Filipa Alves da Costa
J. W. Foppe van Mil · Aldo Alvarez-Risco
Editors

The Pharmacist Guide to Implementing Pharmaceutical Care

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Preface

Pharmaceutical care is the pharmacist's contribution to the care of individuals in order to optimize medicines use and improve health outcomes. The concept, that was first really developed around 1990 by Hepler and Strand, deals with how medicine users should receive their medicines and accompanying medicine information. At the same time, however, the pharmacist is also expected to counsel the patient, and monitor the problems that may occur with the medicine use, the so-called drug-related problems. As part of pharmaceutical care nowadays, pharmacists are also expected to assist prescribers in selecting the optimal medicine treatment or even to prescribe. Many practicing pharmacists have embraced pharmaceutical care, but others do not yet know how to shape it in their practice setting.

The purpose of this book is to comprehensively provide practical support for the implementation of pharmaceutical care. This book is intended to guide and support practitioners in different settings when incorporating pharmaceutical care in their practice. The joint effort of experts from five continents gives this book the relevance and practical utility needed for the implementation of pharmaceutical care at various levels and within different healthcare systems. Their experience forms the basis of this practical guide, aimed at all pharmacists at all levels and settings.

In Part I of the book, the basics of pharmaceutical care are described. A fundamental aspect of the approach of this book is that it is based on a consensus definition of pharmaceutical care, introduced in Chap. 1, and pursued throughout the book. The first chapter also depicts the development of the concept. In Chap. 2, the contribution of pharmaceutical care to the identification and prevention or resolving of drug-related problems is established, making the link to understand in a practical way how this professional activity may be useful to achieve optimal results of therapy for patients.

Part II is centered on the patient and comprises 10 chapters. Chapter 3 presents the pharmaceutical care process in detail, describing the role of the patient in the process and how to assess health-related needs to develop person-centered pharmaceutical care, moving then to the aspects of counseling, instructing patients and increasing health literacy in Chap. 4. The contribution of medication adherence to pharmaceutical care is discussed in Chap. 5, exploring methods to detect and

classify nonadherence in order to target interventions that are meaningful for that person. The importance of interprofessional communication is discussed in Chap. 6, stressing the difference between multidisciplinary and interprofessional collaboration and the impact of the different approaches on effective pharmaceutical care. Chapter 7 focuses on medication reconciliation and review, as an essential part of pharmaceutical care. It describes the different forms of the systematic processes that aim to increase patient safety as well as the effectiveness and efficiency of pharmacotherapy. Chapter 8 sets the scene for aspects of documentation of pharmaceutical care activities, an aspect further detailed during Chap. 9, where quality control is described, including the development and validation of guidelines and protocols to be used in practice. This part concludes with Chaps. 10, 11, and 12, where the related concepts of indicators, the SPO (structure, process, and outcome) paradigm, and the ECHO model (economic, clinical, and humanistic outcomes) are discussed, culminating on the recommendations for the development of Core Outcomes Set (COS) for achieving evidence that may be combined and processed leading to more robust evidence on the value of pharmaceutical care interventions.

Part III, comprising Chaps. 13–17, we aim to provide an overview of the level of progress in the implementation of pharmaceutical care in the five continents, mentioning relevant legislation, practical initiatives, and research. It indicates some of the possibilities for pharmaceutical care that the various healthcare systems offer.

Part IV deals with implementation theory and practice. Chapter 18 provides a comprehensive review of implementation strategies. This chapter is then complemented by Chaps. 19–21, where existing strategies for the implementation of pharmaceutical care at the community level, in nursing homes as well as in hospitals and clinics are presented.

Part V, comprising Chaps. 22–25, focuses on a more holistic approach to pharmaceutical care, detailing aspects of pharmaceutical care in daily practice that are often forgotten. This part covers the role of pharmaceutical care in dispensing new and repeat prescriptions, OTC medication, the provision of medical devices, and in health promotion and disease prevention.

Part VI (Chaps. 26–33) expands pharmaceutical care for patients with specific diseases. These chapters are recommended especially for all pharmacists wishing to provide clinical services to patients with a specific health condition. In reality, most patients will have more than one of the diseases described. But the chapters will be mostly useful to understand the particularities of certain types of interventions, indicators or even outcomes, which can then be effectively combined in practice.

The sustainability of a service, such as pharmaceutical care, depends on ensuring the continuity and improvement of the service over time. For this reason, the economics of the pharmaceutical care services are crucial. Part VII, which includes Chaps. 34–38, deals with the financial and economic aspects of pharmaceutical care, sharing diverse experiences of payment methods established in different healthcare systems, as a reference to use or adapt in other countries.

Finally, because we believe that the future of pharmacy depends also on the coming generations, Part VIII, with Chaps. 39 and 40, discusses the practical aspects of education. They deal with teaching pharmaceutical care in university,

and during continuous professional development. The latter is also applicable to other healthcare professionals contributing to efficient pharmaceutical care delivery, including pharmacy technicians.

We are seriously indebted to all 67 authors of this book, who contributed their knowledge and expertise. Their specific contributions are mentioned in the authors' list.

Each of the parts has a chapter coordinator, who acted as a coeditor and sometimes co-author. This book would not have been possible without their help. These chapter coordinators are people with vast experience and recognized contribution to pharmaceutical care. We are therefore especially grateful to Dave Hackney, Hanne Herborg, Kurt E. Hersberger, Martin Henman, Timothy Rennie and Veerle Foulon for their assistance in creating this book.

All chapters were reviewed by other experts. Often one of the authors assisted in reviewing a chapter created by someone else. But the contribution of external referees is also to be acknowledged as they also greatly contributed to improve the final chapter versions by their constructive criticism. These reviewers are (in alphabetical order): Anna Birna Almarsdottir (Denmark), Ana Margarida Advinha (Portugal), Barry Carter (USA), Beata Bajorek (Australia), Cassyano Correr (Brazil), David Woods (New Zealand), Ema Paulino (Portugal), Louise Mallet (Canada), Mary Tully (United Kingdom), Nejc Horvat (Slovenia), Parastou Donyai (United Kingdom), Patrícia Cavaco Silva (Portugal), Pedro Amariles (Colombia), Peter Schneider (Austria), Sabine Vogler (Austria), Ulrich Jaehde (Germany), and Yolande Hanssens (Qatar).

This book shows the passion of all those who have participated in its writing, for the optimal patient outcomes in pharmaceutical care. It brings together the experiences of the professional careers of its various authors.

We hope that its reading not only provides an inspiration, but we also hope the book is a guide to achieve the increased and thorough implementation of pharmaceutical care in the years to come. This in turn can help the creation of more scientific evidence to support the professional practice of pharmacy and its continuous improvement.

Remember: If you believe it, you make it.

Lisboa, Portugal — Dr. Filipa Alves da Costa
Zuidlaren, The Netherlands — Dr. J. W. Foppe van Mil
Lima, Peru — Dr. Aldo Alvarez-Risco
Coordinating Editors

The original version of this book was revised: The affiliation of editor, Professor Filipa Alves da Costa has been updated. The erratum to this book is available at https://doi.org/10.1007/978-3-319-92576-9_41

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Part I
What is Pharmaceutical Care

Chapter 1
Definitions of Pharmaceutical Care and Related Concepts

J. W. Foppe van Mil

Abstract When using specific terms in health care, one cannot always“ assume that everyone understands the same. In this chapter, we have defined a number of concepts that will frequently be used throughout this book such as pharmaceutical care, drug-related problem, medication review and health care outcome. To avoid confusion with illicit addictive substances, we have also stated that we preferably will use the word “medicine”, and not “drug”, when talking about substances that are used to cure or prevent disease or medical complaints.

Keywords Pharmaceutical care · Definition · Patient · Optimal pharmacotherapy Outcomes

1.1 Names and Definitions

For many things in our life, we know the names, often even in other languages. We all know the words for beer, bière, serveza, cerveza, birre, birra or bier in our own language, and these words mean the same for all people. It is a yellowish or brownish foamy and drinkable liquid with some degree of alcohol, made by the fermentation of sugars, mainly derived from cereal grain starches and with a slightly bitter taste. Thus, the word beer can be easily translated from one language or setting to the other because we all know what beer is. This makes (international) communication about beer easy.

This is different, however, for an abstract concept such as pharmaceutical care because it is not related to a tangible and visual (consumable) object. A term like pharmaceutical care is related to abstract concepts in our mind; what is care, what is pharmacy? Without referring to the descriptive definition, such concepts are difficult to use because in our minds and societies they are shaped by culture, health system and language [1].

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This chapter will clarify a number of concepts that are used throughout this book.

1.2 Drug or Medicine

Throughout this book, the terms drug and medicine are used interchangeably, meaning a substance that can prevent or cure disease or linger its symptoms. The word does definitely not mean an addictive substance that is deliberately used to change the mind, without the support of a health care professional. The word medication or medications is used for the (set of) medicines that are to be used by a specific person.

1.3 Defining Pharmaceutical Care

The first occurrence of a possible definition of the term or concept of pharmaceutical care in literature was in an article by Mikeal et al. published in 1975. The definition reads: (Pharmaceutical care is) "*the provisions of any personal health service involving the decision whether to use, the use and the evaluation of the use or drug, including the range of services from prevention, diagnosis and treatment, to rehabilitation provided by physician, dentists, nurse, pharmacists and other health personnel. Pharmaceutical care includes the complex of personal relationships and organized arrangements through which the health service of a personal nature are made available to the population*". According to the authors, pharmaceutical care is a subset of medical care; is not provided by any one health practitioner exclusively, i.e., not delineated by environment, the writing of a prescription or even a patient consuming a drug [2]. Since more than 200 years, pharmacists had been considered as the experts in developing and preparing medicines. In this definition, the care aspect of the provision of medicines was emphasized for the first time.

The most well-known definition for pharmaceutical care came from Doug Hepler and Linda Strand in their article "*Opportunities and responsibilities in pharmaceutical care*" from 1990 [3]. This was a landmark paper because it marked the start of the international movement to make pharmaceutical care more visible, and get the term and the type of care implemented in hospital and community pharmacy practice. During the following years, both authors worked to make the concept applicable in practice. Hepler and Strand introduced the paradigm shift for the focus of the pharmacist's activities from product to patient. The definition reads: "*Pharmaceutical care is the responsible provision of drug therapy for the purpose of achieving definite outcomes that improve the patients" quality of life*". In this article also the first clear link was made between pharmaceutical care and adverse events and the resulting patient harm. The term drug-related morbidity also became more common. Although in the definition it is left open who should provide that care, from reading further it becomes clear that the authors think it to be the pharmacist:

"*Pharmaceutical care involves the process through which a pharmacist cooperates with a patient and other professionals in designing, implementing, and monitoring a therapeutic plan that will produce specific therapeutic outcomes for the patient*".

In later publications, Linda Strand together with Robert Cipolle even declared pharmaceutical care a practice philosophy for pharmacy. "*Pharmaceutical care is a practice for which the practitioner takes responsibility for a patient"s drug therapy needs and is held accountable for this commitment*" [4]. In this definition, the accountability of the pharmacist is clearly mentioned. Thus, the whole process of pharmaceutical care became a responsibility of the pharmacist, as the International Pharmaceutical Federation, together with the World Health Organization, stated in the GPP Guidelines in 2011 "*Pharmacists are specifically educated and trained health professionals who are charged by their national or other appropriate (e.g., state or provincial) authorities with the management of the distribution of medicines to consumers and to engage in appropriate efforts to assure their safe and efficacious use*" [5].

Additionally, in the years 2000, newer terms like medication management and drug therapy management were introduced. Some found these concepts equivalent to pharmaceutical care.

But, as stated in the introduction, a definition for a concept is rooted in culture and language. And the existing definitions left some aspects unclear:

- Is pharmaceutical care the care of the whole pharmacy team, any team member or pharmacist?
- Is it provided for a patient or for every individual?
- Is it exclusively about medicines or does it encompass medicines plus medical devices?
- Does it cover all medicine-related needs?

And what do we want to achieve, optimal pharmacotherapy or optimal pharmacotherapy outcomes? And what are the activities that pharmaceutical care comprises? Such questions will be answered differently in different settings.

In 2013, a European organization, the Pharmaceutical Care Network Europe (PCNE), created a new definition that could satisfy experts from a multitude of countries. After a review of existing definitions, a number of options were presented to the participants and in a one-day meeting consensus on a definition was reached [6]. This is the definition that this book rests upon.

"***Pharmaceutical Care is the pharmacist's contribution to the care of individuals in order to optimize medicines use and improve health outcomes***".

The ultimate goal of pharmaceutical care (optimize medicines use and improving health outcomes) exists in all practice settings and in all cultures where medicines are used. It involves two major functions: identifying potential and manifest problems in the pharmacotherapy (DRPs), and then resolving the problems and

preventing the potential problems from becoming real for the patient and his therapy outcomes. This should preferably be done together with other health care professionals and the patient through a review of the medication (and diseases). Together with patient and prescriber, the pharmacist will see if the patient receives the most optimal pharmacotherapy. The problems found during this process are called drug-related problems or pharmacotherapy problems. The plan, proposed to solve the problems (the pharmaceutical care plan), is input into the overall individual therapy plan. When the reviewing process uncovers problems, it leads to a continuous quality improvement cycle (Demming cycle) around the pharmacotherapy of the individual patient, as can be seen in Fig. 1.1.

Other basic functions within pharmaceutical care, apart from reviewing the medication, are the counseling of the patient and the support of the prescribing physician. These core activities of pharmaceutical care will be discussed in many places throughout this book.

It is essential to realize that pharmaceutical care, like any other form of care, is a process over time and implies the accountability of the care provider that Strand and Cipolle wrote about. From the perspective of the pharmacist, the fundamental relationship in pharmaceutical care is a mutually beneficial one, in which the patient grants authority to the pharmacist and the pharmacist gives his competence and accepts responsibility for the pharmacotherapy outcomes of the patient.

As the American Society for Health System pharmacy already wrote in 1993:

> "Pharmaceutical care is applicable and achievable by pharmacists in all practice settings. The provision of pharmaceutical care is not limited to pharmacists in inpatient, outpatient, or community settings, nor to pharmacists with certain degrees, specialty certifications, residencies or other credentials. It is not limited to those in academic or teaching settings. Pharmaceutical care is not a matter of formal credentials or place of work. Rather, it is a matter of a direct personal, professional, responsible relationship with a patient to ensure that the patient"s use of medication is optimal and leads to improvements or optimization in the patient"s quality of life".

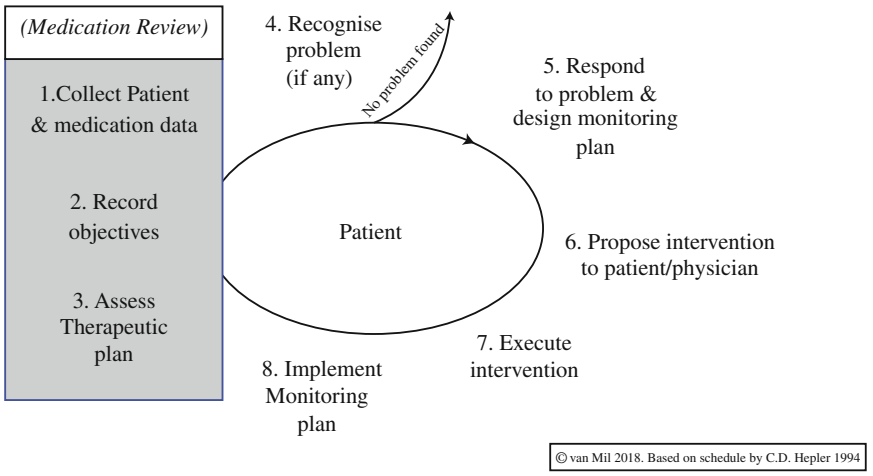

Fig. 1.1 The pharmaceutical care cycle

1.4 Drug-Related Problems and Medication Errors

The term "drug-related problem" (DRP) is slightly confusing because we actually mean medicine-related problem. But this term, first mentioned in the USA, is well known everywhere and indicates a problem related to the use of an approved medicine. However, due to variations in definitions, studies and projects, the mentioned problems are often difficult to compare.

In 1999, when the Pharmaceutical Care Network Europe made its first classification for such problems, a definition was created in which the problem was put in the context of the outcomes.

> ***A Drug-Related Problem is an event or circumstance involving drug therapy that actually or potentially interferes with desired health outcomes.***

DRPs can be potential (in future possibly leading to real problems for the patient) or manifest (the problem already has an impact on the patient and on the therapy outcome). If we take the term drug-related problem too literally, we might forget that it is not only drug-related but also patient-related and disease-related. There also sometimes is a confusion between the problem (that yes-or-no potentially impacts the outcome) and the cause for that problem.

The term "Drug-Related Problem" is not unique for a problem involving pharmacotherapy, and as such other terms have been proposed. For instance, "drug-therapy problem", which was introduced by the group of Cipolle, Morley and Strand in Minnesota [4]. Krska introduced the term "Pharmaceutical Care Issue" in 2002 [7]. That term is sometimes used in the UK. Fernandez-Llimos et al. proposed "pharmacotherapy failure", corresponding to negative clinical outcomes resulting from the use or the lack of use of medicines [8]. All those terms stand for similar concepts as drug-related problems.

Another confusing term is medication error. The medication error has been defined by the National Coordinating Council for Medication Error Reporting and Prevention (NCCMERP) in the USA as "any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer. Such events may be related to professional practice, health care products, procedures, and systems, including prescribing, order communication, product labeling, packaging, and nomenclature, compounding, dispensing, distribution, administration, education, monitoring, and use". This definition seems to be used worldwide. Thus, the medication error focusses more on the use of medication and patient harm. Please note that not all medication errors will lead to drug-related problems, and not all drug-related problems are caused by medication errors [9].

More on these concepts can be found in Chap. 2.

1.5 Medication Review

The structured detection of drug-related problems can take place through several procedures. A full review of all the medication of a given patient is usually called medication review. But even about this concept of medication review, there are several interpretations. These interpretations seem to be caused especially by differences in the health care structure: who has the competence to review medication, who has the necessary data and information, what is the legal position of the different health care professionals, and what are the legal challenges for exchanging patient-related information? Here again, the Pharmaceutical Care Network Europe has spent some time to create an international consensus definition in a series of meetings between 2009 and 2015. This definition reads:

> ***Medication review is a structured evaluation of a patient's medicines with the aim of optimizing medicines use and improving health outcomes. This entails detecting drug-related problems and recommending interventions***.

Medication reconciliation, e.g., a process to collect all information on which medicines the patient uses, has used and is supposed to use, is explicitly a part of this term. One cannot do a medication review without first reconciling the full list of the medications that a given patient is using.

More on medication review can be found in Chap. 6.

1.6 The Structure–Process–Outcomes (SPO) Triad

The final concept that we would like to discuss in the context of the book is the concept of quality, and the related Structure–Process–Outcome paradigm. We owe this concept to Avidis Donabedian, an American who was concerned about the quality of health care and developed his ideas since 1975. To be able to assess the quality of care, for which he defined seven aspects, called pillars [10]. He proposed to evaluate three different parts of health care more or less separately: the structure in which care is given (S), the processes performed to provide care (P) and the outcomes of those processes (on health) (O) [11].

It seems that the most difficult concept to grasp is the outcome. Even an organization like International Society for Pharmacoeconomics & Outcomes Research (ISPOR) had not really defined "outcome" in 2018. They refer to a description in a book:

> "Outcomes are the end results of a health care practice or intervention, and the effect of the health care process on the health and well-being of patients and populations. Outcomes provide evidence about the benefits, risks, and results of interventions… Outcomes or outcome end points include effects that people experience and care about, such as changes in the ability to function and quality of life" [12].

Please note that the word "outcome" is just another word for "(end)-result".

Healthcare outcomes have been described as "measures of the end result of what happens to patients as a consequence of their encounter(s) with the healthcare system" [13].

One should also note that if there has deliberately been no process, there still will be an outcome. If a patient has visited a doctor because he feels ill, and the physician decides that no intervention is necessary, there will be an outcome in the sense of persistence of symptoms, or eventually the passing of the disease.

But what do we look at if we want to evaluate outcomes: clinical data, signs and symptoms, satisfaction, quality of life or money? Another landmark paper divided the outcomes of care into three: Economic outcomes, clinical outcomes and humanistic outcomes. This ECHO model was first described by Chris Kozma and colleagues in 1993 in the context of health care economic research [14].

So, the quality of pharmaceutical care can be evaluated by looking at the structure in which the care is given, the different processes for providing the care and the results of the processes. It will be clear that if a structure changes, this will most probably impact the processes, and thus the outcomes of the care. The principal results or pharmaceutical care, the outcomes, will be economic (time and money investment vs saved care efforts), clinical (improvement of signs and symptoms) and humanistic (satisfaction and quality of life or well-being). More on the SPO triad will at length be discussed in Chap. 10.

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Chapter 2
Pharmaceutical Care and the Role of Drug-Related Problems

Tommy Westerlund

Abstract Identifying, resolving and preventing DRPs are considered cornerstones in pharmaceutical care. The Pharmaceutical Care Network Europe (PCNE) defines a DRP as "*An event or circumstance involving drug therapy that actually or potentially interferes with desired health outcomes*". Another term sometimes mixed up with DRPs is "medication error", defined by the European Medicines Agency (EMA) *as* "*an unintended failure in the drug treatment process that leads to, or has the potential to lead to, harm to the patient*". The natural dividing line between a DRP and a medication error would then be whether the deviation has been committed by a patient or a health professional, respectively, although there is no full consensus on the interpretation of the two terms. Classifying DRPs is desirable for the development of pharmaceutical care practice and research and facilitates documentation and follow-up, important cornerstones of pharmaceutical care. Many different DRP classification systems have been created throughout the years with both similarities and differences. It is of great importance that a DRP classification system is easy to use in daily pharmacy practice, that it is accepted, feasible and validated. The DRP identification rate varies a lot among studies and practices, from less than one DRP per patient to several, depending on a number of factors. Several ways to increase the rate have been tried in different countries.

Keywords Pharmaceutical Care · Drug-related problem · Pharmacotherapy problem · Medication errors · Classification

2.1 Introduction

Detecting and resolving as well as preventing patients' drug-related problems is one of the essential activities of the pharmacist, aimed at ensuring a correct drug use to optimize the therapeutic effect and minimize the possible adverse effect of the

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patient's medications. Ever since the concept named pharmaceutical care was created and spread, it has been regarded the core of the concept.

2.2 Drug-Related Problems, What Is in the Name

The oldest publication including the term "drug-related problems" (DRPs) in its title found in a current PubMed search was in the Canadian Family Physician in 1973 [1], but this study dealt with "nonmedical drug use". That is, with abuse of medications and primarily illicit drugs. The handful publications including "drug-related problems" in their titles that followed in the 1970s were however on DRPs in patients' medical use of drugs, such as adverse drug reactions and non-compliance, as well as about drug-related hospital admissions [2–4]. But the breakthrough of the use of the term did not come until after the epoch-making pharmaceutical care publication by Hepler and Strand [5] in 1990, followed by another one by Strand et al. in the same year on the structure and function of DRPs [6].

The introduction of the concept of pharmaceutical care resulted in an ambition to apply a new philosophy of pharmacy practice, according to its creators Hepler and Strand. "Pharmacists must abandon factionalism and adopt patient-centered pharmaceutical care as their philosophy of practice", as they phrased it and continued "Pharmacy's re-professionalization will be completed only when all pharmacists accept their social mandate to ensure the safe and effective drug therapy of the individual patient" [5]. Identifying, resolving and preventing DRPs are therefore considered cornerstones in pharmaceutical care and have even been labeled as "the heart and soul of the practice of pharmaceutical care" [7].

The first definition of a drug-related problem read as follows: "*An event or circumstance involving drug treatment that actually or potentially interferes with the patient's experiencing an optimum outcome of medical care*" [5] shortly followed by "*an undesirable patient experience that involves drug therapy and that actually or potentially interferes with a desired patient outcome*" [6]. A limitation of these definitions is however that a problem would require a negative experience in the patient to be recognized as a DRP. But there are DRPs, such as a less optimal effect of the drug treatment due to patient non-adherence, which may even make the patient feel better in the short run but may have bad consequences in the long run. Segal's definition "*a circumstance of drug therapy that may interfere with a desired therapeutic objective*" [8] also includes DRPs that the patient may not experience or would not even be aware of and is hence more useful. Based on the previous definitions, the Pharmaceutical Care Network Europe (PCNE) defined a DRP as "*An event or circumstance involving drug therapy that actually or potentially interferes with desired health outcomes*" [9]. Other terms used to designate DRPs have been "drug-therapy problems" [7], "pharmaceutical care issues" [10], "pharmacotherapy failures" and "negative clinical outcomes" [11].

DRPs are primarily caused by the patient's behavior in one way or another, while "medication errors" generally are due to faults committed by health

professionals, although there is a gray area and a lack of a full consensus among practitioners and researchers. Medication errors will be discussed more in detail in Sect. 2.2.

Nor is there a consensus on what constitutes a DRP and a cause of a DRP, respectively, which will be further elaborated in Sect. 2.3 on DRP classifications. Examples of DRP categories according to different classifications are therapy failure, adverse drug reaction, drug interaction, contraindication, under- and over-use of drug, as well as untreated indications and drug use without indication. In the PCNE DRP classification, some of these are however categorized as DRP causes rather than as DRPs.

Pharmacists are in a unique position to identify, correct and prevent the occurrence of patients' drug therapy problems because of their pharmacotherapeutic training and regular contact with patients. In a patient-oriented role, they could, therefore, enhance drug therapy outcomes before they lead to morbidity and mortality. To further demonstrate the meaning of a DRP, the following examples are given:

> Mrs Lorraine Johnson, 55, a regular at your pharmacy comes to get a first refill of her metoprolol depot tablets 200 mg for her hypertension, prescribed by the new, young doctor at her health care center. She thinks however that they are hard to swallow but tells you that she use to split them in half and then chew them carefully. Since years, Mrs Johnson also takes beclomethasone (Easyhaler) 200 mcg twice daily. As well as salmeterol (Diskus) 50 mcg, of which she wants another refill, a couple of weeks earlier than expected.

There are two DRPs, affecting Mrs Johnson's medication. Firstly, depot tablets should not be split and chewed, that is the patient administers the drug in a wrong way and the effect of the drug treatment would not be optimal. Secondly, metoprolol is contraindicated in asthma-patients or should at least be used with great caution. Apparently, Mrs. Johnson's use of metoprolol was the reason for her earlier refill of salmeterol. Hence, another not optimal effect of her drug treatment. The first intervention by the pharmacist would then be patient counseling, that is to inform Mrs. Johnson about how depot tablets work and hence why they should not be split and chewed. A second intervention would be to contact the young doctor at the health care center to suggest a switch of metoprolol to an ACE-inhibitor or an ARB.

> Miss Mary Anderson, 19 years of age, comes to your pharmacy and presents a prescription of metronidazole tablets 500 mg, to be taken three times daily for a week to treat a dental infection. Mary also asks for a refill of her contraceptive pill and is worried that her antibiotic may decrease the effect of her pill and asks you if that's true. She happily tells you about the birthday party she will go to Saturday night together with your daughter and a number of friends in common.

In this case, Ms. Anderson is likely to suffer from adverse drug effects, if she drinks alcohol, due to an interaction between metronidazol and alcohol. However, metronidazol does not decrease the effect of her birth control pills, as rifampicin is the only antibiotic that does. The pharmacist's intervention would be patient counseling to calm her down about her birth control but to inform her about possible risks of alcohol intake during her treatment.

> Mr Joe Trump, 38, known as the great playboy in town, enters your pharmacy and tells you that the hydrocortisone cream and the plasticizer cream he bought over-the-counter more than a week ago did not alleviate the eczema on his hairy arm at all. According to his description, he has apparently used the creams in a correct way.
>
> So, he wonders whether you can recommend any better cream.

Obviously, there is no effect of Mr. Trump's drug treatment despite an apparently correct use, hence a therapy failure. It seems like he would need a stronger cortisone cream on prescription or that his eczema may even be infected by fungus. So, an appropriate intervention besides patient counseling would be referral to a medical doctor.

As indicated by the definitions, a DRP can be either potential (possibly leading to real problems for the patient) or actual or manifest (the problem already impacts the patient and his therapy). Pharmacists have an important role both in preventing potential problems in patients to become manifest and in resolving manifest DRPs. Non-prevented, unattended and unresolved DRPs may cause drug-related mortality and morbidity, resulting in both unnecessary suffering and huge expenditures to society, due to extra doctor's visits and hospitalizations. The Cost-of-Illness Model designed by Johnson and Bootman, which estimates societal costs for drug-related morbidity and mortality in the US, is well-known [12]. Its follow-up by Ernst and Grizzle showed that these costs more than doubled in the span of five years [13]. Several studies have been conducted on drug-related hospitalizations, some resulting in a prevalence of 3–7% [14–16], others in up to 29% [12, 17].

The value of clinical interventions in Australian community pharmacies have been demonstrated both in terms of the quality of care and cost savings [18]. Favorable clinical and economic outcomes of pharmaceutical care in ambulatory patients have also been shown in the US [19]. Data on cost-efficiency of interventions to reduce preventable drug-related morbidity are otherwise scarce, but it was concluded in a Portuguese study that the economic implications of preventable drug-related morbidity are so great that even expensive interventions to tackle the problem may be cost-effective [20]. In a Swedish study, the potential societal cost savings by community pharmacy interventions on DRPs were estimated to be 37 times the expected pharmacy personnel costs for identifying and responding to the DRPs [21].

2.3 Medication Errors

The European Medicines Agency (EMA) defines a medication error *as* "*an unintended failure in the drug treatment process that leads to, or has the potential to lead to, harm to the patient*" [22]. Mistakes in the prescribing, dispensing, storing, preparation and administration of a medicine are the most common preventable cause of undesired adverse events in medication practice and present a major public health burden, according to the EMA. European Union (EU) legislation requires information

on medication errors to be collected and reported through national pharmacovigilance systems. In addition, the European Medicines Agency (EMA) plays a coordinating role and has published a set of good practice guidance [22].

A medication error has also been defined as "a failure in the treatment process that leads to, or has the potential to lead to harm to the patient" [23]—a simple and to the point definition, although it doesn't specify who makes the error. However, it could be any health professional, responsible for the patient's treatment. Examples are doctors' prescribing errors, pharmacists' dispensing errors and nurses' administration errors.

Within the US Food & Drug Administration (FDA) Center for Drug Evaluation and Research (CDER), the Division of Medication Error Prevention and Analysis (DMEPA) reviews medication error reports on marketed human drugs including prescription drugs, generic drugs and over-the-counter drugs. DMEPA uses the National Coordinating Council for Medication Error Reporting and Prevention (NCCMERP) definition of a medication error. Specifically, a medication error is "*any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer. Such events may be related to professional practice, health care products, procedures, and systems, including prescribing; order communication; product labeling, packaging, and nomenclature; compounding; dispensing; distribution; administration; education; monitoring; and use*" [24]. Hence, the medication error definition used by the FDA is broader and more comprehensive than the EMA definition and overlaps the definitions of a DRP, making it harder to distinguish between the two concepts. DRPs then rather become a subgroup of medication errors.

In its document on medication errors, the World Health Organization (WHO) refers to the FDA definition of a medication error and lists a number of factors that may influence medication errors [25–27];

Factors associated with health care professionals:

- Lack of therapeutic training
- Inadequate drug knowledge and experience
- Inadequate knowledge of the patient
- Inadequate perception of risk
- Overworked or fatigued health care professionals
- Physical and emotional health issues
- Poor communication between health care professionals and with patients.

Factors associated with patients:

- Patient characteristics (e.g., personality, literacy, and language barriers)
- Complexity of clinical case, including multiple health conditions, polypharmacy and high-risk medications.

They also list factors associated with the work environment, with medicines, tasks, computerized information systems and primary–secondary interface.

All the factors listed, except for partly the patient factors, are clearly related to the work performed by health professionals. The natural dividing line between a medication error and a DRP would then be whether the deviation has been committed by a health professional or a patient, respectively. The following examples may facilitate the separation between a medication error and a DRP:

An error that is not a DRP, or not leading to a DRP would be 550 mg instead of 500 mg amoxycillin prescribed. A DRP that is not an error is the occurrence of a side effect at normal dose.

DRP classifications are presented and discussed in Sect. 2.3 and like for DRPs there are classifications of medication errors. Contextual classification deals with the specific time, place, medicines and people involved, while modal classifications examines the ways in which errors occur. It has however been argued that classification based on psychological theory is to be preferred, as it explains rather than merely describes errors [28, 29]. In this way, medication errors can be classified as knowledge-based mistakes, rule-based mistakes, action-based slips and memory-based lapses. Lack of knowledge or ignorance of facts could result in knowledge-based errors, while misapplication of good rules or failures to apply them as well as applications of bad rules may lead to rule-based mistakes. An action-based error could, for example, be "a slip of the pen", resulting in a prescribing error. Memory-based errors simply occur when something known is forgotten [29].

2.4 DRP Classifications

Classifying DRPs is desirable for the development of pharmaceutical care practice and research and facilitates documentation and follow-up, important cornerstones of pharmaceutical care. Documenting pharmaceutical care, including DRPs, is covered in Chap. 8. The role and structure of such classifications, however, also is important.

Reasons for classifying and documenting DRPs and pharmacy interventions are several, such as

- Gives a structured and standardized approach to DRP identification and pharmacy interventions
- Increases the pharmacists' attention to patients' drug-related needs resulting in more DRPs being detected, managed and resolved
- Highlights the pharmacists' role in ensuring the correct and safe use of medicines
- "What has not been documented, has not been done", hence documentation provides evidence of practice
- Fosters continuing education in pharmaceutical care practice through a reality-based educational material
- Makes work more fun.

The ultimate purpose of identifying, preventing, classifying, resolving and documenting DRPs is to improve the use of drugs in patients and hence their health and quality of life. There seems to be a general agreement on including not only actual or manifest DRPs but also potential ones, as DRP prevention is an important part of pharmaceutical care. Ideally, potential DRPs are detected prior to becoming manifest and hurting patients.

As previously mentioned, there is however a lack of consensus on separating issues identified as causes of DRPs from issues identified as DRPs. Some may see an issue as a cause of a DRP, such as a drug–drug interaction as a cause of a DRP like therapy failure or an adverse drug reaction (ADR), while others see the issue as a DRP like the interaction in this case and the therapy failure or ADR as a consequence of the DRP. It may be helpful for the separation between causes and problems to decide whether a pharmacy intervention is aimed at rectifying the cause of the DRP or the DRP and you may even end up in philosophical discussions and perplexities.

A number of different DRP classification systems have been created throughout the years, as presented in two publications in 2004 and 2014, respectively [30, 31]. In the first overview, 14 classifications were identified and presented, in the second one 20. Additionally, a number of modifications of previously developed classifications have been used in various studies.

The following requirements for DRP classifications were listed in the first publication:

1. The classification should have a clear definition, both for the DRP in general and for each DRP category.
2. The classification should have a published validation.
3. The classification should be usable in practice (has been used in a published study).
4. The classification should have an open, hierarchical structure (with main groups, subgroups and an open structure to include new problems, preferably on subgroup levels).
5. The classification should have a focus on the drug use process and outcome and separate the problem itself from the cause [30].

Additionally, the classification categories should not be overlapping but mutually exclusive.

However, as concluded in the second publication, there appears to be no consensus on preference or structure of classification systems [31]. Despite the fact that a large number of classifications have been developed, new ones still appear and a universally accepted classification system still doesn't exist. There are many differences between classifications, such as some being non-hierarchical, others not. Some have a classification of DRPs only, such as the initial classification by Hepler and Strand [5]. Others have a classification of DRP causes or interventions as well. The system constructed by the Pharmaceutical Care Network Europe (PCNE), also has a classification of acceptance of intervention proposals and a classification of the status of the DRP, that is the outcome of the intervention [9]. Some classifications

have not been published in an international, scientific article but in a national report only. Not all classifications provide a definition of a DRP and there is in some cases an overlap between the DRP term and other drug safety terms. Some classifications give definitions of their DRP categories, others don't. The number of DRP categories also varies a lot from 6 up to about 60, including subcategories. Where causes are included in the system, the number of categories may be as high as 35. A few classifications have been used in just one published study, while others were applied in several or up to around 80, as with the Hepler and Strand classification, including modifications [27]. One classification, the Westerlund System, was used nationwide in all Swedish pharmacies during more than a decade [32].

To demonstrate the variety of DRP classifications, three examples follow:

The Hepler/Strand Classification [5], the first established classification, contains a non-hierarchical list of DRP categories and has never been revised.

(1) untreated indications
(2) improper drug selection
(3) subtherapeutic dosage
(4) failure to receive drugs
(5) overdosage
(6) adverse reactions
(7) drug interactions
(8) drug use without indication.

The Westerlund System is non-hierarchical as well and has been revised to some minor extent a few times, resulting in the last fifth version [32]. It contains both a classification of DRPs and pharmacy interventions.

DRP categories:

(1) uncertainty about the aim of the drug
(2) insufficient or no therapeutic effect (therapy failure)
(3) underuse of drug
(4) overuse of drug
(5) drug duplication
(6) adverse reaction/side effect
(7) interaction
(8) contraindication
(9) inappropriate time for drug intake/wrong dosage interval
(10) practical problems
(11) other DRP.

Pharmacy intervention categories:

(1) patient drug counseling
(2) information to patient's representative
(3) printed information

(4) practical instruction
(5) contact with prescriber/other health care provider
(6) switch of drug
(7) referral to prescriber/other health care provider
(8) other intervention.

The most comprehensive classification is the one by the PCNE, contrasted by the previous two by being hierarchical with both primary domains and subdomains. It has been revised several times, the current one being version 8.02 [9]. The primary domains are as follows:

Problems

P1 Treatment effectiveness
P2 Treatment safety
P3 Others.

Causes

C1 Drug selection
C2 Drug form
C3 Drug dose
C4 Treatment duration
C5 Dispensing
C6 Drug use process
C7 Patient related
C8 Other.

Planned Interventions

I0 No intervention
I1 At prescriber level
I2 At patient level
I3 At drug level
I4 Other.

Intervention Acceptance

A1 Intervention accepted
A2 Intervention not accepted
A3 Other.

Status of the DRP

O1 Problem status unknown
O2 Problem solved
O3 Problem partially solved
O4 Problem not solved.

Some classification systems have been validated, others have not. Assessment of the internal validity can be found for the Westerlund, PAS and PCNE classifications

and are based on case descriptions and questionnaires [30]. Basger et al. lists references, where interrater agreement and interrater reliability measurements have been stated or presented [31]. Several criteria are to be considered in a validation, such as internal and external validity, appropriateness, feasibility and acceptability. A validation is usually performed by presenting a set of patient case descriptions with DRP situations to a number of pharmacists, such as for the Australian DOCUMENT classification system [33], who then are assigned to find potential or manifest DRPs in the cases and classify them according to the actual system. If there are discrepancies between the pharmacists' DRP classifications, there is a room for improvement of the system, unless the case descriptions have not been clear enough. Ideally, the validation test is repeated a couple of weeks later to examine not only possible interrater discrepancies again but also intra-rater inconsistencies. It is important that the DRP categories are mutually exclusive and that their definitions are unambiguous. DRP causes, interventions and other possible parts of a classification system can be validated in a similar way. It is however difficult to reach a 100% consensus level among pharmacists in a validation and a conformity of 80% may be acceptable.

It is of great importance that a DRP classification system is easy to use in daily pharmacy practice, that it is accepted and feasible. Hence, it should be constructed in a logic way with the actual category easy to find for a pharmacy practitioner, even in a common stressful situation. The Hepler/Strand Classification and the Westerlund System have been used extensively in daily practice, both non-hierarchical with few categories. Too many different categories may then pose difficulties. However, one way to handle a hierarchical system with many categories such as the PCNE classification is to only use the primary domains in regular, daily practice and include the subdomains just during limited periods of time or for one or just a few therapeutic categories at a time, e.g., patients with drugs for hypertension, diabetes or depression.

The DRP identification rate varies a lot among studies and practices, from less than one to several DRPs per patient, depending on a number of factors [31]. Several ways to increase the rate have been tried in different countries. In Australia, electronic prompts or "pop-up alerts" in dispensing software, appearing when filling prescriptions for selected patient groups have been used [34]. An interventional program aimed to increase the rate of clinical interventions has also been undertaken in Australian community pharmacy, including both education and professional remuneration [18]. A communication technique with so-called pharmacy-based protocols has been used in Australia [35]. A similar technique has been tried in OTC drug consumers in Denmark [36]. In Sweden, so-called counseling models (or protocols) have been used in a series of studies. They consist of a number of key questions to be covered routinely in the pharmacy practitioner's dialog with the patient, questions which are often brought up in patient encounters but are asked in a more consistent way to all patients within selected therapeutic groups. The number of detected DRPs was superior in pharmacies practicing counseling models compared to both blind and open controls [37]. Commitment among pharmacy practitioners to the DRP identification, resolution and

documentation is often decisive for the rate and may even overcome possible time constraints [38].

The implementation of medication reviews is another means to facilitate DRP identification and usually results in a much higher rate than in regular pharmacy practice, especially if also clinical patient data are available. See Chap. 6.

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Part II
Pharmaceutical Care Processes

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Part 2 of this book focuses on the key elements of patient-oriented pharmacy as an important concept in pharmaceutical care. It starts with a chapter on the patient, who is central in health care—also in pharmacy (Chap. 3). The chapter shows how the needs of patients can be explored, and how the pharmacist can tailor his interventions and services to these needs in order to provide patient-centered care. This is of extreme importance, as patients form a heterogeneous group and there is plenty of evidence that interventions and services contribute more to therapy adherence and quality of life, if tailored to the patient. In Chap. 4, the counseling role of the pharmacist is further explored, giving examples of communicative strategies that foster patient-centered care.

One of the major problems in pharmacotherapy is a lack of adherence. In Chap. 5, you will find detailed information on the terminology used in this context, how adherence can be measured, which factors play a role, and—most importantly—how the pharmacist can detect nonadherence, including its causes, and which interventions may work. It gives you the essential background to frame interventions to the evidence and to focus on adherence in everyday pharmacy practice.

As the current vision on pharmaceutical care and the ideal healthcare practice not only includes patient-centeredness as a pivotal aspect but also integrated service delivery, we have devoted a full chapter to interprofessional communication (Chap. 6). This should support pharmacists worldwide to engage in collaboration with other healthcare professionals.

One of the advanced pharmacy services that got a lot of attention over the past decade is medication review. It is now considered as a key pharmaceutical care service provided by pharmacists in order to detect and solve drug-related problems, and to optimize patients' medication use. If performed in collaboration with the physician, medication review can further contribute to rational prescribing. The chapter on medication review and medication reconciliation gives a clear overview of the different procedures, as well as practical information on how to perform a review (Chap. 7).

In Chap. 8, we further elaborate on the documentation of pharmaceutical care services, such as medication review. This not only allows to follow-up the patient but it might also be used to demonstrate the role of the pharmacist in patient care, and to obtain a deeper understanding of drug-related problems and in related care issues.

In order to provide high-quality interventions, guidelines are essential. These allow the pharmacist not only to perform interventions that are evidence-based but also to do so in a structured and uniform way to all patients. Chapter 9 gives information on how evidence-based guidelines should be developed, in co-creation with healthcare professionals, authorities, and patients alike.

Indicators can be used to investigate the implementation of guidelines. Chapter 10 describes the different types of indicators (structure, process, and outcomes—the SPO paradigm), the way they are developed and validated, and how they can be used in benchmarking studies.

The ECHO model is an important tool to express the outcomes of health care. Chapter 11 outlines the ECHO model as a framework to evaluate the effectiveness of pharmaceutical care interventions trough measurement of economic, clinical and humanistic outcomes.

Finally, we show the importance of the development of core outcome sets, in order to make sure that when similar interventions (or interventions with similar aims) are evaluated, the same outcomes are assessed (Chap. 12). The latter allows for comparison between studies, facilitates the execution of systematic reviews and meta-analyses, and can enhance the development of robust evidence for specific interventions, also in pharmacy practice.

Chapter 3
Pharmaceutical Care and the Role of the Patient

Sophie Liekens and Veerle Foulon

Abstract In order to effectively implement the gold standard for healthcare practice, person-centered care, communication between the patient and the pharmacist is required. As patients form a heterogeneous group with different needs depending on the disease stage they are in, coping strategies and health beliefs, an accurate understanding of the patient's own motivations, priorities and preferences is critical. Based on the evidence discussed in the current chapter, we strongly believe that drug information embedded in pharmaceutical care contributes more to therapy adherence and patients' quality of life if this information is adjusted to patients' needs. Therefore, the role of the patient in pharmaceutical care is to express his/her needs - and it is the role of the pharmacist to explore those needs and to help patients to articulate them. Consequently, the pharmacists should provide tailored information responsive to patients' needs.

Keywords Pharmaceutical care · Patients · Person-centered care
Patient empowerment · Patient oucomes

3.1 Introduction and Definition of Person-Centered Care

Over the past decades, pharmacists' roles have changed significantly. Alongside these changes, the concept of having the patient as the driving force in decisions related to his/her own health, referred to as "patient-centered care", has evolved and is now largely considered the gold standard for healthcare practice. Patient-centered care has been described by the Institute of Medicine [1] as "*providing care that is respectful of and responsive to individual patient preferences, needs, and values, and ensuring that patient values guide all clinical decisions*."

Recently, the American Geriatrics Society Expert Panel on Person-Centered Care [2] pointed out that there has also been a move toward using the term

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"person-centered," rather than "patient-centered," in order to encompass the entirety of a patient's needs and preferences that is beyond just the clinical or medical.

Person-centered care comprises a shift from a traditional healthcare model (in which healthcare providers such as the pharmacist and the general practitioner are in the primary decision-making role) toward a model that supports the patient's individual choice and autonomy in healthcare decisions.

The American Geriatrics Society Expert Panel on Person-Centered Care [2] stated the following: "*Person-centered care means that individuals' values and preferences are elicited and, once expressed, guide all aspects of their health care, supporting their realistic health and life goals. Person-centered care is achieved through a dynamic relationship among individuals, others who are important to them, and all relevant providers. This collaboration informs decision-making to the extent that the individual desires*" (p. 16).

Eight elements are considered essential to realize this definition, not only in geriatric patients, but for all persons:

- An individualized, goal-oriented care plan based on the patient's preferences;
- Ongoing review of the patient's goals and care plan;
- Care supported by an interprofessional team in which the patient is an integral team member;
- One primary or lead point of contact within the healthcare team;
- Active coordination among all healthcare and supportive service providers;
- Continual information sharing and integrated communication;
- Education and training for providers and, when appropriate, the patient and those important to the patient;
- Performance measurement and quality improvement using feedback from the patient and caregivers.

In order to effectively implement person-centered care, communication between the patient and the provider is required. An accurate understanding of the patient's motivations, priorities and preferences is critical, also for pharmacists.

Pharmacist-patient communication is considered an integral aspect of pharmacist-provided services. The importance of pharmacist-patient communication cannot be underestimated since researchers such as De Young [3] have established that pharmacist-patient communication is not only important for improving appropriate medication use, but also for achieving desired patient outcomes.

3.2 Different Types of Patients

Herborg and Duggan [6] proposed a tool that can be used to typify patients based on their desire for information and their perceived self-efficacy, as shown in Fig. 3.1. The tool is based on the fact that both the desire for information and the perceived self-efficacy can be low or high. Patients with a *high desire for information* acknowledge that they need and/or read as much information about their

medication/illness as possible. Patients with a *low desire for information* don't need information about their medication/illness; they usually agree that too much knowledge is a bad thing. Furthermore, they tend to state that what you don't know (with respect to medication/illness) doesn't hurt you. Patients with a *high perceived self-efficacy* feel confident that they could take their medication as prescribed even if they experienced side effects, felt very healthy or no one reminded them to take their medication. On the contrary, patients with a *low perceived self-efficacy* don't feel confident that they could take their medication as prescribed.

The different combinations of low and high desire for information and low and high perceived self-efficacy results into four different types of patients, represented in Fig. 3.1.

The interesting point about this model is that the different types of patients require different communication styles. Hence, pharmacists can use this model to tailor their counseling according to the type of patient.

"*Eager listeners*" have low self-efficacy and express a high desire for information. For these patients extensive medication counseling by the pharmacist is designated. Furthermore, these patients should have a contact person in the pharmacy, who can provide full information and motivation when sitting down with the patient.

"*Contents*" have high self-efficacy and express a high desire for information. These patients want to know what the medication is used for and how it works. The pharmacist should communicate to these patients "We are there for you!" and see them as expert-patients. Furthermore, these patients benefit from Internet links to specialized sites for more information or written background information.

"*Cash and Carriers*" have high self-efficacy but express a low desire for information. These patients need simple and brief directions on the use of the medication, as they don't need/want extensive medication counseling. Compact written information as a leaflet could be given to these patients. The pharmacist should give contact information for when patients encounter problems or when they would have questions.

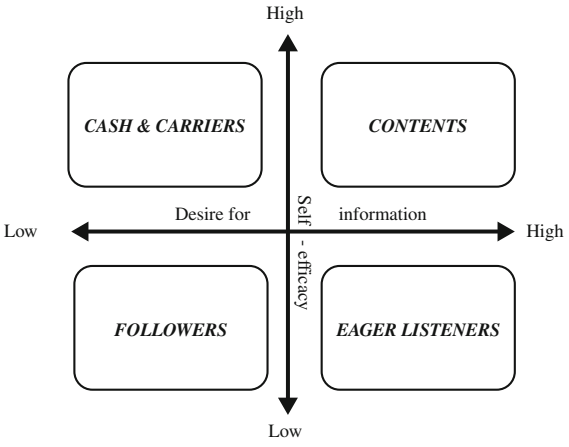

Fig. 3.1 Different types of patients. Adapted with permission from Herborg and Duggan [6]

"*Followers*" have low self-efficacy and express a low desire for information. The pharmacists should offer coaching and technical follow-up for these patients. With a step by step approach, these patients can gain confidence in their treatment. Telephone follow-up or reminders are needed to support these patients.

3.3 What Do Patients Want to Know from the Pharmacist?

Nowadays, most patients want and are intensively seeking information about drug and non-drug treatment options. However, as described in the previous Sect. 3.2 patients form a heterogeneous group with different needs depending on the disease stage they are in, coping strategies and health beliefs. It can be argued that the beneficial factor in targeting this information need is not the mere act of information provision, but rather empowerment that results from tailored information responsive to patients' needs.

Duggan and Bates [4] related the degree of empowerment realized by information provision to two constructs: "intrinsic desire for information" and "worry about changes to medicines." That is: patients who expressed a high degree of worries about changes to their medication and did not want information about their prescription drugs seemed less empowered when given additional information about those changes. One could argue that they were "happy knowing little." For these patients information may even be harmful, since it may cause them to worry and thereby make them less confident about prescribed therapy. On the contrary, patients who expressed a low degree of worry about changes to their medication and a high desire for information about their medication seemed less worried and more empowered when given additional information. Meanwhile, this concept has been explored in many different studies.

A focus group study of patient perspectives [5] identified five specific questions related to drug therapy that patients wanted information on:

1. *What are the side effects and risks?* Patients want information on side effects and risks including information on drug–drug interactions and contraindications. Patients generally believe that they could make more informed treatment decisions based on full disclosure of side effects and risk information.
2. *What are my other treatment options?* Patients want information on the range of treatment options available, including non-pharmacologic and alternative treatments, as well as information on how to apply self-care strategies even before seeing a healthcare professional. Patients tend to use other resources to meet these information needs, as they believe they usually don't receive this information from their physicians or pharmacists.
3. *How long do I need to take the medication?* Some patients want information regarding the period during which they should take the medication and the typical follow-up process when receiving a medication prescription.

4. *What will it cost?* Many patients want to know whether their medication is covered by their drug plan. Furthermore patients are interested in whether there are more cost-effective alternatives available.
5. *Is this medication right for me?* It is important for patients to know that the proposed treatment reflects their individual health situations. That is, whether the medication prescribed is the most appropriate for them personally, rather than a treatment that could have been prescribed to anyone with that condition.

Based on this evidence, we strongly believe that drug information contributes more to therapy adherence and patients' quality of life if this information is adjusted to patients' needs. Therefore, the role of the patient in pharmaceutical care is to express his/her needs—and it is the role of the pharmacist to explore those needs and to help patients to articulate them.

3.4 Patients' Expectations of the Community Pharmacist

Sabater-Galindo et al. [7] have recently summarized the evidence that patients' satisfaction with community pharmacists' interaction is usually high. They have further shown how the high satisfaction can be attributed to patients' low levels of expectations of the community pharmacist: patients' expectations of community pharmacists still appear to be related to their dispensing role. Moreover, patients still appear to be unaware what expanded professional services a pharmacist is able to provide, are not interested in those expanded professional services or prefer other professionals to deliver them. In their study, Sabater-Galindo et al. [7] developed and tested a conceptual model of how patients' perceived image of the pharmacist influences their expectations of the pharmacist's role and how this in turn influences patients' reactions with respect to that role.

The model in Fig. 3.2 shows that the more positive the professional image of the pharmacist (labeled as "perceived pharmacist image"), the higher patient's expectations of the pharmacist (professional expectations and courtesy expectations) and in turn, the greater positive reactions and more limited the negative reactions of the patient.

Perceived pharmacist image implies whether the patient sees the pharmacist as much of a health professional as his doctor, as an expert in medicines and as the person who should manage the patients' medication.

Professional expectations implies whether the patient expects the pharmacist to resolve any doubts the patient has regarding the treatment, to inform the patient about the possible adverse effects of the medications and to follow up the patient' health problems.

Courtesy expectations implies whether the patient expects the pharmacist to greet them when the patient arrives to the pharmacy, to know the patient by name and to ask the patient how he is doing.

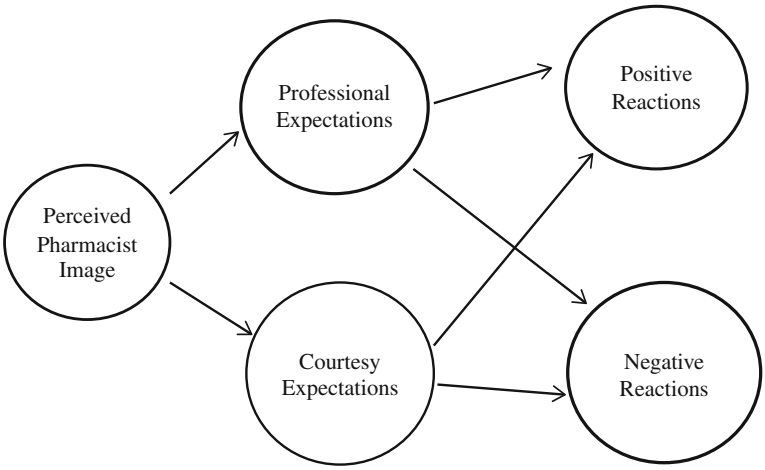

Fig. 3.2 Model predicting patients' expectations and reactions. Figure copied from Sabater-Galindo et al. [7] with permission

Sabater-Galindo et al. [7] conclude that if the professional image of the pharmacist is improved, patients will have greater professional expectations of the pharmacist, and in turn, these expectations will influence the reactions to the community pharmacist.

When the community pharmacist acts in the service provider role, by providing expanded professional services including advanced pharmaceutical care, patients' professional expectations of the pharmacist will increase and generate more positive reactions from patients. Hence, improving the image of the pharmacist is crucial. Therefore, it is necessary for community pharmacists to market and explain their expanded role as a service provider to patients. Worldwide professional associations of community pharmacists strive for more visibility of the role of the pharmacist in an interprofessional team (in which the patient is an integral team member). Furthermore, they develop projects addressed to patients as well as other healthcare professionals to market and explain the added value of the community pharmacist and the benefits of pharmaceutical care for patients.

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Chapter 4
Pharmaceutical Care and Patient Counseling

Afonso Cavaco

Abstract Counseling is an important part of pharmaceutical care to influence patient behavior and adherence. The concepts described in this chapter are a proposal of counseling skills in pharmaceutical care. More than assuring expected medication outcomes, adequate counseling requires communication and relational abilities as tools to provide the best patient care possible. Counseling aims to set a permanent cooperation with patients, thus favoring patient empowerment, self-caring abilities, medication adherence and improved health-related behaviors.

Keywords Pharmaceutical Care · Counseling · Communication
Interpersonal Skills · Patient information

4.1 Counseling: Definition and Scope

Counseling is widely recognized as part of the pharmacists' professional role. It emerges naturally from pharmacists' duties towards people receiving medicinal products as well providing advice to help patients with the use and management of those products.

Counseling can be defined as a process of interaction between a specialized professional and a client, aiming to help the client to clarify and make the right decisions. It is an active and person-centered exchange process, based on a trusting relationship between the professional and client. Counseling assumes that each person has the necessary resources to address the decisions and actions needed. The professional needs to master the abilities necessary to retrieve that person's resources, fostering support and promote the right knowledge and behavior [1].

In pharmacy practice, counseling may arise from a patient asking for advice, or from the duty to provide information to patients, significant others or other

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healthcare professionals. Providing advice usually emerges from uncertainties about an appropriate course of action or knowledge, while the usual pharmacists' duty of information provision has no personal implication for future action. Information, such as directive and factual instructions that should be followed during a drug treatment, tends to receive minimal acknowledgement. This way the actual relevance of counseling is in the interaction itself, rather than on single advice or on the accuracy of the information being provided [2].

The International Pharmacist Federation (FIP) [3] refers to medication counseling as "*an approach that focuses on enhancing individual problem-solving skills for the purpose of improving or maintaining quality of health and quality of life*" (p. 11). It is expected that the pharmacists will provide and discuss medication information, respecting the physical, psychological, sociocultural, emotional and intellectual perspectives, health beliefs and values of the individual. The healthcare professional's responsibility is to support the clients' efforts to develop medication management skills and to move in the direction of self-responsibility. This requires empathy, sincerity and patience.

To further understand pharmacists' counseling, one may follow another definition offered by the American Society of Health System Pharmacists guidelines on pharmacist-conducted patient education and counseling [4]. Here, besides medication-related content such as drug names, expected actions, route and dosages, there is an overall concern with the counseling setting. Environmental features (e.g., room or space ensuring privacy) and especially the process steps, such as those assisting an effective patient interview (e.g., introducing yourself, assessing patient's knowledge, providing information and guidance to reach a decision, etc.), are some of the pre-conditions to adequately counsel a patient. This will be addressed in more detail later.

There are several advantages emerging from pharmacists counseling patients to both patients and pharmacists. From the patient side, they become more capable of making informed decisions concerning the appropriate treatment with prescription and non-prescription drugs, including suitable responses to adverse drug events. Adequate counseling favors the patients' understanding of the usefulness of medicines to maintain or promote well-being, contributing to them participating in their own care. This encompasses an important contribution to patient's functional health literacy, i.e., the patient becomes increasingly "*able to apply literacy skills to health-related materials such as prescriptions, appointment cards, medicine labels, and directions for home health care*" [5]. Advantages to the pharmacists include greater satisfaction with the fulfilment of their professional duties, adding to improved patients' confidence in their service, and other healthcare professionals' approach and recognition of pharmacists' work. Pharmacist-led counseling should be an intervention directed to patients' health-related needs that contribute to reduced morbidity and mortality related to drug therapy while improving interprofessional and inter-institutional communication [6].

4.2 Interpersonal Skills in Counseling

To be able to assist patients' best health-related decisions and influence behaviors such as medication adherence, counseling should entail a clear and objective interpersonal communication [7]. However, to professionally address patient counseling, pharmacists' education and training should go beyond effective communication principles to embrace relationship skills. To deal with all health-significant aspects, pharmacists need to properly respond to patients' emotions aiming to achieve a greater understanding of the patient's biopsychosocial details within the present health condition and treatment.

There are several communication-related features, necessary as the scaffolding of a counseling session. The starting point, as well as a basic underlying feature, is mutual trust. This means both dialoguing persons must believe in the other just as in themselves. The pharmacists must respect the patient's autonomy to make decisions by adapting his/her professional knowledge and actions to patient's needs. Respecting the patient's rights and willingness, and establishing his/her co-responsibility in the counseling process, is the cornerstone of patient counseling. The pharmacist needs to recognize the patient's trust and the acceptance of the pharmacist as a counselor; otherwise, effective counseling will be difficult or even impossible to achieve.

Another critical interpersonal skill is empathy. There are several empathy definitions, including the capacity to place oneself in the position of the other. The professional understands and accepts without any attempts to stop, modify or block the ideas or the emotional content that the patient is disclosing [8]. By feeling acknowledged and secured, the level of detail in the exchange increases, thus enhancing the chances of providing optimal counseling. There is evidence illustrating that an empathic relationship between pharmacists and patients improves pharmaceutical care outcomes, including medication adherence [9].

The empathic behavior should be expressed both verbally and non-verbally. While clear spoken or written language supports effective verbal communication, empathy also requires mastery of the non-verbal communication signs. One main feature for reaching empathic resonance is the quality of paralanguage, in particular, voice features, i.e., how one sounds to the other. The pharmacist should reduce the pitch and decrease the speaking rate if wanting to be perceived as an empathic person. However, a warm voice alone does not turn an unwelcoming pharmacist into an empathic one. Verbal responses need to be preceded by active listening and other effective communication behaviors, e.g., an open body position and an interested look. The empathic pharmacist should "listen with the eyes" to not miss any emotional disclosure. This is a difficult exercise as listening to all empathic opportunities is harder than e.g., asking good questions. Empathic listening also requires physical proximity within a mutually accepted interpersonal distance, full attention to non-verbal information without interruption and showing respect. Empathy also requires attention to one's own body language to avoid emotional signals of disgust, disapproval or annoyance.

In short, a good counselor requires interpersonal qualities such as being approachable and welcoming, friendly and warm, a good and tolerant listener, well focused and self-confident, available to spend time with the other and assuring full confidentiality.

4.3 Pharmaceutical Counseling in Practice: Essential Elements

The pharmaceutical counseling is an interaction between two or more persons, preferably between a pharmacist and a patient, usually in a pharmacy setting. It should start with the patient first sharing a health issue and the professional providing information that comprises possible solutions, their advantages and limitations, so the patient is able to make an informed decision. The pharmacist helps the client to identify, clarify and resolve potential or existing doubts. Concerning therapy issues, the pharmacists should work to guarantee that after the counseling the patient or caregiver is able to show the agreed level of therapy management.

Counseling basic principles and conditions:

1. Professional hard-skills: pharmaceutical, health and social-related knowledge
   - 1.1. Pharmacotherapeutic and health information, e.g., ill-health conditions, drugs, clinical practice, etc.
   - 1.2. Population and social-based information, e.g., prevalent health issues, healthcare organization, community and individual resources (including cultural and economic), etc.
2. Professional soft-skills: interaction competences
   - 2.1. Managing personal barriers, e.g., hearing limitations, different mother tongue, etc.
   - 2.2. Facilitating patient autonomy, e.g., personal attitude with appropriate levels of empathy and assertiveness, etc.
3. Environmental conditions: local setting and organization
   - 3.1. Avoiding physical barriers, e.g., safe and private counseling area, etc.
   - 3.2. Using educational resources, e.g., printed materials, simulated devices, etc.

Main preexisting conditions can be divided into pharmacists' knowledge and skills, as well as on environmental conditions. Knowledge of pharmacotherapy needs to be complemented with knowledge of the diverse cultural and individual backgrounds of patients. The pharmacist should be attentive to patients' attitudes towards the healthcare system as well as patients' own roles and responsibilities for decision-making and self-management. Counseling relies on a certain degree of patients' autonomy not functioning at its best in fully paternalist care environments. Communication competences are tested when social and cultural differences or

system barriers (e.g., shyness and other personality traits, forced spatial separation, unclear organizational structure) or physiological limitations in language use and comprehension (e.g., hearing difficulties, poor eyesight, ill health and psychological distress) exist.

Effective communication also requires controlling for communication noise, from obvious environmental sources (surrounding sounds) to syntactical (wrong grammar) and semantical (diverse interpretations) noises. The physical setting here comprises all features that facilitate patient involvement and learning, i.e., a space that is comfortable (seating position), confidential (enough privacy) and safe (accommodating significant others, if required), including conditions for disabled patients. The desired level of privacy should be guaranteed before initiating the counseling session. Other environmental resources include equipment such as learning aids (e.g., 3D real and virtual models), printed information (e.g., leaflets), charts and graphics, medication administration devices, memory aids and audio-visual resources [4].

4.4 Pharmaceutical Counseling in Practice: Essential Process Steps

Effective counseling requires several pre-conditions and process steps to build trust in the counseling, contributing to a safe and caring environment. Maintaining confidentiality is a pre-condition of effective counseling. The first step is to assess what the individual already knows. The pharmacist should never guess or assume what a person knows or does not know about the issue being discussed. This requires patiently asking questions and listening to clearly understand what the individual is saying or wanting. The empathic pharmacist is non-judgemental and supportive of expressed feelings and fears: you want a true individual account so that a useful solution is offered. Avoid the use of directive communication, i.e., where multiple options exist: the pharmacist should never lead the patient towards their own preferred option.

GATHER [10] is an acronym for a structured approach to counseling that is simple to implement in the pharmacy setting;

Greet—The pharmacists should always greet the patient on arrival to make the patient feel welcome, to make them comfortable and to start building rapport. At the initial exchange, e.g., welcoming the patient at the counter, the pharmacist should determine the primary spoken language, ask the main reasons for the visit to identify the purpose of the counseling and approximate the expected length. At this point, the pharmacist should invite the patient and any appropriate companions to a more private space, ideally a dedicated space or consultation room.

Ask—Ask questions in a friendly manner and using words the patient understands and listens attentively, without expressing judgement. Identify what the patient already knows by asking relevant open-ended questions about personal, social,

family, health/medical condition(s) and therapy/medications. In a following section examples related to drug-focused counseling are provided.
Tell—Provide relevant information to help the patient reach a decision and make an informed choice regarding the health/medical issue. Be neutral in manner and content, presenting the advantages and disadvantages of each option without stating your personal preferences, unless requested by the patient.
Help—Assist the patient to reach a decision, without making choices for him/her. If needed, provide additional and related information so until no doubts persist.
Explain—Once a decision is reached, provide all required information and details to empower the patient regarding the option made including confirmatory questions ensuring patient's learning.
Return—The last step recommends a follow-up after a period. The time elapsed to the return session varies with the counseling initial sessions objectives and patient commitment. For instance, non-drug counseling for diet improvement does not need a specific return time, while using a medical device for the first time might require some feedback from the patient soon after dispensing.

All counseling may present challenges. Difficult moments can occur if the patient stops talking, either as a result of a confidentially concern or perceiving a judgmental attitude from the pharmacist. Emotional expressions (e.g., crying) are also challenging. Use a pause to allow for patients' emotional recovery, offering relevant physical support such as a tissue, glass of water or a seat. If the counseling has become inappropriate or ineffective to, close, the session, the pharmacist can show loss of interest (e.g., standing up) working with the computer or handling other documents. There will be times a pharmacist cannot provide an answer due to lack of knowledge or feeling embarrassed by the subject matter, especially with acquainted patients. In this case, is recommended to refer the patient to a colleague or other healthcare professional.

4.5 Pharmaceutical Counseling and Medication Adherence

Counseling is a patient-focused intervention designed to improve behaviors like medication adherence and persistence. Adherence can be defined as the extent to which a person's behavior, such as taking the medication, corresponds with agreed recommendations from the healthcare provider [11]. This usually involves the voluntary collaboration of a patient in a mutually accepted course of action. In fact, from practical, emotional and unidimensional social support (comprising family cohesiveness and conflict, marital status and the living arrangement of adults), practical support bears the highest correlation with adherence [12]. See Chap. 5 for more considerations around adherence.

In medication counseling, all previous principles, requisites and GATHER steps should be respected with content-specific counseling always adjusted to patient

existing knowledge. When the patient is using a medication for the first time, the initial questioning should comprise patients' understanding of his/her health condition and the, medication purpose, followed by information on what to expect. In medication refills, ask the patient how he/she is using the medication (including demonstration, if required) and to describe any issues being experienced.

Although the previously described approach is most times enough to assess patient knowledge on medication, when aiming at a more detailed counseling, the following topics should be covered:

- Name and purpose of the medication;
- The dosage/quantity that should be taken, when to take it, for how long;
- How to administer the medication, including preparation (if needed);
- What to do when a dosage is missed;
- Precautions when taking the medication, e.g., renal and hepatic impairment, drowsiness and driving, exposure to sunlight, etc;
- Important sideeffects, e.g., GI mal-functioning (e.g., diarrhea, vomiting), CNS disturbances (e.g., sleep disorders, nervousness), etc;
- Interactions with foods, beverages, other medicines;
- How to store the medication at home;
- Proper package and leftovers disposal (if appropriate);
- How to self-monitor effects (if possible);
- How to refill the prescription (if necessary).

Pharmacists engaged in medication counseling should assess their counseling success. This requires more than satisfaction queries but should materialize in follow-up sessions. These sessions should follow a line of enquiring covering how the patient is using the medication (including his/her demonstration, if required) and to describe any issues being experienced, before any advice itself. To better achieve a useful follow-up, pharmacists must develop and implement a plan to monitor patient's progress, detecting risks and employing the measures needed to achieve the agreed outcomes. On the other hand, patients should attend these follow-up sessions. Documentation is essential to accomplish the counselor role and to demonstrate the quality and effectiveness of the service if requested by third parties.

Many times, under routine and time pressures, pharmacists are not immediately able to initiate a dialog conducive to decide on patient's eligibility for medication counseling. This way, it is good to develop a priority checklist, according to local patients and setting. For instance, poly-medicated patients, those receiving for the first time a new drug and those looking confused or known to have visual, hearing or literacy limitations, should be the priority for an initial screening interview. Other patients should also be surveyed for medication counseling, such as those receiving important changes in medication or dosing, complicated directions, significant sideeffects and special storage requirements.

A note should be mentioned regarding the advice-giving in helping patients with minor ailments, designated as counseling non-prescription drugs. Responding to patient symptoms, and confirming the opportunity to treat a self-limited condition,

should entail a structured patient interview with the principles and conditions earlier mentioned, preferably based on self-medication protocols. Otherwise, handling a specific OTC-product request and providing direct information is different by nature from the counseling here proposed.

Finally, any patient counseling needs to respect patient autonomy, to keep data confidentiality, to serve patient welfare, always treating those who have searched for professional help with respect and compassion.

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Chapter 5
The Role of Adherence in Pharmaceutical Care

Parisa Aslani, Rana Ahmed and Filipa Alves da Costa

Abstract Optimal adherence is often a prerequisite for medication effectiveness and safety. Maximizing medication adherence is one of the core activities of the pharmacist when providing pharmaceutical care. This chapter starts by defining and carefully framing medication adherence and placing the different terms and phases of the "patient–medicine relationship" into context. It then provides an overview of the factors that impact on medication adherence, the methods available to measure adherence, and above all, the ways through which practitioners may detect medication non-adherence in daily practice. A list of interventions intended to foster adherence is presented, with their categorisation, together with their pros and cons for development and implementation in daily practice, highlighting those where there is more experience or evidence of success.

Keywords Pharmaceutical care · Medication adherence · Patient compliance Treatment adherence and compliance · Patient education

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5.1 Introduction

Adherence to treatment regimens is a key link to improved patient health outcomes. Ensuring adherence is an important role for the pharmacist, and a fundamental component of pharmaceutical care. At every patient encounter, pharmacists have an obligation to monitor adherence and resolve any medication-taking issues that patients may have, including non-adherence.

Non-adherence is not a condition-specific phenomenon. Low patient adherence to prescribed regimens is a problem which has been observed in a broad range of medical conditions [1, 2]. Depending on the condition and its treatment, patient deviations from therapeutically appropriate treatment regimens can lead to a range of negative humanistic, clinical and economic outcomes. Non-adherence to clinically appropriate treatment regimens has been associated with decreased treatment efficacy, poorer patient outcomes and increased disease burden [3]. It is estimated that only 50% of patients with chronic diseases take/use their medications as prescribed [3]. This, coupled with the growing prevalence and burden of chronic diseases worldwide, emphasizes the significance of the negative consequences of non-adherence for individuals and societies as a whole. Non-adherence represents one of the most significant challenges facing health care providers, policy-makers and researchers today.

5.2 Defining Key Adherence-Related Terms

The complexity of the field of adherence is reflected in the variety of different terms used to account for variations in patients' medication-taking. Interestingly, although some of these terms are used interchangeably in the literature, they are in fact unique terms that are varied in scope.

5.2.1 Compliance

Compliance was, up until recently, the most commonly used term for describing patients' following of treatment instructions. It was first coined in the 1970s and defined as "the extent to which a patient's behavior (in terms of taking medications, following diets or executing other lifestyle changes) coincides with the clinical prescription" [4]. Despite the widespread use of this term throughout medical and pharmaceutical literature, this conceptualisation of patients' medication-taking has been the subject of much debate and controversy, primarily due to the term's negative connotations and paternalistic undertones, with many arguing it implies that patients are expected to passively follow doctors' orders and that there is an inequity of power between the two parties.

5.2.2 Adherence

The introduction of the term adherence reflected a significant shift towards recognizing the important role of patients in their own health care. Adherence emphasizes that patients should be heavily involved in the treatment decisions made. The World Health Organization defines adherence as "the extent to which a person's behavior-taking medication, following a diet and/or executing lifestyle changes, corresponds with agreed recommendations from a healthcare provider" [3]. Perhaps the most important aspect of this definition is the recognition that patients and their health care providers need to reach a point of agreement about the course of treatment.

Adherence is now understood as a multi-faceted construct encompassing patients' understanding of their illness, their belief in the efficacy of a particular treatment and in their ability to control their symptoms by utilizing this treatment. There are three key phases of adherence, *initiation*, *implementation* and *discontinuation* [5]. *Initiation*, which is a discontinuous action, describes the first occasion that a dose of medication is taken by a patient after it has been prescribed. Comparatively, *implementation* represents the extent to which the patient's medication-taking matches the prescribed dosing, administration frequency and timing, and is therefore considered to be a continuous action. *Discontinuation* marks the end of therapy and is indicated by the omission of the patient's next prescribed dose and doses thereafter.

5.2.3 Persistence

Persistence is a measure of treatment continuity, defined as the time from the initiation of treatment to its complete cessation. It is distinct from adherence, whereby a patient who is considered to be persistent with their prescribed treatment regimen may not necessarily qualify as an adherent one. To clarify, a patient who completes a treatment regimen for an acute illness within the timeframe agreed upon with the prescriber would be considered to be persistent. However, if over the course of this treatment, the patient's implementation of the regimen was disparate to that prescribed (e.g., errors in dose amount or timing), they would be regarded as non-adherent.

5.2.4 Concordance

Unlike compliance, adherence and persistence which are quantifiable parameters related to patients' medication-taking, concordance relates to the nature of the relationship between clinicians and their patients in arriving at treatment decisions. First introduced in the late 1990s, concordance was heralded as a model of "shared decision-making and consensual agreement between doctors and patients as equal parties" [6]. Concordance emerged from the understanding that non-adherence is

often the outcome of a prescribing process which neglects the patient's beliefs and preferences. Although concordance initially focussed on the consultation process—where it was expected that clinicians and their patients reached therapeutic decisions only after negotiations respecting the beliefs and wishes of the patient regarding the use of the medication had taken place—over time, the scope of the term expanded to encompass the importance of communication during consultations and patient support in their medication-taking.

5.2.5 Patient-Centered Care

Patient-centered care is a concept which reflects the quality of health care delivered to patients and incorporates the shared decision-making attributes which underpin concordance. Like concordance, the concept of patient-centered care reflected a transition from disease-oriented understandings of patient care. It is defined as "a partnership among practitioners and patients" which ensures that "decisions respect patients' wants, needs and preferences and that patients have the education and support they require to make decisions and participate in their own care" [7]. In this way, the clinician is required to assist patients in arriving at an agreed treatment decision by educating them about their treatment options while at the same time eliciting and considering their beliefs and preferences.

5.2.6 Categories of Non-adherence

Non-adherence can be categorized generally into one of two broad categories [8]. *Primary non-adherence* relates to those patients who do not present their original prescription for dispensing or do not initiate an agreed intervention in the first place. It is estimated that approximately 28% of new prescriptions written by primary care specialists are never filled [9]. Practicing pharmacists are, therefore, less likely to encounter this group of non-adherence. *Secondary non-adherence* refers to when patients do not take their medications or follow the implementation of a particular intervention as agreed with their health care professionals. Secondary non-adherence can be further classified into unintentional and intentional [8]. *Unintentional non-adherence* is observed in those patients who have the intention to adhere to agreed treatment recommendations but are prevented from doing so due to reasons beyond their control. This may include patient forgetfulness or not understanding how to take the medication. *Intentional non-adherence* occurs when patients makes a conscious decision to cease or modify their agreed treatment after consideration of its perceived benefits and risks. In these cases, the risks (e.g., side effects) associated with the treatment are perceived to outweigh the benefits (e.g., alleviation of symptoms).

5.3 Factors Impacting Adherence

There are a number of factors associated with patients' adherence to treatment regimens and these have been explored extensively in the literature [10]. These factors are often organized into one of five categories that are in line with the World Health Organization's dimensions of adherence namely: (i) therapy-related factors; (ii) condition-related factors; (iii) social and economic factors; (iv) patient-related factors; and (v) health system/health care team-related factors [3].

5.3.1 Therapy-Related Factors

The specific nature of treatment regimens and the level of patient involvement required for their maintenance have been shown to influence adherence levels. Complex treatment regimens that involve the use of multiple medications for one or more disease states, have been associated with lower adherence primarily owing to the increased demands such regimens place on patients [11]. Treatment complexity is not only the result of the number of medications taken by patients, but also their administration frequency, duration of treatment, dose administration form and additional directions [10].

The lack of immediacy of beneficial effects associated with prescribed treatments may negatively impact upon patients' adherence [10]. This is especially apparent in the management of conditions which do not present with symptoms for example, hypertension or dyslipidemia, where treatment benefits may not necessarily be noticed by the patient [10]. Concerns about or the actual experience of side effects resulting from prescribed treatments may also negatively influence adherence levels [10].

Patients' inability to access appropriate medical services and medications also impacts upon treatment adherence [12]. This relates both to patients' geographic location with respect to surrounding health services and to the cost of medications [13].

5.3.1.1 Health Condition-Related Factors

Condition-related factors relate to the illness-specific demands faced by patients and have been demonstrated to influence treatment adherence. Some of the key factors include symptom severity and the level of disability caused to the patient, rate of progression and severity of the illness and the presence of comorbidities [10]. Patients who experience severe and impairing symptoms as a result of their condition are more likely to adhere to treatment compared to patients with largely asymptomatic conditions [10]. Furthermore, the nature of progressive conditions such as heart failure or diabetes and the potentially severe consequences of their

mismanagement have also been shown to influence treatment adherence. Comorbidities such as depression, may also impact adherence by potentially impairing patients' motivation or awareness regarding the importance of treatment regimen maintenance [14].

5.3.1.2 Social and Economic Factors

Patients' socioeconomic status has been identified to have an important role in predicting treatment adherence, although the findings of research in this area vary depending on the specific population under examination. The costs associated with certain treatments can be too much of a financial commitment for many patients, especially those from a low socioeconomic background [15]. The financial burden of treatment can extend beyond prescription costs and may also include consultation fees, medical test costs and the cost of transportation to health services. This issue becomes especially pertinent for patients taking multiple medications for prolonged periods of time, as is often the case for patients with chronic illnesses, who may find it difficult to maintain the associated expenses of treatment.

5.3.1.3 Patient-Related Factors

Patient-related factors associated with treatment non-adherence have been the focus of much research and relate to patients' knowledge, attitudes, beliefs, expectations and the resources available to them. There is a vast body of literature regarding these factors. Patients who have difficulty accepting their diagnosis are likely to reject any prescribed treatments [10]. This is particularly prevalent amongst patients with largely asymptomatic conditions such as hypertension or those who have difficulty accepting biomedical conceptualisations for certain conditions such as attention-deficit hyperactivity disorder (ADHD) [16]. Patients' misunderstandings about the nature of their illness and the importance of the prescribed treatments have also been reported to negatively affect treatment adherence [10].

Patients with low education or poor literacy levels have been shown to have less knowledge about and poorer understanding of their condition and its treatment in comparison to those with higher education and literacy levels. These patients' may also have difficulty accessing health and medication information that is presented in a comprehensible format. As a consequence, such patients are more likely to have lower treatment adherence as they may not fully understand the importance of the prescribed treatments and experience difficulty in finding appropriate sources of information [17].

5.3.1.4 Health Care System-Related Factors

In comparison to the factors highlighted above, relatively little is known about how aspects of the health care system impact upon adherence. It is generally understood that a positive relationship between patients and their health care providers may foster treatment adherence [10]. Many health care professionals do not receive direct financial reimbursement for educating patients about treatment adherence. This, coupled with the time demands faced by many health professionals, may lead to reduced willingness and motivation to provide adherence-related advice and support for patients. Consultations with patients may prove too short to adequately inform them about the importance of treatment adherence or to identify and address any discrepancies in patients' medication-taking behaviors. Moreover, health care professional abilities including training and motivation can negatively influence effective communication in fostering adherence.

Problems may also arise when patients are visiting multiple health care providers and there is communication breakdown between them, whereby information is not relayed from one provider to the other and may present a barrier to the identification and management of treatment non-adherence. Good interprofessional collaboration is essential to avoid communication breakdown. Such collaboration whether by face-to-face contact, telephone contact or the sharing of patient treatment records can lead to more holistic patient care. In this way, treatment plans can be optimized when necessary and each health care provider can and be better equipped to monitor and manage patient adherence.

5.4 Factors Promoting Adherence to Prescribed Medications

The findings of adherence-related research have predominantly focused on factors which negatively impact upon adherence. However, there is an increasing trend to investigate factors that encourage adherence to prescribed treatments, which is important as a step towards intervention development (see below). Some of the factors that have been associated with high levels of adherence include patients" feelings of certainty associated with the use of medications; trust in the physician and/or the medications; fear about potential health consequences associated with lack of treatment; motivation and desire to control their health condition; and confidence in their ability to self-manage their health condition [10]. Other key promoters of treatment adherence relate to patients' knowledge and understanding and their beliefs about their health condition and its treatment [10].

5.5 Interventions that Promote Adherence to Therapy

There is no single intervention guaranteed to address the issue of treatment non-adherence. Although there are several interventions which have been demonstrated to significantly improve medication adherence, the consensus in the current literature is that their effectiveness will vary depending on the nature of the intervention itself, the way in which it is utilized and the specific population the intervention is targeted at [18, 19]. Consensus seems to exist, however, that multi-faceted interventions are more effective [20–22].

In order to develop interventions aimed at improving adherence, it is important to consider several factors. Firstly, non-adherence is not associated with a specific disease state. The vast body of adherence-related literature emphasizes that non-adherence is ubiquitous amongst a broad range of diseases and is especially apparent in the treatment of chronic illnesses.

Secondly, there is no specific non-adherent patient. There may be some patient characteristics that are associated with non-adherence, but it is not possible to predict who will be non-adherent. There is likely to be inter-patient variability in adherence, but there is also intra-patient variability in adherence, i.e., where the same patient may have varying degrees of adherence to prescribed regimens over time and across different treatments. It is also important to note that the link between patient's characteristics and non-adherence is very much dependent upon the nature of the condition of interest and its treatment. Therefore, these associations are rarely generalisable to the entire population.

Thirdly, non-adherence is likely to be the result of more than one factor. For example, regimen complexity, lack of clear information and incompatibility with patient's beliefs may all contribute to non-adherence in one patient. Therefore, interventions need to consider the factors that may be contributing to a patient's non-adherence, and be tailored to address the individual needs of the patient.

5.5.1 Educational Interventions

The overarching aim of educational interventions is to provide patients with access to understandable verbal and/or written information about their health condition and the prescribed treatment. In these instances, it is anticipated that improved patients' understanding will lead to improved adherence. However, it should be noted that greater patients' understanding about their illness and its treatments may not necessarily lead to better adherence as it may not be the sole factor influencing patients' willingness to adhere. Educational interventions generally involve one or more of the following [23, 24]:

- *Face-to-face discussions*—Where health care professionals can provide targeted and tailored information to patients, and address barriers to adherence.
- *Educational booklets*—Provision of booklets containing general information about particular health conditions (signs/symptoms, causes, consequences) and their treatments (mode of action, side effects) to patients.
- *Electronic informational leaflets or brochures*—A variety of patient information leaflets relating to various conditions are downloadable from the Internet and may supplement verbal and/or written information provided to patients by their health care professionals.
- *Specific information leaflets*—Patients may also be able to access disease—and treatment-specific information leaflets prepared by pharmaceutical companies or independently prepared by some pharmacies and doctors surgeries.
- *Consumer Medicine Information (CMI) or Package Insert Leaflets (PILs)*—CMI or PIL is a standardized and comprehensive form of medicine information for patients which is available either as an insert in the medication's packaging, print-out or electronically.

5.5.2 Behavioral Interventions

Behavioral interventions generally involve assisting patients in developing necessary skills required to meet the demands of the prescribed treatment regimen. These interventions attempt to broaden patients' capacity to manage their illness and its treatment not only by skill building, but also through the issuing of reminders and providing simplification of treatment regimens where possible. Some examples of behavioral interventions are [23, 24]:

- *Motivational counseling*—This form of health care provider initiated counseling, also referred to as motivational interviewing, uses a patient-centered approach to help initiate change in particular behaviors, e.g., medication-taking habits. The approach is based on the Stages of Change model [25] which proposes five stages of change in relation to patients' health behaviors: (i) pre-contemplation; (ii) contemplation; (iii) preparation; (iv) action; and (v) maintenance. These stages should be used by health care professionals to guide their attempts at improving adherence.

  During motivational counseling, it is essential that the health care professional collaborates with the patient to explore potential reasons for low adherence and identify mutually agreeable goals to address these issues. To achieve this, it is important to assess the patient's readiness or willingness to change and to make recommendations based on the identified barriers to adherence that are in line with the patients' "state of willingness".

  It is useful for health care professionals to be able to express empathy towards the patient which will assist in understanding the patient's perspective and increase patient comfort. Responding appropriately to patient resistance during motivational counseling is also important—health care professionals should not

engage in arguments with their patients, rather they should take time to explore the patient's reasons for resistance and emphasize the need for change in the context of the patient's goals. In doing so, health care professionals will help foster the patient's self-efficacy which is a key driver of patient adherence to prescribed regimens.

- *Specialized packaging*—Specialized packaging of prescribed medications has been found to help improve patients' adherence [26], particularly in instances where patients' non-adherence is the result of forgetfulness. Dosing aids such as calendar blister packages, pill boxes or Webster-paks®, which involve the packaging of several medications in a fixed combination to be taken together, can assist in better organizing patients to take their medications. Other strategies to organize patients' medication-taking include medication calendars or reminder charts which instruct patients to take their medications at the same time each day or help associate their prescribed doses with other daily activities such as consuming a main meal.
- *Adherence reminder aids*—These strategies focus on regularly reminding patients to take their medication(s) and include setting reminder alarms, e.g., on a mobile phone; electronic devices [27]. They also include strategies that remind patients to collect their repeat prescriptions from the doctor or pharmacy, such as telephone, mail or text reminders.
- *Regimen simplification*—This is a common approach used to help improve patients' adherence, particularly in instances where a patient's regimen involves multiple medications as this may increase the risk of unintentional non-adherence. Studies highlight that reducing the complexity of prescribed regimens by decreasing the quantity of medications or their administration frequency leads to significant increases in adherence rates [18].

Therefore, where non-adherence is identified, it may be beneficial for pharmacists to review the patient's regimen to screen for medications which:

- may no longer be necessary
- can be substituted for a non-pharmacological alternative
- can be substituted for an extended-release or long-acting formulation to decrease dosing frequency
- can be substituted for a combination product (containing two or more medications in one tablet/capsule) to decrease the number of medications
- can be administered at the same time.

5.5.3 Intervention Design

The perceptions and practicalities model of non-adherence was proposed by Horne [28], and provides a conceptual distinction between patients' variations in medication use. The model can be a useful guide for the development of interventions to improve

adherence, where the interventions should focus on addressing both the perceptual and practical barriers which may influence patients' medication adherence.

The core aspect of the model is the recognition that non-adherence may be intentional (i.e., the patient won't take the medication) or unintentional (i.e., the patient can't take the medication). The model highlights that intentional non-adherence stems from deliberate patient decisions to alter their medication use, whether by modifying the dosing frequency or not taking the medication altogether. These decisions are based upon the incompatibility of the prescribed treatment with patients' own beliefs about their illness and/treatment as well as their perceived expectations of outcome. For example, where a patient does not understand the need for a particular treatment (e.g., the use of inhaled steroids for the treatment of asthma while asymptomatic), it is unlikely that they will adhere to therapy. In this way, intentional non-adherence can be viewed to be the result of perceptual barriers influenced by patient beliefs.

Comparatively, unintentional non-adherence is a consequence of practical barriers which prevent patients from taking their medications as prescribed. These practical barriers relate to patient capacity and/or resource limitations that may lead to non-adherence despite patients' intentions to follow the prescribed regimen. Such limitations may include deficiencies in:

- memory: e.g., patients who forget to take the medication or forget regimen instructions
- dexterity: e.g., patients who have physical difficulty opening medication bottles/boxes or those who struggle using medical devices such as inhalers
- knowledge: e.g., patients who do not understand regimen instructions or the need to refill prescriptions.

However, it has also been suggested that there may be a gray area between intentional and unintentional non-adherence, which represents those cases where apparently unintentional non-adherence results from intentional non-adherence, i.e., the patient claims to forget but the real reason is because he/she does not value the severity of the underlying disease [29].

5.6 The Pharmacist–Patient Relationship

The aim of this section is to provide the pharmacist with some practical tips to be used during the patient encounter to identify and foster medication adherence.

5.6.1 Methods of Identifying Non-adherence in Health Care Consultations

There are a range of factors which may influence patients' utilization of prescribed treatments. Therefore, it is important that pharmacists are able to recognize potential

indicators of non-adherence and are able to address any concerns patients have about the prescribed regimen as promptly and appropriately as possible. These indicators are closely related to the previously explored factors associated with treatment non-adherence.

Health care professionals often overestimate their patients' adherence [30] and when coupled with the fact that patients are generally reluctant to disclose non-adherence, many instances of non-adherence can often go unnoticed in practice. To avoid this, familiarity with indicators of non-adherence is essential and these are outlined in Table 5.1 (the lists are not exhaustive).

Table 5.1 Indicators for potentialnon-adherence

Patient-related indicators	Condition-related indicators	Medication-related indicators
Patients who: • are unfamiliar with their prescribed medications when asked about them • report missing doses of their medication • are elderly • have poor eyesight • miss appointments with health care professionals • don't refill their prescriptions • appear to be forgetful or have dementia • have a mental illness such as depression • have a low income and/or low social support • have poor coping strategies, poor interpersonal skills and/or low self-esteem • are not well-educated • don't speak or understand the language spoken by the health care professional • have difficulty accepting the legitimacy of the diagnosis or the importance of treatment • do not trust the health care professional • have an unstable work environment, e.g., working changing shifts • travel frequently or are about to travel	If the condition: • is not responding as anticipated to treatment, i.e., symptomatic improvement/change in biological markers is lower than expected • has no or mild symptoms, e.g., hypertension • is one which impairs cognitive functioning • is chronic in nature and will require long-term treatment	If the medication(s): • are large in number and/or involve a complex dosing regimen • are expensive and could place increased financial burden on the patient • have severe side effects • have received negative media attention

5.6.2 How to Measure Patients' Adherence

Whenever patients interact with a health care professional, regardless of the reason whether it be for a follow-up appointment, blood test or simply refilling a prescription, there is an opportunity to discuss medication-taking behavior. Regular review of patients' medication use and ability to systematically document therapy adherence at each visit is of utmost importance for pharmaceutical care. In addition to the potential indicators of non-adherence, there are a variety of tools and methods designed to assist health care professionals in assessing patients' adherence to their prescribed treatments. These methods can be categorized as direct or indirect [1], and the latter further differentiated into either objective or subjective measurement approaches as outlined below.

5.6.2.1 Direct Methods

Direct methods of adherence assessment are regarded to provide the most accurate estimates of patients' adherence levels. Some examples of these approaches include:

- direct observation of therapy: involves physically observing the ingestion of the prescribed medication
- assays of biological samples: involves the measurement of drug or metabolite concentrations by assaying patient's saliva, urine or blood samples or measurement of drug biomarkers.

These approaches have clear advantages, the most important of which is their accuracy in determining patient's adherence levels. However, they can place an increased burden on the supervising health care professional and can be quite invasive for many patients, making it difficult to utilize these strategies in routine day-to-day practice.

5.6.2.2 Indirect Methods

Indirect methods are easier to implement and less invasive compared to direct methods, although they may not provide adherence estimates of the same accuracy. These methods can be classified as objective or subjective depending on the specific nature of the investigative approach, the former providing more direct assessments of adherence rates.

Objective methods

- ***Pill counts***
  This method involves health care professionals determining the number of unused pills remaining in patients' medication bottles or blister packs. If the number of unused pills is greater or less than what is expected based on the patients' prescribed dosing regimen, this may indicate that the patient is potentially under- or over-dosing, respectively. Pill counting is generally quick and easy to perform, providing an objective assessment of patients' adherence to their dosing regimens.
  However, the accuracy of the results may be affected, for example, by patients discarding a certain amount of pills prior to appointments with their health care professional in an attempt to appear congruent with the regimen. Patients may also place pills in other containers such as pill boxes which would also affect pill count findings. Another disadvantage of this method is that while it allows quantification of the total number of pills consumed, it does not provide insight into whether patients are taking the prescribed doses at the correct time throughout the day.
- ***Pharmacy refill records***
  The use of pharmacy refill data provides insight into whether patients' prescriptions have been filled and the regularity with which this occurs. From this information, pharmacists can determine the number of days that a patient has been without their prescribed medication, based on the prescribed regimen and the number of pills supplied with each refill. Refill data are readily available and hence, commonly utilized in the community or hospital outpatient pharmacy. Pharmacists are able to examine patients' electronic prescription records, make assessments about their adherence and follow-up with patients where necessary. It is economical and non-invasive, however the major drawback of utilizing this method is that it does not provide detailed insight into patients' medication-taking behaviors. Computerized patient records may highlight when a prescription has been refilled but they do not indicate whether or not the medication was actually taken by the patient as prescribed or even taken at all. Furthermore, several refill records must be examined before any meaningful patterns in the patients' medication use can be identified, which also requires patients to refill their prescriptions at the same pharmacy.
- ***Electronic monitoring devices***
  Electronic medication monitors are recognized as the gold standard for the measurement of adherence to medications, although their use is also not without potential faults. The medication event monitoring system (MEMS) is a common electronic monitoring device which consists of a chip inserted into the cap of the patient's medication bottle and is capable of recording the dates and exact times that the bottle was opened. The saved information can then be downloaded onto a computer and analysed to determine how accurate the patient was in adhering to the timing and frequency of the prescribed doses. More recently, dosing aids including a chip to record the same information have been developed.

While these devices provide detailed, accurate information about the patients' dosing frequency, they rely on the fact that with each opening of the medication bottle, the patient is removing the correct number of pills. This may not necessarily be the case, as patients may often remove the total number of pills they need to consume for the duration of the day at the same time, rather than opening the bottle on every occasion that a dose is required. Another drawback is that, as with all indirect methods, they do not document whether a patient actually ingested the dose that was removed from the bottle. Furthermore, these devices are expensive and therefore are not used routinely in clinical practice. Importantly, these devices lead to an initial artificial change in patient's medicines-taking behaviour, leading to their potential use as an enabling strategy.

Subjective methods

- ***Interviewing***
  Interviewing patients about their medication use is an easy-to-use approach to assessing medication adherence and should be routinely used in practice. In doing so, it is important to use a combination of open and closed questions to elicit information about the patients' treatment utilization and their beliefs about the treatment. Pharmacists should be empathic, adopt a non-judgemental approach and word questions carefully during these discussions, to increase patient comfort and elicit accurate information.
- ***Patient questionnaires***
  The use of other patient's self-report measures such as patient questionnaires is another practical approach to measuring adherence, although the results obtained may not be as rich as those obtained through patient interviews. Questionnaires are economic, unobtrusive and generally time-efficient but as with patient interviews, they may lead to biased or inaccurate information depending on the truthfulness of responses. Most questionnaires have been primarily created for research purposes, however many are now available for use by health care professionals and can still provide useful insight into patients' medication-taking. When using questionnaires, pharmacists should first evaluate what is being measured as some focus on beliefs and others on the actual adherence measurement.
- ***Patient diaries***
  Asking patients to keep a medication diary is another easy-to-use, cost-effective method for estimating patient adherence and identifying potential barriers to adherence. The diaries may be structured or unstructured and may assist in capturing more than just adherence-related information, but also information about their beliefs and preferences. As with the remaining patient-report measures, this approach is susceptible to misrepresentation as it relies on the accuracy of the patients' accounts.

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Chapter 6
The Role of Interprofessional Communication in Pharmaceutical Care

Veerle Foulon, Joke Wuyts, Sophie Liekens and Giannoula Tsakitzidis

Abstract Pharmaceutical care can hardly be provided without collaboration with other healthcare providers. In its optimal form, interprofessional collaboration entails that providers discuss mutual goals, resources, and responsibility for patient care. In order to support this collaboration, interprofessional education is essential. Collaborating in healthcare is a competency and can be learned. One of the central elements in the competence "collaborator in healthcare" is interprofessional communication. This competency is characterized by different aspects, which apply whatever the medium used.

Keywords Pharmaceutical care · Multidisciplinary care · Interprofessional collaboration · Integrated care

6.1 From Monodisciplinary Approach Via Multidisciplinary Care to Interprofessional Collaboration

In the most recent definition of pharmaceutical care, published by Pharmaceutical Care Network Europe (PCNE), pharmaceutical care is described as "the contribution of the *pharmacist* to the care of individuals in order to optimize medicines use and improve health outcomes" [1]. Although the pharmacist, as an expert in medicines, can play an important role in a patients' medicines use, he usually does not do this on his own. Many healthcare professionals (HCPs) might be involved physicians, nurses, psychologists, etc. As already recommended in 1994 by the

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World Health Organization (WHO), the pharmacist should be a member of the healthcare team, and communication and effectively cooperating with the other members of the healthcare team is essential [2]. In later documents, the WHO further reported that interprofessional collaboration also improves health outcomes [3]. The current vision on ideal healthcare practice therefore not only includes patient centeredness as a pivotal aspect (see Chap. 3) but also integrated service delivery.

6.2 Integrated Services

The WHO has developed the following definition of integrated service delivery: "The management and delivery of health services so that clients receive a continuum of preventive and curative services, according to their needs over time and across different levels of the health system" [4].

For the *user*, integrated service delivery means that the service delivery is coordinated, with a minimum number of stages in an appointment and a minimum number of separate visits. It also means that healthcare professionals (HCPs) are aware of the patients' health as a whole, and that different HCPs across settings communicate as well as to make the care seamless and smooth.

For *professionals*, integration happens when different HCPs work together to provide services.

In its optimal form, integration on the level of the professionals also entails that providers discuss mutual goals, resources, and responsibility for patient care. This is also referred to as *interprofessional care* or *interprofessional collaboration*. This is different from multidisciplinary care, where different aspects of a patients' care are handled independently by different professionals, without a common goal. In multidisciplinary care, each HCP is responsible for his/her own area. This is not the case in interprofessional collaboration. Figure 6.1 illustrates the difference between both concepts. Other terms that are used in practice are "*interprofessional collaborative practice*" and "*interprofessional teamwork*".

When medicines are part of a prevention or treatment plan, a pharmacist is essential to ensure the responsible use of medicines, and by doing so, to contribute to the best quality of patient care [5]. According to the International Pharmaceutical Federation (FIP), collaborative practice should therefore be seen as critical to developing pharmaceutical roles in healthcare systems [6].

Looking at the role of the (community) pharmacist, it is clear that there is a trend to multidisciplinary collaboration, but that interprofessional collaboration is less frequent. The most progressive countries are Australia, Canada, and the US. For the latter two countries, national initiatives promoting collaborative practice and describing the role of the pharmacist have been launched [6]. Australia integrated in 2010 a statement on interprofessional collaboration in the National Competency

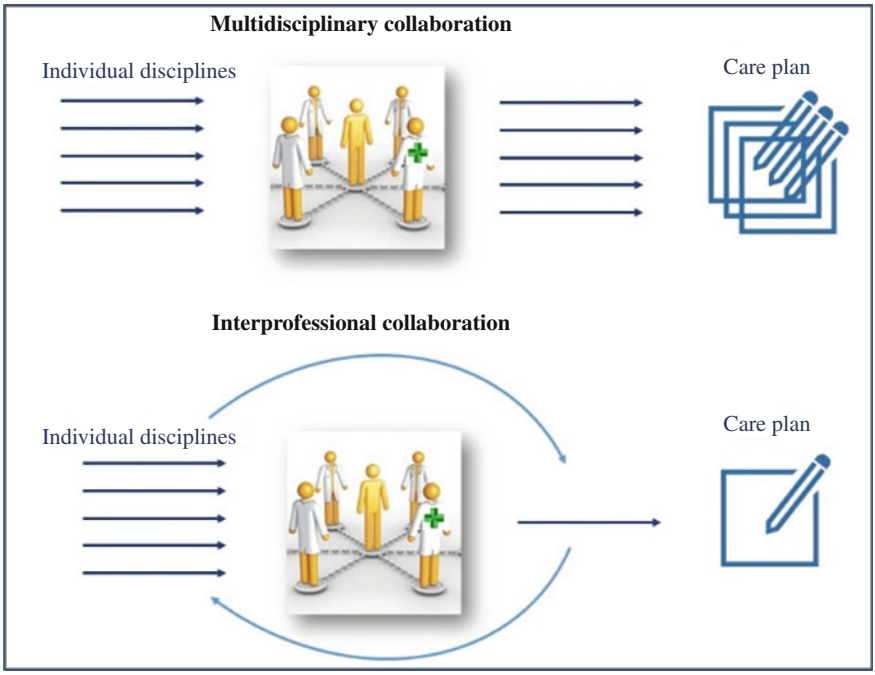

Fig. 6.1 Difference between multidisciplinary and interprofessional collaboration (based on Tsakitzidis et al. [5])

Standards Framework for Pharmacists [6]. In Europe, the Netherlands was the first country to establish working groups between pharmacists and physicians (FTO (local pharmacotherapy concentration) and FTTO (transmural pharmacotherapy concentration)) in order to improve collaboration and optimize rational prescribing [7]. True examples of interprofessional collaboration are often part of a trial and discharge are examples of interprofessional collaboration that have recently been worked out and investigated in studies. Both examples are illustrated in the box (Fig. 6.2). In contrast, a review of medication review (MR) services in Europe (2014) showed that only in a limited number of implemented services case conferences with the physician were fully integrated (3/11 of intermediate MR services; 4/6 advanced MR services) [8]. The Dutch "FTO" (pharmacotherapeutic consultations between GPs and community pharmacists) focuses on optimal prescribing since approximately 1990.

Example 1: taking shared responsibility for appropriate prescribing for nursing home residents
Within the NH, interprofessional case conferences (ICC) are organized on a regular basis. During these ICC, the residents' general practitioner (GP), nurse and pharmacist discuss the residents' medication regimen with the aim to prevent, detect and solve drug related problems. Evidence for rational prescribing, as well as residents' specific factors, including the residents' goals and needs, are taken into account (protocol Come-On study [17]).
Example 2: taking shared responsibility for continuity in drug treatment
At the hospital ward, the clinical pharmacist performs a structured, patient-centered medication review shortly after admission. Proposed changes are communicated with the physician in charge. On discharge, a medication reconciliation is conducted by the clinical pharmacist, including a patient interview with a motivational approach, using a comprehensive summary of changes in the drug therapy during hospitalization. Any drug-related problem not dealt with during hospitalization is mailed after discharge to the individual patient's GP. In addition, a summary note on all changes is sent to the GP, furthermore the GP, caregiver and community pharmacy are contacted by phone (protocol OPTIMIST trial[18]).

Fig. 6.2 Examples of interprofessional collaboration

6.3 Prerequisites for Multidisciplinary and Interprofessional Collaboration

The first challenge for interprofessional collaboration is to have the appropriate range of skills available in the healthcare team. The second challenge is to ensure that the different HCPs effectively work together. One of the ways to achieve this goal, and that has been recognized by WHO and FIP, is to set up interprofessional training or interprofessional education (IPE). This refers to "occasions when members or students of two or more professions learn with, from and about each other to improve collaboration and the quality of care and services" [6, 9]. Learning *with* each other refers to the fact that the content of the training that is offered, e.g., on geriatric pharmacotherapy, is the same for all HCPs (nurses, GPs, pharmacists, etc.). Learning *from* each other means that one HCP can learn from another HCP, e.g., a GP can learn from a pharmacist about drug–drug interactions. Learning *about* each other refers to the fact that while following the same (interactive) training, you get familiar with the knowledge, skills, and attitudes of HCP from a different discipline. In general, IPE results in better knowledge and recognition of each other's expertise; better and more effective communication between individuals and professional groups; better sharing of workload and responsibilities; less tendency to strong specialization and profiling; less rivalry; improved job satisfaction; and higher quality of care [10]. There have been a few examples of IPE involving pharmacy students. Based on qualitative data, Gilligan et al. indicated that although IPE is universally claimed as a "good idea," there is still much room for improvement [11].

6.4 Interprofessional Communication: A Central Element in Collaboration

It is important to know that collaborating in healthcare is considered a competency, and hence that you can learn to collaborate. It also means that collaborating is not something that can just be imposed on people, without knowing how to collaborate or what is important in collaboration. Based on the CanMEDS roles, Tsakitzidis et al. have described seven roles that characterize the competence "collaborator in healthcare" [12]. These seven roles are visualized in Fig. 6.3. Similarly, core competencies in interprofessional collaboration have been described by the Canadian Interprofessional Health Collaborative (CIHC) [13] and the Interprofessional Education Collaborative in the US [14]. In all these models, interprofessional communication is considered as a central domain.

Fig. 6.3 Roles of "collaborator" in healthcare (based on Tsakitzidis et al. [12])

6.5 Interprofessional Communication for Pharmacists

The Interprofessional Education Collaborative Expert Panel has listed eight specific interprofessional communication competencies [14]. Rather than just discussing each of these competencies, we will use the following examples to illustrate how these competencies might be needed and can be reflected in pharmacy practice. As pharmacists mostly collaborate with GPs and nurses, examples will be limited to that context.

Choose effective communication tools and techniques, including information systems and communication technologies, to facilitate discussions and interactions that enhance team function.

> As to achieve integrated service delivery, the pharmacist involved in a long-term care facility supports the development of a shared electronic health record, and takes responsibility for drafting and updating the residents' medication plan (integrated in the electronic health record).

Organize and communicate information with patients, families, and healthcare team members in a form that is understandable, avoiding discipline-specific terminology when possible.

> When trying to explain the reasons for a change in the drug regimen of a patient to the nurse, the pharmacist focuses on the effects that can arise from the combination of the two drugs and the symptoms that may be experienced, rather than on the CYP-mechanism.

Express one's knowledge and opinions to team members involved in patient care with confidence, clarity, and respect, working to ensure common understanding of information and treatment and care decisions.

> When contacting a GP about the dosage of an antibiotic for a 3-year old child, the pharmacist respectfully asks the GP about the dose calculation, without giving the impression of a lack of knowledge on the part of the GP.

Listen actively, and encourage ideas and opinions of other team members.

> In a discussion on the medication regimen of a nursing home resident, the pharmacist carefully listens to the nurse, in order to understand the effects of the drug on the resident, and the fact that the resident is not able to participate in social activities due to the side effects. The pharmacist asks the opinion of the nurse on the proposal to try to reduce the dose of the drug, rather than stopping the drug.

Give timely, sensitive, instructive feedback to others about their performance on the team, responding respectfully as a team member to feedback from others.

> Having sent several unanswered e-mails to a GP in order to make an appointment to discuss the findings of a medication review for a particular patient, the pharmacist calls the GP, informs about the e-mails and the reason why they remained unanswered, and shows in a sensitive way his disappointment on the collaboration so far, as the patient had to wait for an answer on different drug-related problems. The GP apologies for the delay, and asks the pharmacist to clearly mention the subject in future e-mails, as well as the due date, so that he is more aware of the urgency.

Use respectful language appropriate for a given difficult situation, crucial conversation, or interprofessional conflict.

> Being informed about an error in the administration of a drug by a nurse who previously made the same mistake, the pharmacist respectfully questions the nurse on the causes that may have led to this mistake as to avoid similar errors in the future.

Recognize how one's own uniqueness, including experience level, expertise, culture, power, and hierarchy within the healthcare team, contributes to effective communication, conflict resolution, and positive interprofessional working relationships.

> A few months after the recruitment of a recently graduated pharmacist, who takes up more clinical roles, the chief pharmacist actively compliments her on her positive attitude and the way she facilitates the collaboration with the nearby nursing home.

Communicate consistently the importance of teamwork in patient-centered and community-focused care.

> While explaining the interventions based on a medication review of a particular patient, the pharmacist refers to the importance of the preceding discussion with the GP, in order to adapt the medication regimen.

6.6 Interprofessional Communication in Current Practice

While waiting for a full adoption of integrated services and interprofessional collaboration in daily practice, HCPs do communicate among each other and use different media to that extent.

The examples in the box (Fig. 6.4), specifically related to the role of the pharmacist, show the diversity of these media and how they can be used to obtain different goals.

In most countries, developments in e-health encompass the development of a shared electronic patient health record, including a "journal" functionality that allows communication between HCPs. However, there are still quite some barriers to exchanging health information [15] and it is not yet clear to what extent (community) pharmacists will get access to the information.

Whatever medium chosen, all eight aspects discussed before, and characterizing good interprofessional communication, apply. One additional aspect is respecting and guaranteeing the privacy of the patient. This is particularly true for "new" media such as web applications, chat boxes, etc. Hence, in most countries, the development of the e-health infrastructure also contains a thorough development of authentication and role identification procedures, as well as tools to prove a therapeutic relationship with a particular patient.

- *The community pharmacist phones the GP to discuss a drug-drug interaction.*
- *The community pharmacist writes a referral letter for the GP in order to plan a follow-up consultation with an asthma patient.*
- *The community pharmacist sends an e-mail to the clinical pharmacist in the hospital through a secure web-application in order to ask for clarifications on the therapy plan of a patient post-discharge.*
- *As part of a medication review, the pharmacist discusses the possibility to discontinue the statin therapy for a lady of 82 years old, who never had any cardiovascular event, in a face-to-face meeting with the GP.*
- *To organize medication reviews in a more efficient way, the community pharmacist organizes video-conferences with the GP to discuss a patients' medication regimen.*
- *Having completed a medication review, the community pharmacist sends the pharmaceutical care plan as well as the new therapy plan to the GP.*
- *Once every two months, all GPs and community pharmacists of a specific region meet to discuss the use of one class of medication and to build consensus on a plan to optimize the appropriate use of that medication.*

Fig. 6.4 Examples of multidisciplinary collaboration and different media used

6.7 Role of the Patient

As described in the previous chapter, a person-centered approach is characterized by a dynamic relationship among individuals, others who are important to them, and all relevant providers. This collaboration informs decision-making to the extent that the individual desires.

With regard to interprofessional collaboration and communication, this entails that the patient is fully aware of the composition of the team, and is considered part of the team. At minimum, the patient should be informed about all HCPs playing a role in the care process, the different roles they have, and the communication lines between these HCPs. Where possible and desired, the patient should be involved in decisions taken by the team, and hence be offered the possibility to take part in team meetings. This would give an additional dimension to the interprofessional meetings, beyond appropriateness of care and coordination of care, as the patient can express his experiences, preferences, and priorities for care. In most countries, however, this is not yet the case and opportunities to involve the patient in interprofessional case conferences still have to be investigated. At least, two important patient-reported barriers need to be overcome: knowledge and power [16]. Patient knowledge refers not only to knowledge about the condition, treatment options, and health outcomes but also to insight in personal values and preferences. Power reflects the permission to participate, confidence in the own knowledge, and skills necessary to take part.

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Chapter 7
Medication Review and Medication Reconciliation

Nina Griese-Mammen, Martin Schulz, Fabienne Böni and Kurt E. Hersberger

Abstract Medication review and medication reconciliation are systematic processes with the aim of increasing patient safety as well as effectiveness and efficiency on different levels. Whereas medication reconciliation is defined as the formal process of obtaining a complete and accurate list of each patient's current medications with the main aim of detecting and solving discrepancies, medication review is a structured evaluation of a patient's medications with the aim of detecting and solving drug-related problems (DRPs). The available information determines which DRPs can be detected. If a medication list/plan has to be critically appraised, then the list should first be complete and correct. This makes reconciliation automatically a prerequisite for a medication review.

Keywords Pharmaceutical Care · Medication review · Medication reconsiliation Drug-related problems · Classification

7.1 Medication Review

With the introduction of pharmaceutical care came a systematic process for the detection of DRPs to provide consistent and reliable care to patients. The need to regularly review medications in order to detect, solve, and prevent DRPs was shown by the fact that the long-term medications of a substantial number of patients were not even annually reassessed [1] (Fig. 7.1).

In hospitals, pharmacists have participated in optimizing patients' medication therapies since the 1960s, while in community settings, the development of medication review services as one cornerstone of pharmaceutical care started to evolve in the 1990s [2]. Among the first countries to effectively incorporate medication

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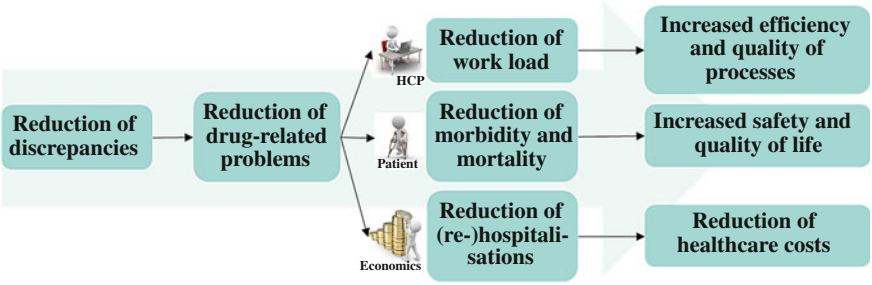

Fig. 7.1 Aims of medication review and medication reconciliation on different levels (HCP = healthcare professional)

review services into health care in community settings were Australia, the Netherlands, United Kingdom (UK), and the United States of America (USA).

Meanwhile, medication review is becoming increasingly important all around the world—in the community as well as in the hospital setting. In both settings, polypharmacy is increasing, and medication review is considered as a tool to reduce problems related to polypharmacy. However, the terms medication review and comparable expressions are used for a broad array of service models [3]. The differences in the process of the review can be related to patients' inclusion criteria, the sources and types of available information, the location of the review, the extent of patient involvement, and the level of multidisciplinary collaboration [4]. Furthermore, the types of investigated DRPs in different models are diverse.

The settings in which medication reviews have been provided include general practitioner (GP) clinics, hospital outpatient clinics, community pharmacies, residential aged care facilities, and the patients' home. Many papers relate to the provision of pharmacy services in aged care facilities or the hospital setting. In many countries, one fundamental difference between the community and hospital setting is the relatively limited or more difficult access to clinical data in the community setting. Another difference is that in the community setting many patients receives medical care and prescriptions from multiple prescribers and sources.

In 2009, the Pharmaceutical Care Network Europe (PCNE), a European association of researchers in this field, started to discuss a definition and classification for medication reviews performed by pharmacists in primary and secondary care. In 2016, this large group of international experts from research and practice reached a consensus on the term "medication review."

This official definition of PCNE is valid for medication review in all settings, and reads:

> Medication review is a structured evaluation of a patient's medicines with the aim of optimizing medicines use and improving health outcomes. This entails detecting drug-related problems and recommending interventions.

In view of the discussions, a position paper that would clarify the different elements of the definition and justify the choices was deemed necessary. This position paper can be found on the PCNE homepage (www.pcne.org).

According to the definition, all healthcare professionals with the appropriate knowledge can conduct a medication review. However, the prevalence and complexity of polypharmacy require that whoever conducts a medication review must have extensive knowledge about both medications and patient-related outcomes if the aims of the optimization of medicines use and of improving health outcomes are to be achieved.

7.1.1 Classification of Medication Review

As mentioned before, the process of medication review varies widely between countries and settings. In some places, the interrogation of a general practitioner (GP) computer system to identify inappropriate prescribing is classified as a review. In others, a dedicated face-to-face consultation is a mandatory part of the review.

The PCNE definition of medication review leaves room for different operational approaches and types of medication review. Besides the definition, PCNE introduced also a new classification for medication reviews. The PCNE classification takes into account the type and source of available information for the medication review (Table 7.1). Using the classification, it is possible to compare studies regarding medication review more accurately.

Due to the differences regarding the available information, different DRPs can be detected by the different types of medication review (Fig. 7.2). Typically, a type 1 medication review uses pharmacy claims data or pharmacy medication histories to

Table 7.1 PCNE classification of medication reviews (MR) considering information sources available

	Information available			
Type of MR	Medication history	Patient interview	Clinical data	
Type 1: Simple MR	+			
Type 2: Intermediate MR				
Type 2a:	+	+		
Type 2b:	+		+	
Type 3: Advanced MR	+	+	+	

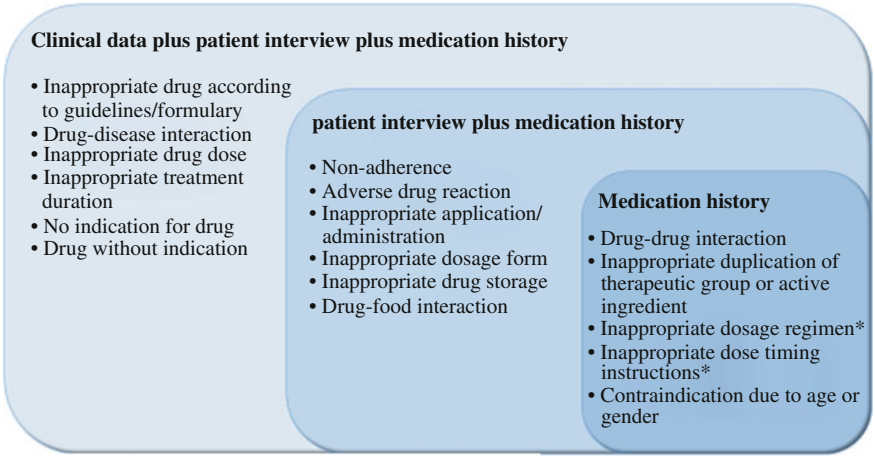

Fig. 7.2 Available information and potential drug-related problems that can be detected (examples)

examine potential problems such as excessive dosage, drug–drug interactions, and therapeutic duplication. When conducting an advanced medication review, the medication history plus clinical data and information from the patient interview are available. With these data, additional DRPs such as a drug without an indication or an inappropriate dosage form can be detected. Therefore, the purpose of the medication review service depends on the available or used information and vice versa. The main aim is always to optimize medicines use by detecting and solving DRPs. However, meeting patients' drug-related needs cannot be a key aim without a patient interview.

7.1.2 Selection of Patients

The target group for medication review services is patients who are at risk of DRPs. Organizations may wish to determine which clients, meeting specified criteria, will benefit most. Inclusion criteria often mentioned in contracts regarding medication review are age over 65 and a minimum number of drugs used. Although age and polypharmacy are predominantly positively associated with the risk of having DRPs, several other risk factors (e.g., comorbidity, renal impairment, and high-risk medication) contribute to the occurrence of DRPs and/or hospital admissions.

The existence of screening criteria enables pharmacists and other providers to direct their effort to patients who would benefit most from this service.

Table 7.2 shows inclusion criteria for medication reviews services often used.

Table 7.2 Examples of inclusion criteria for medication review services

Patients older than 60–65 years
Patients taking 5 or more long-term medications
More than three different (chronic) illnesses
Medication regimen changed four or more times in the last 12 months
History of medication nonadherence
Hospital discharge
Use of drugs that require therapeutic drug monitoring
Symptoms suggestive of an adverse drug reaction
Subtherapeutic response to treatment with medications
More than one prescriber
Patients in need of care who live in a home care setting

The inclusion criteria have to be matched to the type, setting, and the aim of the medication review service.

7.1.3 Process of Medication Review

In contrast to counseling or the validation of a prescription, a medication review is a structured activity or a method in patient care. Medication review as a cognitive service requires the implementation of a comprehensive process, which can differ from country to country. This approach can also be different for different settings and professionals. The term "structured" refers to the need for a standardized approach, which should assure quality.

Even though the approach can be different, the process of medication review consists typically of the following main steps:

- Data collection,
- Detection and evaluation of DRPs,
- Agreement on interventions, and
- Documentation.

These are also major steps in the patient care process: the assessment, the care plan development, and the follow-up evaluation. Therefore, medication review is an important activity of pharmaceutical care and covers important but not all steps of the patient care process.

According to many contracts, medication review services can and should be conducted annually, unless the patient's circumstances have changed sufficiently to justify one or more further consultations during this period. One important reason is, for example, that the patient has recently been discharged from hospital and had changes made to their medicine while they were in hospital.

Data collection

The data collection depends on the type of medication review and the process of data collection on the access to these data. Especially, the access to clinical data differs significantly between settings and countries.

The first step is always the identification of available data sources and their recording. Depending on the availability, both subjective and objective data can be considered. At minimum, the data should include the patient's basic demographics and the medication history.

Medication history

In order to make rational suggestions on interventions, an up-to-date and accurate patient medication history is essential. Ideally, a medication review is based on the "best possible medication history," a complete and accurate list of all the medications a patient is taking (see medication reconciliation).

Sources for information about medications can be the medication records of the pharmacy, the GP, or the hospital together with a patient interview.

The sources listed in Table 7.3 differ in their comprehensiveness (e.g., inclusion of prescription and non-prescription medications), accuracy, clarity, and accessibility. Even sources of medication information that are not complete may still convey valuable. Using different sources of information facilitates the detection of discrepancies between sources and therefore enables to detect potential DRPs.

A medication history or medication list is most useful if it includes current prescription and non-prescription medications, including herbals, complementary healthcare products, compliance aids, and therapeutic devices. Also, medications taken on an as-needed basis (e.g., nitroglycerin spray) or medications taken cyclically (e.g., once monthly) should be included. It is important to document the drug name, dosage form, the dose and/or strength (as required), the route, and the frequency for each.

Patient interview

The patient interview assesses the completeness and accuracy of other sources and highlights issues related to the storage, supply, administration, and handling of medications. The assessment may include immunization status, allergies, and adverse drug events. The patient interview should follow a systematic process and it can be helpful using an interview guide where available. The interview guide should include questions needed to obtain a complete and accurate medication

Table 7.3 Sources of medication information

Electronic medication records (national databases, databases of health insurance companies)
Community pharmacy records
Patient own medication lists or medication plans
Prescriber referrals
Previous admission records/discharge medication information

history and to discover DRPs. In order to achieve this aim, both open- and closed-ended questions can be used.

Open-ended questions	Closed-ended questions
When do you take this medication?	Do you take this medication in the evening?
What do you take this medication for?	Do you take this medication for your diabetes?

During the interview, it is important to determine and document how the patient is actually taking the medication(s). The medication history documented during the interview is a snapshot of the patient's actual medication use, which may be different from what is contained in other sources. The patient's home, the pharmacy, and the nursing home are possible settings to examine the medications and to conduct the patient interview. The patient's home gives the opportunity to holistically assess how the patient is managing his medications in his own environment. If this setting is not possible or appropriate, the brown bag review offers another possibility to get a more holistic view (see box). The interview with the patient can be replaced by an interview with a caregiver or relative, if appropriate.

Brown bag review
The "Brown Bag Review" of medications is a common practice that encourages patients to bring all of their medications to the patient interview. The methodology was first used in a study conducted in the USA. Patients were given brown paper bags and were asked to put all their medications for the patient interview into these bags. The brown bag method is a quite pragmatic approach. Conducting brown bag reviews can help to get a better impression of the patient's medication experience and helps to speak with the patient about his medication in a systematic way. The challenge is getting the patient to bring all his medications.

The patient interview is designed to address some or all of the following:

- Documenting all the patient's medication (medication history),
- Assessing drug-related needs by assessing expected outcomes and potential adverse events,
- Assessing patient-related needs by assessing
  - The patient's medication experience,
  - The patient's understanding and acceptance of their medication, its purpose (=indication according to the patient's statement),
- Identification of barriers to adherence to the agreed medication treatment regimen, and
- Checking the use of devices and administration aids.
- *The role of clinical data*

The role of clinical data

The medical history or clinical data are a major grouping of information that are needed for the medication reviews type 2b and type 3. One main type of clinical data is the diagnoses of the patient. During the evaluation of type 2b and type 3 reviews, it is important that the intended indication for each medication is identified. If clinical data are not available, the indication according to the patient could also give important hints. Clinical and laboratory parameters (such as electrolyte levels, Hb_{A1c}) or other parameters required to monitor medication therapy (such as blood pressure, blood glucose, and peak expiratory flow rates) are the most frequent parameters used to evaluate the clinical outcomes that result from a patient's drug therapy and are important sources to verify DRPs.

Detection and evaluation of drug-related problems

The pharmacist assesses the information gathered from a variety of sources. During this so-called evaluation, both objective and subjective data are evaluated to DRPs. It is important to use a systematic and reproducible method for evaluation. Organizations developing the medication review service should attempt to standardize the tools used for this important step of the review. For each medication review service, it should be defined which DRPs should be reviewed and whether specific tools or methods should be used.

The evaluation is based on the own expertise, taking guidelines into account and other instruments for the detection of drug-related problems.

Tools to evaluate medication appropriateness

Various criteria for detecting DRPs and assessing inappropriate prescribing have been developed. Both explicit and implicit tools can be used.

(1) Explicit instruments

In the early 1990s, Beers and colleagues created the Beers Criteria for potentially inappropriate medication (PIM) use in older adults, a "drugs-to-avoid" list designed to reduce the prescribing of these high-risk drugs in nursing home patients [5]. It is an explicit list of PIMs best avoided in older adults in general and in those with certain diseases or syndromes, prescribed at reduced dosage or with caution or carefully monitored. Since that time, many instruments using explicit criteria were developed internationally to measure various aspects of potentially inappropriate medications. Most of them focus only on drugs best avoided in older adults, while the STOPP & START criteria recognize the dual nature of inappropriate prescribing by including a list of potentially inappropriate medications (STOPP criteria) and potential prescribing omissions (START criteria) [6, 7].

Explicit criteria do not take into account patient preferences, life expectancy, or prescriber's knowledge of the patient. Drug- and disease-oriented explicit criteria require regular updating and are country specific.

(2) Implicit instruments

Implicit judgment is used all the time in clinical practice. Implicit instruments standardize and structure the implicit judgment. They formulate key questions and indicate DRPs to be addressed. Implicit, person-specific criteria are universal and do not need updating, although their use requires up-to-date professional skills.

The medication appropriateness index (MAI) is one of the most common implicit approaches published in the scientific literature. It establishes the appropriateness per drug (Table 7.4). The MAI's purpose was to serve as a sensitive measure of potential improvement in prescribing quality due to a clinical pharmacist intervention within the framework of a randomized controlled trial. The MAI consists of 10 questions that allow 3 rating choices ("1" being appropriate, "2" being marginally appropriate, and "3" being inappropriate [8].

Agreement on interventions

The next step is to define interventions for the detected DRP and the proposed solutions. The pharmacist, if necessary, discusses relevant potential and manifest DRP and their proposed solutions with the physician(s) and/or nurse(s). This requires a coordinated collaboration. In many countries, as a rule, the physician discusses therapeutic interventions with the patient, while the pharmacist discusses pharmaceutical interventions and DRPs related to self-medication/non-prescription drugs (OTC use). As many patients wish to be involved in making decisions about their medications, the patient should be actively involved in the solution of DRP. Where appropriate, ensure that patients and their family members or carers are able to make well-informed choices. Find out what level of involvement in decision-making the patient would like.

Documentation (see also Chap. 8)

Accurate documentation must be initiated and maintained for all steps of the medication review process. A record should be kept of all DRPs identified and of all recommended interventions, including the date and time they were made/taken and whether they were verbal or written. The names of members of the health care who were contacted and the dates of contacts should also be documented. The

Table 7.4 Items of the MAI

• Indication
• Effectiveness
• Dosage
• Direction
• Drug–drug interactions
• Drug–disease interactions
• Direction practicality
• Duplication
• Duration
• (Medical) expense

documentation must be presented in a way that allows colleagues involved in the process to assess the date on which the action was taken, what action was taken, by whom, and whether a follow-up is needed. Other pertinent information related to the medication review service (e.g., completion of a patient interview, brown bag review) and more detailed information (e.g., name of community pharmacy, who interviewed) should also be included in a standardized documentation.

Depending on the medication review service, the following data are part of the documentation:

- Basic patient demographics,
- Medication history,
- Medical history/clinical data,
- Data obtained in the patient interview, and
- Detected DRPs and suggested interventions, what action was taken and by whom.

Organizations developing the medication review service should attempt to standardize both the tools used to document the medication review service and the specific desired documentation practices.

7.1.4 Implementation of Medication Review

Medication review services are complex to implement reliably. Select a relevant patient group to start with (see, Sect. 7.1.2 Selection of patients). Keep your target population reasonably small at the onset of the initiation phase. Implementation is labor intensive at the beginning; so start small. Only increase the scale of implementation once the process is successfully adapted to workflows, tools have been developed and refined, and strategies have been identified and successfully used to manage challenges. More on the implementation of services can be found in Sect. 4 of this book (Chaps. 18–21).

7.1.5 Impact of Medication Review

Most community-based medication review research has been descriptive in nature and conducted in the USA, UK, and Australia. Relatively few studies have involved randomized controlled designs, making it difficult to draw a conclusion about the impact of the medication review service. The various papers on the subject of medication review seem to give conflicting answers to the important question whether the intervention achieves any impact [9]. Many of these differences can be explained with differences in the used methods. There are differences in what is done, who does it, and on whom it is done [9]. When controlled studies have been

performed, the main impact measures have been changes in the mean number of medications per patient and in medication costs per patient.

Reviews or meta-analyses of existing literature on medication reviews and in particular of relevant randomized controlled trials showed that there is at present a lack of clear clinical evidence supporting the effectiveness of the different types of medication reviews in the ambulatory setting [3, 10].

Given the nature of the intervention, the different patient inclusion criteria and the fact that its impact may take a long time to become clear show that the evidence is a relatively complex and costly process. There is still a need for adequately powered RCTs of medication review services to evaluate the effect on morbidity (e.g., hospitalizations) and mortality [11]. Meanwhile, it remains important that relevant data collection and analysis is part of any ongoing implementation project of medication review services.

7.2 Medication Reconciliation

Medication reconciliation is the systematic assessment of all prescribed and currently used medication. It is recommended to be conducted and communicated at every transition of care. Transitions of care occur at every change of care setting (primary, secondary, and tertiary care) or responsible healthcare professional (HCP), e.g., hospital admission and discharge, between wards, between day and night shift, and between general practitioner and community pharmacist.

The term "medication reconciliation" was introduced into the Medical Subject Headings (MeSH) term list in 2011 and is mainly used for the formal process of obtaining a complete and accurate list of each patient's current medications, especially in the hospital. Healthcare professionals and academics have been discussing the activities that medication reconciliation encompasses. Whereas in theory there is a broad agreement that medication reconciliation is the assessment of an accurate complete medication list, in practice, it is not easily separated from a medication review. In this book, we represent the opinion that medication reconciliation and medication review are different activities. Medication reconciliation is considered as a necessary step of medication review, both in the community and the hospital setting. Medication reconciliation can be conducted without the following steps of critical appraisal described for medication review.

This vision is also reflected by the current MeSH definitions and by the NICE guidelines (Table 7.5).

Transitions of care have been known to be critical for patient safety for a long time. Specifically related to medication therapy, this means that patient safety can be compromised due to medication errors. They are likely to occur when medication changes are not communicated between care settings or responsible HCPs.

In practice, it is not uncommon that, depending on whom is asked (the patient, the GP, or the community pharmacist), three different medication lists are received. The differences between these lists are referred to as discrepancies.

Table 7.5 Definitions of medication reconciliation

MeSH 2011 [12]	The formal process of obtaining a complete and accurate list of each patient's current home medications including name, dosage, frequency, and route of administration, and comparing admission, transfer, and/or discharge medication orders to that list. The reconciliation is done to avoid medication errors
NICE guidelines 2015 [13]	Medicines reconciliation, as defined by the Institute for Healthcare Improvement, is the process of identifying an accurate list of a person's current medicines and comparing them with the current list in use, recognizing any discrepancies, and documenting any changes, thereby resulting in a complete list of medicines, accurately communicated. The term "medicines" also includes over the counter or complementary medicines, and any discrepancies should be resolved The medicines reconciliation process will vary depending on the care setting that the person has just moved into—for example, from primary care into hospital, or from hospital to a care home

Figure 7.3 illustrates medication changes that can occur during hospital stay.

The Institute for Safe Medication Practices Canada (ISMP Canada) describes discrepancies as medication changes (dose, frequency, dosage form, etc.), adding medication, and omission. There are intentional documented discrepancies, intentional undocumented discrepancies, and unintentional discrepancies. Undocumented intentional discrepancies are usually a failure of documentation, which can lead to a medication error, whereas unintentional discrepancies are medication errors per se [14]. These definitions are referred to in this chapter to facilitate the reading; however, internationally, there is no consensus on the terminology of discrepancies.

Medication discrepancies have been extensively studied at hospital admission, discharge, and within hospitals. At hospital admission, up to 67% of patients have at least one discrepancy in their medication list, which potentially or actually causes

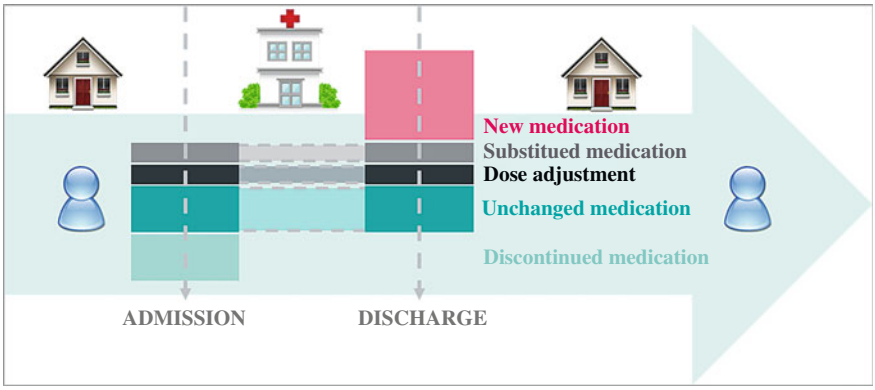

Fig. 7.3 Medication changes at hospital admission and discharge on a patient pathway

adverse outcomes [15, 16]. Patients on long-term medication may be at risk for unintentional discontinuation of medication after hospital admission, especially if they were admitted to the intensive care unit. At hospital discharge, up to 71% of patients had at least one actual or potential unintended discrepancy [17]. Community pharmacies have been detecting more DRPs on hospital discharge prescriptions than on ambulatory prescriptions [18]. These DRPs are likely to lead to adverse drug reactions, which can be a reason for hospital readmissions. A study by Coleman et al. has been able to show that patients with discrepancies were re-hospitalized significantly more than patients without discrepancies [15].

Factors, which increase discrepancies, can be system- and patient-associated. System-associated factors are mainly conflicting information from different sources, discharge instructions that are incomplete, inaccurate, or illegible, and duplications. Patient-associated factors are mainly intentional, non-intentional, nonadherence [15].

At a transition between HCPs within the same care setting, there might be a system in place, for example, the (electronic) patient chart, where information is complete and to which all responsible healthcare professionals have access. In this case, there is usually no need for medication reconciliation. However, in ambulatory care, a transition between responsible caregiver might be between the GP and the community pharmacist. In most countries, the community pharmacist does have some information about the treatment through the patient and the prescriptions (e.g., dispensing history), but has no access to complete health information. The same access problem might be the case within the hospital setting at the transfer of a patient from one hospital to another. In summary, the transitions between care settings and responsible HCPs always require medication reconciliation, if there is no access to the complete health information of the patient, i.e., if HCPs do not work within the same information network. If a dispensing history is available in the community pharmacy, medication reconciliation should be conducted with every new prescription by comparing the new prescription to the dispensing history and, if applicable, updating the patient's medication plan. With a systematic compilation of an accurate medication history at the hospital or in ambulatory care, there might be more clarity throughout the whole medication process and upon hospital discharge, intentional discrepancies can be documented with the accorded reasons and sent out with the discharge prescription.

Ideally, a healthcare telematics infrastructure connects the IT systems of doctors' and dentists' practices, pharmacies, hospitals, and health insurers with each other. It thereby forms the basis for a systematic interchange of information, e.g., electronic health record and medication plan. In this case, a medication reconciliation would only be necessary if a responsible HCP or setting was not included. From time to time, a reconciliation interview with the patient would still be favorable to check if the IT system data are accurate.

7.2.1 Impact of Medication Reconciliation

A vast number of studies have shown that medication reconciliation reduces discrepancies, adverse reactions, rehospitalization, and costs [19, 20]. Most publications emphasize the importance of pharmacy staff in an interprofessional team conducting the medication reconciliation.

From the patients' point of view, someone taking time to sit down with them and check their medication mediates security and gives a feeling of being taken serious. At hospital discharge, patients require an accurate medication plan and their healthcare professionals to share information about their treatment.

On institutional and national levels, guidelines for medication reconciliation have been developed, recommended, and introduced as binding [13]. Most guidelines provide toolkits, like assessment forms and manuals for the interview.

7.2.2 Required Qualifications to Perform Medication Reconciliation

Any healthcare worker, who is trained in medication reconciliation and who possesses the named qualifications, can perform medication reconciliation. However, literature has shown that medication reconciliation performed by pharmacy staff is the most accurate [21]. Innovative models include interprofessional approaches, which use the lean management strategy in health, e.g., conducting medication reconciliation by trained pharmacy technicians under the supervision of a clinical pharmacist.

Recommended qualifications to perform medication reconciliation are as follows:

- Knowledge about the types and names of medications/active ingredients,
- Knowledge about medication-related characteristics, such as dosage forms, dose, regimens, and indications,
- Knowledge about where and how information about medication of a patient can be acquired (e.g., knowledge about general practitioners and community pharmacies of the region),
- Knowledge about the common challenges and errors at the assessment of a correct medication history (e.g., omission, wrong dose, and look-alikes),
- Interview technique for the best possible medication history,
- Skills in being empathic and open toward the patients, to encourage them to communicate openly,
- Skills in communication and teamwork (also important for communication with healthcare professionals in other care settings),

- Skills in evaluating of the completeness of the medication information, and
- Skills in accurate documentation.

7.2.3 *Best Possible Medication History (BPMH)*

The "Best Possible Medication History (BPMH)" is the gold standard method to perform a systematic medication reconciliation. It comprises the elements information sources, anamnesis, medication, medication regimen, and documentation (Fig. 7.4). The aim is the generation of a complete and accurate list of the patient's current medication. At least two sources of information should be considered and ideally, one of them is an interview with the patient and/or relatives. It is of great importance that OTC medication and different dosage forms are asked in direct questions. In addition, details about the medication regimen like strength, treatment duration, and changes in treatment should be carefully assessed. The recommended process encompasses the following steps:

1. Compilation of information on the medication from reliable sources (written, patient's own medication boxes (brown bag method)).
2. Systematic interview of the patient and/or the relatives; during the interview comparison with other sources and documentation of information.
3. Resolving uncertainties and complementation of the documentation.
4. Deposition of the complete medication list in a patient's current file.

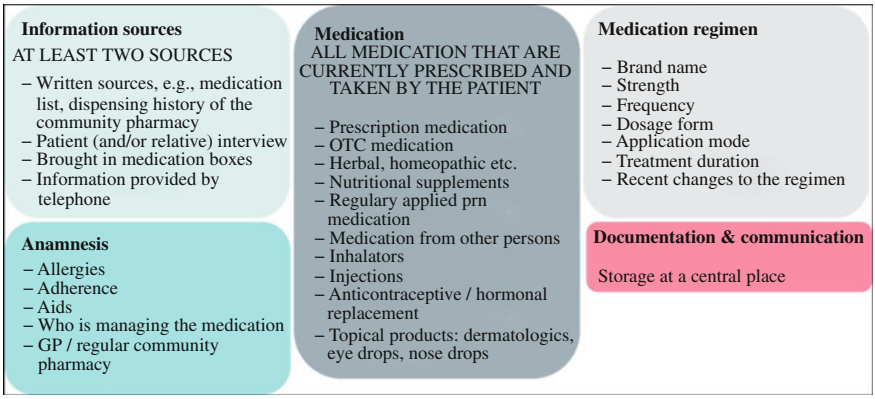

Fig. 7.4 Elements of a best possible medication history (BPMH). PRN = pro re nata (as needed)

7.2.4 Discharge Prescriptions in Community Pharmacies

Generally, hospital discharge prescriptions do not completely correspond to the dispensing history at the community pharmacy. This is a recommended approach for the handling of discharge prescriptions in community pharmacies:

Compare the new prescription to the dispensing history and define discrepancies

When you compare the new prescription and the dispensing history, think about what makes sense and what does not. Use your competencies in pharmacotherapy to decide if you can resolve a discrepancy yourself or if you need further information. Check with the patient for medication that might not be included in the prescription, especially OTC medication including herbals and food supplements.

Set priorities

Before taking actions in getting more information, like ringing up a physician, think about what is necessary to be clarified now, what has to be clarified today, and what can wait until tomorrow. Compile a list of priorities.

Choose accurate information sources

After compiling this list of priorities, reflect on the possibilities of information sources. The patients themselves are often neglected as a source although they usually are able to provide a lot of information. Additionally, they might bring more information material from the hospital than the prescription with them, e.g., a medication plan, a discharge report, or medication to be used during the first days after discharge. Think about who is responsible for the treatment. Hospital physicians usually do not take care of patients after they left the hospital. Questions about potential medication errors can be addressed to them, but questions about the ongoing treatment should be addressed to the general practitioner or to the responsible specialist.

Compile a new best possible medication list

With the information of the dispensing history and other sources, compile a new medication list that is as accurate as possible. Make sure you document the reasons for medication changes. Put the information together in a medication plan for the patient and advise him/her to take this new list and the discharge report to the general practitioner. In some cases, it might make sense to send the new best possible medication list directly to the general practitioner.

Counsel the patient

Counsel the patient about the medication changes (compared to before the hospitalization and to the discharge prescription) and about the new medication. Make sure, the patient understands his/her new medication plan and will be adherent. Provide the possibility to ask questions.

Follow-up and/or check need for medication review

Ideally, phone the patient a few days after hospital discharge to make sure that he/she is able to manage his/her medication and is adherent. Provide the possibility to ask questions. Medication reconciliation often reveals potential DRPs that need to be addressed in a medication review.

7.2.5 Case Scenario

This is an example of a hospital discharge prescription handled at the community pharmacy. A medication reconciliation has to take place at this opportunity.

Mr. Frei, 79 years old, has been at the hospital. He lives alone in an apartment and manages his medication himself. As Mr. Frei is a regular customer of the pharmacy, the dispensing history is available (Fig. 7.5). First thing is to bid Mr. Frei to sit down for a moment, for it is important to take some time for an accurate medication reconciliation. After the comparison (Fig. 7.5), a best possible new medication list is generated. In practice, further activities follow a medication reconciliation (Table 7.6).

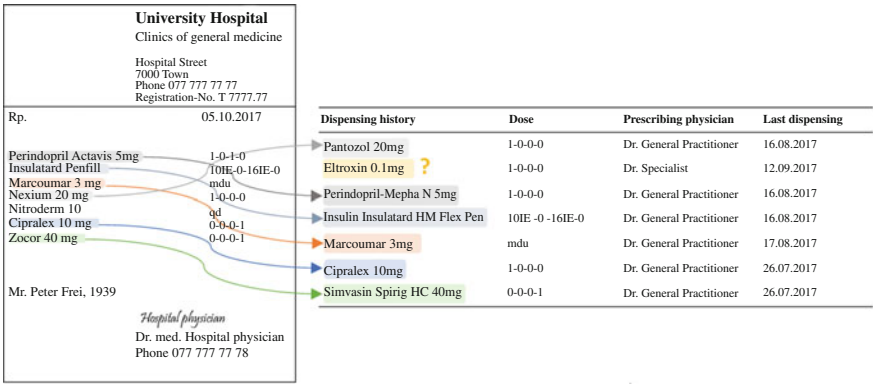

Fig. 7.5 Medication reconciliation with the discharge prescription of Mr. Frei and the dispensing history of the community pharmacy

Table 7.6 Medication reconciliation, best possible new medication list, and actions following medication reconciliation

New prescription	Dispensing history	Action	Best possible new medication list	Actions following medication reconciliation
Perindopril Actavis (perindopril) 5 mg 1-0-1-0	Perindopril Mepha N (perindopril) 5 mg 1-0-0-0	New dose plausible, dispense existing generic brand	**Perindopril Mepha N 5 mg 1-0-1-0**	Check with GP or ask the patient to check with GP at the next visit
Insulatard Penfill (insulin isophane) 10 IE-0-16 IE-0	Insulin Insulatard HM (insulin isophane) Flex Pen 10 IE-0-16 IE-0	Keep existing application mode	**Insulin Insulatard HM Flex Pen 10 IE-0-16 IE-0**	–
Marcoumar (phenprocoumon) 3 mg mdu	Marcoumar (phenprocoumon) 3 mg mdu	–	**Marcoumar 3 mg mdu**	Make GP appointment for INR check
Nexium (esomeprazole) 20 mg 1-0-0-0	Pantozol (pantoprazole) 20 mg 1-0-0-0	Check indication, keep when possible existing brand	**Pantozol 20 mg 1-0-0-0**	–
Nitroderm (nitroglycerin) 10	–	New	**Nitroderm 10**	Counsel patient on the correct application
Cipralex (escitalopram) 10 mg 0-0-0-1	Cipralex (escitalopram) 10 mg 1-0-0-0	Existing dose makes more sense	**Cipralex 10 mg 1-0-0-0**	–
Zocor (simvastatin) 40 mg 0-0-0-1	Simvasin Spirig HC (simvastatin) 40 mg 0-0-0-1	Keep existing generic brand	**Simvasin Spirig HC 40 mg 0-0-0-1**	May be check with GPH if a change to atorvastatin (1-0-0-0) is possible for simplification of the medication regimen
–	Eltroxin (levothyroxine) 0.1 mg 1-0-0-0	It does not make sense to stop, continue	**Eltroxin 0.1 mg 1-0-0-0**	Ask the patient to check with GP at the next visit

bold stands for reconcilled medication

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Chapter 8
Documenting Pharmaceutical Care

Tommy Westerlund

Abstract Documentation of pharmaceutical care has been advocated for close to 30 years for a number of reasons, not least to enable patient follow-up of managed or resolved drug-related problems (DRPs). The first pharmaceutical care documentation was performed in the US, followed by the Netherlands and Sweden, and has also been performed in Canada, in additional countries in Europe and in Australia. The creation of DRP classification systems was necessary for a systematized documentation of pharmaceutical care, which in turn was facilitated by the development of computerized documentation instruments, incorporated into software programs. Statistics on documented DRP data and free text information may serve as educational material for continuing professional development, aimed at further improving the DRP detection skills. The documentation may also be used to get a deeper understanding of both causes and characteristics of DRPs and to demonstrate the potential societal cost savings of pharmaceutical care.

Keywords Pharmaceutical care · Documentation · Classification
Drug-related problems · Patient data

8.1 Why Document?

There are several reasons for documenting pharmaceutical care, as presented in Chap. 2. Documentation is a cornerstone of care provision and therefore also of pharmaceutical care It is necessary to enable patient follow-up of managed or resolved drug-related problems (DRPs). Only those pharmaceutical care activities that are documented can be used for professional and political discussions, promoting the idea of pharmacists becoming recognized (and at a later point in time reimbursed) for their value-adding service. Basic software programs of

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pharmaceutical care therefore comprise standardized forms for the documentation of drug-related problems and the interventions taken to solve them [1]. Documentation of DRPs and pharmaceutical care has been performed in Europe, North America and Australia, and perhaps elsewhere.

8.2 Development of Pharmaceutical Care Documentation

Already in the late 1980s and early 1990s, publications on the need for documenting pharmaceutical care appeared in the US [2, 3], where Strand et al. presented an instrument aimed at standardizing the documentation of a clinical pharmacist's database, patient-care activities and therapeutic plans. A process named "the pharmacist's workup on drug therapy" (PWDT) was created, consisting of the following six steps: (1) establish a comprehensive patient-specific database; (2) identify patient-specific, drug-related problems; (3) describe desired therapeutic outcomes; (4) list all therapeutic alternatives that might produce the desired outcomes; (5) select the drug recommendation(s) that most likely will result in the desired outcomes; and (6) establish a plan for therapeutic drug monitoring that documents that desired effects occur and undesired effects are minimized [2].

In Canada, the need for pharmacists to document their activities in the health care record was brought up [4]. In another publication, researchers concluded that pharmacy lacked a universally accepted, standardized, systematized approach to document the evaluation of a patient's pharmacotherapy [5].

In the Netherlands, around 1996 the Dutch introduced different options to document pharmaceutical care. One computer system introduced an electronic patient dossier (EPD), but it could only be used in free text mode [6]. However, the national pharmacist association introduced, at the same time, a system to document pharmaceutical care by using so-called "Care-records" for all computer systems [7]. These standardized records were formatted as a medicine package record, and thus part of the medicine database that was distributed to all pharmacies. The documentation system allowed a centralized analysis of the care activities of Dutch pharmacies that could be evaluated [8]. A more complete system (called PAS) was proposed by van Mil and Tromp in 1997 [9]. This was the basis for the Pharmaceutical Care Network Europe (PCNE) system, for the first time separating the problem from the cause. A few years later, the Dutch national care record system was updated and revised [10]. The Health Base foundation created their own more detailed system for their specific pharmacy software [11], later followed by the other three Dutch pharmacy software houses, that developed similar tools.

8.3 Use of Computerized Documentation to Generate DRP Statistics

Even if documentation can be made on paper, software programs thus vastly facilitates the compilation of statistics and retrieval of data. In a comparison of documentation of patient-reported adverse drug reactions on both paper-based and electronic medication charts at a tertiary hospital in New Zealand, there were somewhat more discrepancies in ADR information between different information sources in the paper-based (98%) than in the electronic charts (90%) [12].

Pharmaceutical care documentation should include the category of the detected or prevented DRP in the patient, the medication in question, and its dose, the pharmacy intervention category, if possible also the cause, to what extent an intervention was accepted and ideally the outcome. A connection of the documentation instrument to the patient's personal medication record or electronic dossier enables additional documentation, facilitating patient follow-ups. Besides DRP identification and resolution, specific pharmaceutical care activities are sometimes conducted, necessitating other patient-related documentation.

In an evaluation in Sweden, pharmacists first using computerized DRP documentation demonstrated positive attitudes and experiences [13]. In 2001, a DRP documentation tool was incorporated into the dispensing software of all Swedish pharmacies, enabling local statistics at each pharmacy. Three years later, a national DRP database was established, to which all data were delivered, resulting in compilations and analyses on a nationwide level. Figures 8.1 and 8.2 show the

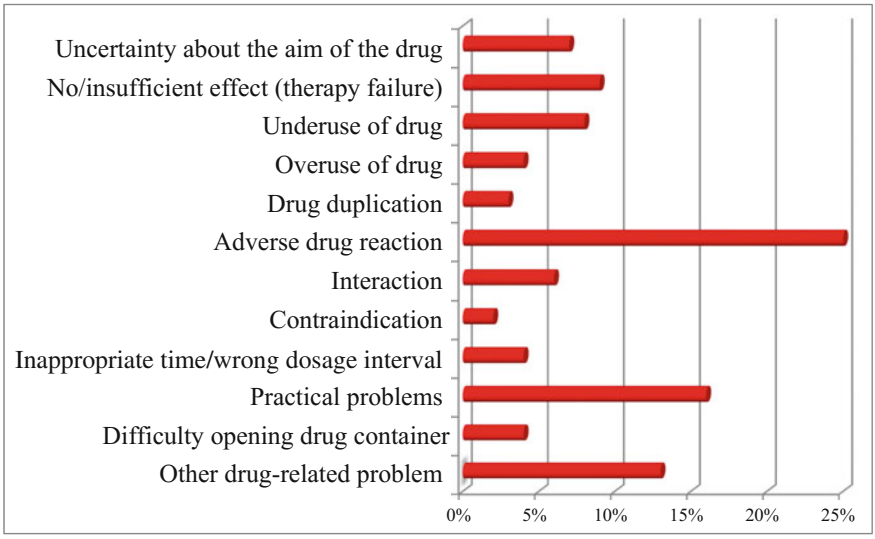

Fig. 8.1 Distribution of drug-related problems in prescription patients 2004–2009 (n = 831,902) [14]

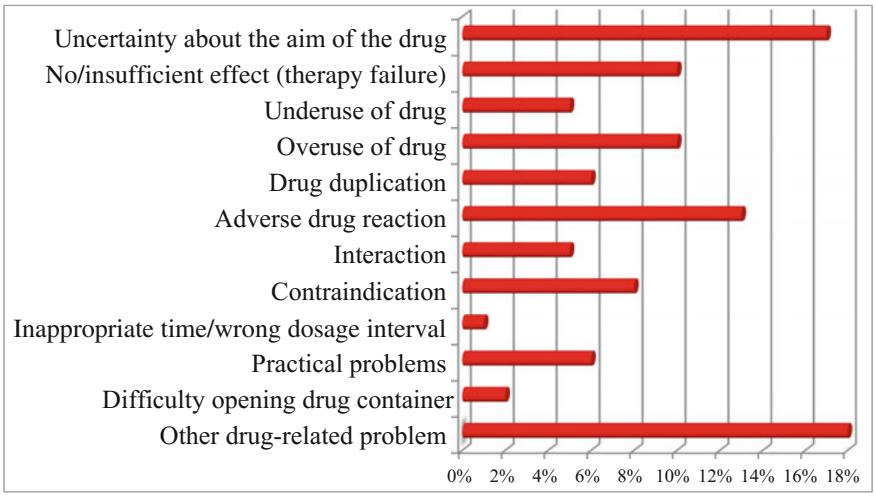

Fig. 8.2 Distribution of drug-related problems in OTC drug consumers 2004–2009 (n = 160,853) [14]

documentation by DRP category of the Swedish national DRP database during 2004–2009 [14].

Thanks to computerized documentation, it was possible to generate a lot of additional statistics on identified DRPs in Swedish pharmacies, distributed to all pharmacies on a monthly basis. Such as types and number of DRP per ATC-group and of pharmacy interventions that could serve as educational material in continuing professional development for pharmacy practitioners, aimed at further improving the DRP detection skills. It was then demonstrated or confirmed that different DRP categories dominate in different therapeutic groups, such as ADRs in patients on antidepressants (e.g., mouth dryness) or on NSAIDs (gastrointestinal disorders), practical administration problems with eye drops and no or an insufficient effect of analgesics. Documentation of pharmaceutical care, especially where free text fields are used to describe the patient cases, may also be used for to gain a deeper understanding of both the causes and the characteristics of DRPs [14] or to demonstrate the potential societal cost savings of pharmacy interventions on DRPs [15]. Hence, pharmaceutical care documentation provides evidence of practice that can be used to further foster pharmaceutical care, as well as to draw politicians' and other policy-makers' attention to the added value of pharmacy practice.

8.4 Additional Rationale for Pharmaceutical Care Documentation

Already in 2003, the American Society of Health System Pharmacists' guidelines for pharmacy documentation in patient medical record (PMR) were discussed in a publication, including types of information pharmacists should document in the PMR, methods for obtaining authorization for pharmacist documentation and role of training and continuous quality improvement in documentation [16]. Swiss pharmacists recognized the importance of documentation of pharmaceutical interventions and believed it may allow traceability, facilitate communication with other health care professionals and increase quality of care [17]. Surveyed general practitioners in Sweden demonstrated very positive attitudes towards the role of pharmacists in improving patients' drug use and managing DRPs. They also found presentations and analyses of their local pharmacies' DRP documentation valuable [18].

As previously mentioned, the use of patient medication records and performance of different types of medication reviews in various settings are very helpful in capturing DRPs. See Chap. 7.

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Chapter 9
Quality Control in Pharmaceutical Care: Guidelines and Protocols

Martina Teichert

Abstract Pharmacy practice guidelines are essential to describe pharmacy care structures and processes at the best evidence available. Guideline development is a laborious procedure that should be well organized and structured by a professional instance with the means to manage revisions and to support implementation in daily practice. During guideline development, practicing pharmacists should be involved as well as patients, other healthcare professions involved in the topic, the healthcare inspectorate, and health insurance companies as external stakeholders. Validated tools are available to grade existing evidence during the formulation of guideline recommendations ("GRADE"). Checklists with acknowledged criteria (AGREE II) can be used to optimize the guideline development process and to appraise guideline quality. Beside guideline development continuous effort must be made for broad guideline implementation in daily practice. This can be done in pilot settings with critical feedback for an update of the guideline recommendations. E health applications may be available to be used in the near future. Additionally, indicators can be used to collect information on the implementation of meaningful aspects and to monitor the progress during time (see Chap. 10).

Keywords Pharmaceutical care · Quality standards · Guidelines
Evidence based health care · Care protocols

9.1 Introduction

Evidence from pharmacy practice research has shown the contribution of pharmacists to patients' health outcomes and medication safety. Additionally, there is a shift from remunerating pharmacists for their logistic services to compensations for their pharmaceutical care. Therefore, pharmacists' services must be clearly defined

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and warrant uniformity at the desired level of quality. Consequently, beside pharmacopoeias for quality definitions of substances, guidelines for pharmaceutical care are needed.

9.2 Terminology

In clinical practice, the terms "standards" and "guidelines" are often used concurrently. In some countries, they are distinguished according to the degree of obligation in following them: in the United Kingdom for instance "standards" are compulsory and must be followed, whereas "guidelines" usually describe best practices without being mandatory.

Here we use the term "guideline" for documents with recommendations based on scientific evidence. After their accreditation they need to be followed and thus become "standards of care". Guidelines support providers, patients, and other stakeholders in making decisions on appropriate health interventions. As such, guidelines are developed by professional bodies within a (national) healthcare setting. This is done by a structured and coordinated program to assure and continuously improve the quality of care.

Guidelines should be distinguished from protocols. Protocols describe specific behavior or technical performance in subsequent steps to implement a distinct guideline recommendation. They are mostly developed locally to support the staff members according to their needs.

9.3 Pharmaceutical Care Guidelines: Young Discipline Compared to Others

Pharmaceutical care guidelines describe the processes and structures to be performed by pharmacists for a specified topic. See here some examples for pharmaceutical care guidelines:

In the Netherlands, pharmaceutical care guidelines cover three domains:

1. Categorical domain addressing specific diseases such as diabetes, asthma, or COPD
2. Generic domain for specific forms of pharmaceutical care such as dispensing, central filling, consultation, or use of computerized medication surveillance signals
3. Organizational domain describing care in cooperation with multidisciplinary teams of healthcare providers for topics such as palliative care, polypharmacy, or sharing medication information within the chain of healthcare providers.

In Germany, the first guidelines with advices for pharmaceutical care in characteristic situations were acknowledged in 2000. These guidelines address specific forms of pharmaceutical care such as medication information, blood pressure measurement, dispensing, compounding, and self-medication [1].

In Australia, Professional Practice Standards formulate the values of the pharmacy profession and name the expected standards of professional behaviour of pharmacists. In 2017, 16 standards were restructured into four key streams: foundations of practice, providing therapeutic goods, providing health information, and delivering professional services. These standards clearly articulate the professional roles and activities that pharmacists have to undertake [2].

In general, during the last decade guideline development for all healthcare professions increased. At present, the library of the Guidelines International Network, GIN contains 6400 guidelines [3]. A membership to this network offers a number of benefits such as sharing of systematic reviews and evidence tables, access to the GIN and Cochrane library, and cooperation within the network for newsletters, training and mentoring, and conferences [3].

Compared to guidelines for medical professions, the development of pharmaceutical care guidelines only started recently in most countries.

For example, in the Netherlands guidelines for General Practitioners (GPs) have been developed for several decades with at present about 100 authorized guidelines. These mainly address the diagnosis, treatment, and prevention of specific diseases. In contrast, the Royal Dutch Pharmacists Association started to develop guidelines on pharmaceutical care only as of 2008. At present, five guidelines are authorized, one categorical guideline "COPD" and four generic guidelines "Dispensing," "Automated dose dispensing," "Compounding," and "Medication review." Additionally, seven guidelines are in development, the categorical guidelines "Diabetes," "Cardiovascular risk management" "Asthma," and the generic guidelines "Medication surveillance," "Pharmaceutical consultation," "Pharmaceutical care at hospital discharge," and "Patient records."

In Germany, the working group of the scientific medical societies has 186 guidelines accredited for the different medical specialists [4]. In comparison, there are 23 guidelines for pharmaceutical care available [1]

9.4 Guideline Development

Guidelines are important tools in defining the quality of care and the implementation of new practices and improvements in health care. Consequently, guidelines should be developed when

(a) there is uncertainty in actual clinical practice, which can be reduced by scientific evidence and
(b) the actual caregiving should be improved [5].

Guideline development starts with the definition of the problem to be addressed. To collect existing evidence, key questions are formulated and translated into search criteria for a systematic literature review of existing evidence. This procedure is based on the conviction that guideline recommendations should be based on the best available scientific evidence to assess the benefits and harms of alternative care options [5]. Additionally, the strength of the recommendations is determined by the quality of the supporting evidence.

> During guideline development in the Netherlands there was an extensive discussion as to what guidelines should describe: the standard care provided by (nearly) every pharmacist—or the best care that should be provided according to existing evidence, independent of the degree of implementation in daily practice. In the end, the choice was made for the latter, the best existing evidence. Thus, the deliberate risk was taken that the guideline recommendations may only partly be implemented by community pharmacists at the authorization date. On the other hand, after accreditation guidelines should be followed as the acknowledged "standards" of care. Thus, they become tools for the implementation of the latest state of knowledge.

When authorized, guidelines achieve a "semi legal" status: their implementation is not mandatory by law, but by the lack of other care definitions, they are used by external stakeholders to test and judge the pharmaceutical care provided. If the care does not meet the guideline recommendations, this may lead to disapproval by the healthcare inspectorate or remuneration loss from health insurance companies. By this, the implementation of professional guidelines is not voluntary, and consequently pharmacists are forced to quickly implement the recommendations in their daily practice. To enable this, during guideline development practicing pharmacists as well as external stakeholders and patients should be involved early in the guideline development and the guideline draft versions are broadly discussed before authorization. During this process pharmacists can indicate bottlenecks in daily practice and the external stakeholders are aware of these for their subsequent use of the guidelines.

Additionally, pharmacists' associations should take the responsibility to support guideline implementation by their members. This covers for instance training courses for implementation. Technical and legal developments for the whole profession can also be stimulated by professional bodies.

> At present, apps and other e-health applications are used. The General Pharmaceutical Council in Great Britain developed an app to provide easy access for all pharmacists to the guidelines. This app is considered as a tool for the dissemination of the professional standards. This is a first step in their further implementation [6].
>
> In the Netherlands, summaries of the medical guidelines are available for smartphones to be used for anamneses [7].

An example for technical and legal support is the development of uniform clinical rules by the Royal Dutch Pharmacists Association to support the signalling, management, and registration of medication surveillance signals in pharmacy computer systems.

Another example is the facilitation of exchanging of meaningful laboratory measurements for medication surveillance. Additionally, to technical supply the professional organization supported this process in contacting the GPs' professional organization for their willingness and acceptance and with legal aspects such as how to provide patients' consent.

9.4.1 Grade Existing Evidence

As clinicians are expected to dutifully apply the guideline recommendations, these need to be based on the best evidence available to warrant the highest benefit at the lowest risk. However, scientific evidence—if available—often is inconsistent. Thus, a rigorous system of rating the quality of evidence must be applied to "grade" the existing results according to the validity of the underlying studies.

As pharmaceutical care guidelines are quite recent, examples of clinical guidelines are presented here to show the importance of grading evidence in guideline recommendations due to advancing knowledge.

In the 1990s, guidelines recommended hormone replacement therapy (HST) in postmenopausal women to reduce women's cardiovascular risk. These recommendations were derived from observational studies. However, these studies had inconsistent results and the evidence of cardiovascular risk reduction was of poor quality. A decade later, randomized controlled trials showed that HST did not reduce cardiovascular risk but might even increase it [8]. It is assumed that a systematic appraisal of the evidence available would have led to less stringent guideline recommendations. A rating procedure furthermore would have revealed a knowledge gap and might have earlier stimulated trials on cardiovascular outcomes in HST-treated women.

Beside this, the failure to recognize high quality evidence can cause similar problems with "false negative" findings instead of "false positives". For instance, expert recommendations lagged a decade behind the evidence from well-conducted randomized controlled trials that thrombolytic therapy achieved a reduction in mortality in myocardial infarction [8].

Therefore, a directed search for evidence during guideline development can help to earlier formulate recommendations based on the latest evidence and to stimulate the acceptance of new insights in clinical practice.

A Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) system has been developed for guideline development and is increasingly adopted worldwide to consistently rate the quality of evidence and the strength of recommendations [8]. To make decisions, patients, and clinicians must weigh up the benefits and risks of alternative strategies. The acceptance of the evidence also depends on their confidence of the results provided.

To achieve transparency and simplicity, the GRADE system classifies the quality of evidence in four levels: high, moderate, low, and very low [8]. Evidence from randomized controlled trials is rated as "high quality evidence." Subsequently according to the confidence in this evidence, the ordeal may be decreased to a lower level. Reasons for devaluation are for instance study limitations, inconsistency of results, indirectness of evidence, imprecision, and reporting bias [8].

Case reports and expert opinion achieve a "very low" level of evidence as they lack a control group and are highly prone to bias. However, when developing pharmaceutical care guidelines, this is often the only evidence available. The questions arising from guideline development reveal the lack of evidence and can stimulate new research to provide evidence for certain care processes.

Corresponding with the quality of evidence, the GRADE system offers two grades for the derived recommendations, "strong" and "weak." Strong recommendations are based on many high quality randomized trials, and further research is very unlikely to change this confidence in the estimation of effect.

Results from case series only without a control group provide weak recommendations. Here further research is very likely to change the outcomes. Uncertainties then remain on the balance between desirable and undesirable effects; there is still variability in values and preferences and uncertainty on the efficiency of resources implied [8].

In the Netherlands, automated dose dispensing came up as a new way to support pharmaceutical care. By the assessment of the GP, those community dwelling patients are eligible for this service who use many different medications at several instances during the day and have problems in organizing their daily living. Often these services are provided by providers outside the pharmacy and thus clarification of tasks, processes, and responsibilities was needed. The remuneration of this service and a lot of questions for quality assurance in this process forced the development of a guideline "automated dose dispensing systems." From cost perspective, medication should be supplied for longer periods and at less dispensing fees. The service started with dispensing for one week, and this was extended to two weeks. Relevant questions were for instance on how long medication should be supplied (for one week or longer) and how to deal with medication changes. With higher stocks of dispensed personalized medication packages, medication changes are more difficult to organize. For safety reasons, some medication changes might not be postponed. Possible solutions were to supply a revised personalized medication package or to replace the medication in question in the existing packages. The latter showed to be very sensitive for medication errors when cutting into the plastic bags and manually

exchanging tablets. Consequently, questions came up on who should decide on whether changing supplied stock and on how to solve this regarding patient safety on the one hand and efficiency reasons on the other. As the service was new, no studies were available to rely on. Thus, the recommendations in the guidelines were formulated by expert opinion from pharmacists, prescribers, and patients. According to the "GRADE" system, this evidence is of "very low" quality and the recommendations based on this are "weak." Consequently, the pharmacists' association supported pharmacy practice research to provide evidence for these recommendations. Based on these results in future, the recommendations for this new pharmaceutical care service can achieve a higher validity level with stronger evidence.

This example shows that guidelines are never finished but need continuous maintenance. This is one of the reasons why guideline development should be laid by instances with the means to manage, develop, and maintain the guidelines for their profession.

9.4.2 From a First Draft to a Published Version

Guidelines are developed in working groups. Preferably this includes pharmacists with special expertise on the guideline topic, preferably working in daily practice and engaged in the field to which the guideline applies. Additionally, other healthcare professions should be engaged who are also involved in the topic. And finally, as the care services should meet patients' needs and expectations, patients should be involved as early as possible. Guideline development in such extended settings contributes to the future acceptance and implementation of the guidelines [5]

The guideline "COPD" for community pharmacists in the Netherlands was developed by the working group consisting of three pharmacists working in community pharmacies and two pharmacists who had experience with guideline development. The Royal Dutch Pharmacists Association (KNMP) had previously developed a procedure for guideline development and implemented a scientific control board to check on compliance to this procedure. During the guideline development, the draft was presented to a special interest group (SIG) for long-term conditions, involving pharmacists working in community or hospital pharmacies or industry. The final draft version was commented by a lawyer, general practitioners, medical specialists for lung diseases, nurses, physiotherapists, and the patient organization for lung diseases. The draft version was then published on the website of the KNMP and open for comments from the KNMP members for several months. The final version was developed in response to these comments and authorized by the scientific control board for five years. It was announced that the guideline would be revised earlier if actual developments in pharmaceutical COPD care would require this. After authorization, pharmacists were invited to contribute new evidence for weak recommendations and pharmacy practice research proposals could be submitted in annual research calls. The insights from new evidence will then be incorporated into the guidelines.

Guidelines should have a logic and uniform structure with a clear and readable layout using understandable language. Often cards are offered that summarize the care provided on a certain topic. The implementation is more successful when the guideline formats are adapted to the readers. Thus, beside professional versions also versions for patients in an accustomed language and addressing the care provided from their perspective are needed to manage patient expectations on pharmaceutical care. Today, guidelines are online accessible by websites and increasingly become available by smartphones.

Pharmaceutical care guidelines in the Netherlands are structured in seven chapters:

1. They start with an introduction on the scope of the guideline describing the type of patients (e.g., COPD patients) and type of pharmacists (e.g., community pharmacists) involved in the care to be provided. Relevant guidelines from other healthcare professionals connected with pharmaceutical care are mentioned. Facts and figures are provided (e.g., disease incidence and prevalence in categorical guidelines or the numbers of drugs dispensed annually in the generic "Dispensing" guideline). The guideline topic is defined and specified (e.g., the definition of "dispensing" in the corresponding guideline with the scope of drugs involved as prescription only, over the counter drugs, etc.).
2. The second chapter describes the pharmaceutical care processes with specific recommendations on critical process steps.

   For the guideline "COPD" this starts with an agreement between patient and pharmacist, including a patient record. Then specific care is described including the drugs involved for the different COPD disease stages and during exacerbations. Relevant issues in medication surveillance for COPD patients are highlighted (otherwise the guideline refers to the generic guideline "medication surveillance") and specific topics for the dispensing of inhalation medication are mentioned (otherwise the guideline refers to the generic guideline "dispensing").

3. In this chapter, the internal and external working structures are described. In the guideline "Dispensing," the internal structures name that pharmaceutical technicians may dispense under a pharmacist's responsibility but that a pharmacist preferably is present or at least can be consulted during dispensing.
4. The fourth chapter describes the process during the development of these guidelines with the persons and organizations involved.
5. In a separate chapter, all abbreviations used are explained.
6. The sixth chapter elucidates the recommendations in Chapter 2 by summarizing the literature cited. Here, different results from relevant studies may be shown and discussed.
7. The last chapter shows the literature cited in the guideline.

These guidelines are publicly accessible by the KNMP website. At present, there are no smartphone versions or patient versions available, but this is a future goal.

9.4.3 Agree on Effective Guidelines

As worldwide the number of medical guidelines increased rapidly, physicians were confronted with multiple guidelines on the same topics. Consequently, a tool was needed to assess the quality of guidelines and to differ between high and low quality. In 2001, the AGREE instrument (Appraisal Instrument for Guidelines, Research and Evaluation) was published and translated into more than 20 languages [9].

At present, pharmacists do not have to struggle with too many guidelines for pharmaceutical care, and as such, the AGREE tool might be not relevant for

Table 9.1 Criteria of AGREE II [10]

Scope and purpose
1. The overall objective(s) of the guideline is (are) specifically described
2. The health question(s) covered by the guideline is (are) specifically described
3. The population (patients, public, etc.) to whom the guideline is meant to apply is specifically described
Stakeholder involvement
4. The guideline development group includes individuals from all relevant professional groups
5. The views and preferences of the target population (patients, public, etc.) have been sought
6. The target users of the guideline are clearly defined
Rigor of development
7. Systematic methods were used to search for evidence
8. The criteria for selecting the evidence are clearly described
9. The strengths and limitations of the body of evidence are clearly described
10. The methods for formulating the recommendations are clearly described
11. The health benefits, side effects, and risks have been considered in formulating the recommendations
12. There is an explicit link between the recommendations and the supporting evidence
13. The guideline has been externally reviewed by experts prior to its publication
14. A procedure for updating the guideline is provided
Clarity and presentation
15. The recommendations are specific and unambiguous
16. The different options for management of the condition or health issue are clearly presented
17. Key recommendations are easily identifiable
Applicability
18. The guideline describes facilitators and barriers to its applications
19. The guideline provides advice and/or tools on how the recommendations can be put into practice
20. The potential resource implications of applying the recommendations have been considered
21. The guideline presents monitoring and/or auditing criteria
Editorial independence
22. The views of the funding body have not influenced the content of the guideline
23. Competing interests of guideline development group members have been recorded and addressed

pharmacists yet. However, beside guideline appraisal the tool has already been used by guideline developers to improve the quality of their guidelines, and the AGREE tool was shown to be effective in this [5]. Thus, the second version of the AGREE criteria is recommended as a checklist during guideline development (Table 9.1).

9.5 Stakeholders

Target users of pharmaceutical care guidelines are pharmacists. They can use the guidelines to organize their care services and to ensure high quality and highlight areas for improvements. In providing recommendations for clinical practice, they are also used as a professional aid in clinical decision making and for education.

To external stakeholders, guidelines show the services to be expected. In the first place, this is relevant for the patients. As pharmaceutical care services are relatively young compared to the traditional tasks of a pharmacist, they still need to become better known by patients, other healthcare professionals, health insurance companies, and the public. Guidelines are an excellent means to advertise pharmaceutical care to all these stakeholders. Patient versions of the guidelines should be developed that describe the specific services offered. Then patients can know what to expect from their pharmacists. They may use the guidelines to ask for specific pharmaceutical care, to compare pharmacies according to the implementation of the guidelines and to actively choose pharmacy services. These activities belong to patient empowerment and self-management, both developments needed in modern healthcare policy.

Secondly, the government and healthcare inspectorate and healthcare insurers are relevant external stakeholders: the government uses guidelines for policy and is mainly interested to prevent unnecessary care, costs, and undesired practice variation. (Practice variation is shown by indicators, see Chap. 10.) The healthcare inspectorate uses guidelines to control the quality of care and to detect safety issues. Healthcare insurers use guidelines as a description of the care to be expected from healthcare professionals when contracting certain care services.

9.6 Guideline Implementation

It has been addressed before that guidelines are a tool for the implementation of innovation by summarizing the existing evidence in recommendations for healthcare providers [5]. To this, the guideline recommendations have to be accepted and supported by the practicing pharmacists. This can be stimulated by involving pharmacists within the guideline development and appraisal (see above). Certain characteristics support guideline implementation (Table 9.2).

Table 9.2 Characteristics of effective guidelines [5]

• Relevance: the recommendations provide answers to relevant questions in daily practice
• Credibility: guidelines were developed by the professional body with transparent procedures and at involvement of acknowledged experts and relevant stakeholders
• Evidence: effort was taken to collect information from latest research and clinical experts
• Applicability: practicing pharmacists were involved and the recommendations were tested for feasibility in pilot settings
• Accessibility: a neat, clear, and attractive format was applied with possibilities for electronic and web-based use
• Maintenance: a professional organization manages guideline revisions, supports guideline publication for the own profession and external stakeholders and stimulates pharmacy practice research for evidence needed

For the development of the concept guideline "diabetes" in community pharmacies in the Netherlands, practice tests were organized. To this, groups of community pharmacists were formed with interest and experience in diabetes care. These pharmacists were invited to score the degree of implementation for the specific recommendations in their daily practice. In groups and assisted by a trainer, they developed an implementation plan and defined individual implementation goals to further or better implement the recommendations in their pharmacy. During the implementation process, critical success factors, barriers, and means to overcome those were noted and discussed within the group. The information from this pilot group was used by the pharmacists' association to revise guideline recommendations or to develop tool boxes for implementation.

This example shows that the measurement of meaningful aspects from the recommendations ("indicators") provides information on how to measure the successful implementation of the guideline recommendations (see Chap. 10). Thus, the development of indicators should be embedded in the guideline development.

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Chapter 10
Structure, Process, and Outcome, and Their Indicators

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Abstract Quality indicators are used for internally monitoring, comparison of national scores ("benchmarking"), and continuous quality improvement. Additionally, indicators are used externally for public reporting, to facilitate deliberate patient choices for healthcare providers, for risk detection by the inspectorate and to enable pay-for-performance policies by health insurance companies. At present, quality indicators in pharmaceutical care mainly address structures, processes, and outcomes of pharmacy processes. To this, most indicator scores are reported by the pharmacists on the presence of structures and in categories for following process recommendations. Routinely collected dispensing data are useful to assess relevant outcomes of dispensing processes on a continuous scale. Feedback reports on individual indicator scores within benchmark information were shown to improve the indicator scores of healthcare professionals over time. When indicator scores are used by external stakeholders to distinguish pharmacies according to their performance, indicators must meet the criteria for acceptance, validity, absence of bias, and discriminative ability. In future, indicators on patient outcomes should be assessed. These can include clinical outcomes, laboratory measurements, patient-reported outcomes, or patient experiences. To this and to further improve drug safety, pharmacists require additional information on diagnoses and laboratory measurements of their patients. Finally, the use of indicators to stimulate quality improvement or to warrant the quality assurance should be accustomed to the scores achieved by the majority of healthcare professionals.

Keywords Pharmaceutical care · SPO paradigm · Healthcare structure
Process indicators · Outcome indicators

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10.1 The Concept of Three Dimensions

Donabedian suggested the dimensions "structure", "processes", and "outcomes" for the evaluation of care [1]. In his concept, structures refer to the setting in which care is delivered as the facilities, equipment, qualification of the care providers, and cooperation needed. Processes are essential professional actions needed to achieve a certain purpose. Guidelines mainly focus on the structures as preconditions needed to perform the processes as described by the recommendations (see Chap. 9).

Outcomes as defined by Donabedian address objective endpoints of care, mostly referring to clinical outcomes such as death or survival, myocardial infarction. Additionally, laboratory measurements are used as a proxy for these "hard" outcomes such as values of blood pressure or renal function [1, 2]. Recently, outcomes in terms of Economic, Clinical, and Humanistic Outcomes, ECHO model, are evolving in clinical research and quality management [2] Outcomes as defined by ECHO also include patient-reported outcomes, PROMs [2], and also patient experiences of the care delivered, PREMs, are used. Additionally, economic outcomes of care are included as part of the continuous process to identify and deliver the most efficient combination of healthcare resources for individual patients [3].

To assess the quality of care consequently meaningful aspects on all three dimensions have to be defined and measured as quality indicators.

10.2 Quality Indicators

Structure indicators provide information on organizational preconditions that are needed to perform pharmaceutical care processes and to achieve the desired outcomes.

> The first set of quality indicators in the Netherlands comprised 66 indicators in 10 domains. Within this set, 29 indicators measured the presence of structures. Examples of structure indicators were "The presence of a valid quality management certificate" or "The availability of protocols for informing on contra indications" or "The availability of automated dose dispensing for eligible patients." [4]

Process indicators give information on activities within pharmaceutical care processes to warrant the outcome at the desired quality level within the existing structures. They can be measured for their presence (dichotomous outcomes for a process being performed by "yes" or "no"). Ideally, these indicators should be measured as percentages of correct actions within all possible actions by (automated) registrations during the working process. At present, however, uniform and automated registration systems for pharmaceutical care actions are scarce. Thus, process indicators are often assessed categorically by personal estimation on their presence by the pharmacists retrospectively.

Within the set of quality indicators in the Netherlands, 24 indicators focussed on processes. Examples of this type of indicator were "Dosage in compounded medication for children up to 6 years is checked by the pharmacist in at least 80% of all compounding for children younger than 6 years" and "Action was taken by the pharmacist in at least 80% of the cases to add antithrombotic medication to nitrate users for whom this co-medication was lacking." [4]

Aspects reported by pharmacists as "outcomes" of their care, in fact, do not reflect clinical patient outcomes but "outcomes of dispensing processes." These aspects are mostly translations of guideline recommendations into dispensing patterns and, in the absence of better, they are regarded as "outcome" measures. As data on medication dispensing are routinely collected in pharmacies in a uniform way, this information can be easily collected. Besides the absence of drug interaction or the presence of protective co-mediation, these data can also be used to assess desired or undesired drug use in the presence of certain diseases. Although pharmacy data usually lack information on diagnoses, the use of (combinations of) drugs is often quite specific for the presence of certain diseases. For instance, dispensing of antidiabetic drugs is predictive for the presence of diabetes disease; concomitant use of renin–angiotensin–aldosterone inhibitors with diuretics indicates heart failure and dispensing of antithrombotics can be linked to the presence of ischaemic cardiovascular diseases.

Examples of outcomes of dispensing are the "Percentage of nonsteroidal anti-inflammatory drug (NSAID) users >70 years with concomitant gastroprotection" or the "Percentage of cyclooxygenase-2 (COX-2) inhibitor (COXib) users without co-medication related to ischaemic cardiovascular diseases within all COXib users."

Real outcomes as clinical patient outcomes are, for instance, death, heart attacks, or hospital admissions. Pharmaceutical care mainly addresses risks associated with medication, better symptom control, a higher level of prophylaxis, and prevention of potential adverse effects. Although these are important and clinically relevant outcomes for the individual patient, they are less "hard", less objective, and less easy to assess [5] "Patient-reported outcome measures, PROMS" as new outcome measures address patients' health status or health-related quality of life [6]. These are mainly used to evaluate medical care as, for example, pain reduction after treatment [7]. PROMS for relevant patient outcomes of pharmaceutical care are not yet developed and it is difficult to detect changes in patient's judgements by pharmacists" interventions. This is due to the fact that benefits can be influenced by many factors outside the pharmacist's control [5]. However, the benefits and the added value of pharmaceutical care still need to be demonstrated to external stakeholders [5]. Beside this, PROMs can be used to accustom the care provided to individual patient's needs.

Recently, a questionnaire was developed to evaluate potentially drug-related patient-reported common symptoms during clinical medication reviews [8]. The intention of this "PROMISE" (Patient-Reported Outcomes Measurement Information System)

questionnaire was to show that medication reviews could reduce these symptoms, compared to normal care. No significant reduction in symptoms was shown between intervention and control group, possibly due to a lack of power in the number of included patients. However, the questionnaire was judged as useful by pharmacists as well as patients to elucidate patient-reported symptoms and to use these in prioritizing medication changes.

Patient-reported scores on the Control of Allergic Rhinitis and Asthma Test, CARAT, questionnaire can be used to assess a patient's need for additional pharmaceutical care [9]. In the SMARAGD (self-management research of asthma and good drug use) study, however, this PROM did not show an added value of individualized pharmaceutical care on asthma disease control.

10.3 Extended Model for the Quality of Pharmaceutical Care

A model is useful to map fields for meaningful aspects to assess the quality of pharmaceutical care. In the 1990s, the European Foundation of Quality Management (EFQM) developed a model for quality management, to be applied to any organization regardless of size, sector or maturity [10]. This model offers nine fields to describe leadership, people, strategy and resources, processes, products and services, and outcomes for people, customer, society, and business. For an application to pharmaceutical care this model was extended from the originally nine EFQM fields to ten fields. This extended model also distinguishes between fields for structures, processes ("enablers" of the original EFQM model), and outcomes ("results" in the original EFQM model). Finally, the Deming Cycle "plan, do, check, act" can be applied (Fig. 10.1). Thus, the model starts with the structure elements "leadership", "staff", "strategy", and "resources", all structural preconditions to plan processes and outcomes. "Leadership" comprises the vision of the pharmacist in charge to determine which form of pharmaceutical care he wants to and perform with his staff and resources. This vision should be accustomed to the location of the pharmacy and actual developments.

"Leadership" is the ability of an individual to guide other individuals. It has become a competence in training program for pharmacists. A community pharmacist should fulfill his legal responsibility for drug supply of his patients at actual safety standards at an increasing efficiency. In this, he depends on cooperation with the General Practitioners, GPs, patients, and their caregivers. This requires a clear view on the corporate identity and expertise level of his team, on the existing resources, and the strategy to maintain and improve them.

The central part of the model are the processes, located in the "do" part of the Deming Cycle. In community pharmacies, these processes can be divided into "pharmaceutical care processes" and "logistical processes". This division makes sense

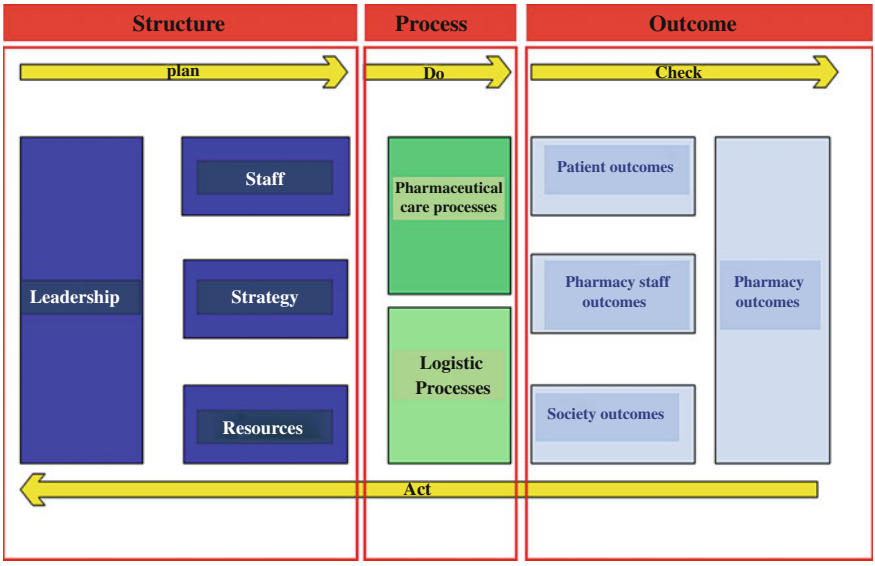

Fig. 10.1 Extended EFQM model [24] for quality measurement of pharmaceutical care

as a different expertise is required to conduct these processes. In principle, pharmaceutical care should not depend on the logistic services, although they are often integrated (see Par. 6.1). New services as medication review are explicitly disconnected from dispensing to enable a comprehensive view of a patient's needs and overall medication use. So, pharmaceutical care can also be provided separately from the logistics, for instance, clinical pharmacists are already providing pharmaceutical care in GP practices or at nursing homes without being responsible for the drug supply [11].

The four fields within the "outcomes" part address patient, pharmacy staff, and society outcomes as parts of the overall outcomes of the pharmacy business. Within the Deming Cycle, these outcomes are used to "check" on the effectiveness of the processes and structures. As an "ist" estimation, they are compared to the "soll" situation from the strategic goals. With the step "act", these insights are carried forward to a new go in the Deming Cycle, starting with "Leadership" and a possibly revised vision.

A comprehensive questionnaire of quality indicators in the Netherlands addressed 10 categories [4]. Information on each aspect was provided by the responsible pharmacist. These categories covered the structure and process fields of the quality model for pharmaceutical care: quality management (leadership), training of pharmaceutical staff (staff), continuity of care (resources), communication with the patient, clinical risk management, compounding, dispensing and over-the-counter (OTC) counseling (all pharmaceutical care), and the agreement with the recommendations of pharmacotherapy guidelines (outcomes of pharmaceutical care). Obviously, the "outcome" fields were not covered by this set. The indicators of the category "agreement with the recommendations of pharmacotherapy guidelines" were marked as "outcome" indicators, however, strictly they addressed "outcomes of dispensing" instead of outcomes in patients.

10.4 Measurement and Validation of Quality Indicators

To measure indicators, information must be collected in a valid and reliable way.

Structure indicators are mainly measured with questions for their presence or absence with dichotomous outcomes "yes" or "no." These questions are simple to answer without additional data registration, and their presence is (relatively) easy to check by external stakeholders.

Process and outcome indicators are preferably measured by routinely collected data. As these are mostly collected for a different aim, data collection is supposed to be unbiased and does not require additional efforts for data collection. However, often in community pharmacies only data on outcomes of dispensing are routinely collected whereas care processes are poorly registered.

This differs from doctors, who are used to routinely collect information on their treatment activities in their automated systems such as the performance of certain diagnostics or treatment initiatives and outcomes from clinical measurements.

> For a pay-for-performance program in family practices in the United Kingdom, 146 quality indicators were developed covering clinical care for 10 chronic diseases, organization of care, and patient experience [12]. An example of a process indicator was "The percentage of patients with severe long-term mental health problems reviewed in the preceding months, including a check on the accuracy of prescribed medication, a review of physical health, and a review of coordination arrangements with secondary care." An example of an outcome indicator was "The percentage of patients with diabetes whose last blood pressure measurement was 145/85 mm Hg or less [4]."
>
> Processes performed by pharmacists without routinely collected data available can be questioned dichotomous by the answers "yes" and "no" or more differentiated in the categories "mostly", "often", "seldom", and "never" [4]. In answering, however, the choice for a category depends on the individual assessment of the healthcare provider and this is likely to differ between the professionals. This makes these answers prone to bias and reduces their use for valid comparisons between healthcare providers.

Routinely collected data in pharmacies are mainly dispensing data. These are collected for remuneration purposes and as such supposed to be reliable. They can, for example, also be used to measure the degree of concomitant dispensing of protective drugs by overlapping periods of drug use with certain risk drugs, according to guideline recommendations.

> An example for this is the degree of laxative co-medication in opioid users or the degree of gastroprotection in older NSAID users [4].
>
> With the help of dispensing data some indications can be found, such as diabetes from the dispensing of blood-sugar-lowering agents. For this patient group, the degree of statin use can be assessed. However, statin use is only necessary in those patients with increased cholesterol levels, and thus only with concomitant information on the laboratory measurements, this indicator is fully valid.

Comparable to the quality assessment of guidelines, good indicators should be judged for their validity, especially when they are used by external stakeholders to compare the quality of care between pharmacies.

> The validation process of a quality indicator set, which had been repeatedly filled by all community pharmacists in the Netherlands, showed that only 13 (25%) of the indicators fully met all quality criteria. The four validity criteria applied were experienced as valuable in this process. Some indicators could be improved for the shortcomings revealed, and other indicators were scratched and replaced by more valid indicators in future sets [13]. The validation was used to appraise the indicators for their appropriateness to serve the expectations of the external stakeholders. Only those indicators were made accessible for health insurance companies for quality-based remuneration that at least partly met all validity criteria.

For comparisons between pharmacies by external stakeholders, quality indicators need to meet certain standards to allow valid comparisons: [13, 14]

- Acceptability: the findings are acceptable to as well those being assessed as those undertaking the assessment.
- Feasibility: routinely available, easily accessible data.
- Content validity, defined as the degree to which the indicator directly reflects the performance of the community pharmacist or the pharmacy team. Ideally, evidence for such a relationship was provided from randomized controlled trials. In the absence of such evidence, expert opinions are used on the existence of such a relationship.
- This characteristic is important for the sensitivity of the indicator to changes in the performance, e.g., that a better performance will lead to improved scores of the indicator.
- Reliability by comparable and consistent measurement:
  - Absence of selection bias as the degree to which differences between populations of pharmacies about age, drug use, morbidity, or social economic status could influence indicator scores and diminish results from the care provided.
  - Absence of measurement bias assessed as differences in data collection between pharmacies that could influence indicator scores.
  - Statistical reliability for numerical indicators depended on a statistical test for enough power to distinguish between indicator scores in a statistically significant way.
- Discrimination between practices enabling benchmarking, select choices, risk detection, and remuneration for better performance

10.5 Application of Indicator Scores in Daily Practice

Indicator scores can help to highlight potential problems in clinical performance, stimulate quality improvement activities, initiate reflections on clinical practice, and identify areas for future research. Besides these applications, indicators are increasingly used to compare performance between healthcare providers, due to growing cost constraints, consumer demands, and a greater focus on accountability. As such they have a broad range for potential use and a wide range of interested stakeholders such as the healthcare providers themselves, managers, purchasers, policy makers, patients, and researchers [4].

In accordance with guidelines the development, measurement, and validation of indicators, their maintenance and reporting require the support of the professional pharmacists' organization. Ideally, indicators are developed as part of the guideline development. Furthermore, they can be used to monitor and improve guideline implementation. Benchmark reports for individual pharmacists on specific indicator scores achieved compared to national scores help to detect aspects for quality improvement. Audit and feedback were reported to have small to moderate effects on improvement of professional practice [15]. However, when indicator scores were used for remuneration, these scores showed a rapid and impressive increase.

Pharmaceutical care as the pharmacist's contribution to the care of individuals in order to optimize medicine use and improve health outcomes [16] mainly addresses risks associated with medication [5] and aims to improve medication safety. For societal outcomes of drug safety, for instance, drug-related hospital admissions can be assessed. This was first done in the report of the Institute of Medicine (IOM) in 1999 "To err is human: building a safer health system." It showed that drug-related adverse events occurred in between 2.9 and 3.7% of hospital admissions; half of them seemed to be potentially avoidable [17]. This report also stated that errors most commonly were caused by faulty systems, processes, and conditions that lead people to make mistakes or fail to prevent them. In a second report of the IOM "Crossing the Quality Chasm: a New Health System for the 21st Century," the wide scope of care-related injuries patients suffered in the US [18] was described. These studies were replicated in other countries with percentages for potentially preventable drug-related hospital admissions ranging from 2 to 12% [19, 20].

In the Netherlands, the measurement for drug-related hospital admissions was repeated after 5 years with information available until 2013. Contrary to the expectations, the number of potentially drug-related hospital admissions increased in subjects older than 65 years from 39000 in 2008 to 49000 in 2013 [21]. Subanalysis showed that this was due to an increase in the number of older people, the increased use of medication, and an increase of hospital admissions in general, possibly due to easier access to hospital care.

To effectively improve medication safety and improve patient outcomes such as less drug-related hospital admissions, closing the gap between the current healthcare system and patients' needs is an overwhelming task. This requires cooperation between all healthcare disciplines including pharmacy. Much attention is given to

the selection of appropriate drug therapy, to the dispensing of the right drug within current medication—however, there remains a great opportunity to improve therapy outcomes through monitoring and managing of therapy after dispensing [22]. Here lies the specific task for pharmaceutical care.

> Research showed that patient interviews were needed to identify more than a quarter of drug-related problems (DRPs) [23]. These DRPs were more frequently assigned a higher clinical relevance than those identified from healthcare records. Additionally, common non-alarming drug-related symptoms might have a substantial impact on the individual patient. However, they are often not recognized as such this by healthcare providers [8].

Consequently, pharmacists and their staff should manage the patient's drug use and assure appropriate drug therapy outcomes. A long-term vision should be built for drug therapy management on effectively targeting those patients in need for additional care and tailoring pharmaceutical care to their needs and expectations to meet individual patient's needs, indicators should allow reasonable deviations from guideline recommendations. This could be measured by additional registrations for the reasons of a deliberate different choice.

> In the Netherlands, clinical rules have been developed with uniform definitions. These rules were implemented in the computerized pharmacy software systems to signalize inappropriate drug use (e.g., interactions, contraindications, double medication). Additionally, these rules facilitate a decision tree to follow the handling of the surveillance signal and to register any deviations from the recommendations. When these registrations can be collected nationally besides dispensing data, the information on these registrations will be included in the quality measurement.

Finally, attention must be paid to the sustainability of indicator scores. Due to long-term attention to some aspects, especially when included in pay-for-performance programs, indicator scores might reach the highest achievable scores in clinical practice. A continued distinction of quality within low variation of indicator scores then results in artificial discrimination of pharmacies and does not correspond with real differences in quality. This will frustrate healthcare providers and does not stimulate them for continuous quality improvement. A solution may be to use those indicators for quality maintenance instead of improvement, for which most healthcare providers reached reasonable scores.

> In the Netherlands, 80% of the pharmacies score between 67 and 84% for the degree of concomitant antilipemic co-medication in diabetes patients. These scores seem not to improve anymore due to patient characteristics (e.g., sufficient lipemic control) and measurement errors (e.g., medication was dispensed in a different pharmacy). Therefore, this indicator is no longer used to discriminate pharmacies for scores above and below the average, but for achieving a minimum score (achieve a score above the 10th percentile).

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Chapter 11
Economical, Clinical, and Humanistic Outcomes and Pharmaceutical Care

Heather E. Barry and Carmel M. Hughes

Abstract This chapter outlines the Economical, Clinical, and Humanistic Outcomes (ECHO) model as a framework for the multidimensional classification of outcomes. Moving on from the traditional disease-oriented model, the ECHO model ensures that economic and humanistic measures are evaluated, as well as clinical variables. Consideration of all three outcome types is important when evaluating pharmaceutical care interventions through well-designed, rigorous trials.

Keywords Pharmaceutical care · ECHO model · Economic outcomes
Humanistic outcomes · Clinical outcomes

11.1 Introduction

Approaches to the assessment of quality of healthcare, including pharmaceutical care provision, have broadened over recent years as the role of the patient has changed from that of a "passive recipient" to an "active consumer" of care [1]. While clinical outcomes are important, researchers and healthcare professionals, including pharmacists, must not forget about patient-centered outcomes and those that are likely to lead to greater efficiency as determined by cost-effectiveness. The Economic, Clinical, and Humanistic Outcomes (ECHO) model, discussed forthwith, provides a comprehensive approach to decision-making about medical and pharmaceutical care processes.

11.2 Rationale for Model Development

Medical decision-making traditionally focused purely on the clinical indicators of disease (which are defined as measurements of a patient physical and biomedical status used to infer the degree of disease, for example, blood pressure, serum

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cholesterol level) and clinical outcomes (defined as events that occur as a result of disease or treatment, for example, hospitalization, death) in order to assess the value of any "treatment alternatives" (i.e., the different treatment options under consideration; Fig. 11.1). Although they are quite different and separate entities, clinical indicators and outcomes are well understood and accepted by clinicians and healthcare providers as they are quantifiable and familiar measures. Thus, traditionally when a patient consulted a healthcare professional for treatment or prevention of an illness, clinical indicators were typically used to evaluate the patient health status and were used as a basis for the selection of treatment alternatives.

However, changes to the demographic characteristics of our population which have resulted in people living longer with chronic long-term conditions, together with a growing interest in consumer-oriented outcomes (such as quality of life, patient satisfaction, and healthcare costs), has meant that clinicians and healthcare providers need to take a more wide-ranging approach when considering healthcare value and medical decision-making. The ECHO model, proposed by Kozma et al. was designed to build upon and extend the traditional medical practice model to include a focus on outcomes, by also systematically assessing humanistic and economic outcomes, together with clinical outcomes [2].

11.3 Principles of the ECHO Model

The ECHO model proposes causal relationships between diseases, health outcomes, and decisions about medical care interventions [2, 3]. The ECHO model recognizes the importance of the traditional medical model, whereby decision-making is centered around the detection, treatment, cure, and prevention of disease. However, it highlights that a multidimensional assessment of the value of alternative treatment options must be made, and balanced simultaneously. The resultant model (shown in

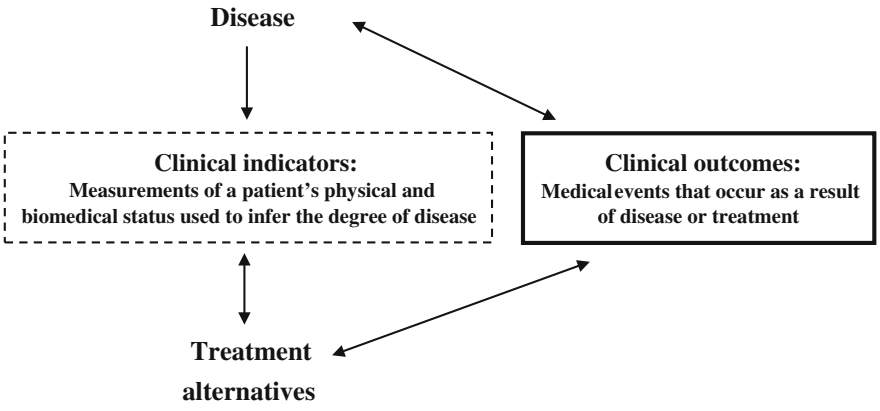

Fig. 11.1 Traditional medical practice model [2]

Fig. 11.2) therefore postulates that outcomes of healthcare can be classified along the following three dimensions: clinical, economic, and humanistic outcomes, which are defined and explained in further detail below.

11.3.1 Clinical Outcomes

Clinical outcomes are events that occur as a result of disease or treatment. So in a randomized controlled trial (RCT) investigating the effects of a new antihypertensive agent, examples of clinical outcomes would be incidence of myocardial infarction, inpatient hospitalization, and death.

11.3.2 Economic Outcomes

Economic outcomes are direct, indirect, and intangible costs compared with the consequences of medical treatment alternatives. Results arising from cost-effectiveness and cost–benefit analyses are examples of economic outcomes, such as cost per life year saved, cost per quality-adjusted life year, and cost per case treated.

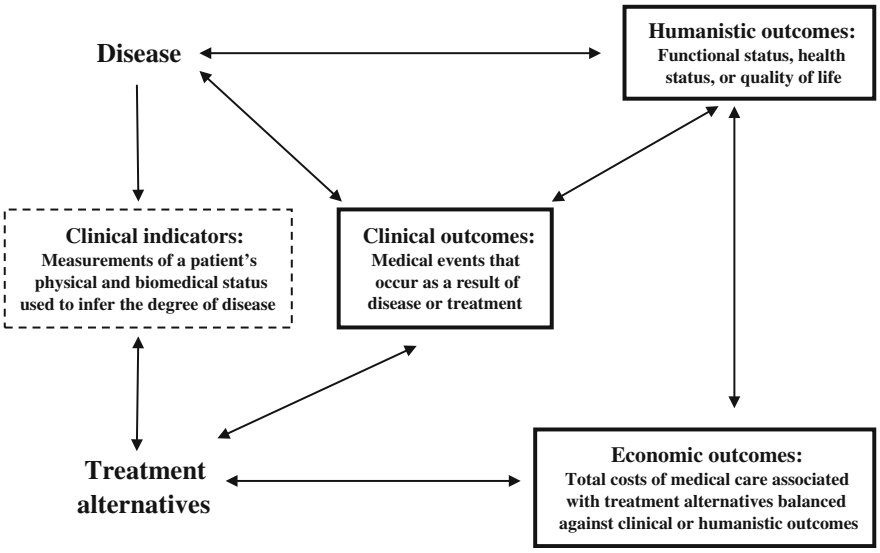

Fig. 11.2 The Economic, Clinical, and Humanistic Outcomes (ECHO) model [2, 3]

11.3.3 Humanistic Outcomes

Humanistic outcomes are consequences of disease or treatment on patient functional status or quality of life (QoL). Examples include physical function, social function, general health, and well-being, and life satisfaction. Humanistic outcomes also include patient satisfaction with healthcare services and the results of treatment.

11.4 Illustration of Theoretical Model

The theoretical relationship between clinical, economic, and humanistic outcomes is illustrated in Fig. 11.3, using chronic asthma as an example. A number of possible examples are indicated under each outcome in the diagram.

Clinicians and healthcare professionals evaluate the clinical indicators of asthma by questioning the patient or by conducting medical tests (for example, spirometry testing), and make decisions regarding treatment alternatives. Clinical indicators are used as the basis for the selection of treatment alternatives, and are surrogates for clinical outcomes. The clinical indicators used to assess asthma would include measures such as forced expiratory volume, wheezing, and breathlessness. Clinical

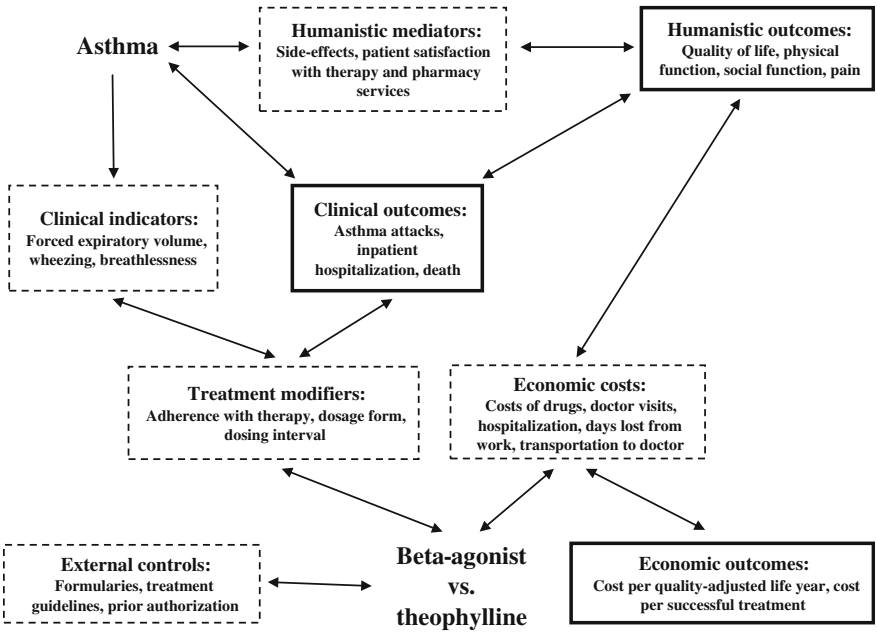

Fig. 11.3 The conceptual ECHO model for chronic asthma [2, 3]

outcomes include events such as incidence of asthma attacks, hospitalization, and death. The model considers two treatment alternatives: a beta-agonist and theophylline. External controls are nonclinical factors that affect the availability or use of treatment alternatives, such as formularies or therapeutic guidelines. Clinical outcomes and indicators may also be affected by "treatment modifiers," which are factors that alter the outcome associated with treatment alternatives. Factors such as adherence with prescribed therapy because of side effects, and issues with theophylline dosing would be considered as treatment modifiers. There are a number of product-specific characteristics that must also be taken into account, such as the dosage form and dosage interval of therapy.

Humanistic mediators, which are the effects of disease or treatment on humanistic outcomes, would include side effects and patient satisfaction with therapy and the pharmacy services provided. The humanistic outcomes of interest include measures such as health-related quality of life and functional status.

Economic outcomes have mediators introduced from both the clinical and humanistic sides of the model. Clinical costs include all costs associated with treatment as well as the direct cost of the pharmaceutical products. Therefore laboratory and hospitalization expenses, and costs of retreatment from treatment failure should be included. Humanistic costs will include indirect or productivity costs associated with time lost from work. Direct nonmedical costs also need to be included, such as travel expenses for hospital or doctor visits. The direct and indirect costs are totalled and balanced against clinical or humanistic outcomes to develop an economic outcome. Such measures include ratios of costs to benefits, effectiveness (for example, reduction in the number of asthma attacks) or utility (for example, quality-adjusted life years).

11.5 Advantages of the ECHO Model

The ECHO model takes a "balance of outcomes" approach, which ultimately ensures that no one outcome is valued over another [4]. As interest in patient-oriented outcomes grew, it was increasingly recognized that outcome types were inter-dependent, and desirable changes in one outcome may be accompanied by undesirable changes in another (known as the "balloon effect"). For example, placing pressure on the balloon in one place (such as by decreasing drug costs) would only cause it to expand somewhere else (such as increased hospitalizations) [4]. Measuring both sets of outcomes in this example would therefore protect against an unanticipated negative impact on the system. Gunter states that balancing outcomes in this way has the following advantages:

It reduces the probability of implementing and running interventions which are ill-conceived and therefore result in unanticipated negative effects;
Outcomes of key interest to a variety of stakeholders are measured and reported;

Instead of thinking about components of an intervention in isolation, it encourages researchers and clinicians to understand the linkages and interactions between intervention components, ensuring that indicators are selected to monitor their impact;
A comprehensive and multidimensional approach is taken to the measurement of healthcare value [4].

11.6 Outcome Selection and Measurement

The selection, measurement, and reporting of outcomes that are relevant, appropriate, and of importance to patients in the "real-world clinical setting" are critical to ensure that a significant impact is made upon patient care [5]. Selecting outcomes to measure in a particular healthcare system requires careful thought due to the limited available resources for data collection and healthcare delivery [4]. Outcomes of interest will often vary depending upon the stakeholder group of interest and the incentives of the healthcare system. For example, clinicians are typically interested in objective clinical outcomes such as reducing incidence of stroke or number of hospitalizations, healthcare service providers are usually interested in economic outcomes such as medical costs, and patients are concerned with humanistic outcomes such as QoL and satisfaction with health services, and may struggle to interpret clinical outcomes [3, 6]. As a result, it is prudent to select a number of outcomes in each of these categories in order to demonstrate the value of a medical or pharmaceutical alternative. Outcome selection should also be informed by an understanding of the structure and incentives of the healthcare delivery system, especially if the primary objective is to foster improvement in the most relevant areas [2, 4]. In recent years, further attention has been paid to outcome selection through the development and use of standardized Core Outcome Sets in trials of interventions in a particular clinical area (see Chap. 12) [5].

Consideration must also be given to the timing of measurement of clinical outcomes in particular; this will depend upon the nature of the condition(s) being studied, the target population to which the study results apply, and clinical judgements where sufficient effects can be captured [7]. Intermediate or surrogate endpoints may be used as a "biological marker" for the condition of interest, and have the main advantage of shortening the follow-up time required to observe possible effects of treatment for the clinical outcome(s) of interest. However, in using intermediate or surrogate endpoints, the researcher may not be provided with a complete picture of the benefits or risk [8]. A recent study by Siaw et al. evaluated the clinical, humanistic, and economic outcomes of a multidisciplinary collaborative care versus physician-centered care in diabetes [9]. Primary outcomes included surrogate endpoints such as glycated hemoglobin (HbA1c), systolic blood pressure, and low-density lipoprotein which were measured at baseline, three and six months. Measures of humanistic and economic outcomes were considered as secondary outcomes. The authors acknowledged that they were unable to assess long-term outcomes due to the short study duration of six months [9].

Monitoring and measurement should focus not only on outcomes, but also on process indicators (see Chap. 10) [4]. This will help to both determine which approach works best, and also to link process and outcome changes. It is prudent, therefore, that time is spent contemplating a rigorous study design to ensure that changes in outcomes result from the intervention itself, as opposed to other extraneous factors.

11.7 Application of the ECHO Model in Pharmaceutical Care Interventions

Decisions regarding pharmaceutical products, services, and interventions should be made through the simultaneous consideration and balancing of all three types of outcomes (clinical, economic, and humanistic) [3]. Furthermore, outcomes should be examined from a broad societal perspective, taking into account that pharmaceutical products and services are only one part of the healthcare system [3]. Outcomes data have many applications within the area of pharmacy practice, for example, in formulary and treatment guideline development, and in the provision of pharmaceutical care [3]. Utilization of the ECHO model ensures that the patient-centered concept of pharmaceutical care is advocated.

Many studies have assessed the impact of pharmaceutical care interventions, in a myriad of clinical areas, on outcomes [10–14]. Bernsten et al. measured the clinical, economic, and humanistic outcomes of a structured pharmaceutical care program provided to older people (i.e., patients aged 65 years and over), which was delivered by community pharmacists in a study performed in seven European countries [10]. Clinical outcomes assessed included number of hospitalizations, and sign and symptom control, while humanistic outcomes included health-related quality of life. Cost analyses including the cost associated with additional time spent by pharmacists providing the intervention and cost of hospitalizations and drugs were also assessed. This study added to the knowledge base significantly as previous studies had only investigated a limited number of outcomes, and it showed that the pharmaceutical care intervention program had had particularly positive effects on humanistic and economic outcomes [10]. Another study by Cordina et al. assessed a community-based pharmaceutical care program for asthma, and measured a number of different clinical and humanistic outcomes [11]. This study showed that the pharmacists" intervention had a small but positive effect on humanistic outcomes such as QoL, and humanistic mediators such as patient satisfaction, with pharmacists being viewed as more approachable and more likely to be perceived as a healthcare professional [11]. Similarly Sadik et al. investigated the impact of pharmaceutical care on a number of clinical and humanistic outcomes related to different aspects of health status in patients with heart failure, and found that such outcomes were enhanced by the intervention, with particular improvements observed with respect to QoL and hospital admission rates [12]. While economic

outcomes were not assessed per se, some preliminary information was reported about costs. The authors of the aforementioned studies have provided useful advice to those considering assessing impact of pharmaceutical care interventions on outcomes. They advise selecting a minimal set of outcomes to be measured when assessing pharmaceutical care, as choosing too many can result in "research fatigue" for both the participants and those delivering the intervention [13]. Mixed methodologies can be utilized in studies assessing pharmaceutical care interventions; qualitative techniques may be particularly useful when investigating aspects of satisfaction and patient and/or healthcare professional perceptions of service provision [10].

Two review articles have assessed the impact of pharmaceutical care services on outcomes using the ECHO framework model: one in community and ambulatory care settings [15], and one in racial/ethnic minority groups of patients [16]. Both reviews found that studies tended to report only one outcome type or a combination of two outcome types; only a very small number of studies had evaluated and subsequently reported a combination of the three outcomes. A further review, which examined the evidence of the impact of the STOPP (Screening Tool of Older Person"s potentially inappropriate Prescriptions) and START (Screening Tool to Alert doctors to the Right Treatment) tools indicating prescribing quality, reported that clinical humanistic and economic impacts have not been well explored [17]. A more recent review by Ganguli et al. which assessed the impact of patient support programs (which includes medication management and counseling) on clinical, economic, and humanistic outcomes, reported that economic outcomes were less often measured in such studies [18]. Loh et al. advise that careful thought should be given to capturing relevant outcomes that reflect the potential benefits of medicines management interventions provided by pharmacists; it would be assumed that this recommendation should apply to the evaluation of all types of pharmaceutical care intervention [19]. These findings reinforce the need to ensure that all three outcome variables are included and measured in order to achieve a balanced, comprehensive, and patient-relevant picture of the impact of pharmaceutical care [18, 20].

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Chapter 12
The Role of Core Outcome Sets for Pharmaceutical Care Research

Anna Millar, Audrey Rankin, Mairead McGrattan, Maureen Spargo and Carmel M. Hughes

Abstract The development and implementation of core outcome sets can help support the generation of high-quality evidence for pharmaceutical care research, which in turn can help improve outcomes for patients. The concept of COSs is relatively new and a robust, evidence-based methodology for developing and implementing COSs is not yet fully established. The processes described in the COMET Handbook (Version 1.0) represents what is known to be best practice at the time of publication. However, there remain some uncertainties regarding the impact of different methodological decisions made during the development of a COS. For example, how to choose the best consensus technique, or how outcomes are prioritized for inclusion in a COS. Furthermore, guidance regarding how to reduce the number of outcomes specified in a COS to a number that can practicably be measured and reported in an RCT is needed. The handbook is likely to be updated periodically as more research is undertaken [4]. A key message for COS developers is to be transparent with regard to the methods used during COS development studies. An accurate description of how and why key decisions during the COS development process are made, and the outcome of those decisions, will not only encourage uptake of the developed COS but will help guide the refinement of COS development methodology.

Keywords Pharmaceutical care · Core outcome sets · COMET initiative
COS development · Patient outcomes

12.1 Core Outcomes

The outcomes that are measured in trials are essential to determine the effectiveness of interventions in pharmaceutical care. These outcomes can be used to compare results between trials and subsequently form the basis of systematic reviews and

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meta-analysis [1]. However, difficulties arise when trials examining similar interventions use different outcome measures. This has been highlighted across the literature, with one systematic review identifying 327 different outcomes used across 47 randomized controlled trials (RCTs) involving medication review in older people [2]. This makes it impossible for interventions to be directly compared, and presents difficulties to policy-makers and other stakeholders involved in decisions regarding funding interventions.

Despite the strengths of RCTs in terms of experimental design, there is still the potential for bias to be introduced during the implementation and reporting phases. There are a number of types of bias which can be introduced within a study, collectively known as selective reporting bias [3]. A subset of selective reporting bias specifically related to outcomes is outcome reporting bias, which occurs when only the statistically significant outcomes are reported in the final results, despite the authors stating other outcomes were measured in the methodology or study protocol [3]. This will have an important impact on interventions, affecting the validity of systematic reviews and meta-analysis aiming to determine their effectiveness, which will subsequently hinder an evidence-based approach to choosing healthcare interventions [3].

One approach to overcoming these challenges is through the development and implementation of "Core Outcome Sets" (COSs), defined as the minimum set of outcomes to be measured in all trials conducted in a particular area of health [1]. Whilst not intended to be the only outcomes measured, they form a standard list of the minimum outcomes which should be reported in such trials, which in turn will facilitate comparison between studies and ultimately reduce bias.

The development of COSs has been endorsed by the Core Outcome Measures in Effectiveness Trials (COMET) Initiative. This chapter will introduce the COMET Initiative, detail the methodology employed to develop a COS and describe other COS initiatives which support COS development. At the end of the chapter, case studies of recent COSs developed in pharmaceutical care will also be presented.

12.2 COMET Initiative

The COMET Initiative provides support by providing resources, networking opportunities and training for COS developers. Specific objectives of the COMET Initiative are to raise the awareness of current problems with outcome selection in clinical trials, encourage evidence-based COS development and uptake, promote Patient and Public Involvement (PPI) and prevent duplication of effort in COS development studies [4]. To facilitate these aims, the COMET Initiative provides a range of resources for use by COS developers. Examples include plain language summaries that describe the COS development process to patients and the public, guidance on the implementation of a COS, and exemplar COS development protocols.

An online database of all ongoing and published COS studies is maintained by the COMET Initiative, (available from www.comet-initative.org) to share examples of good practice and avoid duplication of effort. The searchable database was launched in August 2011, and contains 897 references of planned, ongoing and completed COS development studies (correct as of July 2017). Recently added studies include the development of a COS for immunomodulation in pregnancy and one for effectiveness trials investigating Perthes' Disease of the hip. Prospective COS developers can use the database to determine if relevant work has already been undertaken in specific clinical areas. Likewise, researchers planning trials of interventions can search the database for the existence of a COS that is applicable to the clinical area under investigation. Some funding bodies, such as the National Institute for Health Research (NIHR) in the United Kingdom, now recommend that researchers use the COMET database to identify relevant COSs when preparing funding applications.

The COMET Handbook contains information and guidance about the development, implementation, evaluation and updating of a COS [4]. The first version of the handbook was published in June 2017.

12.3 Methodology

The COMET Handbook [4] outlines in detail the recommended process for developing a COS, the steps of which are summarized in Fig. 12.1. Key aspects in COS development methodology include defining the scope of the COS, identifying existing knowledge, involving key stakeholders and achieving consensus on the outcomes to be included in the final COS.

12.3.1 Defining the Scope of a Proposed COS

The scope of a COS indicates the specific area of research to which the COS is to be applied. This scope of the COS, in terms of specificity, should be considered alongside the relative 'size' of the research area concerned. The scope should therefore be described in terms of the target population, applicable setting(s) and relevant study intervention(s) that the COS will relate to (Fig. 12.2).

As discussed in Sect. 12.1, known challenges relating to heterogeneity of outcome measurement and reporting of outcomes across trials in a specific area will justify the need for a relevant COS to be developed. Once the need for a COS has been established and the scope proposed, it is vital to identify if studies have already been undertaken, or are currently underway, to develop a COS with the same or similar scope.

The COMET Initiative's online searchable database (see Sect. 12.2) can be used to identify existing or ongoing work prior to proceeding with a new COS study.

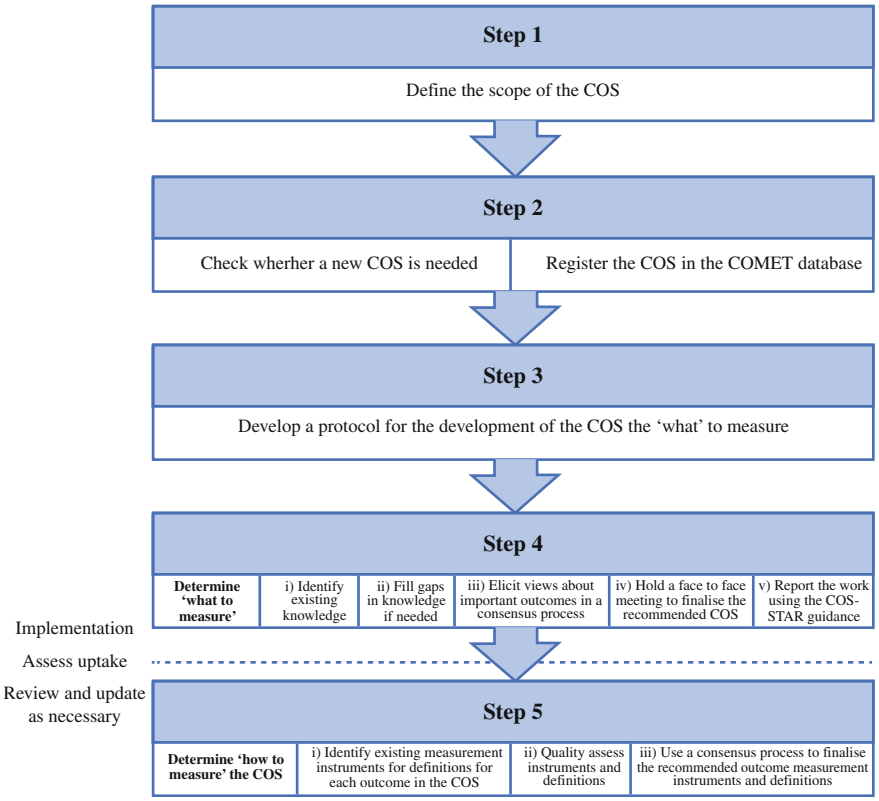

Fig. 12.1 The core outcome set (COS) development process

Population

A COS may be developed which is relevant to, for example, people of all ages, those aged over 65 years, people with type 2 diabetes or people who are prescribed polypharmacy.

Setting

A COS may be relevant to any healthcare setting, or it may specifically be relevant to primary care, hospitals, nursing homes or community pharmacy settings.

Interventions

A COS may be developed for use in any effectiveness trial with the same aim, regardless of the nature of the intervention; or the COS may relate only to a specific type of intervention, for example, medication review by a pharmacist, behaviour change techniques, or electornic prescribing.

Fig. 12.2 Considerations for the scope of a core outcome set

For this reason, COS developers should therefore make early contact with COMET to register their ongoing COS project. COMET also encourages researchers to develop and make publicly available a study protocol, either via the COMET database entry or a publication in an open-access journal.

12.3.2 Identifying Potential Outcomes for Inclusion in the COS

A review of previous trials or systematic reviews, relevant to the proposed scope, is the main method of identifying a list of outcomes for consideration for inclusion in the COS. If required, a review of relevant studies that are not necessarily effectiveness trials (e.g., observational studies and qualitative studies) may also be useful in identifying potential outcomes.

There is no recommended time frame within which to review the published literature, therefore the approach should be pragmatic and guided by the scope of the COS and the size of the body of associated published literature. As large reviews are resource intensive, one strategy could be to perform the literature review in stages, starting with the most recently published studies, until 'outcome saturation' is achieved, i.e., no additional outcomes are being identified [4].

12.3.3 Categorizing Identified Outcomes

It is likely that many identified outcomes could be considered as equal to one other, albeit reported using a range of terminologies across different studies. Such outcomes can therefore be categorized into one descriptive term. COS developers may also choose to group related outcomes into outcome 'domains', i.e., constructs which can be used to classify several outcomes. Such categorisation of outcomes should ideally be conducted independently by at least two researchers.

12.3.4 Stakeholder Involvement

A COS should contain outcomes considered important not only by researchers but by relevant stakeholders, including patients and carers. Other key stakeholder groups may include healthcare professionals, regulators and patient charities or support groups. Stakeholders may be involved in one or more stages of COS development, i.e., stakeholders' opinions may be sought to identify outcomes of importance in the initial stage, thus filling potential knowledge gaps as a result of using only published research to identify outcomes. Stakeholders may also

participate in a consensus exercise to determine the final COS (see later). Decisions regarding the extent of stakeholder involvement, the groups of stakeholders to be involved and the number and proportion from each group will be dependent upon the particular scope of the COS as well as feasibility considerations. COS developers should ideally strive to include stakeholders from across a range of countries to help ensure the widespread relevance and adoption of the COS [4].

Furthermore, involving 'public research partners' in both the design and oversight of the COS development study can be beneficial in accessing particular patient populations and facilitating the design of more appropriate study information (e.g., patient information leaflets). Patient and carer stakeholders may, for example, be identified and recruited via clinics, charity organizations, advocacy groups and carers' support groups [5].

Qualitative methods, such as focus groups, may be used to identify outcomes that are important to patients and carers. Qualitative research methodologies are an accessible way for patients and carers to be involved in COS development as they have the opportunity to explain important aspects of their experiences in their own terms, without the need for them to engage with research-centric language involving 'outcomes' and 'core outcome sets' [6].

12.3.5 Consensus Exercise

Having identified a long list of potential outcomes, achieving consensus on the important core outcomes is the crucial final step in the COS development process. Whilst a variety of methods exist to elicit consensus, the most frequently used technique in COS development is the Delphi technique, which comprises sequential rounds of questionnaires through which the anonymous opinions of participants are sought on the importance of the listed outcomes, indicated by a score.

Following each round, the collated group scores are fed back to the participants. As the participants do not directly interact with each other, the risk of an individual being overly influential or dominant in the group consensus process is reduced. Furthermore, COS studies typically use a 'modified' rather than a traditional Delphi technique. In a 'traditional' Delphi exercise, the outcomes of potential importance would be identified in the first round of the Delphi by participants through the use of an open text question. In the modified Delphi exercise, the participants are presented with the long list of outcomes that have been identified as described previously. However, COMET recommends that Delphi participants should be given the opportunity in the survey to propose additional outcomes not identified in the literature or via stakeholder involvement.

Whilst there is no recommendation for the ideal number of participants to be included in a Delphi panel, it is important to acknowledge that patients, healthcare professionals and researchers may have differing opinions on which outcomes they consider most important [7]. Therefore, careful consideration must be given in advance to the composition of the stakeholder groups within the Delphi panel.

12.3.6 Criteria for Consensus

In COS development studies, Delphi survey participants are commonly asked to score each listed outcome using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) group scoring system, where a score of 1–3 signifies an outcome of 'limited importance', 4–6 'important but not critical', and 7–9 'critical'. Consensus regarding whether an outcome is to be included in the COS is often defined as 70% or more of the respondents scoring an outcome between 7 and 9 and fewer than 15% scoring it as 1–3. Conversely, consensus that an outcome should not be included in the COS is typically defined as 70% or more scoring it as 1–3 and fewer than 15% scoring it as 7–9 [8]. Any other scores would typically be classified as 'no consensus' and therefore the outcome would not be included in the COS.

12.3.7 Face-to-Face Meeting

COMET recommends that, following the Delphi exercise, COS developers hold a face-to-face meeting with stakeholders with the aim of achieving a final consensus on the outcomes to be included in the COS through discussion of the Delphi results and voting, if necessary. Such meetings may involve a heterogeneous group of stakeholders including patients, or alternatively, separate meetings for healthcare professionals and patients may be conducted. Consideration must also be given to the number and proportion of individuals from each stakeholder group. Other issues to consider with face-to-face meetings as well as other aspects of COS development methodology in general are discussed in greater detail in the COMET handbook.

12.4 Other COS Initiatives

The above sections describe the COMET Initiative and outline the recommended methodology as set out by the recently published COMET Handbook (Version 1.0) [4]. Within the handbook, two additional initiatives, Core Outcome Set-STAndards for Reporting (COS-STAR) and COnsensus-based Standards for the selection of health Measurement Instruments (COSMIN) are recommended to COS developers to provide guidance with regard to the reporting of COS studies and selection of measurement tools for outcomes.

12.4.1 Core Outcome Set-STAndards for Reporting (COS-STAR)

Even when robust methodologies (as outlined above) are followed in the development of a COS, inconsistent reporting quality could result in the poor

implementation of relevant COSs. The need for clear and transparent presentation of the methods used during the development of COSs was first highlighted by the COMET Initiative in 2012 [1]. Indeed, a recent qualitative study involving COS developers concluded that reporting guidance would be of benefit to future COS developers [9]. To encourage COS developers to improve the quality of published COSs, the Core Outcome Set-STAndards for Reporting (COS-STAR) guideline has been developed [10]. Additionally, within the four-step COS development process laid out in the COMET Handbook (Version 1.0), the final step recommends that COS developers report their work using the COS-STAR guidance (Fig. 12.1) [4]. The COS-STAR Statement, developed by an international group including COS developers and potential COS users, includes an 18-item checklist, highlighting important methodological aspects of the COS development (e.g., scope, participants and outcome scoring) that should be reported in all COS studies, irrespective of the underlying methods or participants involved [4]. The checklist is also supplemented by an explanation and elaboration document that outlines the need for each checklist item and examples of how each item has been reported properly in published studies [4]. It is, however, important to note that the use of the COS-STAR checklist is not an indication of methodological quality and should not be used as a quality assessment tool [9]. COS developers should endeavor to follow methodological guidance set out by the COMET Initiative and include reference to all the relevant checklist items when reporting their work.

12.4.2 COnsensus-Based Standards for the Selection of Health Measurement Instruments (COSMIN)

The methodology proposed by the COMET Initiative aims to determine what should be measured, as opposed to how it should be measured. A joint initiative between COMET and COSMIN was established to address this by developing a guideline on how to select outcome measurement instruments for outcomes included in a COS [11]. Furthermore, within the four-step COS development process laid out in the COMET Handbook, an additional fifth step recommends that COS developers determine how to measure the COS, including identifying existing measurement instruments and quality assessment (Fig. 12.1) [4]. The checklist focusses on assessing the measurement properties and methodological quality of Health-Related Patient-Reported Outcomes (HR-PROs). However, the measurement properties evaluated are likely to be relevant for other non-PRO measurements instruments, with work currently underway to establish a checklist for these instruments. The four-step process includes: (1) conceptual considerations [i.e., considerations include the construct (i.e., outcome or domain) to be measured and the target population (e.g., age, gender, disease characteristics)]; (2) finding existing outcome measurement instruments; (3) quality assessment of outcome measurement instruments; and (4) generic recommendations on the selection of outcome

measurement instruments for outcomes included in a COS. The COSMIN website also contains a database of systematic reviews of outcome measurement instruments that should be reviewed in Step 2, to determine what measurement instruments are currently available for each outcome included in a COS.

Step 3 involves using the COSMIN checklist to assess the quality of the outcome measurement instruments, in terms of the statistical methods used and the methodological properties based on the COSMIN taxonomy [e.g., internal consistency, reliability, measurement error, content validity (including face validity), construct validity (including structural validity, hypotheses testing and cross-cultural validity), criterion validity, responsiveness and interpretability], which are assessed against certain quality standards and rated on a 4-point scale (1 = poor, 2 = fair, 3 = good, or 4 = excellent). This should result in the selection of only one outcome measurement instrument for each outcome in a COS.

12.5 COSs Developed/Under Development in Pharmaceutical Care: Case Studies

12.5.1 The Development of a COS for Effectiveness Trials Aimed at Optimizing Prescribing in Older Adults in Care Homes

This COS was developed as part of the Care Homes Independent Pharmacist Prescribing Study (CHIPPS). A long-list of outcomes was identified through both a review of published literature in the area, and stakeholder focus groups with GPs, pharmacists, care home staff, residents and relatives. Outcomes were reviewed and refined prior to entering a two-round online Delphi exercise and then distributed via a web link to the Delphi panel, a multidisciplinary team including pharmacists, doctors and PPI representatives. Following both rounds of the Delphi exercise, 13 outcomes [organized into seven overarching domains: medication appropriateness, adverse drug events, prescribing errors, falls, quality of life, all-cause mortality and admissions to hospital (and associated costs)] met the criteria for inclusion in the final COS [12].

12.5.2 Development of a COS for Medication Review in Older People

The aim of this ongoing study is to develop a COS for medication review in older adults. A systematic review has been conducted to identify outcomes used in RCTs and prospective studies, which identified 327 different outcomes across 47 published RCTs as well as 248 outcomes across 32 published protocols. The large

number of outcomes identified by this systematic review reinforced the need for a COS in this area. Further work to develop the COS will include interviews with patients over the age of 65 taking five or more medicines, along with their carers. The final stage will involve condensing outcomes into the final COS through three rounds of Delphi questionnaires, distributed to patients, carers, healthcare professionals and researchers across four European centeres; Belgium, Ireland, Netherlands and Switzerland [12].

12.5.3 The Development of a Core Outcome Set for Use in Interventions Aimed at Improving Appropriate Polypharmacy in Older People in Primary Care

The aim of this study was to develop a COS that can be applied to trials investigating the effectiveness of interventions targeting polypharmacy in older people in primary care. Phase 1 involved three steps: (1) identifying outcomes used in previous studies by updating a Cochrane systematic review on interventions to improve appropriate polypharmacy in older people, (2) identifying outcomes from previously collected qualitative data and (3) initial screening of outcomes from steps 1 and 2, by the Project Steering Group. Phase 2 involved conducting a Delphi consensus exercise with key stakeholders, to reach consensus regarding which outcomes should be included in the COS. The consensus exercise encompassed three rounds of online Delphi questionnaires with key stakeholders (an international panel of 160 stakeholders including 120 experts and a public participant panel of 40 older people). Twenty-nine outcomes identified from the Cochrane review and existing qualitative data were included in a Delphi exercise. After three rounds of Delphi questionnaires, the final COS comprised 16 outcomes, across 6 overarching themes. The seven highest ranked outcomes were ‘serious adverse drug reactions’, ‘medication appropriateness’, ‘falls’, ‘medication regimen complexity’, ‘quality of life’, ‘mortality’ and ‘medication side effects’.

12.5.4 The Development of a COS for Medicines Management Interventions for People with Dementia Living in Primary Care

The aim of this study was to develop a COS for medicines management interventions for people with dementia living in primary care. The first phase of this project involved a systematic review of the literature, to identify outcomes currently used in RCTs in this area. The second phase involved semi-structured interviews with people with dementia, their carers, general practitioners and community

pharmacists to identify which outcomes they felt were important. The final phase involved condensing the outcomes identified from the systematic review and semi-structured interviews into the final COS. This was achieved through three rounds of Delphi questionnaires, distributed to healthcare professionals and researchers from a range of countries. Consensus for inclusion in the COS was reached on 21 outcomes, out of 33 presented outcomes.

12.5.5 Development of a Core Outcome Set for Trials Investigating the Long-Term Management of Bronchiectasis

A study that aimed to develop a COS for trials investigating interventions for the long-term management of bronchiectasis has been completed. The study utilized the findings of existing research on outcomes selection to compile a list of outcomes for consideration by a Delphi panel. An overview of Cochrane systematic reviews provided a list of outcomes that other researchers deemed important to measure when investigating interventions for bronchiectasis interventions. In a consultation with stakeholders (patients, healthcare professionals and academics) in the management of bronchiectasis (conducted as part of an ongoing study to develop an adherence intervention for the condition), expert panel members were asked to suggest and discuss outcomes they believed should be measured in an evaluation of the proposed intervention.

Review of both these studies led to the identification of 20 outcomes for consideration by a Delphi panel in a consensus exercise. Eighty-six participants from 22 European countries were recruited into the Delphi panel. The success of the recruitment strategy was largely attributable to the support provided by a European bronchiectasis network of healthcare professionals and a patient advisory group for bronchiectasis, coordinated by the European Lung Foundation.

The Delphi panel rated the importance of each outcome from 1 to 9 in a series of three sequential online questionnaires using the GRADE criteria (see Sect. 12.3.6). In the first questionnaire, participants were asked to suggest outcomes for consideration in subsequent questionnaires. Outcomes that were rated 'Critical' by $\geq 70\%$ of the Delphi panel (and 'Of limited importance' by <15%) were added to the COS. Eighty-two participants responded to the first questionnaire (42 doctors, 8 nurses, 10 physiotherapists, and 22 patients; response rate 95%). Attrition in response rates between each questionnaire was 5%. Twenty outcomes were rated in the first questionnaire, 32 in the second and 17 in the third. Eighteen outcomes exceeded the predefined threshold for consensus and were included in the COS.

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Part III
Pharmaceutical Care Around the World

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Although the term already exists for many years, pharmaceutical care is still developing around the world. Many achievements and services have already been described in a large number of countries. The below list of international publications compiled by book editors Aldo Alvarez-Risco and Filipa Alves da Costa also reflects this.

In the chapters, we further specify the level of implementation and the type of care and services that can be found in different parts of the world. For better reference and learning, it is helpful to know what is happening where.

As for the current status of pharmaceutical care, literature gives us information on many different countries around the World, such as North America (Canada [1] and USA [2]), Europe as a whole [3–6] (or in individual countries like Austria [7], Bulgaria [8], Denmark [9], Estonia [10], Finland [11], France [12], Germany [13], Greece [14], Lithuania [15], Netherlands [16], Poland [17], Portugal [18], Spain [19], Sweden [20], Switzerland [21], Ukraine [22]), Oceania (Australia [23], New Zealand [24]), Asia (China [25], India [26], Iran [27], Japan [28], Jordan [29], Kuwait [30], Singapore [31], South Korea [32], Taiwan [33]), Africa (Nigeria [34], South Africa [35]), and Latin America (Argentina [36], Brazil [37], Colombia [38], Cuba [39], Peru [40], Uruguay [41]). But, as one can see in literature, implementations are not yet complete in most of the mentioned countries and there are other countries where pharmaceutical care has not yet found any resonance. Please note that this list has been drafted in 2018, and new publications may have appeared since.

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Chapter 13
Pharmaceutical Care in North America

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Abstract Pharmaceutical care in the US and Canada is regulated at the level of the state/province generating differences in the practice of pharmacy across the countries. Pharmacist counseling and utilization review are generally required to be offered at dispensing in community pharmacies. There is a trend toward the development of pharmaceutical care services provided at the community pharmacy, the integration of the pharmacist in the healthcare team, and the implementation of collaborative agreements expanding the role of the pharmacist in patient care. This chapter is divided into two sections, one for the United States of America, and one for Canada.

Keywords Pharmaceutical care · North America · Pharmaceutical services Professional practice · Remuneration

13.1 United States of America

13.1.1 The Community Pharmacist in the US

In 2015, there were 65,280 US community pharmacies [1], representing one pharmacy per 4915 people. US community pharmacies dispensed a total of 4065 million prescriptions with an average of 12.6 prescriptions per inhabitant and a total cost of $379,247 million in the same year [2]. Community pharmacy expenditures represented over 10% of US healthcare expenditures [3]. Public programs including Medicare and Medicaid and other federal and state programs covered over 50% of the pharmaceutical expenditures in the country. In 2015, community pharmacies dispensed 83.3% of the prescriptions and accounted for 68% of the pharmacy expenditures, while mail-order pharmacies dispended 16.7% of the prescriptions and accounted for 31.9% of the expenditures. Pharmacy chains represented 41.2%

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of the stores, dispensed 62.7% of the prescription, and 71.6% of the expenditures of community pharmacy; while independent pharmacies represented 36.1, 22.9, and 14.9%; and pharmacies located in food and merchandiser stores represented 9.8, 14.4, and 13.4%, respectively [4].

There were 305,510 pharmacists employed in the US as May 2016; of which 184,550 (60.4%) worked in community pharmacies, 71,390 (23.4%) in general and surgical hospitals, 3870 (1.3%) in electronic and mail-order pharmacy, 8810 (2.9%) in physician offices and community care centers, and 36,890 (12.1%) in other areas of practice [5].

Pharmacists are required to hold a baccalaureate degree in pharmacy and, after 2000, a doctorate of pharmacy (PharmD) that is accredited by the Accreditation Council for Pharmacy Education (ACPE- a national agency recognized by the US Department of Education for the accreditation of professional degree programs in pharmacy and accreditation of providers of continuing education) [6]. The PharmD program typically requires between 2 and 4 years of pre-pharmacy studies and 4 years of pharmacy studies. Accelerated programs reduce to 3 years the duration of the pharmacy studies by going year round with three semesters per year rather than just two. The last year of the PharmD studies is composed of students' practice rotations in different pharmacy and clinical settings.

To be licensed by a state, pharmacists must also pass the North American Pharmacist Licensure Examination (NAPLEX) organized by the National Association of Boards of Pharmacy (NABP- it includes the boards of pharmacy of the 50 United States, the District of Columbia, Guam, Puerto Rico, the Virgin Islands, Australia, Bahamas, 10 Canadian provinces, and New Zealand) [7]; and the state's practice standards and legislation examination organized by the state's board of pharmacy. Pharmacists may hold licensures from multiple states, and may transfer their license from one state to another, under certain conditions, but they must always hold the licensure from the state where they were originally licensed. Pharmacists must also complete several of hours of continuing education each year to maintain their professional competencies and fulfill the requirements established by the states boards of pharmacy to maintain the pharmacist license [8].

13.1.2 US Regulation of Pharmaceutical Care

The role of the pharmacist is regulated at the federal and state levels. The federal government is responsible for approval, regulation, and interstate commerce of drugs and biologics, enforcement of federal regulations related to controlled drugs, and certain areas of pharmacist activities related to the Federal healthcare programs such as Medicare and Medicaid. Two federal laws, the Omnibus Budget Reconciliation Act of 1990 (OBRA-90) and Medicare Prescription Drug, Improvement, and Modernization Act (MMA) of 2003 expanded the role of the pharmacist in the US.

OBRA-90 required states to provide prospective drug review before an outpatient prescription is dispensed to Medicaid patients at the point-of-sale or distribution and mandated states to establish standards for counseling of Medicaid patients by pharmacists in community pharmacy settings. OBRA-90 represented the federal recognition of the role of pharmacist in patient care and expanded the scope of pharmacy practice.

The prospective review established by OBRA-90 must include screening for potential drug therapy problems due to therapeutic duplication, drug–disease contraindications, drug–drug interactions (including serious interactions with nonprescription or over-the-counter drugs), incorrect drug dosage or duration of drug treatment, drug–allergy interactions, and clinical abuse/misuse [9]. According to OBRA-90 pharmacist counseling requirements, the pharmacist must offer to discuss the following with each Medicaid patient or caregiver who presents a prescription: the name and description of the medication; the route, dosage form, dosage, route of administration, and duration of drug therapy; special directions and precautions for preparation, administration and use by the patient; common severe side or adverse effects or interactions and therapeutic contraindications that may be encountered, including their avoidance, and the action required if they occur; techniques for self-monitoring drug therapy; proper storage; prescription refill information; and action to be taken in the event of a missed dose. OBRA 90 also indicates that pharmacists are not required to provide consultation when patients or caregiver of refuses such consultation.

OBRA-90 also mandated states to ensure that a reasonable effort is made by the pharmacist to maintain a record including demographics, disease related, known allergies and drug reactions, a comprehensive list of medications and relevant devices, and pharmacist comments relevant to the individuals drug therapy.

The MMA established a voluntary prescription drug benefit for Medicare patients, the so-called Medicare Part D, that started in January 2006. The Medicare Part D program is managed by private drug plans under the regulation and supervision of the Centers for Medicare and Medicaid Services (CMS). The MMA requires drug plans to have in place a cost-effective drug utilization management program and a medication therapy management (MTM) program.

According to CMS, MTM is a patient-centric and comprehensive approach aiming to engage the patients and prescribers to promote coordinated care, comprehensive medication review and monitoring of medication therapies. The MTM program aims to ensure optimum therapeutic outcomes and reduced risk of adverse events for patients through improved medication use. The MTM program must be developed in cooperation with licensed and practicing pharmacists and physicians, provided by pharmacists or other qualified providers, and coordinated with any chronic care management plan. Drug plans must to describe the resources and time required to implement the MTM program and establish the fees for pharmacists or others providers.

The MTM program is required for patients who meet all of the following criteria: (1) have three or more chronic diseases, (2) are taking eight or more drugs, and (3) are likely to incur annual costs for Part D drugs greater than or equal to the

specified threshold (US$3919 in 2017). Medicare patients may decline to participate in the MTM program.

The MTM program requires performing an annual comprehensive medication review (CMR) and targeted medication reviews (TMRs) at least quarterly with follow-up interventions as necessary. The CMR is a "systematic process of collecting patient-specific information, assessing medication therapies to identify medication-related problems, developing a prioritized list of medication-related problems, and creating a plan to resolve them with the patient, caregiver and/or prescriber." The CMR must include an interactive, person-to-person, or telehealth medication review, and consultation of the medications (including prescriptions, over-the-counter (OTC) medications, herbal therapies, and dietary supplements) performed in real time by a pharmacist or other qualified provider with a summary of the results of the review and it may result in a recommended medication action plan [10].

The states are responsible for regulating pharmacies, pharmacists, pharmacy technicians, and pharmacy practice within the framework defined by the federal government. Each state's board of pharmacy is responsible for education, licensing, regulation, and enforcement aspects of the practice of pharmacy in the state. As a result, the practice of pharmacy and the role of the pharmacist in patient care change depending on the state.

The ownership and location of a community pharmacy are not regulated in the US. However, a pharmacy is required to have a pharmacist-in-charge and a licensed pharmacist must be on duty while the pharmacy is open.

All states mandate pharmacists to perform drug utilization review and offer patients or caregivers counseling during drug dispensing in order to improve proper use of drugs and maximize patient's outcomes; however, the language and requirements of counseling vary by state, but in general, counseling includes providing information about the purpose of the medication, directions for use, how to identify and how to proceed in case of occurrence of adverse effects, potential interactions and therapeutic contraindications, techniques for self-monitoring drug therapy, proper storage, refill information, and action to be taken in the event of a missed dose.

There are 12 states (Colorado, Idaho, Indiana, Iowa, Nebraska, New Jersey, North Carolina, North Dakota, Tennessee, Texas, Utah, Vermont) that have incorporated the concept of pharmaceutical care as part of the regulation of the role of the pharmacist. States use the concept of pharmaceutical care similar to the one described by the American Pharmacist Association "a patient-centered, outcomes oriented pharmacy practice that requires the pharmacist to work in concert with the patient and the patient's other healthcare providers to promote health, to prevent disease, and to assess, monitor, initiate, and modify medication use to assure that drug therapy regimens are safe and effective" [11].

Idaho, Illinois, New Hampshire, Oregon, West Virginia, and Wyoming have included in their regulation the MTM concept. In general, the states use the definition approved by pharmacy organizations and associations in July 27, 2004, that consider MTM as a "distinct service or group of services that optimize therapeutic

outcomes for individual patients" that encompasses "a broad range of professional activities and responsibilities within the licensed pharmacist's, or other qualified healthcare provider's, scope of practice" [12]. The scope of MTM services described by the states includes similar services than those mentioned by the Medicare Part D MTM requirements.

As of October 1, 2017, all states with the exception of Alabama have implemented collaborative practice agreements (CPAS). CPAs are a formal practice relationship between a pharmacist and a prescriber that specifies functions delegated to the pharmacist by a physician or, in some cases a nurse practitioner or other provider [13]. CPAs functions vary from state to state, and typically include authorizing pharmacists to initiate, modify, and discontinue drug therapy, and ordering and interpreting laboratory tests.

13.1.3 Pharmacists as a Provider in the US

The provision of patient care services has traditionally been an important role of the pharmacist in the US. Clinical pharmacy evolved in hospital pharmacy in the 1960s [14–18], and, later, expanded to outpatient clinics [19–21]. The traditional role of the community pharmacist included dispensing and consultation with prescribers and patients, and health education [22–24]. And some might argue that the diagnoses and recommendations for treatment of self-care issues that pharmacists have been engaged in since the days that pharmacists were apothecaries could be viewed as providing patient care services.

Unlike Physician's Assistants who work as providers under the direct supervisor and under the prescriptive authority of physicians, pharmacist works with physicians as providers in a collaborative fashion due to collaborative practice agreements. A collaborative practice agreement is a signed agreement between a physician or physicians with a pharmacist or pharmacists that allows the pharmacist to assess the patient's medication therapy and make changes to the therapy under certain restrictions such as the specific disease states and or medications.

As a way to create a systematic process of care, in 2014, the American Pharmacists Association and other stakeholders in the Joint Commission of Pharmacy Practitioners created the Pharmacists' Patient Care Process, 2014 [25]. Although this patient care process was created with medication therapy management in mind, it can be used for any patient care process that pharmacists are involved in. In general, the process has the patient at the center of the process and includes the broad components of collecting information, assessing the patient, creating a plan, implementing the plan, and monitoring and evaluating the plan via follow-ups with the patient (Fig. 13.1).

Currently, there are 38 states where pharmacists are designated as a provider in the state pharmacy code or Medicaid provisions [26]. Since pharmacists are not recognized nationally as providers, the American Pharmacists Association and over 40 other stakeholder groups have been working toward the passage of legislation

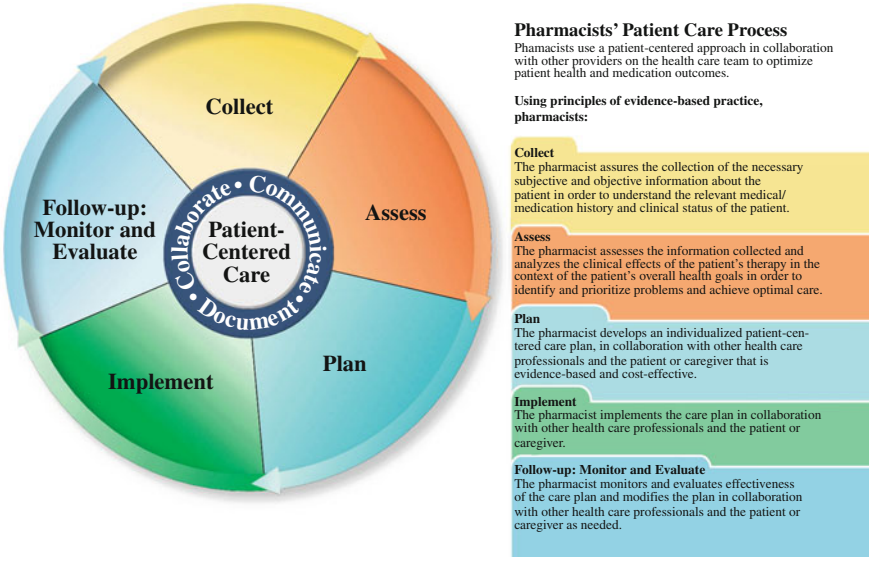

Fig. 13.1 The Pharmacists' Patient care process. *Source* Joint Commission of Pharmacy Practitioners, 2014

that would add pharmacists to the list of authorized providers in the United States Social Security Act. Although the listing of providers in the social security act is primarily for the purpose of determining who can be paid by Medicare and Medicaid for patient care services, the vision is that private health insurance companies would also follow suit and broadly allow pharmacists to get paid for their patient care services.

California has enacted legislation that created a new designation for pharmacist providers, called Advanced Practice Pharmacist (APh) [27]. As of August 10, 2016 pharmacists can be licensed as an APh in addition to the traditional RPh (Registered Pharmacist) designation [28]. An APh is allowed to perform patient assessments, refer patients to other providers, and operate as a collaborative drug therapy management pharmacist in collaboration with a physician. Additionally the APh's role includes the ability to initiate, modify, and discontinue medications.

13.1.4 US Bibliographic Review

Several large projects were conducted in the US to assess the effect of pharmaceutical care on patient care and outcomes. The Asheville Project was a payer-driven and patient-centered program launched in 1997 by the City of Asheville (North Carolina) to provide education and care management for city

employees, retirees, and dependents with chronic health problems including diabetes, asthma, hypertension, and high cholesterol [29]. The Asheville Project has been recognized as a healthcare model for management of chronic diseases. Patient care was provided by a team of primary care physicians, endocrinologists and other specialists, pharmacists, educators, and case managers with the support of data managers and administrators. Community pharmacists provided pharmaceutical care services in community pharmacies. Pharmacists accessed patients' health records from primary care physicians and communicated information back to physicians. The pharmaceutical care services provided in the Asheville Project resulted in improved patient outcomes, lower healthcare costs, fewer sick days, and increased satisfaction with pharmacists' services [30–32].

Project IMPACT teamed up community pharmacists, health clinics, and a mobile health unit to rural, underinsured people in the Appalachian Region of southwestern Virginia [33]. Pharmacists provided no cost patient education about diabetes, medications, and self-management strategies. Pharmacists enroll patients in the program, conduct a diabetes assessment, and identify knowledge gaps. During bimonthly meetings, pharmacists educate patients, record vital signs, and order lab tests. Pharmacists collaborate and communicate with other members of the healthcare team. The Project IMPACT has resulted in improved patient outcomes [34].

Additionally, several systematic reviews including mostly studies conducted in the US have been conducted. The results of those reviews have found that pharmacist care interventions improve health-related quality of life [35]; reduce medication underuse in older people [36]; clinical, and/or humanistic outcomes in patients from racial/ethnic minority groups [37]; As well as improvements in specific diseases such as hypertension, heart failure or diabetes [38–41]. However, those systematic reviews also found limitations in the studies assessing pharmaceutical care that may limit the applicability of the results of the studies [42].

Reviews examining the economic effects of pharmacist care interventions in the US found a positive effect on healthcare costs, however, the reviews also found substantial limitations in the studies' design and analysis [43–45].

13.2 Canada

13.2.1 The Community Pharmacist in Canada

In 2015, there were 9667 Canadian community pharmacies [46], representing one pharmacy per 3745 people. There were 37,265 pharmacists employed in the Canada in 2015 representing a pharmacist per 962 people.

US community pharmacies dispensed a total of 367 million prescriptions [47], with an average of 17.6 prescriptions per inhabitant and a total cost of $ 30,782 million in 2015. Community pharmacy expenditures represented 13.65% of Canada healthcare expenditures [48]. Public programs including federal and provincial

programs covered over 42.7% of the pharmaceutical expenditures in the country. The provinces and territories provide supplemental coverage for pharmaceuticals and other services and products not generally covered under the publicly funded healthcare system to certain groups of people, such as seniors, children, and social assistance recipients [49]. Those who do not qualify for supplementary benefits under government plans pay for pharmaceuticals through out-of-pocket payments and private health insurance plans.

Pharmacists are required to hold a baccalaureate degree in pharmacy accredited by the Canadian Council for Accreditation of Pharmacy Programs (CCAPP) or the US ACPE. The pharmacy program typically requires 2 years of pre-pharmacy studies and 4 years of professional pharmacy studies. To be licensed by a province, pharmacists must pass the Pharmacy Examining Board of Canada (PEBC) Qualifying Examination, and the province's practice-based assessment and jurisprudence examination organized by the province's college of pharmacists. Pharmacists must also complete several of hours of continuing education each year.

13.2.2 Canada Regulation of Pharmaceutical Care

The Federal government is responsible for the regulation of pharmaceuticals, medical devices, and other health-related consumer products. The federal government regulates pharmaceutical products and the use of controlled drugs and substances [50].

The regulation of the practice of pharmacy corresponds to the provinces. The scope of activities, regulations, training requirements, and limitations differ between provinces [51]. The college of pharmacists is the registering and regulating body for the profession of pharmacy in the province. The colleges enforce the legislation, standards of practice, code of ethics, and policies and guidelines relevant to pharmacy practice. The college also ensures that pharmacies within the province meet certain standards for operation and are accredited by the college. Pharmacy ownership is not restricted to pharmacists and there are no restrictions to the establishment of a pharmacy in the country.

Several provinces have granted prescriptive authority to pharmacists to initiate and managed drugs that require a prescription for sale following the diagnosis and professional intervention of a prescriber (schedule 1 drugs) with the exception of controlled drugs (Fig. 13.2). Pharmacist initiation of schedule 1 drugs may be independent (Alberta) or through collaborative agreements (Alberta, Manitoba, New Brunswick, Nova Scotia, Saskatchewan); for minor ailments/conditions (Alberta, Labrador, Manitoba, New Brunswick, Newfoundland, Nova Scotia, Prince Edward Island, Quebec, Saskatchewan); for smoking/tobacco cessation therapies (Alberta, Manitoba, New Brunswick, Labrador, Nova Scotia, Prince Edward Island, Quebec); or in an emergency (Alberta, Manitoba, New Brunswick, Nova Scotia, Prince Edward Island, Saskatchewan). Pharmacist adaptation or management of schedule 1 drugs may be independent (Alberta) or thought collaborative agreements

Fig. 13.2 Pharmacists' scope of practice in Canada. *Source* Canadian Pharmacists Association. Pharmacists' Scope of Practice in Canada. December 2016

(Alberta, Manitoba, New Brunswick, Nova Scotia, Saskatchewan); allow therapeutic substitution (Alberta, British Columbia, Labrador, New Brunswick, Nova Scotia, Prince Edward Island, Saskatchewan); permit changes in drug therapy including dosage, formulation, regime, among other (all with exception of Northwest Territories and Nunavut Yukon); and renew or extend the prescription to ensure continuity of care (all with exception of Nunavut and Yukon). In some provinces, pharmacists can also order (Manitoba) or order and interpret lab tests (Alberta and Quebec). And, while Nunavut and Yukon do not allow pharmacists to provide any of the above services, it should be noted that these provinces account for the smallest Canadian populations at only 0.1% or 36,000 people each.

13.2.3 Pharmacists as a Provider in Canada

Pharmacists in Canada have been providing disease state management and pharmaceutical care services since the late 1990s, and have been expanding their roles ever since. Although there are no initiatives underway to have Canadian pharmacists classified as providers, survey research does show that consumers view pharmacists as healthcare professionals. This 2014 survey of 380 respondents in

Newfoundland and Labrador found that 90% of responders felt that pharmacists were healthcare professionals just like nurses and doctors, and only 10% felt the main role of pharmacists was counting pills [38].

In 2009, the Canadian Society of Hospital Pharmacists approved the statement, "CSHP Advocates prescribing by pharmacists in the provision of high-quality, patient-centered care that is safe, effective, and accessible" [52].

The MedsCheck program in Ontario is a government program similar to the Medicare Part D MTM program in the United States. It is defined as "a one-on-one interview between the pharmacist and the patient to review the patient's prescription and nonprescription medications. The MedsCheck medication review will encourage patients to better understand their medication therapy and help to ensure their medications are taken as prescribed and that patients are getting the most benefit from their medications." MedsCheck is a voluntary program for Ontario residents, with a valid Ontario Health card, who are currently taking three or more prescription medications a chronic condition. These patients are eligible for one annual review, and for a follow-up review within the year if they have a planned hospital admission or were recently discharged, based on a referral from a physician or nurse practitioner, or if the pharmacist determines there is need for a follow-up visit due to changes in the patient's medication profile, evidence of patient noncompliance, or if the patient has transferred their prescriptions to a different pharmacy due to changing their place of residence [53].

13.2.4 Canada Bibliographic Review

Provinces have implemented pharmaceutical care programs in community pharmacy. In 2007, the Ontario launched MedsCheck a government-funded, community pharmacy-led medication review program for patients taking three or more chronic prescription drugs. The purpose of the program is to improve patients understanding of their drugs and appropriate use [54]. In 2016, Nova Scotia has implemented a community pharmacy medication review program reimbursed by the publicly insured seniors' drug benefit program [55]. Since 2007, pharmacists have been working with family physicians and other healthcare professionals as part of the North York Family Health Team to provide pharmaceutical care for patients in Ontario [56].

Pharmacist care interventions in Canada have resulted in increased uptake of immunizations [57], and improve chronic diseases adherence, outcomes, and costs [58–63].

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Chapter 14
Pharmaceutical Care in Europe

Filipa Alves da Costa

Abstract This chapter focuses on pharmaceutical care provision in Europe. It describes the pharmacy structure, pharmacists' workforce and research in pharmacy practice in Europe, while highlighting selected countries with particularities. The diversity of pharmacy services, their complexity, and their influence on the evolution of more structured services is explored. There is a tendency for a greater uptake of simpler services like medication review (type I) with a greater difficulty in establishing long-term care that requires interprofessional collaboration. Examples of milestone research studies are given due to their influence on service provision. The progressive spread of pharmaceutical care from central and northern Europe to south and more recently to eastern countries is also briefly mentioned. The influence of incentives, such as legal recognition, professional collaboration, and remuneration for service provision, has been mentioned contextually, as described in Fig. 14.1. However, it should be noted that the role of the citizens as an engine determining successful implementation has not been explored (see Chap. 3). Similarly, the theoretical influence of the illustrated boxes is not detailed in this chapter (see Chap. 18).

Keywords Pharmaceutical care · Europe · Pharmaceutical services
Medication review · Remuneration

14.1 Pharmacy Practice in Europe

Pharmacy practice may be defined as the act of delivering products and services in a pharmacy by any member of staff.

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Good pharmacy practice (GPP) is defined as "*the practice of pharmacy that responds to the needs of the people who use the pharmacists' services to provide optimal, evidence-based care. To support this practice it is essential that there be an established national framework of quality standards and guidelines*" [1].

Currently, in a European pharmacy, we may find the traditional services focused on the product, where the pharmacist's role is mainly to produce or eventually trade the pharmaceutical, while ensuring the formulation is correct, and the dose and route are appropriate to treat a medical indication. Then, we may find the more patient-centered services which encompass a vast range of services, which will depend not only on the legislation in place but also on the incentives for implementation. These may be classified using different definitions. The Pharmaceutical Group of the European Union (PGEU) is an international association whose members are national associations and professional bodies of community pharmacists from 33 European countries. PGEU aims to advance the contribution of community pharmacists to the healthcare system working through legislative and policy initiatives. The PGEU in 2010 proposed a three-level classification of pharmacy services [2]:

- Core services: essential services provided by all licensed pharmacies during core pharmacy opening hours;
- Basic services: may require separate consultation facilities and special training of pharmacy staff; may need to be available outside core pharmacy opening hours; and
- Advanced services: require separate consultation facilities in the pharmacy and accredited pharmacists to provide it.

Examining sequentially these annual reports issued by PGEU, it becomes quite clear that the core services are easier to implement and disseminate. Surely, every pharmacy in all European countries will dispense prescriptions. In the majority of countries, night services and disposal of medicines are also available. The measurement of biomarkers is another service also consistently reported as implemented in the majority of European countries, although with varying numbers according to the parameter considered (e.g., weigh measurement, blood pressure, glycaemia, etc.) [2–6]. Smoking cessation has also progressively been spreading as a pharmacy service in Europe [6].

14.2 Community Pharmacy Structure

Pharmacies do not look the same in all Europe or are even homogenous within the same country. The legal framework of the country may impose restrictions applicable to the ownership, geographic location, and number of inhabitants served by a pharmacy, minimum areas for the pharmacy to be set, for services, medicines, and products allowed to be made available and even to the professions allowed to work within pharmacies. The variation is enormous within such a small continent and very well portrayed in PGEU reports. In all Europe, you may find prescription-only

medicines, over the counter medicines, medical devices, and cosmetics [7] and in the vast majority, pharmacy-only medicines. Ownership is restricted to pharmacists in an insignificant number of countries (e.g., Spain), although the presence of a supervising pharmacist is compulsory. This pharmacist's role is to supervise all members of staff, to ensure they are adequately trained to provide a good service to the population and to supervise the premises and the enforcement of the legal framework. In most countries, the staff is restricted to pharmacists and pharmacy technicians, although in a few countries there are allied healthcare professionals.

The term community pharmacy arises historically from the idea of having a pharmacy to serve one community of citizens, deeply embedded in the idea of its major focus being disease prevention and primary care provision. However, not in all countries is the location of pharmacies restricted to communities. In some areas, you may find pharmacies in healthcare centers, in suburbs, or in shopping centers. Also, currently in most countries you may have independent pharmacies and chain pharmacies. In restricted countries, there are virtual chains of pharmacies, which maintain their independent ownership but gather to have more benefits in procurement of medicines or even on standardized service implementation. According to GPP, pharmacies should all have an inviting atmosphere, look professional, and be health-oriented.

14.3 Implemented Services

Some services have been important marks for good pharmacy practice in Europe. These are services that may arise only in one country and never be implemented in neighbor countries. They may even have been interrupted in the original country for various barriers encountered. However, they indirectly contribute to the advancement of pharmacy practice in general and to pharmaceutical care in particular, and are therefore worth highlighting.

Service name, (country where it originated)	Brief description of the service
Disease-based pharmaceutical care programs (Portugal)	Programs targeted at patients with specific chronic conditions, where the pharmacist is continuously responsible for detecting, preventing, or solving DRPs, but also engage in related activities that optimize medication use, such as health education, instruct on the use of medical devices, or promote self-management and medication adherence. Existing for three groups: asthma/COPD, diabetes, and hypertension/hyperlipidaemia
Quality Circles (The Netherlands)	Peer review and quality circles are a method for quality improvement in primary care that involves organizing meetings of small groups of pharmacists and physicians (most frequently, but not always) to discuss what activities can be implemented to improve patient care.

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Service name, (country where it originated)	Brief description of the service
	These may encompass overarching activities such as pharmaceutical care for chronic patients or take on a more specific focus such as improving the quality of prescribing in upper respiratory tract infections
Medicines Use Review (United Kingdom)	Service intended mainly for patients on medicines for long-term conditions, targeting first polypharmacy. The pharmacist reviews the patient's use of medication, focusing on patient's understanding of medicines use and reasons for their need. Pharmacists seek to identify any problems and act upon them and, when necessary, provide feedback to the prescriber. The term MUR comes from the UK, but medication review per se may exist in various formats with slight or major differences elsewhere
Polymedication check (Switzerland)	Service targeted at polypharmacy patients which is considered a level II medication review [8]. If adherence issues are detected, the patient may be referred for another service, e.g., the dose administration aid system (blister pack)
New Medicines Service (NMS) (United Kingdom)	Service intended for people with long-term conditions newly prescribed a medicine. The service aims to improve medication adherence, particularly persistence and patient outcomes. Generally organized according to disease subgroups (e.g., NMS type 2-diabetes). The pharmacist provides an in-depth first counseling to instruct the patient on medicines use, and then follows up potentially arising barriers and monitors medicines use at 1 week and periodically during the first 2 months
Pharmacist Prescribing (United Kingdom)	The possibility for pharmacists to prescribe medicines exists under two formats: independent prescribing and supplementary prescribing. The first assumes that the healthcare professional prescribing must have also the responsibility (and ability) to assess the patient who does not have a medical diagnosis established and decides on the necessary clinical management. The act of supplementary prescribing (formerly known as dependent prescribing) assumes that a diagnosis has been established and serves the purpose of ensuring continuity of care. One possible format is by renewing the prescription, albeit with the autonomy to adjust dose or dosage form to meet patients' needs. The intention of this service if also to increase access to medicines. In the UK, pharmacists (and nurses) can prescribe any drug (including controlled) as long as a clinical management plan exists. This plan is established with the patient and with the independent prescriber

14.4 Medication Review in Europe

Medication review (MR) is integral to pharmaceutical care (see also Chap. 7). It has been defined by Pharmaceutical Care Network Europe (PCNE) as a *structured evaluation of patient's medicines with the aim of optimizing medicines use and improving health outcomes. This entails detecting drug-related problems and recommending interventions* [9]. Medication review may be provided in three main levels depending on the sources of information available: The Simple MR or PCNE Type 1 (based on the available medication history in the pharmacy), the Intermediate MR or PCNE Type 2A (when the patient can be approached for information) or 2B (if GP information is also available), and the Advanced MR or PCNE type 3 (based on medication history, patient information, and clinical information). Obviously depending on the type of information available, the problems possible to detect vary.

14.4.1 Value of Medication Review

A recent review focusing on service provision in nursing homes, including eight studies, suggested that the service had a positive impact on the identification of drug-related problems and on the appropriateness of medication but neutral or negative impact on the remaining outcomes evaluated [10]. Medication review may be provided in various settings, an aspect dealt with in Chap. 7, and should not be confused with pharmaceutical care. As detailed in Chap. 1, medication review may be considered one component of pharmaceutical care, but pharmaceutical care is more than that. Pharmaceutical care has two core components: the involvement of the patient and the continuity of care. None of these is compulsory in all types of medication review. Therefore, it is not surprising that pharmaceutical care is much more difficult to implement and disseminate and ultimately to generate evidence of positive patient outcomes.

14.4.2 Implementation of Medication Review in Europe

In 2014, quite a comprehensive study was published where the implementation of the service in various European countries was reported [11]. This study reports on the findings from 16 countries, indicating that medication review is spread in the community setting in 9 and 11 countries, for levels I and II, whereas level III was just reported for 6 countries. Overall, in the outpatient setting, one may expect to find at least one modality of medication review in more than 80% of the countries surveyed. Worth remarking that the three countries where the service was reported as inexistent in the community setting, it was reported for the hospital setting (in

France, Latvia, and Iceland). Some limitations of this study that ought to be mentioned are the restricted sample but also the mailing list used, which arose from PGEU, a political organization, hence reporting bias cannot be disregarded. In fact, according to this same organization, in 2016, there were 13 countries providing medication review as a service whereas in 2017, 100% of the countries reported to provide MR type 1 and 53% MR type 2 [12]. Worth noting that the universe judged by the PGEU, albeit not reported, should encompass 33 countries. The sample is obviously more robust but the respondents again have vested interests in the information broadcasted. Additionally, in all these data sources, we only have access to the reported service provision in the country, but is unknown if the service is locally or nationally implemented. Bulajeva and colleagues tried to explore this aspect but found limited information [11].

14.5 The Effect of Pharmaceutical Care in Europe

Pharmaceutical care is the pharmacist's contribution to the care of individuals in order to optimize medicines use and improve health outcomes, as presented in Chap. 1 of this book. It is therefore depending on the legal framework, either a basic service or an advanced service. In most countries, pharmaceutical care is exclusively provided by pharmacists, who are advised to undergo special training to provide a high-quality service. However, the explicit demand to have an independent accrediting body who will attest the pharmacist's competence to provide the service is not that frequent.

Pharmaceutical care may be named differently in various European countries and sometimes even within the same country at different time periods. This fact makes it more difficult to have an overview of the benefit of services or even of the implementation.

Various systematic reviews have been published in the last decade referring to the value of pharmaceutical care. The service may be named slightly different but when comparing the service characteristics, they are often quite similar although perhaps provided in another setting. This is the case for clinical pharmacy, a concept more commonly used in hospital pharmacy.

Author, year	Term used	Number of studies included	Outcome and conclusion
Nkansah et al. [13]	Outpatient pharmacists' non-dispensing roles: patient counseling, **therapeutic management**, health professional education	43 RCTs	Improved prescribing patterns of physicians

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Author, year	Term used	Number of studies included	Outcome and conclusion
Ryan et al. [14]	Interventions to improve safe and effective medicines: medication review, **medication management**, disease self-management, educational programs	75 systematic reviews	Improved medication use; increased knowledge; reduced mortality
Rotta et al. [15]	**Clinical pharmacy** services	49 systematic reviews	Services focusing on specific medical conditions (e.g., diabetes) showed a positive impact on patient outcomes. The results were inconclusive for other medical conditions

One study worth highlighting, although not a systematic review, is the PINCER trial, which involved nearly 500,000 patients and showed that a pharmacist-led information technology-based intervention had a 95% probability of being cost-effective, which is a fundamental aspect to consider when deciding if a new service is worth upscaling [16]. The service delivered in this study focused on the prevention and correction of three specific drug-related problems and suggested each error avoided saved 95€.

Optimizing medication use is the core of pharmaceutical care, which is achieved by monitoring the occurrence of drug-related problems, which must be prevented or solved by an appropriate intervention, whenever considered that these will benefit the patient's health outcomes. To provide such service, normally pharmacists in Europe use a drug-related problems classification and there are various available, as explored in Chap. 2 of this book. Counseling and other promotion activities mentioned in previous chapters will also contribute to achieve optimal medication use.

14.5.1 Research Conducted Around Pharmaceutical Care Implementation and Practice in Europe

Pharmaceutical Care Network Europe (PCNE) is a research-based organization that joins experts in pharmaceutical care to periodically discuss ways to positively influence practice through research. When this organization was established, one of the initially multicentred projects developed was the OMA (Elderly Medication Analysis) study [17]. This project involved 7 countries in Europe and was set as a controlled trial involving roughly 200 pharmacies monitoring around 2500 elders during 18 months. The most positive outcomes reported were cost savings, and patients' and providers' satisfaction. Additionally, considering this happened at the

end of the 90s, the most important "side effect" was that it created the need for community pharmacists to establish links with the GPs and to initiate collaborative work to rationalize and optimize pharmacotherapy, leading to practice change at least in the participating countries (Northern Ireland, Ireland, Denmark, Germany, Portugal, the Netherlands, and Sweden). However, the sustainability of the interventions was, as in most research studies, limited. Different formats of service provision centered on the elderly and polypharmacy have ever since developed in some of these countries, namely, in Germany, Northern Ireland, and the Netherlands, adopting different names, structures, and even settings (see Chaps. 7 and 26).

Around the same time, the TOM study was initiated. TOM was an acronym created for Therapeutic Outcome Monitoring, which was a model first defined by Hepler for increasing pharmacists' role in primary health care. TOM was based on a continuous quality improvement system applied to pharmaceutical care to detect, prevent, and resolve DRPs in asthma patients. This project was conducted as a controlled intervention study (grouped at the pharmacy level) and focused on medicines optimization for asthmatics, involving close cooperation between pharmacists, GPs and patients. Austria, Belgium, Canada, Denmark, Florida (US), Germany, Iceland, Northern Ireland, and the Netherlands were involved, although some countries reached better results than others. In Denmark, for example, 500 patients were involved and positive outcomes were shown in symptom control, days of sickness, and health-related quality of life [18]. The consumption of β2-agonists decreased aside with corticosteroid increase, suggesting improved asthma treatment [19]. These research projects were important to lead practice, and the TOM project in Denmark is an excellent example of a research initiated service that later culminated in regular service provision, although using a modified structure. Currently, in Denmark, the Inhalation Technique Assessment Service (ITAS) is provided nationwide and remunerated at 8.5 €/session [20]. The service spread to neighboring countries, and currently also exists in Norway with similar implementation level and fee for service. ITAS also exists in the Netherlands.

Simultaneously, the TOMCOR project also developed in Spain, involving over 80 pharmacies and using a similar approach directed at coronary disease patients [21].

The structural aspects of pharmacies, the education, and training of pharmacists and even the social, economic, and political context of the different countries have led to different speeds for service uptake. A series of papers describe the services provided in a selected number of countries around the world, focusing on pharmaceutical care practice, education, and research [22]. Around the same time, an overarching paper describing pharmaceutical care in Europe and focusing on community pharmacy highlighted that in 2006 already pharmaceutical care was included in contracts with insurers, although remuneration was still very limited [23]. A barrier to implementation highlighted at the time was the lack of interprofessional collaboration, often arising during education. A facilitator for implementation was then considered the specialization in a given disease area, which perhaps led to the developments observed in various countries, where disease-led pharmaceutical care programs have become more common.

Nearly a decade later, a survey conducted in 19 countries described the healthcare functioning, education, and training of pharmacists and the state of implementation of various services in pharmacy practice. This study showed that the UK was the country with the widest range of defined services available, including pharmacists prescribing, the sole service unavailable in Portugal. Fourteen countries reported to have pharmaceutical care programs implemented, representing 74% of the sample. Medication review was only reported by 12 of these countries (63%) [7].

In 2006, a PCNE initiated multicentred study led by the University of Belfast was set to assess the provision of pharmaceutical care, using the Behavioral Pharmaceutical Care Scale (BPCS) [24]. The study involved 14 countries and findings suggest a limited provision of pharmaceutical care in Europe. The country attaining the highest score was Ireland. Of notice was the fact that countries where pharmacists were supported by other healthcare professionals in their daily activities, like Ireland or England, higher scores were achieved on the referral and consultation domain. It is worth acknowledging that results may be biased since the survey emerged from one specific healthcare model.

Around 10 years later, this group reassessed the situation in Europe using the same measurement scale in 15 countries and reported that for countries participating in both studies (n = 8) there was a slight but significant improvement in the implementation level. The two countries highlighted as having achieved a more remarkable evolution were Denmark and Switzerland. Additionally, the authors also commented on the wider country uptake. Considering the overall sample, the lowest score was this time found in Moldova and the highest in Switzerland. The trends observed in country distribution suggest countries more recently joining Europe are at a later stage of implementation, i.e. the laggards. There also seem to be clusters of pharmacy practice within Europe with various degrees of differentiation of services, particularly in patient-centeredness. However, it was concluded that the speed of implementation was lower than expected and could be further motivated by external triggers such as remuneration [25]. In fact, remuneration of pharmaceutical care which has been frequently mentioned as a facilitator for implementation has been achieved partly or in full at least in the Netherlands, Switzerland, Germany, and Great Britain. It was once also reported in Portugal, but no longer active.

Acknowledging the varying economic and political context in Europe, and the limitations in previous studies published, the PRACTISE study (*PhaRmAcist-led CogniTIve Services in Europe*) was initiated in 2016 by a working group within PCNE [26]. This project intended to update and explore the existing information on service implementation in Europe and to investigate the associated remuneration for service provision. Remuneration of interest was of a third-party payer, excluding out-of-pocket payments by patients. Preliminary data suggests that the level of implementation varies widely between countries and within each of the countries. The complexity of services seems to be inversely related with the level of implementation, implying core services are implemented in 23–100% of countries in Europe, whereas advanced services range from 3 to 53% of surveyed countries [27].

Although the refinement of data through consensus is ongoing, preliminary analysis suggests that pharmaceutical care may be implemented in 15 countries, representing 44% of the surveyed sample. Worth acknowledging that probably not all respondents understand the essential cornerstones of pharmaceutical care, as defined in this book. The majority considered pharmaceutical care to be an independent service (n = 9), whereas the remainder considered it as part of regular dispensing (n = 6). This may relate to the understanding of the terminology, the legislation in place, and also the existence of a separate fee for service provision.

Reporting PhCare as a separate service	Reporting PhCare to be part of dispensing	Reporting not to have PhCare
Austria	Albania	England[a]
Croatia	Belgium	Estonia
Denmark	Bulgaria	France
Germany	Finland	Georgia
Portugal	Hungary	Iceland
Slovenia	Ukraine	Ireland
Spain		Kosovo
Sweden		Latvia
The Netherlands		Luxembourg
		Macedonia
		Malta
		Northern Ireland
		Norway
		Poland
		Romania
		Serbia
		Slovakia
		Switzerland[b]
		Turkey

[a]MUR is a commissioned service defined differently, but which could be considered as part of pharmaceutical care

[b]Polymedication check is a service intended for improving medication use that may be considered to fit into pharmaceutical care but having particularities

14.5.2 Policy and Practice Around Pharmaceutical Care in Europe

The extent to which pharmaceutical care has been embraced by the different governments in Europe varies widely. In some countries, pharmaceutical care is officially recognized in the legislation, like in Spain or in Portugal. However, that does not imply that the service is structured or standardized, provided continuously and

aiming to detect drug-related problems to optimize patients' outcomes. Also, law recognition does not imply that pharmaceutical care is understood in all Europe as an advanced service, exclusively provided by accredited pharmacists. In some countries, the approach to pharmaceutical care suggested by Strand et al. is used, defined as a practice that encompasses various activities contributing to an improved use of medicines, such as pharmacovigilance, information provision, and adherence programs, to name a few. Interpreting pharmaceutical care as a philosophy where the pharmacist is held accountable for therapy outcomes implies that legal recognition is needed to protect pharmacists from falling into a vulnerable situation. Drug-induced hospitalizations are well documented and mostly preventable.

Service delivery, improvement, and implementation follow different paces, and can be of different qualities. Conscious of that, a policy document has been proposed by the European Directorate for the Quality of Medicines & HealthCare in 2012, intended to capture very general pharmaceutical care indicators, so that they could be used in low-, middle-, and high-income countries and for both community and hospital pharmacy [28]. With the help of these indicators, the implementation level of the quality of care in pharmacy can be monitored. The four basic indicators are number of pharmaceutical care interventions delivered, number of patients counseled about their medicines, number of formal written feedback responses from patients during treatment, and number of adverse drug event reports.

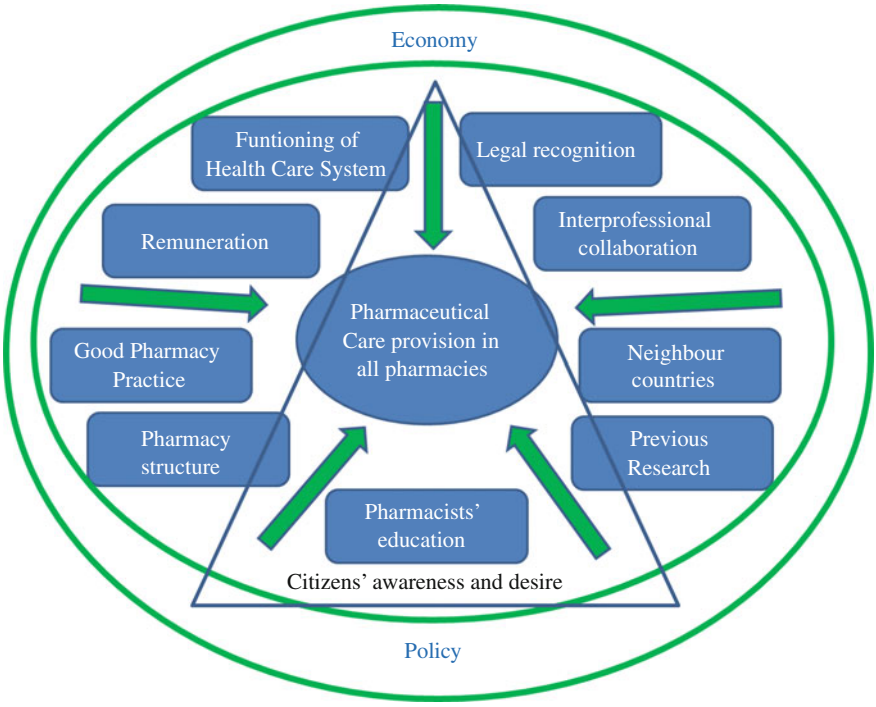

Fig. 14.1 Summary illustration of concepts described in this chapter

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Chapter 15
Pharmaceutical Care in Australia and New Zealand

Timothy F. Chen and Prasad S. Nishtala

Abstract Since the 1990s, pharmacists in Australia and New Zealand have had a strong tradition for providing pharmaceutical care in the form of innovative and advanced patient-focused clinical pharmacy services. The services have been developed over the years by academic pharmacists in collaboration with professional pharmacists' organizations such as the Pharmaceutical Society of Australia (PSA), Pharmaceutical Society of New Zealand (PSNZ) and the Pharmacy Guild in both countries (PGA and PGNZ). These organizations also support pharmacists in the implementation of pharmaceutical care services, such as medication management review and chronic disease management and counseling activities.

Keywords Pharmaceutical care · Australia · New Zealand · Pharmaceutical services · Services implementation

15.1 Community Pharmacy Structure in Australia and New Zealand

Pharmacists in Australia and New Zealand are key members of the health care workforce and can provide services across a number of settings which include community pharmacy, hospital pharmacy (both public and private systems), consultant pharmacy, aged care facilities (nursing homes), government and non-government organizations, industrial pharmacy and academia. The professional roles of pharmacists can vary across different practice settings but include the dispensing of prescription medicines, provision of medicines information, provision of primary care such as advice on management of minor and other illnesses, facilitation of consumer self-care, provision of professional cognitive pharmaceutical services

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(e.g., Home Medicines Review [HMR], Residential Medication Management Review [RMMR]), research and the development of health and medicines policy, amongst others.

There are more than 27,000 practicing registered pharmacists in Australia and about 3500 registered pharmacists and 1200 technicians employed in various practice settings in New Zealand. The majority of registered pharmacists work in primary care in community pharmacy. The network of community pharmacies is extensive, with approximately 5500 sites across Australia. With a current population of over 24 million, this means that each community pharmacy serves approximately 4400 persons, on average. Each year, approximately 300 million prescription items are dispensed, with most prescriptions written by general medical practitioners. Similarly, in New Zealand, approximately 73% of pharmacists work in the community, and based on the national pharmaceutical collections extract supplied by the Ministry of Health of New Zealand, approximately 43 million government funded prescriptions were dispensed in 2016.

The PSA and the PSNZ are the major professional organizations which represent pharmacists and oversee the scope of practice in both countries. These organizations are key providers of professional development and assessment, practice support and tools, and programs for pharmacists and pharmacies, amongst other roles. One significant contribution of the PSA is the authorship and publication of key documents to support pharmacists such as the Code of Ethics for Pharmacists and the National Competency Standards Framework for Pharmacists in Australia [1]. In New Zealand, the Pharmacy Council of New Zealand (PCNZ) also publishes practice standards and guidelines for pharmacists, Code of Ethics 2011 and frameworks and competency standards for medicines management [2].

The Pharmacy Guild of Australia (PGA) and the Pharmacy Guild of New Zealand (PGNZ) provide support and services to community pharmacy owners. The PGA has had a major role in negotiating five year agreements with the commonwealth government, known as Community Pharmacy Agreements. Similar to Australia, the PGNZ provides leadership and negotiates contract with District Health Boards (DHBs) and the Pharmaceutical Management Agency (PHARMAC). PHARMAC is the crown entity that decides funding of pharmaceuticals in New Zealand.

In addition, to assist in maintaining professional competence and development, the Pharmacy Board of Australia requires all registered pharmacists to complete 40 Continuing Professional Development points (40 CPD points) on an annual basis. Importantly, half of the CPD points must be categorized as Group 2 (knowledge or skill improvement with assessment) or Group 3 (facilitation of quality or practice improvement) activities, with the remainder as Group 1 (information without assessment) activities. In New Zealand, pharmacists applying for recertification must be enrolled in a recertification program, complete 20 points per year and 70 points per three year learning cycle. At least 10 points per three years must come from completing two significant learning goals (Group 3) [3].

15.2 Implemented Services

Australian and New Zealand pharmacists have had a strong tradition for providing innovative and advanced patient-focused clinical pharmacy services for past three decades. Many of these services have stemmed from university practice-based research in collaboration with professional pharmacy organizations such as the Pharmacy Guild of Australia, Pharmaceutical Society of Australia, Society of Hospital Pharmacists of Australia, Pharmaceutical Society of New Zealand and The Pharmacy Council of New Zealand.

Under the current 5-year Community Pharmacy Agreement (6th CPA 2015-2020), a variety of professional pharmacy services have been implemented in Australia [4]. These include, but are not limited to the following:

- Dose Administration Aids (DAA)—DAAs are used to facilitate medication adherence. They are sealed, tamper-evident device that allows individual medicine doses to be organized according to the prescribed dose schedule.
- Clinical Interventions—are designed to improve the quality use of medicines by identifying and resolving drug-related problems, usually at the point of dispensing medicines, in community pharmacy.
- Staged supply of medicines—occurs when the pharmacists dispense medicines in smaller quantities than usual (e.g., daily, weekly) to facilitate medication adherence and improved medication safety. The service is designed for consumers with a mental illness, or drug dependency or who have difficulty in managing their medicines safely. Medicine classes include benzodiazepines, antidepressants and analgesics.
- Medication Management Review—these services include Home Medicines Review (HMR), Residential Medication Management Review (RMMR). HMR and RMMR will be described in more detail later in this chapter.
- MedsCheck and Diabetes MedsCheck. These services are designed to facilitate the quality use of medicines and minimize adverse drug events. MedsCheck and Diabetes MedsCheck are in-pharmacy medication review services which focus on a brief consumer-focused review of the medication regimen, and the provision of education and self-management.
- Rural Support Programs—are designed to improve access to medicines and services for people living in rural and remote regions of Australia.
- Aboriginal and Torres Strait Islander Specific Programs—are culturally appropriate services designed to facilitate the quality use of medicines by Aboriginal and Torres Strait Islander consumers.

Specific implemented services in New Zealand include:

- Pharmacist prescribing—Pharmacist prescribers can work collaboratively in multidisciplinary teams' providing services in either primary or secondary care.
- Medicine use review and medication therapy assessment: In 2006, the Pharmaceutical Society of New Zealand (PSNZ) formulated a framework devised by a reference group for consumers, public health organizations, general

practice, community pharmacy, and Maori and Pacific peoples to promote cognitive services. The cognitive services in the order of complexity included Medicines Use Review and Adherence Support, Medication therapy assessment and comprehensive medication review services. In alignment with NZPHCS strategy these services are entrusted to public health organizations (PHOs') to deliver and maintain the aforementioned services.

- Immunization services: Pharmacists in New Zealand are uniquely placed to provide immunization services after completion of a vaccinator training program. Pharmacists must meet the same immunization and quality standards of the Ministry of Health similar to other vaccinators delivering this service. In a new initiative, supported by the Ministry of Health, from 1 April 2017, suitably trained pharmacists are able to provide funded influenza vaccination to pregnant women and older people (aged 65 and over).
- Long-term care services: Registered pharmacists in New Zealand play a key role in recruiting patients into the Long-Term Condition services and are helping optimizing medicines in this high-risk group.
- Anticoagulation management services: Community pharmacists in New Zealand provide anticoagulation management services to a high-risk population requiring anticoagulation services.
- Rheumatic fever prevention program: Registered Pharmacist's in New Zealand also participate in the Rheumatic Fever Prevention Program, whereby pharmacists take throat swabs and provide antibiotic treatment for high-risk populations for rheumatic fever.
- Smoking cessation program: Community pharmacists in New Zealand have also played key roles in smoking cessation program.

15.3 Interprofessional Activities in Australia and New Zealand

At the organizational level, the PSA and PSNZ both support an interprofessional approach to the provision of pharmaceutical care. Indeed, for many professional cognitive pharmaceutical services, close collaboration with other members of the health care team is essential for their effective implementation. In Australia, medication management review services (i.e., HMR, RMMR) are key examples for which interprofessional communication is essential [5–7]. Another approach supported by the PSA is the co-location pharmacists within general practice clinics [8].

In New Zealand, the PSNZ and the New Zealand Medical Association (NZMA) have developed a framework model for pharmacists and general medical practitioners to work in multidisciplinary teams with a view to providing integrated, person-centered care for consumers [9].

In addition, New Zealand is the first country in the Asia Pacific to train specialist pharmacists, working in a multidisciplinary clinical health teams, to prescribe

medicines. Registered pharmacists with extensive clinical experience undertake a postgraduate training certificate course in prescribing, and then register as prescribers with the Pharmacy Council of New Zealand. In 2013, the New Zealand legislation under the Medicines Regulations allowed pharmacists to prescribe. Pharmacist prescribers can work collaboratively in multidisciplinary teams providing services in either primary or secondary care. Pharmacist prescribers are part of multidisciplinary health care teams, and contribute to patient care as well reduce burden on general practitioners. Pharmacist prescribers in secondary care play a key role in reducing medication errors particularly during transition of care from secondary to primary where risk of medication errors at hospital discharge are likely to occur.

At the curriculum level, The Australian Pharmacy Council (APC) is the authority that accredits pharmacy education and training in Australia and New Zealand. Specifically, the APC has the role of accrediting all registerable pharmacy degrees across all schools of pharmacy in both countries (n = 20 universities). Importantly, one of the six learning domains evaluated, Learning Domain 5: Health care systems and the roles of health professionals, has a focus on interprofessional collaboration. It specifically states that interprofessional communication, teamwork and collaborative decision making be included in all curricula. Hence all accredited degree programs must contain elements in their curricula which specifically address interprofessional activities. As an example, The University of Sydney offers a mandatory flagship interprofessional learning activity for all health discipline students (e.g., pharmacy, medicine, nursing, dentistry, physiotherapy, occupational therapy, speech pathology, diagnostic radiography, exercise physiology, nutrition and dietetics) which provides all students with an opportunity to work together in small interdisciplinary teams to solve an authentic complex case study [10].

15.4 Pharmaceutical Care in Australia and New Zealand

Although there have been numerous definitions and descriptions of pharmaceutical care published in the literature, the most well recognized definition of pharmaceutical care was proposed by Hepler and Strand in 1990. They defined pharmaceutical care as “the responsible provision of drug therapy for the purpose of achieving definite outcomes that improve a patient’s quality of life”. In 2013, following a process of expert consensus, PCNE redefined pharmaceutical care as “the pharmacist’s contribution to the care of individuals in order to optimise medicines use and improve health outcomes.” See also Chap. 1. Although the term “Pharmaceutical Care” is not universally used or recognized by health care professionals or consumers in either Australia or New Zealand, the professional role of pharmacists in optimizing medicine use with the goal of improving health outcomes is well established in both countries and embedded within university curricula. Hence the PCNE definition of pharmaceutical care forms the basis for this section.

15.4.1 Counseling About Medicines in Australia and New Zealand

Counseling patients about their use of medicines is a core role for community pharmacists, irrespective of whether the prescribed medicine is for acute or chronic purposes. For the latter, given that the standard quantity of medicines dispensed is for approximately one month's treatment, there is an ideal opportunity to counsel consumers about their use of medicines on a regular basis. More on counseling can also be found in Chap. 7.

In both countries, written information sources, such as Consumer Information Leaflets (in New Zealand) and Consumer Medicines Information (CMI) documents, amongst other sources, are used to facilitate counseling [11]. CMI is a brand specific written information source, authored by pharmaceutical companies, which can be used to assist counseling about the use of medicines. CMI leaflets are available for prescription and some non-prescription medicines. They contain information on the safe and effective use of medicines. Specifically, CMIs contain the following information:

- Name of the medicine
- Names of the active and inactive ingredients
- Dosage of the medicine
- What the medicine is used for and how it works
- Warnings and precautions, such as when the medicine should not be taken
- Interactions the medicine might have with food or other medicines
- How to use the medicine properly
- Side effects
- What to do in the case of an overdose
- How to store the medicine properly
- Name and address of the sponsor
- Date the CMI was last updated.

15.4.2 Medication Management Review in Australia and New Zealand

With the PCNE definition of pharmaceutical care in mind, there are two key government funded services in Australia which have the explicit aim of optimizing medicine use. They are "Residential Medication Management Review (RMMR)" and "Home Medicines Review". Both of these are research underpinned, collaborative, comprehensive and patient-centered medication review services, provided by accredited pharmacists, for residents in aged care facilities (nursing homes) and those living at home, respectively. See Chap. 6 for more about medication review.

15.4.2.1 Australia

The HMR and RMMR programs aim to achieve the quality use of medicines (QUM), that is the judicious, appropriate, safe, and efficacious use of medicines (Table 15.1). HMR, which is also known as Domiciliary Medication Management Review, commenced in 2001 [12]. This Commonwealth-funded program aims to maximize patient benefit from medicines and prevent drug-related problems and their causes through a collaborative process involving both GPs and accredited pharmacists. Accredited pharmacists are those who have received post-registration certification in medication review from either the Australian Association of Consultant Pharmacy and/or the Society of Hospital Pharmacists of Australia. Together with RMMR, HMR forms a major pillar under Australia's medication management initiatives [13].

There is much research evidence to support the HMR and RMMR programs and so only selected findings are reported here. The impact of HMR and RMMR on Drug Burden Index (DBI), an objective pharmacologic outcome measure, have been evaluated. Nishtala et al. conducted a retrospective study of 500 RMMRs from 62 aged care facilities and found a statistically significant reduction in median DBI scores (0.50–0.33 post-RMMR) [14]. Similarly, Castelino et al. conducted a retrospective study of 372 HMRs from 155 pharmacists and also found a statistically significant reduction in median DBI scores (0.50–0.22 post-HMR) in community-dwelling individuals [15]. Hence these studies demonstrated the

Table 15.1 Key steps in the Home Medicines Review and Residential Medication Management Review process

Steps	Home medicines review	Residential medication management review
1	Identification of the consumer, based on need	Identification of the resident in the aged care facility, based on need
2	Referral of the patient to their preferred pharmacy or pharmacist by GP	Referral of the resident to RMMR service provider
3	Pharmacist visits patient at home and obtains a comprehensive medication history	Pharmacist gathers resident information from resident, family or next of kin, aged care facility staff members, and resident's case notes
4	Pharmacist documents their medication review findings and recommendations in a report for the GP	Pharmacist documents their medication review findings and recommendations in a report for the GP and notes that this has been completed on the medication chart and resident's case notes
5	GP and patient formulate a medication plan based on the pharmacist medication review report	Post-RMMR discussion between pharmacist and GP, preferably face-to-face

Adapted from Ref. [12]

effectiveness of both programs using a validated measure. Specifically, higher DBI scores indicate higher exposure to anticholinergic and sedative medicines which are associated with poorer physical and cognitive function [16].

A detailed assessment of the specific recommendations made by pharmacists in 224 HMRs found that 910 or 964 (94.4%) recommendations were directly supported by evidence from recognized Australian national consensus and evidence-based guidelines covering all major therapeutic areas. This study was the first study reported in the literature to assess the quality of HMRs, using consensus and evidence-based guidelines as the measure. It is noted that only a small number of recommendations (n = 54, 5.6%) did not accord with best available evidence [17].

15.4.2.2 New Zealand

In New Zealand, the notion of pharmaceutical care emerged in 1990s. In 2007, the PCNZ endorsed patient-centered services via the National Pharmacy Services Framework. Medication management services outlined in this national framework aimed to optimize medications involving pharmacists working collaboratively with multidisciplinary healthcare teams. The framework outlines 4 tiers of medication management services: Level A-medicines provision, Level B-Medicines use review (MUR), Level C-Medicines therapy assessment and Level D-Comprehensive medicines management (CMM). The MUR and Medicines Therapy Assessment (MTA) services are currently offered in New Zealand whilst the CMM proposed in the national framework has yet to be implemented. The overarching purpose of the MUR is to improve patients' adherence. In contrast the MTA is a comprehensive medication review of the patients' medications undertaken by a pharmacist as a part of a multidisciplinary healthcare team. A retrospective evaluation of medication use review records of 353 patients in NZ found that this service improved patients' knowledge and perceptions of and adherence to medicines [18].

To provide MTA services, pharmacists must be accredited and submit a portfolio of evidence against the Medicines Therapy Assessment Standards endorsed by the Pharmacy Council of New Zealand. The MTA services are not nationally funded in NZ, however some District Health Boards in New Zealand do fund MTA services. A critical evaluation of the MTA service is not feasible given the paucity of either observational or interventional studies in this area.

In New Zealand, pharmacists are granted prescribing rights. Pharmacist prescribing is a separate scope of practice and requires higher level competencies than those required for Levels B, C and D of the medicines management framework. The prerequisite qualification for entry into the pharmacist prescriber program is a Postgraduate Diploma in Clinical Pharmacy or equivalent. The current pharmacist prescribing model requires that pharmacist prescribers are required to work collaboratively in health care teams. The New Zealand model for pharmacist prescribing is that of 'independent prescribing', and pharmacists are independently responsible for prescribing.

15.4.2.3 Medication Management Review Reimbursement in Australia and New Zealand

Both HMR and RMMR aim to achieve the quality use of medicines (QUM), a tenet in line with Australia's National Medicines Policy. In recognition of the value of these services, both pharmacists and general medical practitioners receive a professional fee from the Government for service provision, with no out of pocket expense for patients. Essentially patients are selected for the services on the basis of need with some specific guidelines in place. These include: discharge from hospital in the previous 4 weeks; significant change to the medication regimen in the past 3 months; change in medical condition or abilities (e.g.,, falls, cognition, physical function); use of a medicine with a narrow therapeutic index and that requires therapeutic monitoring; symptoms suggestive of an adverse drug reaction; subtherapeutic response to pharmacotherapy; noncompliance or problems with managing medication-related devices; risk of being or being unable to continue managing own medicines due to changes in dexterity, confusion, or impaired vision.

In New Zealand, patients can receive the MUR service (level B) by a referral from GPs, pharmacists, and nurses or nurse practitioners. The service can be conducted in the pharmacy, patient's home or by telephone. The funding for the services is via DHBs, and not all DHBs fund this service in NZ. On an average, pharmacists are paid up to $200 for four MUR consultations per year. GPs are not reimbursed for this service. MTA akin to the HMR service in Australia is funded by a limited number of DHBs, however the uptake of MTAs since its introduction in 2007 has been limited.

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Chapter 16
Pharmaceutical Care in Latin America

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Abstract This chapter focuses on pharmaceutical care provision in Latin America. We have described the current situation and challenges identified for pharmaceutical care activities, highlighting the situation in specific countries where possible. Different health systems in countries are an important reason for the development of specific strategies for each one. In general, the health literacy level of people in Latin America is rather low. Also, different background and training of pharmacists, and the lack of practice education, explain the low level of skills and knowledge and this leads to only few community pharmacists being active in pharmaceutical care. There are also relatively few hospital pharmacists involved in patient care. There are also positive developments in some countries. A few studies are mentioned in this chapter, because of their potential to influence the professional attitudes. More studies and change of the curricula in Latin America are needed.

Keywords Pharmaceutical care · South America · Pharmaceutical services Care implementation · Pharmacist education

16.1 Background for Pharmacy Practice in Latin America

Every country in The World has specific characteristics that influence the delivery of patient-centered services in pharmacies. The characteristics do not only include a variety of financial and organizational aspects, but also patient-related aspects.

One of the patient-related aspects is health literacy, which is "the degree to which an individual has the capacity to obtain, communicate, process and understand basic health information and services to make appropriate health decisions"

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[1]. The patient demands for services in health care depend on health literacy [2]. The low health literacy in the majority of countries in Latin America is an important barrier for the development and implementation of pharmaceutical care.

Additionally, because only so few care related services are delivered in pharmacy in Latin America, the communities do not see the potential of pharmaceutical care, and thus there is no demand. And lastly, also in Latin America the Internet is growing fast [3], especially in Puerto Rico, Ecuador, Costa Rica, Chile, Argentina, Uruguay, Panama and Brazil. People who browse the Internet for information do not necessarily seek the guidance about their medicines from the pharmacist, and often even the medicines can be ordered through the Internet.

But it is not only the patient; most pharmacists also are not yet ready to deliver pharmaceutical care. In 2011, the Pan American Health Organization (PAHO) released the document "Guidelines for the Development of Pharmaceutical Services in Primary Health Care" [4].

The guidelines described specific weaknesses and challenges for the implementation of pharmaceutical services. The mentioned challenges were:

- Individual, incomplete and fragmented care. The health systems in more than 90% of countries in Latin America are not seamless, and information about medical records of patients is not available in community pharmacy. So the pharmacist is unaware of it when providing care.
- Sporadic care. Pharmaceutical care needs continuity. In Latin America, mainly in big cities, there are pharmacy chains and their staff dedicates a lot of time to administrative activities, making it a challenge to offer personalized and continuous care. On the other hand, because pharmacies are usually small, pharmacists know their patients and can offer them personalized care. But how often will always depend on the available time for the pharmacist and the patient.
- Individual work. Pharmaceutical services and pharmaceutical care need a skillful and knowledgeable staff, at approximately the same level of training. But because there are different levels in the undergraduate programs, different staff members cannot always help the patient at the same care level.
- Lack of protocols. To make sure that every patient receives the same quality care, protocols are needed, independent of the setting, the provider, or the patient. There are hardly any pharmaceutical care protocols in Latin American countries.
- Product-centered professional training. In Latin American, the majority of schools of pharmacy provide training with a general focus on pharmacology, and only a few hours of practice facing patients or clients. There are not many different professors in pharmacy practice, to exchange experiences. There is a lack of specific pharmaceutical care training.
- Product-centered policies. In Latin America only few pharmacy regulations deal with, or encourage, the development or provision of pharmaceutical care.

16.2 The Pharmacy Practice Structure

Pharmacy practice developments are not only different between Latin American countries, but are also different between community and hospital in the same country, and can be even different between regions in same country.

(a) Ownership. In the 1990s the exclusive ownership of pharmacy by individual pharmacists started to change, and now we see that in the majority of countries in Latin America pharmacy chains are active and own pharmacies.
(b) Outlets. Medicines are not only available in pharmacies, but may also be sold in grocery stores [5]. In many countries in Latin America, selling OTC medicines outside the pharmacy is allowed. Usually these stores sell OTC medicines only but due to insufficient control from the regulatory agencies in some countries, they are also selling prescription only medicines without prescriptions, like antibiotics.
(c) Regulation. The lack of a legal regulation of good pharmacy practice (GPP) is prominent. In many countries in Latin America the inspectors of the regulatory agency or Ministry of Health visit pharmacies, but there is no legal document that ensures or enforces good pharmacy practice [6].
(d) Working time. The majority of pharmacies in Latin America do not usually have a licenced pharmacist present all day. In some countries pharmacists must be present all the time the pharmacy is open, by law; In other countries only a few hours. Either way this requirement is not met.

16.3 Pharmaceutical Care Implementation

A number of articles have been published, that describe the status of pharmaceutical care in Latin America. We have seen articles from Argentina [6], Brazil [7], Colombia [8], Cuba [9], Peru [10] and Uruguay [11]. According to the experience of the authors, in comparison to community pharmacies, more clinical or care related activities seem to take place in the hospitals in Latin America. At same time, there is also evidence of the impact of pharmaceutical care on different diseases [12–15].

Like in many other parts of the world, the countries in Latin America have different barriers that impede the implementation of pharmaceutical care. Below we try to list them according to the frameworks of Mehralian [16] and Alvarez-Risco [17].

16.3.1 Resources

16.3.1.1 Lack of Money (Reimbursement)

Currently, in general, there are hardly any systems in Latin America that remunerate clinical and care services by pharmacy or pharmacist. However, in Colombia, there are companies that dispense and deliver medicines to patients with HIV and inform them about effective and safe use; this service is performed outside the hospital setting. The service is paid by the health care system, but it is a payment for the two integrated services; additionally, it is important to mention that pharmaceutical care is a mandatory service in Colombia since 2005. In Costa Rica, within the Costa Rican Social Security Fund, there are pharmaceutical care services that are financed directly by social security. But in general, there is a lack of differentiated payment for providing pharmaceutical care. Also, in Brazil one knows the Sistema Único de Saúde, better known by the acronym SUS. It is Brazil's publicly funded health care system, created in 1990. Under SUS, health care in Brazil is free of charge for any person, including foreigners. Pharmaceutical care is part of this system.

In other countries, the financial barrier could possibly be resolved if stakeholders understand the benefits of pharmaceutical care for patients (social–clinical impact) and for the health care system (clinical and economic impact).

16.3.1.2 Lack of Time

The practice and business models of pharmacy chains (that are present in the great majority of countries in Latin America), usually include a big administrative burden for the pharmacists. This prevents them from having time for the patients. This is a common problem in most community pharmacies in Latin America. It is unlikely that this established business model changes unless the regulations change. But there is hope. The largest pharmacy chain in Venezuela employs an administrator and at the same time two pharmacists per shift in a pharmacy. This facilitates the provision of pharmaceutical care.

16.3.1.3 Lack of Space in Pharmacies

To ensure the privacy of the patient, the provision of pharmaceutical care requires a special area in the pharmacy, regardless of the time and duration of the consultation. But traditionally, the pharmacy model in Latin America focuses on having a large space for selling and presenting over the counter medication and other goods. Mostly, regulations do not require room for such a specific area as is the case in Argentina [18] and Chile [19]. But in for instance Peru [20], the regulations mention that a pharmacy must have a room for providing pharmaceutical care to the patient. Such separate consultation areas can also be found in Ecuador or Bolivia, in

some pharmacist-owned pharmacies. But from a commercial perspective, all space in a pharmacy should generate profits, and as long as the care is not remunerated and a consultation room is not legally required, there is no reason to invest in such a space.

16.3.1.4 Lack of Health Care Networks

In Latin America, there are private health centers that can share patient information between all the services offered. This can sometimes also be the case for state clinics and services that are part of the social security. In some hospitals in Argentina, Brazil, Chile, Colombia, Mexico and Peru pharmacists may have access to the patient's profiles during clinical rounds, and thus can evaluate therapy and make suggestions about the optimal pharmacotherapy of inpatients. In the outpatient setting, where patients can go to any physician or pharmacy, this sharing of information hardly takes place. In the community pharmacies there is no patient information available. The computer systems in community pharmacies have not been developed for patient safety, or for communicating over the Internet or dedicated lines.

16.3.1.5 Lack of Trained Staff

Across Latin American countries, and even within countries, there is a large variety in the content and quality of the university education of pharmacists. In many cases the students do not get any tutoring and the learning is unplanned and unstructured. This may lead to deficient knowledge and poor performance in practice. This also explains the low level of implementation of pharmaceutical care in community pharmacies and even in hospitals. Pharmacy students are expected to have at least 300 h of clinical learning with actual patients, but in most of Latin America they do not get that. There are only a few universities in Brazil, Argentina or Venezuela where there are teaching modules in which students can practice with 'real patients'.

16.3.1.6 Lack of Appropriate Software

To be able to counsel patients properly during consultations, pharmacists need to have information sources at hand. In the large majority of community pharmacies in Latin America, old-fashioned reference books are used, and usually not in an updated version or online. Pharmacy software usually is only made for dispensing and sales, not for providing drug information. In Colombia, Chile and Brazil computer software exists that has detailed information on medicines available, including modules for the automatic detection of interactions. This enables evidence-based decisions at the counter, and supports the pharmaceutical care process. But most pharmacies do not use such software.

16.3.2 Attitude and Vision

16.3.2.1 Inappropriate Attitude of Pharmacy Staff Towards Pharmaceutical Care

Most workers in a pharmacy do not have a patient focus yet, but a traditional focus on products and sales. Staff members will therefore not refer patients to the pharmacist in the case of (potential) drug-related problems or counseling needs. Their professionalization is a result of education, experience and regulations, and the national regulations and required education vary greatly. In some countries such as Colombia and Peru, the technicians must have 3 years of training. In other countries, such as Ecuador, Honduras, Guatemala, Paraguay, Uruguay, Bolivia, Panama, there is only a requirement of 1 year experience, without further dedicated training. Regulations allow the technicians in Colombia and many other countries to practice without a pharmacist being on the premises, but in Peru they must work under the supervision of the pharmacist.

16.3.2.2 Inappropriate Attitude of Pharmacists

During university training many of the current pharmacists did not have clinical training, or very little. They also have not learned how their knowledge might benefit the patient, or had the chance to develop patient-centered skills. Thus, they have had no stimuli to be involved in patient care. And because there are only few pharmacists that work in the area of pharmaceutical care, there also are only few examples from peers, or peer pressure. Other facilitators for adapting the pharmaceutical care approach, such as remuneration or patient demand are also almost absent. All of these aspects shape the attitude of the pharmacists in all Latin American countries. In some countries this is even more outspoken, such as in El Salvador, Nicaragua, Bolivia, Honduras, Mexico, Paraguay, where there is no or very little knowledge about the possible clinical activities of pharmacists.

16.3.2.3 Inappropriate Attitude of Pharmacy Owner Towards Pharmaceutical Care

In many countries in Latin America the pharmacy owner is a company. Almost all companies have a business model that focuses on sales (and not only the sale of medicines). Since clinical or care activities are not remunerated, the clinical activities that their pharmacists can do depend on what companies allow. Even if the pharmacist wants to deliver some care, this can only be occasionally, and only at the counter and for a limited time. If a pharmacy is owned by a pharmacist, there are more efforts to provide clinical services, but still only carried out sporadically and unpaid. That is why they tend not to be sustainable over time.

16.3.2.4 Attitude of Other Health Professionals Towards Pharmaceutical Care

The relationship between pharmacists and health professionals varies in each country in Latin America and even in each context. In general, pharmacists are educated in relative isolation, and for instance not involved in rounds on hospital wards. They also do not seem to work in multidisciplinary health centers or take part in health campaigns or other interdisciplinary work. This most possibly explains the lack of knowledge of other professionals about the role of the pharmacist and their possible clinical competences. But a close collaboration between prescribers and pharmacists has been achieved in several cities in Peru, Chile, Argentina, Colombia, Costa Rica and Cuba. The cornerstone for getting other professionals to know and respect the clinical activities of pharmacists, such as pharmaceutical care, seems to be a joint training of both professionals in, for instance, pharmacotherapy including the discussion of clinical cases.

16.4 Future Developments

Hospital and community pharmacy in Latin America are still under development. Good Pharmacy practice regulations have not yet been defined nor implemented in many Latin American countries. From a health care perspective and for the sake of patient safety, this should be a priority. But this does not mean that isolated developments of pharmaceutical care are not taking place. They may well serve as best examples for the pharmacists that do want to change. However, most pharmacists will need resocialization to prepare them for changes in practice [21]. Therefore, universities have an important role in the further development of the profession and their practice in Latin America.

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Chapter 17
Pharmaceutical Care in Asia

Shaun Wen Huey Lee and J. Simon Bell

Abstract The implementation of pharmaceutical care services has been variable across in Asia. In part this reflects the large disparities that exist within and between countries, including non in countries separation of prescribing and dispensing such as China, Malaysia, and Thailand. Nevertheless, there are increasing reports of innovative services being delivered in hospitals and community pharmacies. Innovation in the development and implementation of community pharmacy services has occurred despite the lack of separation of prescribing and dispensing in countries like Malaysia. Barriers to further implementation include the uneven distribution of pharmacies as well as intrinsic and extrinsic barriers such as negative perceptions from other healthcare professionals and limited confidence among pharmacists to provide new services. However, the widespread investment in new models of education and practice is expected to result the pharmacy profession move forward in the coming years.

Keywords Pharmaceutical care · Asia · Pharmaceutical services
Pharmacist role · Antibiotic stewardship

17.1 Introduction

Asia is the largest and most populous continent, with more than 4.4 billion people living in both densely and sparsely populated regions. Asia's population is living longer, has increasing rates of multi-morbidity, and has greater need for and access to medicines. This demographic shift has changed the need for health care. One of the key changes has been in the provision of medicines and pharmaceutical care, which has evolved considerably over the last decades. Greater access to medicines

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and pharmaceutical care has been instrumental in improving therapeutic outcomes, disease management, patient safety, and quality of life. This has had corresponding implications for pharmaceutical policy and healthcare expenditure.

17.2 Concept of Pharmaceutical Care in Asia

In Chap. 1, van Mil describes how the definition and implementation of pharmaceutical care varies according to the location of practice, legal framework, political context, and healthcare system. This is particularly true in Asia where there is great diversity within and between countries. This lack of uniformity means it is very challenging to summarize pharmaceutical care across Asia. For example, in Asian countries such as China, Hong Kong, Thailand, and Malaysia, physicians both prescribe and dispense medicines. This practice is at odds the practices advocated by organizations such as the Pharmaceutical Society of Australia that maintain that separation of prescribing and dispensing provides flexibility and choice for patients while providing safety through quality assurance and risk management [1]. This is the case in many countries with a shortage of pharmacists, where medicines are often sold with or without a prescription through private "drug stores" that are not necessarily staffed by registered pharmacists. At the other end of the spectrum, tertiary hospitals in many Asian countries provide advanced clinical pharmacy services that are of the highest international standards. Given the diversity of pharmaceutical care across Asia we provide a snapshot rather than a comprehensive examination of pharmaceutical care across the continent. We provide a narrative review of published peer-reviewed literature rather than an overview of pharmaceutical care based on national policies and regulatory frameworks. This peer-reviewed literature was identified through searching major bibliographic databases including PubMed, Embase, and Cochrane Library.

17.3 Pharmaceutical Care in East Asia

Pharmacy in China was predominately focused on the areas of pharmaceutical sciences until the early 2000s. Early development of pharmaceutical care focused on implementation of medication management services to address the issues of medicine-related problems and to ensure rational medicine use. Development has become more rapid and geographically widespread over the past decade. This has been described as being aided by Chinese healthcare reforms and the corresponding introduction of more clinical roles for hospital pharmacists [2]. In a 3-month intervention study, a clinical pharmacy services in an intensive care unit resulted in positive effects on patient outcomes and reduced medication errors [3]. Hospital pharmacists have also taken on new roles in antibiotic stewardship and now offer guidance on antimicrobial use to physicians [4]. However, pharmacy practice in

most community pharmacies remains centered on the traditional roles of medication dispensing and counseling [5]. Community pharmacists have reported barriers to the wider implementation of pharmaceutical care in China include the lack of time, skills, information, and financial incentives [2, 6]. Nevertheless, it is expected that services offered in hospitals will be expanded and offered in community pharmacies in the future. In fact, community pharmacists have expressed that they were optimistic about providing pharmaceutical care services on Traditional Chinese Medicine, which is widely used by the population [7].

In South Korea and Japan, pharmaceutical care services have been expanding and include services such as therapeutic drug monitoring, anticoagulation services, and medication management [8–10]. For example, pharmacists in Japan are now involved in providing clinics for anticoagulation, cancer chemotherapy, and asthma. These clinic-based services began as a pilot program in 2000 and have subsequently expanded nationwide. These clinic-based services are now covered by the universal health coverage in Japan [11]. Barriers that have been reported to wider implementation of pharmacy services include the lack of remuneration, a shortage of pharmacists, and pharmacists lacking the therapeutic knowledge and clinical problem solving skills necessary to implement the range of new services [11–13].

17.4 Pharmaceutical Care in the Eastern Mediterranean Region

Countries in the Eastern Mediterranean region have faced similar issues related to the introduction of pharmaceutical care [14]. Provision of pharmaceutical care in Jordan has primarily been delivered through government and nongovernment hospitals, where there is an increasing number of studies evaluating the impact of a clinical pharmacy services [15, 16]. This has been reflected in the introduction of pharmaceutical care courses in Jordanian universities. Kuwait too is experiencing positive developments in this field, with a push for recent generations of pharmacists to trial new services in hospitals [17]. A recent study by Al Haqan reported that while most pharmacists report they provide medication counseling to their patients, the public and physicians perceive the professional role pharmacists is limited to providing specialist diabetes-related pharmacy services (e.g., glucose monitoring and healthy lifestyle counseling) [18]. Like other countries within the region, Lebanon has introduced clinically orientated pharmacy education. This will provide the basis for the introduction of new community pharmacy services, which up until now have remained mostly centered on compounding and medication dispensing [19]. Pharmacy practice is also developing in other Eastern Mediterranean countries. Like in most other countries across the world, implementation of these new services has been inconsistent. For example, implementation of formal pharmaceutical care services in the United Arab Emirates has mainly been limited to the government settings to date. In Iraq, community pharmacies

have begun to provide medication counseling and monitoring of body weight, blood pressure and blood glucose screening, although this has reportedly been met with resistance from some physicians [20]. More widespread implementation in the community sector has been limited due to lack of remuneration, workload, and a shortage of qualified staff.

It has been reported that pharmacy students and community pharmacists have a good understanding of pharmaceutical care in Saudi Arabia [21, 22]. However, like in other countries most clinical pharmacy services are concentrated in hospitals. These services include discharge medication counseling and monitoring of medication therapy to reduce the risk of any adverse drug reactions. Pharmacist-led mediation adherence clinics are conducted for patients taking anticoagulants. In these clinics, the pharmacists are permitted to adjust medication dosages and switch anticoagulant medications. The breadth of services offered by pharmacists is expected to expand due to the increasing number of graduates from the Doctor of Pharmacy programs [23]. Indeed, there are now efforts to expand postgraduate residency training programs in Saudi Arabia that will increase the capacity of the pharmacy workforce to deliver new clinical services, even if not all the graduates have specialty training in particular therapeutic areas.

Qatar is similarly experiencing an evolutionary phase, due to an expansion of health service, educational initiatives as well as leadership at national and practice levels [24]. For example, most hospitals under the umbrella of Hamad Medical Corporation (HMC) have reportedly offered clinical pharmacy services such as medication therapy management for more than a decade. There are examples of pharmacy programs in Qatar and now offering doctor of pharmacy programs, hospital-based training, and ASHP-accredited postgraduate programs.

17.5 Pharmaceutical Care in South Asia

India has a very large network of pharmacy schools and a large pharmaceutical industry. Drug stores are widespread across India and they are often the first point of contact that patients have with the health system. Most drug stores remain focused on medicine distribution [25]. Nevertheless, there are reports of initiatives that utilize the country's network of drug stores to identify and refer patients with symptoms suggestive of tuberculosis to public sector clinics for diagnosis and treatment [26]. Medication therapy is usually managed by physicians with help from nurses. Given the large pharmacy workforce in India, it could be argued that the expertise of the pharmacist is underutilized. However, many hospitals in India have implemented clinically oriented roles for hospital pharmacists and this has been associated with improved patient health outcomes. Pharmacists in these hospitals have started to provide drug information, participate in ward rounds and monitor patients for adverse reactions [27]. Pharmacy practice in Pakistan and Nepal has been focused on the pharmaceutical industry. However, pharmacists have begun to work in hospitals and community pharmacies with greater focus being given to patient counseling and health promotion [28].

17.6 Pharmaceutical Care in South East Asia

There is great variability in the understanding and implementation of pharmaceutical care in South East Asia. This partially reflects differences in pharmaceutical policies and health systems in each individual country. For example, for historical reasons the structure of the health system in Malaysia and Singapore more closely resembles the British model of healthcare whereas the health system in Indonesia more closely resembles the Dutch model. These differences are reflected in the pharmaceutical care roles performed by pharmacists. In Malaysia, the pharmaceutical services have developed from being solely focused on supply to being focused on the quality use of medications [29–31]. Many hospital and community pharmacies in Malaysia now provide chronic disease management, medication reviews, smoking cessation services, and weight management programs [29, 32]. Other specialized services provided by pharmacists in hospitals include anticoagulant treatment clinics, therapeutic drug monitoring, and antimicrobial stewardship. Thailand has made significant advances in implementation of clinical pharmacy education and practice over the past decade. Hospital pharmacists in Thailand are now involved in conducting medication management outpatient clinics. Thai pharmacists also perform medication reconciliation, patient education and manage medication-related problems. Community pharmacists in Thailand have also begun to provide innovative services such as health assessment, health promotion, and medication usage reviews [33, 34], In Cambodia, specific private pharmacies have worked with the National Tuberculosis Program since 2005 to refer tuberculosis (TB) symptomatic patients to public sector TB clinics for diagnosis and treatment [35, 36].

Clinical pharmacy and pharmaceutical care is relatively new in Indonesia and, therefore, awareness and acceptance by healthcare workers remains inconsistent. Several hospitals now employ pharmacists to deliver clinical services on the ward, monitor medication treatment and provide counseling [37]. Indonesia is a populous and geographically diverse country and so it is likely that it will take years before the full spectrum of clinical pharmacy services is implemented. This situation in the Philippines is similar to that in Indonesia where implementation of pharmaceutical care has an opportunity to expand. Many countries in Asia experience common barriers toward the provision of pharmaceutical care including the lack of awareness and support from physicians and other healthcare professionals [38].

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Part IV
Implementing Pharmaceutical Care in Different Settings

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This part will focus on this field of implementing pharmaceutical care in different settings and different countries. It provides an insight into the theoretical and strategic approaches developed by implementation research as well as an account of the knowledge that has been accumulated in practice research and via daily practice in community, hospital, and nursing home settings.

Pharmaceutical care implementation research really took off in the 1990s. Earlier research had primarily been academic studies documenting drug misadventures and also theoretical concept and model development. This research was now mature enough to move into intervention research. In many countries, the concepts were developed into practice models that were expected to be feasible and deliver evidence for significant outcomes. In some countries, hospital pharmacy was in the lead, in other countries, primary care pharmacy went ahead with the new approach to clinical pharmacy focused on individual patients and on preventing and resolving drug-related problems for those patients. Soon after, also nursing home activities as well as activities for general practice were developed and tested.

It was from the start a realization that the new approach to patient-centered pharmacy needed implementation support. The projects would typically provide manuals describing the philosophy and the process, training materials and forms to document the activity supplemented with various research tools to study processes and outcomes. Training courses would also be provided covering relevant aspects of pharmacotherapy as well as implementations oriented subjects and tools.

However, the experiences from conducting those early projects were variable: Some projects had impressive results, but some did not produce the expected outcomes. Projects using the same process showed varying results in different countries, e.g., the PCNE projects for the elderly [1] suggesting that social factors played an important role.

This pattern leads to new questions: Was the concept no good? Were the research instruments not sensitive? Were the practice models not strong enough?

Were the contextual and financial barriers and facilitators not properly understood and taken into account when designing the local models?

Those experiences lead to a new research field focusing on implementation of pharmaceutical care. This again fostered new generations of intervention research yielding more feasible services with better results and producing a range of pharmacy pharmaceutical care activities and services ready to be rolled out on a larger scale. This development took implementation issues to an entirely new level. Dissemination on a national level has been hard to achieve and has taken much longer time than the pioneers expected. Implementation research would need to broaden its scope and incorporate, e.g., the roles of professional bodies with different backgrounds, national authorities, political agents, local health administrators, third-party payers, roles of other health professionals, etc.

Today, implementation science is well established within the field of pharmaceutical care and health services research [2]. Implementation science is a social science than a clinical science based on randomized controlled trials. Much can and must be learned from other research approaches if we wish to understand the complex social systems where pharmaceutical care needs to be implemented. We need tools to study what happens in real life and to construct implementation models and strategies that can summarize this insight and make it generalizable yet individualized to each context.

In Chap. 18, **Pharmaceutical Care Implementation Strategies and Audience**, *S. I (Charlie) Benrimoj, Victoria Garcia-Cardenas, and Charlotte Rossing* address a number of the overall theoretical and strategic issues in relation to the implementation of pharmaceutical care. They start with stating the fact that there is a significant gap between research and development of pharmaceutical care activities and having those activities implemented and sustained as a routine practice.

Implementation science has developed a range of frameworks, theories, and models attempting to understand the complexity around implementation. The authors refer to several of those and then go on to discuss the evidence-based models that were developed for—mainly community—pharmacy systems.

These include process models pointing to implementation most often going through phases: Exploration; Preparation or installation; Testing or initial implementation; Implementation, full implementation or operation; and finally, Sustainability.

Going deeper, the authors focus on factors influencing implementation, positive as well as negative moderators, distributed across five domains: The service, the individuals, the pharmacy environment, the external local setting, and the system as the outer context. The way the implementation factors can function as barriers and facilitators is complex and may vary in the different phases.

The authors then address the need for implementation strategies stating that individual approaches, as well as multicomponent strategies, are needed, “one size doesn’t fit all”. Finally, the authors describe techniques for practice implementation and approaches to assess implementation success.

In Chap. 19, **Implementation in the Community**, the same authors but in a different sequence, *Charlotte Rossing, S. I (Charlie) Benrimoj, Victoria Garcia-Cardenas* go deeper into the experiences that have been built up in the community setting. Here,

pharmaceutical care is delivered to patients by pharmacists working from either community pharmacies or general practices.

Starting with a structural view of the community pharmacy sector, the authors place pharmaceutical care in the overall structure of the Good Pharmacy Practice framework. Specifics of the workforce in community pharmacies are discussed, and educational models developed by FIP are used to describe goals for implementation of workforce development. Further, the issue of ownership structure is raised. Pharmaceutical care can be delivered from different types of pharmacies, regardless of ownership, but with different implementation opportunities. Online and mail-order pharmacies, however, represent challenges with the personal patient–pharmacist meeting.

Regarding the development of pharmaceutical care activities in community pharmacies, the authors discuss how the focus in implementation research has shifted over time. This development reflects a learning process where the complexity of implementation gradually has gained a deeper understanding.

Pharmaceutical care in community pharmacies is implemented via several different activities. The individual counseling, which is provided when patients come directly in the pharmacy, will in many countries include elements of pharmaceutical care on a broad population level. In addition, pharmaceutical care is being delivered as health services from the pharmacies together with other public health services. Many services have been developed and implemented targeting the population in general, population groups at risk or patients with specific disease states. Some of the most commonly implemented services are medication use reviews, medication reconciliation, new medicines services, chronic disease programs, and medication reviews.

General practice as a setting for pharmacists to deliver pharmaceutical care has been a focus of implementation research in several countries. In the UK, this has resulted in service models that are now routine practice with good evidence for the value of those activities.

The chapter ends with a discussion of the challenges and opportunities that will evolve with new platforms for delivery of drugs, communication, and data. Separating the physical meeting for counseling patients from dispensing of drugs will call for new models for the implementation of pharmaceutical care to meet new patient needs and expectations.

In Chap. 20, **Implementation in Nursing Homes,** *Carmel M. Hughes* states that nursing homes represent a unique setting being, at the same time, a home for the residents as well as a healthcare setting and hence, presenting unique challenges for optimizing quality and safety of care in a home environment.

The paragraph starts with outlining the key characteristics of nursing homes and the challenges for the delivery of pharmaceutical care. Nursing home residents receive up to four times as many medications compared to older people living at home and they have increased risk of adverse drug events. In particular, the use of psychoactive medications such as antipsychotics, hypnotics, and anxiolytics has been documented to be problematic. Explanations have been suggested to be a challenging behavior of residents and a shortage of nursing staff. Initiatives including regulation, legislation, and best practice guidelines have been implemented to reduce unnecessary use of these medications. Likewise, the overuse of

antibiotics has been identified as a problematic area where nursing homes need support in reducing prescribing and minimizing antimicrobial resistance.

We are further presented with the research, which has been carried out in nursing homes to address the challenges of implementing pharmaceutical care. Several models have been tested focusing on the high-risk drug groups in nursing homes and with medication review as the dominating approach, often involving a pharmacist. The effects on improving medication appropriateness have been achieved by different models, but the evidence for effects on outcomes is less certain. There is a need for further research and for development of a set of core outcomes to be used in nursing home studies. Also, there is a need for implementation models that do not only have focus on informing prescribing after it has taken place.

In Chap. 21, **Implementation in Hospitals and Clinics,** *Ulrika Gillespie* describes the challenges that are characteristic for the implementation of pharmaceutical care in hospitals and clinics. The activities must be delivered in very variable settings spanning from acute care, elective surgery, wards for local population to highly specialized medical centers. Patients may appear at the hospital with long medication lists, or they may be subjects to multiple drug changes during their hospital stay, or they may belong to the considerable group of patients who get admitted due to drug-related problems. Common for patients in rehabilitation wards, intensive care units, palliative care, or outpatient care is that they all receive medicines and many will need medication management.

The author states that clinical pharmacists in hospitals mainly perform pharmaceutical care as part of medication reconciliation or medication reviews. The Integrated Medicines Management concept from Northern Ireland is used as an example of an implementation model that has been inspiring many countries to develop similar approaches. The steps in the model and some of the implementation challenges are described. The process should always start with medication reconciliation. It is essential, but as medication reconciliations are labor-intensive, regardless of whether they involve e-record alerts or patient interviews, hospitals worldwide struggle to find mechanisms for identifying patients at risk and focus the resources on those. When the second step, the medication review, involves a pharmacist, there are frequently challenges with integrating the pharmacist fully in the hospital team. Also, the pharmacist will need to acknowledge that all drug-related problems cannot and should not be solved immediately and some recommendations will need to be solved by the next caregiver level.

The chapter ends with discussing upscaling opportunities and the evidence we have for medication review in hospital settings as well as the need for further research.

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Chapter 18
Pharmaceutical Care and Implementation Strategies

Victoria Garcia-Cardenas, Charlotte Rossing and S. I. (Charlie) Benrimoj

Abstract Implementation of pharmaceutical care through professional pharmacy services is a complex process, in which multilevel implementation factors interact and affect implementation processes and outcomes. This process has traditionally been approached in an ad hoc manner, and assuming that positive benefits and diffusion of information through key stakeholders would ensure the service's integration into routine practice. It is now known that this traditional approach is not sufficient to effectively integrate innovations into routine practice of pharmacy, and that more complex, tailored, and evidence-based approaches are needed. The application of implementation science to the implementation of professional pharmacy services will facilitate this complex process and will assist in ensuring their long-term sustainability.

Keywords Pharmaceutical care · Care implementation · Implementation strategy Implementation barriers · Implementation facilitators

18.1 Implementation Background

One of the greatest challenges currently facing healthcare systems is finding strategies to translate evidence-based services into the routine practice of healthcare professionals. Research shows that most of the healthcare innovations proven to be effective in controlled trials either never get or take very long to be implemented [1]. Essentially, there is a high investment of resources on the design, development, and evaluation of evidence-based services that are not translated into routine

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practice, and therefore, fail to benefit patient care at a large scale. The concept of Pharmaceutical Care can be operationalized through the provision of specific professional pharmacy services. These services are essentially a number of interventions, including behavioral, conducted by the pharmacist which lead to optimizing the patient care and health outcomes. Designing and evaluating interventions like professional services are now acknowledged as the first steps in the process of health services research, but not the sole ones. Unfortunately, positive outcomes alone do not ensure effective implementation and additionally, no service can be effective on a long-term basis unless it is appropriately implemented. In the case of pharmacy, as in other disciplines, there is a significant gap between the professional services development, universal implementation and sustainability, which is common in different practice settings (i.e., community, nursing home, hospital, clinic, etc.).

18.2 Implementation Theory

In the past, implementation of innovations or new services in health care was believed to be driven by diffusion (i.e., passive, untargeted, and unplanned spread of innovations) and dissemination (i.e., active spread of innovations to the target audience using planned strategies). This was usually undertaken through information and communication strategies, or intensive clinical training of the service providers. It is now known that this traditional approach is not sufficient to effectively integrate innovations into routine practice within a setting, and that more complex and holistic approaches are needed. Implementation science aims to address this problem through "*the scientific study of methods to promote the systematic uptake of clinical research findings and other evidence-based practices into routine practice, and hence to improve the quality (i.e., effectiveness, reliability, safety, appropriateness, equity, efficiency) of health services and care*" [2]. That is, investigating processes to integrate research findings into real-world settings. Within the field of implementation science a range of frameworks, theories and models attempting to understand the complexity around implementation have been developed. Some evidence-based examples include: the Consolidated Framework for Implementation Research (CFIR) [3], The Promoting Action on Research Implementation in Health Services (PARIHS) [4], Promoting Action on Research Implementation in Health Services (reach, effectiveness, adoption, implementation, maintenance (RE-AIM)), or specifically in the field of pharmacy, the Framework for the Implementation of Services in Pharmacy (FISpH) [5].

A literature review in Implementation Science classified the different theoretical approaches that can assist and guide service implementation. The authors identified five different approaches aiming at: (1) describing or guiding the implementation process (i.e., process models), (2) understanding and explaining what influences implementation outcomes (i.e., determinant frameworks, classic theories and implementation theories), or (3) evaluating implementation success (evaluation

frameworks) [6]. Although in this chapter we focus on community pharmacy practice, these conceptual frameworks have wider application to other pharmacists' practice settings.

18.3 Describing and Guiding the Implementation Process of Pharmaceutical Care and Professional Services in Pharmacy

Process models propose a stepwise approach, guiding implementation through a number of non-continuous and dynamic implementation phases or stages. In practice, however, those implementing change or services in community pharmacies appear generally not to follow a structured approach usually jumping backwards and forwards depending on their experience, context, and circumstances. A structured, evidence-based approach, usually includes [5, 7]:

(1) An Exploration phase, which involves an analysis and evaluation of the pharmacy's system and environment for the implementation of the service. Risk-benefit assessment by decision makers (e.g., pharmacy manager, pharmacy owner) and readiness to change assessment usually drive the decision to adopt or reject the service implementation.
(2) A Preparation or installation phase, which involves the preparation of the pharmacy environment and pharmacy staff to deliver the service, through investing in the acquisition of resources required for service implementation. Initially, a comprehensive analysis of relevant implementation factors, barriers, and facilitators should be undertaken, usually by external practice change facilitators. Second, strategies should be delivered tailored to the findings of this assessment or needs analysis.
(3) Testing or initial implementation. During this phase, the aim is to try the service provision with a limited number of patients, prior to broader implementation. This phase involves the inclusion of all the stakeholders involved in the service implementation within the pharmacy, who attempt to put into practice the new acquired skills and accustomed themselves to new ways of working. This is a crucial stage, as resistance to change and barriers for practice change surface, usually driving participants to return to their comfort zone and restart old ways of practicing.
(4) Implementation, full implementation or operation phase. This phase involves the integration of the service into routine practice of the pharmacy, and the provision of the service to a predefined target number of patients. This means that the service provision becomes usual practice over time. During the implementation phase, there should be an ongoing monitoring of barriers and facilitators, and of implementation processes and outcomes (including fidelity of service provision). Internal champions or practice change facilitators can help ensure that data obtained through this continuous monitoring is transferred

to key stakeholders and it is used to drive decision-making regarding service implementation.

(5) And finally sustainability, in which the service previously integrated into practice during the implementation phase is routinized and institutionalized over time to achieve and sustain the expected service outcomes for all stakeholders including patients, service deliverers, healthcare system, and pharmacy owners and managers [8].

18.4 Understanding and Explaining What Influences Pharmaceutical Care and Professional Services Implementation Process and Outcomes

The evolution through the different implementation stages is driven by a number of core implementation factors, distributed across five major domains, that act as moderators of the service implementation. Although the number can vary depending on the implementation model followed, there are approximately 39 implementation factors that have been identified, spread across five domains and not mutually exclusive to one domain [3].

The five domains across which implementation factors are distributed include (Fig. 18.1): (1) The professional pharmacy service to be implemented. (2) The pharmacy staff involved in the implementation process. (3) The pharmacy environment in which the implementation takes place. (4) The external environment or local setting of the pharmacy in which the implementation takes place. (5) The system or outer context surrounding the service implementation. The *professional service* domain refers to the innovation to be implemented and covers implementation factors such as the complexity of the service, or service adaptability. There might be local protocols and procedures that need to be considered in this domain. The *pharmacy staff* domain covers a range of implementation factors associated with the professionals implementing the service in their work setting. Examples of implementation factors in this domain are: perceived self-efficacy (or staff's belief in their own capabilities to provide the service), knowledge and experience on service provision, including clinical competencies, motivation to implement the service or personal attributes that can act as barriers or facilitators for service implementation. The *pharmacy* domain refers to a range of factors associated to the specific pharmacy setting in which the professional service is being implemented, such as priority assigned to service implementation, structural characteristics of the pharmacy (e.g., layout, availability of a counseling area), pharmacy culture (i.e., norms, values, expectations, and basic assumptions of the pharmacy), team working approaches, leadership, etc. The *local setting* refers to how the local environment of the pharmacy can affect the service implementation, such as patient demographics or beliefs regarding the service need, other stakeholders in the local environment or the existence of a professional network with other healthcare professionals. The

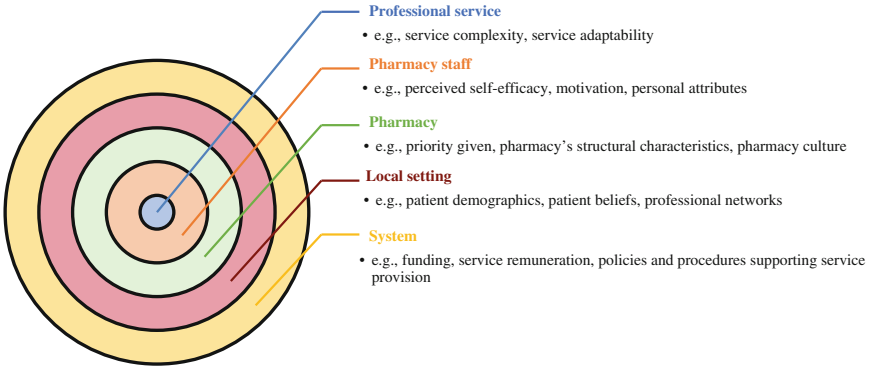

Fig. 18.1 Examples of implementation factors and distribution across domains

system domain covers implementation factors related with the external context surrounding the profession and implementation of services like the healthcare system, availability of funding and service remuneration, professional organizations' policies and procedures supporting service provision and Governmental policies amongst others [9].

18.5 Implementation Factors: Barriers and Facilitators as Moderators

Implementation factors act as moderators of the service implementation process. When these factors act as positive moderators they are usually called facilitators, whereas when they act as negative moderators they are called barriers. Using the implementation factor "incentives" as an example (understood as economic or noneconomic reasons for the participation and engagement in the implementation process, e.g., rewards, performance reviews, promotions, bonus, patient loyalty, Continuing Professional Development (CPD) points, etc.), lack of incentives within the pharmacy would be a barrier hindering the service implementation, whereas the provision of incentives for the pharmacy staff involved in the service implementation would be a facilitator. Most of these implementation factors seem to be interconnected establishing complex cause–effect interactions, which usually vary according to the phase of implementation. For example, in the operation phase "incentives" is a key implementation factor, frequently associated with staff "motivation". In this case, the barrier lack of incentives can be causing a lack of staff motivation to provide the service and hinder the implementation success [9].

Implementation factors are extremely important because they affect both the implementation process (progression rate of the pharmacy through the implementation process) and implementation outcomes (understood as "*the effects of deliberate and purposive actions to implement new treatments, practices, and services*"

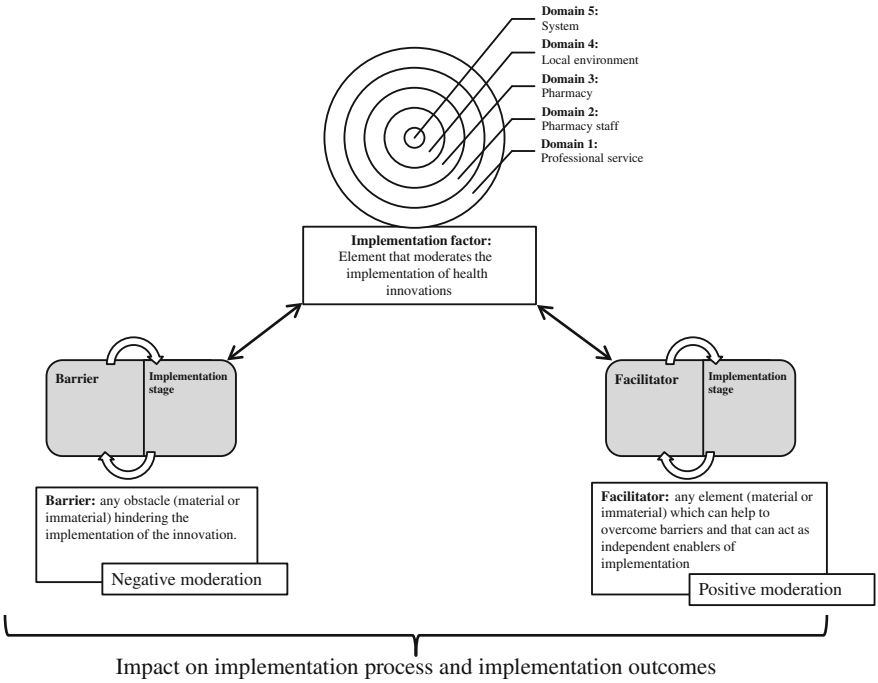

Fig. 18.2 Implementation factors, barriers and facilitators

[10]) and therefore driving the implementation success (Fig. 18.2). An individualized assessment in each pharmacy (or relevant settings) of how these implementation factors are moderating the implementation process and outcomes should be undertaken on a regular basis. Moreover, the cause and effect mechanisms by which they interact should be established. Only based on this assessment, tailored implementation strategies needed to overcome the challenge of effective implementation can be designed.

18.6 Implementation Strategies

Barriers and facilitators should be overcome (in the case of a barrier) or used (in the case of a facilitator) through general and individualized strategies in each pharmacy. Implementation strategies play a key role in the implementation of any professional pharmacy service, as they represent the set of actions designed to achieve successful implementation. They have been defined as "*methods or techniques used to enhance the adoption, implementation, and sustainability of a clinical program or practice*" [11]. Due to the multifactorial and complex nature of service implementation, it is now believed that multicomponent implementation strategies are

needed. As in many other change processes, in implementation "one size does not fit all", and a more individualized approach is needed. This is where tailored interventions (defined as "*interventions planned following an investigation into the factors that explain current professional practice and any reasons for resisting new practice*") come in place. Once the tailored interventions have been provided their success should also be assessed.

18.7 Practice Change Facilitation

Practice change facilitation has been identified as a key technique in the provision of tailored implementation interventions. Widely known frameworks such as the PARIHS emphasize the need for appropriate facilitation to improve the likelihood of implementation success. In the healthcare setting, facilitation has been defined as a technique "whereby facilitators provide support to help individuals and groups realize what they need to change and how to make changes to incorporate evidence into practice". It has also been defined as a role aimed at "working with individual practices on relationship building, education, and quality improvement". "Practice change facilitators" are usually professionals trained to promote organizational change through on-site visits and continuous follow-up. The overall approach to practice change facilitation should follow (Fig. 18.3):

- Step 1: individualized and holistic assessment of implementation factors in each pharmacy. A facilitation assessment tool should be developed, so all relevant implementation factors can systematically be assessed, based on different assessment techniques (e.g., observation, questioning, data gathering).
- Step 2: identification of how those implementation factors are driving the service implementation, and establishing their cause and effect relationships.
- Step 3: planning of a tailored strategy, based on the findings from step 2. A recent systematic review on facilitation strategies used in implementing innovations in healthcare practice identified these can include: provision of

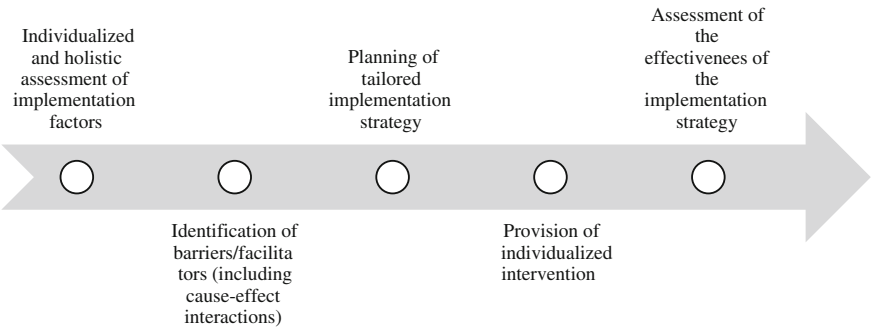

Fig. 18.3 Practice change facilitation approach

feedback, utilization of goal setting, consensus building, provision of staff training, provision of tools and educational material, identification and training of an internal champion, assessment of progress and outcomes and provision of ongoing feedback, or aid in making an improvement plan amongst others.
- Step 4: provision of the tailored strategies designed. These can be delivered through different methods (e.g., in situ, through pharmacy staff workshop, over the phone).
- Step 5: continuous follow-up in order to (1) assess the effectiveness of the strategies delivered and reformulate if necessary, and (2) reassessment of implementation factors over time.

18.8 How to Assess Implementation Success?

During all this process, the impact of the implementation plan should be monitored. This can be done through the assessment of the implementation process (through the monitoring of the progress and movement through the different implementation stages) and implementation outcomes. This is where evaluation frameworks can assist, as they provide a structured plan for evaluating implementation success. This involves the measurement and monitoring of implementation outcomes, so "the effects of deliberate and purposive actions to implement new treatments, treatments, practices, and services" can be assessed [10]. This means they can facilitate the evaluation of the effectiveness of implementation strategies carried out. Moreover, the evaluation of implementation outcomes can allow an optimization of the service benefits, stimulates the dissemination and implementation of the service to other pharmacies and contributes to its long-term sustainability. A diverse range of implementation outcomes has been suggested in the literature, including: Service penetration, reach, feasibility, fidelity, acceptability, appropriateness, integration, implementation efficiency, and implementation costs. Their definitions can be found in Table 18.1.

Table 18.1 Implementation outcomes and definitions [10, 12, 13]

Outcome	Definition
penetration/reach	Level of integration of the service within the pharmacy and its subsystems
Implementation costs	Cost impact of the implementation effort
Feasibility	The extent to which the service can be successfully used or carried out within the pharmacy

(continued)

Table 18.1 (continued)

Outcome	Definition
Fidelity	The degree to which the service is implemented and provided as it was described. Implementation fidelity is usually assessed through different domains that can include: • Adherence (the extent to which service provision is consistent with the service protocol) • Dose (the amount, frequency, and duration of service provision) • Quality of service delivery • Participant responsiveness • Programme differentiation
Acceptability	The perception among implementation stakeholders (e.g., patients and GPs) that the service is agreeable, palatable, or satisfactory
Appropriateness	The extent to which the service is suitable, fitting or proper for the pharmacy and for the local community The perceived fit, relevance or compatibility of the service for the pharmacy; and the perceived fit of the service to address needs of the local community
Service implementation efficiency	The degree to which the service provider improves his/her skills and abilities to provide it over time

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Chapter 19
Implementation of Pharmaceutical Care in Community Setting

Charlotte Rossing, S. I. (Charlie) Benrimoj and Victoria Garcia-Cardenas

Abstract Pharmaceutical care services in primary care have been an area of research from the initial definitions in the early 1990s. The research has resulted in a range of evidence-based services delivered in primary care setting, from the community pharmacies and by the pharmacy workforce. Research has also been focusing on the implementation in community pharmacy practice, taking into account the change in perception of the pharmacy that is needed to deliver pharmaceutical care services. In many countries, pharmaceutical care services are remunerated and to a some extent are delivered to the public, although there is still an implementation gap between what is the potential of service delivery and what is actually delivered. The services are implemented in primary care, primarily delivered by the community pharmacy confirming the role of the community pharmacy in the primary healthcare system.

Keywords Pharmaceutical care · Community pharmacy · Care implementation Professional development · Medicines management

19.1 Structure of Community Pharmacies

Community pharmacies are a significant part of the primary healthcare sector. Community pharmacies are often placed as independent entities where the public gets access without appointment to a healthcare professional. This is the only place in the healthcare system where it is possible to have direct access to healthcare advice. Other healthcare professionals, such as nurses or doctors, can only be reached through prior appointment.

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In many countries, the accessibility to community pharmacies is high. In 2015, Pharmaceutical Group of the European Union (PGEU) published the population to pharmacy ratio which ranges from 1200 inhabitants per pharmacy in Greece to 12,700 in Denmark [1]. In some countries, this results in many small pharmacies in a city, and in other countries there are few large pharmacies serving a larger population.

The practice in community pharmacies has been guided by core frameworks such as Good Pharmacy Practice (GPP). This ensures that the practice of pharmacy is delivered in a quality-assured and uniform way, for the benefit of the patient. The GPP framework has been developed by the World Health Organization (WHO) and International Pharmaceutical Federation (FIP) over the years, and the latest version was published in 2011 [2]. Pharmacy practice is defined in GPP as:

> The practice of pharmacy that responds to the needs of the people who use the pharmacists' services to provide optimal, evidence-based care. To support this practice, it is essential that there be an established national framework of quality standards and guidelines.

This definition is operationalized through the pharmacists' four roles in their daily work:

1. Prepare, obtain, store, secure, distribute, administer, dispense and dispose of medical products
2. Provide effective medication therapy management
3. Maintain and improve professional performance
4. Contribute to improve effectiveness of the healthcare system and public health.

The practice of pharmaceutical care is encompassed in roles 2 and 4, but it is also important to acknowledge that the fundamental of pharmacy practice originally consists in the activities listed in role 1 in the GPP document.

19.2 Workforce in Community Pharmacies

The workforce and roles' distribution within the composition of the pharmacy may vary by country, depending on legislation, the availability of pharmacists and the structure of the pharmacy system in the individual countries. In pharmacies, the two primary categories of professionals are pharmacists and pharmacy technicians. On average, there are 1–4, 18 pharmacists per pharmacy according to PGEU's annual report 2015 [1]. In some countries, there are also bachelors of pharmacy employed at the pharmacy.

Internationally, there appears to be an overall shortage of trained pharmacists, which means that, in some areas of the developed countries, the distribution of medicines and the counseling on medicines are undertaken by pharmacy technicians or non-trained personnel. The individual practice is regulated by national legislation, and in settings with a shortage of pharmacists and pharmacy technicians, the non-trained personnel can work under supervision of pharmacist.

Trained personnel in pharmacies is specialized in medicines, in compounding medicines, and, to some extent, in counseling on medicines. From country to country, there is a great diversity in the training. Only a limited number of universities have focused on the structure of the curricula to systematically support the delivery of Pharmaceutical care services.

The FIP Education (FIPEd) published a report on what is required currently, and in the future, to educate pharmacists to take on the responsibility for Good Pharmacy Practice and Pharmaceutical Care [3]. The FIP also published a set of development goals for the Pharmaceutical Workforce. These goals are inspired by the FIP Needs-Based Educational Model that addresses the process of building capacity in the pharmaceutical workforce based on Needs, Services, Competencies and Education (Fig. 19.1).

The model works from the perspective that the design of the pharmaceutical workforce education should be based on local needs and the health of the population. According to the model, the workforce would be socially accountable to the national healthcare system, and should enhance global connection for a quality-assured workforce that will take care of national needs.

In Table 19.1, the Pharmaceutical Workforce Development Goals produced by FIPEd are presented. They are divided into clusters focusing on Academy, Professional development and systems. Each cluster has a set of individual goals with a short description of what is included in the individual goals.

Besides the Pharmaceutical workforce development goals presented above, the delivery of pharmaceutical care also needs a different set of competencies within the pharmacy.

Research from Australia has focused on the work of implementing pharmaceutical care (Sect. 5.1). Alison Roberts' [4] and Elle Feletto's Ph.D. thesis particularly showed that the focus for new practice should be change management within the pharmacies. It acknowledged that delivery of pharmaceutical care services should follow a strategic decision taken by the pharmacy owner, taking into

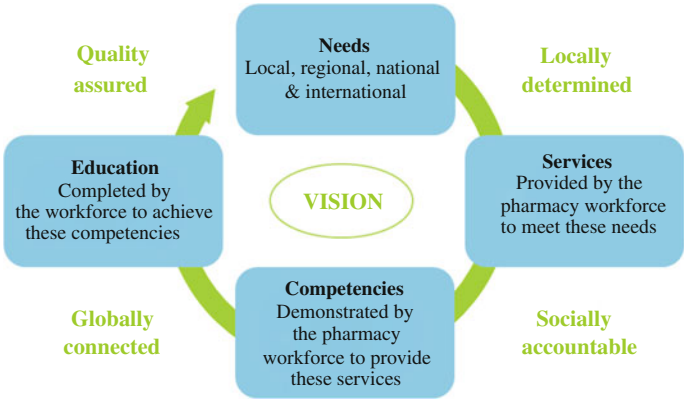

Fig. 19.1 FIP needs-based educational model

Table 19.1 The pharmaceutical workforce development goals (FIPEd)

Cluster	Workforce development goal	Short description
Academy	Academic capacity	Engagement with pharmaceutical higher education development policies and ready access to leaders in pharmaceutical science and clinical practice in order to support supply-side workforce development agendas
	Foundation training and early career development	Foundation training infrastructures in place for the early post-registration (post-licensing) years of the pharmaceutical workforce as a basis for consolidating and processing the novice workforce toward advanced practice
	Quality assurance	Transparent, contemporary and innovative processes for the quality assurance of needs-based education and training systems
Professional development	Advances and specialist expert development	Education and training infrastructures in place for the recognized advancements of pharmaceutical workforce as a basis for enhancing patient care and health system deliverables
	Competency development	Clear and accessible developmental frameworks describing competencies and scope of practice for all stages of professional careers. This should include leadership development frameworks for pharmaceutical workforce
	Leadership development	Strategies and programmes in place that develop professional leadership skills (including clinical and executive leadership) for all stages of career development, including pharmaceutical sciences and initial education and training
	Service provision and education and training	A patient-centered and integrated health services foundation for workforce development, relevant to social determinants of health and needs-based approaches for workforce development
	Working with other healthcare teams	Clearly identifiable elements of collaborative working and interprofessional education and training which should be a feature of all workforce development programmes and policies
Systems	Continuing professional development strategies	All professional development activity clearly linked with needs-based health policy initiatives and pharmaceutical career development pathways
	Gender and diversity balance	Clear strategies for addressing gender and diversity inequalities in pharmaceutical workforce development, continued education, and training and career progressing opportunities

(continued)

Table 19.1 (continued)

Cluster	Workforce development goal	Short description
	Workforce impact and effect on health improvement	Evidence of impact of the pharmaceutical workforce within health systems and health improvement
	Workforce intelligence	A national strategy and corresponding actions to collate and share workforce data and workforce planning activities
	Workforce policy formation	Clear and manageable strategies to implement comprehensive needs-based development of the pharmaceutical workforce from initial education and training to advanced practice

account how the pharmacy can build organizational flexibility. The pharmacy should consider strategic, business and financial planning of the delivery of services, and it should address the image of the pharmacy, secure staff management and consider external support and resources [5].

19.3 Independent Pharmacies and Chain Pharmacies

Historically, the community pharmacy sector has been highly regulated by official bodies. This is both to ensure that the medicines purchased in a pharmacy are of the expected quality, and because, in most countries, governments subsidize medicines. Therefore, community pharmacies in many countries have the exclusivity of prescription only medicines dispensing. The practice involves both the compounding, and the dispensing, of medicines.

In many countries, pharmacies are individually owned by a pharmacist. However, this situation has changed over the past 50 years, and many countries have deregulated their systems and liberalized the community pharmacy sector. There are different models of liberalization—but in all systems, the overall responsibility for Good Pharmacy Practice in community pharmacy remains with the pharmacist.

Community pharmacies are, at a national level, often organized in a Pharmacy Organization. This organization has the task of carrying out the best interest of the community pharmacy sector, and is often the collaboration with government regarding negotiations and legislation in the community pharmacy area. Supporting the delivery of pharmaceutical care services, at a systems level, would also be the task of the professional organization. This can be done through structures for delivery of services, such as manuals and instructions for services, and supporting building capacity to deliver services.

A 2011 report based on a European survey, and illustrated by case studies, showed that in liberalized systems, the trend goes toward an increasing number of

pharmacies, mainly in the metropolitan areas, not in the rural areas. It also shows that pharmacy is still the preferred place to purchase medicines, including over-the-counter (OTC) medicines that are otherwise also available in retail-shops.

In countries where pharmacist ownership is no longer required, the opportunity for commercial chain pharmacies has opened up. There are both national and international commercial pharmacy chains. Looking at the practice of pharmaceutical care in commercial pharmacy chains, the focus in the chains is typically commercial [6]. If the chains take up the delivery of pharmaceutical care services, they are professional and conscious about the commercial delivery of services in their approach and often succeed in implementing services from a financial perspective.

Mail order pharmacies have over the years been available in USA, and one of the more recent developments are online pharmacies. These entities secure the distribution of medicines to areas with low population density.

19.4 What Works?

The development of pharmaceutical care and the focus of pharmaceutical care services are shown in Fig. 19.2. It shows how research has moved from solely focusing on producing evidence for services to implementing services, acknowledging that the delivery of services and change management in the pharmacy is a discipline in itself.

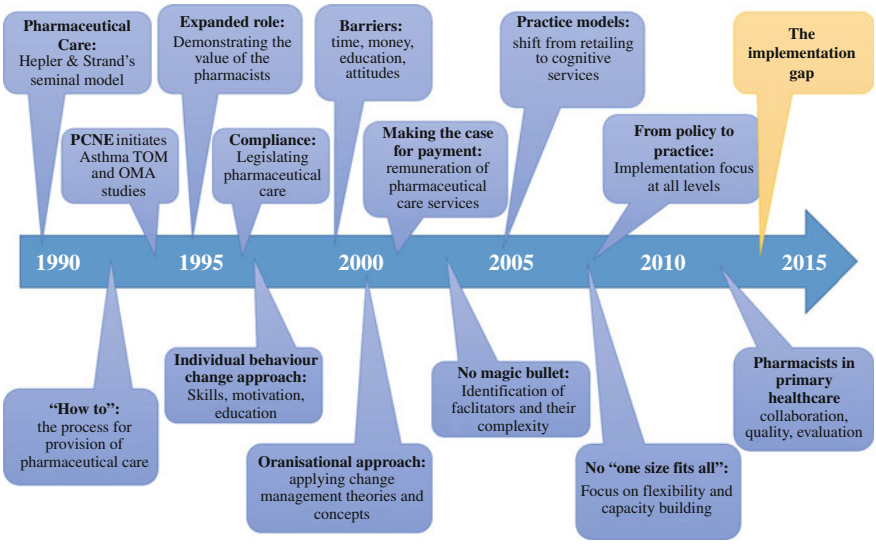

Fig. 19.2 The development of pharmaceutical care research and practice, presented at Pharmaceutical Care Network Europe Working Conference 2013 (PCNE WC 2013); Berlin by Roberts A, Benrimoj S and Rossing C

Looking back at the pharmaceutical care research, different angles can be considered to see how it has evolved over the years. In the early 1990s, the focus on pharmaceutical care was moving in two directions: from the development and later patient outcome-oriented approach to the development of services that could be delivered by a pharmacy [7]. And the focus on pharmaceutical care was a strategy for the profession [8]. The research area needed both the development of evidence-based services and the focus on the pharmacy as an organization that should change practice to reach the state of practice where we are today.

The research on developing pharmaceutical care services concentrated on where the focus was in the services, and who should be the target group for the services [9]. This led to a distinction between population, risk patient and individual patients with chronic disease. In the early days, the services were mostly developed to be delivered directly to the patients, while later research showed the development of services delivered to other primary healthcare professionals, in order to allow them to support the implementation of safe and effective medicines, e.g. among elderly in nursing homes (see Chap. 20).

19.5 Pharmaceutical Care in Community Pharmacies

In community pharmacies, the implementation of pharmaceutical care has been attempted using different initiatives and activities. In many countries today, it is expected that when patients come to a pharmacy they will be counselled on their medicine use and self-management. This may or may not include checking drug-related problems and hence involve basic pharmaceutical care at population level. In some countries, the pharmacies are bound to report medication errors to authorities; e.g. in Denmark, side effects reported by patients or observed by pharmacy staff will be reported to the Danish Medicines Agency.

Pharmaceutical care has also been translated into being the delivery of health services from the pharmacy. Many services have been developed and implemented over the past years. These services are mostly oriented toward better self-management or a safe and effective implementation of medicine treatment.

Figure 19.3 shows the different target groups for pharmaceutical care. At population level, pharmaceutical care can be seen as the general role the community pharmacy has in health promotion and disease prevention. This can be done through campaigns both at the individual pharmacy and in collaboration with other healthcare professionals in primary care. An example of this could be the role of community pharmacies in immunization programmes [10].

Moving from the general level to the specific level addresses patients at risk. These patients are at greater risk of experiencing medicine-related problems due to specific risk factors. They could be elderly patients, with comorbidity or low renal function. It could be patients with low health literacy, having difficulties in understanding the information on their treatment or other patients at risk for not gaining the full potential of their treatment.

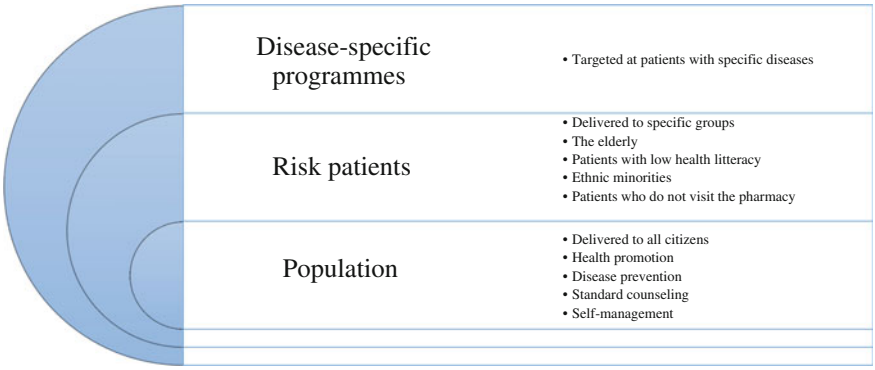

Fig. 19.3 Different target groups of pharmaceutical care [11]

Finally, there are disease-specific programmes, addressing a patient with a specific disease. Often this area is founded on evidence-based programmes documenting the effect on patient outcomes when they receive pharmaceutical care services in the pharmacy.

Pharmaceutical care is care for a patient who uses pharmaceuticals. Therefore, the services should involve the persons who have responsibility for the patient's medicine therapy. This might be the patient himself, an informal caregiver, the staff in a nursing home or the general practitioner. They will all gain knowledge by getting support from pharmacists in the delivery of safe and effective medicines management to the patient [11, 12].

Figure 19.4 shows the services delivered and remunerated from community pharmacy at an international level. The services are divided into Services for Improving the use of medicines, Product Focused Services, primary care and public health services, harm reduction services and other services.

The services that improve the use of medicines are focused on the implementation of rational pharmacotherapy through medication use review, medication reconciliation and new medicines services. Additionally, there are more comprehensive programmes on the known chronic diseases, diabetes, hypertension, Asthma and cardiovascular management.

Medication review has been introduced in many countries as a core service in community pharmacies, both in a nursing home setting, in general practice and directly to patients. The service is always delivered by a pharmacist and includes a structured review of the medicines, addressing medicine-related problems and proposing solutions to the problem.

Many studies on outcomes have been completed, and it has been documented that the delivery of medication reviews made by community pharmacists can improve patients' quality of life and improve patients' empowerment and health status, thus decreasing the number of contacts to the healthcare system, and thereby reducing healthcare costs [14, 15].

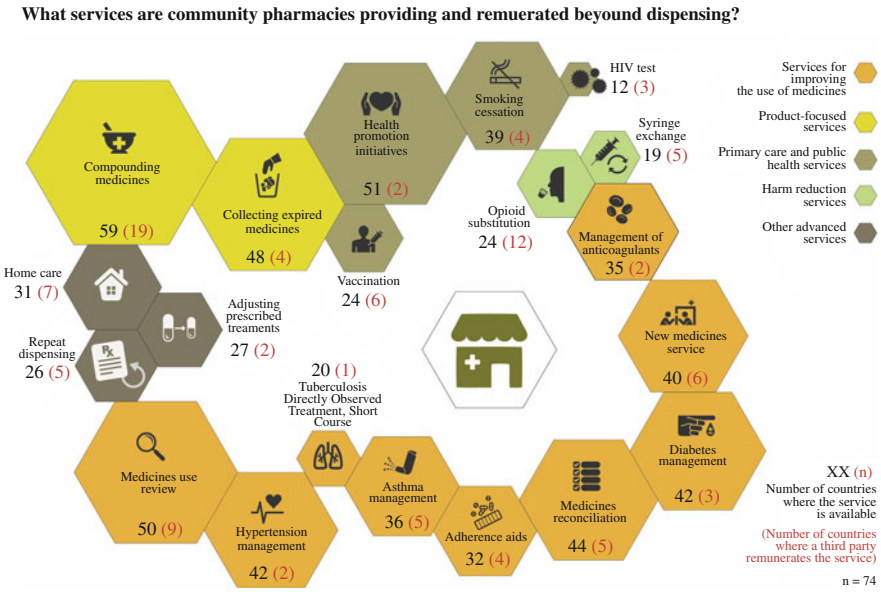

Fig. 19.4 Services pharmacies provide and are remunerated for [13]

For further information regarding the delivery of services internationally, see Chaps. 13–17.

19.6 Pharmaceutical Care in General Practice

Medicines management performed by independent pharmacists in general practice has been tested in different models where pharmacists support general practitioners in their responsibility for the patients' medicine treatment. The studies have proven positive results on risk groups such as elderly polypharmacy patients [16, 17]. This is implemented in practice today in UK and supports the outcomes of the patients regarding medicines management. Different models for pharmacist prescribing support the overall care for the use of medicines at population level and secures accessibility of the medicines.

19.7 The Future of Pharmaceutical Care Delivery

Over the years, dispensing medicines and performing pharmaceutical care have been united at the pharmacy, personalized by the pharmacy workforce. In the future, this may be challenged. E-pharmacies and other web-based shops can

distribute medicines, and they can be delivered by drones. In Switzerland, drones are already applied in the hospital setting, for safe delivery of test responses.

This will challenge the professional counseling regarding medicines as we know it today, because the physical meeting for counseling the patient is separated from the dispensing of medicines. This will call for new models for counseling, new pharmaceutical care services and yet new roles for the pharmacist.

Darrin Baines, a health economist from UK, focused on healthcare and in particular the history of pharmacy and pharmacists. He believes in the profession, stating that pharmacists have always worked with technologies in their practice. In the production of medicines over the centuries, the pharmacist and the pharmacy have been the place where patients go for treatment and the profession they trust to advise them about medicines. To retain this role, pharmacies should rethink their approach to practice. He states five steps to have technology-enabled pharmacies in the future:

1. Refit the "front of the house" as a technology hub that allows patients to connect with the pharmacy, local doctors, the healthcare system, pharmaceutical companies, charities, other patients and the like.
2. Exploit the time that the patients wait for their prescriptions by connecting them to a technology-enabled task, such as reporting on their medicine use, watching an interactive educational programme, completing a questionnaire or being an expert-patient in a study.
3. Network the pharmacy hub into the wider healthcare community, including providers, patient groups and private companies—and by doing so, become the port of first call for patients—and coordinate their care through the pharmacy's technology-enabled networks.
4. Retrain pharmacists in healthcare technology—not just medicines' optimization.
5. Educate and enable the public to become technology-enabled pharmacy users.

The future comprises new platforms for communication, new data to be included in models and new expectations from the patients. The patients will expect availability round the clock, and they will expect the pharmacy to honor this need. Pharmaceutical care services in the future have to honor these needs to be relevant for the patient.

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Chapter 20
Implementation of Pharmaceutical Care in Nursing Homes

Carmel M. Hughes

Abstract Medicines are the most common intervention which patients will receive, and this is particularly the case in the nursing home setting. Research has highlighted the major problems associated with the quality of prescribing of medicines, and the challenges which are presented by this unique environment. Research has also demonstrated that interventions, which often consist of some form of medication review, can improve prescribing, but there is limited impact on other outcomes such as falls, hospitalisations and mortality. This is a population which is in physical and cognitive decline, and providing interventions after prescribing and medication administration have taken place may account for their limited effect. Pharmacists, in the role of prescribers, may offer an alternative approach to pharmaceutical care, and ongoing research may reveal if this model of care can improve outcomes for older residents who live in this unique setting. This chapter will outline some of the key characteristics of nursing homes and how they differ from other healthcare settings, challenges for the delivery of pharmaceutical care in this setting, a description of selected research studies and how the research findings can be translated into everyday practice.

Keywords Pharmaceutical care · Nursing home · Care implementation Vulnerable patients · Fleetwood Model

20.1 Introduction

Nursing homes represent a unique setting for the delivery of healthcare, including pharmaceutical care. A nursing home is an environment in which healthcare is delivered to those who have long-term needs which cannot be met in the community or in hospital. However, a nursing home is also a home for those who reside there. Therefore, it has a dual purpose which can present challenges for those who

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are responsible for the delivery of such care, specifically how to optimize care in a home environment, maintain safety and quality for all residents while ensuring that resident choice and independence are not lost.

20.2 Nursing Homes—A Unique Long-Term Care Setting

As a person ages, the likelihood that they can no longer look after themselves increases. In these instances, long-term care (LTC) may be provided in people's own homes or in institutional facilities such as nursing homes. The terms used to describe such facilities that provide care for older people differ worldwide. In the United Kingdom (UK), the homes are known as "care homes", in the United States (US) they are referred to as "long-term care facilities" (LTCF) and in Australia "aged-care facilities" [1]. Within these categories, further differentiation is made by the type of care provided to residents. For example, care homes in the UK may be defined as "nursing" or "residential", with the former providing 24-h nursing care and must have a registered nurse present. Residential homes, which provide the majority of long-term care for older people, assist with personal care only, i.e., washing, dressing [2]. However, for clarity in this chapter, the term "nursing home" will be used throughout.

Residents of nursing homes are usually frail and have multiple comorbidities and limited life expectancy. Many residents will die within two years of entering a home [1]. The rate of institutionalization increases when dependency levels and needs become too complex or costly to be met at home [3, 4] or by the lack of available community services. Furthermore, the nursing home population is aging in 2011 in the UK, people aged 85 and over represented 59.2% of the older nursing home population compared to 56.5% in 2001 [5].

The most common acute healthcare intervention which nursing home residents receive is the prescribing of medication [6]. Residents may receive up to four times as many medications compared to older people living at home [7]. The use of medicines in nursing homes has been a major focus of research because of concerns regarding the selection of medicines and the overall prevalence of use. Older people living in nursing homes have an increased risk of adverse drug events (preventable medication errors that reach the patient and cause some degree of harm) [8]. Perri et al. [9] found that in a study of 15 US nursing homes, over a period of one month, 47% of residents received at least one potentially inappropriate medicine (PIM—defined as those medications with no clear evidence-based indication—carry a substantially higher risk of adverse effects compared with that associated with their use in younger people, or are not cost-effective [10]), and 13% experienced at least one adverse health outcome (hospitalisation, emergency department visit or death) [9]. Gurwitz et al. [11] found 9.8 adverse drug events per 100 resident-months in two LTC facilities (nursing homes), with 42% being deemed avoidable [11].

20.3 Nursing Homes—Challenges for the Delivery of Pharmaceutical Care

Much research has focused on the type and range of medications which have been prescribed for nursing home residents. Of particular interest and concern has been the use of psychoactive medications, notably antipsychotics, hypnotics and anxiolytics. Much of the seminal research in this field has come from the USA. In the 1970s and 1980s, the frequency of hypnotic use was reported to be between 23 and 34% in the nursing home environment [12–14]. In contrast, medication histories obtained from community-based patients over an 8-year period revealed that the use of hypnotic drugs declined from 8.5% in the period 1978–80 to 6.3% from 1984 to 1986 [15]. Antipsychotic prescribing has also been highlighted as being problematic. Despite uncertainties about the benefits and risks of antipsychotics in older people, the prevalence of their use in this population remains high, especially in care homes, with an estimated 25% in the US [16], 18–22% in the UK [17, 18], 33% in Belgium [19], 28% in Germany [20] and 37% in the Netherlands [21]. The variation in use of antipsychotics is also high between nursing homes within a country [17, 22–26].

It was suggested that such high rates of prescribing were due to these medications being used as "chemical restraints" to sedate and subdue nursing home residents [27]. This was partly in response to so-called "challenging behaviour" of residents, many of whom have dementia, and a shortage of nursing staff [28]. Several initiatives including regulation, legislation and best practice guidelines have been implemented to reduce the unnecessary use of these medications [28].

Although psychoactive prescribing has garnered much attention, other medications have been scrutinized. Antimicrobials which include antibiotics have been identified as a problematic area for prescribing. This is largely as a result of the threat of antimicrobial resistance. Infection control has been recognized as being poor in many nursing homes which, in turn, leads to increased consumption of antimicrobials with the potential for development of resistant bacteria [29]. A large European study, coordinated by the European Survey of Antimicrobial Chemotherapy (ESAC) consortium, investigated antimicrobial prescribing in 15 European countries and 2 UK jurisdictions in April and November 2009 [29]. This was in the form of a point prevalence survey at these two time points in selected nursing homes in the participating countries. Data that were collected included antimicrobial name, total prescribed daily dose, administration route, indication, where it was first prescribed, who prescribed it, whether or not a culture sample was taken before commencing the antimicrobial and the classification according to the Anatomical Therapeutic Chemical (ATC) classification system. The mean prevalence of antimicrobial prescribing in the nursing homes was 6.5% in April and 5.0% in November. The most commonly prescribed antimicrobials were methenamine, trimethoprim, co-amoxiclav and nitrofurantoin. There was large variation in the overall mean antimicrobial prescribing in the selected nursing homes from each of the contributing countries at both time points. For example, means ranged from

1.4% in Germany and Latvia to 19.4% in Northern Ireland in April and 1.2% in Latvia to 13.4% in Finland in November. Furthermore, differences in prescribing were apparent within countries with the largest variation evident in nursing homes in Northern Ireland (21.5%) in April and Finland in November (30.1%). There was no obvious reason for the marked differences between and within countries, but it was recommended that nursing homes needed support in improving prescribing and minimizing antimicrobial resistance [29].

The issues which have been highlighted to date relate to the prescribing of medication. However, the process of administration of medication in nursing homes has also been explored in research. Nursing home care is based on routine in order to facilitate the organization of tasks and to ensure that safety is paramount [30]. Therefore, it has often been assumed that residents will receive their medication on a regular basis and administration will be supervised by nursing home staff) [31]. There are also the over-arching regulatory and legislative frameworks within which nursing homes will operate. In many countries, in order to provide services, nursing homes must be registered with an independent agency which will also perform regular inspections to ensure that homes are attaining minimum standards of quality and safety [32]. Administration of medication will be part of these standards and staff will be expected to record when medication has been administered or if it has been refused by a resident. Indeed, previous research has revealed that nursing home staff's priority is to ensure that all medications prescribed are administered to residents [33], which can be motivated by regulation as administration records will be checked by inspectors. This may lead to problems whereby medication will continue to be given to residents when it is no longer appropriate to do so, leading to the emergence of adverse effects [31]. This will be compounded by the lack of medication review which has been a long-standing problem in nursing homes. Furthermore, the prevalence of dementia and other forms of cognitive impairment in residents may lead to covert administration, i.e., medications concealed in food and drink. The literature has documented cases of this happening in residents who may refuse or spit out medication [31]. Clearly, this runs counter to patient autonomy and the right to make decisions about healthcare; many older people living in their homes are able to make decisions about when and how to administer their medicines. The contrast with the nursing home setting highlights the difficulty of facilitating independence for residents, while ensuring that safe and appropriate practices operate within the home.

20.4 Nursing Homes—Addressing the Challenges for the Delivery of Pharmaceutical Care Through Research

There has been a major research effort which has sought to improve the quality of medicines use in nursing homes, often involving pharmacists providing some degree of pharmaceutical care service, largely focused on a form of medication review.

Much of the early research was conducted in the USA which had implemented legislation to attempt to improve the quality of care provision in nursing homes. Part of this legislative framework required pharmacists to monitor the use of psychoactive medication in nursing home residents, perform a drug regimen review (effectively a medication review) and challenge any unjustified usage of these drugs [34]. The American Society of Consultant Pharmacists, the professional organization for those pharmacists who work in nursing homes in the USA (known as consultant pharmacists), recognized the limitations of this legislative framework, and sought to develop a more holistic approach which they named the Fleetwood Model. This model focused on reducing potentially inappropriate medication use, under-treatment of common diseases, potential adverse drug events and indicators of common geriatric problems associated with medication use [35]. A demonstration project was undertaken (pre-post design) in which 12 nursing homes received the Fleetwood Model intervention, while 13 homes were in the comparison (control) group [36]. The intervention consisted of prospective reviews, direct communication with the prescribers and formalized care planning in residents at highest risk for medication-related problems. Prospective review was facilitated by algorithms incorporated into computer software that was used by prescribers and that could be accessed by the pharmacists, and was also the means by which pharmacists and prescribers communicated to discuss prescribing decisions. Therefore, pharmacists could intervene before a medicine was administered to a resident. Residents at high risk for preventable adverse drug events were those with at least four of the following risk factors based on standing medication orders: use of antidepressant, antibiotic or anti-infective, antipsychotic, anticonvulsant medication, sedative/hypnotic, opioid, anticoagulant, muscle relaxant, three or more cardiovascular medications, or seven or more medications (including over-the-counter and prescription medications). Outcomes which were measured included potentially inappropriate medication use, potential adverse drug events, hospitalizations for any reason and all-cause mortality. Overall, the implementation of the model appeared to have little effect on the preselected outcomes. Intervention residents had similar hospitalization rates, hospitalizations due to adverse drug events and mortality rates in the control homes. There was a decline in the use of potentially inappropriate medications which appeared to happen earlier in the intervention sites compared to usual care, but the difference was not statistically significant [36]. An accompanying process evaluation revealed that pharmacists did appear to deliver the components of the intervention but it was somewhat sporadic [37, 38]. The authors highlighted that residents in nursing homes require comprehensive and holistic pharmaceutical care, but it may be difficult to demonstrate an impact on outcomes [36]. This may be a function of a population which is clinically complex, frail and in decline.

The Fleetwood Model was developed specifically for the American nursing home setting which is quite different to that in other parts of the world. Transposing the Fleetwood Model in its current form to other national settings is unlikely to be effective; therefore, adaptation would be required to account for differences in practice and context. This was undertaken by Patterson et al. [39] who adapted the Fleetwood Model for use in Northern Ireland nursing home settings. The original

model was extremely broad in its scope, and required the availability of sophisticated computer systems for recording and monitoring interventions [36]. The adapted model focused on psychoactive medications (antipsychotics, hypnotics and anxiolytics) as these were deemed to be the most problematic in Northern Ireland nursing homes. It was also recognized that medication review could only be applied in a retrospective manner, i.e., pharmacists would not be able to intervene in real time to make suggestions regarding prescribing changes, as had been possible in the US study [39]. Therefore, the adapted model was tested in a cluster-randomized controlled trial (RCT) in 22 nursing homes; 11 homes received the intervention and 11 homes continued with usual care [40]. The intervention consisted of specially trained pharmacists visiting intervention homes monthly for 12 months and reviewing residents' clinical and prescribing information, applying an algorithm that guided them in assessing the appropriateness of psychoactive medication, and working with prescribers (general practitioners) to improve the prescribing of these drugs. The primary outcome was the proportion of residents prescribed one or more inappropriate psychoactive medicines according to the evidence-based algorithm. The secondary outcome was the rate of change in falls, as these medications have been associated with such events [41]. The results were positive showing that the proportion of residents taking inappropriate psychoactive medications at 12 months in the intervention homes was significantly less than in the control homes (20% vs. 50%, respectively, odds ratio 0.26, 95% Confidence Intervals 0.14–0.49). However, there was no difference observed at 12 months in the rate of falls between the intervention and the control homes [40]. Further analysis indicated that the intervention was more cost-effective than usual care [42]. As with the American Fleetwood Model study, the intervention in Northern Ireland nursing homes appeared to be effective in respect of prescribing appropriateness (albeit on a more restricted group of medicines), but appeared to have no effect on an outcome such as falls. It should be recognized that it is very difficult to demonstrate the effect of discontinuation of medicines on falls as several factors contribute to the latter [43].

Many studies which have focused on prescribing in nursing homes have shown limited effects. This has been confirmed by Alldred et al. [1] in a recent Cochrane review entitled "Interventions to optimise prescribing for older people in care homes". This review included 12 studies involving almost 11,000 residents, and 10 of the interventions included some kind of medication review as one of the components. However, due to heterogeneity across studies, it was not possible to undertake a meta-analysis. It was concluded that interventions led to the identification and resolution of medication-related problems, and improvements in medication appropriateness, but there was less certainty regarding a reduction in drug costs, adverse drug events and mortality. Importantly, the review highlighted the importance of defining, measuring, reporting and analyzing important resident-related outcomes, including quality of life. This reinforces the need for a core outcome set (COS; see Chap. 12), and indeed a COS has been developed for optimizing prescribing for older people in this setting [44]. The value of these outcomes has yet to be tested and it may be the case that a number in combination, i.e., a composite outcome, may be more meaningful.

20.5 Remaining Challenges

Clearly, pharmaceutical care provision must be provided to this very vulnerable population which is exposed to a wide range and number of medications. There needs to be careful consideration as to what can be achieved with conventional medication review in terms of impact on outcomes (see also Chap. 6). Much of the research on medicines has focused on medication review and the recent Cochrane publication has identified this as a central component of most interventions [1]. However, this is usually retrospective and attempts to influence prescribing after it has taken place. An alternative approach is for pharmacists to assume responsibility for prescribing [45, 46]. Indeed, ongoing research seeks to test the model of a prescribing pharmacist in the nursing home setting in the Care Homes Independent Pharmacist Prescribing Study (CHIPPS) (https://www.uea.ac.uk/chipps)—a UK programme grant which incorporates a multicentre cluster-randomized controlled trial to determine the effectiveness and cost-effectiveness of pharmacist-independent prescribers taking responsibility for the prescribing of patients' medicines in care homes. The definitive trial is due to begin in 2018, following on from developmental work which focused on the content of the training, development of the intervention and feasibility testing. Pharmacists will be working closely with family doctors and nursing staff to optimize medicines use, and this teamwork model may represent how care should be delivered in the future.

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Chapter 21
Implementation of Pharmaceutical Care in Hospitals and Clinics

Ulrika Gillespie

Abstract Although there is plenty of evidence that pharmacists performing medication reviews in a hospital setting as well as other pharmaceutical care activities is beneficial in different ways, the evidence is quite heterogeneous, and effects on primary endpoints have not yet been satisfactorily shown. There are still a number of factors that need to be determined; what methods should be used? By which profession and with which education and training? Which patients should be targeted? With an aging population, increasingly complex medication treatments, a shortage of physicians and nurses, the need for pharmaceutical care provided by clinical pharmacists in hospitals seems immense, and the question for the future will probably rather be if there are enough trained pharmacists to fill this gap. This chapter will focus on medication reviews and the opportunities and challenges for pharmacists to provide patients with pharmaceutical care in a hospital setting.

Keywords Pharmaceutical care · Hospital · Care implementation
Medication errors · Seamless care

21.1 Introduction

The main objective for pharmacists providing pharmaceutical care to patients in a hospital setting is to ensure patients receive medicines tailored to their individual need, to make sure they receive maximum benefit and minimum harm from their treatment. In hospitals, especially in the intensive care unit (ICU), this can be a complex and advanced process and that it may, for instance, involve issues with compatibility and administration, high-risk medications and acutely ill patients. Ideally the pharmacist, should be fully integrated into the multidisciplinary team (MDT), proactively involved—making sure the right treatment is being prescribed

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rather than reactively checking and correcting prescriptions. The latter, checking and correcting, is probably the most common way that clinical pharmacists in hospitals practice today but the trend, as practices mature, seems to be toward more integration where pharmacists are seen as partners (with physicians, nurses and patients) rather than advisors. In some countries like the UK, with a long tradition of clinical pharmacy, this is already happening and pharmacists are even taking on a prescribing role. Commonly, but not exclusively, clinical pharmacists in hospitals provide pharmaceutical care through medication reconciliation and medication reviews (see Chap. 6).

21.2 Medication Use in the Hospital Setting

The span of services and specialties within a hospital is immense; there is acute care and elective surgery and procedures, wards for the local population alongside highly specialized international centers of excellence. There are rehabilitation wards where patients stay for extensive time periods and ICU for adults or neonatal children. Patients may be in a palliative stage or have appointments at an outpatient clinic for minor procedures. One thing that unites patients receiving care at a hospital is: nearly all will receive medicines.

All medicines need to be prescribed, dispensed and administered to patients by professionals with adequate competence and training. The patients have very different needs; some are prescribed medicines that they will use long- term, they will need to know the risks and benefits they can expect from the medicine and what the alternatives are. The medicine needs to be safe, effective, easy to take and affordable (to mention a few factors). Patients may need monitoring, motivation and adherence aids. At the other end of the spectrum, patients in ICUs rarely need information on the medicines they receive, but the need for pharmaceutical care services is obvious considering the high-risk medication processes. Then there is always the need to ensure correct transfer of medication information to the next ward/caregiver within the hospital.

21.3 Medication Reviews for Hospital in-Patients

Medication reviews serve a multifaceted purpose: to achieve a safe, effective, evidence-based, practical, and cost-effective medication therapy.

Since patients spend most of their lives outside of hospitals and the healthcare providers they most regularly see are primary care physicians, community pharmacists and nurses, it makes sense that thorough medication reviews should be performed in the community setting, by a physician (or other healthcare professional) in charge of (or at least fully informed of) the patient's full medication. Ideally, it should be someone who has a long-standing, trusting relationship with

the patient and the right competence to cater for all the patient's healthcare needs—pharmaceutical and non-pharmaceutical.

In real life, however, some patients, at least in some countries, do not have a close relationship to one single primary care physician. They may have conditions necessitating frequent hospitalizations and consequently, hospital physicians/hospital Consultants, may be their main prescribers. Patients may present at the emergency department with a long list of medications, which may not reflect their current prescription. During their stay in the hospital, their medication may undergo many necessary amendments, which may occur at any time from admission to discharge e.g. due to rapidly deteriorating organ function. All these factors make medication reconciliation and review crucial within the hospital setting—when a new medicine is started in hospital, it needs to be checked for compatibility with the already prescribed ones, which means (or should mean) assessing and evaluating the complete drug treatment.

Another advantage with medication reviews in a hospital setting is the fact that, if the admission period is long enough, medication changes can be done while the patient's vital parameters, signs and symptoms are well monitored. This is especially useful when making changes in direct-acting, potent medicines and when there is a high risk of adverse drug events (ADEs).

Within the cohort of patients who present to the ED or are admitted to hospital, there are 5–45%, which are due to drug-related problems [1–4]. These patients are obviously in need of a mediation review, where the underlying problems are identified and solved to prevent recurrence. Pharmacists, with their unique skillset and training on medication use, could very well be the ideal healthcare professional to deal with this.

In Northern Ireland, the concept of Integrated Medicines Management (IMM) was invented at the start of this century [5]. Medicines management involves the systematic provision of medicines therapy through a partnership between patients and professionals to deliver best patient outcomes at minimized cost [6, 7]. Having ensured that patients' medication use is known and that they are receiving appropriate medications, the clinical pharmacist has a role in patient education on their disease state, and importantly on their medications, devices, etc., and in monitoring patient outcomes [5]. IMM has been adopted, and slightly adapted, in several European countries, primarily in Scandinavia [8, 9].

21.3.1 Step One—Medication Reconciliation on Admission and Discharge

The first step in the medication review process should always be medication reconciliation. Without knowing the patient's actual use of medications prior to hospitalization, there is little point in scrutinizing the drug regimen for drug-related problems and opportunities for optimization (see Chap. 6).

Medication reconciliation should ideally be performed as soon as possible after the patient arrives at the hospital. When performed in the ED, it can ensure that the patient benefits by having correct and updated medication lists, before being transferred to the ward and/or discharged. Often, however, it is performed at ward level where the patient has been admitted, and one cut-off point often used is within 24 h.

Medication reconciliation in hospitals is currently being performed by pharmacists, physicians, pharmacy technicians or nurses: different settings and countries choose different strategies. The process has shown large benefits in reducing drug-related harm caused by medication errors (omissions, commissions and wrong doses) and is by many seen as a compulsory activity [10–14]. When implementing medication reconciliation services in a hospital, some factors need to be highlighted; while medication errors are frequent, only a small proportion of patients actually experience clinically relevant adverse events due to these errors [15]. Hospitals worldwide struggle to find models where all patients receive a medication reconciliation, mainly since it is a rather labor-intensive activity. Greenwold et al. stated that: "it is important to develop mechanisms for prospectively and proactively identifying patients at risk for medication-related adverse events" [16]. Such an alert system would help maintain vigilance toward these patient safety issues and help focus medication reconciliation resources on high-risk patients. In a recent study by Stuijt et al., they aimed to identify "determinants" that would allow for selecting patients at risk for serious adverse events due to medication errors, who should be prioritized for a medication reconciliation [17]. They found that 75% of 765 included patients had received at least one intervention, something that made prioritization difficult. However, they concluded that if hospitals, forced by resource shortages, need to prioritize reconciliation activities, they should focus on female, acutely admitted patients with a higher number of high-risk medications.

The availability of different information sources, used in the medication reconciliation process, varies greatly between institutions and countries. In Sweden for example, the electronic medical record is often the same in primary and secondary care and includes one, shared list of medication that both parties can access and modify. The prescription history is available with prescriber's name, institution and dates of issue. Data can also be retrieved (with the patient's permission) through the electronic medical record via a national database on all prescriptions that have been dispensed from any pharmacy during the last 15 months. In addition, all medical notes are available for both parties to find out reasons for prescribing or discontinuing a medicine. In wards where pharmacists are working as team members, they will have access to this, as well as physicians and nurses. (Community pharmacists do not have access to any of these sources, except for the dispensing data). In spite of this excess of information regarding patients' prescribed medicines, the medication lists are often not updated and reasons for starting or discontinuing a drug often lacking. This means that no matter what system you have in place or strive for, there is always a need for checking for errors and the person performing the medication reconciliation needs to be alert to the possibility of errors arising.

Many studies have confirmed that the patient/carer interview is the most important part of the medication reconciliation process and should always be performed when possible [18–20]. What is prescribed and dispensed at the pharmacy comprise only two pieces of the puzzle. The patient's actual use of medications is the most important piece, and it can be quite different from the first two.

Medication reconciliation also includes communicating medication-related information (new medication list with instructions, reasons for changes etcetera) to the patient/carer and next caregiver when the patient is leaving the hospital. As stated by Scullin et al., the clinical pharmacist has a role to ensure that the discharge is as seamless as possible, through working with the care team to ensure that discharge prescriptions are accurate and, through liaison with primary care physicians, community home-care providers and community pharmacies, that any hospital initiated medications are available for the patient after discharge [5, 21, 22]. This is vital as medication errors and misunderstandings at discharge have the potential to lead to even more serious events—when patients are left to their own devices at home.

21.3.2 Step Two—Medication Review/Optimizing Pharmacotherapy Including Follow-up

As the rationale for, and processes of, medication reviews is described previously in this book (Sect. 21.3) this section will only touch on factors specifically associated with medication reviews in a hospital in-patient setting.

For a relatively new profession within the healthcare teams, it can be hard for pharmacists to find their roles. The clinical pharmacist will need good communication skills and need to be good at finding opportunities for collaboration. The inclusion of a pharmacist in the team needs to be everybody's business, ensuring appropriate task sharing and that the pharmacist's competence is being used properly. The different professionals need to be cognizant of each other's skills and scope of practice. When the pharmacist has performed a medication review and has suggestions on how to optimize treatment for a specific patient, what sometimes happens is that they choose to put forward these suggestions in writing to the physician, to save time and not disturb the "flow" on the ward. Studies suggest that this should be avoided, however as it leads to fewer recommendations being acted upon, misunderstandings and that the pharmacist is viewed more as an adviser than as a team member [23, 24]. Instead pharmacists should strive for a face-to-face discussion with the physician on how to solve the identified problems and improve pharmacotherapy for the patient [25].

For pharmacists, it is important that they try to be fully informed of the changes in status of the patient, and involved in the plans and decisions made by the team. To achieve this, they may need to participate regularly on ward rounds. There are advantages and disadvantages to this. Advantages are they will be viewed as, and

can act as, formal team members, being useful in a timely manner, it is a great learning opportunity for junior physicians, nurses and pharmacists (as well as for ward-based students) to be exposed to (and take part in) the discussions on appropriate medication selection and problem solving. Disadvantages are of course time constraints. The pharmacist will struggle to find time to take part in the ward round, where many non-drug-related issues are addressed, and nurses and doctors are pressured for time when ward rounds are prolonged by in-depth medication discussions.

One well-known fact is that drug-related problems (DRPs) raised by the patients or identified in patient interviews are generally more clinically relevant (at least the patients think so) and more often resolved [26]. This means that when using tools such as STOPP/START to screen for or identify DRPs, many remain undetected [27]. Often, hospitalized patients are not well enough for discussions, at least initially, but then relatives and carers can (and should) be contacted to shed light on the patient's medication use, including reports on effects, side effects and concerns.

According to the IMM concept, patients should be monitored and educated throughout the admission process [7]. At discharge, they should be fully informed of (and content with) the future medication therapy and aware of the changes made during admission (as well as the reasons for the changes).

When a comprehensive medication review is performed in a hospital setting on acutely admitted patients, it is important to recognize that all identified DRPs cannot and should not be solved immediately. There are problems that are non-urgent and not at all related to the cause of admission that are better to resolve after discharge, and there are specialists' therapies that the ward physician does not want to touch, even though he can see that there may be a problem and there are times when the patient has already had too many medication changes, or is too infirm, that it is better to wait. This is often very frustrating for the person performing the medication review since there is a real risk that these problems will remain unsolved and the recommendations un-communicated after the patient has been discharged. There are ways to address this problem. One is to carry forward the information and recommendations to the next caregiver (usually the patient's primary care physician) in a medication referral. This could be sent by the physician, who may be sending a referral anyway regarding other matters, or by the pharmacist. If the pharmacist sends the referral; however, it is important to make sure there are not conflicting messages being sent out from the hospital.

If there have been many changes to the drug treatment during the hospital admission, or if the patient can be expected to have difficulties managing medications, a follow-up phone call soon after discharge, to ensure understanding and improve adherence, could be a very good idea. Indeed, in one study from Hong Kong, the counseling phone call from pharmacists to discharged patients even showed positive effects on mortality [28].

21.4 Opportunities for Implementation and Scaling up of Practice

When introducing a brand-new service, for example, medication reviews performed by an integrated clinical pharmacist in a hospital setting, it is of course important to consider where the need for such service is the greatest. But another, equally important, factor is to start where the service is wanted and supported by the already existing healthcare team, and especially by the physicians and clinic leads. This can greatly affect the success (or lack thereof) of an initiative. Physicians or nurses who are unaware of the potential benefits of having a clinical pharmacist in the team can be approached in different ways. One way is to perform audits, where the current situation is measured in a small project, conveniently performed by pharmacy students undertaking their Master's thesis, for example. If the results show that there is room for improvement in the field of medication management—identifying, for example, patient risks or low cost-effectiveness—that is a good starting point for discussions on how to proceed with interventions and services that have proven effective in other settings. After agreement, a pilot study can be launched where the intervention is evaluated and refined. Here it is crucial to buy in from the formal and informal decision makers. As physicians and nurses change positions and wards frequently, new services tend to be increasingly requested in new clinics, if they are successful and can show benefit for patients and/or other healthcare professionals as well as for the hospital's economic situation. One factor that is thought to have accelerated the implementation of clinical pharmacy is a general shortage of physicians and nurses. This has meant that innovative solutions are sought to fill the gaps, introducing pharmacists and pharmacy technicians on hospital wards and working with medication reconciliation, medication reviews, patient and staff education as well as prescribing.

21.5 Current Evidence Base for Medication Reviews in a Hospital Setting

Many studies have shown that multi-professional collaborations in a hospital setting, including pharmacists, result in beneficial effects. These studies have focused on the effects on patient safety (reduction in medication errors and ADRs) [29–32], health-economy (reduction in drug costs or healthcare utilization) [5, 24, 33–35] and appropriateness of prescribing [9, 33, 36–39]. It is evident that there is a strong case for preventing drug-related morbidity, for clinical, humanitarian, and economic reasons, and that pharmacy has much to offer [40].

In a couple of recent systematic reviews, studying the effects of hospital- initiated medication reviews, the conclusions have been less positive however [41, 42]. They both included very few studies, mainly because they were limited to prospective randomized controlled trials, reporting on the outcome measures

rehospitalization and mortality. The largest one, which was a Cochrane review concluded: "We found no evidence that medication review reduces mortality or hospital readmissions, although we did find evidence that medication review may reduce emergency department contacts. High-quality trials with long-term follow-up are needed to provide more definitive evidence for the effect of medication review on clinically important outcomes such as mortality, readmissions and emergency department contacts." [41].

It may be argued that the absence of studies showing a positive effect on such multifactorial outcomes as mortality and rehospitalization is probably due to the fact that this is extremely hard to accomplish—when the intervention only targets one associated factor (inappropriate medication use). It may be argued that perhaps these outcomes are not the best to assess the usefulness of pharmacists providing pharmaceutical care in a hospital setting. Another systematic review by Graabaek et al. had a broader scope and concluded that most studied pharmacists' interventions yielded positive effects on the chosen outcomes [43].

There is also an ongoing prospective multicenter study, MedBridge, aiming to address the requests made by the Cochrane collaboration, on producing evidence of effectiveness of medication reviews in a hospital setting on hard clinical outcomes [44]. The main results of MedBridge are expected in 2019.

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Part V
Delivering Pharmaceutical Care in Practice

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In this section, we look at the activities through which pharmacists deliver care and in doing so, we illustrate the specific events and processes comprising the delivery of pharmaceutical care. Foremost among these is, inevitably, providing prescribed medicines, a process usually referred to as dispensing. Throughout the history of health care, prescriptions have been viewed as orders for the supply of items, and patients and others often speak of having them filled, and then of collecting their prescriptions. Prescription dispensing is often thought to be, and is usually costed as, little more than a supply activity, but it can be so much more [1]. As the capacity for the automation of storage, selection, packaging and the delivery of medications, either as original packs, or as pouches containing all of the patient's doses for a particular time and day increases, these supply processes can be seen ever more clearly to be separate from the patient care responsibility that is the main focus of the pharmacist's role today.

Nevertheless, the processes of prescribing and dispensing medications are important at the societal or population health level, since medications are not ordinary goods but ones which may be used to treat conditions and symptoms. Patients may not be able to assess proficiently, the seriousness of the conditions and symptoms and medications are goods which have the capacity to produce benefits and harm not only when taken but also when not taken. It is for these reasons that medications are regulated and that one area of regulation is to classify them according to how they may be supplied and this is closely linked to their clinical use and their safety in use. Medications intended for the treatment of serious conditions and medications which themselves have a significant capacity for harm are classed as prescription-only and may be prescribed only by those with appropriate qualifications.

The range and scope of prescribing by medical and nonmedical prescribers has become more clearly delineated and regulated between and within countries and has come to include pharmacists. Similarly, the classes of medications that may be obtained without prescription have increased as the characterization of the benefits and risks that derive from the use of the product has been more intensively studied.

This comprises an evaluation of the drug, the dose, the form, and the dose regimen required for the specified indication. Regulators of Medications, Health Service bodies and Health Care Professional organizations all contribute to the framework of regulations, guidelines, and codes of practice that circumscribe the provision of medications of all types. Today, this information infrastructure is more accessible to the public and more closely scrutinized than ever before.

When prescription medications are being provided, patients and pharmacists have often taken the opportunity that this encounter provides, of discussing, clarifying or reflecting on what has been prescribed and why, and of reviewing this against past experience. And when the pharmacist is uncertain or unhappy about the prescription they have approached the prescriber to try to resolve their uncertainty or disquiet. As a result, pharmacists have been seen as having the job of checking that all is well with the prescription and that the patient can begin to take their medication. Essentially, it is this activity—the detection and intervention to prevent and resolve problems with prescriptions and the assumption of this professional responsibility that laid the foundation for pharmaceutical care. So while dispensing a prescription is not part of pharmaceutical care, taking responsibility for seeing that a prescription is in the best interest of the patient is.

Pharmaceutical care can be viewed as the formalization of these processes, since it is focussed on the individual and their medications, the actual and potential problems, and the pharmacist's acceptance of the responsibility to provide care for the patient. When receiving a prescription medication for the first time, a patient's need for information and a pharmacist's duty of care to provide that information are both substantial [2]. This poses a significant challenge to both parties since the provision and retention of the complicated and unfamiliar information that is required tests the communications skills of both patients and of pharmacists. Medications and medication-taking must be incorporated by the patient into their daily routine and where it is not clear to the patient what they need to do, the result may be that the medication is not taken as it needs to be and/or that the medication is not taken or not taken for as long as it needs to be. Therefore, the early encounters at the time of dispensing a new prescription are important for the patient, the pharmacist, and the health service.

However, the prescription is only one element in the health care that the patient is receiving. So the prescription must be considered in the context of the patient's prescription medication history. Therefore, Chap. 22 of this section is divided between the dispensing of new or first-time prescriptions and of those that represent the continuation of treatment through the repeat dispensing of a prescription. The presence of patient medication records in pharmacies has not been, and is not, universal for a number of reasons, but its prevalence is growing. Clearly, if the patient–pharmacist consultation at the time of dispensing is to function effectively as a check that there are no concerns about the medications on the prescription, this check must be performed with complete knowledge of any other medications that have been prescribed and which are still required, and any history of the patient's response to medications both those that were ineffective and those that could not be tolerated. As health care and health services become increasingly complicated and

as the prevalence of multimorbidity rises, so it becomes more likely that a patient will receive prescriptions from more than one prescriber—recording and reconciling all of these prescriptions is an important part of the pharmacist's assessment. Furthermore, as patients age, their response to, and their need for, certain medications may change, and this must be taken into account if high-quality care is to be provided. New health needs may require additional medication and conversely, resolution of health needs would allow a medication to be discontinued. Although these new/first-time and repeat prescription scenarios may seem to be no more than variations on a common theme, in each case the concerns about, and attitudes towards, medications, and the willingness to accept the prescribing of a new medication or the deprescribing of an existing medication are very different. In addition, when the readiness and capacity to accept information and to weigh up the benefits and risks of action and inaction, both on the part of the patient, and on that of the pharmacist, are taken into account, it is clear that the nature and content of each situation differs and is more complex than is it first seems.

While in its current and most common use, dispensing is the making up of a medicine according to a prescription, since a minority of medications are made up or compounded in this way today, the provision of medications in a pharmacy, whether prescription or nonprescription may be thought of as dispensing. Self-medication has always been an important action in response to symptoms. Everyone is at one time or another in life a patient or a carer, and makes, consciously or otherwise, an assessment of the need for a medication and of the potential benefits and harm that may come with its use. The scope, depth, and quality of the assessment may vary, and depends on the knowledge and information that is used to form the judgement about whether, and which medication is needed. The availability, the indications for which nonprescription medications may be used, and the number of sources from which medications can be obtained without prescription has increased especially since the Internet has become ubiquitous. Governments all over the world have encouraged patients to take responsibility for treating themselves and the promotion of nonprescription medications via all possible media ensures that everyone is exposed to encouragements to self-diagnose and to self-medicate. However, the widespread availability of medications and the ways in which they may be used creates both individual treatment dilemmas and potential population health problems [3]. Consequently, in many countries, some control of nonprescription medications is considered necessary, so that the dose, quantity, form, and availability from a pharmacy, from other types of retail outlets or from pharmacy or non-pharmacy websites means that multiple sources are available in most countries. Continuous review of the balance of benefits and risks results in the switching of medications from one class to another by regulators; sometimes terms like, downscheduling—moving from prescription-only status to nonprescription and upscheduling, moving from nonprescription to prescription status are used; recent examples would be sibutramine becoming nonprescription in the UK and diclofenac reverting to prescription-only in many countries. For self-medication, the information and advice that is available can be crucial to the effective and safe use of the medication. Pharmacists offer advice and

information about nonprescription medications independently of the manufacturer and also about the symptoms and interpretation of the patient's history. The provision of care in each of these instances, which may or may not be associated with the eventual use of a nonprescription medication, is important when the patient is only using nonprescription medications and also when the patient has assumed responsibility for their self-care in the context of the management of chronic disease (s). These aspects are discussed in Chap. 23 of this section.

Medications that are not taken orally may require a delivery system and a physical container for single or multiple doses. These medication delivery systems are more simply called medical devices and their proper use calls for knowledge and skills that evidence suggests patients require, but do not always receive or manage to retain, for example, inhalers used to deliver medications to the lungs. The physical delivery system and the materials it is made from must be manufactured and tested to the same standard as the medication itself and so syringes and other materials are also classed as medical devices. Similarly, dressings for wounds and burns and joint and vascular supports are regulated as medical devices and may be provided through pharmacies and some of these may incorporate medication into the material in order to release it over sustained period of time. The use of materials science and technology to create new combinations of formulations and devices will continue to increase. The aim of allowing patients to self-administer by different routes will increase the range of medications and the types of devices available for this purpose and the necessity to ensure that these devices can be used to optimal effect. Examples of the way in which pharmacists can provide care with devices are presented in Chap. 24.

While medications are an integral part of the treatment of disease, it is often overlooked that they are also used for prevention, and that medications alone are rarely sufficient to control disease or prevent it from occurring. So, in the same way that trying to discuss the use of a medication with a patient without setting it in the context of the disease and the goals of treatment is unadvisable and ineffective, it is also inappropriate for a healthcare professional not to address any lifestyle factors that could contribute to the patient's care. In addition, since community pharmacies are readily accessible and, in many countries, provide not only medications but also other goods and services, pharmacies are places that people who are not seeking treatment visit. Consequently, pharmacists have a duty of care to take whatever opportunities present to promote the health and well-being of the people who consult them. There is a growing body of evidence in several areas that pharmacists can help patients manage their risk factors as well as take their medication [4]. The final Chap. 25 of this section therefore considers health promotion and the role of the pharmacist and of pharmaceutical care.

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Chapter 22
Pharmaceutical Care and Dispensing Medicines

Luís Lourenço, J. W. Foppe van Mil and Martin Henman

Abstract Dispensing prescription medicines is the most frequent activity performed by pharmacists worldwide. It offers pharmacists and their staff the opportunity to discuss the medications with patients and therefore to contribute, "to the care of individuals in order to optimize medicines use and improve health outcomes" (PCNE). By providing pharmaceutical care around the dispensing of medication, pharmacists may help the patients make the most of their medicines and of treating/controlling their disease(s). A number of protocolised services can be recognized in practice in different countries. For new medicines that are dispensed for the first time, there are several examples of pharmacy services that try to pre-empt non-adherence, amongst others. For repeat prescriptions, maintaining the therapeutic relationship, checking for problems in those most at risk and avoiding normalizing poor and declining health are activities that the pharmacist and the pharmacy staff can take to help patients. Whatever activity pharmacists and their staff undertake, they must be based on the Good Pharmacy Practice guidelines, and be properly documented like all healthcare activities.

Keywords Pharmaceutical care · Dispensing · Prescription review
Medication review · Patient counseling

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22.1 Dispensing and Medication Use Today

For many centuries now, doctors have prescribed medicines, and pharmacists dispensed them. But in order to create the most benefit for the patient, the dispensed medicines should not only be of good quality, but the dispensing process should also assist the patient (or medicine user) to have the most benefit of them. As Hepler and many others stated, the outcomes of the medication therapy should be the concern and responsibility of the pharmacist. This means that the task of the pharmacist does not start nor end with the mere handing over of the medicine.

According to the WHO, when faced with a prescription, "the pharmacist verifies the legality, safety and appropriateness of the prescription order, checks the patient medication record… (when such records are kept in the pharmacy), ensures that the quantities of medication are dispensed accurately, and decides whether the medication should be handed to the patient, with appropriate counseling" [1]. But in many countries, dispensing prescription medications has become a high volume, routine activity. As a result, the focus is on the dispensing only, and undetected errors and problems may occur and patient harm can be caused. On the other hand, dispensing is the moment where the patient, or his caregiver, usually is in the pharmacy and easily accessible for counseling and care provision. A focus on efficient dispensing only may cause this moment not to be used properly.

22.2 Dispensing and Providing Care

Dispensing is a routine activity for a pharmacy but providing pharmaceutical care in many countries may not be. Inserting the elements of pharmaceutical care into routine dispensing requires careful thinking, targeted implementation strategies (see Chaps. 18, 19, 20, and 21), rerouting of routines, motivated pharmacists and staff, and optimal cooperation with other care providers such as doctors and nurses. The routine dispensing process will undoubtedly be affected by providing pharmaceutical care.

Usually prescriptions are generated by a physician. However, increasingly pharmacists also may create a prescription, either through pharmacists' prescribing, or through synchronization procedures for repeat prescriptions. A pharmacist advice regarding OTC medication in some countries may also be called "prescribing".

In the first stage of pharmaceutical care (see the pharmaceutical care cycle in Chap. 1) during dispensing in any pharmacy, the goals of the therapy must be clarified. Then the optimal pharmacotherapy for this individual patient must be assessed, taking into account possible interactions and contraindications. At the dispensing moment itself, appropriate patient-oriented counseling must be given, and after the start of therapy possible drug-related problems must be evaluated and dealt with. And all activities must be properly documented, before, during, and after the dispensing process. Separate chapters in this book are dedicated to most of these activities.

In general, the licenced pharmacist will have the knowledge and skills required for the provision of pharmaceutical care. However, in order to be efficient, usually the pharmaceutical care provision around dispensing is a shared responsibility between pharmacists and their staff. Where in this chapter "pharmacist" is written, one could also read "pharmacy staff member" provided that delegation of activities has been properly protocolised or described, and the staff member has been educated for the task (see Chap. 40).

22.3 Integration of Pharmaceutical Care Processes

22.3.1 Checking of the Prescription

As indicated before, in daily pharmacy practice, the care-related processes must become integrated in the dispensing (handing over) process. At presentation of the prescription in a pharmacy, a validation or review must take place of both prescription and patient. The (new) prescription must be integrated into the pharmacotherapy plan or pharmaceutical care plan. This involves not only a dosage and drug–drug interaction control, but also a (re-)assessment of therapeutic goals. Usually additional information is required, for which the patient or his carer is a primary source. If needed other caregivers can be contacted. To prevent medication errors and drug-related problems, it is essential that medication reconciliation and prescription review are completed before any dispensing starts. Actions such as contacting the prescriber to avoid medication errors or drug-related problems must have been taken before dispensing.

A change in dose, in regimen, or in formulation may be simple to effect, and in some jurisdictions changing prescriptions in this way is within the pharmacists' scope of practice. Changing the medicine—an addition or discontinuation or switch to another medicine—is more complicated both clinically and legally, and usually will require the agreement of the prescriber. Generic switching seems somewhat easier to accomplish.

Such extensive review activities as described above are usually not necessary for repeat prescriptions, unless the patient has developed a new ailment or disease, or the dose of the medicine has been changed. On the other hand, the prescription review may also indicate the need of a full medication review and reconciliation, which then has to be carried through (see Chap. 7).

In terms of patient care, the dispensing of a medication for the first time is often an important clinical event and should trigger an assessment to determine how familiar and prepared the patient is to begin the new medication and to integrate it into the existing treatment and lifestyle. Similarly, it can be important to monitor the second time dispensing. However, dispensing to patients who have been discharged from hospital, or who have just been admitted to a nursing home should also be treated as "new" because moving from one setting to another is a known risk factor for adverse health outcomes, many of which are medication related.

Checking the medicines compatibility with other medicines and diseases of the patient is in some countries done with the help of a computer and patient file and is called medication surveillance.

Table 22.1 shows a list of patient and medication-related information that ideally is required for assessing the appropriateness of a new prescription and counseling urgency, apart from the medication history.

Prescription review, prescription validation or medication surveillance is often described as a purely technical activity that would not necessarily involve the patient or consultation of medication history records. But as with all routine tasks in healthcare, the detection of ambiguities, inaccuracies, errors, and potential errors at this stage will protect patients and trigger the provision of pharmaceutical care for those patients in need of it. It is therefore essential that medication reconciliation and prescription review are completed before dispensing starts and accesses to the patient or caregiver is preferable.

The need for necessary counseling activities can already be signaled during the review, and then initiated when the medicine is handed over the patient.

Table 22.1 Patient and medication-related information for assessing a new prescription

The patient
Age
Kidney function
Liver function
Pregnancy
Breast feeding
Allergies
Previous intolerance to a medication
Mental capacity e.g.,, such as the presence of dementia, intellectual disability
Level of health literacy
Disorder/condition/symptom/presenting complaint
Acute or chronic
Seriousness
Stage and/or complications
Symptoms or asymptomatic
Medication
Indication
High risk medication
Intended dose, route, regimen, and form
Expected benefit and time to benefit
Potential side effects and likely time of occurrence
Potential for drug—drug interactions and drug—food interactions
Patients' ability to operate/handle dose form

22.3.2 Preparing the Medicine(s)

Once the prescription is found appropriate for the patient, the medicine can be prepared. In some countries, this involves also preparing a label with the name of the patient and preparing essential instructions about the medicine use. The required information on a pharmacy prepared medicine label in, for instance, the Netherlands is as follows:

- Name, address, and phone number of dispensing pharmacy
- Date of dispensing
- Prescriber name or prescriber code
- Name and address of the patient
- Date of birth of the patient
- (Daily) use of the medicine
- Warnings concerning the way the medicine must be used (e.g.,, swallow whole)
- Name and strength of the medicine
- Number of dispensed units

As for the information provision, this has to be verbal as well as written. In spite of regulations in most developed countries, there are doubts about the usefulness and quality of the information leaflets that the pharmaceutical industry provides [1]. In some countries, the patient information leaflet (PIL) can be individualized and tailoring information leaflets to patient characteristics and requirements would enhance effectiveness [2]. It gives a nice and useful touch to the provided care. In other countries, there are legal obligations to hand over an information leaflet, be it a customized one or a leaflet prepared by the producer. The written information needs to be prepared and added to the medicine.

Once the medicine with its information is ready, it can be dispensed. In many cases, the prescription review, preparation of medicines, and the dispensing are done by different persons in the pharmacy. The continuity of the process is then an additional concern.

22.3.3 Handing Over the Medicines

Handing over medicines to a patient, or his caregiver, seems a simple task. But this is also the moment that counseling must be given, instructions provided and an assessment must be made as to the health literacy and mental capacities of the patient. It also is the moment where the adherence to medicines can be influenced the best (see Chap. 5). For continuity and documentation purposes, certain aspects that must be stressed at the dispensing moment should have been marked on the prescription, or an added leaflet, during the prescription review and the preparation of the medicine. In several countries, the process of handing over medicines has been protocolised, as to make sure that all care activities are done, where appropriate. This element of quality control is further discussed in Chaps. 9 and 10.

Most people do not appreciate the curious eyes and ears of their neighbors when receiving medicines, so from a pharmaceutical care perspective the counter should be constructed in a way that privacy is possible. Specific instructions for the use of devices such as inhalers, or counseling on sensitive topics should be given in a separate room.

22.3.4 Dispensing Review, Follow-up, and Documentation

Perhaps dispensing review is a "heavy" word, but the dispensing of every prescription should be reviewed; have all checks been done, have all advices been given, did the right patient receive the correct medicine and counseling? Have the chances of medication errors been reduced sufficiently and the optimal chances for positive outcomes of the pharmacotherapy been created? And for future reference, have possible allergies been documented?

The check of such aspects usually is the responsibility of the managing pharmacist. Depending on the computer system, the care activities can be documented on the prescription or in the system. This type of documentation can be compared to what medical doctors are supposed to do. They also must document all their activities and thoughts on a given person, for instance in SOAP notes. For care-providing pharmacists, this is not different. Detected drug-related problems can be documented, often also using SOAP notes, and with the help of the appropriate classifications (see Chap. 8).

A telephone follow-up (also called call-back service) from the pharmacist helps solving patients' problems with a new medicine after the dispensing and can significantly reduce non-adherence and costs.

22.3.5 Protocols for Dispensing

As shown above, dispensing in the context of pharmaceutical care is not a simple task. It requires general pharmacotherapy knowledge and different skills. To assist practitioners in practice to dispense medicines in the most responsible and reproducible way, protocols can be drafted. Such protocols must be adapted to the practice setting, local legal requirements and patient population. Especially the first time dispensing of a new medicine needs a good structure.

In many countries, protocols have been developed by professional organizations in an effort to guide pharmacists to act in a standardized and evidence-based manner. One of the most international recognized guidelines is the FIP-WHO guidelines for GPP—Good Pharmacy Practice, which have evolved over the years incorporating the advances of pharmacy practice [3]. These guidelines can be used as cornerstone for the drafting of practice protocols. In many countries, these GPP

guidelines have been used as a basis for local protocols and guidelines. Adherence to protocols can be self-assessed so that the pharmacy team can improve them, but they should also be regularly audited by an external agency.

The following flowchart indicates the difference between dispensing repeat prescriptions and dispensing a new prescription, and how it may impact the activities in the community (or polyclinic) pharmacy (Fig. 22.1).

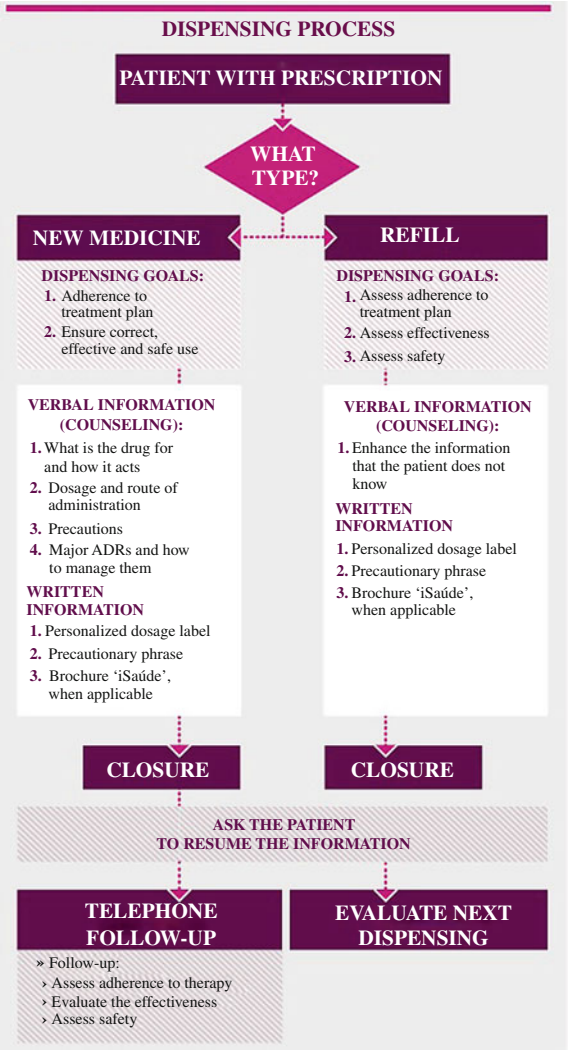

Fig. 22.1 Pathways for dispensing

22.3.5.1 The New Medicine Services

Several countries have established a New Medicines Service, although each with some specifications either regarding the setting and moment of care provision (e.g., post-discharge in the UK), regarding the patient group (e.g., cardiovascular patients in the UK and Norway; asthma patients in the UK and France), or the medication group (e.g., inhaled steroids in Belgium, vitamin K antagonist in France). Despite minor variations, the service has general characteristics which focus on an initial service dealing with the provision of information about the indication of the drug, its necessity and any specific and relevant indications (e.g., how to take, what to avoid). Usually a follow-up visit is also part of the service (may be more than one and may be long distance or face to face) where additional information is transmitted, which focuses on more specific topics that are likely to arise only after the medication has been initiated. In Portugal, although this service is not yet implemented as a nationwide service, some pharmacies have developed their own protocols to guide pharmaceutical intervention, which again follow the same principles. Community pharmacists in the Netherlands are expected to provide additional care and service to all patients who present with a prescription for a new medication.

The service in the UK has primarily been developed to improve adherence and is remunerated separately. It is called an "advanced service", for which a separate accreditation is needed. In most other countries this type of service is regarded as part of the normal pharmacy care services. A study by Elliott et al., published in 2017, suggested that the NMS increased patient medicine adherence compared with normal practice, which translated into increased health gain at reduced overall cost [4].

22.3.5.2 Repeat Prescribing

With repeat prescribing and regular enquiry about the patient's health status, their experience of their treatment and their satisfaction with their treatment may lead to a conversation in which one or more drug-related problems become apparent. Such conversations can be protocolised. The dispensing of repeat medication is an appropriate moment for such conversations. Additionally, a regular medication review for complex patients (complex diseases, complex medicines) may unveil problems too. Since it is not possible carry out an in-depth investigation of every patient receiving repeat medications for long periods, there must be a strategy to select the patient most likely to need additional care.

In several countries, specific patient groups with specific chronic diseases have been targeted for additional pharmaceutical care. Cardiovascular diseases, asthma and COPD, and diabetes are common diseases for which pharmacists give additional protocolised care, sometimes also bridging the gap between different care providers and care institutions (seamless care). In the Netherlands, all patients older than 70 and receiving more than 5 medicines must receive a (regular and

remunerated) Type-3 medication review. Some other countries have similar requirements for patients that receive a certain minimum of chronic medications.

In some countries, the focus of counseling as part of the care for patients with chronic medication has moved to the second time dispensing of a medicine. Some patients are confused when they hear for the first time that they must take a medicine chronically and do not listen properly to the first time counseling [5].

All in all, dispensing repeat prescriptions require a different approach in the pharmacy. They can be a trigger for extended care, extended counseling, or be part of a disease oriented pharmaceutical care plan.

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Chapter 23
OTC Medication and Pharmaceutical Care

Vivien Tong and Parisa Aslani

Abstract With the increasing availability and use of over-the-counter (OTC) or nonprescription medicines by consumers globally, pharmacists have an integral role in delivering pharmaceutical care to support safe and appropriate OTC medication use. This chapter provides an overview of OTC medication use within the context of primary care and self-care. It outlines the role of pharmacists in relation to OTC medicines, details the medication-centered and service-oriented systems for delivering pharmaceutical care relevant to consumer OTC medication use, and discusses current and future scopes of practice within the context of OTC medication and pharmaceutical care.

Keywords Pharmaceutical care · OTC medication · Over-the-counter
Patient counseling · Self-medication

23.1 Introduction

Pharmaceutical care is regarded as "*the pharmacist's contribution to the care of individuals in order to optimize medicines use and improve health outcomes*" [1]. Pharmaceutical care encompasses both prescription and over-the-counter (OTC) or nonprescription medicines (that is, conventional medicines available to consumers without the need for a prescription; complementary and alternative medicines (CAMs) will be discussed separately in this chapter). The increasing and widespread availability of OTC medicines globally has contributed to the need for pharmacists to adapt, refine, and up-skill in order to enable the provision of consumer-centered pharmaceutical care in relation to OTC medicines. Multiple opportunities exist for pharmacists to leverage their expertise and to demonstrate the value of pharmacists and community pharmacy, which include

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- Accessibility, from a logistical perspective due to location and hours of operation, as well as from an economic perspective where professional advice can be sought from pharmacists in many cases without extensive out-of-pocket costs to the consumer;
- Expertise in health and medicines; and
- Immediate access to both healthcare professional advice as well as medications within the same setting.

Pharmacists are key healthcare professionals who are the first point of contact for many consumers with minor ailments and are therefore well-situated within primary care settings such as community pharmacies to deliver pharmaceutical care. As OTC medicines are able to be used by consumers as part of their self-management of minor ailments, the changing landscape of OTC medication use and the widening of the scope of practice of pharmacists have led to a more extensive role for pharmacists within the area of primary care.

23.2 Primary Care, Self-care, Self-medication, and OTC Medicines

The Declaration of Alma-Ata (1978) [2] was seminal in providing a vision for primary health care to help facilitate improved health outcomes for everyone. Within the broader framework of primary health care, primary care is regarded by the World Health Organization as "*first-contact, accessible, continued, comprehensive and coordinated care*" [3]. In light of this, it is clear that community pharmacy and pharmacists are ideally situated and are instrumental in providing primary care.

> Self-care is what individuals, families and communities do with the intention to promote, maintain, or restore health and to cope with illness and disability with or without the support of health professionals such as pharmacists, doctors, dentists and nurses. It includes but is not limited to self-prevention, self-diagnosis, self-medication and self-management of illness and disability. [4] (p. 18)

OTC medication use forms an important element of self-care. A definition compiled and used for the purposes of a project evaluating self-care systems that was commissioned by the European Commission [4] detailed:

Evidently, consumer self-medication using OTC medicines is a key component within the broader self-care continuum. In particular, the role of pharmacists in promoting and enabling self-care has been extensively outlined and discussed in the report recently published by the International Pharmaceutical Federation, entitled "Pharmacy as a gateway to care: helping people towards better health" [5].

Pharmacists are well positioned and have suitable expertise to adequately assist consumers who choose to manage their conditions via self-medication, i.e., the use

of OTC medicines. The contributions of pharmacists are particularly important across multiple contexts, ranging from populations of higher socioeconomic status to areas with limited access to healthcare professionals such as general practitioners (for example in rural areas) to other contexts where accessibility to health care may also be limited for certain populations and/or other reasons (for instance due to affordability of health care).

There has been a clear increase in the number and range of OTC medicines made available over the years. Moreover, the use of OTC medicines is highly prevalent among consumers [6], with consumers reporting a need for pharmacy advice on OTC medicines [7]. Consequently, pharmacists have an increased capacity to help consumers manage minor ailments and meet the increasing requests for OTC medicines. In addition to timely, ready access to OTC medicines for consumers, a number of positive economic benefits for multiple parties/stakeholders [8, 9] may also be seen as a result, such as

- Savings for the healthcare system as a whole, for example, via reduced utilization of limited healthcare resources and/or medication-related costs redirected to consumers;
- Reduced pressures on healthcare professionals, for instance general practitioners, in relation to consultations about minor ailments that are able to be adequately managed in community pharmacy settings; and/or
- Potential savings for consumers regarding reduced wait times associated with seeing a general practitioner, avoidance of unnecessary on-costs associated with visits to the general practitioner, in addition to other indirect benefits of increased convenience.

Thus, increasing self-care and self-management alongside increasing access to OTC medicines via switching medicines from prescription to over-the-counter status has contributed to expanded opportunities for pharmaceutical care to be provided in relation to OTC medicines [5], and within the context of primary care.

23.3 OTC Medicines: The Role of the Pharmacist

Pharmacists are the primary healthcare professionals who advise on, recommend, and participate in the appropriate supply of OTC medicines, much like doctors are the primary prescribers for prescription medicines. The role of a pharmacist is multidimensional, where pharmaceutical care provision by pharmacists is imperative across the treatment continuum for OTC medicines; that is, at all time points that involve the use of OTC medicine(s) in managing the specific ailment(s). Pharmacists' roles and responsibilities comprise

- Appropriate diagnosis of the ailment(s) that may in turn be managed using OTC medicines;
- Provision of appropriate, evidence-based recommendations for OTC medicines for the individual consumer;

- Facilitation of consumer decision-making regarding self-medication;
- Promotion of quality use of medicines, e.g., safe and effective use, prevention of misuse and abuse of OTC medicines;
- Identification and appropriate handling of potential drug–drug interactions, in particular with other prescription, nonprescription, and complementary and alternative medicines (CAMs) being used by the consumer;
- Ongoing monitoring of OTC medication use by consumers;
- Provision of health and OTC medicines information that supports the consumer in engaging in safe and appropriate self-care and self-medication (which can in turn improve consumers' health literacy surrounding self-medication as part of self-care);
- Engaging in and advising on appropriate referral pathways where treatment with OTC medicines has been proven to be inappropriate and/or ineffective; and
- Engaging in appropriate follow-up to ensure continuity of care where a consumer has been referred on to another healthcare professional to manage the medical condition/ailment.

These responsibilities are firmly embedded in pharmacy practice and pharmaceutical care provided for symptom and product-based requests in relation to OTC medicines, as evidenced by existing professional practice standards [10] and protocols such as WHAM [11], ASMETHOD [11], What-Stop-Go [12], and CARER [12]. Importantly, professional practice standards and protocols provide a framework that enable an organized and systematic approach for pharmacists' clinical skills to be actively utilized, and for due care to also be exercised by pharmacists when handling OTC medicine requests. The use of such protocols to guide pharmacists' interactions with consumers allows for potential medication-related problems to be identified in a timely manner that is still respectful of consumers' autonomy in a self-medication context.

23.4 Systems for Delivering Pharmaceutical Care for OTC Medicines

Pharmaceutical care is typically provided for OTC medicines through one of two broad approaches:

- medication-centered systems, which are primarily focused around the supply of specific OTC medicine(s) for appropriate consumer use; and
- service-based systems that seek to facilitate optimized pharmacist engagement in the management of the ailment, which may be complemented by OTC medication use.

23.4.1 Medication-Centered Systems

The availability and ready access to OTC medicines enable pharmacists to provide pharmaceutical care and address the patient's healthcare needs at the point of care

within a primary care setting. Subsequently, the availability and type of OTC medicines, which differs between countries, enables pharmacist interventions and provision of advice to support the use of medicines to manage specific ailments. In addition to this, pharmacists should be cognizant of the quality of written information accompanying OTC medicines found on the label/box and/or accompanying leaflet (where available). The content and language used to convey the OTC medicine information as well as how it is presented in these written information sources may not be optimal across all products available for consumers [13, 14]. Pharmacist-delivered counseling therefore should complement the written information provided with the OTC medicine(s) and ensure that consumers of all health literacy levels are equipped with adequate, understandable information to use OTC medicines safely and appropriately. Furthermore, pharmacists should consciously provide balanced information on all available treatment options that are appropriate for the individual consumer to ensure that evidence-based shared decision-making is promoted between the consumer and pharmacist during minor ailment and OTC medicine-related consultations.

23.4.1.1 OTC Medicine Scheduling: The "Switch" and Pharmacist-Only Medicines

In addition to products being classified as either prescription or OTC medicines, OTC medicines can be further divided into subcategories depending upon the regulatory context (a specific area/region that is governed by the same set of rules and regulations) and implemented legislation surrounding the scheduling of medicines. For instance in certain countries, although some OTC medicines may be sold in retail outlets other than pharmacies, there are certain OTC medicines that are only permitted to be sold in pharmacies. In a 2017 survey conducted by the International Pharmaceutical Federation (FIP) of countries/territories that had at least 1 FIP member organization or candidate member organization (mean response rate 72.6%; n = 72–79 responses, varying between the survey sections), 23 regulatory contexts were reported to have all OTC medicines located behind the counter in the community pharmacy [15]. Nineteen regulatory contexts had OTC medicines available for self-selection in the pharmacy; in contrast, 30 regulatory contexts reportedly had schedules of OTC medicines that are either available for consumers to choose themselves or situated behind the counter [15]. For instance, in countries such as Australia, New Zealand, and the UK, an additional subcategory of OTC medicines known as Pharmacist-Only or P medicines is available. Pharmacists are required to be directly involved in the supply of these medicines, thus ensuring that consumers' symptoms are appropriately assessed by pharmacists and that consumers have access to timely pharmacist advice to support the quality use of these OTC medicines.

Over the years, the scope of pharmaceutical care in the context of OTC medicines has widened in tandem with the increased availability of such medicines for OTC purchase. There have been a number of notable examples of medicines

that have been "switched" from prescription-only to OTC status in multiple countries [8, 16]. A few examples include

- Oral emergency contraceptives, providing women with timely access to emergency contraception when needed;
- Chloramphenicol, enabling pharmacists to facilitate the treatment of bacterial conjunctivitis;
- Proton pump inhibitor(s), which provide an additional treatment option (in addition to other OTC medicines such as H2 antagonist(s) and antacids) for recommendation by pharmacists to those suffering from symptoms of heartburn;
- Orlistat, which provides pharmacists with a pharmacological option that can be recommended to consumers for use as part of weight management;
- Famciclovir, which can be used for the treatment of cold sores;
- Triptans for use in migraines; and/or
- Topical and/or oral antifungal agents for the treatment of vaginal thrush.

Although the above examples are not exhaustive, they illustrate the breadth of health issues that can be managed using OTC medicines provided that their supply is accompanied by appropriate pharmaceutical care delivered by pharmacists.

In those countries with Pharmacist-Only OTC medicine schedules, the relevant pharmaceutical societies/professional organizations have developed practice standards, guidelines and/or resources to support pharmacy practitioners (pharmacists, pharmacy technicians and/or pharmacy assistants) in the appropriate provision of these medicines and broader pharmaceutical care. An example includes the guidelines published by the Pharmaceutical Society of Australia [17]. These guidelines provide pharmacists with informational support to assist in deciding whether the supply of the particular medicine is appropriate, taking into account the range of factors that may impact the decision-making process undertaken by the pharmacist, and reinforce the key counseling points to be delivered to consumers. Notably, with a change in the scheduling of medicines (for instance a prescription medicine becoming available as a Pharmacist-Only medicine), pharmaceutical societies have in general published new and/or updated guidelines to assist pharmacists in ensuring the appropriate supply of such medicines. A few examples of medicines for which practice standards are available from the relevant pharmaceutical society and/or pharmacy council in Australia, UK and/or New Zealand include:

- Oral emergency contraceptives;
- Analgesics containing codeine (note that since 1st February 2018, codeine is no longer available OTC in Australia);
- Proton pump inhibitors;
- Orlistat; and
- Chloramphenicol.

Although many Pharmacist-Only medicines are intended for use in the short term to manage acute symptoms, there are also some Pharmacist-Only medicines available for people to use to manage chronic medical conditions. It is therefore

important for pharmacists to discern appropriate, patient-centered strategies that can be implemented as part of the management of acute and chronic medical conditions. The "Protocol for the sale and supply of Pharmacist Only Medicines for Chronic Conditions" [18], published by the Pharmacy Council of New Zealand, aims to support pharmacists in differentiating between the use of Pharmacist-Only medicines for acute and chronic conditions. It is compulsory for pharmacists to adhere to this protocol when a person presents with a chronic medical condition, such as obesity, for which a Pharmacist-Only medicine can be used and is supplied by the pharmacist to treat the condition [18]. Other examples of medicines that can be supplied without a prescription in certain situations by pharmacists in New Zealand for chronic conditions include sildenafil for erectile dysfunction and topical adapalene for acne.

The key components of the protocol include [18]

- The need for a face-to-face consultation (unless there are permissible circumstances that deem this to not be feasible);
- Availability of a private consultation area for the face-to-face consultation;
- Recording and secure storage of the consumer's personal and clinical information in a consumer-specific file;
- Determination of the appropriateness of the medicine, with due consideration of non-pharmacological options, other medicines, or referral for medical attention;
- Appropriate recommendation of a Pharmacist-Only medicine to manage the chronic medical condition;
- Provision of spoken and written medicine information;
- Electronically recording the supply of the medicine (similar to that for the supply of a prescription medicine); and
- Supply of the medicine in the original packaging to ensure that written consumer medicines information is provided.

23.4.1.2 Facilitation of Safe and Evidence-Based Use of Complementary and Alternative Medicines

Complementary and alternative medicines (CAMs) are available for purchase by consumers in a number of settings where there may or may not be immediate access to advice from a healthcare professional. As many consumers do obtain such medicines from pharmacies, pharmacists have a particularly important role in providing evidence-based recommendations tailored to the individual consumer to support their safe and effective use. A systematic review conducted by Ung et al. [19] identified and outlined key roles and responsibilities for pharmacists in relation to CAMs, which were to

- Recognize and enquire about their use by consumers,
- Possess knowledge about CAMs,
- Facilitate the safe and effective use of CAMs by consumers,

- Record consumer CAM use,
- Engage in the reporting of adverse drug events associated with CAM use,
- Educate consumers, and
- Engage in interprofessional collaboration in relation to consumer CAM use [19].

As an example, the Pharmacy Council of New Zealand has published "Complementary and alternative medicines—best practice guidance for pharmacists" [20]. This guidance reiterates many of the above key roles and responsibilities. Accordingly, pharmaceutical care relating to OTC medicines is also inclusive of CAMs. Moreover, it is important to recognize that there is no fundamental distinction in the pharmaceutical care that should ideally be provided by pharmacists between the types of OTC medicines available. There is a need for pharmacists to acknowledge the role of CAMs from the consumers' perspective in facilitating self-care and ensure that consumers' use of CAMs is considered and discussed as part of an integrated, holistic approach to patient-centered care. Similarly, in instances where consumers choose to utilize CAMs for which there is less evidence for efficacy, appropriate unbiased information should be offered to consumers by pharmacists. However, if consumers choose to proceed in engaging in self-medication using CAMs in situations where there are minimal safety implications, the choice to do so should be respected.

23.4.1.3 Clinical Interventions

Pharmaceutical care provided in relation to OTC medicines is an opportunity for timely medication reconciliation regarding OTC medicines used by consumers. Moreover, despite their OTC availability, ill-considered and/or inappropriate use of OTC medicines still carries a number of risks for the consumer. Consumers do not always discuss or want to discuss their OTC medication use with their doctor [21], and doctors may not always enquire about their OTC medication use during a consultation [22]. Thus, pharmacists are in an ideal position to optimize consumer self-medication strategies via timely clinical interventions, as well as be the link between consumers and doctors, strengthening interprofessional collaboration, and effective consumer self-management. These important efforts can be initiated by pharmacists to promote the health and well-being of consumers.

As with prescription medicines, there is also the ongoing potential for medication-related problems to arise with OTC medicines. A study conducted by Westerlund et al. [23] over 15 years ago found that over a 10-week period, 1425 medication-related problems and 2040 interventions were reported by 308 pharmacists from 45 Swedish pharmacies [23]. Similarly, Eickhoff et al. [24] found that medication-related problems linked to OTC medicines were identified in 17.6% of consultations (2206/12,567) with consumers, as documented by study pharmacists. Broad types of medication-related problems pertaining to OTC medicines previously identified include [25]

- Inappropriate product requests/self-medication,
- Incorrect dosage or planned treatment duration, and/or
- Suboptimal understanding of the medicine's indication.

Williams et al. [26] estimated that approximately 485,912 interventions were conducted within Australian community pharmacy settings per year in relation to OTC medicines that can only be sold in pharmacies (Pharmacy and Pharmacist-Only medicines). They calculated and extrapolated data from two studies, where actual data were obtained from each study pharmacy (n = 934 and n = 101, respectively) for a designated study period of 2 weeks between November 2004 and September 2005. Furthermore, 101,324 interventions (21%) were classified as potentially being life-saving and/or avoiding serious harm [26]. When considering the number and nature of interventions that would be conducted by pharmacists as part of routine practice within community pharmacies globally, the impact of these interventions in both preventing and addressing medication-related problems emphasizes the unique opportunities for pharmacists to influence OTC treatment decision-making, medication use, and safety, thus continuing to be an important part of the overall healthcare system.

23.4.2 Service-Oriented Systems

Many pharmaceutical care-related activities conducted by pharmacists are closely linked to the supply of OTC medicines, whether it be via direct product requests or symptom-based requests that may or may not eventuate in the actual supply of OTC medicine(s). Service-oriented systems, although complemented by medication-oriented systems, help to facilitate the added engagement of pharmacists in delivering services that can help treat and/or manage specific medical conditions in addition to pharmacists' baseline supply functions. Thus, the primary focus of a service-oriented system is the service itself, rather than the medicine, which is targeted at addressing a specific consumer health need. The services provided are sometimes known as cognitive pharmaceutical services or professional pharmacy services.

23.4.2.1 Cognitive Pharmaceutical Services/Professional Pharmacy Services—Examples

The provision of pharmaceutical care by pharmacists in community pharmacy settings has increased over the years; however, there are differences in the uptake and types of services being offered internationally. In order to better utilize pharmacists' expertise in helping consumers manage their medical conditions, cognitive pharmaceutical services, also known as professional pharmacy services, have been developed and implemented in practice. Such services may exist at a local level,

i.e., services specifically developed to meet the needs of the population serviced by a single pharmacy, or may involve more standardized services that are remunerated via government funding. Services developed to address a particular health need or medical condition which may involve the use of OTC medicines and/or therapeutic goods include, for example,

- Condition-specific management and services delivered as part of broader minor ailment schemes;
- Wound care services, which may involve the dressing of wounds, and relevant consumer education and counseling to support the cleaning/dressing of wounds at home;
- Smoking cessation services, facilitated by the OTC availability of nicotine replacement therapy options; and
- Weight management services, which may involve the use of products such as OTC orlistat or very low calorie diet products that are sold in pharmacies, recommended in conjunction with counseling on diet and lifestyle factors which may or may not be part of a structured, branded weight loss program.

Of particular relevance are minor ailment schemes or services. Previous systematic reviews of remunerated pharmaceutical care services have identified minor ailment schemes that are offered in countries such as the UK and Canada [27, 28]. As a remunerated service, such schemes provide pharmacists with the opportunity to manage certain minor ailments in the community pharmacy setting. This involves the pharmacist completing a consultation with the consumer which would involve appropriate questioning to enable the diagnosis of the minor ailment, provision of treatment where applicable, appropriate counseling, and/or appropriate referral provided. Depending on the schemes' inclusions, minor ailments covered may encompass conditions such as [29]

- Symptoms relating to colds/coughs;
- Hay fever;
- Dermatological-related ailments such as nappy rash, dermatitis, eczema, and athlete's foot;
- Head lice;
- Oral/vaginal thrush; and/or
- Gastrointestinal-related ailments such as indigestion, diarrhea, constipation, and hemorrhoids.

A systematic review of the evidence for UK minor ailment schemes found that 68–94% of consumers who utilized the scheme had reported complete resolution of the ailment [29]. Positively, many studies noted overall consumer satisfaction with the service provided as part of the minor ailment scheme and consumer willingness to utilize the service again in future [29]. Although further comprehensive, ongoing economic evaluations of the minor ailment schemes are still needed, it has been reported that the costs associated with reimbursing pharmacists' consultation times for managing minor ailments are in general less than that associated with general

practitioner consultations [30]. This is suggestive of positive savings for the overall healthcare system as well as the easing of pressures across other primary care settings.

NetCare, an initiative of pharmaSuisse, is an example of a collaborative primary healthcare service delivered through community pharmacies. It has involved the development of evidence-based decision support tools for 24 medical conditions commonly presented by consumers in primary care [31]. The decision support tools can be utilized by a trained pharmacist in a private consultation area within the pharmacy, with information documented using a standardized form [31]. When an eligible and willing consumer is assessed using the relevant decision support tool (s), there are three possible outcomes [31]:

(1) The pharmacist manages the ailment, with medicine(s) provided OTC where necessary;
(2) The ailment is managed by the pharmacist with support from a doctor via videoconference (thus providing a pathway for appropriate triage and an opportunity for interprofessional collaboration in the management of the consumer's ailment(s)); or
(3) The consumer is referred for medical care from a GP and/or emergency services as required.

In a study by Erni et al. [31] 3146/4118 netCare cases (76%) documented between April 2012 and January 2014 only required pharmacist intervention; and upon follow-up, the majority of these consumers reported complete symptom resolution or marked symptomatic relief [31]. Although not specific to OTC medicines, this is one example, similar to minor ailment schemes, where system-based approaches have sought to optimize and highlight the potential for effective pharmaceutical care delivered in the context of common ailments in primary care.

23.5 Current Practice and Future Scope for Practice

Pharmacists are trained health and medicines experts. When considering the prevalence of poly-pharmacy as well as the varied health needs of consumers, the provision of pharmaceutical care relating to OTC medicines is not conducted in silo to other systems of pharmaceutical care that are nonspecific to OTC medicines, for instance medication reviews/medication therapy management. Patient-centered care that supports the appropriate consumer use of OTC medicines within their overall healthcare plan or regimen should remain the mainstay for pharmaceutical care that seeks to facilitate self-care and self-medication.

As the availability of OTC medicines continues to increase, future medication switches will further opportunities for pharmacists to contribute to self-management within the OTC treatment options available within each specific regulatory context. This is applicable to medicines switched from prescription to OTC status, and vice versa, where medication risks have been associated with their OTC availability.

Opportunities for continuing consumer education and counseling within this context reinforce and ensure that pharmacists and the pharmaceutical care provided by pharmacists in relation to OTC medicines remain highly relevant.

Although cognitive pharmaceutical services being provided by community pharmacists have increased over the years, the supply function inherent within community practice settings that are more skewed toward medication-oriented systems financially supports the employment of pharmacists and pharmacy staff to provide these services. Development and availability of alternative funding systems that reimburse for pharmaceutical care linked to OTC medicines, as seen with minor ailment schemes, will enable pharmacists to be remunerated for their time rather than solely via the sale of an OTC medicine or product. The importance of this is reiterated in one of the recommendations in the recently adopted FIP Statement of Policy "Pharmacy: Gateway to Care" [32] which recommends that "*government and insurers… assure proper compensation for pharmacist self-care services, and encourage health sector collaboration to optimize efficiency, safety and value*" [32] (p. 5). The expansion of minor ailment schemes to other countries and the inclusion of additional minor ailments covered as part of existing schemes will enable pharmacists to broaden their scope of practice and be remunerated for helping consumers manage their minor ailments using appropriate treatment options. Minor ailment schemes can help to reduce the multifactorial pressures experienced by other sectors of the healthcare system that are otherwise critically supported and dependent on government funding. Moreover, further ongoing research is needed to ascertain the overall impact of pharmaceutical care provided in relation to OTC medicines to elucidate a more comprehensive understanding of the impact that such pharmaceutical care has on the economic, clinical, and humanistic outcomes of consumers engaged in self-care and the respective components of self-care.

Although there is significant potential for pharmacists to deliver pharmaceutical care relating to OTC medicines, a critical need exists to improve the way in which pharmacists handle requests relating to OTC medicines (in particular direct product requests) [25]. Community pharmacists' and pharmacy staff's information gathering has been reported to be inconsistent or incomplete, signaling room for improvement [25]. Furthermore, pharmacists' level of receptivity toward practice changes, as well as their willingness and readiness to implement these changes, can act as barriers to pharmacists contributing toward pharmaceutical care. Despite the vast potential for pharmacists to contribute toward self-management and self-medication within the broader context of self-care, "pharmacists as a barrier to self-care" [5, 33] is an issue that needs urgent attention. As a profession, pharmacists have a duty of care to strive to continue to develop and appropriately apply clinical skills in facilitating quality use of OTC medicines. Additionally, although consumers acknowledge that there can be risks associated with OTC medication use, many also believe that OTC medicines are safe [34].

Pharmacists need to acknowledge and address consumers' perceptions of the safety of OTC medicines when providing pharmaceutical care associated with OTC self-medication. Further training to better enable pharmacists to appropriately supply OTC medicines, such as the accreditation training requirements for the supply of

certain medicines without a prescription by pharmacists in New Zealand, can support this up-skilling and professional development. A range of training opportunities can be used to support and provide feedback on current practices surrounding pharmacist supply of OTC medicines, for instance via the use of mystery shoppers or pseudo-patients as one approach [35]. Furthermore, existing standards, guidelines, or protocols can be used and adapted by countries where there may be limited professional practice standards and/or guidelines that support pharmaceutical care provision with respect to OTC medicines. For instance, the detailed approach and protocol utilized in New Zealand for the supply of Pharmacist-Only medicines for chronic medical conditions [18] is one such system that may be of use for other countries to reference and adapt accordingly. Improved documentation associated with pharmaceutical care delivered for consumers regarding OTC medicines, for instance, may facilitate improved medication reconciliation and review, and improved continuity of care and information exchange between members of the healthcare team. Utilization of emergent eHealth and mHealth initiatives such as electronic health records (where available) as part of this process may also become more prevalent and therefore necessary when moving forward.

When considering that self-care, by its definition, can be undertaken by consumers with or without the support/help of healthcare professionals, suboptimal health literacy levels of consumers can significantly impact self-management and subsequent self-medication using OTC medicines. Inadequate health literacy within the broader population remains a prevalent and ongoing issue. Consequently, there will be an ongoing imperative role for pharmacists both as part of current practice and future scope of practice to continually seek ways to improve consumers' health literacy. These concepts have been aptly encapsulated in the recommendations for pharmacists included as part of the aforementioned FIP Statement of Policy (reproduced in Table 23.1), and should continually drive pharmacists to seek ways to fulfill their duty of care and enhance the pharmaceutical care provided to consumers of OTC medicines, in order to improve consumers' health outcomes and quality of life.

Table 23.1 Recommendations for pharmacists included in the "FIP Statement of Policy–Pharmacy: Gateway to Care" [32] (p. 5–6)

1. Assist individuals to:	Seek to be better educated in caring for themselves. This education, sourced from local or global health providers, health promotion resources of the local or national health system or patient organizations, will yield greater patient confidence in managing one's health and personal level of health literacy; Share and educate others on their inherited and indigenous cultures and beliefs with the goal of having clearer communication among the patient's health providers; Be aware of the health determinants and indicators for themselves and their children

(continued)

Table 23.1 (continued)

2. Develop and adopt standard operating procedures for quality management of self-care presentations, such as, but not limited to:	Applying the pharmaceutical care concept to self-care; Assuring quality and safety of self-care though proper documentation of their work and provision of services such as medicines reconciliation, adherence support and medication management; Ensuring accurate use and interpretation of results derived from current best self-care technologies; Pharmacists' triage, including appropriate patient referral to and from alternate services within the healthcare system
3. Advocate, promote, support and engage in:	Collaboration with the patient and their health team, and as a patient advocate within the health system; Various health promotion activities and health education; Best legislation on factors that affect self-care; Enhancing their personal communication and coaching skills under the theme of health literacy—"listen to learn" rather than "listen to respond"

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Chapter 24
Care Around Medical Devices: Infusion Sets and Devices

Claire Chapuis, Lise Bernard, Pierrick Bedouch and Valérie Sautou

Abstract Patients who receive intravenous (IV) medications as a rule should be given special attention. As pharmacists we want to assist to optimize the treatment and prevent medication errors. Intravenous drug administration is complex and subject to iatrogenic risk. The choice of the appropriate medical devices is therefore important in each infusion setup. By his knowledge of injectable drugs and medical devices, the pharmacist can contribute to the selection of appropriate tools to control infusion rates, avoid drug incompatibilities, container–content interactions, prevent allergies or infectious complications, and improve the patient comfort.

Keywords Pharmaceutical care · Medical devices · Hospital · Infusion sets Patient comfort

24.1 Introduction

Intravenous (IV) drug administration is complex and prone to medication errors that may course drug-related problems in patients. Pharmacist can help to prevent such errors and problems by assisting in the choice of appropriate devices for administration.

The optimal drug delivery through IV infusion depends on a number of critical parameters such as the choice of infusion devices, the internal volume of the IV delivery system, the performance of the IV administration set, and the presence of valves or filters on the main infusion line, as well as the size of the common space in which drugs can be mixed. All these parameters have their influence on flow-rate variability, affecting the volumes delivered per time unit and this has potentially negative clinical consequences for patients. Additionally, iatrogenic infections must

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also be prevented. Clinicians should recognize these factors, because the safety and efficacy of IV infusions depends on them. In this chapter, we will try to provide some important information and data on how to secure and optimize the use of infusion devices, for optimal patient safety and comfort.

24.2 Control of Drug Infusion Rate

An accurate infusion of fluids and IV drug administration is important for the optimal management of (critically ill) patients. The patient should receive the right amounts of medicine at the right moments. To be effective, infusion sets should therefore minimize the lag time between the time a change is made in the pump flow rate and the time the medicine is delivered to the patient at the new mass flow rate. The concentration of the drug being delivered can be reduced considerably as it mixes with the carrier solution in the infusion set [1].

Especially in multidrug infusion two main points are essential: (1) the common dead volume of drugs delivered simultaneously with potential consequences on the accuracy and amount of drug delivery and (2) the prevention of drug incompatibilities and their clinical effects [2]. The first point can be solved by choosing the right medical devices, the second point by choosing the right mix of medicines and infusion fluid.

Available infusion techniques include three main types of devices (Table 24.1): gravity-driven infusion systems, positive displacement pumps (volumetric and syringe pumps), and elastomeric pumps.

The flow rate of fluid in gravity-driven systems is often controlled by a simple roller clamp. Other technologies include manual flow regulators, which allow for finer changes in flow resistance compared with roller clamps, and may show a more linear flow response to controller position by limiting the effects of creep. However, the lack of accuracy and the variations in flow rate between brands may limit clinical use. Claps and other flow regulators are not recommended in critical care.

For critically ill patients (especially with bad kidney functions and young patients), requiring multiple infusions, the amount of administered fluid can cause volume overload. This stimulated the development of micro-infusion strategies wherein drug solutions are highly concentrated and infused at low rates.

In acute care, well-controlled intravenous delivery of common medications, such as inotropic agents, vasoactive drugs, insulin, and heparin via infusion pump, is the preferred mode of therapy. This is especially true for drugs with short half-lives: IV delivery helps to maintain a constant serum concentration. To prevent fluid overload, infusion pumps are also indicated to administer fluids in neonates with compromised renal, cardiac, or pulmonary function. The use of infusion pumps is preferred over the manual flow control system because it assures a precise and accurate delivery of prescribed fluid volumes over a specified time, and it helps in better nursing management [3].

Table 24.1 Comparison of the different drug infusion systems

	Gravity-driven flow infusions (with manual flow regulator)	Large-volume peristaltic and cassette pumps	Syringe pumps	Elastomeric pumps
Type of infusion	Macro-infusion	Macro- and micro-infusion	Micro-infusion	Macro-infusion
Flow rate	0.1 to 90–100 ml/h	7–50 ml/h	0.1–10 ml/h	0.5–250 ml/h
Volumes	No limit	$\geq$ 60 ml	10–60 ml	100–555 ml
Dead volume	10–15 ml	25–30 ml	2–5 ml	2–10 ml
Ease of use	Simple, fast	Pump programming required	Pump programming required	Simple, long duration
Energy source	No	Battery	Battery	No
Drug libraries	No	Yes	Yes	No
Precision	No	Yes	Yes	No
Authorized deviation in rate	No norm	$\pm$5%	$\pm$3%	$\pm$15%
Air detection	No	Yes	No	No
Back pressure/ occlusion alarm	No	Yes	Yes	No
Alert when reservoir is near empty	No	Yes	Yes	No
Practical use	Standard infusions (glucose, saline…)	Artificial nutrition	NTI (e.g., heparin) small volumes, small rate, catecholamines…	Antibiotics, local anesthetics, chemotherapies

Smart infusion pumps are new-generation infusion pumps that incorporate software including a "drug library" with hospital-defined drug infusion parameters, such as acceptable concentrations, infusion rates, dosing units, maximum and minimum loading and maintenance dose bolus limits, for 60 or more medications. Such pumps can be preprogrammed and are intended to prevent adverse drug events. They are likely to be used along with computerized prescriber order entry and automatic medication dispensing systems.

Management of catecholamine infusion
Hemodynamic instability following the changeover of vasoactive infusion pump (CVIP) is a common problem in the intensive care unit (ICU). Adverse events could be decreased by the use of algorithms and procedures. The name of drug and its concentration should be clearly notified on the syringe. Several empirical methods are used to achieve CVIP, for example, the "quick change method" of CVIP using two syringe drivers. The manual changeover of CVIP frequently leads to hemodynamic instability. A study was conducted, during which CVIP was successively performed manually then automatically. The frequency of hemodynamic incidents related to the relays, which were defined as significant variations of mean arterial pressure or heart rate, was assessed. The results demonstrated the benefits of automated CVIP using smart pumps in limiting the frequency of hemodynamic incidents related to relays [4, 5].

24.3 Reduction of Infusion System Dead Volume

The dead volume of a drug infusion system is defined as the volume between the point where drug and inert carrier streams meet and the patient's blood. This volume is potentially caused by distal parts of infusion tubing, connectors, manifolds, and catheter lumens. In addition to the risk of unintended drug administration at some later time, residual drug in the dead volume is undelivered. This may have implications for medicines that need to reach threshold serum concentrations rapidly such as some antibiotics. The dead volume becomes a "reservoir for forgotten drugs" when the infusion flow slows or stops. Even if the infusion flows properly, some drug always resides within the dead volume. This amount of drug can be accidentally delivered to patients if for some reasons medications are pushed upstream, carrier flows are suddenly increased, or another drug infusion is started at a high flow rate. For all of the above reasons, the use of drug infusion systems with a small dead volume is preferred [3, 6].

Multi-access infusion devices with reduced dead-space volume and anti-reflux valves seem to be a good solution. They reduce perturbations in drug delivery (lag time, backflow, bolus, physicochemical incompatibilities). The multiple drug stream compartments are separate so that the carrier and the drug meet only at the downstream connector to the catheter, thus also avoiding incompatibilities [7].

Potential risks associated with the dead volume may be magnified with micro-infusion, where smaller volumes of highly concentrated medicines are used [3]. Care providers must consider dead-space volume and the presence of an anti-reflux valve when choosing their infusion sets [1].

Anti-reflux valves
Anti-reflux and anti-siphon valves are two types of one-way valves. Drug delivery can only proceed in one direction. Anti-reflux valves (or anti-backflow valves) prevent backflow of the infused solution into the IV line (figures). Anti-siphon valves (ASV) are used to prevent possible siphoning of the syringe and the administering of a bolus when moving the syringe pump. The ability of an infusion set to deliver a specific amount of drug to the patient can be directly related to the presence of an anti-reflux valve and dead-space volume. Anti-reflux valves are widely used in conjunction with patient-controlled analgesia devices. However, it is important to note that they can achieve a potential "stored volume" if occluded and they may, as part of the administration set, retard fluid administration [2, 8].

24.4 Prevention of Drug Incompatibilities, Particles Formation, and Container–Content Interactions

Drug incompatibilities can jeopardize the safety and effectiveness of intravenous drug therapies especially in the ICU where patients receive many injectable drugs. Drug incompatibility can provoke physical and/or chemical reactions. These can lead to the formation of visible or subvisible particles, degradation of the drug, and/or the formation of toxic substances with potentially serious consequences for the patient (catheter obstruction, occurrence of potentially fatal embolism, systemic inflammatory response syndrome, and loss of therapeutic efficiency). When drugs are known to be incompatible and separate infusion not possible, using separate lumen of a multi-lumen catheter avoids contact between drugs and incompatibility risk. However in the ICU, the number of infused drugs is often higher than the number of available lumens of the catheter. Thus, it is essential to consider the design of each infusion line taking the incompatibilities into account and preferably use multi-access infusion devices containing reduced dead-space volume [2, 9].

An in-line filter is often used to prevent particle infusion when drug incompatibilities lead to a precipitate, but their use must be adapted to the infused mixture. Not all drugs are filterable, such as suspensions, micellar solutions, liposomes, that have a high viscosity or risk to be absorbed by the filter. On the other hand, the presence of an in-line filter on the infusion line reduces flow irregularities [10].

During infusion, interactions may also occur between the medicines and the infusion set. Polyvinyl chloride (PVC), a material widely used in for infusions (e.g., in extension lines), has interactions with many drugs, especially with lipophilic molecules. The absorption can lead to a significant loss of the active drug and then potentially reduces therapeutic efficacy. This problem is especially prevalent when medicines are administered at low flow with syringe pumps. In order to prevent this risk, the use of co-extruded PVC/PE tubing (a thin polyethylene (PE) layer inside

the PVC tubing) is recommended. PE may present some interactions with drugs (such as insulin or monoclonal antibodies) but these are limited and controllable. A simple rinsing of a PE or PVC/PE tubing by the drug generally can be effective. When using PVC, additives (in particular plasticizers) can migrate from the material to the infused drug mixture and into the patient's system. One of these compounds, the diethylhexyl phthalate (DEHP), is known to be reprotoxic and its use is restricted in medical devices [11, 12]. The use of PVC/ PE lines whose PVC is plasticized with TOTM (trioctyl trimellitate) or DEHT (diethylhexyl terephthalate) is a good choice [13, 14].

24.5 Prevention of Allergies

Hypersensitivity reactions to a drug are often feared because they represent a risk for the patient that is difficult to control. In the field of medical devices, allergies are scarce and limited to the well-known allergy to latex due to contact with some specific medical devices such as surgical gloves, urinary or digestive catheters, cannula, drains, tube connections, infusion stoppers, etc. Latex is no longer used in most operating rooms.

Some case reports of contact dermatitis or other allergic reactions exist for the use of medical devices with polyurethane or silicone such used in neonatology. Since these substances are known to be inert and biocompatible, the reactions were probably caused by the isocyanate components in polyurethane [15, 16]. Allergy could also be triggered in response to the particles of ethylene oxide from the sterilization procedure in the medical device [17].

Problems may be prevented through specific protocols which enforce the choice of inert/non-sensitizing materials for medical devices. It is important to collect data from the literature and if possible, from the industry about the allergic properties of materials. When an allergic risk is suspected, the roles and responsibilities of the healthcare professionals, including the pharmacists, have to be identified and clearly defined.

24.6 Prevention of Infectious Complications

Indirectly related to the system used, measures must be taken to reduce the risk for catheter-related bloodstream infections (CRBSI). Two measures reduce the CRBSI risk for patients. These are:

- Skin disinfection

Alcohol is the most effective, with 70% isopropyl alcohol being microbiologically superior to 69% ethanol. But the effect disappears quickly. The action of chlorhexidine or povidone iodine is slower and less profound, but persists longer. In the CLEAN trial, it was proven that chlorhexidine–alcohol provides greater

protection against short-term catheter-related infections than povidone iodine–alcohol. Chlorhexidine–alcohol should be included in all bundles for prevention of intravascular catheter-related infections [18].

- Impregnation of central venous catheters (CVCs)

A recent Cochrane review (2016) showed that the impregnation of catheters significantly reduced CRBSI and catheter colonization. There were no significant differences between the impregnated and non-impregnated groups in the rates of adverse effects, including thrombosis/thrombophlebitis, bleeding, erythema, and/or tenderness at the insertion site. But still, the authors call for caution in routinely recommending the use of antimicrobial-impregnated CVCs across all settings [19].

The EPIC3 revision, for catheter and catheter site care (IVAD20), now recommends that 2% chlorhexidine-impregnated gel dressings should be considered, in addition to 2% chlorhexidine-impregnated sponge dressings, for antimicrobial protection of insertion sites in catheterized adult patients [20].

24.7 Improvement of Patient Comfort: Ambulatory Drug Infusion Systems

One major limit of continuous drug infusions is the low level of comfort and mobility of the patient. Ambulatory drug infusion systems have gained popularity at home and specific ambulatory settings. These systems offer an alternative to traditional infusion systems needing a regular nurse intervention. The following systems allow ambulatory administration of chemotherapy, anti-infective therapies, pain management, total parenteral nutrition and others, by infusion [3].

– Electromechanical pumps: The main advantage of these systems is they have programmable software that allow to adjust drug doses. They are useful for direct patient-controlled-controlled infusion and are especially used in pain management (i.e., patient-controlled analgesia).
– Elastomeric pumps: These systems use the elastic properties of the drug reservoir to provide flow when pressurized. They are portable, low-cost, simple to use, and do not require a power source. Depending on the compatibility between drug and device, they allow for long duration continuous infusion (e.g., chemotherapy, antibiotics, local anesthetics).
– Total implantable catheters: Also called port devices (i.e., Port-a-Cath). These catheters have a reservoir (i.e., port) and a catheter implanted into subcutaneous tissue, usually in the upper chest. Beyond the reduction of the risk of infection, the main advantage for patient is that these catheters allow unrestricted activity, and also reduce infection risk. These devices are very popular for chemotherapy in ambulant patients.

– Peripherally Inserted Central Catheters (PICC) and Midline Catheters [21, 22] are used for central and peripheral venous infusion respectively. PICC and midline catheters can stay in place for weeks or months. These devices have the potential to reduce cost, and lessen patient exposure to hospital procedures and complications of venous access. They improve in patients' comfort and satisfaction [23].

24.8 Conclusion

The optimal administration of injectable drugs is guided by the choice and good use of medical devices. Care around medical devices used for IV administration is a fundamental element of the pharmaceutical care given to the patient. The design of the infusion lines must be based on a consultation between physicians, pharmacists and nurses, particularly in neonatal, pediatric, and adult ICU, where the infusion process is complex and at high risk. To provide optimal care for the patient, pharmacists should also receive (continuing) education on these aspects of drug delivery.

The use of other medical devices in pharmaceutical care is closely linked with specific diseases and will be discussed in the appropriate chapters: Chap. 27 for the respiratory devices and Chap. 28 for the devices used in diabetes.

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Chapter 25
Pharmaceutical Care, Health Promotion, and Disease Prevention

Claire Anderson

Abstract After discussing the exact nature of health promotion, disease prevention, and pharmacy practice, I argue that pharmaceutical care should not be separated from holistic approach to patient care. If pharmacists are going to contribute to healthcare and improving all health outcomes for patients, they need of course to focus on their area of expertise, medicines, but also on broader health and lifestyle issues. This gives them a role in health prevention and disease prevention. There are several practice examples where this has already been achieved.

Keywords Pharmaceutical care · Public health · Disease prevention
Holistic patient care · Lifestyle

25.1 What Is Health Promotion?

Like definitions of health, there are numerous definitions of health promotion. Health promotion may include a wide range of activities and interventions including those that encourage individuals, families, communities or whole populations to adopt healthy lifestyles, encourage better access to health services and involvement in health decisions, seek to promote an environment where healthy choices are easy choices and educate people about their body and keeping healthy. Health promotion aims to maintain and enhance good health and prevent ill health. It has been argued that,

> the overall goal of health promotion may be summed up as the balanced enhancement of physical, mental and social facets of positive health, coupled with the prevention of physical, mental and social ill health. [1]

The term encompasses a range of activities and issues including both individual and societal aspects. At one end of this range are government policy and legislation

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affecting health. These include actions with a direct influence on health (for example, legislation to ban tobacco smoking in public places) as well as those which affect the determinants of health (for example, social welfare and benefits policies). At the other end is an individual's lifestyle choices. The shift from infectious diseases to chronic long term conditions has highlighted the role of lifestyle in disease causation, and therefore, the importance of prevention. One problem in examining pharmacist's health promotion activities is the lack of a single, stable, and bounded definition for each of the terms "ill health prevention" and "health promotion". It should be noted that public health and health promotion are often used interchangeably in the literature on pharmacy although traditionally public health has focused on populations rather than individuals.

25.2 Disease Prevention

A number of viewpoints is possible for preventing disease, with different terms.

Primary prevention is concerned with preventing the onset of ill health and to detect high risk groups. Activities are designed to reduce the instances of an illness in a population and thus to reduce (as far as possible) the risk of new cases appearing, and to reduce their duration. Examples include immunization, health education campaigns.

Secondary prevention is about detecting a disease in its earliest stages, before symptoms appear, and intervening to slow or stop its progression. Activities include educating people about their medicines, education on healthy eating for people with diabetes, screening for and treating Chlamydia.

Tertiary prevention is about interventions designed to stop the progress of an established long term condition, to control it and to reduce disability and increase quality of life. It seeks to change health damaging behaviors and prevent the progression of ill health. Activities might include educating people with diabetes about diet and foot health, ensuring people with atrial fibrillation adhere to their treatment.

25.3 The Uniqueness of Pharmacy

Pharmacists are in a unique position in society, they are available for at least eight and for up to twenty four hours a day without an appointment; they regularly see the healthy as well as those with illness, and those living with long term conditions; their position at the center of communities enables their premises to be used for health promotion campaigns which will reach a large number of people; the relationship that a pharmacist builds up with patients customers and their families over years; they have opportunities to promote health every day.

25.4 What Is the Evidence Base for Pharmacists' Role in Health Promotion?

A recent Public Health England Commissioned review of pharmacy's role in improving the health of the public [2] identified twenty relevant review papers. In the literature on the contribution of community pharmacy to public health is extensive and growing. A considerable body of evidence exists for the role of community pharmacy in a range of services, not only aimed at improving general health, but also at maintaining the health of those with existing disease. The evidence for positive outcomes is strongest in services including smoking cessation, emergency hormonal contraception (EHC) EHC supply, cardiovascular disease prevention, blood pressure management, diabetes, and possibly asthma and heart failure. There was strong evidence of improvements in lipid levels that were sustained for at least one year in both primary and secondary prevention of coronary heart disease. Community pharmacists can make an important contribution to the management of people with diabetes for screening, improved adherence with medicines and reduced blood glucose levels or HbA1c.

Although published evidence is currently less strong in other areas such as COPD, infection control, substance abuse, weight management, and minor ailments schemes, there are some reports of successes in the community pharmacy provision of these services. However, further research is required to justify the role of community pharmacy in these areas.

This review did not identify any UK papers on immunization and vaccination, although there is more recent evidence indicating that UK community pharmacists are providing services in this area, for example [3, 4]. Vaccination is an established pharmacy service in several countries, the USA, Portugal, and Ireland, for example.

25.5 How Far Should Pharmacist's Role in Health Promotion Move?

There has long been discussion about how far pharmacy's role in health promotion should move from their role as experts in medicines and providers of pharmaceutical care [5]. It is easy to see a role in health promotion when it is linked to the sale or supply of a medicines, like nicotine replacement therapy in smoking cessation or advice about healthy eating or exercise to someone with a prescription for coronary heart disease medicines. However, should pharmacists provide brief interventions for problem drinkers or promote exercise classes when these activities are not linked to medicines? Should they provide health checks and offer health screening?

Van Mil and Fernadez-Llimos asked, if *"pharmaceutical care" should always be associated with the existence of medicine treatment in a given patient?* and by inference if we should therefore perhaps exclude educational activities or health promotion activities performed by pharmacists from the scope of the

"pharmaceutical care"? [6]. They asked if other pharmacist activities that are not necessarily associated with medicines are parts of the concept, like smoking cessation programs, condom use promotion, needle exchange, or screening and if they should be included as part of pharmaceutical care. In other words, is pharmaceutical care the care by the pharmacist, or care around pharmaceuticals?

To understand these arguments, we need consider the patient for whom we are caring. Can we separate people's medicines related outcomes from people's health outcomes? Do we offer a medicines centered approach care or a more holistic approach to healthcare? If we narrowly focus on the medicines will we miss key factors that will affect a person's treatment, recovery, and well-being? If we focus on an individual's health outcomes lifestyle, behaviors and well-being all become important parts of the treatment.

25.6 Does Pharmaceutical Care Link to Health Promotion?

If we take the PCNE definition of pharmaceutical care at face value it appears to be about the pharmacists' care of individuals to both optimize medicines use and improve health outcomes.

> Pharmaceutical Care is the pharmacist's contribution to the care of individuals in order to optimize medicines use and improve health outcomes.

It could be argued that those health outcomes are those linked directly to the medicines and not to broader lifestyle or well-being issues. Conversely it could be argued that if health outcomes are included then health promotion becomes inextricably linked to the pharmacists' or perhaps the pharmacy's role in medicines optimization. The PCNE definition provides an approach that can easily include health promotion as well as medicines optimization.

Let's take a simple example, a 70-year-old male patient who is also a carer for his wife who has Alzheimer's disease, comes into the pharmacy for a review of their coronary heart disease medicines. The pharmacist carries out the review and ensures that they understand the medicines and how to take them correctly and that they are having the appropriate outcomes. She also asks him if they have had their "flu vaccination" this year? The pharmacist notices that the patient smells of smoke and has nicotine stained teeth. She asks him how his wife is doing,

If the pharmacist were only to concentrate on the medicines, the patient's smoking habit would be ignored and so would his wife and the effect her illness might have on his health outcomes. Carer's often neglect their own health and are less likely to get "flu immunizations". However, if the pharmacist broaches the subject of smoking and how it will affect the disease progression and treatment and then offers support to help the patient to quit smoking as well as offering the "flu immunization" it could be argued that more complete, holistic care had been offered which will plead to better health outcomes.

25.6.1 An English Example of the Link Between Pharmaceutical Care and Health Promotion

In England all community pharmacies provide healthy living advice to patients as part of the public health element of the community pharmacy contractual framework and provision of relevant healthy living advice is also part of the Medicines Use Review (MUR) service and the New Medicine Service (NMS). MURs and the NMS are key medicines optimization services which all community pharmacist contractors in England are encouraged to offer to eligible patients to help them to ensure that they get the most benefit from their prescribed medicines. In the MUR service specification, the pharmacist is expected to provide healthy living advice alongside advice and information about the patient's medicines in the following areas:

a. diet and nutrition
b. smoking
c. physical activity
d. alcohol
e. sexual health
f. weight management
g. other (free text information can be entered in the clinical record)
h. healthy living advice not applicable at this consultation.

The majority of community pharmacies will also provide at least one locally commissioned public health service, such as provision of emergency contraception, stop smoking, or supervision of methadone and buprenorphine.

The Healthy Living Pharmacy (HLP) framework provides a positive approach to focusing the whole pharmacy team and not just the pharmacist on promotion of healthy lifestyles and associated service delivery [7]. The development of support staff skills and increased motivation to provide services has been a positive achievement of the HLP concept. The Department of Health (DH) introduced a quality payments scheme as part of the contractual framework in 2017. The following requirements must be met before a pharmacy can be registered as a HLP Level 1,

- the pharmacy has a consultation room which is compliant with the Advanced Services standards and is appropriate for the services on offer;
- in the past year, the pharmacy has participated in the provision of both Medicines Use Reviews (MURs) and the New Medicine Service (NMS), and has proactively engaged in health promoting conversations;
- in the past year, the pharmacy has participated in the provision of the NHS Community Pharmacy Seasonal Influenza Vaccination Advanced Service or has actively referred patients to other NHS providers of vaccinations;
- the pharmacy complies with the General Pharmaceutical Council's Standards for Registered Premises and Standards of Conduct, Ethics and Performance; and
- the pharmacy complies with the NHS Community Pharmacy Contractual Framework (CPCF) requirements.

This illustrates that the provision of medicines-oriented services such as the MUR, are a prerequisite for HLP Level 1 registration.

25.7 What Approach Should Pharmacists Take?

Pharmacists have been criticized for being passive rather than opportunistic in their health promoting role. Even though information in itself is unlikely to result in behavior change, it is an important part of attempts to persuade people to adopt healthy choices. There is now a body of evidence upon which to base efforts to change behavior [8].

There is evidence that even the shortest of interventions can be effective providing they are delivered in a way that has been shown in research to work.

Types of pharmacy intervention [8]:

Very brief intervention

A very brief intervention can take from 30 s to a couple of minutes. It is mainly about giving people information, or directing them where to go for further help. It may also include other activities such as raising awareness of risks, or providing encouragement and support for change. It follows an "ask, advise, assist" structure. For example, very brief advice on smoking would involve recording the person's smoking status and advising them that stop smoking services offer effective help to quit. Then, depending on the person's response, they may be directed to these services for additional support.

Brief intervention

A brief intervention involves oral discussion, negotiation or encouragement, with or without written or other support or follow-up. It may also involve a referral for further interventions, directing people to other options, or more intensive support. Brief interventions can be delivered by anyone who is trained in the necessary skills and knowledge. These interventions are often carried out when the opportunity arises, typically taking not more than a few minutes for basic advice.

Extended brief intervention

An extended brief intervention is similar in content to a brief intervention but usually lasts more than 30 min and consists of an individually focused discussion. It can involve a single session or multiple brief sessions.

25.8 Health Promotion and Pharmaceutical Care in Practice

Pharmacists wishing to integrate health promoting activities into their pharmaceutical care need to adopt a style of consulting which involves listening and negotiating rather than telling, crucially taking into account the individual's social circumstances. This may involve the role of family members, carers or friends in the management of medicines, while taking into consideration living conditions, health status, and socioeconomic resources. Pharmacists should adopt a holistic approach and think creatively about the opportunities to promote health whenever they are talking to patients about their medicines. By holistic, I mean addressing issues not traditionally associated with pharmacy or medicines, but which may actually be linked to the sale or supply of medicines or health-related goods.

25.9 Conclusion

In conclusion, it must be clear that pharmaceutical care cannot and should not be separated from holistic approach to patient care. If pharmacists are going to contribute to improving health outcomes for patients, they need of course to focus on their area of expertise, medicines, but also on broader health and lifestyle issues.

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Part VI
Pharmaceutical Care for Specific Patient Groups

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In this section, we focus on pharmaceutical care for chronic patients and we selected some important diseases to address general and specific issues, challenges, pitfalls, helpful tools, and some illustrative examples of best pharmaceutical care practice.

Globally, the population is aging and the "oldest old" cohort, i.e., those aged 80 years and older, is also aging. The drivers for the demographic shift are well known, and recently the World Health Organization (WHO) launched a Global Strategy and Action Plan on Ageing and Health. The vision of this plan is to ensure "a world in which everyone can live a long and healthy life". The practice of pharmacy and the provision of pharmaceutical care services play an important role, and hence the implications for the pharmacy profession within this vision are significant. Understanding the aging processes, specifically pharmacodynamics and pharmacokinetics, and how prescribed therapy can be optimized, will help to understand the pharmaceutical care needs of people (older and younger), and ultimately help to realize the WHO's vision of enabling people to live a long and healthy life. Thus, with the exception of the chapter on pediatrics, the topics addressed in most chapters in this section comprise polypharmacy, adherence, medication review, and related screening tools as well as challenges in practice implementation.

Some authors also discuss the current evidence of pharmacist-led services. The latter remains a big challenge and we still struggle to prove that pharmaceutical care can improve clinical outcomes compared with usual care. We also wonder if such improvements translate to improved humanistic and economic outcomes. However, looking at cardiovascular disease, Schulz et al. report in Chap. 29 strong evidence that pharmacist intervention improves BP control in outpatients. At the same time, they claim that randomized controlled trials (RCTs) are still urgently needed with robust designs, studying large populations, adequate follow-up periods, and sufficient power to detect clinical relevant differences in endpoints. Similarly Chap. 27 reports, with respect to asthma and COPD, that with the exception of improvement of inhaler technique, it is challenging to find evidence

demonstrating pharmacists' positive impact on clinical, humanistic and economic outcomes. And in Chap. 26, on the aged, again positive results are known for process outcomes (e.g., improved prescribing, adherence) but evidence showing impact on healthcare services resource utilization, e.g., hospitalization and mortality is still lacking.

But, there are also positive examples. Kamal et al. conclude in Chap. 33 that, pharmacists can have direct influence on clinical outcomes in HIV, namely on viral load and CD4 count. Supporting/enhancing adherence to ARVs and co-treatments is the intervention. Throughout all chapters and all described diseases, improving adherence is a crucial task for pharmacists and lack of adherence is a major drug-related problem to be addressed through pharmaceutical care interventions. See also Chap. 5.

A further aspect seen in all chapters is the need for strengthening interprofessional collaboration and the need to get access to clinical data, namely diagnoses and the medical history. This is, for example, quite essential in pharmaceutical care for cancer patients (Chap. 32) and increasingly pharmacists get involved (at least in the hospital) in multidisciplinary teams of healthcare professionals.

Taking into consideration the individual patients beliefs about their condition, their attitudes in relation to their medication are of paramount importance. Understanding the individual patient's needs, including assessing the level of literacy and identifying which intervention works best, will enable the development of a more effective personalized approach. Patients need to be supported and empowered to take increased responsibility for their treatments and to actively participate in the management of their condition. Another keyword frequently addressed is shared decision-making with an increased involvement of the patient, and eventually his caregiver, into any design of a treatment plan.

In some diseases, the pharmaceutical care issues comprise nonmedicine-related interventions, namely on lifestyle. Management of type-2 diabetes (Chapter 28) starts with lifestyle modification before medicines are used and drug-related problems arise. And lifestyle interventions are also essential in patients with asthma and/or COPD (smoking cessation) and in all cardiovascular diseases. However, in some countries, such interventions are not provided by pharmacists and not considered part of pharmaceutical care, although of increasing importance to achieve optimal outcomes of pharmacotherapy.

To sum up, this section on eight specific diseases or patient groups provides a rich insight in different pharmaceutical care models. All reflect the setting and circumstances of the respective authors. Reading all chapters provides knowledge and skills to students and rich food for thinking and inspiration to the advanced practitioners. Finally, in the chapters on diabetes (28), cardiovascular disease (29), anticoagulation (30), and viral diseases (33) precious patient case scenarios are presented.

Chapter 26
Pharmaceutical Care in the Aged

Cristín Ryan and Máire O'Dwyer

Abstract Prescribing for older people is complex particularly in the presence of multi-morbidity. Ensuring the appropriate balance of prescribed medicines requires a consideration of pharmacokinetic and pharmacodynamics parameters, a knowledge of the potential adverse effects as well as the potential for inappropriate prescribing. Adopting a systematic approach to ensure that patients receive the maximum benefit from their prescribed treatment is essential. While various approaches can be used, it is important that the approach undertaken is tailored to individual patient needs and what is achievable within the clinical practice setting.

Keywords Pharmaceutical care · Older people · Medication review
Polypharmacy · Medication adherence

26.1 The Aging Population

Globally, the population is aging, with the proportion of people over 60 years of age set to increase from a current estimate of 962 million to a projected 2.1 billion by 2050 [1]. The relative proportion of people aged over 60 years is also projected to rise, and will reach one in five by 2050. On a European level, currently, 24% of the population is aged 60 years or over, a figure projected to increase to 34% by 2050 [1].

The "oldest old" cohort, i.e., those aged 85 years and older, is also aging. Globally, it is estimated that 14% of people are in this cohort, the proportion of which is expected to increase to 19% by 2050. Consequently, there will also be an increase in the prevalence of disability, as more older people suffer from disability when compared to a younger population (the prevalence of disability among

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persons under 18 years is 5.8%; this prevalence increases to 44.6% among 65–74-year olds, and increases further to 84.2% in those aged 85 years and over).

Drivers of this demographic shift include: the improved provision of healthcare services; advancements in diagnoses and treatments of conditions; advancements in public health strategies; improved nutrition and sanitation; an increase in life expectancy; and a decline in birth rates as well as migration [1].

In response to this demographic shift, the World Health Organization (WHO) recently launched a Global Strategy and Action Plan on Ageing and Health whose vision is to ensure "a world in which everyone can live a long and healthy life" [2].

There are five key strategic objectives linked to achieving this vision, which include:

- Commitment to action on Healthy Aging in every country;
- Developing age-friendly environments;
- Aligning health systems to the needs of older populations;
- Developing sustainable and equitable systems for providing long-term care; and
- Improving measurement, monitoring and research on Healthy Aging.

The practice of pharmacy and the provision of pharmaceutical care services play an important role within each of these objectives and hence the implications for the pharmacy profession within this vision are significant.

Understanding the aging process and mechanisms by which prescribed therapy can be optimized will help realize the WHO's vision of enabling older people to live a healthy and long life.

26.2 Chronic Conditions and Multi-morbidity

The prevalence of all chronic conditions and the presence of multi-morbidity (the coexistence of two or more long-term health conditions) increase with age [3, 4]. Current estimates suggest that by the age of 65 years, over 60% of adults will have two or more chronic conditions, >25% will have four or more, while 10% will have six or more chronic conditions [4].

Cardiovascular disease is the leading cause of morbidity and mortality in older people, and is associated with significant multi-morbidity. Over 50% of patients who have heart failure or stroke also have at least five comorbid conditions [4]. The most common concomitant conditions in patients with heart failure, stroke or atrial fibrillation are arthritis, anaemia and diabetes mellitus, with chronic kidney disease, chronic obstructive pulmonary disease depression and cognitive impairment, also being common [5].

The prevalence of cognitive impairment, Alzheimer's disease and other dementias is low at younger ages, and nearly doubles with every 5 years of age after the age of 65. It is estimated that 25–30% of the population aged 85 years or

older have dementia. Patients with Alzheimer's disease are more at risk of medication errors than those without, which may in some cases be due to non-adherence or indeed over-adherence [5].

In general, the occurrence of multi-morbidity also leads to the prescribing of polypharmacy (Section X). Because the majority of evidence-based guidelines are written for single diseases, knowledge and understanding of how medicines are handled in the body with increasing age is fundamental to the provision of pharmaceutical care for older people.

26.3 Pharmacokinetics and Pharmacodynamics

Physiological changes that occur heterogenically with aging affect the body's handling of medicines, i.e., pharmacokinetics, and it's response to medicines, i.e., pharmacodynamics, to varying extents. These changes result from the loss of functional capacity of several organs as well as the reduced efficacy of homeostatic mechanisms [6, 7].

26.3.1 Pharmacokinetics

Pharmacokinetics involves four components: absorption, distribution, metabolism, and elimination. Knowledge of each of these parameters is important to ensure the appropriate design of patients' medication regimens, to ensure efficacy and to prevent toxicity [8]. The clinical implications for each of these vary, and certain drug properties need to be considered when predicting the extent to which each individual drug is affected. Table 26.1 summarizes the key physiological changes that affect each pharmacokinetic parameter, the impact these changes have on each parameter and some examples of their clinical significance.

26.3.2 Pharmacodynamics

Pharmacodynamics refers to the change in the response to drugs with time [9]. Pharmacodynamic changes that occur with aging may result from organ system changes, alterations in homeostatic functions or from receptor and cellular changes [10]. Table 26.2 provides a summary of commonly occurring pharmacodynamic changes associated with aging.

Table 26.1 Age-related changes in pharmacokinetics [6–9]

Pharmacokinetic parameter	Age-related change	Pharmacokinetic effect and clinical significance
Absorption	Increased gastric Ph Delayed gastric emptying Reduced splanchnic blood flow Decreased absorption surface Decreased gastrointestinal motility	Rate and/or extent of absorption altered Clinically inconsequential for most drugs Exceptions: Absorption by active transport of iron, calcium, vitamin B12 is ↓ Absorption of levodopa is ↑ Onset of action of bucally administered medication may be delayed
Distribution	Increased body fat mass	Vd of lipophilic drugs ↑, e.g., haloperidol, resulting in a ↓ serum concentration
	Reduced body total water	Vd of hydrophilic drugs ↓, e.g., theophylline, resulting in ↑ serum concentration
	Reduced body lean mass	Vd of drugs that distribute into muscle ↓, e.g., digoxin
	Reduced serum albumin	↑ concentration of unbound acidic drugs, e.g., diazepam, NSAIDs
Metabolism	Reduced overall liver mass and hepatic blood flow, resulting in a reduction in metabolizing enzymes, and the concentration of drug being delivered to the liver	↓ in metabolizing enzymes results in higher systemic bioavailability of medicines that undergo 1st pass metabolism, e.g., nitrates Prodrugs that require activation by 1st pass metabolism will have a ↓ systemic bioavailability
Elimination	Reduced renal blood flow and glomerular filtration rate, extraction capacity of the liver and hepatic blood flow	Elimination of drugs by the renal system, e.g., water-soluble antibiotics, diuretics and the hepatic system will be ↓ resulting in an ↑ bioavailability

Key: *Vd* Volume of distribution; *NSAIDs* Nonsteroidal Anti-inflammatory drugs, ↓ decrease; ↑ Increase

26.3.3 Pharmacokinetics and Pharmacodynamics in Practice

The application of the known potential pharmacokinetic and pharmacodynamic changes that occur with increasing age facilitates the prediction of therapeutic outcomes and consequently the occurrence of adverse events may be avoided. Table 26.3 provides some examples.

Table 26.2 Pharmacodynamic changes associated with aging [6, 7, 10]

Drug	Pharmacodynamic Effect	Clinical Significance
Anticholinergics	Central effects	↑
Antihypertensives	Postural hypotension	↑
Benzodiazepines	Sedation, postural sway	↑
Diltiazem	Antihypertensive effect Acute PR interval prolongation	↑ ↓
Furosemide	Peak diuretic response	↓
Neuroleptics, metoclopramide	Extrapyramidal symptoms	↑
Morphine	Analgesic effect Respiratory depression	↑ ↔
NSAIDs	GI adverse reactions	↑
Verapamil	Acute hypertensive effect	↑
Warfarin	Anticoagulant effect	↑
Neuroleptics, TCAs	Anticholinergic effects	↑

Key: ↑ Increased, ↓ Decreased; ↔ No change, *NSAIDs* Nonsteroidal Anti-Inflammatory Drugs, *GI* Gastrointestinal, *TCA* Tricyclic Antidepressant

Table 26.3 The application of pharmacokinetic and pharmacodynamic changes to commonly encountered medicines in older adults

Drug properties	Pharmacokinetic and pharmacodynamic changes	Clinical significance
NSAIDs		
Lipid soluble	↑ Vd	↑ likelihood of side-effects, e.g., GI bleed, renal toxicity
Extensively protein bound	↑ concentration of unbound drug	
Renal excretion	↓ clearance, ↑ plasma concentrations	
Digoxin		
Hydrophilic drug	↓ Vd, ↑ plasma concentrations	↑ susceptibility to digoxin toxicity
Distributes into muscle	↓ loading dose if lean body mass ↓	
Renal excretion	↓ clearance, ↑ plasma concentrations	
Benzodiazepines		
Protein bound	↑ in active unbound drug concentrations if albumin is ↓	↑ sedative effects
Lipid soluble benzodiazepines Hepatic degradation and clearance	↑ Vd → ↑ $t_{1/2}$ and accumulation ↑ $t_{1/2}$ benzodiazepine	

Key: ↑ Increase, ↓ decrease, *Vd* Volume of distribution, $t_{1/2}$ half-life, *NSAIDs* Nonsteroidal anti-inflammatory drugs, *GI* Gastrointestinal

26.4 Prescribing for Older People

26.4.1 Polypharmacy

Predicting the pharmacokinetic and pharmacodynamic effects of medicines is more challenging when several medicines are prescribed. To that end, "polypharmacy" describes the prescribing of multiple medicines and has been noted as "one of the most pressing prescribing challenges" [11]. Despite the fact that the term "polypharmacy" is widely used in the literature, there is a lack of consistency with how polypharmacy is defined. Polypharmacy is commonly assigned a numerical value, of four or five concomitant medicines, but has also been viewed historically in a negative light, i.e., "the prescribing of too many medicines", or the "prescribing of more medicines than are clinically indicated".

However, due to the growing prevalence of multi-morbidity (Sect. 7.2), the enhanced availability of primary and secondary preventative treatments and evidence-based guidelines that advocate for the prescribing of multiple medicines, the prescribing of many medicines may be entirely appropriate, indicated and necessary in order to maximize patient outcomes [12].

This transition in thinking, or paradigm shift (Fig. 26.1), has led to the adoption of the term "appropriate polypharmacy", which provides for the prescribing of several medicines "where medicine use has been optimized and prescribing is in

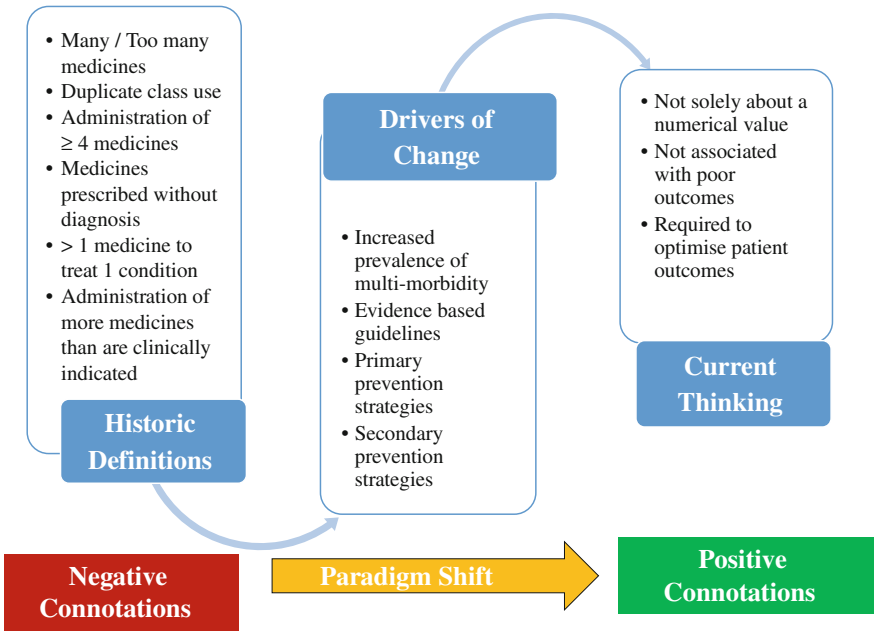

Fig. 26.1 Defining polypharmacy

accordance with best evidence" [13]. In essence, this recognizes that the prescribing of several medicines is often required, and ensuring that these medicines are optimized is imperative to achieve "appropriate polypharmacy".

Polypharmacy has often been viewed in a negative light because the use of several medicines can lead to medication-related problems such as adverse drug reactions (Sect. 26.4.2), potentially inappropriate prescribing (Sect. 26.4.3) and poor patient adherence (Chap. 5).

26.4.2 Adverse Drugs Reactions

The risk of the occurrence of an adverse drug reaction (ADR; defined as "*any response to a drug which is noxious and unintended and which occurs at doses normally used in human beings for diagnosis, prophylaxis or therapy of disease and excluding a failure to accomplish the intended purpose*") [14] increases with age, owing to pharmacokinetic and pharmacodynamics changes described above (26.2), polypharmacy (26.4.1), multi-morbidity (Sect. 26.3), inappropriate prescribing and monitoring.

The most commonly occurring ADRs in the older population include: renal failure, orthostatic hypotension, falls, delirium, gastrointestinal and intracranial bleeding, and the most commonly associated medicines with ADRs-related hospital admissions include: diuretics, NSAID, antiplatelets, anticoagulants, anti-diabetics, and medicines with sedative properties.

Many ADRs are preventable by adopting strategies such as minimising inappropriate prescribing and unnecessary polypharmacy by undertaking regular medication review, considering the potential risk–benefit ratio of treatment, using the minimal effective dose of medicines and limiting the number of medicines prescribed [15].

26.4.3 Potentially Inappropriate Prescribing

Potentially inappropriate prescribing (PIP) encompasses a set of prescribing practices, where the risk of prescribing a particular medicine outweighs the potential benefits to the patient, and includes (i) over-use, (ii) mis-use and (iii) under-use of medicines [16].

The word "potentially" is used as, without engaging with the prescriber, it is not possible to determine if, in fact, the prescriber had considered the risk(s) associated with prescribing the particular medicine, possible alternatives to that medicine and their associated risk(s) or the individual patient's preferences. Considering these factors, it is possible that the prescriber made an informed decision to continue the particular medicine in question.

The *over-use* of a medicine results from the prescribing of a medicine at a dose, frequency or duration that exceeds evidence-based recommendations. For example, the use of digoxin at a long-term dose of >125 micrograms when renal impairment is present, or the use of long-acting benzodiazepines or benzodiazepines with long-acting metabolites for a long term (i.e., > 1 month).

The *mis-use* of a medicine involves the prescribing of a particular medicine that has certain associated risks, whereby there is a safer, more-effective alternative available. For example, the use of Selective Serotonin Reuptake Inhibitors in patients with a history of clinically significant hyponatraemia, or the use of theophylline as monotherapy for patients with Chronic Obstructive Pulmonary Disease.

The *under-use* of medicines occurs when a medicine that is clinically indicated for either primary or secondary prevention is not prescribed, and there is no apparent contra-indication to that medicine. Examples include: the omission of calcium and vitamin D supplementation in patients with known osteoporosis, or the omission of folic acid supplementation in patients taking methotrexate. In comparison to other components of inappropriate prescribing (i.e., over-use and mis-use), under-use of medicines is poorly understood.

26.5 Strategies to Enhance Prescribing for Older Patients

Various initiatives are recommended to ensure that patients' medicines are prescribed appropriately in order for patients to get the maximum benefit from their prescribed treatments with minimum risk of adverse events. These include: medicines reconciliation and medication review (Chap. 7, Sect. 26.5.1), medicines optimization (Sect. 26.5.2) and using screening tools within a review (Sect. 26.5.3). Guidance on improving prescribing for multi-morbid patients has also been recently published by the National Institute for Health and Care Excellence (NICE) [17].

26.5.1 Medication Review in Older People

One medication review strategy specifically designed to target prescribing of polypharmacy for multi-morbid patients has recently been published by the Scottish Government [18]. This guidance recognizes that "necessary polypharmacy is a feature of modern therapeutics", and suggests adopting a "7-step" approach to medication review. These steps involve establishing the aim, need, effectiveness, safety, cost-effectiveness and the patient's adherence to each medicine prescribed (Table 26.4).

Evaluation of the impact, and clinical implications of this guidance, has not yet been reported.

Table 26.4 The 7-step approach to medication review [18]

Domain	Step	Process
Aims	What are the aims and objectives of drug therapy?	Identify therapeutic objectives regarding: Management of existing health problems Prevention of future health problems
Need	What are the essential drugs required?	Identify essential drugs that: Prevent rapid symptomatic decline, e.g., ACE Inhibitor in LVSD Have essential replacement functions, e.g., levothyroxine
	Does the patient take unnecessary drug therapy?	Identify and review need for drugs with: Temporary indications, e.g., Sedative Higher than usual maintenance doses, e.g., Proton Pump Inhibitor Limited benefit in general for the indication they are used for Limited benefit in the patient under review
Effectiveness	Are therapeutic objectives being achieved?	Identify the need for adding/intensifying drug therapy in order to achieve therapeutic objectives to: Achieve symptom control Achieve biochemical/clinical target Prevent disease progression/exacerbation
Safety	Is the patient at risk of ADRs or suffer actual ADRs?	Consider: Interactions (Drug—disease, Drug—drug) Robustness of monitoring mechanisms for high-risk drugs Risk of accidental overdose
Cost-effectiveness	Is the drug therapy cost-effective?	Consider more cost-effective alternatives
Adherence/ Patient centeredness	Is the patient willing and able to take drug therapy as intended?	Consider: Pharmaceutical form; can the patient take this? Convenience of dosing schedule Discuss treatment with patient/carer

Key: *ADRs* Adverse Drug Reactions; *ACE* Angiotensin Converting Enzyme, *LVSD* Left Ventricular Systolic Decline

26.5.2 Medicines Optimization

Medicines optimization is another, similar concept to a medication review, aimed at maximizing patient benefit from prescribed treatments and is defined as a "person-centred approach to safe and effective medication use, to ensure people obtain the best possible outcomes from their medicines" [19].

The Royal Pharmaceutical Society in the United Kingdom (UK) produced guidance on how pharmacists should approach the process of medicines optimization, and suggests the following four principles should be followed:

- Aim to understand the patient's experience,
- Ensure medicine choices are evidence-based,
- Ensure medicines use is as safe as possible and
- Make medicines optimization part of routine practice.

In contrast to a medication review, patients must be present as art of a "medicines optimization" consultation. The long-term clinical implications of adopting this process have not been reported.

26.5.3 Screening Tools

The use of screening tools to help facilitate the undertaking of a medication review is becoming increasingly popular, due to its positive effects on patient outcomes. Screening tools contain either explicit (rule-based/specific statements of inappropriateness) or implicit (judgement-based) criteria or a combination of both, and there are a variety of each type used in various clinical settings. Examples of screening tools include: the FORTA (Fit fOR The Aged) list; [20] STOPP/START (Screening Tool of Older Persons Prescriptions/Screening Tool to Alert Doctors to Right Treatment); [21] PRISCUS; and [22] the Medication Appropriateness Index [23] and Laroche's list [24]. The majority of these criteria were developed using expert consensus methodologies and are based on robust evidence; they vary in length, the countries in which they were developed, various aspects of potentially inappropriate prescribing targeted (e.g., the START component of the STOPP/START tool lists potential prescribing omissions) by the criteria and the clinical setting for which they were designed. Selecting the most appropriate criteria for use is important, and some time should be spent researching various options. Some of the key considerations are summarized in Table 26.5. While these factors should be considered, it is also important to bear in mind that each screening tool can be tailored/modified to reflect local prescribing practices and priorities.

Once a screening tool has been chosen, there are other key factors that should be considered to ensure the maximum benefit from the screening tool within specific areas of practice. These include: the patient information available, individual pharmacists' rapport with prescribers, prescribers' preferences and resources available.

These are summarized (Table 26.6). This information has been compiled from a combination of reports from clinical practice and from research studies.

Table 26.5 Factors to consider when selecting a screening tool to facilitate a medication review

Consideration	Example	Suggestion
Country of origin of the criteria, and county in which the criteria will be used	Was the criteria developed for any specific country or can it be used globally?	Pick a criteria that will tailor to prescribing practices in country of use
Level of information available	Are biochemical data available?	If not, tailor criteria to exclude those that reference biochemical data Consider using medicines prescribed as proxies for clinical indications
Clinical setting	Tailor expected patient outcomes relative to the patient setting	For example, aim to reduce the occurrence of medication-related hospital admissions in secondary care
Patient care priorities	Do you want to target any specific area of prescribing, e.g., the occurrence of falls?	Select criteria that include a section specifically targeting medications associated with an increased risk of falls
Clinical effectiveness	Is there evidence to support the use of the tool in achieving the desired outcome?	STOPP/START has been shown to reduce adverse drug events and falls [25]
Inter-rater reliability	Can the criteria be used reliably amongst healthcare professionals?	A peer-learning approach to using the criteria could be adopted

26.5.4 Managing Multi-morbidity

As noted previously (Sect. 26.2), the prevalence of multi-morbidity increases with age. The NICE in the United Kingdom (UK) has recently published guidance on how healthcare professionals should manage multi-morbid patients (Table 26.7) [17].

Their recommendations are summarized under the five main headings below:

- Discuss the purpose of an approach to care that accounts for multi-morbidity
- Establish disease and treatment burden
- Establish patients' goals, values and priorities
- Review medicines and other treatments taking into account evidence of likely benefits and harms for the individual patient and outcomes important to the person
- Agree an individualized management plan with the patient

In essence, the process of managing multi-morbidity in older patients as recommended by NICE encompasses many of the principles of medication review, medications optimization and the use of screening tools, already discussed in the sections above.

Table 26.6 Challenges of using screening tools in every day practice

Challenge	Reason for challenge	Potential solution to challenge
Access to the prescriber	Access to prescriber varies depending on setting, e.g., community pharmacists are more isolated from prescribers than pharmacist in secondary care	Establish a rapport with local prescribers, particularly if in the community pharmacy setting. Seek to involve them in the planning of medication initiatives, irrespective of setting.
Prescriber's willingness to change	Previous failed attempts to change Prescribed treatment initiated by a different clinician, e.g., specialist Knowledge of patient preferences	Early engagement with the prescriber Highlight that recommendations are evidence-based, Adopt a peer-learning approach to reviewing medicines Engage in prescriber training if appropriate
Large number of criteria to become familiar with	Some criteria have over 100 individual rule of avoidance to contend with	Increased familiarity with criteria reduces the time taken to use them
Length of time required to use criteria	Undertaking a review using a screening tool can take in excess of 30 min	Adopt a structured approach to undertaking a review, e.g., per physiological system
Criteria do not list all erroneous scenarios	None of the screening tools developed have been designed to replace clinical knowledge and judgement	Pharmacists need to bear this in mind when undertaking a review
Resources	Lack of alternative/supportive services in the local area to help make the recommended change successful	Be aware of supportive series that exist for older people in local area
Underlying conditions	Patients in secondary care are usually acutely unwell, care priorities may not include the undertaking of a medication review	Engage with other clinical pharmacists and prescribers to encourage review
Types of medicines prescribed	Instigating change may be more challenging for specific medication classes, e.g., psychotropic medicines	Present prescribing recommendation along with supporting evidence
Desired patient outcomes	Change in quality of life might not be the most appropriate measure for nursing home residents as they might rate this poorly by virtue of being a nursing home residents	Tailor desired outcome to specific population

Table 26.7 Mediation review for multi-morbid patients [17]

Action	Purpose
Refer to the database of treatment effects	Establish the: Effectiveness of treatments Duration of treatment trials Population included in treatment trials
Consider using a screening tool (e.g., STOPP/START) [21]	Identify: Medication-related safety concerns Medicines the patient might benefit from but is not currently prescribed
Consider changes to medications	Consider any medicines or non-pharmacological treatments that might be started as well as those that might be stopped
Ask patient if treatments are providing benefit or causing harm	If the patient is unsure of the benefit or is experiencing harm from treatment: Discuss reducing or stopping the treatment Plan a review to monitor effects of any changes made and decide whether further changes are needed
Consider the possibility of lower overall benefit of continuing treatments, if limited life expectancy/frailty	Potential to reduce medication burden
Discuss with patients who have limited life expectancy/frailty whether they wish to continue treatments which may offer limited overall benefit	Potential to reduce medication burden
Discuss any changes to treatments that aim to offer prognostic benefit with the person	Take the following patient views into account: The likely benefits and harms from individual treatments Their personal goals, values and priorities
Patients taking bisphosphonates for osteoporosis for at least 3 years should be informed that	There is no consistent evidence of: Further benefit from continuing bisphosphonate for another 3 years Harms from discontinuing bisphosphonates after 3 years treatment

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Chapter 27
Pharmaceutical Care in Asthma and Chronic Obstructive Pulmonary Disease

Maria Cordina

Abstract The pharmaceutical care philosophy and framework fit in perfectly with the needs of patients with asthma and COPD. Ample evidence exists to demonstrate the positive impact that pharmacists have had in these patients when conducting interventions in inhaler technique, reviewing medication, and managing drug-related problems (DRPs). Pharmacists taking the lead in coordinating the patients' medication matters will contribute to overcoming issues arising from fragmented healthcare systems. Caring for patients by personalizing interventions is the key to achieving optimal outcomes.

Keywords Pharmaceutical care · Asthma · COPD · Inhaler medication Medication adherence

27.1 Disease Characteristics

Asthma and Chronic Obstructive Pulmonary Disease (COPD) are two common chronic conditions affecting the lower respiratory tract. Although they tend to present with similar symptoms and are managed using the same types of medication, they are two distinct conditions with varying underlying pathophysiology. This is appropriately illustrated by the definitions provided by the two global bodies dedicated to asthma and COPD, Global Initiative for Asthma, GINA [1] and Global initiative for Chronic Obstructive Lung Disease, GOLD [2].

Asthma is a heterogeneous disease, usually characterized by chronic airway inflammation. It is defined by a history of respiratory symptoms such as wheeze, shortness of breath, chest tightness, and cough that vary over time and in intensity, together with variable expiratory airflow limitation [1].

Chronic obstructive pulmonary disease is a common, preventable, and treatable disease that is characterized by persistent respiratory symptoms and airflow

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limitation that is due to airway and/or alveolar abnormalities usually caused by significant exposure to noxious particles or gases [2].

There are some patients, usually above the age of 40 years, who may present with characteristics of both asthma and COPD. This is *characterized by persistent airflow limitation with several features usually associated with asthma and several features usually associated with COPD. It is therefore identified in clinical practice by the features that it shares with both asthma and COPD* [1, 2].

27.1.1 Asthma

It is estimated that there are approximately 235 million people worldwide who currently suffer from asthma [3]. Asthma is found in all age groups; however, it is the commonest chronic disease in childhood. If inappropriately managed, asthma can lead to death. The World Health Organization (WHO) estimates that in 2015 there were 383 000 deaths due to asthma [3].

The risk factors for the development of asthma are both genetic and environmental, with atopy being a major risk factor [3]. Asthma is characterized by airway inflammation which is due to the release of chemical mediators from inflammatory cells, mucus hypersecretion leading to bronchoconstriction and reversible airflow obstruction [4]. Generally, patients may have extended periods of being well controlled and yet may still experience a severe exacerbation.

- Comorbidities in asthma

Patients who present with asthma may also have comorbid conditions which need to be managed for optimal control of asthma. Allergic rhinitis is the commonest comorbidity in asthma. Lack of treatment or inappropriate treatment of allergic rhinitis in patients with asthma may lead to ineffective control of asthma [5]. The ARIA Guidelines—Allergic Rhinitis in Asthma—provide detailed information for pharmacists' intervention in this patient group [6]. Other atopic conditions are also frequently present and need to be managed accordingly. Obesity makes asthma more difficult to control and weight management needs to be addressed in obese individuals [7]. Mental health problems, particularly anxiety and depression, are a frequent occurrence and if left untreated will have a significant negative impact on asthma control and quality of life [1].

27.1.2 Chronic Obstructive Pulmonary Disease

COPD currently affects over 300 million individuals and it is estimated to become the third leading cause of death by 2030 [8]. Patients with COPD tend to be over 40 years of age, with a history of smoking and/or exposure to noxious substances

which may be environmental and/or occupational. Younger patients who present with COPD usually have predisposing factors which are genetic such as alpha-1-antitrypsin deficiency and abnormal lung development. The most frequently encountered respiratory symptoms of COPD are dyspnea, cough and/or sputum production. The presence of wheeze and chest tightness is variable, while fatigue, weight loss, and anorexia may also be present when the condition becomes severe. COPD is characterized by exacerbations and comorbidities [2, 8].

- Comorbidities in COPD

Patients with COPD tend to be multi-morbidity patients presenting with other chronic conditions which may impact the progression of COPD and need to be managed according to their respective treatment guidelines. The main comorbidities present in COPD patients include cardiovascular diseases (in particular heart failure), osteoporosis, anxiety, depression, metabolic syndrome, diabetes, bronchiectasis, obstructive sleep apnea, and lung cancer [2]. Most of these comorbidities may also be caused by smoking or may be associated with medication used to treat COPD [9].

27.1.3 Treatment Goals

The treatment goals presented here are mainly based on GINA [1] and GOLD [2]. Many countries and possibly regions have their own guidelines which take into account the local healthcare system, the specific needs of the population, local resources, and cultural issues. Using guidelines which have been adapted to local communities makes treatment goals more achievable and is in line with WHO's vision of responding to the needs of the specific communities [10].

- Multidisciplinary management

Asthma and COPD both necessitate multidisciplinary management, with guidelines highlighting the essential contribution of pharmacists in optimizing medicines use and improving health outcomes [1, 2]. Building a working professional relationship with other healthcare professionals takes time, commitment, and various skills. Establishing methods of open effective communication, both formal and informal, will improve the chances of functioning in the best interest of the patient [11]. Pharmacists' ability to take the lead in coordinating matters pertaining to the patient's pharmacotherapeutic management will contribute significantly to fulfilling the treatment goals.

- Knowing your patient and personalizing interventions

When setting treatment goals it is necessary to take into account the patient's own goals and not just the standard expected outcomes of therapy. Taking into consideration the individual patient's beliefs about their condition and attitudes in

relation to their medication is of paramount importance. Understanding the individual patient's needs, including assessing the level of literacy and identifying which intervention works best, will enable the development of a more effective personalized approach. Engaging patients, listening to their concerns, and expectations while communicating effectively will contribute considerably to achieving the desired treatment outcomes [12].

- Attaining and maintaining the treatment goals

Attaining and maintaining both the long-term and short-term goals of treatment, which become apparent over the course of patient care, necessitate routine and systematic monitoring and assessment [13]. Appropriate documentation is essential to review patients' progress toward attaining and maintaining treatment goals.

27.1.4 Treatment Goals for Asthma

While the management of asthma is dealt with separately in terms of age group, the treatment goals are the same. The ultimate aim of asthma treatment is complete control, which is defined as no day or night time symptoms, no need for reliever medication, no limitation on activities and normal lung function, this being achieved with ideally no or negligible adverse effects from medication [1, 13].

- Achieving good symptom control

The symptoms of wheeze, shortness of breath, chest tightness, and cough are very disturbing and limiting for patients. Patients may experience any one, all or any combination of the above with varying intensity. They may be experienced at different times throughout the day or, if less well controlled, during the night. With appropriate management, patients are able to lead a relatively symptom-free life. Patients should not accept their symptoms or allow them to pose limitations on their lifestyle.

- Maintaining normal levels of activity

The first step is to identify what the individual patient's "normal" is and aim at that level. For children, attending school, engaging in games with friends, activities and sports without feeling different from their peers may be the desired normal. For young people, normal could be going to work and having a social life without needing to explain their symptoms. Other people may want to conduct normal daily activities such as shopping, gardening or simply walking, and climbing stairs without taking frequent breaks. Engaging in sports and physical activity is encouraged and having asthma should not be considered a barrier to being fully active.

- Minimizing risk of exacerbations

Patients may experience an exacerbation whether they are well controlled or not. However, the less controlled they are, the higher the probability of experiencing an exacerbation.

- Limiting side effects of treatment

The aim is to achieve optimal control and quality of life using the least number of medicines, at the lowest possible dose with a minimum of adverse effects. Adverse effects of medication, may, at times, go unnoticed by the patients themselves or they may be prepared to accept them and not bring them to the attention of the practitioner. Alternatively, they may unilaterally decide to modify their prescribed therapy or stop their therapy altogether.

27.1.5 Treatment Goals for Stable COPD

The treatment goals for stable COPD may broadly be seen as twofold: symptom reduction and risk reduction [2]. The aim is to achieve these goals with a minimum of adverse effects from the medication being used to treat both COPD and the comorbidities present [8].

- Symptom reduction

As the condition progresses, the characteristic symptoms of COPD increase in frequency and intensity, imposing significant limitations on exercise and daily activities as well as having a general negative impact on health status. Patients tend to accept their symptoms and adapt their lifestyle to their increasingly limiting symptoms, which may lead to underestimating the severity of their condition. The aim is, therefore, to relieve symptoms, improve exercise tolerance, and improve overall health status.

- Risk reduction

The higher the exposure to risk factors, such as tobacco smoke, indoor and outdoor air pollution, and occupational exposure, the higher the probability of disease progression, exacerbations, and mortality. The treatment, therefore, aims to prevent the progression of COPD, to prevent and treat exacerbations, to prevent and treat complications, and to reduce mortality.

27.2 Management of the Diseases

The management of asthma and COPD requires both a pharmacological and non-pharmacological approach. Generally, the management entails pharmacotherapy, education including supported self-management, appropriate use of inhalation devices and monitoring.

Medication delivered by inhaled therapy is the hallmark of the pharmacological management of these two conditions. Both conditions necessitate the selection of appropriate drugs and delivery devices which have a crucial role in achieving the successful outcomes of therapy. While there is a significant overlap in the medication used to manage asthma and COPD, it is essential for the delivery of optimal pharmaceutical care to be aware of the appropriate diagnosis since the medication is used differently in different conditions. Education, coupled by appropriate interventions to support behavior change, is an essential component of management. Education needs to impart to patients and their caregivers the necessary skills to cope with their condition. An educational intervention has a better chance of having an impact if commenced after a professional relationship and partnership with the patient has been established. It is essential to address issues that are important and relevant to the patient, taking into account any misconceptions, fears, concerns and should be culturally sensitive. The intervention needs to be delivered in a manner and a language which can be understood by the patient. Educational interventions target the patient as well as the family and carergivers. Education is an ongoing process and key messages should be reinforced at every opportunity [14].

Monitoring of various parameters is an integral part of management to be conducted by both healthcare professionals as well as the patients themselves and, when appropriate, their caregivers. Patients need to be supported and empowered to take increased responsibility and actively participate in the management of their condition.

Recent systematic reviews have clearly demonstrated that pharmacists' educational and monitoring interventions delivered as structured programs are highly effective in achieving the desired positive outcomes in asthma [15, 16].

With the exception of improvement in inhaler technique, it is rather more challenging to find evidence demonstrating pharmacists' positive interventions when delivering a structured program for COPD patients. There are abundant reasons for this, some of which are the following: since it is a highly complex condition, patients require complex interventions which include the monitoring and control of comorbid conditions as well as medications for those conditions. Education and monitoring of COPD in isolation is unlikely to yield the desired results. COPD is a progressive disease; therefore, even if there is improvement in various parameters, this may be offset by the nature of the disease. The study designs of publications related to pharmacists' interventions in COPD are also problematic, as very often they include both asthma and COPD patients and have the same outcomes. The two diseases should be studied separately and studies designed accordingly. There is evidence to demonstrate that pharmacists' interventions in COPD had a positive impact on knowledge, adherence to therapy, medicines beliefs, and drug-related problems in addition to inhaler technique [17–19]. A systematic review studying educational programs in COPD management argued that while most of the interventions were carried out by nurses, physicians, and physiotherapists, including pharmacists could lead to better management and outcomes [20].

27.2.1 Inhalation Devices

There is robust evidence demonstrating the positive outcomes achieved following pharmacists' interventions on inhaler use in asthma and COPD [21]. Prior to instructing the patient on the use of an inhaler, it is essential for pharmacists to have mastered the use of the devices available and have the resources to use in teaching the appropriate technique.

There are a plethora of different types of inhalation devices available. These include pressurized metered dose inhalers (pMDIs), [8, 13] used with or without spacers, breathe-actuated pMDIs, soft mist inhalers, single-dose and multidose dry powder inhalers, and nebulizers. Inhalation devices are complex, with their design and construction, taking into account the need to generate a respirable aerosol and the patients' ability to inhale the aerosol into the lungs. The projected therapeutic effect of the drug being delivered by an inhaler is based on the assumption that the inhaler will be used as instructed. Incorrect use of the device will lead to a decreased therapeutic effect and loss of control of the disease and the possibility of increased adverse effects as in the case of inhaled corticosteroids. Pharmacists are the healthcare professionals whose training best equips them to fully appreciate the basic science behind the device as a delivery system, the pharmacological effect of the drug delivered and the practical needs of the patient.

- Assessing suitability

Assessing the suitability of the inhaler device prescribed is important both in the case of a patient being prescribed a specific type of inhaler for the first time as well as for a patient who has been using the inhaler for some time. Various factors need to be taken into account when assessing suitability, such as the patient's inspiratory ability and the patient's physical and mental ability to use the device [22]. The choice of device is at times closely linked to the drug selected and this can be a limiting factor for selecting the most appropriate device for the patient. Another issue is accessibility. Prescribing devices that are not affordable to the patient leads to nonadherence. Cost and availability of devices vary in different countries. The choice of inhaler should take into account the individual patient's needs, circumstances, and preferences [23].

- Instructing and assessing technique

The importance of teaching patients how to use their inhalers is of paramount importance. Based on the assessment of the patients' abilities, an appropriate inhaler technique education intervention can be drawn up. This may vary from one individual to another, and the more the intervention is tailored to the individual, the better the chances of success. Using placebo inhalers to teach the technique has been found to be effective. In the absence of placebos, the patient's own inhalers may be used. Verbal, audiovisual [1] and written instructions are all useful methods. Using the "teach back" method will enable the pharmacist to assess the effectiveness of the intervention. More instructions may be needed at that point. Depending

on the patient, the pharmacist must decide whether to continue with the intervention or set a follow-up appointment. Pharmacists need to be aware of common errors which patients make when using inhalers and should be well equipped to identify and intervene appropriately [24]. It may be evident from the start that the patient is unable to use the prescribed inhaler, such as when there is limited physical dexterity, or is unable to comprehend instructions, etc. Communicating the problem/s to the prescriber and suggesting another type of inhaler/therapy would be the preferable approach.

- Reviewing technique

Reviewing the patient's technique on a regular basis, on average every 4–6 weeks, is also important as the ability to use the inhaler properly can diminish over time [1]. Regular reinforcement of inhaler technique is essential for the patient to maintain the ability to use the device properly. Checking the steps of use for the specific type of inhaler against a standard list of steps is practical and relatively easy to conduct [25]. Any steps which the patient has carried out incorrectly can easily be identified, corrected and the technique once again reinforced.

- Simplification of therapy

Some patients present with a range of different types of inhaler devices. The use of several different types of devices makes it confusing and more difficult for the patient to master the various steps required for the diverse devices prescribed. Recommendations to the prescriber to, as much as possible, select the same type of device will enhance the probability of appropriate inhaler technique. Maintaining the number of devices to a minimum should also be taken into account. It is advisable for a medication review to include an assessment for the need of the number of devices prescribed. Whenever indicated, recommendations for a decrease in the number of devices ought to be made. Simplification of therapy will make it less confusing for patients, contribute to a better inhaler technique, and adherence to therapy [22].

- Spacers

Spacer devices are used in combination with pMDI, especially in children and in those individuals who are unable to use a pMDI appropriately. Spacers selected should be fully compatible with the pMDI prescribed. Patients need to be taught how to use this device and how to clean and maintain the device as per manufacturer's instructions [13].

- Oxygen cylinders

Patients on domiciliary oxygen using oxygen cylinders and concentrators need instruction and counseling on their appropriate use and care.

27.2.2 Pharmacological Management of Asthma Based on Symptom Control

Inhaled corticosteroids (ICS) are the cornerstone of therapy in asthma and are considered to be first-line therapy. They are usually referred to as controllers or preventers. In most patients, treating with regular low-dose ICS will lead to a reduction in asthma symptoms, increase in lung function, improvement in quality of life, and a reduction in risk of exacerbations, hospitalizations, and death. It is only in patients who experience very occasional day time asthma symptoms that ICS are not currently recommended. The dose of ICS is increased or decreased and used in combination with other medications depending on the patient's clinical need [1, 13].

Inhaled Beta-2-agonists may be short-acting (SABAs) which are relievers or long-acting (LABAs) which are classified as preventer/controllers. SABAs are recommended for "as required use" in all asthma patients to relieve symptoms. In patients who only experience symptoms infrequently, such as occasional wheeze lasting for a short period of time, they are currently the only recommended therapy. It is currently recommended that LABAs are added on to regular ICS when the desired outcomes are not achieved with low-dose ICS alone [1].

Oral leukotriene receptor antagonists (LTRA) are also classified as preventers/controllers. They may be an alternative in patients unwilling or unable to use ICS; however, they are less effective than inhaled corticosteroids. They may also be used in combination with ICS/LABAs to achieve and maintain control [1, 13].

Other add-on therapy options include: Tiotropium, which is a long-acting muscarinic antagonist (LAMA) delivered as a soft mist inhaler, is used in adult patients with a history of exacerbations; however, the evidence supporting this use is not robust [1, 13]. Oral theophylline is sometimes used in adults although not recommended for regular use. The chromes, inhaled nedocromil sodium and sodium cromoglycate, are still available; however, they have a rather low efficacy. In patients who have severe allergic uncontrolled asthma, anti-immunoglobulin E (anti-IgE), omalizumab, is an option [1, 13], while in severe uncontrolled eosinophilic asthma, subcutaneous mepolizumab, and intravenous reslizumab are available in some countries [1]. Low-dose long-term oral steroids may be used in adults with severe asthma, who have failed to achieve control on inhaled controller/preventer therapy [1, 13].

- Common DRPs in patients with asthma

Table 27.1 uses the PCNE DRP classification [26] to illustrate some of the common DRPs that are manifest in patients with asthma.

- Education, supported self-management and monitoring in asthma

Patient education is essential to empower patients and support them to manage their condition. Various resources are available which can be used in educational interventions [27–29]. Providing a brief overview of asthma, its underlying causes,

Table 27.1 Commonly encountered DRPs in asthma patients

Problem	Cause	Comment
Treatment effectiveness		Lack of effective treatment leads to loss of control, with increased symptoms and potential exacerbations. This poses an increased burden on the patient and the healthcare system
	Drug selection	Prescription of a SABA alone, when inhaled corticosteroid is necessary Prescription of a LABA as monotherapy, when it should be used as add-on therapy Practitioners may be reluctant to prescribe oral corticosteroids such as prednisone/prednisolone, even in severe cases where they are necessary Alternatively they may over use oral prednisone/prednisolone
	Drug form	At times, the type of inhaler device selected may not be suitable for the individual patient
	Dose selection	The dose of ICS prescribed may not be commensurate with asthma severity (status of control) or the combination of inhaled preparations prescribed are not in doses sufficient to maintain control Alternatively, current dosing too high, therapy may be stepped down, i.e., asthma is not managed at the appropriate guideline step
	Dispensing	Patient has not been given sufficient instruction on how to use the device
	Drug use	Inadequate inhaler technique and inappropriate use of inhaler
	Patient-related causes	Lack of adherence to prescribed regimen, especially ICS Possible reasons: Non-intentional nonadherence: – Forgetfulness – Regimen does not fit lifestyle – Prescribing too many different types of inhalers – Polypharmacy – Lack of fully appreciating the need to take medication – Barrier to access, e.g., financial; inability to have prescription filled – Mood disorders and mental health issues Intentional nonadherence: – Concerns about medication outweigh necessity to take medication – Fear of steroids (in general) – Real or perceived adverse effects – Perception that prescribed medication is ineffective – Belief that does not need prescribed medication

(continued)

Table 27.1 (continued)

Problem	Cause	Comment
Treatment safety		
	Adverse effects from drug therapy	ICS can lead to several adverse effects especially in patients on high doses over a prolonged period of time Specific adverse effects may be more pronounced in children or in other specific patient groups Often encountered: Oral candidiasis, dysphonia, hoarseness, easy bruising Oral corticosteroids: encountered with long-term use; numerous, serious, e.g., increase in blood pressure, osteoporosis, diabetes, hyperlipidemia, cataracts The most commonly encountered adverse effects of inhaled beta-2- agonists are palpitations and tachycardia usually associated with overuse of inhaler
	Drug disease interactions	Aspirin or any other NSAID may precipitate an exacerbation in asthma patients who are aspirin sensitive Beta-2-antagonists may induce bronchospasm in asthma

manifestation/symptoms, risk factors, what to expect from the disease and how it may affect lifestyle will help patients better understand their condition. Addressing triggering factors and appropriate avoidance strategies as well as delving into patient-specific modifiable risk factors could contribute to maintaining better control. Enabling patients to identify the deterioration in condition/loss of control, which may lead to an exacerbation and how to deal with the situation, including how to access help, is an essential part of the educational intervention. Educating patients on their different types of medication, preventer/controllers, relievers, how they work, why they are needed, when to take them and how to appropriately use the various inhalers is imperative. Depending on the individual patient, advising on smoking cessation and avoidance of tobacco smoke and weight loss in cases of obesity is also a necessary part of the intervention.

Individualized action plans where patients adjust their medication requirements depending on their level of symptom control and peak expiratory flow rate have been shown to be highly effective [1]. Empowering patients to take increased responsibility in the management of their asthma leads to positive outcomes [30]. Personalized self-management plans are drawn up by the care team and tailored to the needs of the individual taking into consideration the ability and the desire to follow the plan, as well as level of literacy. Pharmacists' involvement in drawing up the plan, monitoring and intervening to enable the patient to attain and maintain the treatment goals is an integral part of the delivery of care. Additionally, facilitating a plan for those individuals who require one is another essential intervention.

Monitoring of various parameters in patients with asthma is essential to maintain control and have a good quality of life. The British Thoracic Society clearly highlights the parameters that need to be monitored, all of which pharmacists can contribute to through the delivery of pharmaceutical care [13]. Reviewing the patient in a structured and planned manner leads to better outcomes than using a casual unplanned approached [31].

Symptoms can be monitored by pharmacists in a structured manner using a variety of tools available such as the 30 Second Asthma Test [32] and the widely used Asthma Control Test – ACT [33]. These tools are easy to use and take up very little time.

Lung function can be monitored using a peak flow meter. Patients can use a peak flow meter to monitor their lung function and these can be reviewed by the pharmacist. Monitoring peak flow is mostly useful in those patients with severe asthma [13].

Asthma exacerbations, the use of rescue courses of oral glucocorticoids, as well as the number of days taken away from work or school also need to be monitored as these give an indication of the degree of control of the patient's asthma [13].

Inhaler technique can be monitored as explained earlier. Standardized asthma checklists like those produced by the National Council of Australia are useful as they offer a structured categorical approach to assessing inhaler technique [34].

As indicated in Chap. 5, adherence to therapy is an important parameter that needs to be monitored, certainly in asthma. It is well known that adherence is low in patients with chronic disease. It is indeed a challenge to accurately assess adherence to preventer therapy. Some ways include checking how many prescriptions have been filled or asking patients how many times they have forgotten to take their medication over a short period of time [1, 13]. While none of these approaches provide accurate information, they do give an indication of the degree of adherence by the patient.

Short-acting bronchodilator use monitoring provides information as to whether patients are overusing their reliever inhaler, which is another indicator of inappropriate management and loss of control. Using more than one short-acting bronchodilator per month is a clear indicator of poor asthma control.

Pharmacists should monitor patients for any DRPs including the emergence of adverse effects of their current therapy. This will allow for timely interventions.

27.2.3 Management of Chronic Obstructive Pulmonary Disease

- Pharmacological management of COPD

Pharmacological management of COPD has been shown to positively impact a number of parameters including a reduction in symptoms, a reduction in frequency and severity of exacerbations, as well as an improvement in health status and

exercise tolerance. Each treatment regimen in COPD needs to be individualized [2]. However, none of the therapy used to date has managed to have an effect on the long-term decline in lung function [8].

Bronchodilators: In COPD, the mainstay of therapy is bronchodilators which are primarily used to prevent or reduce symptoms. SABAs and LABAs are most commonly used, although the use of SABA on a regular basis is not a preferred option. The use of LABAs has a positive effect on lung function, dyspnea, health status, exacerbations, and hospitalization rate. LAMAs have been found to improve health status, pulmonary rehabilitation and lead to a reduction of exacerbations and hospitalizations. Combining Beta-2-agonists and antimuscarinics will usually have an enhanced therapeutic effect without leading to an increase in adverse effects. Various inhalers containing a combination of bronchodilators are available. Methylxanthines, such as theophylline, are also used in COPD; however, the optimal manner in which they should be used is still open to debate [2, 35].

Anti-inflammatory agents: The use of ICS in COPD is still unclear and their use needs to be balanced with the risks involved. While the use as monotherapy is not recommended, there are some advantages in using them in combination with LABAs and LAMAs. Triple therapy of ICS/LAMA/LABA has been found to improve lung function, symptoms, health status, and exacerbations when compared to either LAMA alone or the ICS/LABA combination [2, 35].

Phosphodiesterase 4 inhibitors reduce exacerbations in those who have chronic bronchitis, severe to very severe COPD, and a history of exacerbations. They do not appear to have much effect on symptoms and quality of life [2, 35]. The use of the macrolides azithromycin and erythromycin is useful in reducing exacerbations over a one-year period. The regular use of mucolytic and antioxidant agents may be useful to reduce exacerbations and improve health status in COPD patients not on ICS [2].

Patients with chronic respiratory failure who present with severe resting hypoxemia benefit from long-term administration of oxygen (>15 h per day) by increasing survival [2].

Important Safety Considerations: While the management of asthma and COPD involves the use of inhaled corticosteroids and bronchodilators, their safety recommendations are opposite. In the case of asthma, LABAs and LAMAs should never be used without ICS; in COPD, treatment is initiated with LABAs and/or LAMAs without ICS [2].

- Drug-related problems in COPD

COPD is a multicomponent disease which affects various organs. When treating and managing COPD, one does not just focus on the lungs but the entire system. Patients with COPD tend to use many medicines to treat their various comorbidities. The DRPs which they experience are multiple and do not just relate to respiratory medicines. Therefore, a review needs to take into account all these issues. For practical reasons, Table 27.2 addresses mainly DRPs related to respiratory drugs; however, this only presents a partial picture and is far from comprehensive.

Table 27.2 Commonly encountered DRPs in COPD patients

Problem	Cause	Comment
Treatment effectiveness		The most challenging issue with treatment effectiveness in COPD is if COPD has been appropriately diagnosed using the correct diagnostic tools, i.e., spirometry
	Drug selection	Drug selection more appropriate to treat asthma rather than COPD Inappropriate drug selection to treat comorbidities
	Drug form	At times, the type of inhaler device selected may not be suitable for the individual patient such as limited physical dexterity and possibly limited cognitive ability
	Dose selection	Inadequate dosing of medication, possibly due to inadequate frequency of review to step up dosing in line with decrease in lung function Inadequate dosing for drugs to treat comorbidities
	Dispensing	Patients and/or caregivers have not been given sufficient instruction on how to use the device Inadequate counseling provided as how to manage all medications prescribed
	Drug use	Inadequate inhaler technique and inappropriate use of inhaler/s Inadequate drug use of medicines to treat comorbidities
	Patient-related causes	Lack of adherence to prescribed regimen Possible reasons: Non-intentional nonadherence: – Polypharmacy – Forgetfulness – Regimen does not fit lifestyle – Prescribing of too many different types of inhalers – Lack of fully appreciating the need to take medication – Barrier to access, e.g., financial; inability to have prescription filled – Physical and mental health issues – Inadequate social support Intentional nonadherence: – Concerns about medication outweigh necessity to take medication – Real or perceived adverse effects
Treatment safety		This is a highly significant issue in COPD patients
	Adverse effects from drug therapy	These are usually multiple and result in increased morbidity. They arise from medicines used both to treat COPD and to treat comorbidities

- Education, supported self–management and monitoring in COPD

Educational interventions in COPD require addressing by a multidisciplinary team which may include, among others, physicians, nurses, pharmacists, physiotherapists, occupational therapists, and psychologists [20]. The educational intervention, therefore, requires a structured and coordinated approach. Pharmacists' primary contribution is in engaging patients in smoking cessation programs and addressing exposures to other irritants and risk factors. Educating patients about their condition, its progression, early recognition of exacerbations, and how to handle the situation is an essential part of the educational strategy. Pharmacists can council patients about their different types of medication, how they function, the rationale behind their use, and what to expect from their therapy, including the recognition of possible adverse effects together with instructing on inhaler technique as described earlier and provide advice on appropriate vaccinations [2, 20].

Supporting patients to develop self-management skills has been found to positively influence outcomes in COPD [2]. The main skills that pharmacists can address include helping patients to: identify and control triggers and control symptoms; handle an acute episode or an emergency; navigate the healthcare system and services and making appropriate use of the various healthcare professionals. The skills related to medicine taking including how to use their inhalers always need reinforcing. In addition to these skills, there are various other skills such as dietary interventions, physical, and psychological techniques which are usually addressed by other members of the team. The best outcomes are achieved when these skills are part of an action plan drawn up for the individual patient [20, 36].

Monitoring for the appropriate use of therapy, adherence to therapy and for the emergence of DRPs especially ADRs is vital in the management of COPD. Symptom monitoring could be conducted using various tools which are available such as the COPD Assessment Test (CAT™) [37]. These tools only provide an indication to the pharmacist and are by no means a comprehensive assessment of COPD. Monitoring of comorbidities according to the relevant guidelines is important as they significantly influence mortality and hospitalization [2].

27.3 Delivery of Pharmaceutical Care to Asthma and COPD Patients

- Developing patient-centered pharmaceutical care for patients with asthma

The philosophy and care model of pharmaceutical care fits perfectly with the needs and management model for asthma. Delivery of pharmaceutical care to asthma patients has resulted in positive therapeutic and patient outcomes coupled with high patient satisfaction [38]. Fig. 27.1 provides an overview of the pharmaceutical care cycle for asthma.

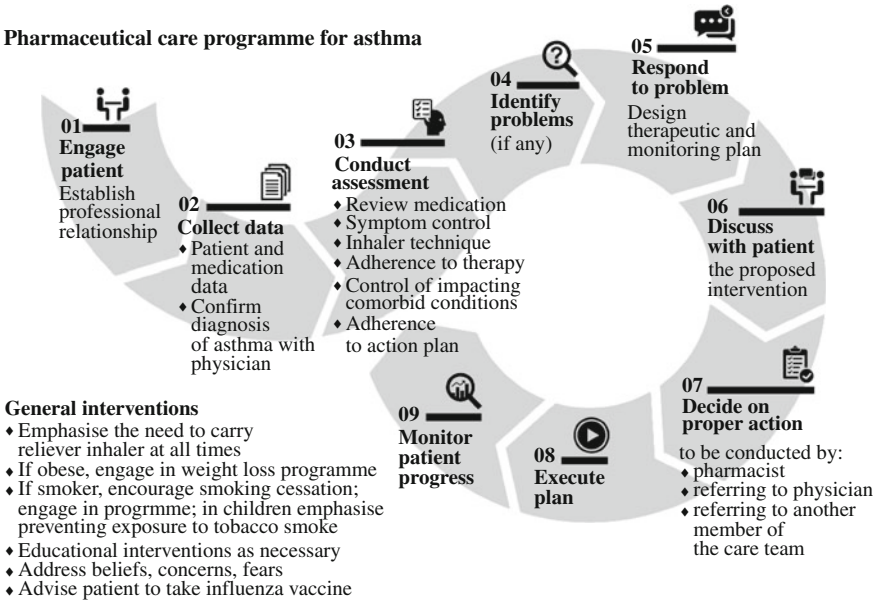

Fig. 27.1 Pharmaceutical care program for asthma

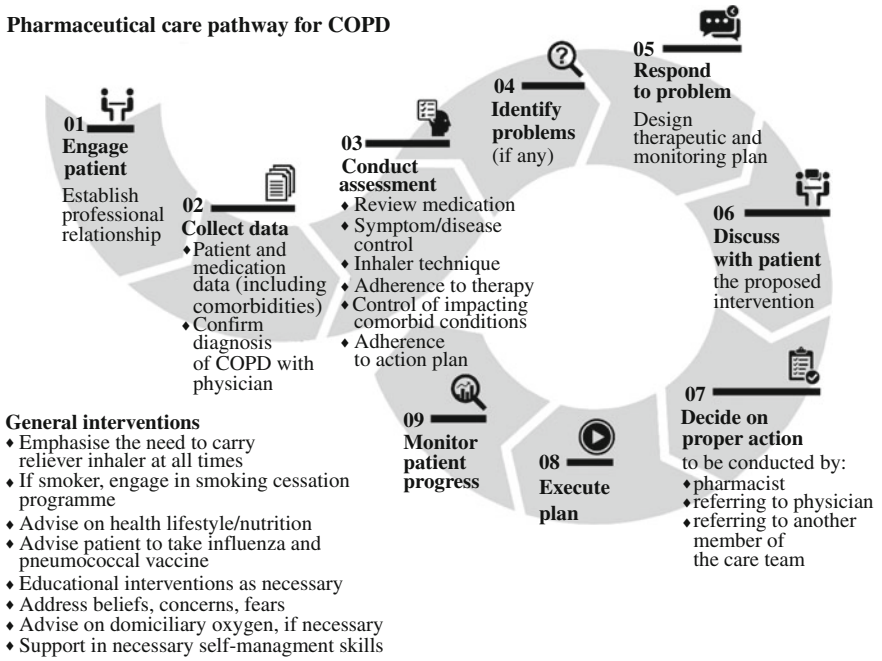

Fig. 27.2 Pharmaceutical care pathway for COPD

- Delivering patient-centered pharmaceutical care for patients with COPD

The increased knowledge gained about COPD over the past years has presented a better opportunity for the delivery of pharmaceutical care to patients with COPD. Currently, the recommendation is for a highly flexible programme dependent on the stage of the condition and the needs of the individual. Figure 27.2 provides an overview of the pharmaceutical care cycle for COPD.

Case Scenario

Ms FC is 30-year-old overweight female with a hectic lifestyle who usually collects her asthma prescriptions from your community pharmacy. One early Autumn afternoon, she presents at your pharmacy to collect her elderly mother's prescription. You notice that she has an upper respiratory tract infection, a chesty cough and you also detect a slight wheeze. You ask her if she is managing her cold and symptoms. She replies that she does not want to take any medication because she is trying to get pregnant. In fact, she has also stopped taking her asthma medication and felt fine during the summer months. She tries to put up with her symptoms as much as possible and takes a few puffs of her reliever—salbutamol, as a last resort; however, now it is getting to be very difficult. She wants her body to be "free from steroids" when she gets pregnant. On checking her profile, you note that her current prescription is for a combined dry power inhaler of Formoterol 6 micrograms/dose and Budesonide 200 micrograms/dose, to be taken as 2 puffs daily (1 puff every 12 h), in addition to salbutamol as a metered dose inhaler, to be taken as required. The last time that she collected her prescription was over 3 months ago.

Pharmaceutical care interventions: There are a number of important issues that need to be addressed by the pharmacist.

Initial assessment and identification of problems: Ms FC is clearly misinformed about her asthma medication use before and during pregnancy. This has led to nonadherence to therapy and loss of asthma control. Her cold is about to precipitate an acute attack.

Therapeutic Plan

Immediate action

1. Counseling

Counsel Ms FC on the importance of taking her preventer medication both when preparing for pregnancy and during pregnancy;

The importance of asthma being well controlled during pregnancy for both mother and fetus;

Highlight benefits of asthma-inhaled medication use as opposed to risks of lack of use;

Encourage an open discussion regarding this issue;

Provide information, possibly also reliable asthma education websites.

2. Assessment of symptom control using a tool such as ACT.

3. Insist on patient recommencing her preventer therapy immediately.

4. Refer to physician for immediate (same day) review to prevent further loss of control and precipitation of attack.

5. Advise to keep reliever with her at all times.

The following day Ms FC returns from her doctor with a prescription for oral prednisolone 40 mg daily for 5 days, Formoterol 6 micrograms/dose and Budesonide 200 micrograms/dose, to be taken as 2 puffs twice daily, in addition to salbutamol as a metered dose inhaler, to be taken as required. She is also prescribed paracetamol as required.

1. Update Ms FC's profile including necessary documentation of issues encountered.

2. Dispense medication, advice on dosage regimen of preventer (highlighting changes from previous dose), advice on oral hygiene following preventer inhaler use and advice on administration of prednisolone.

3. Assess inhaler technique for both the dry powder inhaler and metered dose inhaler against standardized checklist. Conduct any necessary intervention to ensure appropriate inhaler technique.

4. Reinforce counseling regarding the importance of asthma medication use and pregnancy. Encourage patient interaction regarding this issue.

5. Enquire about any other risk factors for asthma and advice/discuss accordingly.

6. Advice on upper respiratory tract infection management and use of paracetamol.

7. Set a follow-up appointment with Ms FC in about 3 weeks. Encourage her to contact you earlier if she needs to.

Follow-up

Ms FC returns for her follow-up appointment. Her condition has improved significantly.

1. Initiate a discussion about medication. Attempt to determine *if* she is taking her asthma medication and *how* she is taking it.

2. Open discussion about medication during pregnancy and importance of asthma control during pregnancy and try to ascertain if she is convinced of the need to adhere to medication.

3. Assess of symptom control.

4. Encourage her to take the influenza vaccine.

5. Recommend folic acid supplementation.

6. Discuss and propose the adoption of a healthy lifestyle, including moderate exercise and a healthy diet.

7. Encourage her to drop by or contact you if she needs to do so before picking up her next prescription.

Monitoring

Two months later, Ms FC returns to collect her prescription for her asthma medication. She looks well and happy. She informs you that three weeks ago she found out that she is pregnant. She is happily following your advice. She is taking her preventer asthma medication regularly, with hardly any need to use her reliever. She is feeling even better than before. She is doing her best to stay healthy, taking folic acid, eating healthy food and incorporating walking in her daily routine. Her pregnancy is being monitored by her doctor and midwife.

1. Assess asthma symptom control
2. Assess inhaler technique
3. Advice as necessary
4. Encourage her to contact you whenever is necessary.

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Chapter 28
Pharmaceutical Care in Type-2 Diabetes

Ines Krass and Kreshnik Hoti

Abstract There are many opportunities for pharmacists to make valuable contributions to the care of patients with diabetes. The application of a systematic pharmaceutical care process as outlined in this chapter will facilitate identification of a range of DRPs which may be preventing the patient from deriving the maximum benefit to be gained from their pharmacotherapy. Pharmacists should appreciate the needs of their patients and establish systems and infrastructure to permit the provision and documentation of effective pharmaceutical care.

Keywords Pharmaceutical care · Diabetes · Type 2 Diabetes · Lifestyle Medication adherence

28.1 Disease Definitions Around Diabetes

Diabetes mellitus is a complex heterogeneous metabolic disorder characterized by chronic hyperglycemia. The clinical presentation and disease progression are related to the disease phenotype and depend on the degree of dysfunction of insulin producing pancreatic beta cells and/or the responsiveness of target tissues, such as liver muscle and fat, to the action of insulin [1]. The current classification of diabetes distinguishes four categories [2].

1. Type 1 diabetes (T1DM) is due to autoimmune destruction of beta cells leading to absolute deficiency in insulin;
2. Type 2 diabetes (T2DM); the most common form of diabetes mellitus, characterized by insulin resistance and progressive loss of insulin secretion.

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3. Gestational diabetes mellitus (GDM)—carbohydrate intolerance resulting in hyperglycemia of variable severity, with onset, or first recognition, during pregnancy.
4. Diabetes due to other causes, e.g., mature onset diabetes of the young (MODY); other endocrine diseases, pancreatic diseases (e.g., cystic fibrosis), or iatrogenic causes, e.g., corticosteroid therapy.

Current global estimates suggest that approximately 415 million adults have diabetes and that this will increase to 642 million by 2040. While the proportion of the population with T2DM is increasing in most countries, three quarters of these live in low- and middle-income countries [3].

28.1.1 Diabetes Complications

Chronic uncontrolled hyperglycemia causes damage to blood vessels and nerves which leads to both microvascular and macrovascular long-term complications. Microvascular complications include retinopathy, nephropathy, and neuropathy. Diabetic retinopathy consists of vascular leakage and ischemia in the retina and is the leading cause of new cases of blindness in adults aged 20–74 years. Diabetic nephropathy is the most common cause of end-stage renal disease in developed countries and also an independent risk factor for cardiovascular morbidity and mortality. Neuropathy is a highly variable complication initially affecting the peripheral nerves, and is a major cause of morbidity. It has several clinical complications, including foot ulceration, amputations, gangrene, sexual dysfunction, and even cardiac arrhythmia leading to sudden death [4].

Macrovascular complications related to diabetes, including coronary heart disease, stroke, and peripheral vascular disease, account for more than 50% of the mortality in people with T2DM. A person with diabetes has a threefold greater risk of a myocardial infarction compared to someone without diabetes [4]. The atheroma and myocardial damage are likely to occur at least in part as consequences of hypertension, altered vascular permeability, and ischemia. However, long-term glycemic control remains the best predictor of cardiovascular disease (CVD) risk in people with both T1DM and T2DM. Other complications include depression, sexual dysfunction, and dementia [4].

Therefore, a multifactorial approach is essential in the treatment of people with diabetes. Since T2DM account for the majority of diabetes cases managed in primary care and community pharmacy practice, this chapter will focus primarily on the pharmaceutical care of T2DM.

28.1.2 Goals of Therapy

A strong body of evidence supports the benefit of control of glycemia, blood pressure, and lipids in the prevention of microvascular complications and

macrovascular complications in patients with diabetes [5]. Optimal glycemic targets are especially important early in the course of T2DM as this will confer a "legacy effect" in the longer term protection from complications [5].

There are international guidelines for the management of diabetes. The current International Diabetes Federation (IDF) guidelines, recommendations [3] valid for T2DM, are as follows.

Glucose control

The general target for glucose control in T2DM should be an HbA1c less than 7% (53 mmol/mol). Lower HbA1c targets are desirable or at least should be considered, as long as hypoglycemia and weight gain can be avoided using appropriate treatments.

An HbA1c target between 7.5 and 8% (58–64 mmol/mol) may be more appropriate in patients using multiple medications including glucose-lowering drugs (GLDs) where predicted survival is short.

Glucose monitoring is mandatory for patients using insulin. Glucose monitoring is useful during treatment adjustment, acute illness, or as an education tool for self-care.

Blood pressure

Patients with T2DM and hypertension should be treated to a diastolic blood pressure (DBP) target of 80 mmHg and an systolic blood pressure (SBP) target of 130–140 mmHg. The lower target for younger people or when additional cardiovascular risk factors or microvascular disease are present. Angiotensin-converting enzyme inhibitors (ACEI) or angiotensin receptor blockers (ARB) are the preferred antihypertensive medication due to their reno-protective effects.

Lipids

All people with T2DM and without established CVD who are ≥ 40 years old and have LDL cholesterol >100 mg/dL (2.6 mmol/L), should start treatment with a statin (primary prevention). In people with T2DM who have established cardiovascular disease—the LDL cholesterol target is <70 mg/dL (1.8 mmol/L) (Secondary prevention).

28.2 Management of T1DM

All people with T1DM require insulin replacement therapy either with multiple daily injections (MDI) including basal and bolus inulin or insulin delivered by an insulin pump. The preferred insulin regimen for people with T1DM is the basal–bolus regimen which involves four/five injections of insulin per day; three (or more) injections of rapid-acting insulin to cover mealtime needs with one or two injections of basal insulin covering insulin requirements between meals. This regimen mimics

the normal physiological pattern of insulin release. Insulin pumps continuously deliver a fast or short-acting insulin into the body according to the patient's needs. The pump is preprogrammed to give small background doses of insulin continuously throughout the day and night depending on the patient's needs. Every time a patient eats carbohydrate, they have to activate the pump to give a burst of insulin. The amount of carbohydrate that is eaten for a meal or a snack needs to be fairly accurately estimated in grams or exchanges. It is critical to match insulin dosing with carbohydrate intake to prevent hyper or hypoglycemia [2]. Table 28.1 includes types of insulins.

The most common acute complication of T1DM is hypoglycemia which typically occurs when a patient's blood glucose level falls below 4 mmol/L, at which point homeostatic physiological counter-regulatory responses occur. Hypoglycemia is one of the most important limiting factors to the achievement of near-normoglycemia in the management of T1DM and is one of the most feared complications. Factors that contribute to the unpredictability of diabetes control and the likelihood of hypoglycemia include:

- the uncertainty caused by differences in insulin absorption rates;
- the variable effects of exercise;
- the variability of food absorption;
- the variable effectiveness of different foods to raise blood glucose level;
- the uncertain effects of physical and psychological stress.

Most people with T1DM are under the care of diabetes care team including an endocrinologist, diabetes nurse or diabetes educator, and a dietitian. In some places, a pharmacist will be part of this team where they can contribute to optimizing medication therapy.

28.3 Management of T2DM

Management involves lifestyle management, including weight management, nutrition, and physical activity and pharmacotherapy. Figure 28.1 gives an overview of the management of Diabetes.

28.3.1 Lifestyle Modification

Following diagnosis of T2DM, the initial management usually commences with lifestyle modification focusing on both carbohydrate and energy restriction and increase in physical activity. Modest persistent weight loss, defined as sustained reduction of 5% of initial body weight, can delay the need for initiation of pharmacotherapy. However, to achieve optimal outcomes in control of glycemia, blood

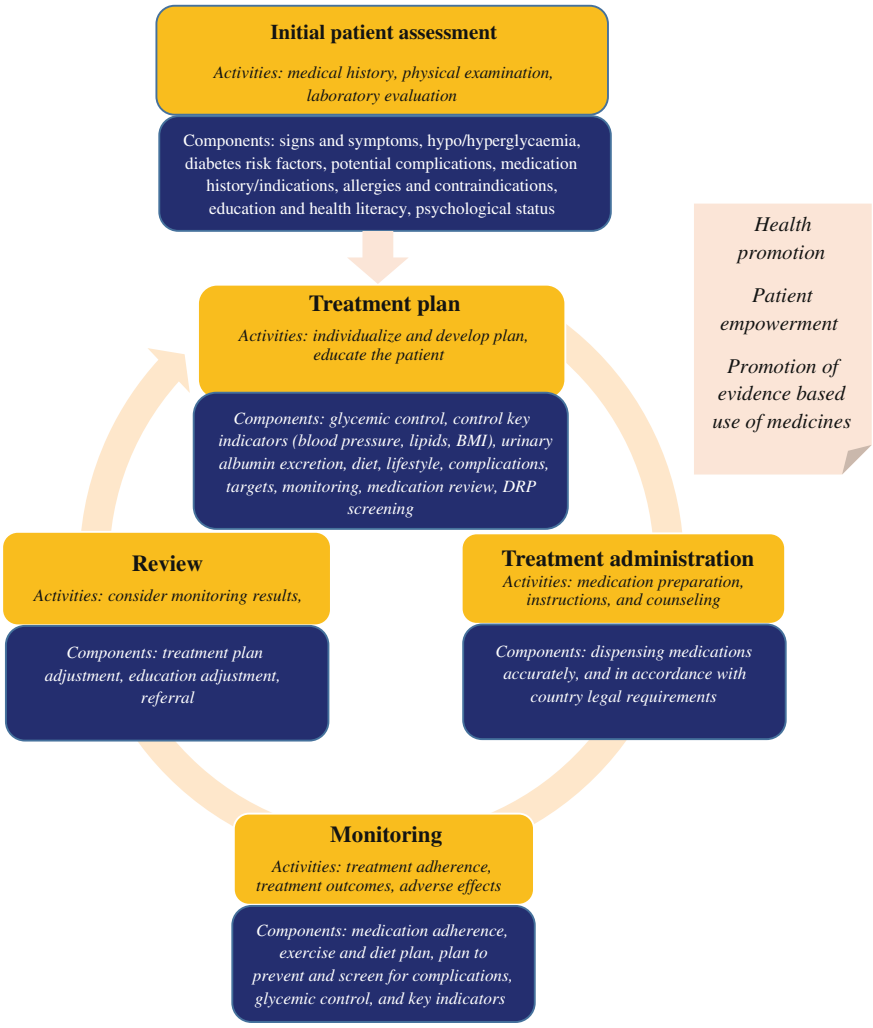

Fig. 28.1 A model of systematic approach to pharmaceutical care delivery in patients with T2DM [14]

pressure and lipids, a sustained weight loss of 7% is recommended. This can be challenging for many obese individuals with T2DM. This degree of weight loss can be attained with lifestyle programs that achieve a 500–750 kcal/day energy deficit or provide; 1200–1500 kcal/day for women and 1500–1800 kcal/day for men, adjusted for the individual's baseline body weight [2]. Physical activity recommendations to assist in weight loss and reduce insulin resistance include undertaking at least 150 min/week of moderate-intensity aerobic physical activity (50–70% of maximum heart rate), spread over at least 3 days/week with no more than 2

consecutive days without exercise, reduction of sedentary activity undertaking resistance training at least twice a week and include exercise programs [2]. Other lifestyle measures that need to be considered in the treatment plan for patients with T2DM are moderate alcohol consumption (≤ 1 drink for women, ≤ 2 drinks/men) and reduction in sodium intake especially in patients with comorbidities such as hypertension.

28.3.2 Pharmacotherapy

If a 6–12 week trial of lifestyle modification is not successful in controlling glycemia or if blood glucose levels are very elevated and/or the patient has symptoms at the time of diagnosis, pharmacotherapy is indicated. There are now 9 distinct oral pharmacologic classes and a variety of insulin and noninsulin injectable medications available for the treatment of T2DM. Metformin remains the first-line treatment option for most patients. It targets one of the key pathophysiological features of T2DM, namely insulin resistance. However, T2DM is also characterized by other types of dysfunction in organs such as the liver which produces too much glucose, the pancreas where α cells increase glucagon secretion and β cells produce less insulin and the gut with reduction in Glucagon-like peptide-1 (GLP-1) levels and increased intestinal transit time for food and the kidney with increased glucose reabsorption. In adipose tissue (visceral fat) dysregulation of hormones such as adiponectin and the production of inflammatory cytokines contribute to insulin resistance [6].

The progressive nature of T2DM and the need to tackle all areas of dysfunction imply that combination therapy with classes of medication with complementary modes of action is more likely to achieve glycemic control and importantly preserve β-cell function, the ultimate goal of therapy [6, 7].

Current guidelines advise clinicians to select second and third agents from among the available classes adopting a patient-centered approach, taking account of patient preferences, tolerability, and individualized glycemic targets [2]. Table 28.1 summarizes the current classes of oral and injectable agents, their mode of action, efficacy (HbA1C lowering), risk of hypoglycemia, effect on body weight, and common side effects.

However, studies have shown that many patients do not meet targets for glycemic control, blood pressure, and lipids, putting them at higher risk of developing complications. Both physician and patient factors contribute to this. Inappropriate prescribing or therapeutic inertia (i.e., failure by physicians to intensify therapy to meet recommended targets) or patients' failure to adhere as prescribed to their medication regimen due to a range of drug-related problems (DRPs) [8].

Table 28.1 Classes of antidiabetic agents and effects [6, 7, 13]

Class	Available agents	Mechanism of action	HbA1C (%)	Risk of hypoglycemia	Effect on body weight	Effect on CVD outcomes	Other adverse effects
Biguanides	Metformin	Insulin sensitiser Numerous effects on inhibition of glucose production	1–2	No	Mild weight loss due to anorectic effect	(Risk reduction (UKPDS)	May cause nausea, vomiting or diarrhea after commencing therapy lactic acidosis (rare) Vitamin B12 deficiency
Sulphonylureas	Glyburide Glipizide Glimepiride	Increase pancreatic insulin secretion; may decrease insulin resistance	1–2	Yes (increased by advanced age, renal or hepatic impairment and interacting drugs), weight gain	Weight gain	Risk increase (observational trials and meta-analyses)	Less common nausea, diarrhea, metallic taste, headache, rash
Alpha-glucosidase inhibitors	Acarbose	Delays intestinal absorption of carbohydrates by inhibiting alpha-glucosidase enzymes in the small intestine; reduces postprandial hyperglycemia	0.5–0.8	No		Unknown	Flatulence, diarrhea, abdominal pain, and distension

(continued)

Table 28.1 (continued)

Class	Available agents	Mechanism of action	HbA1C (%)	Risk of hypoglycemia	Effect on body weight	Effect on CVD outcomes	Other adverse effects
Thiazolidinediones	Rosiglitazone Pioglitazone	Insulin sensitizer Decrease free fatty acid accumulation, reduce inflammatory cytokines, increase adiponectin levels, and preserve β-cell integrity and function, all leading to improvement of insulin resistance and β-cell exhaustion	0.5–1.4	No	Weight gain	(Risk reduction Pioglitazone PROactive)	Peripheral edema, Headache, dizziness, arthralgia, Decrease in hemoglobin and aematocrit Fractures (rare) Bladder cancer (rare) Heart failure when combined with insulin
GLP-1 analogs	Exenatide Liraglutide Dulaglutide	Binds to GLP-1 receptor on pancreatic ß-cells, promoting glucose-mediated insulin secretion, reduced glucagon secretion and slows gastric motility	0.5–1.5	No (Only in combination with sulphonylureas)	Weight loss	Reduction/ neutral (liraglutide LEADER, semaglutide; SUSTAIN 6 ELIXA)	GI side effects are common; 30–45% of patients experience one or more episodes of nausea, vomiting or diarrhea
DPP-IV (Dipeptidyl peptidase-IV) inhibitors	Alogliptin Linagliptin Saxagliptin Sitagliptin Vildagliptin	Reduce degradation of endogenous GLP-1 and GIP	0.5–0.9	Low (mainly when used with insulin or a sulphonylurea),	No effect	Neutral (sitagliptin; TECOS, saxagliptin SAVOR-TIMI; aligliptin; EXAMINE)	Runny nose, sore throat, headache, musculoskeletal pain (may be severe) constipation (uncommon)

(continued)

Table 28.1 (continued)

Class	Available agents	Mechanism of action	HbA1C (%)	Risk of hypoglycemia	Effect on body weight	Effect on CVD outcomes	Other adverse effects
SGLT-2 (sodium-glucose transport -2 protein) and inhibitors	Dapagliflozoin Canagliflozin Empagliflozin	Inhibit sodium-glucose co transporter 2, reducing glucose reabsorption in the kidney (and increasing its excretion in the urine)	0.5–0.7	Low (when used with a sulfonylurea or insulin),	Weight loss	Reduction (empagliflozin; EMPA-REG OUTCOME)	Genital infections polyuria, dysuria, UTI, dyslipidemia, increased hematocrit, constipation, nausea, thirst, renal impairment, e.g.,
Insulins	Rapid-acting (analog insulins) Short-acting Regular Intermediate Long-acting (Basal)	Hormone replacement therapy	1–2.5	Marked	Weight gain	Neutral (glargine; ORIGIN)	Lipoatrophy lipohypertrophy at injection sites Allergy to injection components

28.3.2.1 Drug-Related Problems

DRPs including adverse drug reactions, interactions, contraindications, and nonadherence can undermine the effectiveness of T2DM therapy. Since patients with T2DM generally use multiple medications, DRPs are likely to occur in this population and can negatively influence diabetes control. Research has shown that a substantial proportion of DRPs that exist within the healthcare system are related to patients with diabetes. Two recent studies, which applied the PCNE classification for DRPs explored the prevalence of DRPs among patients with T2DM (i) in the community setting [9] or (ii) in the hospital setting as contributing to the hospitalization [10]. The former study comprised home visits to 54 diabetes patients by students interned in 79 Swiss community pharmacies. The most common DRPs identified were; confusion between trade and generic names, risk of nonadherence; gaps in knowledge about potential interactions and purpose of medication; and hoarding of prescription and OTC medications [9]. The investigation of hospitalization resulting from DRPs involved a retrospective review of 300 patients from hospitals in both UK and Saudi Arabia. The main problems identified were lack of effectiveness and adverse drug reactions caused predominantly by polypharmacy and nonadherence, with older age, and using insulin both significant predictors of the occurrence of a DRP. However, in the UK cohort, adverse drug reactions were the most common DRP, whereas in the Saudi Arabian cohort, it was lack of therapeutic effectiveness due to inappropriate drug and dose selection [10].

28.3.3 Self-management

Self-management is a fundamental aspect of diabetes care which recognizes that the achievement of strict glycemic control is highly dependent on the extent to which an individual is able to self-manage their condition. Successful self-management of T2DM requires individuals to engage in various cognitive and behavioral processes on a daily basis to maintain blood glucose levels within the normal range, including lifestyle modifications, adherence to medications, self-monitoring of blood glucose (SMBG) and regular visits to their healthcare professionals (HCPs). For many people with T2DM, self-management is challenging as they do not possess adequate knowledge, skills, and motivation to initiate and maintain behavioral changes to help them control their illness.

Diabetes self-management education provides a framework to enable an individual to develop the necessary knowledge and skills required to self-manage their condition. Topics include elements of optimal nutrition concerning control of glycemia (i.e., carbohydrate intake), blood pressure (salt) lipids (fats), recommended physical activity, identification, and management of hypoglycemia (especially for people on insulin/secretagogues), sick day management, smoking cessation (if applicable), alcohol use, foot care, instruction on medications, and the importance of regular monitoring for complications [2].

In addition to knowledge, people with T2DM also need the self-efficacy and motivation to successfully implement effective self-management. The use of motivational interviewing and collaborative goal setting by pharmacists as complementary strategies to facilitate self-management support have been shown to be effective in improving health outcomes in T2DM [11]. Motivational interviewing is based on asking open-ended questions to identify ambivalent thoughts and feelings, and explore patient beliefs about perceived difficulties in changing their behavior. The collaborative goal setting technique involves the pharmacist and patient negotiating several small, achievable, and specific goals to tackle their most pressing problems. Each goal is supported by a strategy designed to help the patient achieve those goals. The achievement of behavior change is optimized through the patient's personal investment in this process [11].

Another valuable tool to assist people with T2DM to achieve optimal control is the use of self-monitoring blood glucose (SMBG). At the time of diagnosis, it serves to enhance an individual's understanding how their diet, lifestyle, and medication influence their blood glucose levels. It may also provide a means for people to actively and effectively participate in the control and treatment of their diabetes, modifying their behavior and pharmacotherapy as needed, in consultation with their healthcare provider. SMBG use requires an easy procedure for patients to regularly monitor the performance and accuracy of their glucose meter. Many blood glucose meters have companion software to facilitate downloading of blood glucose results which may be reviewed in consultation with their pharmacist and other healthcare professional in their care team. The intensity and frequency of SMBG is tailored to take account of the individual's specific educational/behavioral/clinical needs (to identify/prevent/manage acute hyper- and hypoglycemia) and to produce data on glycemic patterns and the impact of changes in therapy [12].

Thus, pharmacists need to work with patients to assist and support them to make and sustain the necessary behavior changes in lifestyle, to undertake self-care and SMBG and adhere to the medication regimen throughout their patient journey.

28.4 Pharmaceutical Care in T2DM

As a complex and multifaceted chronic condition, T2DM offers a good context for provision of pharmaceutical care within all levels of healthcare where pharmacists are involved or plan to expand their current roles. Pharmacists are ideally placed to ensure provision of responsible drug therapy to achieve optimal clinical outcomes and improve health-related quality of life in patients with T2DM, i.e., fulfilling core objectives of pharmaceutical care.

Provision of effective pharmaceutical care in T2DM demands a systematic approach, especially considering the difficult clinical task of optimizing diabetes therapy [13]. In this regard, pharmacists should be guided by a model that allows them to assist patients achieve the treatment goals set by the IDF (see above IDF recommendations) [3]. From the pharmaceutical care perspective, the process of

achieving the IDF goals should consider improving glycemic control without adversely causing hypoglycemia and weight gain and through interventions that have a positive impact on key indicators such as blood pressure and lipid levels. A systematic provision of pharmaceutical care can be ensured through an initial assessment of patient's medical history, physical, and laboratory results status. This is then followed by considering patient's treatment plan, treatment administration, monitoring, and review [3]. More details of this process, including components involved within the types of pharmaceutical care interventions are provided in Fig. 28.1. This process ensures that there is a system in place that addresses ongoing identification of patient issues, providing continued care and optimal outcomes for the patient.

It should be emphasized that during provision of pharmaceutical care, multidisciplinary collaboration of pharmacists with other health professionals should be considered, given that the activities involved in pharmaceutical care provide a good platform for collaboration [15]. This multidisciplinary collaboration ensures optimal treatment selection and achievement of best outcomes for the patient, ultimately leading to improved management of T2DM.

There is substantial body of evidence reporting the value of pharmacy-based/pharmacist-delivered pharmaceutical care interventions, leading to patient support and improvement of T2DM management [14].

Studies have evaluated pharmaceutical care interventions in T2DM by measuring effectiveness in terms of improvements in outcomes such as in control of glycemia, blood pressure, and lipids levels, body mass index (BMI), adherence to treatment, and resolution of drug-related problems. Economic and humanistic and social outcomes (patient's satisfaction, quality of life, knowledge and beliefs, self-care, and lifestyle) have also been evaluated [14].

28.4.1 Summary of Types of Activities with Accompanying Evidence

Studies have reported positive effects of pharmaceutical care interventions on the abovementioned outcomes [14]. Collectively, these studies provide evidence supporting pharmacist's involvement in diabetes care in various practice settings including community pharmacies, hospitals, outpatient clinics, and primary healthcare centers. It should be noted, however, that evaluated interventions were multifaceted and with variations across studies, it is difficult to pinpoint which particular interventions are associated with greatest benefits for the patient. A summary of the evidence supporting pharmacists' interventions in key clinical and nonclinical outcomes is provided below [14].

28.4.1.1 Glycemic Control

The literature supports the positive impact of pharmaceutical care interventions in improvement of glycemic control. HbA1c level reductions were reported within ranges of −0.18 to −0.98%. It is interesting to note that the positive impact of pharmaceutical care interventions did not significantly differ between settings (i.e., community pharmacy vs. other outpatient settings). Furthermore, evidence suggests that most significant positive effects on glycemic control were reported in patients with more poorly controlled glycemia prior to the intervention and in younger population groups; as age of participants increased the effects of pharmaceutical care interventions decreased) [14].

28.4.1.2 Blood Pressure and Lipid Levels

The review of pharmaceutical care interventions in T2DM also highlighted significant improvements in blood pressure control, with studies reporting reductions in systolic blood pressure ranging from −5.6 mmHg to as much as −20.05 mmHg. Diastolic blood pressure was reported to be reduced from −3.90 to −6.2 mmHg. Total cholesterol, low-density lipoprotein cholesterol, and BMI were also improved through pharmacy-based interventions. The literature also supports the benefits of pharmaceutical care interventions in improvement in cardiovascular disease major risk factors [14].

28.4.1.3 Humanistic and Social Outcomes

Delivery of pharmaceutical care interventions results in improvement in humanistic outcomes such as patient's health-related quality of life. However, demonstration of this improvement is often difficult and dependent on quality of life measures employed as well as the duration of studies. Nevertheless, significant reduction of hyperglycemic and hypoglycemic episodes among patients participating in a six-month diabetes management and education program was demonstrated. These outcomes can inevitably have positive effects on a patient's quality of life. Positive economic effects were also reported through involvement of pharmacists in a patient's diabetes care [14]. In this regard, it is worth noting that although pharmacists' interventions may result in increased medication costs, they are usually offset by total medical costs of hospital attendances and admissions.

Improvement in medication adherence of patients with T2DM is supported by evidence. This is an important aspect of diabetes management that can be addressed by pharmacists given that poor medication adherence is a major contributor to patients failing to achieve adequate glycemic control. Furthermore, this issue becomes more pressing to address given that poor medication adherence is widespread among diabetes patients with studies reporting medication adherence in the

range from 38 to 93% (worth noting that this difference is mainly due to various approaches in the methodology employed by these studies) [16].

During provision of diabetes-based pharmacy services, pharmacists must ensure a range of conditions are met that ensure successful delivery of pharmacy services and interventions. These conditions include: an appropriate counseling area that ensures patient's privacy, a fully equipped (e.g., with devices that enable accurate measurements of diabetes indicators such as BGL, blood pressure, BMI) healthcare area for dealing with patients with T2DM and adherence to relevant ethical and professional practice standards [17].

28.4.2 Documentation of Care

Documentation of patient care is an essential component of care ensuring quality, efficiency, continuity of care, and improved patient safety. See also Chap. 8. In relation to pharmacist interventions, documentation of care also supports the decision-making process and facilitates communication with other health professionals. In general, documentation of care should be legible and accurately reflective of pharmaceutical care provided by pharmacists in various stages, i.e., patient assessment, treatment plan, monitoring parameters, and review outcomes. Furthermore, the progressive nature of T2DM makes it essential that pharmaceutical care for these patients is supported by ongoing documentation that ensures prioritization of issues and provision of continued patient care. From the perspective of identifying DRPs, the initial patient assessment outlined in Fig. 28.1 ensures pharmacists have the information needed to proceed with review of patients' drug therapy (i.e., treatment plan), leading to potential identification of DRPs.

During identification of the DRPs and delivery of subsequent intervention, a number of classification systems have been developed to assist pharmacists and other health professionals in documenting DRPs during the process of pharmaceutical care provision. The Pharmaceutical Care Network EUROPE (PCNE) has developed a classification which focuses on the problem, cause (including possible causes for potential problems), planned intervention, intervention acceptance, and status of the DRP. Each of these domains is then elaborated in more detail in specific sub-domains [17].

The PCNE classification system can be employed during identification and resolution of DRPs as a means of facilitating the process of recording and documentation in patients with T2DM. Figure 28.1 outlines a step-by-step approach to identifying DRPs and subsequent inclusion into a pharmacist's care plan (Table 28.2).

Table 28.2 Summary of Mrs. N's DRPS and Interventions using the PCNE classification [17]

DRP	PCNE code	Interventions	PCNE code
Suboptimal glycemic control Non adherence to diabetes medications has contributed to introduction of vildagliptin, Cessation of simvastatin therapy Halving the dose of gliclazide	P2.1 P1.2 C7.1 C7.1	Education on diabetes and the importance of medication adherence Explore reasons for nonadherence Discuss the pharmacotherapy for glycemia with doctor Educate patient about the important of statin in CVD prevention Educate the patient about correct administration of dose	12.1 12.2 11.4
Ankle swelling is an adverse effect of amlodipine; furosemide-treating amlodipine-induced ankle oedema	P2	Recommend/decrease the dose of amlodipine or cease it (provided that her blood pressure is well controlled) Furosemide treatment only until amelioration of swollen ankles	11.3
Not on aspirin which may be beneficial given her cardiovascular risk	P1.3 C1.6	Discuss the addition of aspirin therapy with prescriber	11.4

Case scenario– *Mrs. N*

Consider the case of Mrs. N. She is a long-time customer of your local pharmacy; she is 67 years old and has come to the pharmacy today with a new prescription for Vildagliptin, following an appointment with her GP. Mrs. N has had T2DM for 13 years as well as a range of other chronic conditions.

Her current medications:
Amlodipine 10 mg mane (in the morning)
Atenolol 50 mg mane (old MI)
Irbesartan 300 mg mane (ACEI induced cough in past)
Gliclazide 80 mg × 1.5 bd (twice a day)
Metformin 500 mg × 2 bd
Furosemide 40 mg mane
Simvastatin (Zocor) 20 mg nocte (only took for 1 box "course")

Her current concerns

Mrs. N has been battling with her weight (BMI = 35 kg/m^2) for some time. She is also unhappy about having to take yet another type of tablet; she believes that she is already taking too many and even skips some of her

evening medications. Mrs. N considers her diabetes to be well under control given that (according to her): (a) her latest HbA1c level (done 12 months ago) was 8.5%, (b) without doing too much testing at home she never had a hypoglycemic episode and c) doctor told her today that her blood pressure and lipids are good. Upon further questioning you understand that Mrs. N also does not understand the value of her losing weight and that she is largely inactive and has an irregular diet. Furthermore, she complains about the remembering to take all of these pills and at the right time. Given that she lives alone, Mrs. N has no assistance in managing all her pills, which adds on to her stress related to medication management.

There are a number of key activities which pharmacists can undertake with the view of being actively involved in supporting Mrs. N's T2DM. These activities may be delivered within the five key stages (i.e., initial patient assessment, treatment plan, treatment administration, monitoring, and review) and through use of specific pharmaceutical activities as outlined in Fig. 28.1:

Stage 1: Initial assessment

Following the initial assessment of Mrs. N, it can be identified that her new prescription for vildagliptin is likely to be an attempt to escalate therapy in response to Mrs. N's HbA1c of 8.5% and that the forosemide is being taken for swollen ankles. However, the GP is unaware that this lady is not taking her evening doses of gliclazide and metformin. It can also be identified that Mrs. N would benefit from education on her T2DM including medications, complication risk factors and diet, and lifestyle.

Stage 2 Treatment plan

When considering Mrs. N's treatment plan, a number of issues can be addressed, including key indicators (blood pressure, lipids, BMI), diabetes complications, diet, and lifestyle indicating the need for a medication review and DRP screening. DRP screening may be assisted using the PCNE classification system enabling categorization of DRPs in addition to documenting [17].

During the medication review, it can be ascertained that medication adherence has contributed to introduction of vildagliptin, making education on medication adherence one of the priority areas to address. Medication adherence should become part of her pharmaceutical care plan and a model of ongoing documentation of medication adherence is provided in Table 28.3. As part of this plan, it may be beneficial to explore her reluctance to take the evening doses and pursue this before adding an alternative medication. In this regard, both education and medication access will need to be considered in her pharmaceutical care plan. You also note that she has stopped the statin therapy. Although currently Mrs. N suggests that her blood pressure and lipid profile are satisfactory, it would be beneficial to ascertain this through communication with her doctor.

Given that furosemide is being taken for swollen ankles, it may be that this is an adverse effect of amlodipine, hence making further investigation of this potential issue a priority DRP to address. If this was the case, then the options would be to recommend/decrease the dose of amlodipine (given that peripheral edema due to amlodipine is dose dependent) or cease it (provided that her blood pressure is well under control). Upon further screening for DRPs, it can be noticed that Mrs. N is not currently taking aspirin which may be beneficial given her cardiovascular risk (i.e., treatment missing). This would be discussed with the GP and may require considerable consultation with Mrs. N given her reluctance to addition of new medications.

Furthermore, it can be ascertained that her treatment plan needs to consider modifications in diet and lifestyle. Exploration of weight loss options with Mrs. N could be very helpful considering local support resources such as dietitian, exercise opportunities, psychologist if food is being used as a comfort and medication.

Stage 3 Treatment administration

During this stage, the pharmacist would need to ensure that all medications are being dispensed accurately and in accordance with country legal requirements. The pharmacist would need to ensure that all medication is being administered correctly and counseling is provided. Mrs. N is currently taking 120 mg of gliclazide meaning that she is halving the 80 mg tablet to achieve this. The pharmacist should ensure that this is being done adequately.

Stage 4 Monitoring

As part of a continued care for Mrs. N, medication adherence, exercise and diet plan, plan to prevent and screen for complications, glycemic control, and key indicators for T2DM will need to be monitored. Table 28.3, has an example of activities and strategies that can be undertaken as part of an ongoing glycemic control monitoring.

Stage 5 Review

The results of the above interventions should be reviewed at this stage. Specifically, if following consultation with the doctor vildagliptin was not added (i.e., due to the plan to address adherence of metformin and gliclazide first), then the results of improved medication adherence will need to be reviewed in relation to glycemic control. If not satisfactory, then introduction of vilgagliptin could be considered at this stage, requiring referral to her doctor. Likewise, ankle swallowing resolution post dose reduction or cessation of amlodipine is reviewed as well as the effects of lifestyle and diet interventions in her overall T2DM management.

Table 28.3 Examples of a documentation system for activities undertaken as part of a continued pharmaceutical care plan model addressing medication adherence and glycemic control

Medication adherence	Visit date	Visit date	Visit date
Education (*Patient health beliefs, knowledge, and adherence.*) Possible strategies:			
1a Clarify any inaccurate perceptions the patient may have about diabetes and its treatment			
1b Provide information on the long-term benefits of good diabetic control			
1c Give the benefits of taking a medication and explain why it has been prescribed (e.g., anti-stroke pill)			
1d Explain the consequences of not taking a medication			
1e Acknowledge and investigate complaints about side effects			
1f Provide written information on treatment plan			
1g Address other concerns about medication			
1h Help patient to remember to take medications: select reminders or cues (such as clock time, mealtime, bathroom ritual) use repeat refill reminders (telephone call, letter) encourage use of unit dose compliance aids (e.g., Webster Packs) encourage patient to enlist family member to remind to take medication			
1i Encourage patient to monitor condition and agree on achievable goals			
1j Ask patient to verbally agree to take medication—set goals			
1k Ask patient to sign a concordance			
1l Refer to GP			
Medication access (*Relates to physical barriers to adherence, e.g., difficulties self-injecting, opening containers, reading instructions)* Possible strategies:			
2a Consider easily managed dose forms, e.g., liquids, crushable tablets			
2b Consider repackaging medications, unit dose systems			
2c Encourage patient to involve spouse/family member to help them take medications			
2d Organize large print labels			
2e Ensure that nothing is labeled with “take as directed”			
2f Where cost is an issue, consider generic brands			
1. Technique Check for problems with SMBG and correct any problem areas:			
1a Finger pricking			
1b Blood Application			
1c Timing			
1d Meter operation			
1e Sharps disposal			
1f Reading and recording events			
1g Calibration and control tests			
1h Meter maintenance			
1i Strip expiry			

(continued)

Table 28.3 (continued)

Medication adherence	Visit date	Visit date	Visit date
2. Hypoglycemia (a reading <4 mmol/L on home meter or hypoglycemic episode)			
Possible strategies:			
2a Ask what action normally taken			
2b Check patients understanding of hypoglycemia, reinforce causes, symptoms and treatment and prevention			
2c Give written information			
2d Check SMBG technique especially blood application and meter care			
2e Refer to GP			
3. Hyperglycemia (a reading >15 mmol/L on home meter)			
Possible strategies:			
3a Check patient's understanding of hyperglycemia and reinforce causes, symptoms and treatment			
3b Ask about sick day management/hyperglycemia management			
3c Give written information of sick day management			
3d Assess if patient has signs and symptoms of infection or acute illness			
3e Refer to GP			
3f If no acute illness check SMBG technique, including hand washing and testing time			
3g Check adherence with medication			

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Chapter 29
Pharmaceutical Care and Cardiovascular Diseases

Martin Schulz, Katrin Krueger, Nina Griese-Mammen and Ross Tsuyuki

Abstract Cardiovascular diseases (CVDs) are often accompanied with comorbidities and, therefore, with multiple drug regimens. Drug-related morbidity and mortality due to drug-related problems (DRPs) represent a serious problem in these patients. Pharmacists' intervention can detect and solve or prevent DRPs. However, DRPs in CVDs are currently not a validated surrogate outcome. Nevertheless, suggested interventions are medication reconciliation and reviews, patient education and counseling (to improve self-care and medication adherence), additional written information (medication plan) and pillboxes (weekly dosing aids) to improve adherence, and monitoring of clinical parameters, among others. Apart from hypertension and CVD risk reduction, randomized controlled trials (RCTs) with robust designs, studying large populations, adequate follow-up periods, and sufficiently powered to detect clinical relevant differences in endpoints are needed. The evidence gained will provide standards for the interventions and outcome measures, both to compare studies and approaches to implement them reimbursed in daily pharmaceutical practice.

Keywords Pharmaceutical care · Cardiovascular diseases · Medication adherence Hypertension · Angina pectoris · Myocardial infarction · Heart failure Cerebrovascular diseases

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29.1 Introduction

Cardiovascular diseases (CVDs) are the number one cause of death globally. The World Health Organization (WHO) reports that 17.5 million people die each year from CVDs, an estimated 31% of all deaths worldwide. Four out of five CVD deaths are due to heart attacks and strokes. Over 75% of CVD deaths occur in low-income and middle-income countries [1].

CVDs are caused by disorders of the heart and blood vessels, such as raised blood pressure (BP; hypertension (HT)) and coronary heart disease (CHD). They include angina, acute coronary syndromes (ACS) including myocardial infarction (MI), heart failure (HF), cerebrovascular diseases (stroke and transient ischemic attacks (TIA)), peripheral artery disease (PAD), rheumatic heart diseases, and congenital heart diseases. Individuals at risk of CVD often have hypertension, dysglycemia, and dyslipidemia as well as overweight/obesity. These can all be easily measured and monitored by pharmacists. Identifying those at highest risk of CVDs and ensuring they receive appropriate treatment can prevent premature deaths. The major lifestyle risk factors of CVD are tobacco use, physical inactivity, an unhealthy diet, and harmful use of alcohol [1].

It is possible to prevent CVD by addressing these behavioral risk factors. People with CVD or at high CV risk need early detection and management including counseling and pharmacotherapy [1–3]. The WHO identified cost effective interventions for prevention and control of CVD, e.g., comprehensive tobacco control policies, taxation to reduce the intake of foods that are high in fat, sugar and salt, building walking and cycle paths to increase physical activity, and individual healthcare interventions to be targeted to those at high CVD risk. For secondary prevention of CVD in those with established disease, treatment with medications like aspirin (ASA), beta-blockers (BB), angiotensin-converting enzyme inhibitors (ACEI), and lipid-lowering drugs (mostly statins) is necessary [1].

The complexity of the guideline-recommended therapies increases as the disease progresses due to increasing comorbidities requiring additional treatment by different specialists. This increases the probability of drug-related problems (DRPs) such as drug/drug and drug/food interactions, contraindications, duplicate medications, and adverse effects (AE). Moreover, actual medication intake by patients often differs from the recommendations made by healthcare professionals. Medication nonadherence is, hence, another major issue. For many patients, it is difficult to self-manage their many pharmacological and non-pharmacological treatments. More on medication adherence can be found in Chap. 5.

So, multidisciplinary approaches to treatment and care are promising to reduce hospitalizations and mortality, eventually [1]. The benefits of these interventions are largely independent, but when used together with smoking cessation, nearly 75% of recurrent vascular events are potentially preventable. Currently there are, however, major gaps in the implementation of these interventions particularly at the primary healthcare level [1].

29.2 Disease Characteristics

Hypertension and dyslipidemia are the most common CVD risk factors, and CHD and HF are by far the most common CVD. Therefore, this section covers these four conditions.

29.2.1 Dyslipidemia

Dyslipidemia is a major risk factor for CVD including stroke [1–3, 22]. The most common dyslipidemia is elevated low-density lipoprotein cholesterol levels, which directly relate to risk of atherosclerotic vascular disease.

Dyslipidemia targets recommended by major cardiovascular guidelines are all based upon calculation of an individual's risk for CV events (see the guidelines for various CV risk calculators). The approach to LDL-C targets vary by guideline, and either call for a 50% reduction in LDL-C, targets based upon CV risk (e.g., a target of <2.0 mmol/L in those at high CV risk) (see www.onlinecjc.ca/article/S0828-282X(16)30732-2/pdf and https://www.eas-society.org/?page=dyslipidemia_guide), or simply to use high-dose statins in all patients at high CV risk (see circ.ahajournals.org/content/circulationaha/133/18/1795.full.pdf).

29.2.2 Hypertension

Hypertension is a condition in which the blood vessels have persistently raised pressure. Raised BP is one of the leading risk factors for CHD, HF, both ischemic and hemorrhagic stroke, and subsequently, for global mortality. In some age groups, the risk of CVD doubles for each increment of 20/10 (systolic/diastolic) mmHg of BP, starting as low as 115/75 mmHg [1].

29.2.3 Coronary Heart Disease (CHD)

CHD, as a result of coronary artery disease (CAD), causes exercise- and stress-related ischemic symptoms due to narrowing of $\geq 50\%$ in the left main coronary artery and $\geq 70\%$ in one or several of the major coronary arteries. CHD is characterized by episodes of reversible myocardial supply mismatch, related to ischemia or hypoxia commonly associated with transient chest discomfort and pain (angina pectoris).

The various clinical presentations of CHD are associated with different underlying mechanisms that mainly include (i) plaque-related obstruction of epicardial arteries, (ii) focal or diffuse spasm of normal or plaque-diseased arteries, (iii) microvascular dysfunction, and (iv) left ventricular dysfunction (LVD) caused by prior acute myocardial necrosis and/or hibernation (ischemic cardiomyopathy) [2].

29.2.4 Heart Failure (HF)

HF is a highly morbid and costly condition with a growing impact on public health affecting approximately 1–2% of the adult population in developed countries. Hospitalizations for acute decompensated HF (ADHF) are common, and the mortality is high despite guideline-directed treatment [3]. HF is characterized by typical symptoms (e.g., breathlessness (various degrees of dyspnea), ankle swelling, and fatigue) that may be accompanied by signs (e.g., elevated jugular venous pressure, pulmonary crackles, and peripheral edema). It is caused by a structural and/or functional cardiac abnormality, resulting in a reduced cardiac output. Before clinical symptoms become apparent, patients can present with asymptomatic structural or functional cardiac abnormalities. Identification of the underlying cardiovascular problem(s), mostly undiagnosed or poorly managed hypertension or CAD, is crucial.

HF is categorized by the percentage of the left ventricular ejection fraction (LVEF). There are patients with normal LVEF ($\geq 50\%$; HF with preserved EF (HFpEF)), with reduced LVEF (<40%; HF with reduced EF (HFrEF)), and with an LVEF in the range of 40–49% (HF with midrange EF (HFmrEF)) [2].

29.3 Treatment Goals

29.3.1 Hypertension

BP-lowering drugs are strongly recommended to reduce the risk of CV outcomes (e.g., stroke, ACS/MI, and HF) in all individuals with HT [2]. Treating systolic and diastolic BP to a target below 140/90 mmHg is associated with a reduction in CV complications [1]. Treatment includes lifestyle modifications which is first line. The introduction of pharmacotherapy is linked to overall CVD risk: diuretics (including thiazides, chlorthalidone, and indapamide), BB, calcium channel blockers (CCBs), and ACEI or angiotensin receptor blockers (ARBs) are all suitable for the initiation and maintenance of antihypertensive treatment [2].

29.3.2 Coronary Heart Disease

Management of CHD aims to reduce symptoms, improve prognosis, as well as prevent CV events. It includes lifestyle modifications like healthy diet and increased/appropriate physical activity, control of risk factors (like smoking, overweight/obesity, high lipids, high BP), evidence-based pharmacological therapy, and patient education. Anti-ischemic drugs like nitrates and molsidomine, BB, CCB, and ivabradine (an inhibitor of the "funny channel" reducing only the heart rate in patients in sinus rhythm) are used.

To prevent CV events (like MI or acute thrombotic events), pharmacological or lifestyle interventions are used which: (i) reduce plaque progression; (ii) stabilize plaque by reducing inflammation, and (iii) prevent thrombosis. Therefore, antiplatelet agents like low-dose aspirin and $P2Y_{12}$-inhibitors such as clopidogrel, prasugrel, or ticagrelor, lipid-lowering agents (statins), and renin-angiotensin-aldosterone system (RAAS) blockers like ACEI are recommended [2].

29.3.3 Heart Failure

The goals of guideline-recommended therapies for heart failure (HF) are: improvement of symptoms (dyspnea, fatigue, and exercise tolerance), slowing of disease progression, improvement in quality of life (QoL), and decrease in hospitalizations and mortality, requiring a long-term therapy with multiple drugs [4]. Neurohormonal antagonists (ACEI or ARB, BB, and mineralocorticoid receptor antagonists (MRA)) have been shown to improve overall survival (all-cause mortality) in patients with HFrEF. In addition, a first-in-class composite angiotensin receptor–neprilysin (NEP) inhibitor (ARNI; valsartan+sacubitril) reduces the risk of HF-related hospitalizations and mortality in patients with HFrEF. Ivabradine reduces the elevated heart rate often seen in HFrEF and has also been shown to improve outcomes in HFrEF.

The use of diuretics, especially loop diuretics, should be modulated according to the patient's clinical status. Treatment of hypertension is recommended to prevent or delay the onset of HF. Also counseling on appropriate fluid/sodium intake, appropriate physical activity, smoking cessation, and reduction in alcohol intake is recommended [2].

29.4 Common Drug-Related Problems Often Encountered in Patients with CVD

CVDs are often accompanied with comorbidities and, therefore, with multiple drug regimens. One study found that nearly 30% of CVD patients taking ≥ 5 drugs (a common threshold for polypharmacy) had at least one DRP. Inappropriateness of

the drug (especially inappropriate drug combinations) or the dose was the most common drug-related problems (DRPs). A need of additional drug therapy and lack of therapeutic monitoring are common risk factors causing DRPs [5].

The most inappropriate drug class for CVD patients is nonsteroidal anti-inflammatory drugs (NSAIDs, ibuprofen, diclofenac, naproxen, among others) including COX-2 inhibitors (coxibs). Whenever possible, NSAIDs should be avoided in combination with ACEI, ARB, or diuretics due to the risk of raised BP and worsening of renal function. NSAIDs or coxibs are not recommended (contraindicated) in patients with HF, as they increase the risk of HF worsening and HF hospitalization [6].

Many antihypertensives are associated with clinically significant drug interactions which may affect BP-lowering or result in adverse drug reactions (ADR). BB may mask signs and symptoms of hypoglycemia when used with insulin or oral antidiabetics and may impair glucose tolerance leading to poorer glycemic control. Drug/drug interactions resulting in increased plasma levels of statins increase the risk of ADRs such as myopathies.

In HF, drug classes causing many DRPs include ACEI, ARB, BB, MRA, diuretics, potassium supplements, and digoxin [6]. Regular monitoring of both potassium levels and renal function is recommended. Moreover, thiazolidinediones (glitazones) and the CCBs diltiazem and verapamil are not recommended in patients with HF, as they increase the risk of HF worsening and HF hospitalization [2].

Pharmacists' intervention can help to monitor and prevent the risk of developing DRPs, and contribute to improve clinical outcomes in patients with or at risk of CVD [5]. In one non-randomized study without a control group, 94% of the DRPs in HF patients were classified as preventable. During the 6-months follow-up, pharmacist interventions solved or prevented the health problem in 83% of the cases [6]. It should also be emphasized that many patients with, or at risk for CVDs are undertreated for their risk factors—these are DRPs that should be a target for pharmacist interventions.

29.5 Interventions in Patients with or at Risk of CVD

There are few studies evaluating pharmacists´ intervention in patients with or at risk of CVD, and randomized controlled trials (RCTs) are rare. However, RCTs in pharmaceutical care are often challenging to conduct. Most studies have investigated the impact of interventions in hypertension, followed by HF, and CHD.

Pharmacists' intervention may improve the clinical management of major risk factors for CVD, can detect, solve, or prevent DRP, and may increase medication adherence. In one RCT with 723 patients, and after adjusting for baseline values and center effect, there was a 21% difference in change in risk for CVD events ($p < 0.001$) between the intervention and usual care groups. The intervention group

had greater improvements in LDL-C (−0.2 mmol/L; $p < 0.001$), systolic BP (−9.37 mmHg; $p < 0.001$), glycosylated hemoglobin in those with diabetes (−0.92%; $p < 0.001$), and smoking cessation (20.2% reduction; $p = 0.002$) [7].

A systematic review and meta-analysis identified the following interventions: patient education, patient reminder systems, measurement of CVD risk factors, medication management and feedback to physician, or education of other healthcare professionals [8]. Pharmacist care was associated with a significant reduction in systolic/diastolic BP (19 studies [10,479 patients]: −8.1 mmHg, 95% CI [−10.2 to −5.9]/−3.8 mmHg [−5.3 to −2.3]); total cholesterol (TC) (9 studies [1121 patients]: −17.4 mg/dL [−25.5 to −9.2]; LDL-C (7 studies [924 patients]: −13.4 mg/dL [−23.0 to −3.8], and a reduction in the risk of smoking (2 studies [196 patients]: relative risk, 0.77 [0.67–0.89]) [8].

Another systematic review of studies, which evaluated the impact of pharmaceutical care on patients with CVD, showed that 20 of 24 included RCTs resulted in significantly improved risk factors, i.e., high BP, elevated LDL-C or blood glucose levels, or CV risk in general—with high BP and elevated cholesterol levels as the most common surrogate outcomes with significant differences after the intervention [9]. Interventions with significant results were medication reviews, patient education and counseling, additional written information, pillboxes (weekly dosing aids), and monitoring of clinical parameters [9]. More on medication review and counseling can be found in Chaps. 4 and 7 of this book.

29.5.1 Hypertension

The control of BP is a major challenge in primary care. The primary outcomes of studies evaluating pharmaceutical care in patients with hypertension are, apart from BP, medication adherence and QoL with systolic BP as the outcome most positively impacted by pharmaceutical intervention [10].

There is very strong evidence that pharmacist intervention improves BP control in outpatients compared with usual care. In a large systematic review, pharmacist intervention—for example, patient education and counseling about lifestyle, medication use and adherence, feedback to physician (including DRP identification and recommendations for medication change), and medication management (e.g., drug monitoring)—showed a reduction in systolic BP (−7.6 mmHg, 95% CI [−9.0 to −6.3]; $I^2 = 67\%$), and diastolic BP (−3.9 mmHg [−5.1 to 2.8]; $I^2 = 83\%$) when compared with usual care [11]. The effect tended to be larger if the intervention was led by the pharmacist and was delivered at least monthly.

Moreover, a recent study demonstrated better BP outcomes and cost savings with a pharmacist prescribing intervention for patients with hypertension in Canada [12].

29.5.2 Coronary Heart Disease

For CHD, a systematic review of RCTs evaluated the impact of pharmaceutical care interventions on cardiovascular events, hospitalizations, and mortality [13]. Secondary outcomes were medication adherence, BP, and lipid management. The authors found only one study that assessed the primary outcomes with no significant effects; and four that assessed secondary outcomes—with significant effects on medication adherence, BP, and lipid management. Interventions delivered by pharmacists included patient education, medication management (e.g., medication review, tools to improve/measure medication adherence, monitoring therapy), feedback to other healthcare professionals, and disease management (e.g., assessment of targets for medication therapy such as BP) [13].

29.5.3 Heart Failure

For HF, a recent systematic review identified three important fields for primary (ambulatory/community) pharmacist care: (I) medication reconciliation and reviews, (II) self-care and symptom control, and (III) medication adherence. Eight RCTs were included and seven systematic reviews were analyzed additionally [14]. Pharmacist interventions consisted of a structured interview with the patient (e.g., guided and documented by an assessment tool such as "The One Minute Clinic for Heart Failure" (TOM-CHF) [15] where drug use and reasons for medication nonadherence were discussed as well as a follow-up of the supply with electronic devices (MEMS®), regular communication with the patient about the therapy, monitoring with MEMS® and written instructions, medication reconciliation, and reviews to optimize medical treatment according to guidelines and to improve medication safety, written information for the patient and instructions for self-care, home visits including a medication review as well as advice on symptom self-management and lifestyle [14]. Primary outcomes were a combination of the 2 min walk test, BP, body weight, pulse, forced vital capacity (FVC), and QoL, medication adherence, adverse drug events (ADE) and medication errors, hospital admission, as well as a composite of hospital admission and death [14].

Six RCTs found statistically significant effects on primary outcomes, whereas two studies found no significant differences [14]. This systematic review showed an improvement in CV risk factors due to pharmacist intervention, a reduced risk of hospitalizations due to collaboration between pharmacists and physicians including medication reviews, as well as due to pharmacists' monitoring for contraindications and drug interactions. Moreover, educational and counseling interventions including instructions on self-monitoring, recommendations to physicians, and adherence aids were identified as promising interventions.

Two meta-analyses of RCTs in HF have reported reductions in all-cause hospitalizations of 21% and 29%, respectively, when the multidisciplinary intervention contained elements of pharmacist care [16, 17].

With a largely static therapeutic armamentarium in HF, maximal application of existing RCT-proven therapies is increasingly important. The dangers of deferring HF therapy are obvious: "*Drugs can't work in patients who don't receive them*". A structured medication review offers the opportunity not only to reconcile the medication but to identify undertreatment of HF both in terms of drug classes and doses prescribed/used. Pharmacists can play a critical role in addressing the ever-growing complexity of polypharmacy for HF, incorporating medications for comorbid conditions, and orchestrating dose titration of cardiovascular medications as well as integrating newer medications such as sacubitril–valsartan or ivabradine [18, 19].

29.6 Disease Management Programs

Adequate patient education, with special emphasis on adherence and self-care are common components of management programs for patients with HF. These programs should employ a multidisciplinary approach (cardiologists, primary care physicians, pharmacists, nurses) [2]. The 2017 update of the German national guideline on chronic heart failure (CHF) included a specific statement supporting the integration of pharmacists in the care of HF patients. A further statement recommends a standardized medication plan (a complete list of prescribed and OTC drugs) for every HF patient. Physician and pharmacist should coordinate issuing and updating the medication plan with the main aims to improve patient safety and medication adherence [20]. A consolidated medication plan shall be a result of a coordinated medication review. However, assuring that patients understand the standardized medication plan and can transfer the given information into practice is necessary. In addition to aid the patient, a complete and up-to-date medication plan also informs healthcare professionals about a patients' current medication. Hence, bridging the gap between providers and settings. It, therefore, can help to detect, solve, and prevent DRPs and to support medication reconciliation [21].

29.7 Outcomes that Matter

Evidence of cost-effectiveness of pharmaceutical care on major and patient-centered outcomes in CVDs is currently not strong enough to draw firm conclusions. Possible issues are the diversity of pharmaceutical care interventions, a lack of precision in defining the scope of the intervention, the size of the study population, and the lack of RCTs which have investigated relevant clinical endpoints. Clinical endpoints such as hospitalizations and mortality are often not captured. Most often,

surrogate parameters like BP or LDL-C levels have been evaluated (although that may be appropriate). The detection and resolution of DRPs and the presentation of the number of DRPs need to be put into the context of patient outcomes. Most studies have investigated the number of DRPs, but had no control group to compare relevant patients′ outcomes. Hence, DRPs in CVDs are currently not a validated surrogate outcome. Often, the study population is small, and therefore the studies are underpowered to detect significant differences in usual composite endpoints in CVD, hence morbidity (CV- or HF-related hospitalizations, MI, or stroke) and CV or all-cause mortality. In addition, the follow-up period is too short to assess mortality as an outcome.

A review further criticized the low quality of study designs according to the Jadad scale [10]. Differences in the design quality as well as differences in interventions and measurements have made it difficult to compare studies, and the conduct of meta-analyses. This does not apply to pharmacists' intervention studies in hypertension, however.

In addition to hospitalizations and mortality, health-related QoL (HRQoL) of CVD patients is widely considered to be of increased importance as an outcome measure. It is included in Health Technology Assessments (HTA), and a number of validated instruments are available. For example, the Minnesota Living with Heart Failure questionnaire (MLHF) or the Kansas City Cardiomyopathy Questionnaire (KCCQ) is widely used in HF trials. In CHD, the Seattle Angina Questionnaire (SAQ) or the Quality of Life after Myocardial Infarction (QLMI)/MacNew Heart Disease Quality of Life Questionnaire (MacNew) are valid and accepted instruments.

For all CVD patients, HRQoL is noticeable and influences the entire daily routine. Therefore, future, preferably randomized controlled CVD trials of pharmacist care interventions should assess both generic (e.g., EuroQoL/EQ-5D) and disease-specific QoL as secondary (patient-related) outcome measures. Economic analyses should also be conducted to determine value for the money spent on pharmacist care interventions.

Case Scenario

Hypertension and Dyslipidemia → CAD → Myocardial infarction (MI) → HF

Patient Mr. X, male, 69 years old, 179 cm, 87 kg (BMI: 27.2 kg/m^2)

Medical history-I (<2011)
Diagnoses: COPD, psoriasis, gout, ulcerative colitis

Pharmaceutical care-I

Check elderly patients for CV risk factors i.e., measure weight and height and calculate BMI, assess smoking history, and measure blood pressure (BP), heart rate (HR), and lipids (at least total (TC) and low-density lipoprotein cholesterol (LDL-C)).

Note: BP measurement should be performed according to standards: patients/clients should be seated quietly in a chair with back support, with both feet flat on the floor for at least 5 min prior to obtaining a measurement. BP should be checked in both arms at the first examination, at least, and the arm with the higher pressure should be used for subsequent monitoring assessments. It is recommended that the average of at least two readings should be taken at an interval of at least 1 min to represent the patient's/client's BP. If the difference between the first two readings is more than 5 mm Hg, one or two additional readings should be obtained, and the average of the multiple readings should be used.
CV risk factors screened by pharmacists: slightly elevated BMI, current smoker (>40 years), high BP (150/92 mmHg), and elevated LDL-C level (185 mg/dL [4.8 mmol/L], non-fasting).
Offer structured smoking cessation program including nicotine replacement therapy (NRT). Refer to GP with documented CV risk factors.

→ GP diagnosis of CV risk conditions: hypertension and dyslipidemia.
CV-Medication prescribed (Rx): enalapril 10 mg b.i.d. (*bis in die* = twice a day), atorvastatin 20 mg daily.

Pharmaceutical care-II

Monitor for medication nonadherence and potential AE/ADR; intervene as appropriate.

Medical history-II (2012)

Large anterior MI; single vessel disease.
CV-Medication: ASA 100 mg daily, bisoprolol 10 mg daily, enalapril 10 mg b.i.d., atorvastatin 20 mg daily.

Medical history-III (2016)

Hospitalization for decompensated HF.
New diagnoses: Heart failure (NYHA III-IV, re-compensated), type 2 diabetes. BP: 105/70 mmHg (right arm sitting).
HR: 85 bpm (sinus rhythm (SR)).
Lab: K^+ 4.8 mEq/L; eGFR: 45 ml/min/1.73 m^2
CV-Medication: ASA 100 mg daily, furosemide 40 mg b.i.d., bisoprolol 10 mg daily, enalapril 10 mg b.i.d., atorvastatin 20 mg daily. Other: metformin 500 mg b.i.d.

Pharmaceutical care-III

Medication review (3 weeks following discharge).
Make an appointment for a medication review and ask patient to bring his entire medication (Rx and OTC) in a "brown bag".

Results:

GP file (Rx)	Pharmacy dispensed (Rx/OTC)	Patient interview including brown bag and dose according to patient	Drug-related problem (DRP)	Remarks/ Intervention
Bisoprolol 10 mg	Bisoprolol 10 mg		Missing drug; only used sporadically and if HR is high	Inform GP and suggest a starting dose of 1.25 mg and up-titrate every 14 days, if tolerated, to at least 5 mg
Enalapril 10 mg b.i.d.	Enalapril 10 mg b.i.d.	Enalapril 10 mg b.i.d.		
Furosemide 20 mg b.i.d.	Furosemide 20 mg	Furosemide 20–40 mg	Frequent awakening for urination	Take 20 mg in the morning and 20 mg not later than 4 pm. Counsel on appropriate fluid intake and regular monitoring of weight
ASA 100 mg	ASA 100 mg	ASA 100 mg		
Atorvastatin 20 mg	Atorvastatin 20 mg	Atorvastatin 20 mg	Check LDL-C level	LDL-C 105 mg/dL (2.7 mmol/L)
Metformin 500 mg b.i.d.	Metformin 500 mg b.i.d.	Metformin 500 mg b.i.d.	Renal function and HbA_1c?	Ask GP
	Allopurinol 100 mg	Allopurinol 100 mg	GP unaware of this drug	Inform GP
		Diclofenac 25 mg b.i.d.	NSAIDs may worsen HF and drug/drug interaction with ACE inhibitor	Switch to non-NSAID analgesic
		Simvastatin/ Ezetimibe 10/ 40 mg	Duplicate medication; prescribed by other physician	Clarify with both physicians

Document drug-related problems (DRPs) and intervene as mentioned above.

Follow-up (mid 2017)

NYHA II
BP: 115/78 mmHg

HR: 82 bpm (SR)
CV-Medication: ASA 100 mg daily, furosemide 20 mg daily, bisoprolol 1.25 mg daily (+ 1.25 mg every 14 days) → 5 mg daily (if tolerated), enalapril 10 mg b.i.d., atorvastatin 40 mg daily.
Other: Metformin 500 mg b.i.d., allopurinol 100 mg daily, COPD medication.
OTC: Paracetamol 500 (acetaminophen) 1000 mg prn (max. 3 g daily).

Pharmaceutical care-IV

Check inhalation technique (metered dose (MDI) and dry powder inhaler (DPI)) and intervene as needed.
Check HR during and after up-titration of bisoprolol (goal 60–70 bpm).
Offer follow-up medication review (as above).
One result of this medication review is a **medication plan** for Mr. X, consolidated by Mr. X, his GP, and his pharmacist (see below).

Medication Plan for Mr. X (as of 6 September 2017)

(insert) Rx name	Generic name	Dose	Reason
	Bisoprolol	2.5 mg (for next 14 days; than increase to 5 mg)	Heart failure
	Enalapril	10 mg b.i.d.	Heart failure
	Furosemide	10 mg early morning and 10 mg between 2 and 4 pm	Dyspnea/edema
	Acetylsalicylic acid (ASA)	100 mg	Prevention myocardial infarction (MI)
	Atorvastatin	40 mg	Prevention MI, high cholesterol
	Allopurinol	100 mg	Gout
	Metformin	500 mg b.i.d.	Type 2 diabetes
	Fenoterol/ ipratropium 50/20 (MDI)	Daily 3–4 times 1 puff	Chronic obstructive pulmonary disease (COPD)
	Tiotropium 18 (DPI)	OD	COPD
	Paracetamol (acetaminophen) 500	1000 mg (2 caplets) prn (up to 3 g per day = 6 caplets)	Pain

b.i.d. = *bis in die* (twice daily); DPI = dry powder inhaler; HR = heart rate; MDI = metered dose inhaler; OD = once daily; prn = pro re nata; SR = sinus rhythm
Make sure that Mr. X has fully understood his medication plan!

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Chapter 30
Pharmaceutical Care for Patients Receiving Anticoagulation

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Abstract The main anticoagulants traditionally prescribed were predominantly vitamin K antagonists, and the more recent introduction of NOACs has increased the options available to patients and the associated potential drug-related problems. Pharmacists can play a vital role in the pharmaceutical care of anticoagulation management from patient education to ongoing clinical monitoring.

Keywords Pharmaceutical Care · Oral Anticoagulation · Anticoagulation clinic DOAC · Warfarin

30.1 Introduction

Anticoagulants remain the primary strategy for the prevention and treatment of thrombosis. The indication for anticoagulation is widespread and includes prevention and treatment of venous thromboembolism (VTE), acute coronary syndrome to prevent clot extension and most commonly to prevent strokes in people with atrial fibrillation.

Historically, most patients who required parenteral anticoagulation received heparin, whereas those patients requiring oral anticoagulation received vitamin K antagonists (VKA), such as warfarin. Due to the narrow therapeutic index and need for frequent laboratory monitoring associated with warfarin, there has been a desire to develop newer, more effective anticoagulants. Consequently, there have been several novel anticoagulants developed often termed as NOACs for non-vitamin K antagonist oral anticoagulants or DOACs for direct oral anticoagulants and include direct thrombin

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inhibitors (e.g., dabigatran) and factor Xa inhibitors (e.g., rivaroxaban, apixaban, edoxaban) designed to target different points of the coagulant cascade.

Although oral anticoagulation has a beneficial effect on patients' long-term survival and the prevention of thrombotic events [1, 2], the use of these medications is not without risk. Decreasing the ability of the blood to clot decreases the thrombotic risk at the risk of increasing major bleeding, such as gastrointestinal or intracranial bleeding [2, 3]. Most emergency hospitalisations for recognized adverse drug events in elder people result from a few commonly used medications, with a substantial proportion of these events being related to VKA use and bleeding complications being the most common reason for medication-related hospital admissions [4, 5].

As the population gets older, the need for and the prescribing of anticoagulation will increase further, it is becoming essential for any pharmacist involved in managing patients with long-term conditions to become aware of the indications for anticoagulation as well as ensuring appropriate monitoring.

30.2 Treatment Options

30.2.1 Vitamin K Antagonists: VKAs

For many decades, the vitamin K antagonists (VKAs) have been the only oral anticoagulant drugs available for clinical use for the primary and secondary prevention of venous and arterial thromboembolic events. VKAs include warfarin, acenocoumarol or phenprocoumon, but warfarin is the most common oral vitamin K antagonist utilized worldwide [6].

Vitamin K antagonists (VKAs) such as warfarin function by blocking the vitamin K-epoxide reductase, thereby preventing the formation of the active form of the vitamin K-dependent clotting factors [6]. The VKAs have an initial pro-thrombotic effect, by initially blocking proteins C and S, followed by a delayed antithrombotic effect, through the inhibition of coagulation factors II, VII, IX and X.

30.2.1.1 Warfarin

Indications for the use of warfarin include long-term anticoagulation following a thrombotic event or prevention of thrombotic events in patients at high risk, including postoperative states, atrial fibrillation (AF), and those with artificial valves [7]. In view of the initial procoagulant effect, warfarin is often co-administered with a parenteral anticoagulant, which can be discontinued after therapeutic levels are achieved and stable over the course of 24 h. Warfarin is metabolized primarily through the CYP450 system. Induction or inhibition of the isoenzymes involved with warfarin's metabolism can potentially influence INR

significantly. Furthermore, alteration in oral vitamin K consumption can create significant fluctuations in INR [8].

The level of anticoagulation with warfarin is expressed as the International Normalized Ratio (INR), which is derived from the ratio between the actual prothrombin time and that of a standardized control serum [9]. Indeed, the efficacy of warfarin depends on maintenance of the INR within the designated therapeutic range. For instance, the available evidence indicates a higher incidence of ischemic stroke in patients with AF with insufficient anticoagulation (INR < 2), and a higher incidence of bleeding events in over-anticoagulated patients with non-valvular AF (INR > 3) [10].

Therefore, based on achieving a balance between stroke risk with low INRs and an increasing bleeding risk with high INRs, an INR of 2.0–3.0 is the optimal range for prevention of stroke and systemic embolism in patients with non-valvular AF [9].

So while warfarin continues to be widely used in clinical practice and although it has shown to reduce the risk of stroke by 60% [1], its efficacy is dependent on achieving a time in therapeutic range (TTR) above 65% [11], which has often proven to be challenging to attain and requires doses to be tailored to the individual based on the INR. An evaluation of outcomes among patients randomized to warfarin therapy according to anticoagulant control has continuously shown that poorer control as assessed by TTR (<60%) is associated with greater mortality and major bleeding as compared to good control (TTR > 75%) [12]. National and International guidelines recognize the complexity of managing warfarin and have recommended that for any person receiving a VKA, the adequacy of anticoagulant control be assessed and if control is poor, taking into account possible factors that may have contributed to poor anticoagulation control, e.g., adherence, interacting drugs, etc., to review choice of agent in particular following the introduction of the more recent NOACs within their license [9, 11]. The complexity of dosing to attain good INR control has also led to pharmacogenetic studies undertaken to assess the utility of genotype testing in choosing an initial dose of VKA and initial suggestions are that it may offer improvements in INR-related and clinical outcomes [13].

Several studies have assessed the impact of pharmacist-managed anticoagulation clinics, demonstrating that pharmacists impact positively warfarin management leading to better INR control and reduced rates of thromboembolic complications compared with standard care [14, 15].

In order to overcome some of these limitations, four NOACs—dabigatran, rivaroxaban, apixaban, and edoxaban—have been approved as options for the prevention of stroke and systemic embolism in patients with non-valvular AF, treatment of VTE and with the exception of edoxaban at the time of print prophylaxis of VTE post hip or knee replacement [16–19].

When compared to warfarin, NOACs offer several advantages with their rapid onset of action, short half-life, less drug interactions, no dietary interaction and fixed dose response without the need for frequent monitoring [2] These agents have been demonstrated to be as safe and effective as warfarin [2] being now the preferred option in European guidelines [9].

30.2.2 Non-vitamin K Antagonist Oral Anticoagulants: NOACs

In simplified terms, the NOACs act at either of two specific levels of the clotting cascade. Dabigatran is a direct thrombin inhibitor, whereas apixaban, rivaroxaban and edoxaban are direct factor Xa inhibitors [2]. Therefore, direct targeting of factor Xa or thrombin allows for a rapid onset of anticoagulation effect, expected to begin 2 h following the first dose; as well as the loss of anticoagulant effect within 24 h after discontinuation of these drugs [9]. Characteristics of each of these agents are displayed in Table 30.1 (adapted from ESC 2016 guidelines) [9].

NOACs have predictable pharmacokinetics and pharmacodynamics and a lower potential for food and drug interactions. These agents can, therefore, be given at fixed dosing schedules without the need for routine coagulation monitoring [9]. All NOACs are partially eliminated via the kidney. Therefore, the assessment of kidney function is important to estimate their clearance from the body. Based on these properties, apixaban, edoxaban, and rivaroxaban [16, 17, 19] are not recommended in patients with AF who have CrCl < 15 mL/min and dabigatran [18] is

Table 30.1 Pharmacokinetic and pharmacodynamic properties of NOACs

	Dabigatran	Apixaban	Rivaroxaban	Edoxaban
Mechanism of action	Oral direct thrombin inhibitor	Oral factor Xa Inhibitor	Oral factor Xa inhibitor	Oral Factor Xa inhibitor
Bioavailability (%)	6	50	60–80	62
Plasma protein binding (%)	35	87	92–95	55
Time to peak levels (h)	0.5–2.0	3–4	2–4	1–2
Half-life (h)	12–14	12	5–13	10–14
Dosing frequency NVAF VTE treatment and Prevention recurrent VTE	Twice daily Twice daily after heparin lead in	Twice daily Two tablets Twice daily (7 days) then twice daily	Once daily Twice daily (21 days) then once daily	Once daily Once daily after heparin lead in
Excretion	85% renal	27% renal	66% renal	50% renal
CYP metabolism (%)	None	25	≈66	<10
Transport proteins	P-gp	P-gp, BRCP	P-gp, BRCP	P-gp

BRCP breast cancer resistance protein, *CYP* cytochrome P450, *P-gp P-glycoprotein*

contraindicated in patients with CrCl < 30 mL/min. However, there are no effectiveness and safety outcome data for NOACs in patients with advanced CKD (CrCL < 30 mL/min), and the current ESC Guidelines recommend against their use in such patients [9].

NOACs are all substrates of P-glycoprotein (P-gp), a transport protein present in enterocytes and the liver which reduces the bioavailability of its substrates [20]. Hence, even if the potential for drug–drug interactions is less with NOACs compared to VKA, there is still a significant potential for interactions and caution is required when they are co-administered with drugs such as verapamil, amiodarone and dronedarone [20]. By contrast, drug–food interactions are not expected with the NOACs as vitamin K intake does not influence their mechanism of action [20].

30.3 Pharmaceutical Intervention: The Role of the Pharmacist

Oral anticoagulants are often classified as high-risk medicines, based on serious and often fatal errors that occur with these drugs, emphasizing the particular effort and role of the pharmacists to improve medication safety [21].

Besides the risk of drug-related problems due to pharmacological properties of oral anticoagulants (bleeding and interactions), both healthcare professionals and patients should be actively supported to ensure safe and effective medication care. Studies have indicated the potential for errors associated with oral anticoagulants. Oral anticoagulants are often under dosed, inadequately monitored, inadequately stored and not taken as prescribed, increasing the risk for adverse drug events in patients receiving oral anticoagulation [22].

Both the European Heart Rhythm Association (EHRA) and the European Society of Cardiology (ESC) reiterate the need for a structured follow-up of anticoagulated patients as essential for patient safety in their updated versions of the guideline for NOACs [23] and the guideline on the management of atrial fibrillation [9], respectively. Recognizing the numerous healthcare providers (e.g., physicians, nurses, pharmacists, general practitioners, anticoagulation services) involved in the management of patients receiving oral anticoagulation therapy, efficient multidisciplinary collaboration and communication is required to ensure safe patient care between different care settings.

A study conducted in Denmark with the purpose to describe the severity of adverse medication incidents caused by oral anticoagulants in hospitals showed that all fatal and almost all serious adverse medication incidents were associated with the prescribing phase of the medication process. In addition, this study also showed that during admission and surgery, prescribing excess anticoagulant was the most frequent problem and, on the other side, during discharge, prescribing insufficient anticoagulant was the most frequent problem [24].

Reviews highlight the importance of patient counseling, ensuring the individual understands the purpose of the anticoagulant therapy. More about counseling can be found in Chap. 4. An outline of the relevant information to include is listed below [25].

- Indication for the anticoagulation;
- Start date and expected duration of treatment;
- The dose of anticoagulant;
- What to do in case of missed dose;
- The importance of adherence;
- When to seek medical attention;
- Potential drug interactions and adverse effects;
- The need for regular blood tests as well as dietary advice (for patients prescribed warfarin);
- The importance of carrying an anticoagulation alert card.

Patient education on anticoagulation is key to monitor and manage adverse drug reactions such as bleeding. Patients should be advised to manage minor bleeding symptoms by applying pressure to the affected area, if there is a small wound or minor nose bleed. Whereas nose bleeds lasting longer than 10 min and blood in urine or black tarry colored stools which may indicate internal bleeding are examples of red flag symptoms, which require the patient to seek medical attention immediately. Co-prescribing of drugs that may increase the risk of bleeding is also a common problem, such as nonsteroidal anti-inflammatory drugs (NSAIDs) which can be bought over the counter. The use of antiplatelet agents alongside anticoagulants should also be avoided unless specifically indicated, for example, following an acute coronary syndrome or percutaneous coronary intervention [2].

While persistence with NOAC therapy has been reported to be greater than with warfarin [26, 27] and routine monitoring (besides renal function) is not required, pharmacists have a critical role to play in supporting NOACs adherence. In particular, the half-lives of NOACs are shorter than that of warfarin, so the anticoagulation effect of NOACs declines more rapidly when scheduled doses are not taken. Therefore, nonadherence to NOACs might have larger adverse effects than warfarin and the adherence itself may be related to the index medication [28]. NOACs dosing frequency differs in that apixaban and dabigatran are twice daily whereas rivaroxaban and edoxaban is once daily and rivaroxaban requires to be taken with food to optimize absorption. Dabigatran being moisture sensitive is therefore not suitable for use in a medicine compliance aid.

Pharmacists have a role in ensuring appropriate dosing of NOACs is undertaken based on renal function. However, it is worth noting that the clinical trials of NOACs for stroke prevention in atrial fibrillation (AF) used the Cockcroft–Gault (CG) equation to estimate creatinine clearance as a measure of renal function and subsequent assessment of drug eligibility and dosing were determined. A cross-sectional study demonstrated when using the Modified Diet in Renal Disease (MDRD) formula (a more widely available and more commonly used

equation for assessing Creatinine clearance) instead of the CG formula (used in clinical trials), patients would receive higher doses or be deemed incorrectly suitable for eligibility for NOAC treatment, yet the safety and efficacy of using the MDRD equation have not been established [29].

To safeguard appropriate prescribing for NOACs in non-valvular AF (NVAF), a simple ABCD can be used whereby (Fig. 30.1);

- A—age—certain NOACs require a consideration for dose reduction depending on age
- B—body weight—certain NOACs require a dose reduction if body weight <60 kg
- C—creatinine clearance (Cockcroft–Gault)—all NOACs are dependent on renal function and require a dose reduction as renal function decreases
- D—check for drug interactions—all NOACs may interact with p-glycoprotein inhibitors or drugs that may induce or inhibit cytochrome P450 system—check against summary of product characteristics.

Many patients may need to undergo surgery, and a number of factors are required to be considered in regards to anticoagulation when a patient is due to undergo an invasive procedure such as whether to interrupt therapy, when to interrupt, whether to bridge, how to bridge and finally how to restart patients usual therapy. Evidence [30] suggests that forgoing bridging anticoagulation was non-inferior to bridging warfarin with LMWH for low-risk AF patients. Therefore, a risk stratification for the bleeding and thrombosis needs to be adopted to guide the management in the perioperative period.

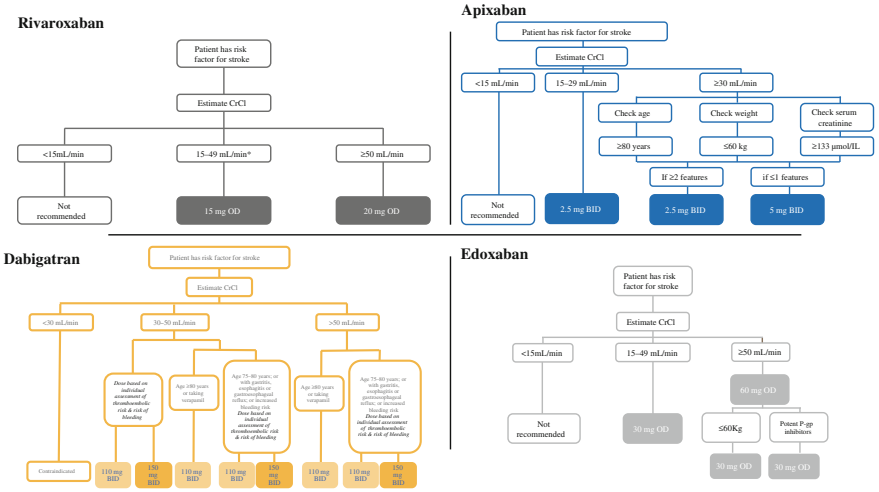

Fig. 30.1 Dose adjustments for NOACs in non-valvular AF and application of the ABCD rule

Case Scenario

Mrs MC, 76 year old, 80 kg comes in your pharmacy with a prescription for enoxaparin 120 mg to be administered once daily to start 3 days preoperatively given to her in pre-assessment clinic. She tells you that she is having a hip operation next week and has to stop the warfarin **5** days before the operation. She is concerned about stopping the warfarin and not being on any medication for 2 days before starting the injections, she asks whether her heart will be protected.

On reviewing the warfarin monitoring booklet, you discover the indication is atrial fibrillation (AF) and her INR test carried out today is 2.5.

Other past medical history:

- Hypertension
- Heart failure
- Diabetes
- Angina—PCI 10 years ago

Step 1: Initial assessment

In view of the vast indications for anticoagulation, it is important to ensure that the patient understands the reasons for their prescribed medication. For patients that are established on therapy, it should not be assumed that they know why they are taking it. Here the role of the pharmacist is to educate Mrs MC that the anticoagulation is for stroke prevention rather than correction of the electrical activity of the heart. As Mrs MC is worried about not taking any anticoagulant for 2 days, the pharmacist can explain that warfarin can take up to 3 days for it to be cleared from the body based on its long half life. Therefore Mrs MC can be reassured that there still is an anticoagulant effect after missing a dose of warfarin. Once the INR is subtherapeutic, enoxaparin is administered instead.

This encounter with the patient is also an opportunity to advise the patient to inform their anticoagulation clinic of this interruption in therapy as many healthcare professionals are involved in the patients' pathway of anticoagulation management. This is important in view of many errors involving these high-risk medications that are associated with the transfer between different care settings.

Step 2: Treatment plan

Mrs MC is due to undergo a major surgery which is associated with a high bleeding risk therefore warfarin interruption is required. For INR readings between 2 and 3, warfarin discontinuation is recommended 5 days before procedure.

To determine whether to bridge with LWMH, a risk stratification of thrombosis should be calculated. For AF patients, the risk of stroke is calculated using the CHA_2DS_2VASc score as per table below:

Risk factor	Score for the risk factor	Mrs MCs' score
Congestive heart failure	1	1
Hypertension	1	1
Age ≥ 75	2	2
Age 65–74	1	0
Diabetes	1	1
Stroke/TIA/Thromboembolism	2	0
Vascular disease	1	1
Female	1	1
Total	9	7

A CHA_2DS_2VASc score of 7 or higher is considered as high risk, therefore bridging with a LMWH is required.

As the formulation of anticoagulation has now changed, it is key to ensure that the patient either is aware on how to administer the subcutaneous injection or arrangements are in place for administration by a carer or district nurse.

Six months following the hip operation, Mrs MC comes into your pharmacy with a new prescription for apixaban 5 mg twice daily. Since her operation, she has been getting her INR tested weekly in view of her poor control and has been finding it difficult getting to the hospital. The doctor told her that her TTR is 50%, therefore a decision to switch to a different anticoagulant has been made. She tells you that she is happy that no more frequent monitoring is required.

Step 3: Monitoring

The parameters for monitoring when switching between anticoagulants is variable dependant on the agents are involved. When switching from warfarin to a NOAC, the INR should be less than 2 before starting the NOAC.

On initiation of a NOAC, the monitoring of bleeding advice would be similar to that of warfarin. Whereas NOAC-specific monitoring would involve checking patient adherence and supporting with medication aids or reminders if this issue arises. The dose of apixaban is dependent on the patients' Age, Body weight, renal function (Creatinine clearance) and any potential Drug interactions (ABCD algorithm), therefore dose adjustment should be made accordingly. The ongoing monitoring of the renal function is guided by the baseline creatinine clearance (CrCl) by using the following formula; CrCl/10 = x months. For example if the baseline creatinine clearance is 50mls/min, this will mean that ongoing monitoring function should be approximately 5 months.

Other factors to monitor would be to check for any changes in patient's medication therapy which could potentially interact with the NOAC as well as monitoring the patients' blood pressure as uncontrolled hypertension can add to the patients bleeding risk.

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Chapter 31
Pharmaceutical Care in Pediatrics

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Abstract When providing pharmaceutical care to the pediatric population, pharmacists need to take extra care, and be vigilant to try to prevent some of the common drug-related problems that have previously been reported too commonly for this cohort. Through the medication review process (see Chap. 6), pharmacists make recommendations on appropriate dose adjustments, intercept potentially harmful medication errors, determine patient adherence, identify drug-related problems, and take action where necessary such as educating parents and children themselves. Considering that pediatric patients are more likely to experience adverse drug misadventures, they may need a narrower follow-up period than their adult counterparts, and pharmacists are able to apply advanced pharmaceutical and therapeutic knowledge to monitor for adverse, as well as positive outcomes.Some important general principles when treating children should be followed:

1. If the infant is very young (less than 3-6 months), then most often a referral would be appropriate.
2. If the child is very ill (lethargic, listless, and inconsolable), referral is required.
3. If a medication is to be given, then make sure the dose explained to the caregiver is correct (many medicines will be dosed according to weight).
4. Show the caregiver how to effectively administer/use the medication (e.g., show them how to use a syringe for measuring liquid medications).
5. Involve the child (when old enough to take part) in their own care and encourage communication between the child and their parents, because at some stage the child will be responsible for their own medication use.

Keywords Pharmaceutical care · Pediatrics · Medicine administration
Adverse events · Parental supervision

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31.1 Introduction

Pharmacists can assist caregivers to manage children's minor ailments or even children's chronic diseases through the provision of pharmaceutical care. The principals in providing pharmaceutical care in pediatrics are not so different to those that we apply to adults, although it must be noted that depending on the age of the child, pharmacist may be speaking and educating predominantly the caregiver. However, as children get older it is recommended that they become involved in their own pharmaceutical care. In fact, research suggests that children perceive themselves as active participants in medication use and claim they are more autonomous than their parents perceive [1, 2]. This pinpoints the need to educate both children and their caregivers about rational medication use.

It should be acknowledged that while pharmacists as health care professionals (HCPs) are at the forefront of promoting children's empowerment in medication use, parents should not be left out. Studies have illustrated that parents are not only influential in affecting their child's medication use and health outcomes, but also health-related orientation and expectations to use medication in the future [3]. This is because children indirectly adopt their parents' perception, knowledge, and habits through daily interaction, a process also known as the socialization pathway [4]. As shifting of primary responsibility of medication use from parents to children is unavoidable as part of the growing up processes, the USP has encouraged parents to empower children by involving them in and negotiating gradual transfer of responsibility in medicines use with their offspring [5]. These are essential things to consider when thinking about providing pharmaceutical care to the pediatric population.

This chapter uses pain and fever, colic, coughs, and colds, in the minor ailments category highlighting in these scenarios the important information to be disseminated to parents predominantly as these are minor ailments often occurring frequently in very young children. In the chronic conditions space eczema and asthma have been used as examples to highlight pharmaceutical care provision involving both children and parents as active partners.

It must be noted that as well as the extra complexity of needing to provide information to both children and caregivers, the use of medicines in children has a number of additional challenges that may not exist in treating the adult population. Firstly a child's age and size can affect the pharmacokinetics and dynamics of many medicines. This means that we often need to classify children according to age and size and not just treat them as mini adults. Most doses in children also need to be calculated by weight adding extra complexity. Errors in dosing either at the prescribing or the administration stage are also common. And finally there are many medicines used in pediatrics that are used outside their approved guidelines. This is known as "off-label" prescribing. It is these complexities that make it essential for pharmacists to be extra vigilant when providing pharmaceutical care to the pediatric population.

31.2 Patient Group Definitions

The definition of a child can vary from reference to reference, hence, cohorts of children that pharmacists provide services to under the umbrella of pediatrics can be from birth to 21 years of age (adulthood). However, for the purpose of this section, we will be focusing mainly on children from birth to 12 years of age, where the dosing of most medicines in this cohort are more specific and often extra steps in dose manipulations are required in these age groups.

Neonates are classified as children from birth to one month of age. The neonatal period is a period where a vast amount of physiological change occurs. This means that there are some very specific doses of medicines given to babies in this period that take into account theses rapid changes as well as the varying rates of gastric emptying, the extent of drug absorption, and renal and hepatic clearance of drugs. As neonates are a specific category of children that should be under specialist medical care if requiring medicines, treatment of this age group is outside the scope of this book.

Infants are defined as children from 1 month to 2 years, *young children* are considered from two to six years and a *child* is defined as being from 6–12 years. This section of this book will be covering medicine administration predominately for common minor ailments as well as looking at Asthma as an example of a common chronic condition for children in these age categories.

31.3 Dose Considerations

The majority of doses in pediatrics will be calculated based on the child's weight. That is they will be dosed by multiplying the child's weight by the recommended number of milligrams (mg) for a particular medicine. For example, paracetamol's standard dose for a child under 12 years is 15 mg/kg per dose. However, in children that have a significantly different weight to their ideal body weight, for example in an obese child, there will be times that the dose will be calculated on ideal body weight based usually on the medicine's ability to disperse into adipose tissue. Therefore, in an obese child, extra dosing considerations need to be made to calculate the dose based on ideal body weight for height.

Dosing errors are unfortunately far too common in children and often occur at the time of prescribing or at the time of dose administration. Due to the increased need for dose calculations, dilution, and manipulation of medicines, a substantial proportion of preventable dose errors are reported to be 10 and 100 fold errors [6]. Dose errors however also extend into the home environment where research has revealed that the majority of caregivers when asked to state and measure a dose of paracetamol for their child will administer an inaccurate dose for the child's weight [7, 8]. Other research has shown that parents often choose a household spoon rather than a standardized graduated measure such as a syringe, also leading to inaccurate doses [9].

31.4 Management of Minor Ailments

In this section we will cover three minor ailments. (1) Colic which affects a large number of infants; (2) Pain and Fever; and (3) Coughs and colds which affect all children. As all parents/caregivers will find themselves needing to manage common ailments, and while medicines are available to treat many symptoms, often these common ailments require non-pharmacological management, and pharmaceutical care services to parents/caregivers require pharmacists to provide more advice and reassurance, than medicines.

31.4.1 Colic

Colic refers to "paroxysmal abdominal pain associated with severe unrelenting crying" commonly occurring in children aged under 6 months. Colic is often the label that is given to describe the reason for crying in infants but it must be noted that all babies cry, with crying intensity peaking at about 6 weeks and abating by 12–16 weeks. Colic itself has been defined as inconsolable crying for more than three hours a day and more than three days per week for a period longer than 3 weeks. It affects approximately 10–40% of infants [10]. Crying is often worse in the late afternoon or evening. Wind is often blamed as the culprit as many infants will draw up their legs, arch their back, redden their face, frown or grimace as well as pass wind. However, it has been suggested that these are in fact normal infant crying behaviors and not necessarily gastrointestinally related. Many parents/caregivers, however, feel that there may be a gastrointestinal cause to their infant's crying and hence turn to over-the-counter (OTC) or prescription products for help.

Medications Medication that have been indicated for colic treatment have included Infant drops containing belladonna alkaloids atropine, hyoscine, and hyoscyamine or other anticholinergic agents such as dicyclomine. These work on the basis of reducing gastrointestinal motility, however current guidelines recommend avoiding use due to adverse effects. In some countries these medicines were available over-the-counter whereas in other countries they were restricted to physician prescription. Simethicone drops are also commonly used for colic on the basis that they will act as a surfactant to merge small wind bubbles together. Other agents sometimes used include homeopathic formulations containing bryonia, chamomilla, colocynthis, magnesium phosphate, or Gripe water in which ingredients vary according to manufacturers but variously include: dill seed oil, caraway oil, cinnamon bark oil, clove bud oil, cardamom oil, coriander oil, fennel oil, peppermint oil, filipendula ulmaria (Meadowsweet) extract. More recently probiotics have been trialed for colic, and finally, sometimes proton pump inhibitors are prescribed [10]. What is most important however is that there is conflicting evidence as to whether any of these treatments provide relief and whether they are necessary [10–14].

Medication Errors/Drug-Related Problems Infant Drops containing belladonna alkaloids or dicyclomine have been indicated for use in infant colic, however use of these drops has resulted in anticholinergic toxicity; symptoms include agitation, sedation, irritability, seizures, and coma in serious cases [15]. In Australia data indicate a number of calls to poison's information centers before these belladonna alkaloid products were discontinued with 10- fold dosing errors of colic medicines in general being a common reason for calls to the centers [15, 16]. In a USA study, the most common reason for errors when dosing colic medicines was also found to be a misunderstanding of the instructions. Often parents administered full droppers of medicine instead of a discrete number of drops. Furthermore, caregivers admitted to administering these medicines more frequently than advised [17].

Caregiver Management of Colic Parental support and reassurance are the key components of colic management especially for first time parents [10]. Firstly, pharmacists should be ensuring there are no symptoms that would suggest something other than colic and hence require immediate referral. These could include lethargy, feeding refusal, fever or a distended abdomen that could implicate serious underlying illness if associated with inconsolable crying. Other questioning should be about the infant's bowel habits, checking for diarrhea or constipation and also checking if the infant has been vomiting. Again these symptoms lend themselves to more sinister pathology and referral would be appropriate. Furthermore, questioning around feeding and weight gain is also required. If the child has no other signs or symptoms of serious pathology and seems otherwise well, most commonly advice and reassurance is what is required. When it comes to selecting medicines the following issues should be considered.

The probiotic *Lactobacillus reuteri* has been shown to reduce colic symptoms in some trials; however, the latest evidence suggests it is only effective for colic treatment in breast-fed infants. Simethicone, while widely available and commonly used, seems to be safe, however has not been shown to be effective in reviews. Herbal and Homeopathic drops have limited evidence for their efficacy. Anticholinergic agents such as dicyclomine are contraindicated in infants less than 6 months due to adverse effects and should not be recommended. Proton Pump Inhibitors have also not been shown to be effective in reducing crying time.

Therefore in general, when providing pharmaceutical care to a colicky baby, as they are in the infant stage, the care is directed to the parent/caregiver only due to age. The pharmacist has a role in guiding caregivers in their treatment choices and making sure referral to the physician occurs when required. Trailing a change of infant formula and seeking advice about specialized formulas could be recommended in formula fed babies and assisting maintenance of breast feeding in breast-fed infants should also be encouraged.

31.4.2 Pain and Fever

Pain is often formally defined as "an unpleasant sensory and emotional experience, associated with or expressed in terms of actual or potential tissue damage" [18]. An alternative definition is "Pain is whatever the experiencing person says it is, existing whenever the experiencing person says it does" [19]. Both of these definitions highlight that pain is more than just tissue damage triggering a response from the nervous system, hence its treatment involves more than just treating tissue injury. To further complicate the issue, children and especially infants are often unable to describe or express the pain they are suffering, making treatment even more complex.

When assessing pain in children it is important to ask questions regarding intensity, duration, description, the impact the pain is having on activities and factors that may influence a child's perception of pain which may include past history, or family or cultural aspects.

Fever is a normal physiological response to infections and is recognized as a core body temperature of 38 °C or greater [20]. Depending on where the temperature is taken (rectal, oral, axillary, tympanic), fluctuations in thermometer readings will however be seen. It is recommended that for most children in the home setting that an axillary thermometer is used as they are cheap to purchase and relatively easy to use. Fever is a common occurrence especially in children, and nearly all caregivers will find themselves needing to manage fever for their children at some stage. While there is evidence that the analgesic agents will decrease temperatures by a modest amount, it is important to realize that fever itself does not require treatment and that the benefit of these analgesic agents is therefore on the pain associated with fever and even these benefits are not conclusive. However, fever in children three months or younger should be immediately referred for further investigation.

Medications Paracetamol and ibuprofen both are effective in relieving pain with or without fever in children and they both have few side effects when used correctly for short-term use.

The recommended dose of paracetamol is 15 mg/kg every 4–6 h with a maximum of 4 doses in 24 h (60 mg/kg), and this should be used for up to 48 h only at this maximum dose in the community setting. In the hospital setting slightly higher doses may be seen, but these are reserved for severe pain usually in an Intensive Care Setting. The recommended dose of Ibuprofen is 5–10 mg/kg every 6–8 h hence a maximum of 40 mg/kg/day.

Although many of these products are available for administration via the oral, rectal, and intravenous route, the oral route is preferred. In fact, the rectal route has highly unpredictable absorption and is therefore not a recommended administration route if it can be avoided [21].

Medication Errors/Drug-Related Problems Paracetamol and Ibuprofen use, and misuse, in children is ubiquitous. They are the most commonly used over-the-counter

(OTC) medicines in children and the most common medicines kept at home [22, 23]. The published literature demonstrates that most misuse can occur due to accidental ingestion; [24] inappropriate administration; false parental/caregiver beliefs of efficacy and safety; and inability to use as directed. Moreover, most parents remain unaware of the side effects of OTC medicines and there is evidence suggesting that medicines are often used for inappropriate indications, including the use of paracetamol to sedate children.

In overdose both Ibuprofen and Paracetamol are dangerous, so correct dosing is paramount. There are many dosages of liquid paracetamol and liquid ibuprofen available. With these formulations, there are different marketing strategies guiding the various strengths to be used. For example, the strongest paracetamol liquid is marketed for use in babies, so that very small doses are to be given. In contrast the weakest liquids for both ibuprofen and paracetamol are often marketed for 1–5 year olds. In addition in many countries there are age and weight dosing instructions on the packaging with often the dose indicated as a range such as 6–8 mL. Due to all these factors it is easy for parents to make errors when calculating or measuring a correct dose of medicine for their children [7, 8].

Furthermore, unfortunately research continues to demonstrate that caregivers inappropriately manage fever and adopt practices not stipulated in current guidelines. Studies have reported that caregivers respond to fever with significant concern, perceiving it as harmful with detrimental bodily effects such as neurological damage, organ damage, and death which are not true [25, 26]. Some recent research at the University of Sydney revealed that negative attitudes toward fever, aiming to reduce the temperature, misinformed views of medications, and misunderstanding of package labeling were the main factors driving inappropriate behavior of caregivers when treating fever. This research also revealed that fever management was only appropriate in 15% of caregivers interviewed [27]. These data suggest that pharmacists need to spend time counseling caregivers on appropriate pain and fever management, and if a medicine is to be used, explaining how and when to dose as suggested above, is important.

Caregiver Management of Pain/Fever For pain that involves inflammation like a sprained ankle for example, Ibuprofen may be more suitable than paracetamol in this case, due to its anti-inflammatory effects. For other simple pain, a choice of one or the other agent should usually be made and often paracetamol is first choice for many due to its long safety history when given correctly. For moderate to severe pain, sometimes a combination of products can be recommended, however commonly in children with mild pain or fever, one agent alone will be enough. There are also non-pharmacological things that can be done in conjunction with analgesia to comfort a child in pain. Some of these include having a parent comfort the child, allowing the child to ask questions if they are able, or advising the child to focus on deep and steady breathing. Distraction methods can also be very helpful, so the use of books, video games, or television are commonly used distractions. Play is an excellent distraction also, but it should be noted that just because a child is able to play, it does not mean the pain has gone away. Positive affirmation like—"you are

doing great" are also recommended as well as comforting the child through plenty of cuddles and attention. Ice packs or heat treatments are also sometimes used. For fever, removing one layer of clothing and keeping the child hydrated are also very important.

As pharmacists it is important that we guide parents to the weight-based dose instructions, and we give caregivers an exact dose to measure based on the child's weight (unless the child is obese). We should give an oral syringe to assist with dose measurement and show caregivers how to use this syringe. Research has shown that only about one third of parents will get the dose right for their child [7, 8], hence this advice is extremely important. In the community setting, it is best to advise a caregiver to choose only one medicine and stick to it. For example, if Paracetamol is the medicine chosen, then this should be the only medication used for the condition. While a combination of both paracetamol and ibuprofen may be required for some more severe pain in children, this is best only used on the advice of a doctor, as mistakes with one product are very common, hence mistakes with two products would seem to be much more likely if combinations are used. While we see the practice of using two medications commonly, particularly for fever, there is no need to alternate or dose two medicines together, as the fever is normal biological response to infection that does not need treatment. Instead as pharmacists we should be encouraging practical non-pharmacological management such as removal of clothing and increased fluids and rest.

When thinking about the pharmaceutical care issues involved in pain and fever management in a pharmacy setting, if the child is verbal they should be involved in the decisions around their treatment and included in the choice to medicate. As errors in the use of analgesics are so common, the pharmaceutical care dosing principles should be passed onto parents, and in turn their children as early as possible, to perhaps break this cycle of poor medication administration.

31.4.3 Cough/Cold

The common cold is most often a self-limiting virus which can affect people of all ages. The average child will have six to eight colds per year, with those attending childcare having on average 10 colds per year [28, 29]. Symptoms generally include nasal blockage or rhinorrhea, sneezing, coughing, headache, and fever. Medicines available OTC for colds and flus only provide symptomatic relief, and no study has proven the efficacy of cough and cold medicines in improving the rate of recovery in young children. Generally, children will eventually improve on their own in 10–14 days without any treatment.

Medications, Medication Errors, and Drug-Related Problems Many OTC cough and cold products contain multiple substances, including a decongestant, antitussives, antihistamine, and sometimes analgesics/antipyretics. When taken in high doses, decongestants such as pseudoephedrine result in central nervous system

stimulation, hypertension, and tachycardia. Serious complications after ingestion include hypertension, tachycardia, bradycardia, seizures, stroke, and cerebral hemorrhage [30, 31]. These concerns have resulted in the release of safety advisories from various regulatory bodies in developed countries, discouraging the use of these medications in young children in recent years.

For blocked noses in adults, we would use decongestants. Oral decongestants may include: phenylephrine and pseudoephedrine. In children, there is no evidence that these products improve symptoms and unfortunately there are case reports of adverse drug events. For this reason, these products are not to be sold over-the-counter for children under two and are not recommended for use in children under twelve due to their limited efficacy data, in many developed countries. Topical decongestants (Oxymetazoline and Xylometazoline) are less well studied, but with the limited studies available, there is still no evidence to recommend these products for children. Other products that are common in cough and cold preparations to treat nasal symptoms are antihistamines. The evidence regarding sedating antihistamines contained in cold and flu products for children is clear that these have no benefit in treating colds, and are associated with an increased risk of adverse effects and even sudden infant death. Preparations containing sedating antihistamines cannot be recommended for children under two years of age. Vapor rubs and essential oils have been associated with case reports of seizure, although most of these follow accidental ingestion rather than topical application. The evidence however for the effectiveness of these rubs is also lacking, and only the baby balsam formulas can be used for children under two.

For dry coughs the usual recommendation in an adult might consist of a cough suppressant. In children however, we also have no evidence to support the use of such products. In fact, a recent review found that cough mixtures were no more effective than placebo for both children and adults. Cough suppressants should not be recommended for children in general, and cannot be sold legally without a prescription for children under two.

The research surrounding cough mixtures for chesty coughs is also unclear and while there may be less safety concerns with some of these products (e.g., bromhexine), we still do not have firm outcomes on their efficacy in children.

Caregiver Management of Coughs and Colds Nasal saline drops have proved to be safe for blocked and runny noses and therefore can be used. It is important to encourage children to clean out the nasal passages through blowing their nose, to avoid secondary sinus infections. Saline drops can certainly help with this. Honey can help sooth coughs; however this should only be in children over 12 months of age as in children less than one year of age honey has been associated with infantile botulism. Common sense prevails and of course children should be advised to intake more fluids (water) and rest. Paracetamol or Ibuprofen can be given if the child is very miserable due to pain/fever, but if they are eating, drinking, and still happy, no doses are required. The use of a steam vaporizer or humidifier could be used, although if this is recommended, a very firm warning for parents to put these out of reach of children is warranted, as they have been associated with steam burns if they are in a child's reach.

It is important to provide patients information regarding their children's colds and give them realistic expectations. They should be advised that there is no cure for their child's cold and practical things such as rest, increased fluid intake, and adequate nutrition are the mainstay of treatment. Although there are many liquid medicated cough and cold products (usually containing a combination of decongestant and a drowsy antihistamine or an expectorant or a cough suppressant) available to treat children, most of them are not suitable for children under six years of age. With this in mind, nondrug treatments should always be your first choice when treating children.

Pharmacists should recommend caregivers to see a physician when there is:

- Persistent symptoms for more than a week especially persistent nocturnal cough
- Fever—38 °C or higher for more than 3 days or in a child under three months
- Suspected dehydration
- Blood in sputum
- Cold causing exacerbation of asthma
- Tonsillar exudate
- Or sudden worsening of a child's symptoms that are worrying to the caregiver

As for pain and fever, children that are verbal should be involved in the decision-making around their treatment of the common cold, again in order to empower the next generations to break the cycles of nonevidence-based treatments. We must try to educate the public (both adults and children) that the common cold still has no magic medicine available to cure it.

31.5 Pharmaceutical Care in Chronic Conditions/ Complex Situations

When it comes to managing chronic conditions in children, it could be perceived as even more important that children are involved in their pharmaceutical care as soon as possible, and that as they grow, more and more autonomy is given to them. A snapshot of literature illustrated that delegation of responsibility is not an easy decision for parents to make. For chronically ill children, premature transfer of responsibility could lead to poor health outcomes [32] due to children's inability to cope with the increased responsibility. On the other hand, delayed transfer and "miscarried helping" can interfere with the development of children's autonomy and promote excessive reliance on others. Moreover, studies have demonstrated that deterioration in health outcomes is usually observable during adolescence, the time when parents allocate more self-management responsibility for chronic illness to their offspring, despite the rise in children's knowledge and skills. These findings call for the establishment of collaboration between pharmacists, parents, and children so that a smooth transition that upholds the quality use of medicines can be achieved.

31.5.1 Eczema

Atopic dermatitis or (eczema) is a common inflammatory skin condition which is associated with other atopies such as allergic rhinitis and asthma. Most children who develop atopic dermatitis will do so before the age of two years and it is estimated that around 20% of infants under two years will experience it. Indeed, the prevalence of atopic dermatitis is growing rapidly. While atopic dermatitis is considered a chronic condition (and this should be made clear to the family), most children will experience flare-ups interspersed with periods of time when the skin is not inflamed. The goal of treatment is to completely clear the skin between flare-ups and to swiftly reduce inflammation when the skin flares up.

In order to minimize the chance of flare-ups the following, lifestyle measures can be undertaken to improve the barrier nature of the skin's defense.

- Using soap-free washes where possible
- Having shorter showers and running more tepid (than hot) water
- Avoiding known irritants like chlorine, grass, and sand
- Using simple emollients, particularly when the skin begins to look dry and flaky.
- When the skin is inflamed, the first-line treatment is topical corticosteroids.

Using Topical Corticosteroids (TCs) Effectively Topical corticosteroids (TCs) should be used early, liberally, once daily to all areas of inflammation including broken skin and even up to the borders of wounds. They are best applied when the skin is damp, such as after a shower or bath. They should be used for at least 1–2 weeks and stopped only when the skin is looking not inflamed and restarted again if needed. Some patients will require long-term treatment. For longer treatment periods, intermittent therapy such as every other day, weekend-only application or a resting period of 1–2 weeks between cycles may be an option.

In the past, many medical practitioners and pharmacists have been very cautious in their recommendations about using TCs. Pediatric dermatologists, now commonly voice their frustration that GPs and pharmacists are too conservative and provide patients with outdated risk messages such as; use TCs sparingly, apply them thinly, or avoid them altogether. For example, even in 2016 a high proportion of Australian caregivers' reported that they had been told these risk messages "often" or "always" by both GPs and community pharmacists [33]. These messages are perpetuated by members of family and friends and appear in online searches about TCS [34]. Of course the main reason for such conservatism is the concern that TCs might cause side effects such as skin thinning (atrophy). However, the good news is that an Australian observational study showed that even when potent steroids had been used for children for around one year, there was no evidence of atrophy [35]. Indeed, current consensus is that skin thinning, hypopigmentation, hypertrichosis, osteoporosis, purpura, or telangiectasia do not occur in pediatric dermatology when used appropriately as per guidelines [36]. While practitioners should be concerned to avoid atrophy through overuse, it is far more likely to occur

when highly potent TCS are used chronically (without rest) for a long time. Care should also be used when using TCs on the face because perioral dermatitis can be aggravated by TCs.

How much TCs to use, the appropriate potency and strength to select is available from Consensus Guidelines [36]. The fingertip unit (FTU) was developed in 1991 [37] and is a useful tool to think about the amount to use. A FTU is defined as the amount of steroid preparation squeezed from a tube that will fit along an adult's index finger to the first crease. How much to use depends on the site [36].

There are three bases which can be used to deliver topical corticosteroids to the skin, lotions, creams, and ointments. Lotions, which contain a high proportion of water, can give a cooling effect but also the can sting and are best avoided. Creams contain water with an oil component. Creams too can cause stinging when the skin is inflamed and should be avoided during flare-up. Creams may be useful if the skin is not very inflamed. Ointments are the most appropriate option when the skin is inflamed and/or dry. They cause less irritation and deliver topical corticosteroids better. Occasionally, caregivers do not like ointments as they feel sticky and messy, but they are quite effective in improving hydration.

While itching (pruritus) is a hallmark of eczema, there is really no role for antihistamines. Occasionally, topical corticosteroids are not effective and in these cases, referral to a pediatric dermatologist is warranted because there is a high prevalence of Staphylococcus aureus which may require specific antibiotic therapy and referral to a medical practitioner. There is increasing interest in the use of bleach baths and/or nasal mupirocin ointment to reduce staphylococcal load in difficult-to-treat atopic dermatitis [35].

31.5.2 Childhood Asthma

Past research has identified many issues that have been poorly dealt with, with respect to childhood asthma management including: lack of parental knowledge about asthma and asthma medications, lack of information provided to parents, parental beliefs and fears, parental behavioral problems, the high costs of medications and devices, the child's self-image, the need for more child responsibility, physician nonadherence to prescribing guidelines, "off-label" prescribing, poor understanding of teachers, lack of access to educational resources, and specific medications [38]. With asthma being the most prevalent chronic disease of childhood with approximately 14% of children worldwide experiencing symptoms of asthma, pharmacists need to be working hard to ensure that asthma management education is being provided to the child and parents, as well as to the supporting community that has responsibility for children with asthma. The following case study highlights that even in a simple straightforward case of dispensing two medications for a child, there is a plethora of information and skills that needs to be divulged to a large range of people.

The following case illustrates the specific aspects of the treatment of asthma in children.

Asthma Case Scenario

Mrs Dunda and her 6 year old daughter Mishka enter your pharmacy with a new prescription for Fluticasone and Salbutamol metered dose inhalers. For the past few months over the winter, Mishka has had several colds that she hasn't been able to fully get rid of, and she has been waking at night coughing. A few times this term at school, when she was running in the playground, she got so out of breath, the school teachers had to administer salbutamol via a spacer to relieve her breathlessness. After investigation, Mishka has been diagnosed with asthma and active regular preventer treatment has been deemed necessary.

In this particular case, there is a huge amount of pharmaceutical care that needs to be provided by the pharmacist, and the information must be given both to Mishka and to her parents, and some information may also need to be disseminated to the other support community involved in Mishka's care, including teachers. Some of the types of information and services that need to be provided include:

1. Explanation of what asthma is and why it needs treatment
2. Explanation of the different puffers—reliever and preventer
3. Demonstration of inhaler use with a spacer
4. Checking technique of individual and caregivers
5. Explanation of peak flow monitoring
6. Explanation and demonstration of what to do during an asthma exacerbation
7. Development of an asthma action plan and how to monitor for signs of worsening control
8. Discussion on adherence to treatment
9. Discussion of environmental control and avoidance strategies
10. Discussion regarding side effects and how to avoid them

These particular services could take up to half an hour and may need to be repeated each time a new prescription is dispensed, as there is so much for one to try to take in and remember. Of course accompanying this information with written materials is also required. Also placebo devices and demonstration spacers will need to be used.

While the principles for asthma management are no different to those described in Chap. 27, the extra steps in educating children and their surrounding community are also really important. Studies have highlighted that hands-on skills training in how to use a reliever device and spacer provided by pharmacists can vastly improve the way an acute exacerbation is handled

[39]. Furthermore, education provided by pharmacists to children with asthma and their parents have shown improvements in knowledge, quality of life, and inhaler technique [40].

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Chapter 32
Pharmaceutical Care for Cancer Outpatients

Jaqueline G. Hugtenburg, Lonneke Timmers and Jan Jacob Beckeringh

Abstract In recent years, the number of oral anticancer agents (OACA), protein kinase inhibitors (PKI or "nibs"), in particular, has sharply increased. In the near future, the rise is likely to continue. OACA are used in the treatment of both common cancer types and a wide variety of less commonly occurring cancers and hematological malignancies. Due to the spreading use of OACA in cancer treatment pharmacists (and staff) of outpatient pharmacies are becoming more closely involved in the disease's main treatment and directly interact with predominantly older cancer patients and other caregivers. Providing pharmaceutical care for cancer outpatients requires specific knowledge of cancer (drug) therapy, pharmacogenomics, contraindications, interactions of OACA with other drugs and food, side effects, and their management and patient education.Within the framework of a multidisciplinary team effort, the pharmacist dispensing OACA must assess the suitability of its use for the patient and address eventual problems that the treatment entails, notably with respect to supportive and current medication for chronic diseases. The pharmacist is also responsible for adequate patient counseling. Adherence to OACA treatment and effects brought about by OACA and co-medication require careful monitoring of the patient and his/her use of medication. Close collaboration with other healthcare providers, both in the case of prescribing OACA and co-medication and with respect to events occurring during the course of treatment as the result of disease progression, side effects or incorrect medication use, is the most appropriate way to resolve eventual problems and adequately adjust treatment. In the present chapter, the various steps of the pharmaceutical care process, conditions for its successful completion and the role of the pharmacist in it, are lined out and the main topics that have to be addressed during this process including the detection and management of drug interactions, the reporting and management of side effects, (non-) adherence and adherence supportive care, and last but not least, patient counseling are discussed. The basic

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approach is that pharmacists are partners of (primary care) physicians as they collaborate on a wide variety of care activities including the optimization of treatment, medication reconciliation, patient education, and medication safety.

Keywords Oral anticancer agents · Pharmaceutical care · Oncology
Adverse events · Adherence · Drug interactions · Outpatient care

32.1 Introduction

Since the highly successful introduction of capecitabine and imatinib in the years just after the beginning of the present century, the number of oral anticancer agents (OACA), protein kinase inhibitors (PKI or "nibs") in particular, has sharply increased. In the near future, the rise is likely to continue [1, 2]. OACA are used both in the treatment of common cancer types like breast, colorectal, lung, and prostate cancer and a wide variety of less common cancers and hematological malignancies including chronic myelogenous leukemia, multiple myeloma, kidney, and liver cancer. As the result, the number of cancer outpatients on active treatment has considerably increased.

Since most OACA are (very) expensive, in many countries they are only available under special arrangements and/or are dispensed by hospital, hospital outpatient, or specialist pharmacies. However, supportive medication like antibiotics, anti-emetics, antiviral drugs, bone stabilizing drugs, and analgesics as well as medication for chronic diseases is often still dispensed by community pharmacies. Pharmaceutical care for cancer outpatients clearly requires specific knowledge with respect to cancer (drug) therapy, adverse effects, contraindications, interactions of OACA with other drugs, and patient education. Therefore, it is highly important that pharmacists have the capacity to adequately deal with cancer patients using OACA and their specific health problems [3–7].

32.2 Etiology

The term "cancer" covers a wide range of malignant diseases that cause irreversible tissue damage by uncontrolled cell growth which results in the formation of neoplasms in organs and tissues (solid tumors) or an abnormal increase and accumulation of malignant cells in bone marrow and the lymphatic system (hematological disorders). This is the ultimate effect of a defect in our genetic material (DNA/RNA) caused by a hereditary or acquired (somatic) mutation, a virus infection, radiation, or exposure to a chemical or otherwise toxic substance. Cancer-related alterations predominantly concern the genes of proteins involved in processes like cell division and growth, programmed cell death (apoptosis), and DNA repair. Abnormal gene activity and the resulting interaction of the various proteins

produced and/or malfunctioning of signal transduction pathways disrupt the normal cell cycle. This results in a decreased or less effective regulation of normal cell growth and an increased risk of neoplasm formation. In the case of a solid tumor, the affected cell forms a microscopic tumor which develops into a primary tumor. In a subsequent phase the tumor spreads to other organs and tissues and causes metastasis: at the site where cells originating from the primary tumor are nesting the process of tumor formation repeats itself [8].

32.3 Cancer Treatment

32.3.1 Curative Treatments

Curative treatment intending to cure a cancer or achieve long-time control of tumor growth or the accumulation of malignant blood cells, usually results in a substantial extension of life. Curative treatment strategies have shown to be particularly effective in patients with whom the disease has not yet spread. Treatment primarily consists of tumor removal by means of surgery or the eradication of malignant stem cells and their replacement by normal cells (stem cell transplantation). Radiotherapy may also be used to eradicate tumors, or reduce their size after which the remainder can be dealt with by means of surgery. Malignant cells that not have been cleared by primary treatment or the (possible) presence of non-detectable (micro-)metastases can be challenged by radio-, chemo-, and/or immunotherapy [8].

32.3.2 Adjuvant and Neoadjuvant Treatments

Adjuvant treatment concerns the use of chemo-, hormonal, or immunotherapy after surgery in order to eliminate remaining malignant cells and reduce the risk of recurrence. Neoadjuvant treatment usually relates to chemotherapy given prior to surgery. The simultaneous application of radio- and chemotherapy is referred to as chemoradiotherapy [8].

32.3.3 Palliative Treatment

After spreading of the disease (metastasis) to other tissues or the uncontrollable formation of massive amounts of dysfunctional blood cells curative treatment is no longer an option. Treatment is now restricted to addressing the symptoms resulting from disease progression, particularly the relief of pain and preservation of bone integrity, and combating infections as well as uphold the quality of life. In the

treatment of advanced or metastatic disease chemo- and immunotherapy are the most important options. Surgery and irradiation have now largely become supportive (combination-) treatments [8].

32.3.4 Treatment Lines and Treatment Intensity

Common cancers are treated with a major part of the older anticancer drugs, mostly in fixed combinations. New drugs, particularly OACA and monoclonal antibodies, are constantly being added. Marketing authorizations for new cancer drugs are mostly obtained only for use in second line or later treatment (i.e. treatment after one or more other therapies). In the case of successful drugs, with additional studies, use in first line (i.e. as treatment of first choice) often follows over time. Patients are generally treated till disease progression and then switch to the next line. Sometimes, patients are treated beyond progression with the aim of slowing this process on the basis of residual activity (e.g. the continued use of trastuzumab in patients with metastatic HER2-positive breast cancer). If patients are not treated continuously, anticancer treatment often consists of a number of cycles (usually 4–6) comprising a period of active treatment followed by a period without treatment (often to recover from adverse effects) [8].

The patients' overall health status, usually expressed by an ECOG (0, 1, 2, 3, 4, 5) or Karnofsky (50, 70, 90%) score is an important parameter determining both the choice of the first-line treatment and its intensity (dose and dosage interval). A low ECOG score (0) or high Karnofsky score (> 90%) means that the patient is not yet, or only to a very limited extent, restricted by the disease in performing her/his daily activities and is in a reasonable or good physical condition, and therefore can be treated more intensively. Age is also an important treatment parameter. Among several other factors, as the consequence of a reduced liver of kidney function, elderly patients generally tolerate intensive treatment less well than younger patients. The same holds true for patients with comorbities which as such are also more frequently present in elderly patients. Since the activity of enzymes involved in drug metabolism is increasingly associated with their genetic make-up (genotype), the prominence of genetics as a factor determining the intensity of treatment as required for not only an effective and but also safe use of OACA is rising (see below) [8].

32.4 Anticancer Agents and Their Use

32.4.1 Conventional Agents

For decades systemic anticancer treatment mainly consisted of intravenously administered chemotherapy with alkylating agents, antimetabolites, vinca alkaloids, antibiotics, platinum compounds, and taxanes. Use in the (neo-)adjuvant setting or

as first-line therapy of metastatic disease generally concerns treatment with combinations of these agents in cyclic dosing regimens (4–6 cycles) in which each cycle of 2–3 weeks consists of a number of days of administration and a short break (1–2 weeks) to recover from side effects. With the exception of carboplatin which is dosed on the basis of the AUC, conventional systemic chemotherapy is usually dosed on the basis of the patient's body surface area but adjustment is required in the case of over- and underweight patients. Dosing also depends on organ function. Treatment with conventional agents often produces serious (hematological) side effects [8].

32.4.2 Oral Anticancer Agents and Monoclonal Antibodies

32.4.2.1 Conventional Oral Anticancer Agents

Older OACA mainly comprise alkylating agents and antimetabolites like cyclophoshamide, chlorambucil, melphalan, and methotrexate. Capecitabine, the oral pro-drug of the antimetabolite 5-fluorouracil (5-FU), has been one of the first widely used newer OACA. In contrast to 5-FU, given by bolus infusion in a combination regimen or continuously over 1–4 days at the start of a treatment cycle, capecitabine is mostly used on the basis of a twice daily regimen for two weeks followed by a 1-week rest period. Apart from the hand-foot syndrome, its toxicity profile is more favorable than that of 5-FU. In addition to its use in metastatic breast cancer, capecitabine has now largely replaced 5-FU in colorectal cancer treatment regimens combining 5-FU with oxaliplatin (FOLFOX → CAPOX) or irinotecan (FOLFIRI → CAPIRI) [8].

The use of OACA in hormonal therapy (HT) is also well established. Aimed to prevent recurrence after initial curative treatment of early hormone receptor (HR-) positive breast cancer, estrogen function is suppressed by adjuvant HT using tamoxifen, a Selective Estrogen Receptor Modulator (SERM) or an aromatase inhibitor like anastrozole, exemestane, and letrozole. Since they lower estrogen production in fat tissue, the use of aromatase inhibitors is restricted to post-menopausal women. In HT OACA are used alone or given consecutively over a five to 10-year treatment period. In women with metastatic HR-positive breast cancer HT is used to retard disease progression [8].

In the case of hormone-sensitive metastatic prostatic cancer (90% of patients) HT comprises the use of nonsteroidal androgen receptor blockers, especially when the disease has become castrate resistant. These OACA include bicalutamide, enzalutamide, flutamide, and nilutamide. Metastatic castration-resistant prostate cancer can also be treated by androgen synthesis inhibitors such as ketoconazole, aminoglutethamide, and abiraterone acetate (last treatment line). The daily use of HT continues until the disease becomes refractory [8].

32.4.2.2 Newer Oral Anticancer Agents and Monoclonal Antibodies: Targeted Therapy

The vastly increased knowledge of genomics and molecular biology including the role of tumor-associated genetic mutations and signaling pathways involved in processes like cell proliferation, programmed cell death (apoptosis), tumor angiogenesis, and cell migration, has led to the development of drugs that specifically target abnormally functioning proteins and intracellular signaling pathways sustaining the growth and proliferation of cancer cells. Successful application of **targeted therapy**, as the clinical application of these new drugs is referred to, therefore often requires genetic testing as part of the diagnosis. Targeted therapy can be administered either intravenously (monoclonal antibodies or "mabs") or orally (small molecules like PKI and immunomodulants). The majority of PKI are multikinase inhibitors acting simultaneously on several kinases (e.g. serine, threonine, and tyrosine kinases). In contrast to mabs which interact with proteins on cell surfaces and present in blood, PKI interact with protein kinases that are part of an intracellular signaling pathway. Most PKI are used continuously in a fixed-dose regimen [1, 8].

32.5 Pharmaceutical Care

The increasing use of OACA in cancer treatment leads to a pharmaceutical care process in which pharmacists of outpatient pharmacies are more closely involved in the disease's main treatment. In a coordinated effort with other healthcare providers (HCP) pharmacists (and pharmacy staff) now directly interact with the patient and other caregivers. Importantly, as compared to conventional hospital-based cancer care and treatment, patients themselves now carry ultimate responsibility for taking their medication and reporting side effects. This, however, may cause patients to adjust or even abandon treatment, particularly when side effects are not recognized as such or inadequately attended to. Collaboration with other HCP in the form of a **multidisciplinary team** (MDT), accompanied by continuous consultation and exchange of information (or access to), especially in the case of problems and disappointing treatment results, is another critical factor in the successful completion of this care process [3, 4, 6]. See also Chap. 5.

The pharmaceutical care process **at the start of OACA treatment** essentially consists of three stages that can be clearly defined: (1) check and verification (especially with regard to existing co-medication), (2) dispensing of medication and patient counseling, and (3) monitoring of treatment, eventual adjustment, and providing patient support (Table 32.1) [3, 4, 6, 9, 10].

The first phase mainly consists of checks and verification: is the medication record complete, does the selected medication (OACA and co-medication) suit the patient with respect to genetic profile, health status, and living conditions, are there

Table 32.1 Collaborative Pharmaceutical Care Process

Pharmacist[a,b]	Patient/medication	Physician[a]
	Malignancy => (and eventual comorbidity and [drug] treatment of comorbity)	
	Disease status (early—metastatic) – age, condition, – particulars, life expectancy	**=>Diagnosis** – Medical – Laboratory – Genomics
Input (=) => – Pharmacogenomics – Contraindications – Interactions (drugs/food) – Dose and regimen – Use – Disposition – Supportive medication – Co-medication	**<= Consultation =>** **Considering Treatment Options** **<= Needs and Wishes = >** **Consent =>**	**<= (=) Treatment Plan** – Options with respect to nondrug treatment (and eventual supportive medication) – Options with respect to drug treatment (dose, regimen, and use, supportive medication): efficacy and side effects – Existing comorbidity and [drug] treatment
Preliminary Medication Treatment Plan (=) => – OACA – Supportive medication and eventual co-medication – Use of data from input – Monitoring plan	**<= Consultation =>**	**<= (=) Prescribing** – OACA (dose, regimen, use) – Duration of (initial) treatment – Ibid. supportive medication and co-medication
Dispensing and Patient Education => (final treatment plan following [structured] patient interview) – Mechanism of action – Dose and regimen – Use and handling (+disposal) – Effects (efficacy) – Side effects (management and reporting [tools]) – Adherence (counseling and tools)	**<= Needs and Wishes = >** **<= Consent**	

(continued)

Table 32.1 (continued)

Pharmacist[a,b]	Patient/medication	Physician[a]
Monitoring/ Evaluation of Effects/ Refills => – Adjustment (medication and use) – Side effects – Adherence	**<= Consultation =>** **Reports on** **<= Treatment/ Medication/ Quality of life =>**	**<= Monitoring/Evaluation Disease and Treatment Effects** – Efficacy – Side effects & management – Adjustment – Duration of drug treatment(s)
Refills and/or Re-run of Previous Steps => – Short-term, occasional and long-term medication	**<= Consultation =>** **Reports on** **<= Treatment/ Medication/ Quality of life =>**	**<= Prescribing of Alternative Treatment and/or Follow-up Treatment (as previous steps)** – Monitoring and adjustment (short- and long-term)

(=) =>: Column beyond the adjacent one
<= Consultation =>: HCP interaction without patient involvement
[a]Including pharmacy staff and oncology nurses
[b]Later steps also apply to pharmacists not dispensing OACA

any (potentially) harmful interactions with other drugs (including contraindications), have the appropriate dose and dose regimen been selected?

In addition to dispensing, subsequent steps (stage 2) are mainly focused on the provision of information and advice, particularly with regard to the handling and use of the medication, treatment effects that can possibly be observed by the patient, anticipated side effects, and their management and the setting up of a treatment support structure (as part of the MDT effort) (Table 32.1). The best means to achieve this is to discuss these matters with the patient on the basis of a structured questionnaire (structured interview). Issues emerging from the first phase should be verified and discussed. In this respect, the patient should also be asked about the use of OTC drugs and dietary supplements. Treatment finally needs to be tailored to the limitations, needs, and wishes of the patient, especially when OACA and/or co-medication have to be taken on an empty stomach. Providing information on specific measures regarding contraception of the patient and his/her partner is often also required [3–7, 9, 10].

This first meeting is ideally suited as a start in building a relationship of trust with the patient (and his/her carers) as needed to achieve optimal treatment outcomes. However, an important condition for maintaining this much needed relationship is that a patient should always be able to contact a HCP he/she already knows and who is familiar with the patients' case. In this context it is also highly appropriate if the pharmacist already has been introduced to the patient by prescribing MDT members, and that in turn the patient is introduced to pharmacy staff involved in the pharmaceutical care process of dispensing and monitoring.

Follow-up (stage 3) essentially consists of two phases. In addition to dispensing the first refills, short-term monitoring (2–12 weeks) mainly consists of asking the

patient after his/her experiences with the new treatment, the occurrence of acute side effects, and offering support in managing these effects (Table 32.2). Subsequent refills and long-term monitoring depend on a wide variety factors including the disease and its course, treatment aim (curative, preventive, palliative) and duration, efficacy of treatment, and side effects and the attitude and condition of the patient as well of his/her living conditions. It is also important to adjust doses in the case of serious weight loss and stop any medication that becomes redundant (deprescribing). The main objective is to enable the patient to successfully continue OACA treatment and co-medication as long as deemed necessary and useful. Main pharmacist activities therefore consist of monitoring treatment with respect to elicited effects and adherence, and supporting the patient in the management of side effects and symptoms of disease progress as well as addressing anxiety and concerns about treatment in a collaborative fashion with the prescribing HCP and oncology nurse (3–7, 9, 10). In the case of any major change of medication, possibly as the result of adjustment due to disease progress, intolerance or side effects, the entire process or certain relevant parts of it should be repeated but in a fashion as described in Chap. 6.

Particularly with respect to the steps involving checks and verification (dosage, interactions, contraindications, co-medication), current information from (electronic) medical and pharmaceutical files is indispensable. Data review is faster when these databases are linked (or have been integrated) and the information can be shared without additional effort. In later stages of the process electronic (pharmacy) information systems are also highly useful, notably for the recording of information about the course of the treatment and interventions (5, 6). However, the use of these systems does not mean that the different steps of the care process can be conducted in a less careful manner than without their involvement. Moreover, successful implementation of the pharmaceutical care process requires commitment, continuous training, consultation, and evaluation as well as ample experience [3–7, 9, 10].

The rapidly growing number of anticancer drugs including OACA is accompanied by a massive flow of data which must be classified, evaluated, and made accessible to the HCP involved in the daily treatment of cancer patients. It has become virtually impossible for these HCP to perform these activities themselves. Therefore, national or regional centers should be established where relevant information concerning all aspects of treatment is collected, evaluated, and processed, and made available (e.g. by means of a dedicated app or website) and/or linked to the electronic information systems used by HCPs involved in cancer care [3–6, 8].

Although being elaborate, the abovementioned pharmaceutical care effort for cancer (out-)patients, as it is closely linked with the medical care process, is likely to pay off in the form of better treatment outcomes, less problems and hospital admissions, and an increase in patient satisfaction [3–7, 9, 10].

32.6 Dosing of Oral Anticancer Agents

When OACA treatment has been decided upon pharmacists must ensure that the correct dosing regimen is selected. However, largely as the result of side effects or as a measure to avoid their occurrence, dose regimens frequently need to be adjusted particularly in the case of elderly patients and patients with a reduced liver and renal function [8–11]. As in the case of OACA like capecitabine, lenalidomide, and sunitinib which are used with predetermined rest periods, it might be required to insert additional rest periods [8, 9].

With regard to metabolic issues, genetic testing prior to treatment should be used to optimize individual dosing regimens, notably with respect to cytochrome P450 (CYP)-enzymes in the liver (see 7.7.7.2). It is well known that patients with (partial) dihydropyrimidine dehydrogenase deficiency (DPD) using 5-FU or capecitabine without proper dose adjustment experience severe or lethal toxicity due to a lack of metabolic capacity [12]. Although guidelines for dosing patients with DPD mutations are available, in clinical practice DPD status is as yet not routinely assessed.

Dosing can be personalized by means of adjustment on the basis of the actual drug exposure as obtained by means of therapeutic drug monitoring (TDM) [3, 9, 10, 13]. As yet TDM is not commonly used in oncology. One of the main conditions for TDM is the existence of a clear relationship between exposure (e.g. the area under the plasma concentration time curve [AUC]) and the response to treatment (efficacy/toxicity). However, the number of OACA for which a relationship between drug exposure and treatment outcome has been established, is growing. A more widespread use of the dried blood spot (DBS) sampling technique may also contribute to the development of more personalized TDM-based treatment regimens with OACA. In DBS a minute amount of whole blood, obtained by means of a finger prick, is collected on paper by the patient at home and sent by the patient to a laboratory for analysis. In the near future, this method, which has shown to be feasible and cheap, may be of major importance in optimizing OACA dosing [14].

32.7 OACA and Drug Interactions

32.7.1 Monitoring of Drug–Drug Interactions

Cancer patients often use a considerable number of drugs. Not only those required to treat their malignancy and its symptoms but also drugs to contend with treatment-induced side effects and comorbidity largely in the form of a chronic disease. OACA generally have a narrow therapeutic index. Particularly patients continuously treated with OACA are therefore highly susceptible to drug–drug interactions (DDI). DDI may affect the effectiveness of cancer treatment and that of other drugs, result in or exacerbate side effects, and ultimately contribute to a reduced quality of life. The likelihood of DDI increases with age mainly as the

result of the increased use of drugs in the elderly, their decreased metabolic (liver function) and excretory (renal function) capacities and altered eating habits or decreased appetite. Indeed, (potential) DDI have found to be very common among (elderly) cancer patients using OACA. Both the number of comorbidities and the number of "over-the-counter" drugs used have been identified as determinants [3, 8–10, 15].

Although the detection of (potential) DDI is therefore an integral part of the prescription process (or at least should be executed immediately afterward), DDI monitoring must be continued throughout the entire period of treatment. At present electronic pharmacy information systems generally feature the automated monitoring of interactions and also give recommendations to avoid interactions. Adequate monitoring, however, can only be performed when the medication record is up-to-date and complete (and preferably includes data on the use of OTC medicines, relevant lab values, and nutritional supplements). Monitoring, however, is a problem in cancer patients using OACA as they are treated both by (hospital) specialists and general practitioners (GP), and medication is often provided by various pharmacies like hospital outpatient and community pharmacies or specialist dispensing services. Verification of medication prior to the check on interactions is therefore always mandatory. To this end a transfer of medication data should accomplished as soon as patients are admitted to or discharged from hospital or otherwise change from one care setting to another. The availability of integrated electronic patient and medication records may solve this issue [3–5, 9, 10].

32.7.2 OACA-Related Drug–Drug Interactions

OACA use is susceptible to both pharmacokinetic and pharmacodynamic DDI [8, 15]. The latter category refers to interactions brought about by drugs with a similar mechanism of action or exerting directly interacting effects. The effect can be additive, synergistic, or antagonistic. The latter effect may result in toxicity like QT_c prolongation, occurrence of GI and CNS effects, or increased toxicity due to NSAID-induced impairment of kidney function. DDI in OACA treatment most frequently observed are those between OACA and coumarins (e.g. capecitabine), quinolones, anti-epileptics (carbamazepine, phenytoin), and diuretics (especially hydrochlorothiazide) [8, 11, 15].

Absorption can be impaired by drug-induced mucositis and diarrhea. These side effects commonly occur as the result of anticancer drug treatment. Several OACA require acid conditions for absorption. The simultaneous use of drugs that decrease acidity in the stomach like H_2-antagonists, proton pump inhibitors (PPI), and antacids, therefore, affects the absorption of several PKI including axitinib, dasatinib, erlotinib, gefitinib, imatinib, lapatinib, and pazopanib and reduces their bioavailability. OACA absorption can also be affected by an interaction with intestinal P-glycoprotein and the intestinal cytochrome P450 3A4 enzyme (CYP3A4). Finally, a (drug-induced) increase or decrease of the volume of

distribution as caused by edema and dehydration, respectively, may also affect OACA bioavailability [8, 11, 15].

A great number of (potential) interactions regarding the metabolism of OACA is brought about by CYP enzymes in the liver which account for about 75% of the total drug metabolism [3, 8, 12, 15]. OACA CYP-mediated metabolism as such may be influenced by genetic polymorphisms, notably those present in the CYP2D6, CYP2C19 and CYP2C9-enzymes [12]. The presence of certain polymorphisms accelerates or reduces CYP-mediated metabolism. This may be the cause of substantial inter-individual OACA plasma level variability which often also has considerable clinical impact. Likewise, polymorphisms altering drug efflux transporter activity in the intestine, lever, and kidney influence the uptake and excretion of several OACA. Pharmacogenetic screening of patients using OACA is therefore increasingly used as a tool to optimize treatment efficacy and avoid excess toxicity [3, 4, 8, 12, 15].

OACA themselves may also increase or decrease the activity of CYP isozymes. In this respect, the majority of PKI is primarily metabolized by CYP3A4. Hence, both CYP3A4 inhibiting and inducing drugs may exert substantial influence on OACA metabolism and thereby cause treatment inefficacy and/or adverse drug reactions. Likewise, the reverse may also occur: inhibition of CYP3A4 by imatinib may cause plasma levels of simvastatin and atorvastatin to rise leading to myopathy. Certain PKI including lapatinib, nilotinib, and sunitinib induce QT_c interval prolongation. CYP3A4 inhibition by co-medication (e.g. antiemetics, antibiotics, and antifungals) might result in life-threatening toxicity [3, 4, 9, 11, 15].

32.7.3 Drug–Food Interactions

Drug–food interactions (DFI) of PKI may be related to the concomitant use of grapefruit juice which is a potent inhibitor of (intestinal) CYP3A4 and therefore increase the bioavailability of these drugs. The reverse effect can be observed in the case that St John's wort is used concomitantly as it induces CYP3A4 and P-glycoprotein [3, 8, 16].

Although food raising the gastric pH may affect the absorption of certain OACA, combining the intake of OACA, particularly of certain PKI, with (fat) food often improves the bioavailability of these drugs [16]. On the other hand, this (potentially) increases variation and may be the cause of toxicity. In order to avoid problems, the marketing authorization of several OACA recommends using these drugs in the absence of food [16]. However, in daily practice for many patients the use of their medicines under fasting conditions is highly inconvenient and they do not comply with this requirement. For a number of PKI including erlotinib, lapatinib, nilotinib, and pazopanib, the effect of the simultaneous intake of food on their bioavailability has been investigated. Although dose adjustments may be required, preliminary study data suggest that they can be safely used in combination with food. Particularly in combination with TDM, the standard use of OACA used at

lower dose levels in combination with food may become an option. Nevertheless, in the case that OACA cannot be used in combination with food patients should be carefully informed and given advice how to handle this intake restriction [8–11, 14, 16].

32.8 Management of Disease Symptoms and Side Effects

Nearly, all patients using OACA experience side effects which may be caused both by their anticancer medication and their supportive treatment which is generally used to treat symptoms stemming from the (metastatic) disease itself or side effects (in-)directly resulting from treatment with anticancer drugs (e.g. blood and laboratory abnormalities, bone effects, pain, seizures, and skin effects) or other means (e.g. irradiation, surgery) [3, 5–11, 17].

Disease-related symptoms are mostly organ-specific but often also have a general or psychological nature including loss of weight, reduced appetite, fatigue, and depression. In view of their exhaustive and demoralizing effect, these symptoms should be explicitly dealt with within the context of the MDT effort. Suppression of bone marrow activity leading to thrombocytopenia, neutropenia which increases the risk of infections, and/or anemia causing fatigue, is a prominent and often dose-limiting side effect that is not only specifically related to the use of most conventional IV-administered anticancer agents but also to PKI inhibiting BCR-ABL and JAK proteins, as well as radiotherapy. Dependent on the type of stem cell most sensitive to a certain anticancer drug, the use of these anticancer drugs usually results in a specific pattern of bone marrow suppression. Neutropenia-related infections are commonly treated with antibiotics and/or antimycotics. However, neutropenia and it consequences can be attenuated or even prevented by growth factor co-treatment [8, 9].

Non-hematological side effects of conventional (oral) chemotherapy include alopecia, mucositis, nausea, vomiting, diarrhea, neuropathy, and changes in fertility and sexuality. Toxicity brought about by newer OACA is strongly related to their mechanism of action and (combinations of) side effects are often unique to certain drug categories. In addition to the above mentioned effects, specific effects commonly observed in patients using targeted therapy include skin rash (EGFR, HER2, mTOR and RAS/RAF inhibition), hypertension (VEGFR inhibition), proteinuria (VEGFR inhibition), wound-healing complications, hand-foot-skin reactions, and various vascular complications (VEGFR inhibition), various laboratory abnormalities (ALK inhibition), cardiac abnormalities, and hypothyroidism (BCR-ABL inhibition). PKI treatment may also result in hyperglycemia (BCR-ABL, PI3K, AKT, and mTOR inhibition) and is also associated with specific ocular and pulmonary toxicity [3, 8, 9].

Although the cause of side effects usually lies in the toxicity of the anticancer drugs themselves, DDI and DFI may reinforce or intensify side effects and even may be the cause of death. On the other hand, side effects may also result from

"over-adherence" to treatment as patients interpret their occurrence as an expression of efficacy [17]. Disease progression is likely to exacerbate the burden of side effects. Particularly when side effects rather than disease symptoms obstruct cancer patients in their daily activities, they exert a strong demoralizing effect [6–9, 17, 18].

Close monitoring of side effects is also urgently required because the long-term safety of many newly approved OACA, particularly those approved on a conditional basis, has not yet been established. In cancer treatment, adverse event (AE) reporting has evolved to a continuous systematic process. In clinical trials data collection is predominantly clinician-based and highly regulated by the National Cancer Institute (NCI)-Common Terminology Criteria for Adverse Events (CTCAE) system. Being an important source of information after approval, patient-reported outcomes (PROs) not only have been recognized as highly useful but their systematic collection in routine practice also brings forth a high degree of patient engagement and compliance. Recently, the NCI developed a PRO measurement system as a companion to the CTCAE, called the PRO-CTCAE. Longitudinally collected clinician-derived CTCAE assessments were found to better predict unfavorable events, whereas patients reports better reflected daily health status [19].

If not managed adequately both disease symptoms and side effects will affect life expectancy in a very negative sense not least because by their effect on a patients' quality of life they detract from adherence and persistence to OACA treatment. Indeed, between 30 and 50% of patients with side effects report their occurrence as the reason for discontinuation of treatment. Adequate (non-)pharmacological treatment of symptoms and side effects including extensive counseling, psychological support, and lifestyle adjustment, is therefore a highly important aspect of cancer care [3, 6–9, 17].

Thus, in view of their often profound effect on the treatment result, side effects should be continuously monitored by all HCP involved and patients alike. Moreover, in addition to providing information on side effects and their pharmacological treatment, and dispensing the drugs required, pharmacists should actively ask their patients and their caregivers after their experiences and discuss these reports with other HCP involved (oncologist, oncology nurse). Electronic diaries and mobile apps appear to be excellent tools for patients to record their symptoms and share their experiences [5–7, 9].

32.9 Adherence

Apart from the issues about adherence discussed in Chap. 4, there are additional concerns in patients using OACA's. It is generally assumed that patients with a life-threatening disease take their medication as prescribed. However, adherence to anticancer drugs in long-term treatment has proved to be a constant source of serious concern. Adherence rates of patients using OACA range from less than 20–100% [6, 17, 18]. Effective HT in adjuvant treatment of breast cancer requires women to take

Table 32.2 Adherence and support to OACA treatment: contributing factors, interventions, and tools

Factors contributing to (non-) adherence	Actions/interventions (and eventual tools)
Patient-related: – Younger age – Forgetfulness – Depression and antidepressant use – Level of health literacy – Perceived need to use medication – Breaks from daily routine – Limited social support – Cost of treatment	– Increasing focus on needs and wishes of the patient (structured interviews) – Increasing focus on comorbidity and symptom/side effect treatment – Stepping up of educational support (plus providing of accessible and easy to understand [written] information) – Use of (electronic) reminder and reporting devices and/or services (e.g. (bi-) weekly pill box/roll, mobile phone app, website) – Enhancing patient support quality – Signposting of patient associations – Coordination/integration of informal care with HCP-provided care (creating less interrupted as well as more structured care) – Providing of both adequate and affordable care/health insurance
Disease-related: – Comorbidity – Quality of response – Limited overall survival/ higher risk all-cause mortality	- Timely adjustment of disease and comorbidity treatment – Adequate monitoring of treatment response – Adequate treatment of symptoms
Treatment-related: – Perceived lack of efficacy – Toxicity and side effects – Efficacy of supportive medication/treatment – Co-medication – Treatment duration	– Use of therapeutic drug monitoring – Adequate monitoring and management of side effects – Increased focus on patient-reported side effects – Consistent follow-up of patient-reported side effects
Provider-HCP related: – Less experience with disease – Inadequate communication – Limited number of patient contacts – Inadequate counseling – Inadequate monitoring	– Collaborative approach to treatment (MDT framework) – Adherence to treatment protocols and data recording – Enhancing data accessibility and exchange between HCP – Use of adequate (electronic) data registries – Employment of pharmacy staff and oncology nurses (as full/ integrated members of MDT) – Increasing the number of patient contacts (engage staff) – Focused training – (adherence) monitoring program. Particular focus on long-term treatment – Improving access to (informal) care and support services

their medication once daily for a period of at least 5 years. However, because of side effects about 30–50% of these patients discontinue treatment prematurely while intake interruptions are frequent [18]. Adherence to capecitabine seems to be higher and amounts to 80–100%. Of patients with CML treated with imatinib about one third was found to be not or only partially adherent [20].

Overuse of anticancer medication may occur as well. Overuse has even been reported in the setting of a clinical trial in which patients are more closely observed than in daily practice and may be intended ("over-adherence") of unintended. Over-adherence particularly occurs in patients with complex dosing regimens. The consequences of over-adherence can be serious as overdosing may produce serious side effects [17, 18].

Suboptimal medication adherence may have serious consequences. An adherence rate (AR) of 90 or 95% is often considered the threshold for sustained effectiveness of OACA treatment. The impact of nonadherence on the response to imatinib therapy in CML is well known. Only 29.3% of patients with an AR of $\leq$ 95% achieved a major molecular response, whereas 94.5% of the patients with an AR of > 95% achieved this outcome [20]. In patients with NSCLC using erlotinib a threshold AR of 95% was associated with the extent of disease control. Furthermore, in children with an AR < 95% to treatment with 6-mercaptopurine the risk of relapse of acute lymphoblastic leukemia was increased by 2.7-fold. These examples clearly show that in cancer treatment high ARs are mandatory to achieve a successful long-term outcome [6–9, 17, 18]. However, either in a disease- or drug-dependent manner a certain level of nonadherence might be tolerated since the lowering of initially prescribed doses of capecitabine in the course of treatment as necessitated by side effects was found not to compromise effectiveness [17, 18, 20].

The occurrence of (serious) side effects is one of the most important factors promoting nonadherence (Table 32.2). Other factors of nonadherence directly related to treatment are the number of co-medication, duration of treatment, and higher out-of-pocket costs for the medication. Patient's beliefs about the medication are also an important factor as well as age (elderly and adolescents) and depression [6–10, 15, 17, 18, 20].

HCP-related factors (usually related to physicians or nurses) also influence medication adherence. A positive effect was associated with a strong HCP–patient relationship, trust in the HCP, and shared decision-making. A lack of HCP support, insufficient information about treatment options, the experience of side effects of which patients were not informed in advance and the frequent change of physicians during follow-up were related to a negative effect (5–7, 17).

Although improving medication adherence to OACA treatment is urgent, it has been shown to be a challenging task. In spite of decades of intensive research, evidence for effective interventions to improve medication adherence and thereby clinical outcomes, is still thin. Current intervention methods to enhance medication adherence for chronic health problems are mostly complex and evidence demonstrating their effectiveness is mostly inconsistent. However, several projects to promote adherence by applying e-health- and m-health-based tools to involve and motivate patients seem to yield promising results [3–7, 9, 10, 13, 17].

32.10 Tailoring OACA Treatment to the Patients' Need and Patient Education

When initiating anticancer treatment comprising OACA it is important that HCP approach the patient in the context of a comprehensive and well-coordinated MDT effort that ensures a clear and uninterrupted process of collaborative care without unnecessary visits burdening the patient (seamless care) [3–8]. In addition, with respect to the relationship between patient and HCP, the current premise is that with the exception of technical matters, decisions regarding treatment and use of medication are carried out in accordance with the principle of shared decision making. This implies that patients are not only adequately informed on their disease, its treatment, and the consequences thereof, and invited to discuss these matters with their HCP, but also that they are explicitly and timely asked after their preferences and wishes [3–8, 17, 20].

Following the course of the pharmaceutical care process as described in paragraph 32.5 (Table 32.1), both the first dispensing of the medication and subsequent refills are part of a predetermined set of appointments at which treatment effects (results, side effects, social impact of treatment) are evaluated and necessary adjustments are made. It is necessary that prescribing HCP (oncologist, hemato-oncologist, surgeon) pass the treatment plan including all information relevant to the use of the medication on to the pharmacist and make data (e.g. lab values, pharmacogenomic data) accessible in time. In the context of this collaborative approach, it is self-evident that there is mutual consultation between prescribing HCP and pharmacist [3–6, 9, 10]. In this manner, the dispensing of medication can be efficiently prepared and tailored to the patient in a preliminary manner (Table 32.1). This process also ensures that information about OACA (and co-medication), its use and expected effects provided to the patient by the pharmacist (or designated pharmacy staff) is in line with information provided by the prescribing HCP and oncology nurse. Moreover, thorough preparation prevents the situation that missing data still has to be retrieved in the presence of the patient.

Using the preliminary treatment plan at first dispensing, the patient is informed on the relevant particulars of the selected OACA (mechanism of action), its use (dose and dose regimen), and treatment effects (therapeutic effect, side effects) that can be expected to occur. If applicable the information is extended both to supportive medication to treat or prevent side effects and co-medication (and their interaction with OACA treatment). Information given by the patient on the basis of a structured interview may lead to adjustments with respect to OACA dose and regimen and use of eventual co-medication. The patient is explicitly asked to consent to the finalized treatment plan. The first meeting with the patient is also used to discuss monitoring of treatment and follow-up (weekly to every 3-month), adherence matters and the importance of reporting side effects. It is clearly agreed whom the patient may contact for information and questions between appointments. Relevant data and specifics that have been discussed at the first and subsequent dispensings are documented in the patients' electronic health/medication record [3–5, 9, 10].

An important element of the dispensing of subsequent OACA prescriptions after scheduled assessments of the therapeutic effect, is asking the patient (by means of a structured interview) after his/her experiences with OACA treatment with respect to side effects and impact on social life. If necessary, the patient's remarks should lead to treatment adjustment, interventions that correct nonadherence, or other measures aimed to uphold quality of life [5–7, 9, 17, 18].

At the start of anticancer treatment patients often receive (too) much information in a short time interval and are not receptive to information or unable to properly process all data. Apart from the possibility to arrange a follow-up meeting, printed information in a (personalized) form that is understandable to the patient, should therefore be available and given to the patient. Moreover, in addition to information presented in leaflets and brochures, patients should also be alerted to websites where relevant information can be viewed online (hospital, pharmacy, patient association) and made aware of patient associations. It can also be highly useful to introduce tools supporting the patient in the form of medication cards and electronic reminder/reporting services (mobile phone app/interactive website) [5–7, 9, 10, 15].

32.11 Role of the Pharmacist in Supporting Patients Using Oral Anticancer Agents

Over the last decades the pharmacy profession has experienced a change from traditionally drug-oriented toward patient-oriented services. As the result pharmacists (and staff) in community and hospital outpatient pharmacies now play a significant role in the care of patients with chronic diseases. Due to the rapid progress in cancer treatment including the introduction of targeted therapies for a growing number of patients, at least some cancer types have also become a chronic disease. Moreover, the increased availability of effective OACA has reduced the hospitalization rate of cancer patients and improved their quality of life. However, these possible benefits can be jeopardized by an inadequate use of medication, a poor management of side effects or an insufficient adherence to medication. The latter case particularly applies to patients whose disease has been greatly reduced for a long time or who use OACA preventively after previous treatment [3, 5–10, 17].

On the basis of their knowledge and skills pharmacists may timely identify the increasing number of (potential) medication-related problems and contribute to their solution. Close collaboration with other HCP, both in the case that these problems are related to prescribing or that they occur during the course of treatment as the result of disease progression, side effects, or inadequate medication use, is the most appropriate way to resolve these problems. Increasingly pharmacists are seen as partners of (primary care) physicians as they collaborate on a variety of care activities including the optimization of medication, medication reconciliation, patient education, and medication safety [3–7, 9, 10].

Clearly, as they dispense OACA and co-medication on a regular basis, pharmacists should play a more prominent role in the care process of cancer patients.

Within the MDT framework this means that the pharmacist (or designated staff) proactively informs and advises the (often elderly) patient about the medication, its use, and the consequences thereof with an emphasis on side effects and their management, and adherence preferably in the form of a therapeutic monitoring program with patient-tailored interventions applied if necessary. Several pharmacist-led care interventions to improve adherence to OACA increasingly using modern ICT applications indeed have shown to be effective. Thus, supporting patients in adhering to their medication has now become a responsibility of community and outpatient pharmacists as well as playing a prominent role in patient education [3–7, 9, 10].

However, in view of the growing complexity of cancer treatment and cancer patient care requiring extensive knowledge and experience, and the often very small populations of many less commonly occurring malignancies, the management of the majority of cancer medication can only be properly handled by hospital- or specialist pharmacy-based pharmacists familiar with all aspects of cancer treatment with these drugs and other means (specialist care). As the result in many countries "Oncology Pharmacy" has evolved into a new pharmaceutical discipline [3, 4, 9].

Notwithstanding this requirement, to a lesser extent it also applies to community pharmacists who do not dispense OACA but are responsible for the pharmaceutical care of patients using OACA and co-medication on a day-to-day basis [5–7, 10]. As the result, these pharmacists (and designated staff) will be much more focused on safe medication use, supporting patients with regard to adherence, and the management of side effects brought about by both the anticancer and other (chronic and/or supportive) medication. However, with respect to specific problems related to the use of OACA, these pharmacists must have direct access to the knowledge available to the specialist dispensing pharmacists (e.g. by means of help desks and/or an electronic knowledge base) [3–6, 9, 10]. In this respect, it would be helpful to establish local or regional information centers where relevant information regarding cancer drugs and cancer treatment is collected, evaluated, and made available either in the form of a help desk or electronically by linking it to the pharmacy information systems. In this manner and with specific training, community pharmacists indeed provide the link between hospital-based cancer treatment with OACA, first-line care by general practitioners and the patient [3–7, 10]. Finally, in addition to selecting, prescribing, and dispensing the right treatment, personal contact, commitment, and familiarity with all HCP participating in the MDT effort are indispensable contributions to the success of pharmaceutical care for cancer patients.

Case Scenario

Case 1—EGFR-mutated NSCLC treated with erlotinib and co-medication

Mrs L, 86 years, widowed since 8 years, has angina pectoris since 10 years. Twelve months ago she was diagnosed with metastatic epidermal growth factor receptor (EGFR)-mutated non-small cell lung cancer (NSCLC) for

which she was prescribed erlotinib (initially 150 mg/day, after 2 months 100 mg/day). As recommended she takes erlotinib one hour before breakfast on an empty stomach (because food increases erlotinib bioavailability which is associated with an increased risk of QTC prolongation). Each month the erlotinib tablets are dispensed by the hospital outpatient pharmacy. Mrs L responds well to erlotinib. With some help of relatives she still lives independently and loves to be in her garden. She has also a good cognitive function.

Mrs L also uses the following co-medication: acetylsalicylic acid (ASA) 80 mg, once daily for 10 years, metoprolol 50 mg, once daily for 10 years, simvastatin 40 mg, once daily for 10 years, omeprazole 40/20 mg, once daily for 7 years, and minocycline 100 mg, once daily for 8 months. Mrs L visits the local pharmacy to collect her chronic medication for a 90 days period.

As its solubility is decreased at pH above 5, the bioavailability of erlotinib is decreased when used in combination with drugs that increase the pH in the stomach. It is therefore recommended to avoid the use of a proton pump inhibitor in combination with erlotinib. However, in view of the need to use ASA, Mrs L's age and her history of mild reflux esophagitis, at the start of erlotinib the hospital pharmacist suggested to continue omeprazole but at the lower 20 mg/day dose.

Although her malignancy responded well to erlotinib, soon after starting treatment Mrs L developed serious skin toxicity in the form of papulopustular skin eruptions (grade 3) which in spite of topical treatment, led to a dose reduction from 150 to 100 mg/day as she felt tempted to discontinue treatment. As a further measure to manage skin toxicity she was prescribed minocycline (tablet 100 mg, once daily). Twice daily she also uses a moisturizing emollient cream.

When collecting her chronic medication and cream from the local pharmacy, the pharmacist asked her after her experiences with erlotinib and her skin problems. She told the pharmacist that as such treatment was now tolerable but that she observed more and more dark spots on her skin (hyperpigmentation is a well-known side effect of minocycline in dermatology). She also said that she felt somewhat nauseous during the day which, however, usually improved during the evening. Increasingly, she also suffered from aching muscles which effect she attributed to a lack of physical activity as the result of fatigue. Following consultation with her GP Mrs L switched from minocycline to doxycycline tablets (100 mg, once daily) with the advice to avoid sunlight. The pharmacist also proposed to stop using simvastatin and add vitamin D to (tablet 800 IE, once daily) to her medication. Moreover, the pharmacist also suggested Mrs L to take erlotinib two hours after dinner for a trial period of two weeks and to make a consultation after two weeks. Mrs L accepted this proposal.

After two weeks, Mrs L returned to the pharmacy and shared her experiences with her modified medication with the pharmacist in the pharmacy's consulting room. Mrs L said that although the feeling of fatigue had not completely abated, she felt now much better not only by taking erlotinib in the evening but also because the pain in her muscles had disappeared.

Simvastatin use was stopped not only because of Mrs L's age and life expectancy (deprescribing) but also since the combination of erlotinib and a statin has been related to an increased risk of statin-induced myopathy. Vitamin D was considered necessary because of Mrs L's reduced physical activity and the advice to avoid sunlight as a consequence of using doxycycline.

Case 2—AHT following early breast cancer treatment and co-medication

Mrs B, 68 years, is a type 2 diabetes patient since 8 years. As treatment she uses metformin 500 mg, once daily, gliclazide 30 mg SR, once daily, and simvastatin 40 mg, once daily in the evening. She also has atrial fibrillation for which she now only uses metoprolol 50 mg, once daily, and warfarin. Being diagnosed with early hormone receptor-positive breast cancer she recently has been successfully treated with surgery, radiotherapy, and chemotherapy. According to the guidelines, the oncologist advised her to use tamoxifen 20 mg, once daily for a 5-year period. The prescription for tamoxifen was sent by e-mail to the local pharmacy.

Unfortunately, Mrs B has not been convinced that she should use tamoxifen. This because she already uses four medicines and meanwhile has developed a strong fear of side effects as she has read on the internet about the horrible side effects of adjuvant hormone therapy (AHT). When she visits the pharmacy to collect her medicines, the pharmacy technician supplies her with a box of 30 tamoxifen 20 mg tablets and asks her what the oncologist has told her about tamoxifen. Mrs B says that she was told that tamoxifen is an antihormone which use is required to prevent breast cancer recurrence, but that its use would be accompanied by particularly annoying side effects, such as not feeling well, depression, and dry skin. Mrs B complains that she already is not feeling well, not only because she feels not recovered from her recent cancer treatment but also because she thinks her diabetes is going out of control. Especially because of the prospect of having to use tamoxifen for such a long period, she has therefore little inclination to start with using tamoxifen. The pharmacy technician feels that Mrs B needs more support for starting tamoxifen treatment and asks the pharmacist to counsel Mrs L about the pros and cons of AHT. The pharmacist knows Mrs B, because she is a frequent visitor of the pharmacy and is included in the program of the yearly performed clinical medication reviews. In the pharmacy's consulting room, Mrs B is provided with information on AHT, the various side effects including hot flushes, urinary symptoms, tiredness, night sweats, and emotional problems, and their actual risk of occurrence in relationship to the

information Mrs B found on the internet. Because of her ambivalent attitude and many questions, the pharmacist particularly addresses the effect of AHT on the recurrence of breast cancer and tells her that in case of side effects she should contact her oncologist. In addition, the pharmacist indicates that tamoxifen can be taken in the morning simultaneously with metformin, gliclazide, and metoprolol. The pharmacist also explains that there is no interaction of tamoxifen with her current medication. However, since tamoxifen may enhance the effects of warfarin, the pharmacist will report her starting with tamoxifen to the Thrombosis Service which will monitor this interaction and may adapt the scheme for the intake of warfarin. At the end of the consultation, Mrs B receives a brochure with all the information and is signposted the websites of breast cancer patient and research associations. After a few days, Mrs B decides to start tamoxifen and calls the pharmacy to tell it. As agreed, for the first half year she is dispensed tamoxifen monthly, keeping her in a diary how she feels and what side effects she suffers.

Although Mrs B continues to use the tamoxifen without too many problems, after several months she becomes depressed and visits the pharmacy with a prescription for paroxetine. The pharmacy technician enters the prescription in the pharmacy information system. Subsequently, an alert showing a drug–drug interaction with tamoxifen appears. The interaction comprises CYP2D6 inhibition by paroxetine leading to a reduced formation of the potent tamoxifen metabolite endoxifen which affects the effectiveness of tamoxifen treatment. The pharmacy contacts the GP, discusses the interaction, and proposes the use of citalopram instead.

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Chapter 33
Pharmaceutical Care in Viral Diseases (HIV and Hepatitis C)

Susan Kamal, Olivier Bugnon and Marie-Paule Schneider

Abstract Pharmacists are well positioned within the care continuum to help patients achieve their treatment outcomes as they are easily accessible, are in contact with the patients when they visit the pharmacy at treatment initiation and overtime for refill visits, and they have education and training in the management of drug–drug interactions and adverse effects. In this chapter, we highlighted evidence-based pharmaceutical care interventions in adherence, which is an important DRP in HIV and hepatitis C infections.

Keywords Pharmaceutical Care · AIDS · Hepatitis · Prevention
Medication adherence

33.1 Introduction

There are about 2.4 million people living with HIV in Europe, 36.7 million people worldwide [1]. Globally, 150 million people have chronic hepatitis C viral infection, which is about 2–3% of the world's population. In industrial countries, it is the most frequent cause of chronic hepatitis and hepatocellular carcinoma and the main indication for liver transplant. 10–30% of people living with HIV (PLWHIV) also have hepatitis C coinfection [2], which accelerates the impairment of the liver. However, since directly acting antivirals (DAAs) against hepatitis C have good clinical outcomes for patients mono-infected with HCV or coinfected with HCV and HIV, the World Health Organization (WHO) guidelines state that HIV+ patients coinfected with hepatitis C virus (HCV) no longer need to be considered as a hard-to-treat population [2]. However, the main actual challenges are risks of drug–drug interactions for HIV+ individuals coinfected with HCV, and for individuals

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with HIV or HCV suffering from other comorbidities (e.g., cardiovascular, depression, tuberculosis), medication nonadherence and access barriers to these expensive drugs. Knowledge in pharmacology and pharmaceutical care are key factors to ensure the success of HIV and Hepatitis C treatment, which means ensuring the clinical and economic efficiency of the treatment as well as the patient safety.

33.2 Disease Definitions

33.2.1 HIV

Human Immunodeficiency Virus (HIV) is a retrovirus that causes HIV infection, and over a long period for untreated individuals, causes acquired immunodeficiency syndrome (AIDS). HIV attacks the host's immune system, destroying a specific subset of T cells—CD4 lymphocyte cells reducing their numbers, which leaves the host prone to several opportunistic infections, e.g., pneumonia or infection-related cancers, e.g., Kaposi's sarcoma. It also infects other cells such as plasma cells, macrophages, and causes tissue inflammation throughout the body, which is strongly predictive of the risk of morbi-mortality. The three stages of HIV infection are: [1] acute HIV infection, [2] clinical latency and [3] AIDS.

The acute HIV infection stage occurs within 2–4 weeks after HIV exposure in about one-half of all patients. The infected individual experiences flu-like symptoms, which is the body's natural response to HIV infection. Symptoms include fever, adenopathy, pharyngitis, headaches, muscle aches, and sore throat. Dermatologic symptoms such as ulcers are also common. The virus is using CD4 cells to replicate, which destroys them. During this period, the host is very infectious and can transmit HIV to others through sexual contact or needle sharing. Toward the end of this phase, the host's immune response will bring the viral levels to a relatively stable level and the CD4 count begins to increase to normal levels, but still below pre-HIV infection levels. Then the infection progresses into the clinical latency stage. During this stage, the virus is replicating at a very low level, and is in symbiosis with the host without producing any symptoms; this is why it may also be called "asymptomatic HIV infection". This phase may last 10 years or longer in untreated individuals. Then, when untreated, the viral levels will start to rise and CD4 count will progressively decline over the years. When the level of CD4 cells falls below 200 copies/mL, or when the host suffers from one or more opportunistic infections, the HIV infection has progressed into AIDS. Without treatment, people with AIDS typically survive about 3 years.

The progress of the disease differs among hosts due to several factors including: host and virus genetics, how healthy individuals were before acquiring HIV infection and whether or not they were diagnosed and linked into care immediately after their exposure, which would improve their prognosis.

33.2.2 Hepatitis C

Hepatitis C is an infection caused by HCV, affecting the human liver. It is a bloodborne infection and can be transmitted through the transfusion of unscreened blood or blood products, or sharing needles among infected individuals. The infection can be both acute and chronic. Acute Hepatitis C infections occur in 15–45% of the cases; the infection is often asymptomatic, and the virus is cleared out without any treatment in 6 months. Chronic Hepatitis C infections occur in 55–85% of the cases; after an incubation period between 2 weeks and 6 months, infected individuals exhibit symptoms such as fever, fatigue, abdominal pain, nausea, vomiting, and jaundice. HCV infection is the leading cause of chronic liver disease, cirrhosis, and hepatocellular carcinoma, as well as the most common indication for liver transplantation in many countries [3].

33.3 Management of the Disease

33.3.1 Lifestyle

A new HIV diagnosis is devastating for many patients. HIV still has no cure. Thus, the dissemination of prevention and health promotion information is a public health priority. The impact of treatment on HIV transmission can be of greater effect when combined with behavioral change such as safer sexual practices, and harm reduction for people with intravenous drug use history. In addition, as a high level of antiretroviral (ARV) therapy (ART) adherence (90–95%) is required to achieve viral suppression [4], behavioral change such as adapting to regular daily medication intake is needed to maintain it in the long term. As PLWHIV are getting older due to the success of ARV therapy, pharmacists along with other healthcare providers (HCP) must pay attention to life style modifications to reduce risk of cardiovascular disease (e.g., increased physical exercise and smoking cessation).

Individuals with an untreated HCV infection are encouraged to make certain lifestyle changes. Most importantly, to refrain from drinking alcohol as much as possible, as it speeds up the progression to liver disease. It is also advisable to avoid blood contact with others through sharing razors, toothbrushes, or needles to prevent transmission to others.

33.3.2 Medications

To the moment of writing this book chapter, no cure exists for HIV, but long-term viral suppression can be achieved through continuous treatment with ARVs. Treatment involves six classes of ARVs and each drug is classified according to the part of the replication cycle of HIV that the drug inhibits.

HIV infection starts when HIV enters the human body and infects human CD4 lymphocytes. The first drug class is called "Entry/Fusion inhibitors" and it binds to CD4+ receptors and the chemokine CCR5 or CXCR4 co-receptors expressed in CD4 host cells, or viral gp41 or gp120 to prevent viral entry into the human cell. As HIV is an RNA virus, therefore it needs to reverse transcribe its RNA into DNA using the viral reverse transcriptase enzyme to be integrated within the nucleus of a human cell. Two drug classes inhibit the viral reverse transcriptase enzymes: "Non-nucleoside reverse transcriptase inhibitors (NNRTIs)" and "Nucleoside reverse transcriptase inhibitors (NRTIs)". The fourth class is "Integrase inhibitors (INI)" and they prevent the integration of viral DNA strands into the host's DNA. The fifth class is "Protease inhibitors (PI)", which prevent the cleaving of viral proteins needed to form mature viruses. Improvement of the pharmacokinetic properties of PIs can be done through the addition of a small dose of ritonavir (RTV) or Cobicistat, i.e., "boosting". There are several novel ARVs that are less widely used or are still in clinical trials such as attachment inhibitors, maturation inhibitors, and capsid inhibitors.

ART is usually used in combination. Typical combinations include two NRTIs as a "backbone" along with one NNRTI, INI or boosted PI as a "base". Currently, the first line of combined ART (cART) consists of a single pill, taken once daily to be started as soon as an HIV+ diagnosis is established. Pre-Exposure Prophylaxis (PrEP) is recommended for HIV negative people with a substantial risk of getting an HIV infection and who do not always use condoms (e.g., individuals who engage in chemsex) by getting a daily or intermittent dose of ARVs according to medical recommendation. In addition, postexposure prophylaxis (PEP) is possible within 48–72 h after exposure to HIV in order to prevent infection (e.g., unsafe sex, needle stick accident). PEP includes counseling, and administration of a 28-day course of ARVs. Pharmacists play an important role in helping patients initiate treatment and prevent early discontinuation.

Treatment of chronic hepatitis C is a fast evolving field with rapidly changing recommendations. Current treatment guidelines recommend DAA once daily. There are four classes of DAAs that directly target HCV nonstructural (NS) proteins essential to viral replication through different mechanisms: Nucleoside and Nucleotide NS5B Polymerase Inhibitors, NS3/4A Protease Inhibitors (PIs), NS5A Inhibitors and Non-Nucleoside NS5B Polymerase Inhibitors (e.g., Simeprevir, Paritaprevir, Daclatasvir, Ledipasvir, Ombitasvir, Sofosbuvir, and Dasabuvir).

Treatment with DAAs can cure most patients within 12 weeks and a maximum of 24 weeks. However, the cost of DAAs remains very high in many countries. There remains a limited role for older regimens with pegylated interferon and ribavirin in certain cases.

Despite the strong recommendation for treatment of nearly all HCV-infected patients, pretreatment assessment of a patient's understanding of treatment goals and provision of education about adherence and follow-up are extremely important, in addition to the essential Viral genotype evaluation. A well-established therapeutic relationship between clinicians and patients remains crucial for optimal outcomes with direct-acting antiviral (DAA) therapies. Additionally, in certain

settings there remain factors that impact access to medications and the ability to deliver them to patients. In these settings, clinicians may still need to decide which patient should be treated first. The descriptions of unique populations discussed in these guidelines may help physicians make more informed treatment decisions for these groups [5].

Several treatment guidelines can be accessed online for more guidance on HIV or hepatitis C treatment such as: European treatment guidelines [6], recommendations of the International Antiviral Society–USA Panel on antiretroviral treatment of HIV+ adults and the Swiss Association for the Study of the Liver (SASL) expert opinion statement on the treatment of chronic Hepatitis C [7].

33.3.3 Drug-Related Problems

DRPs such as side effects, drug–drug interactions and poor adherence can be problematic, especially in cART that is a lifelong treatment. Novel ARVs may have fewer side effects than older generations. Table 33.1 summarizes side effects by antiretroviral class for the most widely used treatment classes. There are also some adverse effects related to drug–food interactions and drug–drug interactions between two or more ARVs and also between ARVs and co-treatments. For example, as PIs are metabolized by cytochrome (CY) P450, hence their concomitant use with other drugs that are metabolized by CYP450 can result in significant drug–drug interactions with prescribed, OTC and herbal treatments (e.g., simvastatin, midazolam, ethinylestradiol, ergot derivates, St John's wort) [6]. Boosters such as low dose ritonavir or cobicistat are potent inhibitors of CYP450. Anti-acid drugs modify the bioavailability of several ARVs. The University of Liverpool websites [8] are a significant resource for pharmacists to check for drug–drug interaction in HIV therapy.

Table 33.1 Antiretroviral treatment classes and severe side effects

HIV antiretroviral class (most prescribed drugs)	Common or severe side effects
NRTI (TDF, TAF, FTC, 3TC, ABC)	Anorexia, nausea, vomiting, hepatoxicity, lipoatrophy, hyperlactatemia, peripheral neuropathy, tubular injury, rash, hypersensitivity, anemia
NNRTI (ETV, RPV, EFV, NVP)	Hepatotoxicity, sleep disorders and psychological stress, rash, hypersensitivity, eosinophilia
Boosted PI (ATV, DRV, LPV)	Anorexia, nausea, vomiting, hepatoxicity, hyperglycemia, osteoporosis, nephrolithiasis, alopecia, dry skin
INI (RAL, DTG, EVG/c)	Diarrhea, nausea, fatigue, headache, insomnia

NRTI = nucleoside reverse transcriptase Inhibitors, NNRT = non-nucleoside reverse transcriptase inhibitors, PI = protease inhibitors, INI = integrase inhibitors, TDF = tenofovir disoproxil fumarate, TAF = tenofovir alafenamide, FTC = emtricitabine, 3TC = Lamivudine, ABC = abacavir, ETV = etravirine, RPV = rilpivirine, EFV = efavirenz, NVP = Nevirapine, ATV = atazanavir, DRV = darunavir, LPV = lopinavir, RAL = raltegravir, DTG = dolutegravir, EVG = elvitegravir

On contrary to former interferon and ribavirin-based treatments, DAAs are well tolerated and easier to take (e.g.,, some DAAs are available as one pill a day). Main side effects are nausea, diarrhea, headache, and fatigue. Other side effects such as rash, photosensitivity, pruritus (e.g., simeprevir) or cardiovascular (e.g., sofosbuvir) are more drug specific. Some DAAs such as Dasabuvir and Elbasvir/grazoprevir are substrates of CYP450 and other DAAs are moderate inhibitors of CYP450 such as asunaprevir, therefore they have a direct drug–drug interaction with ARVs and other CYP450 inhibitors or inducers (an interactions checker is available on the Liverpool's University website [9]. HCV-infected patients with liver cirrhosis may have an impaired CYP450 function that puts them at a higher risk of drug–drug interactions and drug toxicity.

Adherence to medication is an important aspect, especially in the treatment of viral infections (see also Chap. 5). Nonadherence to ART is associated with virologic failure, development of drug-resistant viral mutations and a higher risk of mortality, hence better understanding of what factors predict poor adherence is needed. The scientific literature is inconclusive about different social and demographic factors such as ethnicity, education level, income level, housing situation or gender as predictors of nonadherence. Even though individual studies in specific populations may find a link between particular factors and nonadherence, meta-analyses lack consistent findings. In the context of HIV infection, alcohol use, depression, anxiety, and cognitive disorders are associated with a greater risk of nonadherence in several studies, and lower adherence was observed among adolescents infected with HIV. As HIV is still highly stigmatized among different communities in different parts of the world, patients may be more liable to develop anxiety or psychological disorders, which put them at a risk of nonadherence.

As DAAs are relatively newer drugs, wide scale studies measuring adherence to DAAs are not yet published. However, existing evidence from the US shows high adherence over 12 weeks of DAA intake [10]. Adherence to DAA therapy is easier than with older interferon-based regimens due to markedly decreased toxicity, easier dosing schedule, shorter course of treatment, and providers' adherence reinforcement due to the costs of DAA.

33.3.4 Treatment Goals

For HIV patients, the ultimate treatment goal is a durable viral suppression (below 50 copies/mL HIV RNA viral load) and a normal CD4 lymphocyte count (above 400 cells/mm^3). For Hepatitis C patients, the treatment goal is to achieve a sustained virologic response (SVR) defined as undetectable HCV RNA for 24 weeks following completion of therapy. There is evidence that SVR can reverse the early effects of fibrosis and prevent the progression into hepatocellular carcinoma.

33.3.5 Self-management

Self-management involves several concepts such as patient education, integrated person-centered care, and behavioral change. Patients can learn to self-manage their treatment using several tools such as: electronic pillboxes, phone applications (Apps) or alarm reminders about medication intake timing and pillbox organizers that were shown to decrease unintentional nonadherence. Technology-based tools include telephone support (including SMS) and web based interventions (including the aforementioned Apps). Such tools have the potential to keep the patient in close contact with the provider and help the provider address regularly, both patient intentional and unintentional nonadherent behaviors and adjust the treatment to patient's needs. Therefore, patients should be encouraged to share their electronic/digital data with healthcare providers including pharmacists.

Regarding self-management of side effects, several methods can be of help to patients. In case of mild depression, insomnia, or anxiety, regular exercise and relaxation exercises can help alleviate symptoms. For gastric discomfort, addressing patients' needs in terms of best food–medicines combinations, timing of medicine intake, and eating habits provide relief for many patients. For dry skin, using moisturizing creams that are available over the counter can be of help. Finally, in case of dry mouth, drinking plenty of water and brushing teeth regularly is suggested. In case of more severe side effects, alternative regimens might be the best solution, which have to be discussed with the prescriber.

33.4 Pharmaceutical Care in HIV and HCV

33.4.1 Existing Evidence

Several studies in HIV provide evidence on the positive impact of pharmacists on the clinical outcomes expressed by: higher rates of viral suppression and greater increases in CD4 cell count [11, 12], reduced pill burden and dosing frequency and higher adherence of HIV patients [13]. A study that compared two treating arms for 1571 HIV+ individuals initiating their antiretroviral therapy, one including a pharmacist and the other not, showed that patients exposed to a pharmacist were more likely to achieve viral suppression than those who did not [14]. Another study showed that pharmacist-led interventions, such as adherence counseling and regimen adjustment were associated with better treatment outcomes such as sustained undetectable viral load [15]. A pharmacist-led behavioral intervention among nonadherent HIV+ individuals also demonstrated increased retention to pharmacy refill and clinic appointments, fewer hospitalizations, and decreased number of opportunistic infections [16].

For Hepatitis C infections, clinical pharmacists play an important role in: checking for hepatitis A and B virus immunizations for those infected with HCV,

managing drug–drug interactions and in patient counseling, education, and adherence monitoring. An interprofessional intervention including pharmacists, showed comparable clinical outcomes of sustained SVR among the community-based intervention participants to those who participated in clinical trials [17]. The addition of pharmacists to a team of hepatologists and nurses resulted in an increase in medication adherence and SVR rates in HCV patients [18]. Finally, including pharmacists with experience in HCV in care provision, demonstrated better HCV viral load monitoring and appropriate management of DAA-related side effects [19].

33.4.2 Approach to Care/Interventions

According to many pharmaceutical care guidelines, the pharmacist's role in caring for patients with HIV/AIDS and/or HCV infection is part of the Medication Therapy Management Services (MTMs) which include:

(1) Patient counseling and education about their disease, either directly or through referring patients to specialist centers or trusted information sources such as books, leaflets or online websites (see also Chap. 4).
(2) Checking patient readiness before treatment initiation, especially because, since recently, cART is started just after diagnosis,
(3) reinforcing medication adherence on the long term and
(4) monitoring response to therapy, managing adverse effects, and dug–drug interactions.

In this chapter, we will focus on the role of the pharmacist in adherence enhancing interventions.

Based on the dimensions of adherence defined by the WHO, described in Chap. 5, the barriers and facilitators to adherence and consequently the levels of an adherence enhancing intervention can be grouped into 3 main factors/levels:

(1) Cognitive and psychosocial factors\
(2) Environmental and organizational factors and
(3) Treatment-related factors.

Even though the role of pharmacists in the treatment of HIV and HCV patients is well documented in the literature, the impact of their role in evidence-based intervention studies that include adherence data, and have a large sample size is not well described. However, there are few examples that we can share in this chapter.

Pharmacists should ensure continuous access to ARVs whenever it is in their capacity to avoid any treatment discontinuation and a risk of viral rebound. For example, by maintaining contact with the treating physicians to guarantee a continuous access to ARV by renewing prescriptions as timely as possible. Further, due to the success of ART, the HIV population is aging and is at risk of developing comorbidities. That necessitates that the pharmacist should reinforce medication adherence of all prescribed treatments from various prescribers while minimizing

the pill burden and side effects. They should also invite their patients to inform them if they collect different treatments from different pharmacies or online to advise them on possible drug–drug interactions. This may be of special importance as some patients may obtain their HIV treatments from pharmacies that differ from the pharmacies where they obtain their other co-treatments to maintain their confidentiality. In some settings, pharmacists can play a role in HIV testing and counseling high-risk groups (e.g., when providing the morning-after PEP pill).

Drug holidays can be detrimental in HIV and HCV. Hence, it is the role of the pharmacist to advice patients on how to make up for missed doses. For example, the timespan during which a missed dose can be taken, to take the next dose at the scheduled time and not to take multiple doses at once to compensate for their missed doses.

HIV-related stigma has been known as a barrier to access to treatment, care, and prevention. Pharmacists along with other HCPs can also play an important role in reducing HIV-related stigma. This can be done through providing a welcoming environment for HIV+ individuals who come to their working places within the healthcare system (e.g., pharmacies or hospitals).

At the Community Pharmacy of the Department of Ambulatory Care & Community Medicine (University of Lausanne, Switzerland) in collaboration with the Infectious Diseases Service of the University Hospital, a medication adherence program has been implemented. Motivational interviewing is combined to longitudinal medication adherence monitoring via electronic monitors (MEMS^{TM}, Aardex MWV, Sion, Switzerland), and pill count. Electronic adherence data are shown to the patient as feedback and a report is sent to the physician and nurse after each interview to ensure continuity in care [20]. HIV+ patients who participated in this intervention were shown to have an increased retention in care versus patients who did not [21]. A cohort study in Canada compared patient's adherence when cared for in a tertiary AIDS care hospital outpatient pharmacy (where pharmacists provided medication counseling, individualized regimens, and adverse effect monitoring) with those cared for in family physicians' offices. Results show higher adherence rates (> 90%) among those who had contact with pharmacists (70% of patients who had contact vs. 55% of patients who did not have contact with pharmacists) (22). In a liver unit in Spain, a multidisciplinary support program (MSP) among 447 HCV patients showed that adherence and SVR rates were higher among participating patients versus control group (94.6 and 77.1%, respectively, for MSP vs. 78.9 and 61.9% for controls) [18].

33.4.3 Biomarkers

Important biomarkers in HIV infection are plasma HIV RNA levels which can be determined through using polymerase chain reaction (PCR) assay with a lower detection level of either 50 copies/mL or in new generation equipment 20 copies/ml. HIV RNA levels can be dichotomized into detectable or not, based on the lower

detection level of the PCR assay. CD4 lymphocyte count is the second important biomarker and can be measured using standard flow cytometry. A normal range for CD4 cells is about 500–1200 cells/mm3.

In chronic HCV infection, liver-related biomarkers have been developed to predict liver fibrosis or cirrhosis and hepatocellular carcinoma. These include HCV genotype, serum HCV RNA load, stage of fibrosis, and Child–Pugh score (total bilirubin, albumin, INR, ascites, and encephalopathy).

33.4.4 Outcomes that Matter

Outcomes that have to be addressed in HIV and hepatitis C can be classified according to the economic, clinical, and humanistic outcomes (ECHOs) model of pharmaceutical care services.

In HIV, pharmacists can have direct influence on direct clinical outcomes namely viral load and CD4 count. Indeed, their role is crucial in supporting/enhancing adherence to ARVs and co-treatments, by reducing pill burden and frequency of dosing, increasing retention in care, reducing incidence of opportunistic infections and reducing ARV-related toxicity. Nonadherence to antiretrovirals can lead to unwanted outcomes such as viral resistance that is difficult to treat and costly to the healthcare system. In addition, the cost of treating HIV-related opportunistic infections can be burdensome to the healthcare system as well. Evidence shows that patients with sustained undetectable HIV RNA viral load and higher CD4 cell counts, fewer HIV symptoms, lower pill burden, and higher adherence have improved survival rates, higher health-related quality of life (HRQOL) and can attend to daily living tasks. Therefore, increasing the HRQOL of PLWHIV has become an important treatment goal. HRQOL can be enhanced through several physical, psychological, and social determinants of health. Pharmacists can play an important role in health promotion, patient therapeutic education, and psychosocial counseling. Pharmacists should encourage practical and emotional support whenever possible from significant others of patients to facilitate long-term medication adherence. They can decrease the stigma surrounding HIV patients through their professional, empathic, and supportive attitude. They should also support pregnant HIV+ women on cART adherence to avoid vertical transmission to their newborns.

Patients with HCV are known to have reduced work productivity and HRQOL, high rates of all-cause hospitalizations and mortality, which represent an economic burden to the patients and the healthcare system. Successful treatment should reduce liver-related morbidity and mortality, hospitalization rates, and reduced risk of developing hepatocellular carcinoma. Further, as hepatitis C is curable for the first time with the introduction of DAAs that are very costly, it is the role of the pharmacists to ensure access to treatments for eligible patients, reinforce patient's strict persistence and adherence to treatment, help patients manage their side effects if any and check the presence of drug–drug interactions.

33.4.5 Documenting Care Provided

Appropriate documentation of activities of pharmaceutical care is important for efficient communication among HCP, regarding the patients and to collect evidence on the role of the pharmacist in the care continuum (see also Chap. 8). Documentation can be in patient records or medical charts or in individual pharmacy records. The records can be in digital form or paper-based and can also be part of a standalone computer database or, whenever possible, part of an integrated electronic health records database.

Case Scenario

In this case scenario, we will work on enhancing adherence by identifying the barriers and facilitators to adherence within the three main levels as described earlier. This approach is applied in a pharmacist-led interdisciplinary adherence enhancing intervention in Switzerland, and can be adapted elsewhere in the world. The three levels are: (1) Cognitive and psychosocial factors; (2) Environmental and organizational factors; and (3) Treatment-related factors.

Female patient in her forties, originally from West sub-Saharan Africa, has four children and is single. She was diagnosed with HIV 4 years ago following sexual assault. She was prescribed efavirenz/emtricitabine/tenofovir disoproxil fumarate once daily. The viral load when starting treatment was 39,000 copies/ml. The viral load one month later was undetectable with CD4 count 550 cell/mm^3. Her taking adherence as measured by electronic monitoring is around 95%, with regular medication intake until one year later after starting treatment. Starting the following year, she stopped going to her pharmacy and medical visits, her adherence level dropped, and viral load was detectable again.

1. Cognitive and Psychosocial Factors

Barriers: She is single, as she believes that it is impossible to find a partner who would accept her HIV diagnosis, and she does not want to grow old alone. She does not share with her relatives that she is HIV+, feels socially isolated and sometimes she cries herself to sleep.

Facilitators: She accepts her treatment and she can see the effect of treatment on her health. She has a strong will to live to look after her four children. She knows how to regularly discipline her medication intake around the same time every night, before she goes to sleep.

2. Environmental and Organizational Factors

Barriers: Sometimes she works in the night so the medication intake hours are affected as they are different to her usual habits, taking them before going to bed.

Facilitators: She knows how to associate medication intake timing with a daily behavior, which is going to bed, which makes it hard to forget. She also keeps her medicine in a drawer next to her bed so it helps her remember.

3. Treatment-Related Factors

Barriers: She complains from nausea especially if she takes her medication on an empty stomach. She also suffers from fatigue and headaches.

Facilitators: She says that her side effects are less frequent over time, compared to daily symptoms in the beginning of the treatment initiation.

The main difficulties with this patient are that she has a difficult social status being a single mother to four children without a fixed employment. She also feels stigmatized by her HIV status. Pharmaceutical care support should combine best pharmacological knowledge with advanced communication competences (e.g., motivational interviewing). For example, to empower her by evoking her ARV success in the past, and what this means for her today in terms of eventually resuming her treatment intake. The pharmacist should monitor the evolution of fatigue from one visit to the next one. In case the fatigue is persistent, it might be a side effect of efavirenz and the pharmacist should evaluate the possibilities to switch to a non-efavirenz containing ARV regimen with the prescriber. If the patient has difficulties adhering to an evening dose due to working night shifts, the pharmacist can recommend alternative ARVs that can be taken in the morning. As physicians are attentive to side effects that impair clinical functionalities (e.g., liver, kidney, heart), it is the role of the pharmacists to pay attention to the patient's HRQOL by monitoring milder side effects such as nausea or fatigue in this case study. If psychosocial aid is possible, the pharmacist can recommend a psychologist or psychosocial nurse that can work with the patient to help her overcome her distress about her HIV status, and work with her in view of the decreased risk of HIV transmission among sero-discordant couples (one partner is HIV negative and the other is HIV positive) when specific clinical conditions are met and discussed with the infectious disease physician. Lastly, the pharmacist should establish with the patient the potential use of refill reminders to keep her in care.

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Part VII
Remuneration of Pharmaceutical Care

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Introduction

Pharmaceutical care implies a shift in the pharmacy practice model. The shift started in a period where all over the world pharmacists' earnings were based on fixed markups on the medicine costs. However, pharmaceutical care is much more about providing a service than about delivering a product. Therefore, the existing remuneration models quickly became unfit.

In most countries, medicines have a fixed price. This price is usually decided by the license holder together with the regulatory agency. These negotiations take place outside and often distant from pharmacy practice. This means that the practitioner does not have to think about how much he should charge for the medicine, he simply needs to think how efficient he can be in dispensing as pharmaceutical care evolves, some of the activities may indirectly lead to less medicines consumption. This implies that, while doing well, the pharmacist earns less. This led pharmacists to rethink their service delivery and the remuneration models. Pharmacists had to change their mindset and charge additionally the cost of the pharmaceutical care services. How much time does it take? What are the resources needed? What is the perceived value for the recipient of the service? To be able to answer such questions, pharmacists need to start documenting what they do, timing activities, and valuing their services from the patient's perspective. Additionally, they must develop a whole new set of activities for which they were traditionally not trained.

In this part, we start by presenting the basic functioning of healthcare systems in view of pharmaceutical care, in Chap. 34. This knowledge is fundamental to understand the deeper concepts, later referred to. The payment methods in healthcare systems are then further detailed in Chap. 35, which we believe is also necessary for understanding the following chapters. In Chap. 36, we discuss how pharmacists may determine the price of a service, which in fact is part of health technology assessment. Some pharmacy services, including pharmaceutical care,

are already being paid in specific areas. Without aiming for a full review of these, in Chap. 37, we provide some examples of remunerated services, focusing on the payment models. This part finishes with a chapter entitled "Paying for Pharmaceutical Care", where we selected some of the mentioned experiences to further detail the costing methods used, while discussing their advantages and disadvantages. Based on the literature around barriers to implementation, we have then assumed that a simple exercise would be needed to demonstrate how we can make pharmaceutical care more profitable by managing it in a leaner way.

The overall idea of this part is to provide pharmacists with fundamental concepts of economics that can be helpful to determine the price of their pharmaceutical care services in practice. Although we certainly believe that additional reading in specific literature [1, 2] may be needed for policy makers, we hope this part is useful for practitioners who want to start costing their services, or think of alternative ways for valuing their services.

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Chapter 34
Introduction to Healthcare Systems

Mitja Kos

Abstract Various healthcare systems have developed around the world, which tend to follow some general patterns. They all use, to a larger or smaller extent, elements of The Bismarck model and The Beveridge Model. In contrast to the two models, the out-of-pocket model represents another possible approach, which however, does not embrace an intention toward universal coverage.

Keywords Pharmaceutical care · Healthcare system · Bismarck model Beveridge model · Out-of-pocket model

34.1 Introduction

Universal health coverage, as defined by WHO, requires all people to have access to needed health services without the risk of financial hardship associated with accessing services [1]. For that purpose, various healthcare systems have developed around the world. Although they can vary in many different aspects, they all tend to follow some general patterns. They all use, to a larger or smaller extent, elements of The Bismarck model and The Beveridge Model (Fig. 34.1). These two distinct models of health care are important also from the historical perspective. Some countries base their system upon one model, while others choose a combination. In contrast to the two models, the out-of-pocket model represents another possible approach, which however, does not embrace an intention toward universal coverage [2–4].

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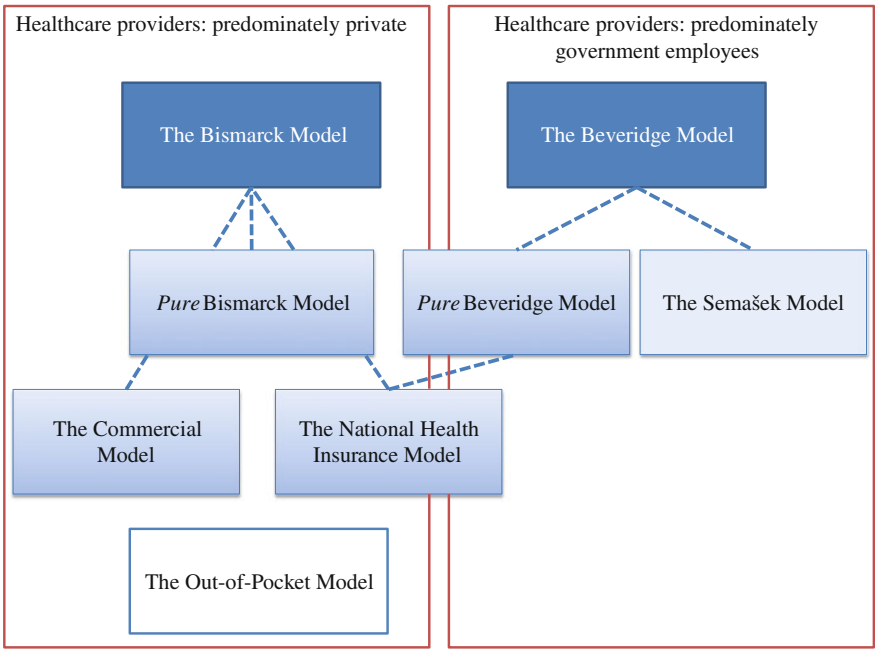

Fig. 34.1 Models of healthcare systems. Models are presented in light blue. They follow the two distinct types of models: The Bismarck and The Beveridge model. An exception in this regard is the Out-of-Pocket Model

34.2 The Bismarck Model

The Bismarck model was named after the Prussian Chancellor, Otto von Bismarck, who implemented the system in 1883 as part of the concept of welfare state during the unification of Germany. The Bismarck model is a social insurance model where it is compulsory for all citizens to belong to an insurance fund. In its origin, it is a multi-payer model. For that purpose, it uses several insurance agencies, also known as 'sickness funds'. They are financed through social contributions or premiums jointly paid by employers and employees. The premiums are usually in the form of payroll deductions and hence costs can be still controlled by the government to an extent. Insurance agencies have a high level of autonomy, which means that the finances cannot be used for other purposes than health care. They are run as nonprofit organizations and are required to accept all citizens without discrimination. Solidarity is built into the system that also guarantees citizens without any income to have access to health care. Healthcare providers tend to be largely private. The role of the state is minor and is primarily related with regulation and its control in practice. Healthcare systems based on this model may be found in Germany, Austria, Belgium, France, the Netherlands, Japan, and to a degree, Latin America [5].

In Fig. 34.1, three different models are related to the Bismarck-type model. Apart from the "pure" Bismarck model in its origin, The Commercial Model and The National Health Insurance Model are presented, which both use insurance programmes as the base of the system.

34.2.1 The Commercial Model

Systems based on the commercial model have typically multiple payers that offer private insurance programmes. Health insurance companies can be for-profit enterprises, unlike in the pure Bismarck-type model. The system is based on the demand/supply basis with the possibility to freely choose among different insurance programmes. The premiums are based on risk assessments and the insurances can also refuse the request for insurance. The state has a very limited, regulatory role. The typical example of such a system could be found in USA before the Patient Protection and Affordable Care Act into law by President Barack Obama in 2010 [6, 7].

34.2.2 The National Health Insurance Model

The National Health Insurance system is a form of the Bismarck model, although some authors classify it as a separate model or describe it as having elements of both Beveridge and Bismarck model. It is a single-payer, state-run insurance programme, which is compulsory for all citizens. Payroll contributions are often supplemented by general taxation or other public funds. According to the higher involvement of the state, it makes it similar to the Beveridge model. Existence of the insurance programme as well as predominately private facilities and providers of health care increases the similarity to The Bismarck model. This model is distinct from the pure Bismarck type, which has multiple payers (insurance funds) and not only one. The most typical National Health Insurance Model can be found in Canada, with some younger developments in Taiwan and South Korea [8].

34.3 The Beveridge Model

The Beveridge model requires the state to assure social as well as health security. The system is named after Sir William Henry Beveridge who designed Britain's National Health Service as a reaction to the unacceptable poverty after the Second World War. It became operational in 1948. In this system, health care is financed by the government (single-payer system) through tax payments. Many healthcare facilities are owned by the government, and the healthcare workers are government

employees. Although private initiatives are allowed they are often financed by the government. The government, as the only healthcare payer, has total control over the costs of the system. Countries that use a variation of Beveridge plan include the United Kingdom, Portugal, Spain, Italy and most of Scandinavia [9, 10].

34.3.1 The Semašek Model

The Semašek model is similar to the Beveridge model where the state plays the crucial role in assuring social and health welfare. The model is based on the socialistic ideology and was typical for the former Soviet Union as well as for other socialistic countries developing in parallel to the Beveridge model [11, 12].

34.4 The Out-of-Pocket Model

The Out-of-Pocket Model is based on direct payments from patients to healthcare workers at the time of treatment. Such a system does not present a systematic approach that would assure health care to all citizens in need. On the contrary to what one would expect, the model is present in the majority of countries as perhaps only one-quarter of all the countries have an established and organized healthcare system, accordingly to one of the previously described models.

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Chapter 35
Payment Methods and Pharmaceutical Care

Filipa Alves da Costa and Mitja Kos

Abstract This chapter provides an overview of payment methods used in health care in general, expanding on those that have been adopted for pharmaceutical care. A critique is made for the different approaches, while recognizing some particularities of pharmaceutical care provision that would suggest different and new methods need development. The chapter finalizes with a proposed model of payment for pharmaceutical care.

Keywords Pharmaceutical Care · Remuneration · Pay for Performance
Pay for Service · Outpatient service · QALY

35.1 Payment Methods in Healthcare Systems

The most common forms of payment for healthcare provision are divided into prospective and retrospective analyses of service provision.

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35.1.1 Retrospective Analysis Models

The retrospective analysis models include the fee-for-service model, traditionally used in the outpatient setting, namely, by general practitioners (GPs) or specialist services. This is a model increasingly being adopted in pharmacy practice.

35.1.2 Prospective Analysis Models

The prospective analysis models of payment include the payment for case, capitation, and global budget. The payment for case is traditionally used in the hospital setting, where the diagnosis-related group system is used. This system attributes a cost to each patient entering the hospital, where each unit of product and service is estimated and added up to come to the most approximate estimation of the cost of an illness episode. However, pharmaceutical interventions are not listed and as such are not accounted for in this cost estimation. The capitation system is the typical model used in primary care in many countries, where GPs get paid according to the number of patients enrolled in their lists, and the cost will cover the provision of a range of services. The term capitation is also used in pharmacy practice in some countries to describe the eventually existing rules for opening a new pharmacy; for instance, a pharmacy is established for every 2500 inhabitants. As such, in theory, this system could also be used to establish the cost of a range of pharmacy services being provided to that given population.

The global budget is also a prospective model of payment generally applicable to hospitals, a range of services are included but the main difference resides in the fact that the payment is independent of the actual service provision [1].

35.1.3 Pros and Cons of Different Models

All these models of service payment are based on the structure or on the process, making the parallelism with the structure–process–outcome (SPO) paradigm. These systems do not favor efficiency of the healthcare systems, because the providers always get the same amount regardless of the quality of services provided. In some of these models, it may even encourage bad quality, because the more patients are served the more is earned. Additionally, these methods encourage defragmented healthcare provision, where costs are estimated by setting and by provider and the patient is not seen as a holistic entity. As a result, more recently, different models of payment have developed. These try to focus on the outcome of service provision, and the pay-for-performance model is one example being incorporated in various countries. In an Organisation for Economic Co-operation and Development (OECD) report from 2012, more than half of the countries had at least one

pay-for-performance scheme, mostly found in primary care. This model assumes that the service provision should be either rewarded or penalized according to the clinical outcomes of the patients (sometimes also humanistic and/or economic). The difficulty in this model is to determine the division of the payment by each of the providers involved in the patient pathway. As an example, we can think of a diabetic patient discharged from hospital and transferred to the community, where he is efficiently monitored during 6 months by a nurse, a nutritionist, a pharmacist, a GP, and an endocrinologist. All these providers contribute to a given extent to the final outcome measured, which is optimal glycaemic control. The award is a payment correspondent to the amount of saving one amputation. How is this money to be distributed? Did all providers contribute equally? Were all of them really providing a good service? Obviously for such systems to flourish, developed technology infrastructures must exist, as well as the most appropriate indicators.

Another drawback of this model is that service planners do not necessarily take into consideration all providers involved in patient care. The Portuguese example of a pay-for-performance scheme is applied to family health units. The figure of the family health providers has been created for these units, but the sole professionals considered compulsory are the family physician, the family nurse, and the family administrative staff. Nonetheless, we believe that once a balance has been reached, an adaptation of such methods may be useful as it should be aligned with health policy objectives.

35.2 Difficulties in Using Pay-for-Performance Methods in Pharmaceutical Care

One important aspect to consider in pay-for-performance methods is that while some interventions aim at treating patients or curing lives, some other interventions focus on preventing illness. In the treatment model, society pays for the cost saved when the condition is controlled and the consequences of disease aggravation do not exist due to better care provided. In the prevention model, in fact society is paying for something that does not happen. Therefore, we may consider more difficult to estimate its true economic impact, also because the effect being prevented could, without such intervention happen after some days, months, or years. Let us think of some pharmaceutical care typical activities, which focus on preventing drug-related problems.

We all know that the clinical relevance of drug-related problems may vary widely, and so will their clinical potential consequences. Also, some drug-related problems may express themselves in the short-term or in the long-term. As an example we may consider the immediate effect of a benzodiazepine taken concurrently with alcohol, where if detected in the context of a pharmaceutical care intervention, could prevent a car accident, which costs may be eventually extrapolated. Even this simple example can have cost variations, if we consider a car accident with no third parties involved or a major accident involving others.

Nonetheless, the main difference is if we want to cost the long-term effect of preventing dependency from benzodiazepines with associated memory loss, or even the high likelihood that as age increases, the physical dependence and years of use lead to a dose escalation, culminating in a hip fracture. In such scenario, the prevention exercise should also take into account that the costs will not be the same in 10 or 50 years, and this is often very difficult to predict as it depends on much more than simply the inflation rate.

35.3 A Proposed Model of Pay for Performance Applied to Pharmaceutical Care

Models where performance is measured and paid according to results obtained have been emerging worldwide and in Europe [2]. In most of these, simulation is used and high and low performing care units or care providers may be differentiated according to primary outcomes obtained. Obviously such models may only be valid when matching is possible to enable prognosis and risk factors or risk modifiers to be taken into account. In pharmacy practice, we are very far from such models, mostly because we often focus on less tangible outcomes. Despite that, the principles may be applied and should be possible to extrapolate.

A similar rationale may be used when we assume that an outcome may depend on various contributing factors. Researchers who focus on diseases with multiple causality and complex models, such as cardiovascular diseases have long struggled with the need to isolate the contributions from various sources. Taking cardiovascular disease as an example, we know that improvements observed over the most recent years may result from changes in lifestyle, from better pharmacological treatments, most modern surgery procedures, or simply greater uptake of all of the available treatments (both by clinicians and by patients). Each of these groups is complex and improvements may result from one single factor or from a conjugation of factors, e.g. smoking cessation, lipid and/or blood pressure treatment, and diabetes control, to name a few. The Improving Mood—Promoting Access to Collaborative Treatment (IMPACT) model is one example where retrospective population data has been used to define the relative contribution of each factor to the outcome of interest [3]. We propose here the PHARMACARE model, where one would estimate the relative contribution of each pharmacist-led service to the control of the disease, ultimately entering the IMPACT model or equivalent (depending on the disease).

The value attributable to pharmaceutical care would then be a result of all the individual contributions leading to better disease outcomes where each of them would be weighted. In Fig. 35.1, we have used an illustrative example taken from the authors of the IMPACT model who have stated that 8% could not be explained by their model. This is merely an example, because in fact the IMPACT model was developed with different purposes. Therefore it has considered the contribution of

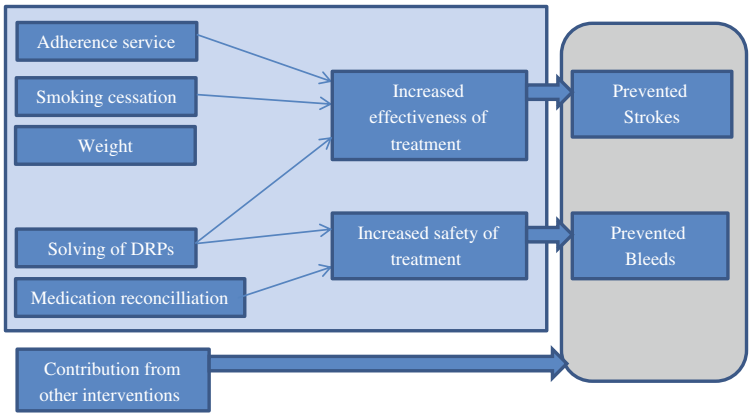

Fig. 35.1 The PHARMACARE model, inspired by the impact model [3]

pharmacological treatments as a whole, i.e. as unit measure, where in fact in our model would assume various individual contributions to an optimal pharmacological treatment. In our concept, optimal treatment results not only from an efficacious drug, but also from one being taken as directed by physician and agreed by literate patients who also take concurrent medications, i.e. an effective and safe treatment as ensured when the patient is being monitored through pharmaceutical care. In the IMPACT model, approximately 50% was attributable to increased uptake of treatments, so in fact, part of this proportion may be a result of pharmaceutical care.

So, the first step would be to estimate the true contribution of pharmaceutical care to better disease outcomes.

The second step is in fact quite straightforward and has been traditionally estimated in the most prevalent, if not all, disease conditions, which is to determine the costs of prevented negative outcomes. The complexity of the measure chosen may vary, but disability-adjusted life years (DALYs) or quality-adjusted life years (QALYs) are possible measures to consider, for which current data are available [4]. Taking atrial fibrillation as the example, we would need to define the costs of, e.g. stroke and bleeds, and add them.

The third step would be the modeling of the costs of the outcome prevented into the future. In this step, we may assume that some outcomes would manifest themselves within 1 year and others within 10 years, if the care would not have been provided.

The final step would be to determine the payment of service provision. The payment of the service provided should then be a result of the savings its provision generates. Of course, variants would then be possible to apply, using different methods for pricing the services, as further detailed in Chap. 36.

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Chapter 36
How to Determine the Price of a Service

Mitja Kos

Abstract Pricing of services depends on the healthcare system, established procedures, and the way service is going to function in the system. The ideal would be a remunerated service by the healthcare payer. Labor, material, and overhead cost should be considered for pricing services. Most often, the following methods are used for pricing the service: cost-plus pricing, competition-based pricing, and value-based pricing. Health technology assessment is a formal procedure of evaluating health technologies, including new pharmacy services. It can, however, differ in the extent and nature of its implementation in healthcare systems and can, but not necessarily, also include a thorough health economic evaluation.

Keywords Pharmaceutical Care · Remuneration · Service costs
Health technology assessment · Cost analysis

36.1 Introduction

Pricing of services very much depends on the healthcare system and established procedures (see Chaps. 34 and 35). The major aim of any healthcare system is, of course, to assure health. Therefore, from the healthcare payer perspective, it can be easily understood that the cost of the service that provides benefit to patients is covered and that the service needs to have an assured financial sustainability. On the contrary, earning profits with healthcare services beyond reasonable amounts will be for sure an issue for consideration and debate.

When preparing a new pharmaceutical care service, one should first define how the service is going to function in the system. The ideal would be a remunerated service by the healthcare payer. However, this is not always possible. In fact, in the past decades pharmacists have struggled to get remuneration of such services.

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Although changes in the role of pharmacists have been advocated since the 1990s [1] most of the struggle was very much connected with the barriers related to "newly" established roles of pharmacist. With regard to the payer, the service could be, depending on the country, also offered to patients on out-of-pocket basis. On the one hand, privately funded health services offer some more flexibility, but on the other hand also pose additional challenges to patients, which risk overpaying services. Nonetheless, the price of the service can be more directly reflected based on patients' willingness to pay.

When talking about the price of the services, it is necessary to distinguish between:

- *cost of the service to the provider*, which is the amount spent to perform the service,
- *price of the service*, which is the financial reward for providing the service and is the fee established by the provider for the service,
- *value of the service*, which is what patients and/or healthcare payer believe or have estimated based on evidence the service is worth,
- *cost of the service to the healthcare payer*, which is the amount spent by the payer to buy the service,
- *cost of the service to the patient*, which is the amount the patient pays out-of-pocket for the service [2].

36.2 Types of Costs to Be Considered for Pricing Services

The price of the service should cover at minimum the cost related with the development, implementation, and provision of the service to patients. This includes:

- *Labor cost*: Pharmaceutical care services based on the knowledge and expertise of pharmacist and other potential staff, directly related to the provision of the service. Therefore, the cost of direct labor to provide a service is of primary concern. These are the wages and benefits paid to employees and/or subcontractors who perform, supervise, or manage the service. Established national and union agreements should be considered. The cost of the labor can be also quite significant in the development and implementation of the service. Furthermore, in order to assure quality of services continuing professional development needs to be stimulated and financially supported.
- *Material cost*: They include costs of goods needed to provide the service. Cognitive pharmacy services mostly based on relations with the patients, where access to patient documentation as well as professional sources is necessary. The e-health approaches have largely replaced the traditional paper-based documents. Therefore, appropriate Information Technology (IT) infrastructure needs to be assured as well as the access to literature and databases. Furthermore, some of the services demand products such as point of care tests and other materials used to perform the service.

- *Overhead cost*: These are the indirect costs in providing services to the patients. They include labor for other people, e.g. assistants, cleaners, and administration, and should consider monthly rent, taxes, insurance, depreciation, marketing, office supplies, utilities, mileage, etc. A reasonable amount of these overhead costs should be billed to each service performed.

In most cases, costs can be also divided into:

- *fixed costs*: which are those that are always present, regardless of how much or how little of the services is performed, e.g. rent and salaries, and
- *variable costs*: which are those that rise as the service is performed in a greater extent, e.g. financial stimulations for the performance of the service and cost of additional material.

36.3 Different Methods for Pricing the Services

In general, three basic approaches of pricing the services are used:

- *Cost-plus pricing*: This is a standard method of pricing that first requires costs of the service are determined, and then an extra amount is added to represent the desired profit.
- *Competition-based pricing*: This is the approach that takes into account competitors performing similar services. Pharmaceutical care services are usually developed based on specific competencies of pharmacists. Therefore, they are unique and normally complementary to services performed by other health professionals. Nevertheless, some of the services might be or look similar, e.g. physicians and nurses performing medication reviews. Moreover, benchmarking can be used to determine the relevant prices based on other services already remunerated by the healthcare payer or offered directly to patients.
- *Value-based pricing*: This approach is based on the willingness to pay for a perceived value of the service by the patient and/or healthcare payer. Such approach, particularly if based on patients' perceptions, could also lead to irrational pricings as health is one of the highest needs. Namely, according to Maslow the safety needs come just after the physiological needs [3]. Therefore, willingness to pay for individual services could be relatively high. On the other hand, healthcare systems all have scarce resources and limited budget that needs to be spent wisely. Consequently, healthcare systems developed systematic approaches for evaluation and uptake of health technologies.

36.4 Health Technology Assessment

Elements of health technology assessment, which primarily supports the value-based approach to pricing, can be found in every system. Health technology is a term that beside products, e.g. medicines and medical equipment, embraces also

diagnostic, treatment, and prevention methods, including pharmaceutical care services [4, 5].

Health technology assessment (HTA) is a multidisciplinary process that summarizes information about the medical, social, economic, and ethical issues related to the use of a health technology in a systematic, transparent, unbiased, and robust manner. In most countries, the HTA of medicines reached the highest possible standard, whereas evaluation of other technologies follows the experiences from medicines. Usually, HTA is done based on a predefined set of criteria. EUnetHTA [6], a network for HTA across Europe, suggests health technologies are assessed based on the following information:

1. Health problem and current use of technology
2. Description and technical characteristics of technology
3. Safety
4. Clinical effectiveness
5. Costs and economic evaluation
6. Ethical analysis
7. Organizational aspects
8. Patients and Social aspects
9. Legal aspects

Economic evaluation [7] As described above, economic evaluation represents one of the relevant criteria for HTA. Value of the pharmaceutical care service is a prerequisite to discuss the uptake of the service by the healthcare system. Nevertheless, economic evaluation normally appears as one of the crucial and challenging steps. The task of economic evaluation is to define whether the proposed health technology is cost-effective and what will be its impact on the healthcare budget.

The concept of cost-effectiveness embraces two sides and relates them to one another: the cost and the effectiveness/benefit. Cost in this regard is not solely the cost of health technology itself, but could include also other direct medical and nonmedical costs, as well as indirect cost due to lost productivity related to the implementation and performance of the health technology in practice. The cost included in the evaluations is most often studied in observational and cost of illness studies and defined by the perspective of the analysis, e.g. the healthcare payer perspective would only include cost relevant to the payer, whereas the societal perspective would include also other costs, including indirect cost. Technically, four different types of full scale economic evaluations are distinguished:

1. *cost-minimization analysis*: a determination of the least costly among alternative interventions that are assumed to produce equivalent outcomes.
2. *cost-effectiveness analysis*: a comparison of costs in monetary units with outcomes in quantitative non-monetary units, *e.g.* reduced mortality or morbidity

3. *cost-utility analysis*: a form of cost-effectiveness analysis that compares costs in monetary units with outcomes in terms of their utility, usually to the patient, measured, *e.g.* in quality-adjusted life years (QALYs).
4. *cost—benefit analysis*: compares costs and benefits, both of which are quantified in common monetary units

Cost-effectiveness is usually expressed as incremental cost-effectiveness ratio (ICER), which defines extra cost per extra effectiveness of the new technology compared to the standard of care. Effectiveness can be expressed in different healthcare measures, e.g., blood pressure, low-density lipoprotein (LDL) cholesterol. A generic index that can be used for the evaluation across different diseases and health technologies is often the Quality-Adjusted Life Years (QALY). QALY at the same time embraces information about the survival and quality of life of the patients. The ICER is then expressed in euros per QALY gained and is compared with the national threshold. Despite several methodological approaches, the threshold is normally arbitrarily defined [8]. The threshold represents the maximum extra cost the healthcare system is willing to pay for the additional benefit. If ICER of the health technology is below the predefined threshold, the technology is proclaimed as a cost-effective therapy. The threshold varies from country to country and currently amounts to around 20,000–80,000 EUR per QALY gained. When using other effectiveness measures for ICER calculation, a benchmark needs to be established similarly to the previously explained threshold. This might be challenging and depends on the level of current decision procedures. Nevertheless, there is also a special case, which appears in the situation when the overall cost of the strategy with the new health technology is lower than the standard treatment. In such a case, we talk about the cost-saving strategy, which adds value for less overall cost.

Budget impact analysis represents the second part of the economic evaluation. Normally this means a clear presentation of the predicted cost in the next 3–5 years. The costs are presented as cost of the health technology, as well as other relevant costs related to the health technology. Such an analysis also takes into account the rate of the uptake of the health technology in practice.

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Chapter 37
Overview of Different Outpatient Pharmacist Care Services Being Paid Worldwide

Filipa Alves da Costa

Abstract Payment for services is quite common in health care, and the same goes for the payment of services in pharmacies or to pharmacists. This chapter gives a large number of examples of paid services. We do not claim that this is a comprehensive overview, because the systems and payments are continuously shifting and changing. But the examples may help the reader to develop ideas about possible remuneration policies.

Keywords Pharmaceutical care · Remuneration · Pharmaceutical services Medication review · Payment models

37.1 Introduction

In the previous chapter, we have outlined the different models of remuneration for healthcare services, and their differences. There is no standard remuneration for pharmacy or pharmacist services internationally, because the systems differ. The payment for some services is included in a general dispensing fee, or in the percentual profit margin, other services are paid separately. What is included in a separate fee, can be excluded the next year or included in yet another remuneration fee. In order to receive remuneration, sometimes special licenses or trainings are compulsory. This chapter provides an overview of the payment models of the different services that can be part of pharmaceutical care. There is currently no published information on the remuneration of services in Asia or South America.

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37.2 Remunerated Services in Europe

The remuneration of medication review services has been briefly described in a paper by Bulajeva et al. [1]. In this publication, payment of level I medication review, also called prescription review, has only been reported in Switzerland. The payment of type II medication review, or adherence review, was the most commonly reported, stated to exist in seven different countries (Denmark, Finland, Netherlands, Portugal, Switzerland, and the UK). No detailed information on the payment in each of these countries has been provided, albeit stated that it ranged between 20 and 80€. However, complementing this information with other sources, slightly more detail may be obtained.

Type III medication review services were only reported to exist in Denmark, Finland, and the Netherlands, and according to the authors, the information on the payment depends on the individual contract between the practitioner and the payor (mostly the insurance), which is highly sensitive information and therefore not reported [1].

In Denmark, there is dose dispensing, a system implemented nationwide in 2001 where the medicine is dispensed by central units of packing pharmacies, for 14 days at a time, and then the local pharmacy will distribute the pouches at the patient's home or at nursing homes. This service is paid at 8€/week by the patient and the fee is reimbursable [2]. Recently, a similar approach to the new medicines service (NMS) has been launched and pharmacies are being reimbursed for this provision. Similarly, in Norway, following the successful rollout of the NMS, negotiations are being held for reimbursement based on time spent on service provision, estimated to be around 30 min (first dispensing and first contact at one week).

In Finland, there are a few of municipalities paying for the provision of pharmaceutical care. The most common approach, however, is developing medication review in the context of unit dose dispensing, which exists on a larger scale since 2012 [3].

The Netherlands is probably one of the most advanced countries in Europe and with the widest variability of services provided in community pharmacy. There is the dose administration aid (DAA) system, a service that in the outpatient setting must be prescribed by a General Practitioner (GP) to be provided. The service is then paid at around 2.6€/week dispensing fee and the cost of the medicine is added to that figure. If a 2-week dispensing system is arranged with the pharmacy, then the fee is 4.75€. When it is the first dispensing, there will be an additional fee (around 6€). However, to provide such service, a medication review (type III) must be performed and cannot be charged separately. In the nursing homes, there is a pack of services annually negotiated between the pharmacy and the insurer and provided based on a fixed fee/patient/month. The fee will include the cost of the medicines included in the weekly pouches and also include medication review and regular pharmacotherapy quality circles organized in collaboration with GPs. There might be different budgets whenever the drugs taken include high-cost medicines.

It is therefore a flat fee regardless of the drugs included. The annual payment could be around 1500€/patient/year to be paid on a monthly basis. Another existing service in the Netherlands is the medication sheet, which consists of creating and keeping up to date the drug use profile and is paid at 6€/patient. Monitoring adherence is performed automatically by a pop-up system included in software that alerts the pharmacist for early or late refills. That is not charged separately as it is considered to be included in the normal dispensing fee. Medication review level III is the most comprehensive service, with additional complexity, levels of monitoring, and involvement of other healthcare professionals and paid at an average of 75 €/patient.

Currently, there is a pilot running in selected regions of Spain where pharmaceutical care services are being delivered and remunerated at 45€/patient/month. Cataluña and the Basque region have some tradition already of paid services, unlike other regions, although more in the area of public health. Examples are the methadone directly observed treatment (paid for long at 30€/patient/month [4]) and more recently the bowel cancer screening (paid at 1.5€/sample collected). Another incentive being given by the local authorities is the provision to pharmacies of these tests free of charge, a format also used for the human immunodeficiency virus (HIV) testing. Pharmacies may charge a fee to the patients for the HIV test (on average, 10€), generating income, although there is no direct reimbursement.

In Portugal, the payment referred to by Bulajeva, was for the provision of disease management pharmaceutical care specifically for diabetes patients. This agreement was established between the National Association of Pharmacies and the Portuguese Government with a value set at 15€/month/patient, the government covering 75%, and the remainder paid by the patient out of pocket [5]. This agreement lasted between 2003 and 2010, not being active at the time of this publication. Public health services, like the needle exchange program, are since 2016 remunerated, where the pharmacy receives a fixed fee of 2.40€/kit exchanged.

In Switzerland, the service is entitled “Polymedikation Check”, which is directed at patients prescribed with four or more drugs taken for a period over 3 months. The service is provided following a suggestion from the pharmacist, agreed by the patient, and independently from the prescriber. The service is paid at 40€ and this check can only be remunerated twice a year. However, during the delivery of this service the pharmacist may identify the patient who would benefit from an additional service, which is the dose dispensing service, a weekly prepared pillbox or punch card for patients who take three or more different drugs. This service is then paid by the insurer at 20€/week [6].

Implemented since 2005, the Medicines Use Review is the UK approach to pharmaceutical care. In the UK, services are divided according to their complexity and requirements in three levels, similar to what has been described by the Pharmaceutical Group of the European Union (PGEU) in Chap. 14, but using different names. The more complex level in the UK is entitled Advanced services and includes six services, among which the Medicines Use Review (MUR), paid by the National Health Service (NHS) at 30.5€ in the case of MUR. Also included in the Advanced Services is the New Medicines Service, directed at enhancing

adherence to newly prescribed medicines. These services are not compulsory; the pharmacy will choose if they want to provide it as long as they meet the minimum requirements. The next level is named Enhanced services and includes a level III Medication Review, named Full Clinical Review.

Although not reported by Bulajeva and colleagues, in some regions of Germany there is also a medication review service that may be provided once a year and which covers checking for implicit criteria such as drug-related problems (DRPs), and explicit criteria such as potentially inappropriate medicines (PIMs), most commonly using the Priscus list. This service is negotiated with the insurer and some of the payments reported are around 45€/patient.

Outside Europe, there are interesting reports of services provided and paid by a third-party payer. Although, our intention is not to provide an exhaustive overview, selected examples will be provided.

37.3 Remunerated Services in Canada and the United States

In Ontario, since 2007, there is a government-funded medication review service. It is named Medication Therapy Management (MTM) and any pharmacist working in any community pharmacy may provide it, without needing specific training [7]. The program is called the MedsCheck and is similar to the polymedication check in the sense that the pharmacist's intervention is to review the prescriptions in detail and is also directed at patients taking three or more chronic medicines. The intervention lasts approximately half an hour and the pharmacist writes a detailed list of all medicines taken by the patient, including nonprescription, a list to be kept at the pharmacy and also provided to the patient, contributing to empower him/her. This was the first reimbursed service in Ontario and the price set was initially 34€ per year (later upgraded to 41€), with 17€ for the follow-up. This service may indirectly contribute to adherence but that is not its main aim. If, however, in a MedsCheck, the pharmacist discovers that there is an area of opportunity to optimize the patient's drug regimen, he can make a recommendation to the physician, and get reimbursed for that act regardless of the physician's acceptance of the recommendation. There are variants to the service according to the province. For instance, in Saskatchewan, the service is directed at elderly residing in nursing homes, and is more comprehensive. However, the payment is quite similar. A different service is the prescription adaptation, which, depending on the province, may include alteration or refusal to fill the prescription. This service is remunerated at 10€ in Nova Scotia and at 14€ in Alberta, for instance.

The compliance aid program, which in Europe seems to have a tendency for reimbursement, is a service offered in Canada, where pharmacists are not able to charge for it. There is not any reimbursable compliance program. Some of the third-party insurers have been discussing it but nothing has been implemented. In some specific chains (e.g., Shoppers Drug Mart), there are programs where

pharmacists work in a call center and proactively call patients to remind them to pick up their prescriptions that have been refilled automatically; this same chain also just launched a "digital adherence platform" which is an online portal/app which gives patients access to their medication profile and allows them to fill prescriptions automatically. Both these services are totally free and are used as a way to make the patient loyal to a given chain and improve the quality of services offered. Very recently, a comprehensive pharmaceutical care service including pharmacist prescribing for patients with hypertension resulted in positive clinical outcomes and cost savings, while showing to fill in a care gap in terms of service provision [8].

The United States (US) has been reported in a systemic review as the country where most third-party funded programs exist [9]. The average payment for the initial medication review in the US was 46.5€, with 16€ for the follow-up and 10€ for prescription adaptations. In the US, as the prescription reimbursement rate has declined, the investment in quality measures awarded financial incentives has been described as an enabler for service implementation. This happens because one quality measure considered by payers is the provision of medication management services [10].

37.4 Remunerated Services in Australia and New Zealand

Medication review in New Zealand may take three different formats, all of which are reimbursed since 2007. Medication use review and adherence support may be described as the service with the lowest level of complexity, paid at around 57.5€/patient for the initial consultation and additional 15€ for the follow-up. The second level is the medicines therapy assessment, which is provided in a multidisciplinary context and paid at 69€/patient for the initial assessment and 34.5€ for the follow-up. The last level is the comprehensive medicines management (also multidisciplinary) and paid at 92€/patient for the initial assessment and 46€ for the follow-up [8]. Since 2016, there is also a nationally funded service arising from the successful experiences in piloting (since 2006) a community pharmacist-led anticoagulation management service. The service involves active interprofessional collaboration and timely data sharing, so that interventions are developed whenever needed to control the time in therapeutic range (TTR) [11].

In Australia, there are several funded services. The dose dispensing aid service, for instance, is funded since the 4th agreement. Currently, the sixth agreement dictates that the pharmacy may claim 4€/patient/week. However, from 2018 onwards this value can increase to 21.5€/patient/week if the patient is monitored for 6 months. There are then several medication management funded programs. The Home Medicines Review (HMR) is provided at a patient's home (see Chap. 15) and under the sixth agreement is reimbursed at 150€. The meds check and diabetes check are similar programs but delivered in the pharmacy. There is a fee for the initial evaluation of 45€ for the Meds check and of 67€ for the Diabetes

MedCheck. A separate fee may be claimed if additional patient data are collected. There is, however, a monthly cap of 20 services for any of the formerly mentioned formats of medication review. These services may also be provided at a residential facility (residential medicines management service). In such case, there must be a GP referral and the service is then paid at 75.5€ [12, 13].

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Chapter 38
Paying for Pharmaceutical Care

Filipa Alves da Costa and Kurt E. Hersberger

Abstract This chapter aims to provide a summary of different approaches to the payment of pharmaceutical care that have been adopted in selected countries. Each of them is described in brief, with the ultimate goal of highlighting the pros and cons of each approach. The second part of the chapter elaborates on a possible solution to make pharmaceutical care not only a clinical activity which is essential to ensure the patient receives optimal therapy to attain better outcomes, but also to transform this practice into a profitable service. We believe this option is essential for pharmaceutical care to flourish worldwide.

Keywords Pharmaceutical care · Remuneration · Lean management
Cost–benefit analysis · Organizational optimization

38.1 Selected Cases of Remunerated Services Where Different Costing Methods Were Used

Although still not being remunerated, the cost of medication review has been recently estimated for **Spain** [1]. The approach taken was based on the time-driven activity costing method, an approach that quantifies all costs involved in service delivery. For the estimate, there is a need to time the service delivery, something not routinely done in pharmacy practice. In the model used, named Medication Review with Follow-up (MRF) seven stages were considered: face-to-face interviews;

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initial assessment of clinical situation; study phase; advanced medication review focusing on the identification of DRPs and negative outcomes; action plan; delivery of interventions to address the identified DRPs; and the follow-up visits. The mean time spent on service provision was around 6.5 h per provider during 6 months. This included all visits undertaken during that period, which accounted for around 40% of the time estimated. Additional detail is included on the original manuscript referring to the timings allocated to the various stages of the process. The potential service price ranged from 237 to 628 €/patient/year, suggesting that reallocation of tasks so that less expensive staff were involved could be considered, as long as the quality of the service delivery could be sustained.

A similar methodological approach has been taken in **Portugal** looking at different types of service, including dispensing of medicines, patient counseling and screening programs [2]. According to Gregório and colleagues the cost of these services are, respectively, around 4, 1.3 and 3.5€. It is worth mentioning that none of these three services is currently remunerated in Spain or in Portugal.

One other service currently remunerated in Portugal is the needle exchange program, paid by the Public Health Service at 2.40€. This achievement was a result of a study using a two scenario analysis, considering the existence of the program in pharmacies and its absence, over 5 years. The gains were estimated considering the infections avoided according to the model of Jacobs et al. where epidemiological data were taken into account [3]. The model ascertained that along 5 years (2015–2019), the involvement of community pharmacies would result in a reduction of 22 HIV and 25 HCV new cases. The number of exchanged needles was forecasted at 87,761 in the first year and 169,347 in the following years. As a result, the overall costs per needle exchanged were estimated to be 3.09€ [4].

Another recently published study, yet with no consequences in terms of reimbursement, used a decision model to estimate the social and economic value of the pharmacist. The model used information collected in literature about effectiveness of services, quality of life gains and use of health care resources, which were then adapted to Portugal through an expert panel. The authors estimated that considering all the current pharmacy services result in a quality of life gain of 8.3%, valued at nearly 900 M€. This value was considered to include 342.1 M€ attributed to non-remunerated services and 448.1 M€ in avoided costs due to the use of health care resources [5].

Since 2010, **Swiss community pharmacies** can offer a ‘Polymedication-Check’ (PMC) to patients on ≥ 4 prescribed drugs taken over ≥ 3 months. Referring to the different types of medication reviews, defined by the Pharmaceutical Care Network Europe (PCNE), the PMC is identified as an ‘intermediate’ medication review. Information is available from the medication history, which is mandatorily kept in Swiss community pharmacies, and from a structured patient interview. The check focuses on adherence problems, patients’ knowledge, and handling problems. At the end of the interview, the patient signs the documentation form and the pharmacy can charge a fee of 40€ to the health insurance irrespective of the time spent. This fee is a result of negotiations with the authorities based on the assumption that this medication review only takes 20 min. After introduction of the

service, research showed that the time needed is around 30 min which might be one reason for the very disappointing uptake by Swiss community pharmacies with only about three checks per pharmacy per year and a large majority of pharmacies not offering this service [6].

Through the PMC, pharmacists can evaluate a patient's need for a weekly pill organizer (WPO). If the patient agrees and is taking at least three different medicines, the pharmacy can prepare a pill organizer/blister pack. Likewise, the GP can prescribe the provision of a WPO. This service is remunerated by 20€/week. Again, this fee is the same for all pharmacies and is a result of negotiations, which are not based on time requirement or any proof of cost-effectiveness. This service is very well implemented in Swiss community pharmacies reflecting their economic interest in this service [7].

Very recently, new services received remuneration if provided by specialized pharmacies and if the patient voluntarily affects a supplementary insurance. Using the example of asthma, a certified "Air Way Pharmacy" can include patients suffering at least one problem of the asthma control test (ACT) into a comprehensive asthma care program. The service comprises spirometry, individualized counseling on best use of asthma medicines and up to three follow-up visits. The fee of 220€ per patient per year is paid if at least two follow-up visits were reported. Similar services with similar fees paid by supplementary insurances cover, *e.g.,* migraine, musculoskeletal pain, and hypertension.

38.2 The Lean Management of Pharmaceutical Services: How Can We Boost Service Provision and Make It Profitable?

In order to provide pharmaceutical care services in a cost-efficient way and to reduce the workload of pharmacists while service provision is enhanced, different approaches can be considered:

First, we should organize the workforce in our institutions. Pharmacy technicians are able to take on a larger role in pharmacy practice. For illustration, performing medication reviews comprises distinct activities within a structured process. Initially, a best possible medication history is needed which often involves a reconciliation of medicines prescribed currently versus in the past. Often, a brown bag analysis of the medicines in the hand of the patient is additionally performed. These preparatory tasks could be delegated to pharmacy technicians [8, 9]. Eventually, patient interviews focusing on adherence and handling problems could be delegated as well. On the other hand, the clinical assessment of potential and manifest drug-related problems associated with efficacy and safety issues need a clinical judgement by a pharmacist. Thus, medication reviews could be performed in the pharmacy setting in collaboration and with support by a technician. Similarly, all kind of screening services including point of care testing and smoking cessation

counseling are feasible tasks for pharmacy technicians if adequately trained [10]. Overall, increasing staff productivity is the highest priority with respect to the delivery of cost effective pharmaceutical care.

Second, prioritizing of patients served and of their problems is key in order to achieve outcomes with a reasonable effort. For prioritizing of pharmaceutical care delivery at ward level, a simple self-assessment questionnaire to screen for hospitalized patients at risk for drug-related problems has been developed, enabling targeted pharmaceutical care during the hospital stay and upon discharge [11]. More challenging is the priority setting during a medication review of polypharmacy. Multiple DRPs become evident and a clinical judgement is needed to address the most relevant problem for intervention. Again, a collaborative approach could be used with delegation of interventions to the best-suited health care professional. Likewise, a lot of follow-up activities can be delegated as well, *e.g.,* to a pharmacy technician.

Third, short and easy to use checklists, standard operating procedures and validated tools can be supportive in daily practice. Such tools need to be tailored for practice (and not only retrieved from research) and must be adapted to local situations. The NHS Medicines Use Review service worksheet can be cited as a good example [12].

Fourth, technology can assist with delivery of pharmaceutical care. The question is how we could better use ehealth (or ePharmacy). Not only to support dispensing and administrative/logistic processes but also for patient care. However, little information is available concerning the implementation of clinical decision support software in community pharmacy practice [13]. Fortunately, ehealth will push on traditional practices. Information systems and technologies will have an important role in shaping future health care provision. And, online pharmaceutical services will emerge such as ePharmacare [14].

Fifth, training is essential. Moreover, the best training only can result in efficient service provision if the service is frequently provided to become at least weekly routine. Therefore, a kind of specialization within a team of pharmacists might be a solution, but only feasible in large community pharmacies.

In short, through optimized organization of both, the workforce and the processes in the pharmacy the imperative target of lean management of pharmaceutical care services can be achieved.

38.3 Conclusion

We have provided some examples of services being remunerated in different countries, briefly explaining the grounds for the fee estimate. So far, in pharmacy practice, we have identified four major approaches to estimate the fee of a service:

(1) based on the time spent to provide the service, irrespective of the result;
(2) based on the results achieved, which depending on the disease or the setting could be cases of disease prevented, controlled, or cured;

(3) fixed fee based on meeting a minimum set of quantity and/or quality requirements; and
(4) negotiations with the payer with no solid grounds (these may be market research, for instance, where the cost results from what is "normal" in other countries or when the service is provided in other venues or by other healthcare providers).

Each of these approaches has advantages and disadvantages, and highly dependent on the functioning of the health care system and also on the culture in place. Some services might benefit from one way of remuneration in an initial phase and then an adaption into a different model of payment. One possible evolution is to start with model 1 (to foster adoption), then evolve into model 4 (to improve quality), and finalize with model 2 (to ensure patients and payers indeed benefit from the service).

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Part VIII
Teaching Pharmaceutical Care

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Before pharmaceutical care was normalized in the collective pharmacy psyche and in pharmacy practice, the process of instituting the practice of pharmaceutical care would have to begin with the teaching and training needs in any setting. Those educational needs depend on current trends in health care, innovative practice methods, unique practice settings, and the political landscape. There are countries in the world where the population of pharmacists outnumber the total population of other countries and some countries still do not have formally established pharmacy education, or are limited to the training of specific cadres in the profession be they pharmacists, technicians or assistants. Regardless of the healthcare model (e.g., public, private, government funded), the resources, disease burdens, and the interface of pharmacy practice within those organizations will impact the education and training needs. Hence, the training needs of pharmaceutical care in one setting may focus on nurse competence rather than pharmacy students; primary care rather than specialized care; rural rather than urban; and graduate education rather than undergraduate. Pharmaceutical care is still a relatively new concept that many settings have not embraced or are struggling to implement. However, even in a vacuum of pharmacy education, there is still a pharmacy presence and to elicit any change will require resources of time, effort, and advocacy.

Overview on Pharmaceutical Care Education

If pharmaceutical care focuses on optimizing drug therapy such that it is safe and efficacious, it stands to reason that the pharmacist holds the responsibility to actively engage the patient and health professionals to optimize drug therapy. The two core pharmaceutical care competencies include the identification and resolution of drug therapy related problems. Hence, the emphasis of pharmaceutical care education is for learners to acquire the competencies (including the combination of knowledge, attitudes, and skills) of identifying and resolving drug therapy related problems. The success of a pharmaceutical care training program requires that it is done in context and involves interprofessional collaboration. Furthermore, pharmaceutical care education should emphasize comprehensive patient care including

drug therapy related problems in addition to nursing and medical needs. Inter-professional education/learning (IPE/IPL), therefore, is a critical element in education of pharmaceutical care. The approach towards the education of pharmaceutical care determines the success of the program. Even though pharmaceutical care is a practical clinical discipline, early integration of learners into a clinical environment without appropriate knowledge, attitudes and skills may frustrate the learning efforts and in an unsupported environment even endanger the lives of patients. Learners should have basic knowledge and skills on diagnosis and resolution of drug therapy problems and interprofessional cooperation before being integrated into a clinical setting; by doing this in a collaborative and organized way, it is also likely to protect patient care. Pharmaceutical care curricula should include horizontal and vertical integration of theoretical and practical activities and over time increase the difficulty of the case studies or scenarios. Finally, and arguably most important, a robust structure to implement a pharmaceutical care program is required. This should start with curriculum development, built around a particular context, involve appropriate stakeholders and be mindful of resource limitations. If done correctly, this process will likely implement and integrate well with preceptors and training facilities.

Chapter 39 discusses why pharmaceutical care is necessary to be addressed through pharmacy education at preservice (undergraduate) level following the historical shift in the practice and various recommendations that have emerged. It moves on to look at the development of training through competency-based curricula relating to the context that encompasses practice-related issues. Furthermore, examples of the methods of education are discussed in detail as well as the assessment methods necessary to quantify and evaluate the learning process.

Achieving Competences in Pharmaceutical Care Education

A systematic approach is critical to effectively educate students in the practice of pharmaceutical care. For example, the Subjective, Objective, Assessment, Plan (SOAP) method is a widely used approach for clinical reasoning by medical, nursing, and pharmacy professionals. An important emphasis in the SOAP approach is the assessment and resolution of drug therapy problems. The pharmaceutical care students must demonstrate the ability to collect and interpret subjective and objective data from nursing, medical, and pharmaceutical perspectives to affirm and resolve the drug therapy problems.

To achieve competencies in pharmaceutical care around the eight drug therapy aspects, students must demonstrate the basic skills of performing a medication history interview and medicines reconciliation and review as to progress and ultimately be able to develop a pharmaceutical care plan. Medicines reconciliation enables learners to identify medication errors between transition points—including errors of duplication, errors of omission, commission, and transcribing. A review of the medication enables students to identify the drug therapy problems. However, to perform a medication review, learners should be in a position to collect data from the patient, medical records and/or the health care provider treating the patient. In addition, students should develop the skill of prioritizing the medicine-related

problems and develop a care plan. The care plan is based on the main drug-related problem from which goals of therapy, intervention, communication, and monitoring plans are developed and implemented. The development of the plan requires that the students have working knowledge of pharmacotherapy and evidence-based medicine. The competencies relate equally to education in undergraduate and postgraduate/in-service levels as appropriate to the context.

Chapter 40 addresses the context of learning Pharmaceutical Care for qualified and practicing pharmacists—as well as other health professionals—and discusses the approach to pharmacy education in that service provision/practice context. Considerations of this heterogeneous population of practitioners are discussed and addressed through a systematic process from standards that ultimately relate to patient care and outcome.

It is worth considering some examples of the journey of education and training of pharmaceutical care in specific settings (Box 1 and Box 2). Box 1 provides an example of pharmaceutical care education for pharmacists during their undergraduate education, in line with what is further detailed in Chap. 39. Box 2 expands on the scope of the education of future pharmacists to address also education to non-pharmacists, as explored during Chap. 40. These are merely illustrative and should foster the reader's interest to dig deeper into the educational methods to transform pharmacy education, as detailed in the next chapters.

Box 1: Instituting Pharmaceutical Care Through Education: The US and European Movements

As a developed country with over a century of professional organization of pharmacy, the United States (US) was well placed to experiment through education with the concept of pharmaceutical care. The debate for having a Doctor of Pharmacy (PharmD) educational program began *circa* 1950 with the University of Southern California offering the first PharmD program. Though a few other institutions followed suit, it was not until federal funding was issued in the 1970s that there was accelerated expansion of the PharmD degree, and subsequently clinical pharmacy. With the backing of representative and regulatory bodies declaring that they would only support PharmD programs, the PharmD became the entry-level degree to practice pharmacy in the US. Summarizing in a few sentences nearly 70 years of history, one may conclude the initial intention of the pharmacy profession to move towards a pharmaceutical care model was only realized with the support of funding, regulation and standards to support delivery. Following the evolution of pharmacy education was the creation of postgraduate training in the form of residency programs for pharmacists. These one to two-year educational programs have experienced significant growth since the late 1990s where pharmacists are placed directly into patient care environments where they are often collaborating interprofessionally. This transformation of pharmacy education has been valued by other healthcare professionals and may stem from the growth of new medicines, the complexity of disease state

management, along with changing political and healthcare systems. With the standardization and accreditation of residency training programs, educational and healthcare institutions began to invest more resources. In this respect, the emerging need of pharmacy residency training was ultimately matched through education [1]. Similar examples are observed in other settings such as the United Kingdom and wider European region; the Bologna Declaration in 1999 sought, among many things, to align pharmacy education among member states of the European Union through harmonization with the hope of promoting cooperative mobility in the region [1, 2]. The UK shift from a 3-year BPharm to a 4-year MPharm undergraduate degree can be seen as a product of this movement, a change that occurred across the entire United Kingdom in 1997. Academic institutions that responded to educational change have also responded to the need for patient-centered pharmaceutical care through clinical and postgraduate training, including the Joint Program Board Post-Graduate Diploma in General Pharmacy Practice. Initially funded by the government, this training is offered by a collaboration of universities and National Health Service training centers [3], and the Centre for Pharmacy Postgraduate Education (CPPE) that executes a broader remit around post-graduate and post-registration training.

Box 2: Case of Pharmaceutical Training at the University of Namibia (UNAM)

The Bachelor of Pharmacy degree offered by the University of Namibia is a needs and competency-based curriculum that began in 2011, the first of its kind in Namibia. Over one-quarter of the curriculum is taught alongside medical students with clinical skills being introduced in the second year. During this interprofessional course, entitled “Introduction to Medical and Nursing Skills”, students are taught skills in a skills lab-based environment to build vital competencies, such as infection control and first aid, before being introduced to in-patient ward-based care.

Subsequently, in the third and fourth year of study, there are two major sequential modules that encompass pharmaceutical care: Pathophysiology and Pharmacotherapy I and II. In the first module, students are introduced to the pathophysiological basis of pharmacotherapy including the five disease processes—metabolic, inflammatory, neoplastic, degenerative, and congenital diseases. The students are also taught to perform medication history, reconciliation, and reviews in parallel with the approach to pharmaceutical care, such as the SOAP method, to identify and resolve the eight drug therapy problems. The module also covers subjective and objective data collection and interpretation with an emphasis on vital signs, physical exam findings, and laboratory results. The educational emphasis in the first module is didactic coursework supplemented with case-based learning with case

presentations and analysis. Students undertake a one-month supervised hospital placement between the two modules to apply their didactic knowledge in the clinical setting with the aim to integrate them into clinical care. During this month, their education is augmented with workbook assignments and instruction from clinical pharmacists. Then, throughout the fourth and final year of study, the students attend clinical rotations in defined areas of infectious disease, oncology, and mental health where their training is overseen by recent graduates (interns), graduate students, and practicing pharmacists. During these rotations, students review patient charts, collect, and analyze data, develop pharmaceutical care plans, and present them to their clinical instructor. This training program is intended to prepare students for their one-year preregistration internships before qualifying as pharmacists, improve the quality of pharmaceutical care and clinical pharmacy services being delivered, and transition students to the clinical Masters of Pharmacy degree, ultimately creating a greater measurable impact of pharmaceutical care in Namibia.

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Chapter 39
Teaching Pharmaceutical Care at University Level

Inês Nunes-da-Cunha and Fernando Fernandez-Llimos

Abstract The practice change and needs of the pharmacy profession have created a shift in pharmacy education. Schools of pharmacy globally attempt to respond to the recommendations issued by the WHO and FIP, by modifying their curricula, especially with the introduction of clinical and social content. However, it appears that pharmacy education in Europe, compared to the U.S., maintains a greater focus on basic sciences. Competency frameworks for pharmacy education and practice have emerged. Their use in curriculum development is extremely important, but to ensure that the competencies are achieved by graduates to enter pharmacy practice, the syllabi must align competencies, educational contents, learning activities, and assessment tasks. The teaching of pharmaceutical care benefits from the use of active learning methods, such as problem-based learning and team-based learning, allowing students to develop skills of communication, teamwork, and critical thinking. Although curriculum integration presents some implementation difficulties, its use allows students to integrate concepts from different areas throughout the curriculum. The use of assessment methods based on student performance, such as OSCE and OSATS, is most appropriate to evaluate students regarding the development of competencies in relation to pharmaceutical care and technical skills.

Keywords Pharmaceutical care · Education pharmacy · Academic education Competency framework · OSCE

39.1 Pharmaceutical Care in the Academic Pharmacy Education

Following the shift from a product-centered to a patient-centered practice, international organizations such as the World Health Organization (WHO) and International Pharmaceutical Federation (FIP), recommended that the pharmacist'

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education should mirror these changes. In 1993, at the second meeting on "The role of the pharmacist: quality pharmaceutical services—benefits for governments and the public", the WHO established a list of recommendations that the profession and educators should follow to provide pharmacists with pharmaceutical care skills [1]. The first recommendation emphasized the continuous review of the outcomes, content, and process of the undergraduate curriculum, to ensure pharmacy education prepares graduates to practice pharmaceutical care. For this, it is necessary to ensure an adequate balance of curricular contents of basic sciences, pharmaceutical sciences, biomedical and clinical sciences, socioeconomic, and behavioral sciences with practical experience. The introduction of courses related to the implementation of patient-centered care such as communication, was also recommended. In addition to these curricular changes, it was also suggested more practical and problem-oriented teaching methods, interprofessional education, and a clinical internship period was necessary for achieving competencies in pharmaceutical care. In the field of continuing education and postgraduate studies, the WHO also recommended adopting the philosophy of pharmaceutical care (see Sect. 9.2) [1].

39.1.1 WHO and FIP Pressure

In 1997, the WHO continued emphasizing the need for an education that allows students to obtain the knowledge, skills, attitudes, and behaviors for the practice of pharmaceutical care. Although each country has its own educational needs, related to its own context, the WHO recommended that there are common core elements essential to all pharmacy curriculum. For example, educational results can be related to the concept of the seven-star pharmacist (caregiver, decision-maker, communicator, leader, manager, lifelong-learner, and teacher), educational methods should become student-centered, and educators should continually update the curriculum as a dynamic process to meet the changing needs of the profession [2].

FIP also recommended improvement of pharmacy education, stressing the importance of clinical education and patient-centered care curricula. In the curriculum design, FIP proposed that educators ensure that the competencies required to enter pharmacy practice are attained by all graduates. For that, schools of pharmacy should: "systematically evaluate and validate its curricular structure, content, organization, teaching and learning methodologies, and outcomes" [3].

39.1.2 Changes in Pharmacy Education Around the World

Pharmacy schools around the world attempted to respond to WHO and FIP recommendations through changes in pharmacy education. The curricula of countries such as Australia, Canada, the United States, and New Zealand have undergone

notable changes with the introduction of disciplines from the clinical pharmacy and social, administrative and behavioral pharmacy areas.

In the United States, the main change in pharmacy education was the creation and implementation of the doctor of pharmacy (PharmD). This program is the sole degree required to enter professional practice, and should follow the Accreditation Council for Pharmacy Education (ACPE) standards and guidelines (see Box 1). The ACPE requires at least two academic years or the equivalent college-level course work prior to the admission into a PharmD program (four academic years). The pharmacy curriculum was designed to comprise an appropriate balance of biomedical, pharmaceutical, social/behavioral/administrative, and clinical sciences, and an integration of pharmacy practice experiences in different settings [4]. Currently, only some Canadian pharmacy schools offer a PharmD degree. However, the Association of Faculties of Pharmacy of Canada recommended that all pharmacy schools change the entry-to-practice degree for pharmacy from the Bachelor of Science in Pharmacy to the PharmD by the year 2020. Other countries such as Japan, Saudi Arabia, and Thailand have also adopted the PharmD as their entry-level degree for the profession.

In Europe, the ministers of education from 29 countries signed the Bologna Declaration in 1999, creating the European Higher Education Area (EHEA) [5]. With the Bologna Declaration the European higher education institutions work in an integrated and harmonized way, allowing students from any European university to begin, continue, and complete their education and obtain a European diploma that would be recognized in any of the EHEA universities. To make this possible, a system that encompasses easily comparable degrees was adopted among the EHEA Members States. This system was based on two main cycles (undergraduate and graduate) and a system of credits (ECTS—European Credit Transfer and Accumulation System) was established [5]. Presently, 48 Member States participate in the Bologna process. As a result of the Bologna process, the European Parliament and the Council of the European Union has approved legislation on the recognition of pharmacist professional qualifications, defining knowledge, skills, and core competencies that pharmacy students must achieve to become pharmacists [6]. The pharmacy degree became organized into two training cycles with the duration of at least 5 years, including a 6-month traineeship at a community or hospital pharmacy during or at the end of the program. At the end of the 5 years of study, a total of 300 ECTS is required to complete the pharmacy degree. Following the Bologna Declaration, the European pharmacy schools conducted curricular revisions, including the introduction of some clinical sciences and social aspects associated with pharmaceutical practice. However, despite these changes, European pharmacy education maintains a greater focus on basic sciences and a lower emphasis on patient care-centered course load compared to the United States pharmacy curricula [7]. This suggests that European countries should consider reviewing their pharmacy curriculum so as to comply with the WHO and FIP recommendations.

39.1.3 Competency Frameworks in Pharmacy Education

A curriculum must be developed taking into account the needs of society as to prepare students with the necessary competencies to respond to the individual patient and to population health-related needs [3]. When developing a curriculum, these competencies must be expressed in course curricula or discipline syllabi. The syllabus is an important document that includes the course plan, and works as a tool that improves student learning, assists faculty teaching, promote communication between faculty members about courses, and increases curricular quality. A course syllabus should contain information such as general course information, course instructional team, course goals, course objectives (skills, knowledge, and attitudes that students need to acquire), description of course content including the sequence of topics/readings and learning activities/assignments, time schedule, learning and teaching methods, student assessment and grading, and academic policy information. Competencies should direct the syllabi that in turn inform the alignment of learning outcomes, learning activities, and assessment.

The development of competency frameworks for pharmacy education and practice has emerged worldwide, and is established in countries such as Australia, Canada, Ireland, New Zealand, Portugal, Singapore, Spain, Thailand, the United Kingdom, and the United States. The global competency framework created by FIPEd (FIP Education Initiatives and partnerships with WHO and UNESCO), contains a core set of competencies that can be used to indicate the achievement by graduates to enter pharmacy practice. This framework serves as a mapping tool and undergoes changes with the evolution of the pharmacy profession [8]. Other competency frameworks for pharmacy education and training have also been developed, for example, the PHAR-QA project in Europe that is used as a quality assurance system of pharmacy education [9].

Competency frameworks are extremely important in guiding curriculum development, but it is critical to ensure that students' actually achieve these competencies. However, the translation of frameworks into practice competencies does not always occur, and there are reports of competencies misuse [10]. Ideally, the competency framework should be created by the profession, and disciplines should have their programmatic content perfectly aligned with each topic of the competency framework [10].

39.1.4 Pharmaceutical Care Educational Contents in the Pharmacy Curriculum

With the aim of assisting in the creation of an undergraduate pharmacy curriculum, which focuses on preparing students for a patient-centered practice, a catalog of educational contents was created through a qualitative analysis of the educational contents included in the syllabi of the disciplines from undergraduate pharmacy

curriculum in Australia, Canada, New Zealand, and the United States [10]. The selection of these countries was based on the fact that they have a wide implementation of pharmacy services and have undergone a curriculum change to incorporate more clinical models. All courses with patient-centered educational contents (topics described under clinical sciences and social/behavioral/administrative sciences) were included for content analysis. Educational content related to pharmacy practice were analyzed and extracted from 1703 syllabi belonging to 110 pharmacy schools in Australia, Canada, New Zealand, and the United States. Using the ACPE "Guidance on the Science Foundation for the Curriculum" [4] as a coding framework, a final coding tree with 4 hierarchical levels and 355 topics of educational contents for a patient-centered undergraduate pharmacy curriculum was created. The first hierarchical level comprises four main groups in which the area of pharmacy practice could be divided: (1) Clinical Sciences Aspects, covering topics related to patient care, the processes associated with patient care, and clinical health outcomes; (2) Social and Behavioral Pharmacy Sciences Aspects, includes topics on the relationship with the patient and society (in the role of public health); (3) Administrative Pharmacy Sciences Aspects, covering procedural and technological aspects that support the role of the pharmacist as a health professional; (4) Miscellaneous, including cross-sectional educational contents for the groups above, such as the design and interpretation of research and the history of pharmacy. Figure 39.1 shows the two higher hierarchical levels of educational contents for a patient-centered pharmacy curriculum [10]. Universities should follow competency-based curriculum design, but each competency must be scrupulously aligned with the corresponding educational contents.

39.2 Teaching and Learning Methods

Teaching methods are the principles and strategies used by instructors to promote student learning. In addition to facilitating the achievement of learning outcomes, teaching methods can help students engage in the learning process, support their responsibility for self-directed learning, and promote peer interaction and collaboration.

Teaching philosophies can be divided into teacher-centered approaches and student-centered approaches. A teacher-centered instruction model emphasizes the lecturer taking a more authoritarian role and assuming control of the classroom, while students act as passive subjects who receive information provided by the professor through lectures, with a final aim of assessing their knowledge. In teacher-centered education, the student engagement in the learning process, participation in the class, and the development of communication and teamwork skills is low. The transition to a student-centered teaching model has several advantages, beginning with responsibility for the learning process. The role of the instructor changes from authoritarian to facilitator leading to an increase in student participation, responsibility for self-directed learning, and involvement in the assessment

Fig. 39.1 Two higher hierarchical levels to code the educational contents for a patient-centered pharmacy curriculum [10]

process. In a student-centered model, teaching and assessment are linked since student learning is measured continuously during the teaching process. The use of a student-centered approach to learning, with the use of active learning strategies, seems to be more appropriate for the patient-centered education aimed for in pharmaceutical care.

39.2.1 Different Teaching Methods

Different teaching methods relate to different contexts, and the chosen teaching method (or mix of methods) depends mainly on the subject area being taught and the characteristics of the learners. Additionally, the educational philosophy and beliefs of the teacher, the teaching context, the resources available, and the school mission are several factors that influence the choice of a particular teaching method.

Higher education institutions and teaching methods have evolved according to the social, economic, and political contexts. Until the nineteenth century, the lecture was the most traditional method used in the classroom teaching. In the late twentieth century with the rise of the digital age, new teaching methods began to emerge. The presence of technology in the classroom for teachers and learners has become commonplace, including laptops, tablets, mobile phones, and digital projection of content (e.g., PowerPoint®). The focus of teaching has changed from the simple transmission of information to knowledge management, "where students have the responsibility for finding, analyzing, evaluating, sharing and applying knowledge, under the direction of a skilled subject expert" [11]. The use of active learning strategies engages and motivates learners and assists them in understanding and retaining information. These new strategies include laboratory experiences, case studies, small group discussions, brainstorming of ideas, games, peer teaching, role plays, and other practice-based exercises. In active learning, the instructor must carefully structure the activities in which the learner will be involved, such that regardless of the methods used, the student is actively engaged in the educational process.

With the educational evolution from basic sciences to clinical and integrated courses, the use of active learning strategies in pharmacy education was essential to provide pharmacy graduates with the necessary integration of knowledge, skills, attitudes, values, and behaviors to a patient-centered practice. According to the Standards for Curriculum published by ACPE, the pharmacy curriculum should promote lifelong professional learning through an emphasis on active, self-directed learning [4]. The integration of active learning strategies in the didactic and practice-based coursework is fundamental to the development of critical thinking, problem-solving skills, communication, and teamwork; all which construct the foundation of the effective delivery of pharmaceutical care.

There are numerous studies that address the implementation of active learning methods in pharmacy education such as problem-based learning, team-based learning, case-based learning, cooperative learning, project-based learning, simulation-based learning, ability-based education and assessment-as-learning, game-based learning, and blended learning. The next section will focus on the most widely used teaching methods in pharmacy education that prepare students for a patient-centered practice.

39.2.1.1 Lecture-Based Learning

Lecture-based learning (LBL) is a traditional method where the instructor is in the center of the teaching approach. In this passive learning method, the instructor delivers the information to students who receive and attempt to memorize the content. During the lecture, the students can take notes while they are listening to the instructor, but there is less opportunity to interpret and use concepts. There tends to be poor engagement with the students with LBL and student attention and retention of information decline progressively after the first 10 min of lecture.

Although this teaching method is not the most appropriate to provide pharmaceutical care skills to graduates, it is one of the oldest methods and is still widely used in pharmacy education. It is a highly effective and efficient method of transmitting information to a large group of individuals, does not involve a large investment in material resources, and if the instructor is a good speaker, can captivate the audience. To make the LBL method more effective, the instructor can incorporate some active learning strategies during the lecture. For example, the use of question-and-answer techniques and group discussions increases feedback between the teacher and students, and helps to absorb and understand the information. In addition, if the instructor introduces real-life examples during the class, it may be easier for students to understand the information and relate to practice.

39.2.1.2 Problem-Based Learning

The problem-based learning (PBL) model emerged in 1969 in the medical education at McMaster University in Canada. Since then, this method has been used among health sciences education programs successfully. An example of the student-centered PBL approach is the case studies model where a small group of learners, usually less than 10, are guided through a patient encounter by a faculty facilitator. A typical scenario of PBL is as follows: In the first class of the week, a case is presented to the students. During this week the students discuss the case and research the issues that arise, then present their interpretation in the second class of the week. Each week a new case is presented to the students along with a list of learning objectives which align with the corresponding educational content. The purpose of PBL is not to simply focus on problem-solving, but also for students to recognize their own learning needs as they make efforts to understand the problem. At the same time they gather and synthesize information and deepen concepts related to the problem, they apply a self-directed learning approach and enhance while enhancing group collaboration and communication skills, ultimately assuming responsibility for their learning.

Schools of pharmacy have implemented PBL in their curricula to be in line with the demand of the pharmacy profession, producing graduates that may be better prepared to provide quality pharmaceutical care. In the literature, there are several reports of the implementation and use of the PBL method in pharmacy education to supplement the traditional learning approach. For example, the University of Mississippi employs the PBL model in the third year of the professional degree in a course called “Pharmaceutical Care”. In this course series, the educational contents previously covered in different courses were integrated into clinical case scenarios and discussed by students in small groups oriented by a faculty facilitator [12].

Although the inclusion of the PBL method in the curriculum has several advantages, there are some barriers and limitations to its implementation and use. This method requires more human resources and more time invested by faculty in the preparation of patient cases. There needs to be a transition among the faculty to move from a traditional teaching method to a more innovative and active teaching

approach, which may be opposed by faculty who have successfully instructed their students for decades through LBL. Also, students are not always receptive to PBL because of their comfort as a passive learner. PBL also requires educational institutions to be well equipped with the necessary resources of books, journals, computers, and internet access which allows students to research effectively. However, if the students are not properly resourced or guided by the instructors, they could be overwhelmed with the information they identify. The use of PBL also requires instructors to change the student assessment, which usually requires lengthy grading of cases, redirecting learning and research, and incorporating the evaluation of noncontent characteristics such as participation, teamwork, and communication.

39.2.1.3 Team-Based Learning

Team-based learning (TBL) is an active teaching method originally developed by Larry Michaelsen in the late 1970s when he was a professor of business at the University of Oklahoma and later adopted by health professions education.

TBL strategically organizes students into teams of 5–7 students with diverse backgrounds that remain fixed throughout the entire term. Furthermore, the educational course content is structured into main units or course blocks (6–10 h of coursework) with the goal of developing team learning simultaneously as students achieving course objectives. TBL consists of three phases: the preparation, the readiness assurance process (RAP), and the application. In the first phase, prior to class, the students read and study the assigned materials related to the unit of study. The second phase occurs in the classroom where students are assessed, usually by multiple-choice quiz, about the material studied previously provided. The students may then initiate an individual readiness assurance test (RAT) and subsequently answer the same RAT as a team where they reconcile their individual answers with the team. The instructor provides immediate feedback on their performance and clarifies doubts that have arisen during assessment with both individual and team RAT contributing to the final grade. In the last phase of the TBL method, students apply concepts and content that they have learned and tested to real-world problems through discussions, team activities, and exercises. The engagement of students with the TBL is higher, since the students spend more time in the preparation of the class and take more accountability for their own learning.

Several pharmacy schools in the United States have incorporated the TBL method into their curriculum to be in line with the ACPE Standards, which recommend active learning strategies that develop critical thinking, problem-solving, communication, and teamwork skills. The incorporation of TBL in pharmacy education provides for self-directed learning and allows students to solve clinical problems, while they build teamwork skills, essential to the delivery of patient-centered care as a member of the healthcare team.

The limitations to the implementation and use of the TBL method are similar to PBL and include faculty resistance, lack of training, increased workload, and the

costs of the resources needed to facilitate. As an economical alternative to the digital learning management systems, paper can be used to respond to the RATs, although it takes more time for the instructor to give feedback to the students and to grade them.

TBL with PBL have been compared extensively in academic literature, however, the main differences of the TBL method are the four essential principles: (1) creation and management of heterogeneous teams; (2) students are responsible for their individual and teamwork; (3) students should receive frequent and immediate feedback; and (4) group application activities must be designed to promote learning and team development. The TBL requires that students to attain knowledge before the class, while in PBL a new "problem" is presented to the students during the class where only after they apply a self-directed study to resolve it. In TBL, the instructor facilitates the discussion after all teams have submitted solutions (one instructor per classroom); in PBL, the instructor facilitates each team during the discussion (one instructor per group). Although the application of these two teaching methods differs, they both highlight critical thinking, communication skills, and student responsibility and engagement in their learning.

39.2.1.4 Game-Based Learning

The use of educational games as a teaching method in pharmacy education is progressively increasing. Two different systematics reviews have been conducted with the aim of analyzing educational games adopted in pharmacy schools and to evaluate the effects of implementing games in the pharmacy curriculum [13, 14]. Different games have been used to introduce active learning into the curriculum to engage and motivate student learning. The literature identifies and describes the implementation of games such as bingo, Clue®, crossword puzzles, quiz shows, card/board games, and simulation games. For example, the University of Florida College of Pharmacy has created an educational tool, called Medication Mysteries Infinite Case Tool, for teaching pharmacy students to conduct medication history interviews and to perform medication reconciliation [15].

Although more studies are needed to prove that the use of games as a teaching method improves students' learning, the literature shows that students enjoy these strategies and their motivation, interaction and participation in the class are stimulated. While playing, students develop critical thinking, communication skills, and social collaboration, fundamental to the practice of pharmaceutical care. Another advantage of the game-based learning is that the instructor could use real-world situations but in a safe environment, being less stressful to the students.

The main limitations to the implementation and use of educational games as a teaching method relate to the challenge of designing an effective game, the time consumed, and the costs involved. Additionally, some games are difficult to apply in large classrooms, they may require the presence of more than one instructor for facilitation and moderation of the game, and some students may take the competition too seriously, increasing their anxiety and conflict.

39.2.1.5 Blended Learning

Internet-based learning (e-learning) has emerged as an innovative method in which teaching is conducted online through internet-based tutorials, online reading materials, virtual patients, e-mail, online forums, videoconferences, online chat, and instant messaging. Through this method the communication between instructor and students can be synchronous, involving real-time interaction between participants over the internet (e.g., videoconference), or asynchronous, where instructor and student are not online at the same time (e.g., e-mail). The main advantage of the e-learning method is the access to educational content can occurs anytime and anywhere, depending only on internet access and the equipment necessary to access the internet.

In pharmacy education, this distance method is widely used for continuing education programs. However, the lack of interaction between students and instructor makes this method less appropriate to obtain the skills needed for patient-centered practice. As an alternative to e-learning, the blended learning (b-learning) method emerged. Blended learning is a student-centered learning approach that combines online resources with face-to-face classroom methods. With this model, also known as the "flipped classroom", the instructor makes the educational content available online. The students study the lecture material at home before class and during the class they apply the knowledge through work assignments.

Some studies have described the implementation and use of b-learning in pharmacy education. For example, in the University at Buffalo School of Pharmacy and Pharmaceutical Sciences, a b-learning model that combines online videos with TBL, case-based learning and clinical skills laboratory was integrated into a "patient assessment" course sequence in the first professional year. This approach was well received by students and related with improved academic performance [16]. A list of best practices for the use of blended learning in pharmacy education was recently published, containing advice such as the inclusion of a schedule of the course activities on the syllabus, including a length of time for out-of-class activities; availability of materials on the online platform at least 2 weeks prior to the classroom lesson; review of the difficult content topics at the beginning of each class [17].

Although the b-learning method offers the advantages described above for the active methods, the main disadvantages are the high costs related to the preparation of online materials, costs of maintaining an electronic learning platform, and faculty online time. It should also be taken into account that technological resources should be affordable, reliable, up to date, and easy-to-use for students and instructors. Finally, the impact of blended learning on the student's ability to deliver pharmaceutical care has not been evaluated and creates opportunities for future academic research.

39.2.2 Integrative Teaching and Learning in Pharmacy Education

The ACPE standards state that graduates must develop, integrate, and apply basic sciences knowledge to solve clinical problems, which has led to most colleges of pharmacy in the United States to develop some approach to integrate their curriculum. This educational strategy allows for the integration of contents from the basic sciences with clinical sciences, subsequently combining theory and practice, enabling a better assimilation and application of concepts by the students. Also a pharmacy curriculum with a complete integration of biomedical, pharmaceutical, social/behavioral/administrative, and clinical sciences was developed [18]. Evidence from the literature suggests that by integrating curricular content, students learn and understand concepts more quickly and easily by identifying connections from various areas across the curriculum. Additionally, curricular integration supports the development of problem-solving skills where students can apply basic science concepts to solve drug-related problems.

A curriculum can have "horizontal integration", when related educational content from different courses are taught at the same time, or "vertical integration", when content are taught at different stages of the program. A "spiral curriculum" model occurs when horizontal and vertical integration are adopted. Following this approach, at the beginning of the program, content and concepts are taught in a simpler way, increasing complexity over time. In curricular integration, it can be useful if the educational contents are organized by themes, such as discipline, organ system, chronological, and problem-based themes. Durham University in the United Kingdom has applied curriculum integration where modules are organized according to body systems, where each module does not correspond to a specific discipline, but is rather organized around the management of diseases specific to an organ system. For example, in studying the cardiovascular system, the student addresses hypertension taking into account pathology, public health, pharmacology, therapeutic drug monitoring, drug formulation and clinical therapeutics. The modules are linked to each other, and material is recurrently reintroduced throughout the program in more complex clinical situations. The curriculum works as a whole instead of the sum of the parts [19].

Despite the benefits of curricular integration in pharmacy education, the implementation of an integrated curriculum presents some limitations. The main barriers are the complex design process, the need to develop integrative pedagogical and evaluation strategies, and the time and resources consumed. Other obstacles to curricular integration are that traditionally, academic institutions are discipline-based, instructors from basic sciences and clinical sciences express different interests in this teaching model, and student's resistance to a new pedagogy.

39.3 Assessment Methods

The students' assessment process and the methods of reporting students' results is a fundamental part of the teaching and learning process. Assessment methods are strategies and instruments used to determine whether students have achieved the desired course learning objectives and is characterized by being a systematic and continuous process, which enhances student learning, and focuses on the improvement of curricular programs.

According to ACPE standards, every pharmacy school must develop and implement a plan to assess the attainment of educational outcomes to ensure that graduates are fit for practice. This assessment plan should combine systematic, valid, and reliable knowledge-based and performance-based formative and summative assessments. The assessment of student learning must comprise "student self-assessments and faculty and preceptor assessments of student development of the professional competencies and demonstration of professional behaviors". In addition, the instructor may document, for example, in student portfolios that graduates have achieved the desired competencies [4].

In 1990, George Miller responded with the article "The assessment of clinical skills/competence/performance". Miller presented a framework for clinical assessment, which consists of a pyramid describing clinical competence with four hierarchical levels (Fig. 39.2). At the base of the pyramid is the knowledge (knows), followed by competence (knows how), performance (shows how), and action (does) [20]. The "knows" represents the knowledge that a student must achieve, and the "knows how" is the interpretation and application of this knowledge. These two base levels are within the scope of cognitive knowledge, and could be assessed using traditional assessment methods with written tests, multiple-choice questions, and oral exams. The "shows how" level is where students can demonstrate what they have learned and can be assessed in controlled situations through lab practicals, simulations, objective-structured clinical examinations (OSCE), and objective-structured assessment of technical skills (OSATS). The "does" corresponds to what happens in real-life practice and assessing the performance in the work environment. The upper two levels of the pyramid are related to behavioral

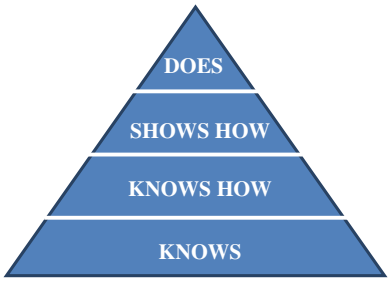

Fig. 39.2 Miller's pyramid of clinical competence [20]

components. Research shows that the cognition area ("knows" or "knows how") and the behavior area ("shows how" or "does") have a weak correlation. For example, a pharmacy student who knows how to do a certain task does not automatically mean that they will perform as a competent pharmacist in practice. In order to help students to apply their knowledge in real life—to be competent—it is critical to select methods that allow them to "show" and "do".

There are several methods to assess student learning outcomes and the selection of the assessment method depends on the learning outcome supposed to be tested. The use of multiple methods in the student evaluation process could be useful to ensure that all student learning outcomes are assessed, sometimes termed as 360° assessment. There are direct and indirect methods of assessment. While in the first, the students are asked to demonstrate their learning (e.g., tests and presentations), in the second, the students are asked to reflect on their learning (e.g., course evaluation survey and syllabus review).

The students' assessment could be formative or summative. The formative assessments observe and help inform the student learning during the teaching-learning process, while the summative assessments occur at the end of a program or course. Formative assessments (also known as "low-stakes") are used for collected information and feedback about the students' progress in the course, such as what they know and can do, if they have misunderstandings or any learning needs, and if some gap on the educational process exists. This type of information allows the teacher to adopt strategies that improve the students learning. There are several examples of formative assessment techniques such as: prior knowledge assessment; written reflections such as minute paper or muddiest point; "wrappers" (set of reflective questions); case studies; and checks for understanding using audience response systems (used for quizzes, voting, and active learning). The summative assessments ("high-stakes") are used with accountability purpose to check what students have learned and what they are able to do at the end of the teaching-learning process, resulting in the assignment of a score or determining the progression of the student in the program. Tests and exams, portfolios, OSCE, papers, projects, and presentations are examples of summative assessment techniques.

39.3.1 Traditional Assessment Methods

The most widely used traditional assessment methods are written examinations. These examinations may include mid-term exams, final exams, pop-quizzes, and mini tests, depending on the intention of the assessment (formative/summative). The content of the exam may include any combination of question types allowing students to demonstrate their knowledge, and fall in the categories of short answers, true/false questions, multiple-choice questions (MCQs), matching questions, or essays.

The main advantages of traditional evaluation methods are that they are easy to prepare, administer and evaluate, consume less time and resources, and are economical. In addition, it is a standard approach that evaluates the student's knowledge in an objective, reliable, and valid way. However, interpersonal skills, lifelong learning, professionalism, and integration of fundamental knowledge into decision-making can be underestimated. Since the traditional approach typically only evaluates the "knows" and "knows how" in the Miller's pyramid, these methods are not the most appropriate for assessing students abilities for practicing pharmaceutical care. Also, with this type of assessment, students are generally encouraged to memorize knowledge in producing the right answers, and in the particular case of MCQs or true/false questions, the correct answer is suggested to the students, reflecting the student's ability to take a test rather than the knowledge acquired.

39.3.2 Simulation-Based Assessment

The integration of simulation methods in pharmacy education arose from the need to assess whether students were able to translate their knowledge into practice. Simulation-based assessment includes role plays with colleagues, standardized patients or clients, clinical skills-based assessment (e.g., prescription filing and checking), virtual patients, and human patient simulation (high-fidelity mannequin models). Simulation attempts to imitate real practice, but without resorting to real patients, since the use of real patients has some limitations such as patient accessibility and wellbeing, and the necessity to provide a controlled student assessment. Standardized patients or clients may be trained as actors that perform a specific role repetitively and systematically, being able to interpret a patient, caregiver, or health care provider.

Simulation activities allow students to apply their knowledge into practice, and developing patient care skills such as communication, history taking, information-gathering, professionalism, active listening, counseling, problem-solving, and decision-making. Assessment in the simulated environment has the advantages of reflecting real life, being immediate, reliable, and consistent, and applied to formative feedback or summative evaluations. However, the use of isolated and poorly structured simulations does not allow students to be evaluated in a standardized, objective valid, reliable and feasible, as with the objective-structured clinical examinations.

39.3.3 Objective-Structured Clinical Examinations

Objective-structured clinical examinations (OSCE) are an example of competence-based evaluation introduced in 1975 by Ronald Harden et al. at the University of Dundee, Scotland, with the aim of avoiding the disadvantages of the

traditional clinical examination in medical education [21]. The OSCE method was designed to assess student's clinical competence in a systematic and objective way, and is still employed today in various health care disciplines to assess student performance.

During the OSCE, the students typically rotate through a series of 12–16 stations and spend between 5 and 10 min at each station. The number of stations and the time spent at each one can vary depending on the OSCE design. There are procedure stations, where student must perform a real-world task such as history taking, physical examination, or interpretation of laboratory analysis and the examiner uses a checklist to score student performance. There are also question stations, where students must answer questions related to the information and findings attained from the prior station with evaluations usually consisting of multiple-choice questions. After the examination, the examiners' checklists and the students' multiple-choice answer tests are marked according to an established rubric. With this method, the use of a simulated patient (trained actors representing patients) can be substituted in the place of a real patient, since the OSCE is repeated a large number of times according to the number of students in the discipline [22].

In the assessment of competence in the history taking, a brief description of the patient is given to the student. During the student performance, the examiner listens and scores their performance on a checklist made previously in the examination, and the result must be reliable and objective. Examiners make notes on the student performance regarding their relationship with the patient, history taking technique, and inquiring about the key points in the history. The examiner marks with a tick on the checklist whether the student, during their performance, asked the patient certain key points. After the student performance on the procedure station, they must complete an MCQ test about the patient history. In assessing competence on physical examination, the student examines a limited area and the examiner evaluates his or her performance using a checklist with previously established topics. After that, the student also answers MCQs related to their findings about the physical examination. With the OSCE, in addition to being able to assess the student's competences in taking a patient history or doing a physical examination, the examiner can evaluate other situations such as inspection of a patient or images, interpretation of patient charts or laboratory data, and provision of health education to the patient [22].

The use of the OSCE as a method to assess pharmacy student performance has become more common in pharmacy schools worldwide. In Canada, it used as an assessment component of entry-to-practice examination for pharmacists, in the United States it is commonly employed as an evaluation method in pharmacy education, and it has been adopted globally in countries including the United Kingdom, Switzerland, Malaysia, Japan, and Australia. The use of the OSCE in pharmacy education parallels that described previously in medical education, but with the focus of the evaluation on the delivery of pharmaceutical care. Stations may include a scripted simulated interaction with a patient, caregiver, or health care provider aimed at assessing communication skills, patient counseling or demonstrating use of a medical device, where other stations may have students performing

pharmaceutical calculations or checking prescriptions for errors [23]. Furthermore, the OSCE methodology has been recognized as a valid, reliable, and feasible assessment tool through the use of specific checklists for scoring performance, increasing agreement among examiners [24, 25].

Ultimately, the logistics of using the OSCE are complex and require significant human and financial resources. Yet, when well planned and effectively executed, becomes a feasible assessment method, whether formative or summative, in different stages in the education of a variety of health care professions [24].

39.3.4 Objective-Structured Assessment of Technical Skills

The objective-structured assessment of technical skills (OSATS) is a reliable and valid method that has been used to evaluate technical skills. This method has been developed and used to measure technical skills of surgical trainees, but it can be adapted to evaluate students from other areas of health, namely pharmacy. In pharmacy education, OSATS is useful to assess competencies relative to isolated techniques and complete procedures, such as administration of vaccines, inhaler devices techniques, glucometer usage, blood pressure assessment, and individual medication preparation. Students' technical skills are evaluated according to task-specific checklists that should be performed during the procedures. In the student performance evaluation, the examiner also use a global rating scale and a pass/fail judgment. Although this method is costly both in terms of time and resources, it allows students' technical skills to be assessed in a feasible and effective way.

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Chapter 40
Teaching Pharmaceutical Care to Pharmacists and Other Health Professionals

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Abstract Educating pharmacists about pharmaceutical care begins with re-orientating them to the provision of care rather than the supply of a medicine. Then the pharmacist's knowledge and understanding must be developed and tailored to the steps of providing care; assessing the problem, identifying and prioritizing problems, planning the interventions, implementing changes, monitoring, and follow-up. In order to do this, it is necessary to have integrated academic and work-based learning with appropriately qualified and experienced professionals who take on the roles of facilitators, supervisors, mentors, and coaches as necessary. Suitable methods of assessment help the learner to gage their progression.

Keywords Pharmaceutical care · Education pharmacy · Continuing education Pharmacy staff education · Practice learning

40.1 Reasoning for Pharmaceutical Care in Practice

Teaching, learning, and applying the concepts of pharmaceutical care to the practicing professional is challenging, but essential to maximizing patient outcomes. One of the first documents to consider pharmaceutical care and pharmacy education was written by a working group of the European Faculties of Pharmacy in 1999 [1]. Although the concept of pharmaceutical care has continued to be widely endorsed since this document was published, its inclusion in continuing education, postgraduate qualifications and continuing professional development reflects the different interpretations of pharmaceutical care and the challenges of incorporating it into pharmacy practice.

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Teaching pharmaceutical care is important and often described as a philosophy, implying it is of fundamental importance, but describing an idea as a philosophy implies it is theoretical and not practical. However, the idea of pharmaceutical care arose as pharmacists thought about how they could provide care with medications, rather than just dispensing/supplying them. As this pragmatic view is taken, several themes become obvious:

- Applying the knowledge and skills of the pharmacist to provide "care" should be central
- Pharmaceutical care integrates the relevant knowledge from the patient's medical, family, and social histories in order to identify the factors that influence the patient's use and experience of medications
- The development of a therapeutic relationship between the health care professional and the patient underpins all of the activities that are needed to provide care
- Assuming responsibility for the process of care requires the pharmacist to practice patient-centered care and collaborate with other health care providers.

For these reasons, it is important that curriculum clearly indicate why pharmaceutical care is needed, what impact it can have on patient outcomes and how it can be effectively employed, otherwise, its value as a transformative educational idea will be lost. For example, the relationship between pharmaceutical care and other pharmacist activities and responsibilities, such as responding to requests for nonprescription medication may not addressed, and so limiting the scope and impact of the idea of pharmaceutical care. Furthermore, as health care changes, new approaches to education, and care delivery are needed [2]. In education and health care, understanding and employing these concepts are essential because as the development of any health care professional progresses from novice to expert, it requires growth in knowledge, skills, competence, judgment, collaboration, and leadership [3, 4].

Pharmacy educators must be able to clearly articulate these concepts when teaching pharmaceutical care so that pharmacists can optimize patient outcomes by appropriately managing medication use. If a formal qualification is to be awarded to certify the pharmacist for a specific type of practice, then the requirements and standards of the practice will also have to be factored into the description, structure, and assessment methods used in the program.

Unlike undergraduate students, pharmacists are mature and adult learners with a body of experience and expertise to draw upon. They may be engaging with a formal pharmaceutical care education programs as part of their continuing professional development, but they could also be taking an active learning approach and changing their practice model or introducing new services. This relates both to professional requirements and obligations as well as a need to "skill-up" in order to enable a new output/service-related aspect. Many pharmacy settings enforce compulsory CPD that seeks to ensure fitness to practice and protects that patient but in addition there may be requirements to demonstrate a certain competence—such as following deregistration of medicines for pharmacists to provide over the counter—in order to perform that role.

The ultimate goal of teaching pharmaceutical care to pharmacists is to optimize patient drug therapy. That is to ensure that pharmacists gain and improve skills on diagnosing and resolving drug-related problems in various patient populations. In order be able to diagnose and resolve drug therapy problems, the teaching program should empower pharmacist staff with a set of skills, knowledge, and behaviors—in other words competence—for optimal pharmaceutical care. First pharmacists should ensure that their knowledge and understanding enable them to make accurate, appropriate and timely clinical decisions. Second, pharmacists should be taught on how to perform certain skills such as undertaking a medication history and reviews with clinical reasoning to optimize drug therapy through good communication. Thirdly the pharmacist needs to have developed behaviors and exhibit attitudes towards patients and members of the health care team towards achieving the full complement of pharmaceutical care.

40.2 Pharmacists

Education for pharmaceutical care necessitates re-orienting pharmacist's roles and responsibilities from suppliers of medication to providers of care. Pharmacists in practice may take a traditional approach and start with the medication and work backwards to considering the patient's condition and finally to the patient themselves. Typically, task-oriented procedures and protocols support the use of rapid screening processes to identify problems associated with a prescription, a nonprescription request, or a request for advice about symptoms. While these provide structure, and enable quality assurance to be carried out and are a reasonable approach to managing the workflow in a pharmacy, other skills, and procedures are required in order to provide care. Pharmaceutical care is similar to task-oriented procedures as both are logically structured and systematic, but differs because it is outcome oriented, holistic, patient-centered, and interprofessional.

As some currently practicing pharmacists may not have received formal instruction in the concepts of pharmaceutical care in their undergraduate curriculum, these individuals need to be educated so that they can provide patient-centered services in their respective practice setting. Central to the ability in providing pharmaceutical care is understanding the six stages of the care cycle: assessing the problem, identifying and prioritizing problems, planning the interventions, implementing changes, monitoring and follow-up. This complex process has been a part of the education of other health care professionals for many years, and requires the combination of knowledge, skills, and judgment to effectively execute.

Educating the practicing pharmacist creates unique challenges not often faced in other educational settings, and if work-based learning is to be effective, it will require commitment and planning [5]. To learn and employ the principles of pharmaceutical care, there needs to be some reconstruction and re-organization of knowledge, modification of perspective, and development of new processes. Some of the skills may not be familiar to a pharmacist; for example, reflection and

reflective practice has long been used in nursing education but may seem an unusual tool to some pharmacists [6]. Communication skills and self-directed learning of the mature learner to be refreshed in a way that engages the practicing professional, and subsequently the teacher assumes the role of facilitator, advisor, mentor, and coach. Furthermore, the educational setting should involve traditional didactic environments coupled with patient care settings, utilizing simulated and real-life patients for instruction and assessment. Interprofessional educational opportunities should be encouraged to allow for a more patient-centered learning approach, diverse and comprehensive care plan, and develop interprofessional trust and respect [7]. The need for a competency framework depends upon the educational setting, instructional methods, and whether individual behaviors or global assessment of performance is being evaluated. A list of suggested educational methods for pharmacists can be found in Table 40.1.

Table 40.1 Suggested components of a pharmaceutical care education program

Preparation and re-orientation
Systematic and holistic assessment
Patient-centered processes and care
Therapeutic relationship and continuity of care
Collaborative and shared care
Outcome focused—short, medium, and long term
Pathology and therapeutics of the disease states that form part of the syllabus
Medication-related problems, risk assessment with medications and balancing risk and benefit
Subject matter
Sources of information and of evidence in the health service and the published literature
Evidence-based practice and therapeutic guidelines; their strengths and limitations
Multimorbidity, patient preferences and patient-oriented -outcomes
Clinical judgment and prioritization
Health-related quality of life
Medication use: patient's ideas, concerns, and experiences
Process of care as distinct from a tool-driven biomedical process
Patient-centered care and communication, shared understanding and action
Recording consultations and linking/integrating records into existing pharmacy systems
Communicating with other professionals and shared decision-making
Teaching and learning methods and assessment
Assessment of knowledge relevant to the disease states and the operation of the health service and sources of information using summative methods
Assessment and reflection upon pharmaceutical care and existing practice to explore the re-orientation and educational and professional goals of the student, using formative methods
Care planning on paper and its implementation
Observation of, discussion of, and reflection on pharmaceutical care practice by self and with mentor/coach

(continued)

Table 40.1 (continued)

Preparation and re-orientation
Pharmaceutical care practice with simulated patients assessed by mentor/coach and by simulated patient
Workplace learning of pharmaceutical care practice with and without mentor/coach oversight
Assessment of process
Assessment of patient outcomes
Portfolio of patient cases
Skills
Negotiation
Leadership
Judgment
Advocacy
Collaboration

40.2.1 A Programatic Approach to Pharmaceutical Care Education

Education of practitioners in pharmaceutical care should therefore be systematic with clear exit outcomes based on the individual and/or institutional needs. In this section, we propose and discuss the Monitoring, Training, and Planning (MTP) model for effective teaching on pharmaceutical care to pharmacy staff [8]. The first step is to monitor and evaluate the current practices of pharmaceutical care in any given practice setting amongst the various pharmacy personnel present; this will help in the identification and quantification of the teaching needs. In addition, the assessment of the training needs provides a baseline for monitoring implementation of a particular teaching program. Once the training needs have been identified—for example, through a rigorous external needs assessment or through individual self-assessment such as in the use of a learning diary—training curricula or teaching/training guide should be developed to implement teaching strategies that would address competence through the knowledge, skills, and/or behavior gaps in pharmaceutical care. Different modes of training, resources, methods, and approaches may be adapted to closing the specific pharmaceutical care gap(s) identified. Once the teaching has been implemented, a plan should be put in place to demonstrate that there is improvement in the practice of pharmaceutical care; for example, this could be reported by the individuals concerned or through external evaluation of the training program after some time has elapsed by means of valid specific and structured assessment tools. The plan should have clear goals of what is expected to improve within a specified time line and should also enable the pharmacist access to the most appropriate resources as well as resourceful persons (such as learning or practice mentors) to achieve the intended outcomes.

40.2.2 Pragmatic Approaches to Pharmaceutical Care Education

One core aspect of a teaching curriculum or guide is the unit standards, which express the extent and depth of learning. The unit standards are key elements in the training of pharmaceutical care to pharmacist staff members. Unit standards indicate and describe the competencies to be acquired and include a defined set of knowledge, skills, and behaviors. Two main unit standards are assessing and resolving drug therapy problems. Overall, this requires the development of skills in clinical reasoning as well as interprofessional practice. Another important unit standard is one aimed at developing the clinical approach of pharmacists. This unit standard would focus on imparting skills such as handling clinical information (clinical records, medical notes, drug administration charts, common medical abbreviations) and interpretation of clinical laboratory tests as well as patients' vital signs. In this approach the education of pharmaceutical care amongst pharmacists is iterative.

40.2.3 Training on the Assessment of Drug Therapy Problems

Box 40.1 Knowledge of Drug Therapy Problems
The pharmacist staff should be knowledgeable of the eight drug therapy problems in general—that are:

- Adverse Drug Reactions
- Choice of therapy,
- Inappropriate indications:
  - drugs without indications
  - indications without drugs
- Drug–Drug interactions, and
- Inappropriate Dosage adjustment:
  - underdose/overdose or
  - duplications
- Compliance to therapy.

The pharmacist should be trained on basic concepts on how to assess and resolve each of the above drug therapy problems and medication errors. In this section, we discuss in detail what aspects should be emphasized in the general teaching on medication errors and drug therapy problems. In addition, the pharmacist should be

trained to obtain a medication history, undertake medication reconciliation, and perform an appropriate type of medication review to identify the drug therapy problems. It is important that each pharmacist knows how to take a medication history—this training should ideally be done at the patient bed side with support from a senior pharmacist mentor, and a standardized protocol for taking history should be used. The teaching of medication history should focus on sources of medication history, how to effectively carry out the medication history interview and documentation of a complete and accurate medication history as part of the patient's clinical record. Training on medication history should be followed by a teaching on medicines reconciliation where the pharmacists are taught on techniques to identify discrepancies in the documented medication history and the patient's current therapy. Medicines reconciliation should be undertaken preferably in patients on high risk medicines, and/or in busy environments or transitioning between health facilities and practitioners. The teaching of medication reconciliation should emphasize errors of duplication, omission, commission, and transcribing. Pharmacists should also be taught skills on the review of drug therapy as a whole for its appropriateness, safety, and cost-effectiveness. The need for subjective patient data as well as objective patient data should be emphasized in the identification and prioritization of the drug therapy problems. The pharmacist should be introduced to the different levels of a medication review (level 1–level 3)—from a review of a prescription to performing a thorough review of the clinical case including the patient and treatment (see also Chap. 6). The teaching of medication review may require emphasizing training on the patient behaviors, disease (pathophysiology), and the pharmacotherapy as well as clinical reasoning. The pharmacist should be taught the clinical presentation of the diseases and the diagnostic criteria used to identify diseases as well as their appropriate drug therapy. Training should also focus on the pathophysiology of five major categories of disease states including—metabolic, inflammatory, neoplastic, degenerative, and congenital/hereditary disorders. For each patient case, the pharmacist should review the clinical presentation, lesions, etiology, and pathogenesis of each disease state.

Box 40.2 Awareness of Common Medication Errors
The Pharmacist should be aware of the common medication errors that may lead to drug therapy-related problems—these errors include:

- Duplication of medication
- Omission of a medication
- Commission errors, and
- Transcribing errors.

In addition, for each disease state, the pharmacist should be familiar with the pharmacotherapy including the drug classes of choice, the rational of use, adverse effects and mechanisms, and unique pharmacokinetic aspects of the drugs. This basic

knowledge of pathophysiology and pharmacotherapy should be reviewed by the pharmacist and verified and validated by senior pharmacists and fellow pharmacists before pharmaceutical interventions are made and communicated to other members of the multidisciplinary health care team. Once the pharmacist demonstrates competency in obtaining medication histories, undertaking medicines reconciliation, and medication reviews, the pharmacist should be taught how to develop and implement a pharmaceutical care plan as will be discussed in the next sections.

40.2.4 Resolving Drug Therapy Problems

The pharmacist should be taught on how to collate subjective and objective data to identify and prioritize drug therapy problems, and ultimately how to intervene appropriately to ensure the best desired outcome for the patient. The pharmacist should be able to use criteria and evidence to justify the potential and/or actual occurrence of drug therapy problems and also estimate the risk or contribution of the drug therapy to the patient's problem. This requires clinical reasoning with knowledge of pharmacotherapy and pathophysiology and well as patient assessment. Pharmacist staff should be encouraged to collaborate with other members of the health care team—interprofessionalism—to validate the drug therapy problems that they may have identified. Pharmacists should be taught on skills of interprofessional collaboration and practice that include, for example, effective communication strategies in a specific cultural context, and assertiveness. This should subsequently lead to training on the development and implementation of a Pharmaceutical Care Plan. It is advised that a standard tool for a care plan should be used during training of pharmacist staff; this should have aspects of the priority problems, the goals of therapy, the options for therapy, the most appropriate interventions for the patient, and the plan to communicate the intervention to the health team as well as monitoring the goals of therapy. Specific emphasis in the plan is the development of SMART goals of therapy (Specific, Measurable, Achievable, Realistic, Timely) and communication to the patient and the rest of the health care team as well as documentation. The pharmacist should be taught on how to use evidence of up-to-date data development and interpretation to optimally develop and implement a care plan. Pharmacists with adequate knowledge of pharmaceutical care planning should regularly attend clinical rounds to advise on therapeutic decision making in real-time and further develop their pharmacotherapeutic relationships with patients and other clinicians.

40.2.5 Clinical Pharmacy Reasoning Tool Kit

Most importantly, pharmacists should be taught to adopt and apply a clinical reasoning approach. The SOAP approach (Subjective, Objective, Assessment, and

Plan) is the most commonly used clinical reasoning tool by health care workers. The pharmacist can be taught on how to use the SOAP approach to identify and resolve drug therapy problems and also collaborate with other team members to best identify the main health problem. This will involve engaging in the process to validate the current subjective and objective presentation of the health problem with relevant and appropriate evidence in literature and/or criteria and methods—this may be aggregated into local, national, or international clinical treatment guidelines, for example. The key steps in clinical pharmacy reasoning are to:

1. Identify the subjective and objective data from the case;
2. Use appropriate and valid evidence to associate the subjective and objective data with a medical (disease), pharmaceutical (drug therapy), and/or nursing (psychosocial) problem;
3. Check the relationship between the drug therapy problems and the medical and/or nursing problem in order to establish and validate the current drug therapy problem(s) and prioritize the health problems.

Subsequently, a care plan should be developed and implemented based on the drug therapy problem.

40.2.6 Monitoring of Changes in Practice

In order to monitor changes in practice as an impact of pharmaceutical care training on practice, professional audits of practice should be undertaken. An audit of both pharmaceutical outputs (self-reported pharmaceutical interventions) and patient outcomes associated with the interventions can be carried out. This would require that pharmacists document their interventions along with the corresponding patient outcomes. These audits can reveal the most common interventions made and at what point of the patient journey (admission, in-hospital patient stay, and discharge) the interventions are made. Feedback can be sought from the wider interprofessional team in a systematic manner on the pharmacists' role and input. In addition, research can also be undertaken as a more substantive approach to measuring impact and monitoring changes in practice to inform any change in education.

The content and focus of the next training should be informed by results of professional audits, feedback, and research undertaken to monitor the impact of initial training on practice.

40.3 Other Health Care Professionals

Other health care professionals may arguably better understand the six stages of the care cycle and have a defined scope of practice. Therefore, the items described in Table 40.1, for example, are not new, it is the idea that the cycle may be applied to medication-related problems that is novel. They may be learning about

Table 40.2 Examples of assessment tools for pharmaceutical care in practice

Assessment tool	Assessed domain	Setting	Place in assessment
Clinical evaluation method	Clinical practice	Clinical; prospective	Usually formative
Case-based discussion	Clinical reasoning and understanding	Clinical; retrospective	Usually formative
Peer-assessment tool	Perceived practice competence by others	Virtual; peer review	Usually formative
Directly observed practice	Technical practice	Technical; prospective	Usually formative
Multiple choice questions	Knowledge	Non-practice; retrospective	Usually summative
Observed structured clinical examination	Knowledge/skills/attitudes	Simulated	Usually summative

pharmaceutical care for one of two reasons: (1) to understand what pharmacists mean and intend by pharmaceutical care and (2) to improve the outcome of use of medication by their patients. The material presented in Table 40.2 is relevant for both reasons and will help them to review their perspective of health care and inform them about the pharmacist's role, how patients view and use medications, and how to improve medication usage to maximize patient-oriented outcomes.

Teaching pharmaceutical care to other health professionals requires a range of skills and mixture of styles from facilitator to expert, and from mentor to coach.

As in the case of teaching pharmacists, if a formal qualification to certify the recipient to practice, is to be provided, the details of the requirements and standards will fundamentally influence both what is taught and learnt and how it is assessed.

40.4 Assessment of Learning in Practice

Assessments used to measure and evaluate pharmaceutical care learning in undergraduate and preservice are well described in Chap. 39 and include many tools that can also be applied for learning in practice and amongst practicing pharmacists. The focus of competency-based assessment becomes even more important, however, as pharmacist learners will need to demonstrate improvement in competence in their practice. This can be broken down, for example, by assessing knowledge through multiple-choice question (MCQ) style assessment that can be orientated in different ways (true/false responses; single/multiple answer formats; extended MCQs, etc.) but there are a number of valid methods for assessing learning in practice that give a 360° evaluation of the learner [9]. The challenge will always be to assess learning as close to the intended competency as possible and some assessments should be carried in the learner's practice. For example, the Clinical Evaluation Exercise (CEX) can be applied in the clinical practice setting with the pharmacist being assessed in their real

interaction with a patient and being assessed for their applied clinical knowledge, attitudes, and behavior. The outcome of this type of assessment shifts from a graduated score (e.g., percentage correct) to a system more rational to the setting, such as, "above expectations/meets expectations/does not meet expectations" or "competent/not yet competent". Obviously, this assessment cannot be systematically reproduced learner to learner but over the course of time the learner should start to develop, show improvement in their assessment, and consistently demonstrate competence in most situations they are presented with. Directly Observed Practice (DOP), similar to the OSATS in Chap. 39, can be applied in more technical areas of practice, for example, aseptic/sterile production of medicines or quality assurance settings. Otherwise, the learner can be afforded more time for reflection and peer review such as in the Case-based Discussion (CbD) that is retrospective in nature whereby the learner and assessor discuss the course of action and intervention of pharmaceutical care that has already taken place between the learner and patient. A broader peer review assessment tool exists in the Peer-Assessment Tool (PAT) that combines the feedback from a range of interprofessional clinical colleagues that work alongside or practice with the learner. This feedback is systematically gathered and is measured against the learners' self-assessment against the same criteria of various domains of practice and can also be compared against a group mean of learners undertaking the same education in pharmaceutical care. These examples of assessment tools, alongside the OSCE (see also Sect. 39.3.3), can be used in formative and summative assessment and give a broad picture of the competence of the learner as demonstrated in practice settings, simulated practice, self- and peer-assessment that reflect the competence. Assessment and examples of practice and learning can be brought together in a portfolio of practice, such as those used in Continuous Professional Development [10]. Learners can then be signed off in their assessment of practice through their portfolio's before progressing in their studies.

As a practical tool, below we give some scenarios that trainers or instructors may encounter, when formulating new learning.

Scenario 1: You work as a trainer for the provider of continuing professional development (or continuing education) for community pharmacists and pharmacy staff. You are new to the role and have been tasked with 'freshening up' the learning approach. This will involve a better understanding of the learning needs and how the implementation of learning will actually impact on improving the competence of the clients.

What initial questions do you think you need to ask?

What approach would you use to identify the learning needs in the target population?

How do you think you could demonstrate or evaluate the impact of your learning on competence?

Do you think it is important to evaluate competence as an outcome?

Scenario 2: You are a clinical instructor employed in the local teaching hospital under the training and education division. You have to deal with a seemingly constant flow of undergraduate pharmacy students on placements in your hospital, new internship/pre-registration graduates of pharmacy, and pharmacy residents for whom you have to tailor training at the appropriate level and in the right setting.
Ultimately, what do you think is your first duty of care (hint: in relation to medical ethics) and what tools can you employ or measures you can put in place to ensure this?
How will the training you provide for the various groups differ in terms of their orientation, depth of training, supervision, and responsibilities given to patient care?
Sketch out some learning strategies for each of the pharmacy learner groups described above. How would you approach their training?

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