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Polypharmacy in elderly people

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Summary Polypharmacy characterizes ongoing prescription of multiple medications in a patient. Following the demographic change and growing number of elderly patients, polypharmacy is of major concern due to the associated risks and even mortality. Many causes made this geriatric syndrome more common in the past decade. First, the management of comorbidities is often lacking in disease-specific guidelines. Second, multimorbidity is rising due to the ageing population. Third, deprescribing methods are sparse, and results are conflicting. This mini review integrates the effects of polypharmacy on mortality and morbidity, the causes and confounders of polypharmacy, and presents a practical stepwise manual of deprescribing. The work is based on a literature search for randomized control trials and reviews in English and German from 2015 onwards in the PubMed database, with integration of relevant citations as a result of this search.

Keywords Multimorbidity · Frailty · Deprescribing · Potential inappropriate medication · Tools

Definitions of polypharmacy

Polypharmacy is often defined as prescription of multiple medications in an individual using qualitative or quantitative parameters [1]. On a quantitative basis, it is defined as the regular intake of five or more medications [2]. Although no consensus on a definition of polypharmacy exists, this number is used in ongoing review articles [3]. The term hyperpolypharmacy describes clinical situations where more than ten medications are taken regularly [4]. For future activities to evaluate the effect of deprescribing methods to meliorate the negative aspects of polypharmacy, a clear definition is needed for different clinical situations and settings [1]. Patients exposed to polypharmacy are threatened by medication taken for too long, at the wrong frequency, without effect on symptoms or prognosis, outdated medication, with drug–drug interactions, or with interactions with comorbidities, summarized with the concept of potential inappropriate medication (PIM). About 26% of the community-dwelling patients and 49% of patients living in nursing homes in Europe are exposed to PIM [5, 6]. The inappropriateness of prescriptions in Europe and the USA is comparable [3]. Previous studies have identified PIM as one of the main risk factors for adverse drug events (ADEs) in older adults [4]. To identify PIM on medication lists, explicit or implicit tools can be used as mentioned in the "Management of polypharmacy" section [7, 8].

Adverse effects of polypharmacy

Despite the beneficial effect of polypharmacy in reducing mortality in multimorbidity and relieving symptoms, the complexity of different types of medication, the risk of drug–drug interaction, drug–disease interaction, and the risk of medication errors rising with the number of prescriptions may, in turn, cancel out the benefits of modern medicine. The vulnerability of older patients as part of the geriatric syndrome frailty even enhances these risks [9]. In a Japanese study on 584 patients in a university hospital in Japan admitted for hepatectomy, pancreaticoduodenectomy, gastrectomy, or colectomy, logistic regression analysis revealed that polypharmacy was significantly associated with prolonged hospitalization [10]. But not only economic index is driven with polyphar-

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macy, severe threats to to health such as falls, frailty, functional decline, self-perceived health, reduced adherence, adverse drug events, quality of life, cognitive impairment, and even mortality follow polypharmacy [11, 12]. The risk of these threats varies between different health care institutions and geographical sites, and must be considered due to these circumstances. In hospitalized geriatric patients in Korea, 46% of patients experienced polypharmacy and a higher mortality rate of 25% and a higher rate of hospitalization of 18% in the following 5 years [13]. But also in community-dwelling older adults can the adverse effects of polypharmacy be shown: In a systematic review, Hsu found polypharmacy to be present in 7–45% of the older adults and a positive association with poor self-perceived health status, limitations in physical activity, falls, depression, and pain [3]. The high rate of variation is due to the fact of different national guidelines in clinical practice, definitions of polypharmacy and PIM, and geographic peculiarities [14].

Risk factors for polypharmacy

To manage polypharmacy in older patients, it is useful to identify the risk factors that are associated with this geriatric syndrome. The risk factors are differentiated into factors found in health care systems and those found in patients themselves [15]. On the one hand, poor medical records, automatic prescriptions of ongoing medication, transition errors, and prescriptions focused solely on disease-specific needs are listed [16, 17]. On the other hand, on the patient's side, the greatest risk factor for polypharmacy is age [18]. Hospitalizations are common in elderly patients and drug burden is high in the last years of life. Discharge home are arranged with additional prescriptions for potentially futile medications [19]. A gender effect was evident in one systematic review on that topic, with a higher risk of polypharmacy in women [20]. Cognitive impairment, frailty, multimorbidity, residency in a long-term care facility, and specific illnesses (diabetes, heart disease, neoplasms, metabolic syndromes, and obstructive pulmonary disease) express a higher rate of polypharmacy [21, 22]. Osterberg et al. concluded in a review article that adherence to prescribed medication is hampered by factors identified in the health care system, providers, and in patients [23]. All factors for an appropriate medication can be checked using the Medication Appropriateness Index presented by Hanlon J et al. [24, 25].

Management of polypharmacy

Good medical practice

Improvements in polypharmacy can be based on the six-step model of rational prescribing of the World Health Organization: step 1: define the patient's problem; step 2: specify the therapeutic objective; step 3a: choose your standard treatment; step 3b: verify the suitability of your treatment; step 4: start treatment; step 5: give information, instructions, and warnings; step 6: monitor and stop treatment in case of adverse effects or treatment failure. Now, the principal of good medical practice goes even further, with prescribing of drugs only established on adequate knowledge of the patient's health and functionality [26]. The General Medical Council in the United Kingdom proposed a guidance for good medical practice adapted in 2019 (https://www.gmc-uk.org/guidance): provide medication on best available evidence, take all possible steps to alleviate pain and distress in all clinical situations. Consult colleagues where appropriate and respect the patient's right to a second opinion. Check the medication list for compatibility with other medication and interference with comorbidity, including over-the-counter medication. Avoid treatment of yourself and of patients you personally know [27]. Critical reading of guidelines, recognizing their pitfalls and exclusion criteria, is a precondition for prescribing a new medication in older patients. Adapting therapy for older adults means not only extrapolating effects of drug therapy in middle-aged persons for the geriatric part of the population. In fact, it is necessary to coordinate diagnosis, prognosis, and medication based on the integration of functionality in older patients and the identification of geriatric syndromes for their eminent effect on prognosis [28].

Identification of PIM

An effective approach to identifying medications that do more harm than good is to signal it as PIM. PIM in older patients causes a higher risk of hospitalization, ADEs, and poorer health-related quality of life [29]. Proposed assessment tools for the identification of PIM were explicit and implicit [7, 8]. Responsible prescribing is as important as responsible deprescribing, a therapeutic intervention to reduce mortality and clinical risks caused by PIM [30, 31]. For explicit measures, expert lists were published on a national basis [32–35]. Medications on these lists are qualified by experts using a physiological system-based screening tool (STOPP screening tool of older persons potentially inappropriate prescriptions) or school grading system [34, 36, 37]. Implicit methods can identify PIM using algorithms and questionnaires [25, 38–40].

Identification of anticholinergic drugs and drugs with higher risk

Medications with anticholinergic or sedative side effects jeopardize older patients even more than PIM, increasing the risk of falling and worsening cognitive impairment. A tool to identify this medication is the

Drug Burden Index (DBI) [41, 42]. It evaluates the exposure of an individual to medications with anticholinergic and sedative activity. Higher DBI scores have been associated with poorer physical and cognitive function in community-dwelling older people [43]. The Anticholinergic Risk Scale is a categorically ranked list of medications that predicts an increased risk of anticholinergic adverse effects in elderly patients [44].

Deprescribing

"If my doctor said it was possible, I would be willing to stop one or more of my medicines." A meta-analysis found that the proportion of participants who agreed or strongly agreed with this statement was 84% [45]. Although it seems feasible and easy to deprescribe unnecessary of even harmful medication, patients often do not agree [46]. Deprescribing means a systematic process to identify and discontinue medication in clinical situations in which potential harms outweigh benefits in view of patients' goals, functionality, life expectancy, and preferences [47]. Pharmaceutical care appears to improve prescibing for older patients, especially when a multidisciplinary element (integrating a clinical pharmacist) is included in the deprescribing process [48]. For these situations, a straight algorithm was presented by Garfinkel in his war against polypharmacy in a palliative setting, and was even adjustable for community-dwelling elderly people [38, 49]. In these studies, the decision for stopping or shifting to another drug was constructed on the facts of evidence-based consensus using a drug, the relevance for the patients' age and disability level, the balance of adverse drug reactions and benefit, the existence of a better drug in the situation, and the absence of risks in case of deprescribing. An eight-step algorithm was proposed, applicating these clinical decisions using the acronym ACADEMIA using the following process [39]:

- *A*ssess—counting all medications of current use, also over-the-counter medication and medication used from other sources (maybe using the so-called brown bag method—all medication used is packed in a bag and presented to the doctor).
- *C*omprehensive Geriatric Assessment—to assess the functionality, presence of geriatric syndromes, and estimate the prognosis on lifespan of the patient.
- *A*dherence—using pill organizers, calendars, delivered blister packs with the specific medication for each patient, involvement of caregivers, collaborative work with the patient, prescribing a simple regime of medication.
- *D*evelopment—newly developed proposal coordinated with the personal wishes of the patient and his/her moral conceptions.
- *E*mergence—reconcile current medication and identify medication without indication, mismatch to the given priorities, and even missing therapies.
- *M*inimization—using the techniques of deprescribing.
- *I*nterdisciplinarity—coworking with a pharmacist regarding drug–drug interactions; pharmaceutical care plans and recommendations are submitted.
- *A*lertness—for rebound, new adverse drug events—monitoring and reevaluation [24].

All these tools for deprescribing in older persons and limited life expectancy can be summarized in three steps [40]. First, using models of framework, considering goals of care, time to benefit, life expectancy, clinical status, and alignment of treatment goals with these parameters [50]. Second, by assessing the entire

Table 1 Websites offering deprescribing tools

Organization	Aims	Website
Deprescribing.org Website was developed by Dr. Barbara Farrell, Dr. Cara Tannenbaum, and their research teams at the Bruyère Research Institute (Ottawa) and Université de Montréal	Share and exchange information about deprescribing approaches and deprescribing research. It offers tools to help patients and providers participate in deprescribing and links to people around the world who are interested in deprescribing	https://deprescribing.org/
US Deprescribing Research Network	Develop and disseminate evidence about deprescribing for older adults. Funded by the US National Institute on Aging	https://deprescribingresearch.org/resources-2/resources-for-clinicians/
PrescQIPP	Help NHS commissioners to improve patient outcomes and manage medicines budgets effectively Reduce duplication and support collaboration across NHS commissioning areas Highlight and spread prescribing good practice and innovation	https://www.prescqipp.info/our-resources/webkits/polypharmacy-and-deprescribing/
American Geriatric Society	Toolkit provides guidance for discontinuing unnecessary and potentially harmful medications	https://geriatricscareonline.org/ProductAbstract/ags-deprescribing-toolkit/TK013/?param2=search
Rxisk	Is operated by Data Based Medicine Americas Ltd. (DBM), based in Toronto, Canada. Educating and empowering patients to have better conversations with their doctors. Collecting data on the unintended consequences of prescription medications	https://rxisk.org/

medication list and judging it on comorbidity, clinical status, functionality, and prognosis. In this step, prioritization of the medication list, identification of medication for deprescribing, and monitoring must be set. Third, medication-specific guidance on deprescribing/tapering, discussing, and monitoring will be established.

Despite these numerous attempts to improve ongoing prescriptions in polypharmacy, an updated Cochrane review highlights the lack of existing intervention studies of suitable quality aimed at improving the appropriate use of polypharmacy in older patients [8]. A list of online tools for deprescribing may be helpful (Table 1).

Avoid prescription cascade

To avoid prescription cascade—a clinical situation in which doctors prescribe another medication for adverse drug reactions—the most prevalent adverse drug reactions were listed in a brochure of the Austrian Geriatric Society (ÖGGG). An expert panel chose the most prominent medications causing each symptom. So, if an older patient presents with one of these symptoms, doctors should check first for possible adverse drug effects and think on deprescribing before setting another treatment [51].

Conclusion

Polypharmacy can be a threat or a benefit for older patients with multimorbidity and is per se value free. It turns out to be threat when a stable clinical situation changes with a new medication added, worsening of organ function due to advancing age, emerging disease, or environmental changes. An older organism proposed to frailty and quick deterioration due to lacking compensating function has a higher risk of developing ADEs. On the given definitions of polypharmacy, identification of PIM and the presented tools for deprescribing rises the alertness for the risks for polypharmacy and encourages doctors to intervene in an appropriate manner.

Conflict of interest P. Dovjak declares that he has no competing interests.

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