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Aging Research - Methodological Issues

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Preface

Aging of the population all over the world is one of the most important drivers of the future, specially for developing countries because of the speed of the process and the implications in several dimensions – social, economic, and health services, among others.

Health services have been particularly challenged due to an increase of health demands and a peculiar pattern of disease, characterized by chronic conditions, lack of specialized health human resources, and also but more important a lack of health policy agenda. In some way this situation has increased interest in the topic of aging, and several students, pre- and postgraduate, health staff, and professional researchers are beginning to do research in the aging area.

The key origin of this book began with several discussion sessions among the editors, all involved in aging research since several years ago. We thought that even when the interest in the topic has grown exponentially, the lack of an aging perspective in the available research was evident in many cases.

Consequently, we decided to invite a group of recognized researchers in aging, geriatrics, and gerontology to point out specific conditions, issues, and special features that have to be taken into account when research in aging is done. The idea behind this project was not to do another methodological health research book, because several extraordinary texts already exist and the principles when applied to this specific group of age are essentially the same. The aim was to integrate several characteristics that are core features in aging research, such as clinical concepts – as multimorbidity, frailty, and functionality – but also specific methodological concepts, for example, the consequences of certain exclusion criteria, the balance between risks and benefits, and heterogeneity of those subjects labeled as older persons.

With this in mind, we attempted to integrate in this book chapters that review the classical epidemiological and clinical research types of studies, such as descriptive, case control, longitudinal, and clinical trials, incorporating in addition three other perspectives: biomedical research, qualitative studies, and mixed-method studies. To close this section systematic reviews and meta-analysis are also analyzed. The general purpose of the chapters was to identify the basic structure of the design, the main advantages and disadvantages of each one, but more important, the specific variations and conditions that have to be considered when one of these studies is focused on persons older than 60 years. Examples of representative studies in every design are presented.

The book also includes other chapters that cover a wide perspective. A review of the scientific method is presented as the first chapter, after the introduction. We believe that reviewing the general principles of science, in a very clear and concrete way, is a good way to keep in mind the main reason of doing research which is pursuing new knowledge.

A discussion about the relationship between technology and aging is also included, how technologies may be introduced and connected with health research and also how to reduce the digital gap. Also the last chapter is a discussion about the transference of health research results into aging policy. There is an urgent need of evidence in all the health systems to make better decisions, and there is no doubt that scientific research could bring objective data into the process of public policy. However, to answer how to connect these two very different arenas is one of the reasons of this chapter.

We have to say that omitting some topics or sections in this book was unavoidable. Specific issues as sample size or statistical analysis were not included because the aim was to impulse aging research more than a presentation of specific techniques.

This book was written with several audiences in mind. We hope that pre- and postgraduate students who are interested in aging research for the first time find this book challenging and useful. Senior researchers who have not done research in the area also can find a different perspective, and refreshing concepts may be found all over the diverse chapters.

We want to acknowledge several people who contributed to the preparation of this text: Ken Emmond, for his dedicated translation into English; Aurelio García-Cortés for helping us in the design of several figures and graphs; Leslie V. Robles-Jimenez, MD, and Pamela Tella-Vega, MD, for their assistance in helping us to review several times all the chapters; and the National Institute of Geriatrics from Mexico, for providing a grant for the edition of this book.

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Chapter 1
Introduction

Mario Ulises Pérez-Zepeda, Carmen García-Peña, Victoria E. Arango-Lopera, and Luis Miguel Gutiérrez-Robledo

Abstract In this chapter a brief review of how aging is becoming a topic of increasing interest in different areas of science and in particular in health sciences. Older adults are a heterogeneous population group with characterizing features that should be taken into account when making research on age and aging.

Keywords Research methodology • Geriatric research • Research on age • Health in old people

1.1 General Points

One of the great challenges our society faces is the aging of the population [1], and it will increase noticeably in the coming years. The problems this will create in health care are so complex that perhaps they have never been seen before in the current system. They will require the convergence of all sectors to provide adequate care for the needs of this age group [2]. In addition to health, this demographic change will also have an impact in other population spheres: social, cultural, economic and the workforce, to name a few [3].

Research into age and aging is essential to confront this phenomenon. Seen as a system, the articulation of knowledge from the moment it appears and translating it to the various disciplines – from the basic to the clinical, from the clinical to public policies of social and health care – is a fundamental piece in the puzzle of setting up

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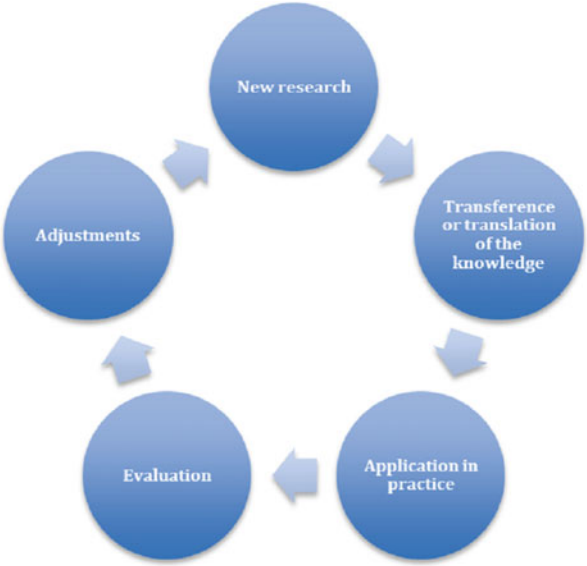

Fig. 1.1 Cycle of knowledge creation

a strategy for the aging population (Fig. 1.1). In this spirit, the 2012 Report on World Health of the World Health Organization (WHO) was titled "No health without research." It argues that to achieve universal and equitable access to health services (one of the millennium goals), one feasible way is through research and policies based on the knowledge generated [4, 5]. However, it has been found that in fact, fewer than 10 % of public health policies are based on scientific evidence [6].

This cycle takes on special importance in age and aging research, since the effective acquisition of knowledge about the subject matter will make possible the improvement of conditions for this population segment that is growing so fast [7]. In addition, it is known that in terms of health, this age group often suffers from so-called non-transmittable chronic illnesses. They are the main users of health services and the main consumers of the specific therapies available to them (including pharmacological) [8, 9]. Finally, another type of suffering is recognized for which there is limited information as to its epidemiology, pathophysiology, interactions, diagnostic classification, intervention and prognosis. Such is the case of geriatric syndromes, frailty and cognitive deterioration [10, 11]. Recent data from the 2012 National Survey of Health and Nutrition (ENSANUT 2012) showed that two of the illnesses with the greatest repercussions on the functioning of the older adult are the vascular cerebral illness and cardiac insufficiency. However, it was also found that geriatric syndromes (such as cognitive deterioration, neurosensory deficits, depression and falls, to name a few), as well as having a high impact on function, are highly prevalent. In addition to the foregoing, the presence of multimorbidity, with its endless mixtures of conditions, places an enormous negative weight on function and on sanitary costs. It is a markedly common situation in this age group.

1.2 Distinctive Features and Research on Age and Aging

Once the aging of the population and the lack of information on this age group is recognized as a problem, the question arises about what distinguishes scientific research on health in this area from other disciplines [12].

Research into age and aging uses the scientific method to generate knowledge, not unlike other disciplines. However, it incorporates many more elements than those generally used in "traditional" health research. One of the main differences is the focus on the preservation of function of older adults at different levels (with difficulty, independent, dependent, etc.), in contrast to the objective of preserving life, which is more usual in health research in other age groups [12]. On the other hand, the reductionist focus of other medical specialties (internal medicine, surgery, orthopedics, etc.) makes it difficult to study the phenomenon of aging and it is more useful, both conceptually and in practice, to focus on the biology of systems, or a holistic approach [13]. Another type of focus that can be useful is called "subject-centered", in which the weight of the signs of discomfort by the persons involved acquires more relevancy than the numbers from biochemical measurement [14].

The incorporation of more topics of investigation than is the case at present will be done in the years to come. Among the new items to consider are: services (access, quality, innovation, technology), the incorporation of social determinants of health, deep analysis of these determinants, a multi-disciplinary approach, systematic incorporation of the evidence for creation of public policies, and molecular biology (genomics, proteomics, metabolomics) [12]. As well, in a world of limited resources, research in the economics of health is a fundamental ingredient for the creation of knowledge for improving the clinical care of older adults. Those changes (if any) will have to be adapted to the group of older adults.

Research into age and aging is no different from other research; it simply has emphasized some characteristics that are often harder to investigate in this age group, such as: defining what is normal (normal changes in aging vs. pathological changes), "normalization" of problems/illnesses of age, nihilism (thinking that whether or not something is done, why do research in this age group if they will soon die or be incapacitated?), non-specific manifestations of problems, coupled with homogenous definitions – bias in classification – (the case of frailty, whose variability shows up in studies of it), the need for adequate sources of information (valid scales, trained interviewers and optimization of obtaining and analyzing data, to name a few) [12, 15].

1.3 Different Categories of Older Adults

With the goal of having a framework of heterogeneity in age, what follows is a description of different groups, very differentiated within this population segment. With the advances in knowledge about aging in recent decades, a group that previously appeared to be homogeneous now is known to be made up of distinct sub-groups, whose characteristics must be taken into account in the various domains at the time of doing the research [16]. Even though there is agreement about the age at which a person should start to be called old (older than 60 years), this does not always correlate biologically [17]. There are sub-groups with specific characteristics, whose differences must be taken into account throughout the design and development of any research project into age or aging: sampling (over-sampling of barely representative groups), selection criteria, stratification, allocation of the intervention, statistical adjustments, in a way that real conclusions are arrived at and not derived from population differences established a priori (Table 1.1). Another characteristic that generates different sub-groups, and that it is crucial to take into account, is related to the losses in the trials, since in some cases they are highly characteristic, for example, in subjects with dementia.

Therefore, it is necessary to thoroughly know these different groups within the group of older adults, in order to be able to make the pertinent adjustments in the design of the protocol, or in the last instance, if this is not possible, at least to describe the population group and its distinct characteristics. The following is a detailed description of some of the characteristics that produce the marked differences:

1.3.1 Age

The easiest way to look at for this category is chronological: the more years that have passed, the higher the probability of suffering one or more illnesses, and the same with loss of function, frailty and the appearance of geriatric syndromes. Therefore, the division of these groups by age in research has a clinical logic. In addition, and depending on the outcome – following the Gompertz curve – it is known that the probability of dying is greater with advancing age, a situation to take into account, for example, when comparing groups of subjects of 60 and 90 years of age. If one wants to evaluate the effect of a particular intervention, wants to show the impact on mortality, and is unable to find any, the difference by age – expected and not adjusted – would be the explanation [18]. Finally, the group most advanced in age, the people older than 100 years of age, is much less represented in the studies, being one of the most forgotten groups in all types of research.

Taking into account the foregoing, conventionally the most common way to divide groups of older adults by age is: “old-young” 60–79; “old-old” 80–90; “ancient old-old” 90 and over; “nonagenarians” 91–100; and “super centenarians” greater than 101 years [19, 20]. As can be observed, this is an arbitrary division and within each group there is also a lot of heterogeneity, given that health strategies not only provide for an increase in life expectations, but also an increase in the expectation of a healthy life. Alternatives to the division by age groups could be those given by levels of functioning, the extent of non-transmittable chronic illness, specific pathologies (cancer, dementia, etc.), level of health care required or frailty status.

Table 1.1 Different groups to take into account in age and aging research

Groups	Categories
Age	Young-old 60–79
	Old-old 80–89
	Extremely old 90 and above
	Nonagenarian 91–100
	Super centenarians older than 101
Function	Effective function without difficulty
	Effective function with difficulty
	Ineffective function without difficulty
	Ineffective function with difficulty
	Loss of function in some activities, with dependence with assistance
	Loss of function in some activities with dependence without assistance
	Loss of function in all activities with dependence with assistance
	Loss of function in all activities with dependency without assistance
Multi-morbidity/ polypathology	Without non-degenerative chronic illnesses
	With one non-degenerative chronic illness
	With multi-morbidity/polypathology
Life prognosis	Without terminal illness
	With a terminal illness but without probability of dying in the next 6 months
	With terminal illness with probability of dying within the next 6 months; not moribund
	Moribund
Specific pathology	Without a specific pathology
	Dementia
	Cancer
	Frailty
Level of care	Ambulatory
	Acute hospital care
	Chronic hospital care
	Residence
	Hospice
Caregiver	Without a caregiver
	Without caregiver burden
	With caregiver burden

1.3.2 Function

Defined as the capacity to be able to carry out, independently and autonomously, the activities necessary to take care of oneself under optimal conditions and within one's own surroundings, function is an effective way to classify the elderly. There is a large spectrum between the two extremes (independence and dependence), with a number of activities within which is also a different range of effectiveness in capacity to carry out these functions (independence in function, difficulty in doing this, and total dependence on someone else to be able to do some of the activities). Taking into account the potential effect function can have on a particular intervention improves the possibility of obtaining other appropriate outcomes. Research can also be carried out on specific groups of levels of functionality, as is the case in researching the cause of pressure sores in people almost totally dependent; testing an intervention on injuries to cure them. The fact of not taking into account functional status could give the false impression of the effectiveness of the intervention.

1.3.3 Multi-morbidity

Recently there has been emphasis on this concept (suffering from more than one non-transmittable chronic illness for which the person is taking medicine regularly), because it appears that it could involve a problem with characteristics different from the rest of the population and an entity in which there would have to be special care taken in carrying out clinical tests at the time of reporting the interactions.

1.4 Conclusions

To better understand the problems that could be presented at each stage of the research in areas of age and aging, knowledge is created clearly and with a solid scientific structure that contributes to improvement in the quality of care for older adults and a clearer understanding of the processes that could have impact on their overall health.

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Chapter 2
The Scientific Method

Ruben Fossion and Leonardo Zapata-Fonseca

Abstract It is surprisingly difficult to define what makes something scientific. It is not what is being studied, i.e. the topic, but rather how the study is carried out, i.e. whether a correct methodology – or the so-called scientific method – is being used. The scientific method is not very different from the common sense with which we interpret events in our daily life, but with the important difference that the successive steps of observation, hypothesis and empirical verification are well articulated and controlled. Two different views exist on the scientific method. On the one hand, there are the philosophers who try to define a universal method that is valid for all scientific disciplines and for all times. From the philosophical point of view, scientific research is not 100 % objective, and it turns out impossible to confirm or refute any theory in an absolute way, which seems to be in paradoxal contradiction with the profound success of scientific research in all domains of human achievement. On the other hand, there are the working scientists who are interested in a pragmatic method that in the first place must be applicable to their daily research activities. According to the latter view, a theory does not need to be absolutely certain but instead has a certain level of probability based upon how well it fits into the coherent network of all scientific knowledge; an individual scientific investigation might be subjective up to a certain degree, but science as a whole converges to objectivity.

Keywords Scientific method • Common sense • Iterative process • Idealistic vs. pragmatic view • Paradigm • Complexity

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2.1 Philosophy of Science and Common Sense

The most direct contact between society and science is probably through technology-based products derived from a specific scientific specialty: the computer, the mobile telephone, satellite television, or medical applications such as tomography and organ transplantations, among others. A less tangible but no less transcendent contact is the way in which different scientific disciplines have changed our perception of Nature, the cosmos and our place in it –e.g., Darwin's theory of evolution, which demonstrated that we are not the owners of the flora and fauna as taught in the Bible, but rather part of it; or the Big Bang theory, according to which we are not the center of the universe, but rather the insignificant inhabitants of just another planet circling a mediocre star in a far-away corner of the Milky Way. Although science is sometimes plagued with a negative connotation because of abuses and degradations such as the atomic bomb, pollution and global warming, society esteems science for its presumed quality of being based on objective facts, so that scientific research has more weight and authority than a personal opinion [1]. But what makes something scientific? It is not the object or the topic under study but rather the methodology with which a study is carried out and the standards that are used to judge the obtained results [2]. The methodology that is used in science, or the so-called *scientific method*, is not very different from the way in which we use common sense to interpret events in our daily lives. *Common sense* analyzes the information we receive through our senses (sight, hearing, touch, smell, taste, proprioception and vestibular orientation) as being real and independent from the observer. Without thinking consciously about the steps taken, our common sense is based on a sequence of observation, evidence and verification; scientific thinking follows the same logic, but the scientific train of thought is slowed down for the purpose of increasing transparency and control during the various steps. Transparency is important because it enables both peers and colleagues to repeat experiments, verify results and construct more advanced theories based upon them [2]. Science is a collaborative activity, and recent examples of this are the peer review process and open access journals.

The study of the scientific method is a science of science, also called *meta-science*, and therefore belongs to the field of *philosophy of science* (Fig. 2.1). Philosophy is a forum to question and clarify concepts that other disciplines believe to be obvious without having investigated them explicitly [2]. Philosophy of science analyzes the various steps of a scientific investigation. The experts who have written on the scientific method are the philosophers [1–3] and less frequently the scientists themselves [4–6], resulting in two completely different approaches to the topic. On the one hand, scientists learn and apply the scientific method implicitly in their daily activities, usually without noticing the abstract pattern that underlies every scientific investigation. On the other hand, instead of concentrating on the object or topic under study, philosophers are more interested in the research method that is employed and they investigate the logical structure of the sequence of scientific activities carried out [3]. Consequently, the philosophical approach tends to be abstract and idealistic, and the goal is to define an absolute and universal scientific method that is valid for all disciplines and for all times; in contrast, the scientific

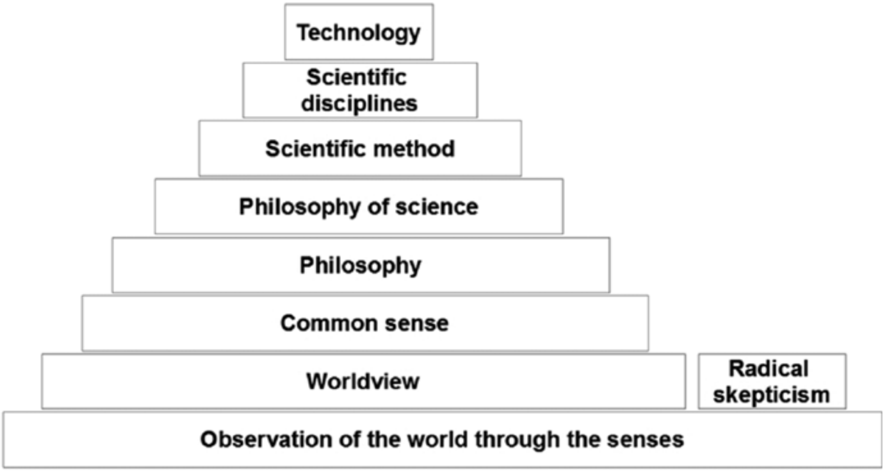

Fig. 2.1 The scientific method is founded on philosophy of science, which in turn depends on philosophy, common sense, and a worldview (for example, atheism, humanism, materialism, Christianity, Buddhism, etc.). The scientific method gives support to scientific specialties and technology. Radical skepticism treats the physical world that we observe through the senses as being non-existent, unknowable or illusive, and is not compatible with common sense or with the scientific method (modified from [5] with kind permission from Cambridge University Press)

approach is more realistic and conformist, and scientists are satisfied with an approximated scientific method that in the first place must be applicable to their daily research activities. Not surprisingly, scientists who are active both in research and in teaching tend to be the most pragmatic in their understanding of the scientific method [5, 7].

2.2 Foundations of the Scientific Method: From the Ancient Greeks to the Scientific Revolution

History of science is another discipline that belongs to the field of philosophy of science. The history of science illustrates how the scientific method developed gradually through time [6].

The ancient Greeks were pioneers in establishing a science independent of religious dogmas. Plato (427–47 BC) and his mentor Socrates (469–399 BC) developed a contemplative science based on some abstract axioms to which they applied *deductive logic*[1] to obtain new statements. Aristotle (384–322 BC), although he studied in Plato's Academy in Athens, preferred to combine abstract thought with passive

[1] Deduction is a tool of logic that allows obtaining conclusions from accepted premises. If the initial premises are correct, the conclusions are necessarily also correct; in other words, the truth of the premises ensures the truth of the conclusions.

observations of Nature and used *induction*[2] to obtain new hypotheses. Today, in retrospect, Aristotle is criticized for his exaggerated generalizations not verified with experimental data. The teachings of Aristotle continued to influence the development of science –though sometimes to their detriment– for the two following millennia.

In the dark ages of Europe's Medieval Period (500–1000 or 500–1300, depending on the source), much of the scientific knowledge of the Greeks was lost. Fortunately, a lot of that knowledge could be recovered thanks to the Arabs (700–1500), who had adopted the science of the ancient Greeks. The contribution of the Arabs to the scientific method was to include active *experimentation*, which proved to be an important step forward, because since then it became customary to check theoretical predictions with experimental results.

The next important period is the *scientific revolution* (1500–1800), whose development was due to the contribution of many factors, some of which will be mentioned in the following. The first universities in Italy, France and England, founded starting from the tenth and eleventh centuries, resulted in a gradual "liberalization" of the sciences leading to a more pluralistic vision not dictated by a few authorities, such as Aristotle in the centuries before. Humanism was a new philosophical and ethical current having as one of its purposes to explain all natural phenomena without any reference to the supernatural. During the scientific revolution, active experimentation was responsible for important advances. One example is the dissection of human cadavers, through which Andreas Vesalius (1514–1564) could gain a better understanding of human anatomy and which culminated in his main work *De Humani Corporis Fabrica*. In particular, Vesalius described the interconnected system of veins and arteries, refuting the scientific dogma of the ancient Greek physician Galen (130–200 AD), who had postulated two independent systems, a theory that was well accepted from the second century of our era till after the Middle Ages. Technological inventions further accelerated the advance of science: the telescope enabled Copernicus (1473–1543) and Kepler (1571–1630) to refute the theory of the geocentric system of the ancient Greek astronomer Ptolemy (90–180 AD) and to propose a new heliocentric system to describe the movement of the planets in our solar system; the microscope made it possible for Robert Hooke (1635–1703) and Antonie van Leeuwenhoek (1632–1723) to study the life of microorganisms for the first time. Another important factor driving science forward in many fields of knowledge was *mathematical modeling*, which allowed researchers to make not only *qualitative* predictions (e.g., the temperature will rise) but also *quantitative* predictions (e.g., the temperature will rise with exactly 2°C). The ability to make quantitative predictions increased dramatically the power of verification of the scientific method, because in this way it became possible to distinguish between two or more competing theories if one explained the numerical results of an experiment more satisfactorily.

[2] Induction is a tool of logic that simplifies and generalizes patterns observed in a limited amount of data into a theoretical principle (hypothesis, law, model, conjecture). Induction is a creative and imaginative step associated with the inspiration and genius of the researcher. The conclusion does not have absolute certainty, but rather a certain level of probability, which depends on the quality of the evidence. A classic example of induction is observing that all European swans are white and generalizing that all swans must be white. This conclusion was shown to be false when black swans were discovered in Australia.

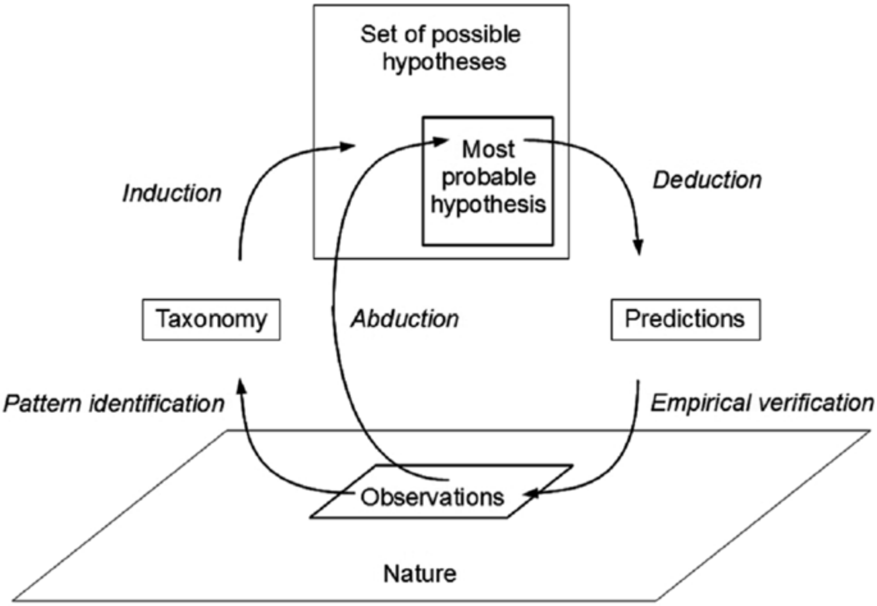

Fig. 2.2 The process of scientific reasoning is iterative and alternates between deduction, induction and abduction. Induction generalizes observed patterns in nature in theoretical models. Abduction selects the most probable working hypothesis from a set of possible hypotheses to explain an observed phenomenon. Using deduction, predictions are made from the hypothesis to be verified with data from controlled experiments, so that the hypothesis can be checked and corrected if necessary

The structure of the scientific method, in its most basic form, can be summarized as successive repetitions of the following sequence (Fig. 2.2):

$$Observation \rightarrow Taxonomy \rightarrow Hypothesis \rightarrow Prediction \rightarrow Empirical\ Verification$$

In the *observation* phase, relevant data about a natural phenomenon of interest are recognized. The *taxonomy* stage detects and classifies regular patterns in the data. The induction phase enables the researcher to generalize and simplify these patterns in one or more *theoretical hypotheses* to explain the phenomenon. *Abduction*[3] is a type of logical inference that is used to select the most probable hypothesis from a set of possible hypothesis to explain a given phenomenon (see also Sect. 2.3.2). Applying deductive logic to the working hypothesis allows deriving predictions, which can be *verified* with the results of carefully controlled experiments. A *controlled experiment* is one where a certain (independent) variable is varied to study the consequent changes in another (dependent) variable. It is preferable that all the other variables remain constant to avoid confusion factors. When new observations are

[3]Abduction is a tool of logic that infers a premise from a conclusion. For example, since grass becomes wet when it rains, observing wet grass in the morning, a good working hypothesis might be that it must have rained during the night. Abductive reasoning is prone to the fallacy of affirming the consequent.

made, and new experimental data are obtained, the working hypothesis may be retained, modified or refuted. It is assumed that the repetition of the sequence Observation → Taxonomy → New Hypothesis → Prediction → Experimental Verification → … will converge to an accurate description of the true state of Nature [4–7].

2.3 An Idealistic Interpretation of the Scientific Method According to Philosophers

In day-to-day scientific practice, the following properties are often taken for granted:

- The data are previous to and independent from theory;
- The data constitute a firm and reliable base for scientific knowledge;
- The experimental data are obtained by impartial observation through the senses.

However, philosophers have identified some problems with these assertions, such as theory-ladeness and subjectivity, confirmation and rejection of the theories, and how to evaluate scientific progress [1].

2.3.1 Theory-Ladeness and Subjectivity

The American philosopher of science Norwood Russell Hanson (1924–1967) argued that all observations are *theory-laden* [8]. The most intuitive way to illustrate the concept of theory-ladeness is with an optical illusion, where what is perceived depends on previous knowledge and assumptions (or prejudices) of the observer [1] (Fig. 2.3). The concept of theory-ladeness gives rise to several philosophical problems because it introduces *relativism* to the choice of theories, which means that empirical evidence does not always distinguish among different hypotheses. The question then would be: what is it that limits the choice of theories? If the theory-laden observations cannot limit those choices, the restrictions that operate are the subjective preferences of the scientists or the rules of conduct of groups of scientists. The logic of confirmation appears to be intrinsically contaminated by idiosyncratic and social factors, threatening the very idea of scientific rationality [9].

2.3.2 The Problem of the Confirmation of Theories

Many theories make statements about things that are not directly observable (as were germs before the era of the microscope, or quarks in today's subatomic physics), which makes *direct empirical verification* impossible in these theories. It is possible to carry out *indirect empirical verification* by means of observable implications from the theory using the *hypothetical-deductive method* [2], which deduces a prediction

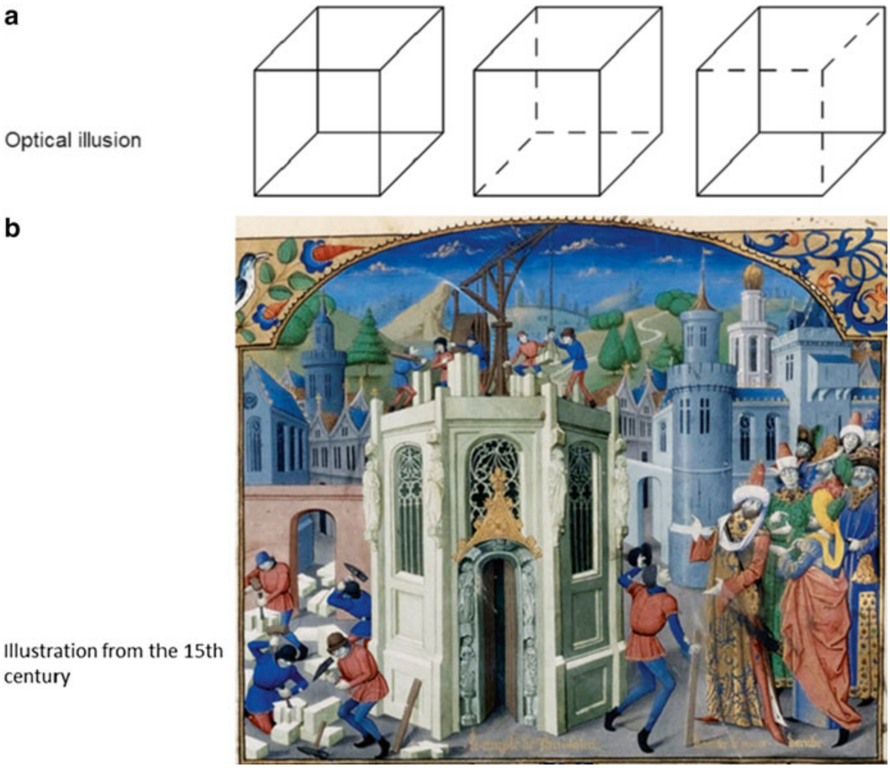

Fig. 2.3 Illustration of the concept of theory-ladeness. (**a**) The two-dimensional representation of a three-dimensional cube constitutes an optical illusion where, depending on the perspective, the front face can be the bottom one, and the upper face the rear one. The interpretation of graphical perspective depends on a previous knowledge of geometry; as a convention, continuous lines are interpreted to be visible whereas discontinuous lines represent invisible features. (**b**) Paintings from before the Renaissance do not present the graphical perspective correctly because knowledge of geometry was insufficient at that time. As an example, shown is an illustration of the reconstruction of the temple of Jerusalem from the fifteenth century in the manuscript "Histoire d'Outremer" by William of Tyre (National Library of France, Paris). The figure is from the public domain taken from Wikipedia, from the article "Perspective (graphical)"

(p) given a certain hypothesis (H). Checking the data, if prediction p is true, one can conclude that hypothesis H is also true, or symbolically,

If H, then p
p

H

For the American philosopher, logician, mathematician and scientist Charles Sanders Peirce (1839–1914) this way of reasoning is the basis of the third type of logical inference, namely abduction. One has to be careful because it is possible to commit the *fallacy of affirming the consequent* [2]. This can be seen more clearly with the following example: let us suppose that malaria causes fever (hypothesis H), so everyone who has malaria will also have fever (prediction p); if we diagnose fever in a patient (so that p is true), we cannot confirm that the patient in question has malaria (hypothesis H), because there are many other illnesses that could cause fever in addition to malaria. However, Peirce argued that abductive reasoning has evolved in humankind and that humans have become experts in choosing the best hypothesis to explain a given phenomenon. In the case of a patient with fever, as in the example mentioned, a treating physician would make a mental list of several possible causes and then would select the most probable cause (perhaps the flu?) as a working hypothesis to be further examined by comparison with additional data.

2.3.3 The Problem of Refuting Theories

The Austrian-British philosopher of science Sir Karl Raimund Popper (1902–1994) is best known for his *falsifiability* approach to the scientific method [10]. Falsificationism is an attempt to avoid induction (the creative and thus subjective step) in the scientific method. Popper suggested that, in order to explain a given phenomenon, it is possible to generate a very large number of hypotheses and try to reject them; a theory that survives several attempts to be falsified is not necessarily true, but is interpreted as a relative improvement to competing but falsifiable theories. From this perspective, scientific progress may be described as the replacement of falsified theories with new theories that up to that moment have withstood every attempt of falsification [10, 1]. However, the falsification of a theory turns out to be just as difficult as its confirmation, which can be understood considering again the *hypothetical-deductive method* [2] with a working hypothesis (H) and a deduced prediction (p). The negation of the prediction ($\neg p$) implies the rejection of the hypothesis ($\neg H$). However, a hypothesis usually does not stand alone but is supported by *auxiliary theories* and/or assumptions (A_1, A_2, …). For example, any use of a microscope is supported with auxiliary theories of optics that explain how and under what circumstances a correct magnification is obtained for the object being studied. In such a case, the negation of the system of a hypothesis *and* auxiliary theories results in the negation of the hypothesis *or* in the negation of one of the auxiliary theories. In symbolic form,

Case of a single hypothesis:	Case of a hypothesis with auxiliary theories:
If H, then p	If (H and A_1 and A_2 and…), then p
$\neg p$	$\neg p$
————	————————————
$\neg H$	$\neg$ (H and A_1 and A_2 and …)
	Which is equivalent to $\neg H$ or $\neg A_1$ or $\neg A_2$ or …

The *Duhem-Quine thesis*, after the French physicist Pierre Maurice Duhem (1861–1916) and the American philosopher Willard Van Orman Quine (1908–2000), establishes that a theory can never be definitively falsified because it is impossible to rule out that an erroneous prediction is caused by an untrue assumption or a false auxiliary theory [1]. The Hungarian philosopher of science Imre Lakatos (1922–1974) nicknames the system of auxiliary theories a *protective belt* that prohibits the definitive falsification of a hypothesis [11].

2.3.4 Paradigm Shift and Scientific Progress

The American physicist and philosopher of science Thomas Kuhn (1922–1996) revolutionized the way in which *scientific progress* is perceived. Before Kuhn, scientific progress was interpreted as a gradual process; it has been suggested that our textbooks are to blame for reinforcing this view of a continuous accumulation of ideas up to the current state of science, whereas Kuhn argues that scientific achievements of the past need to be interpreted within the context of sociological factors and scientific perspectives of the time in which they were developed [6]. It appears that within each scientific specialty, prolonged periods of stability and consolidation precede short bursts of major conceptual revision, which Kuhn called *paradigm shifts* [12] (Fig. 2.4a).

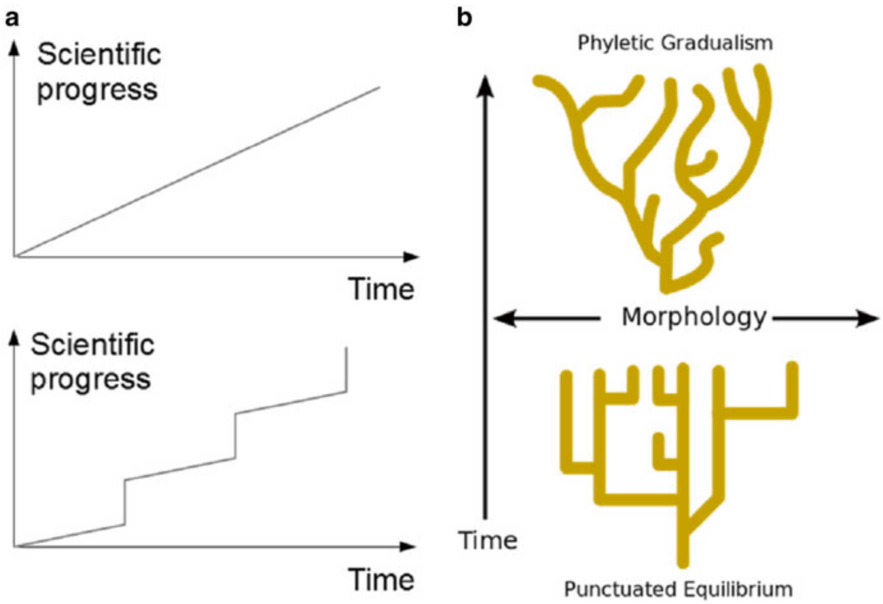

Fig. 2.4 Similarities between (**a**) scientific progress and (**b**) biological evolution. Traditionally, advances and changes were thought to be gradual, whereas more recent interpretations suggest an intermittent equilibrium. The figures from panel (b) are from the public domain, taken from Wikipedia, from the article "Punctuated equilibrium"

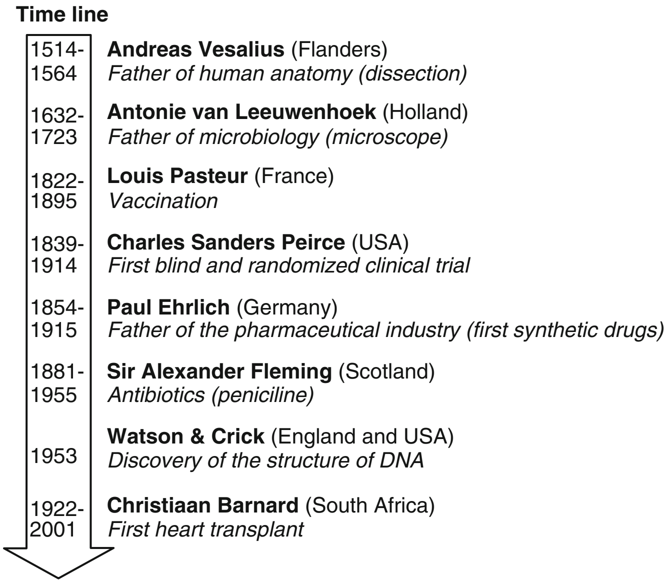

Fig. 2.5 Some key moments in the history of medicine that possibly constituted a paradigm shift

A *paradigm* is a coherent set of theories and concepts that guides interpretations, the choice of relevant experiments, and the development of additional theories in a field of study. Examples of contrasting paradigms in physics are: Newtonian dynamics as opposed to Einstein's theory of general relativity, and classical physics versus quantum mechanics. In medicine, possible examples of paradigm shifts are the dissection of human cadavers as introduced by Vesalius, the use of the microscope and the development of synthetic drugs (Fig. 2.5).

Standard science works within the framework of an existing paradigm that guides a field of research. In this case, almost all of the research relates to the paradigm: research is carried out according to a fixed scheme, and it is the paradigm that indicates which topics for research are appropriate and worthwhile; theoretical and experimental studies imply the collection of data to verify predictions of the paradigm, and consider also efforts to extend the paradigm in order to include apparent problems or ambiguities. Research within an existing paradigm is sometimes described in a pejorative way as "cleaning up." In a new field, that is, a field in a *pre-paradigm* state, no fixed scheme exists that indicates how experiments should be done or how data should be interpreted. To draw an analogy: data collection within the framework of an existing paradigm is like a hunter pursuing a prey, whereas without the guidance of a paradigm it rather resembles going for fishing in a lake to see what comes out [6]. In the absence of a paradigm, lots of data may be available but they are extremely complicated to interpret, and the general pattern and the main principles are vague; several currents of reasoning compete without agreement on which phenomena are worth studying, and no single current of reasoning is capable of providing a more general view of the field (see also Sect. 2.5).

The progress of science has been interpreted as a *punctuated illumination*, very similar to the theory of *punctuated equilibrium*, also known as interrupted equilibrium or intermittent equilibrium [6] (Fig. 2.4b). Punctuated equilibrium is a theory of evolutionary biology that proposes *stasis*, i.e., stability or only minor changes during most of the time of existence of a species; in contrast, evolutionary changes accumulate during the process of *speciation*, i.e., the formation of a new species which is sudden and of brief duration in comparison with the geological time scale [13]. Whereas neo-Darwinists defend the idea that evolution develops over time according to a linear or phylogenetic pattern, the punctuationists support the idea of evolution as a mosaic, in other words, branched. The idea of the former is a linear succession from one species to another; for the latter, an ancestral species gives place to multiple descendent species that in turn either become extinct or continue to branch out.

2.4 A Pragmatic Interpretation of the Scientific Method According to Scientists

2.4.1 From the Myth of Objectivity to Pragmatism

Scientists are interested in general concepts and principles, not in personal subjective perspectives. However, from the philosophical point of view (Sect. 2.3), it is possible that scientists cling to a *myth of objectivity*, in other words, scientists believe that objective knowledge of the true state of Nature is accessible, whereas in reality this might not be the case [6]. This does not imply that objectivity is a fallacy or an illusion, but that it could be an unattainable ideal. According to the great German quantum physicist Werner Heisenberg (1901–1976) science does not provide an objective explanation of Nature; rather, it describes what is exposed of Nature through the specific method of questioning being used [6]. This results in the following paradox: how is it possible to reconcile the apparent and profound success of science with the problem that scientific objectivity might be an elusive ideal because of the inherent subjectivity in perception? Apparently, science depends less on absolute objectivity than is thought traditionally. It can be argued that scientists are in the first place *pragmatists*: the challenge is to use methods and assumptions, bearing in mind that they are subjective and imperfect, and at the same time try to obtain an as objective as possible understanding of the patterns and principles of Nature [6, 14]. Certainly, any scientific investigation must necessarily use a biased scale to weigh and evaluate data because all scales are biased; but if we are fully conscious of the bias in the scale, it can be used effectively. To increase the precision of the scale, we need to know the sources of error. In order to achieve this, we need to understand the limits of our methods and it is important to understand, too, how the process of perception affects our observations and thus be able to recognize our own biases.

2.4.2 Full Disclosure

A first step toward the recognition of possible biases in research is complete transparency, or *full disclosure*, to reveal all the elements and steps taken to arrive at a scientific conclusion. Already Aristotle was interested in the transparency of scientific reasoning: "What is it that goes in so that scientific conclusions come out?" he asked. A modern model of transparency is the PEL model [5] (Fig. 2.6). The first element of the PEL model is the list of *presuppositions* (*P*), which offers a basic and indispensable image of the system being studied. The presuppositions are important because they enable one to restrict the set of all possible hypotheses, which are infinite, to a limited set. Without constraint, the set of possible hypotheses would be infinite and it would be impossible to reject all the absurd hypotheses and keep the realistic ones, based on the finite quantity of empirical evidence accessible to us. Evidently, presuppositions do not differentiate between the credibility of each of the realistic hypotheses because the presuppositions are what all hypotheses have in common. On the other hand, *evidence* (*E*) is data that can distinguish among the different hypotheses. Finally, l*ogic* (*L*) combines the premises of presuppositions and evidence with logical reasoning (deduction, induction and abduction) in order to arrive at a conclusion.

It is possible to incorporate the PEL model of full disclosure into the iterative process of *Observation* → *Taxonomy* → *Hypothesis* → *Experimental Verification* (Fig. 2.7). Full disclosure enables the scientific community to evaluate the possible biases in a research project (e.g., are all the presuppositions reasonable?); one important aspect of science as a joint activity is the peer review process of scientific articles before they are accepted for publication [15].

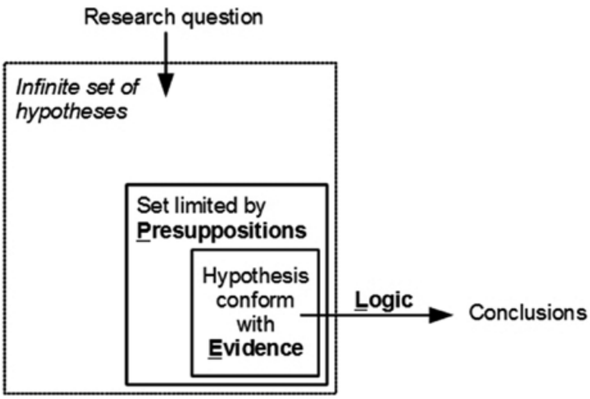

Fig. 2.6 Complete transparency, or *full disclosure*, of a research project according to the PEL model. The set of all possible hypotheses is infinite. The presuppositions (*P*) enable to discard unrealistic hypotheses. The evidence (*E*) allows to choose an appropriate working hypothesis. Logic (*L*) combines the presuppositions and the evidence to arrive at a conclusion

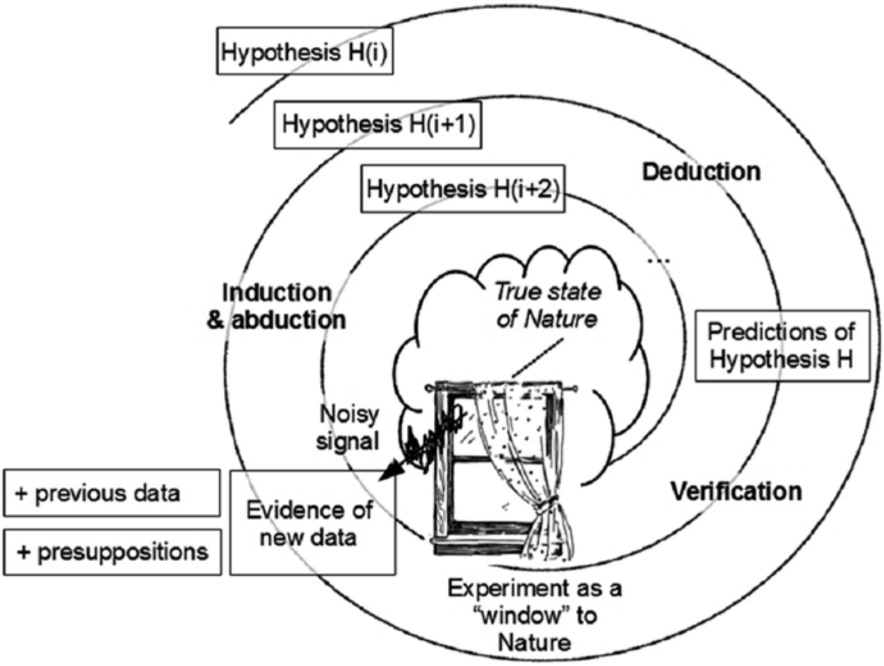

Fig. 2.7 Diagram of the scientific method that combines the iterative process of scientific reasoning (Fig. 2.2) with the PEL model of full disclosure (Fig. 2.6). The purpose is to make the working hypothesis converge towards an accurate description of the true state of the Nature (Modified from Ref. [4] with kind permission of John Wiley & Sons, licence number 3602580414728)

2.4.3 Certainty Spectrum and Knowledge Network

The scientific method is based on evidence and logic, but the details of empirical verification show that evidence and logic by themselves do not solve the problem of which hypotheses are absolutely true and which are absolutely false. As was mentioned in previous sections of this chapter, no isolated proof can definitively confirm or refute a hypothesis. In general terms, empirical proofs are never decisive: a false hypothesis can result in a true prediction and a true hypothesis could give a false prediction. Despite this, empirical verification is not useless because, from a pragmatic point of view, a true prediction provides some probability that the working hypothesis could be true, while a false prediction obliges us to rethink some aspects of the combined system of hypothesis, presuppositions and auxiliary theories [2]. The scientific method and its companion from daily life, common sense, have the important limitation that they never result in perfect or *absolute certainty*. In science as in life, we are always confronted with uncertainty and we are sensitive to *levels of certainty*: everything exists on a spectrum between mere conjecture and absolute certainty. The objective of the scientific method is to localize a particular theory within this spectrum; when evidence accumulates, the position of the theory on the spectrum can change. To increase our confidence in a hypothesis large numbers and varieties of different tests are necessary. One good way to gain confidence in a hypothesis is to verify how it fits within a coherent network of other theoretical statements and experimental claims. The concept of a *coherent network of ideas* plays an important role within the scientific method. The most important requirement for coherency is *logical consistency* because a network of knowledge does not tolerate contradiction. This does not mean that inconsistencies that persist in diverse scientific specialties cannot exist, but when such inconsistencies are identified they need to be studied and in the end usually give way to new scientific discoveries; that is why contradictions in science cannot be ignored. In addition to being consistent, scientific claims have to be *cooperative*, which means that they need to generate connections between different ideas, such that a new claim in one field of science can play the role of an auxiliary theory in the same or in other scientific disciplines. There is a variety of links between different theories, resulting in an interrelated and coherent network of scientific claims. When evidence accumulates and a new theory becomes better interconnected with other theories, the classification of this theory as uncertain slowly disappears and the theory converges toward the side of certainty on the spectrum. When a hypothesis arrives at equilibrium within a network of scientific knowledge, confidence in its certainty is established; this is also part of the scientific method [2].

2.5 Complexity Sciences: Towards a New Paradigm?

Since the 1970s an epidemiological transition is being observed, from a predominance of acute infectious diseases to a higher prevalence of chronic-degenerative illnesses [16]. *Acute infectious diseases*, e.g., a bacterial infection or a bone fracture, are usually relatively simple to diagnose and treat because often it is possible to localize and delimit the affected part of the body, and although several risk factors can be in play, the causes of the symptoms are quite clear in general. In contrast, *chronic-degenerative illnesses* like cancer, diabetes, frailty associated with aging, chronic stress, fibromyalgia, etc. seem to be more complex. Those afflictions are usually *systemic*, whereby several organs or biological processes are affected simultaneously, and *multifactorial*, with a broad spectrum of risk factors ranging from the microscopic (e.g., genetic predisposition) and mesoscopic (e.g., lifestyle) to the macroscopic (e.g., health policies). Often it is impossible to identify a clear cause-effect relationship, possibly due to a complicated interaction among the multiple risk factors.

It is possible that the current paradigm of the scientific method as used in medicine is not the most suitable one to study those more "complex" illnesses. It is noteworthy that many fields of knowledge presently face problems that at a first glance might appear very different but that are similar in terms of their inherent complexity e.g., species in danger of extinction in ecology, financial crises in econ-

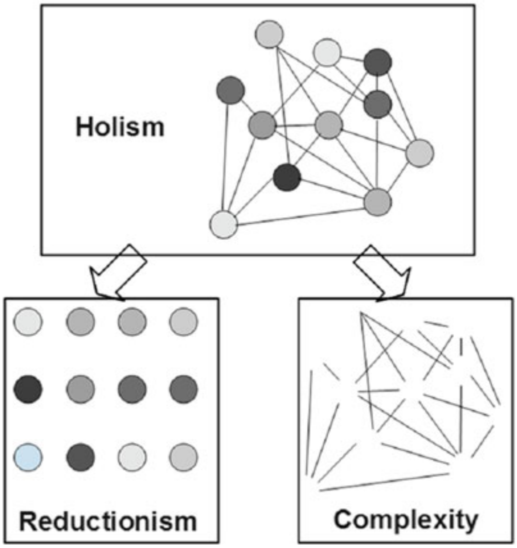

Fig. 2.8 Holism attempts to study systems in their totality, which is not always possible. Reductionism and complexity are different approximations of reality. *Reductionism* focuses on the components of a system and neglects information on time, space, interactions and context. *Complexity sciences*, or *systems biology*, focus on the interactions and the dynamics, giving less importance to the study of the individual components

omy, global warming in climatology, etc. [17]. The current scientific paradigm is characterized by *reductionism* and high specialization, which tend to focus on individual factors and lose sight of the context and interactions among factors that cross the borders of individual disciplines [18–20] (Fig. 2.8). There are many efforts to break free from the different limitations of the prevailing paradigm: *multi-, inter-* and *transdiscipline* try to integrate different scientific disciplines and make them interact [21]; *data mining* investigates patterns in huge quantities of crude data and translates the generated knowledge into predictive models that can be used in decision-making [22, 23]; *network theory* describes the interactions among elements or factors of a set [24]; *time series* statistics analyzes the temporal evolution of a specific observable [25], etc. Although all the techniques mentioned form part of the toolkit of the so-called *complexity sciences* or *systems biology*, each technique has its particular focus, and a general overview of the topics being studied is lacking. It would appear that the application of complexity sciences to economy, ecology and climatology and to the understanding of complex ailments in medicine, such as age-related frailty [26], are still in a *pre-paradigm state* (Sect. 2.3.4): the taxonomy of the phenomena observed has not yet been established clearly, and a general descriptive theory still needs to be constructed.

2.6 Conclusions

It is not the *topic* which determines whether something under study is scientific or not, but rather the *way* in which it is studied; in other words, whether the study follows the scientific method. The scientific method is similar to the common sense that we use in daily life but with the sequence of the different successive steps *Observation → Taxonomy → Hypothesis → Prediction → Verification* well articulated and well documented.

There are two different approaches to the scientific method. The philosophers, on the one hand, are idealists and try to define an absolute and universal method, with one of the unresolved questions being: "how can one obtain objective knowledge if some of the steps in the method are subjective?". Scientists, on the other hand, are realists and conformists, and are satisfied with an approximate description of the scientific method that can be applied in daily practice. Key aspects of this pragmatic approach to the scientific method are full disclosure of any investigation, interaction with the scientific community, and fitting the research into a coherent and cooperative knowledge network. In this pragmatic approach, individual research projects might be subjective, but science as a whole converges toward objectivity.

The current paradigm of the scientific method has been based on reductionism; on the other hand, many problems of the modern world are characterized by such a high level of complexity that they cannot be solved using the reductionist approach. Complexity science is an attempt to establish a new way of thinking and possibly represents a paradigm shift in the making.

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Chapter 3
Biomedical Research

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Abstract There is evidence that aging is the biggest risk factor for developing chronic diseases that can lead to death. Globally multiple investigations in the biomedical area are trying to identify the molecular, genetic, genomic, transcriptomic and proteomic factors (among others) involved in the aging process, in order to be translated into an adequate health status for an aging population. However, most studies have low power to detect small changes in relation to age in animal models or in humans. This raises the emerging need for studies to increase the power and contemplate the effect of the interaction of multiple factors in the aging process. The aim of this chapter is to present a review of some transcendental methodological aspects to be taken into account in the development of biomedical research protocols, without forgetting that there is no approach that is unanimously considered as the best.

Keywords Geroscience • Aging mechanisms • Biogerontology

Acronyms

Acid ATP	Adenosine Triphosphate
Acid FOXO3a	Forkhead Box O3a gene
ApoC	Apolipoprotein C
ApoE	Apolipoprotein E
DNA	Deoxyribonucleic
EGF	Epidermal Growth Factor
GWAS	Genome-Wide Association Study
IGF 1	Insulin-like Growing Factor 1
JNK	Jun N-terminal Kinase 1
MIM ID	Mendelian Inheritance in Man Identification
miRNA	Micro Ribonucleic Acid

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SIRT 1/2	Sirtuin 1/2
SNPs	Single Nucleotide Polymorphisms
TOMM 40	Translocase of Outer Mitochondrial Membrane 40 Homolog
TOR	Target of Rapamycin
TUBBY	Tub Protein Gene
β-Gal	Beta Galactosidase

3.1 Introduction

Aging is a process in which multiple changes occur in an organism over time [1]. It is considered extremely important given the biological, cultural and social changes that accompany it [2]. Aging has been studied since ancient times, and yet has resisted efforts to its definition [3]. From a biological point of view, most agree that it is a slow and gradual process of deterioration of the functional capacity of the organism, after maturity, and eventually leading to disability or death [4]. Even within the same process, there is wide variability among populations, and that chronological age does not correlate at all with the functional age.

There is evidence that aging is the biggest risk factor for developing chronic diseases that can lead to death (heart failure, neurodegenerative diseases, cancer, diabetes, etc.), although these diseases are not part of the aging process, are a consequence of it [3, 5]. There are also other conditions associated with aging, not being direct causes of death are responsible for the deterioration in the quality of life of the elderly, for example, sarcopenia [6], osteoporosis [7], arthritis, autoimmune disorders [8], decreased resistance to infection and loss of regenerative capacity [9].

Globally multiple investigations in the biomedical area are trying to identify the molecular, genetic, genomic, transcriptomic and proteomic factors (among others) involved in the aging process, in order to be translated into an adequate health status for an aging population. The results of these studies have shown that many biological mechanisms are involved and cause aging, have identified some of the molecular pathways that may decrease the effects of aging, but unfortunately the mechanisms and pathways that are capable of being modified, are extremely complex [5, 10]. Aging causes defects that include damage to DNA in the nucleus and mitochondria (mitochondrial dysfunction in turn leads to increased production of reactive oxygen species and decreased production of ATP), oxidative damage to proteins (and other macromolecules), protein misfolding and aggregation, glycation of proteins, induction of proinflammatory cytokines, telomere shortening and cell senescence [10].

Diverse and increasingly interesting approaches have been carried out for the study of aging, among which include: parabiosis [5, 11, 12]; study of nonagenarians and centenarians, as well as their families, to identify genetic factors that explain longevity of these individuals [5, 13, 14]; bioinformatic studies to identify new genes and pathways involved in human aging, with a potential custom application, transcriptomics, proteomics, epigenomic and individuals in various age groups to identify differences between them [5], and studies of SNPs (single nucleotide polymorphisms) and haplotype conformation suggesting new genes and pathways involved in extreme longevity or otherwise in accelerated aging [5, 15]. Moreover, some studies have also taken into account environmental factors, examples of this are: inadequate nutrition that leads to obesity and later to diabetes mellitus, and that of increasing pollution of air and reducing water quality leading to cell damage. However, most studies have low power to detect small changes in relation to age in animal models or in humans. This raises the emerging need for studies to increase the power and contemplate the effect of the interaction of multiple factors in the aging process.

The aim of this chapter is to present a review of some transcendental methodological aspects to be taken into account in the development of biomedical research protocols, without forgetting that there is no approach that is unanimously considered as the best. Rarely a study by itself can be considered very good or very bad and not enough to judge a study methodology; no study can be assessed only by its methods, since both the methods and the results are often important [16].

3.2 Units of Analysis in Biomedical Research on Aging

3.2.1 Non-human Models

Cell lines, eukaryotic models and animals, and even human models, are used as units of analysis to try to understand the factors associated with longevity, aging and associated with this disease [16].

3.2.1.1 Cell Cultures

Although it has come to question whether cell culture studies accurately represent what happens in an organism, the study of cell cultures, particularly fibroblasts, has allowed the identification of some biomarkers of aging such as IGF-1 (Insulin-like Growth Factor 1) growth, EGF (Epidermal Growth Factor) and β-Gal (beta-galactosidase associated with aging), among others. Experiments in cell culture has also led to the development of therapies that slow some adverse changes associated with aging [17].

The study of cultures of normal somatic cells is a model that mimics the cellular and molecular changes associated with aging. Even that the cell cultures show replicative senescence; it has been proposed that the limit in the replicative life is due to the inability of these cells to adapt to an artificial medium. The hypothesis of the relationship between replicative senescence and aging comes from the observation of decreased life expectancy in culture skin fibroblasts as a function of age of donor cells, however this has not been fully confirmed [17, 18]. In fact, it has been reported that when certain pathways and cell culture conditions are modulated for a senescent phenotype, this occurs independently of cell proliferation. Furthermore, the cell culture continuously requires to undergo proliferation, which does not occur in an organism, in addition metabolic requirements and growth conditions are also different.

3.2.1.2 Animal Models

The aging process occurs similarly in many species, therefore the underlying molecular mechanisms may be the same or at least similar enough across species. There is evidence of molecular homology between species and of the great utility of research on aging from unicellular eukaryotic to animal models. The study of aging in various animal models has been very important, for example, insulin signaling pathway/IGF-1, lipophilic hormones, oxidative stress response, TOR signaling, TUBBY and JNK-1, and caloric restriction genes involved in mitochondrial function, SIRT2 deacetylase activity and telomere length [19]. The latter, in order to assess possible interventions with potential relevance and application in humans [3]. To be considered a model of aging, it is required that the candidate shows signs of age-related deterioration that can be used as biomarkers, the phylogenetic distance between the model and the human should be as short as possible to facilitate external validity or extrapolation and generalization of the results to humans, and that the life expectancy of the model also be as short as possible to minimize the time required to perform the experiments and make relevant conclusions [20].

Compared to other biological systems, the relative ease and speed at which life span is measured, make yeast one of the most appealing organisms to model aging. In particular, there are two main models of aging in yeast: replicative aging, a model of mitotically active cells where the life span of the parent cell is defined by the number of mitotic divisions (daughter cells produced) before senescence and usually requires manual separation under the microscope of the mother and daughter cell; and chronological aging of post-mitotic cells which, in which life span is defined by the number of cells that survive in a non-dividing state or quiescent and similarly require to measure the ability of individual cells to form a colony (colony forming unit) state [21–23]. Although some aspects of aging are specific for these organisms, many features have been evolutionarily conserved in species of invertebrates and rodents [3, 23, 24].

Saccharomyces cerevisiae, used industrially in the manufacture of bread, beer and wine, is one of the most important unicellular eukaryotic organisms used in investigating the molecular mechanisms that modulate longevity due to the high evolutionary conservation of its genome between this yeast and mammals [25, 26]. This model has allowed the identification of various regulatory mechanisms involved in longevity, including nutrient signaling pathways, machinery acetylation/deacetylation (mainly sirtuins), response to stress [27] and autophagy. In addition, caloric restriction that is the main environmental factor associated with extension of life by reducing nutritional supplementation without inducing malnutrition [25, 28], has been experimented in this yeast. Other species of yeast *Schizosaccharomyces pombe* as [29] and *Kluyveromyces lactis* have provided useful and valuable information, with alternative models in the study of aging. In recent years, it has also been tried to study the replicative aging *Candida albicans* [30] and *Cryptococcus neoformans* [31].

Because of its short half-life (2–3 weeks), *Caenorhabditis elegans*, a nematode that is 1 mm in length, is another model for studying aging, given its low maintenance cost and that the total life span can be covered in short periods of experimentation; it has allowed the identification of hundreds of genes that, when mutated, increase life expectancy and in many cases maintain the physiological vitality [32], however, the great evolutionary distance it has with the mammals, complicates the extrapolation of data to human [20]. Notwithstanding, there are currently, diverse and varied approaches in the study of aging in *C. elegans* (evolutionary studies, population, diseases associated with aging, environmental manipulation as caloric restriction and hormetic treatments, as well as trials of drugs and substances that increase the expectation life) [3, 33–35].

On the other hand, the fruit fly, *Drosophila melanogaster*, which has a short life expectancy, low cost and easy maintenance, has allowed the identification of several genes of TOR signaling pathway in regulating longevity [36, 37]. *D. melanogaster* allows continuous study of aging and avoids the influence of newly divided cells because their cells are post-mitotic (except for some cells of the gut and gonads). Its longevity is altered by various environmental manipulations such as, temperature, reproductive status and dietary food or drug content [37]. *D. melanogaster* shares evolutionarily conserved pathways that regulate aging in mammals and has been useful to describe the presence of various populations of adult stem cells in ovary, testis and intestine, which play an active role in maintaining homeostasis of local tissue (similar to the occurring mammalian stem cells), and is a useful model for the study of the relationship between stem cells and aging [3, 38, 39]. Recently, genomic and epigenomic changes that were associated with mating and aging in females of *D. melanogaster*, including changes in expression of microRNAs, associated target genes and epigenetic modifications associated to histone three pathway [39].

Regarding to rodent mammals models constitute the best options in terms of biology and genetics. Mice and rats are valuable models due to their small size, short life expectancy (24 months on average), and easy to maintain in captivity; some pitfalls of these models include the habit of nocturnal behavior that causes some complications during phase activity [20]. Research on aging mice and rats has been used extensively to generate mutants with different life spans from to long ones [40], as well as studies of caloric restriction [3, 41]. A study of mutant and wild mice with *SIRT1* (sirtuin 1) showed that wild mice in which induced degeneration of coccygeal spinal discs was delayed when treated with resveratrol, on the other hand those rodents *SIRT1* deficient had an accelerated degeneration of the discs [42].

Larger mammal models are of increasing interest because of a similar life span to that of humans. These larger species include moles, beavers, porcupines and squirrels [41]. However, smaller mammals with longer life spans have also been studied, as in the case of naked mole rat with a life expectancy of 17 years and the little brown bat (*Myotis lucifugus*) with a life expectancy of about 34 years in the wild [3, 43, 44].

Furthermore, there are studies in the process of aging in birds –living organisms with three times span of that of a mammal of the same size, which is indicative of their relative resistance to degenerative processes associated with aging. Even this slow aging in birds, it has been observed that age-related deterioration is similar to humans and mammals [43, 45]. Research on birds and mammals, has shown the involvement of early growth pattern and reproductive history on age-related changes; pointing to the fact that the rate of aging can be influenced by genes and maternal age when the individual is born [46].

It is noteworthy that other animal models have been used in the study of aging, among which include: (a) Fish, the largest group of vertebrates, with a variety of species differ widely in terms of their longevity and versatility as experimental models, with great power of adaptation to a wide range of environmental conditions, with the ability to lay many eggs at the same time and with low maintenance costs through its lifecycle [20, 47]. Some species (of the order *Cyprinodontiformes*) and zebrafish (*Danio rerio*), guppie fish (*Poecilia reticulata*) and killifish (genus *Nothobranchius*) have been considered study models from the biogerontological point of view [20, 48–51] (b) Bees have been used as model organisms in relation to vertebrates, since they experience biochemical changes with aging, among which include, reduced proteolytic and antioxidant enzymes, in addition to increased levels of methylation in aging [52, 53] recent study in Western bees (*Apis mellifera*) showed that exposure to caffeine in a dose-dependent manner (safe dose of 5 mg/ml), delays the biochemical changes associated with aging and slowing the process of global DNA methylation [53]; (c) Other models like domestic dogs [54], cats and horses [55], have also been used to study more specific conditions, such as the study of degenerative macular disease in beagles.

Research in primates is also a valuable approach to elucidate the nature and causes of aging observed in human as well as evaluation of potential interventions. One of the advantages of using primate models is their genetic homology with humans (92.5–95 %), in addition to the fact that these animals are well suited for laboratory research, including breeding, nutrition and veterinary medicine. Some of the disadvantages are low availability, maintenance costs, genetic heterogeneity and risk of disease transmission between species, in addition to the implications in time, resources and efforts that involve longitudinal studies [56].

Finally, is important to recognize that even the enormous efforts in these models, there has recently been a significant lack of the association of genes that increase longevity in animal models with respect to those observed in humans. According to the data base GenAge (aging related genes), over 1,000 genes have been associated with longevity and/or aging in model organisms, including more than 100 in mice, of which 51 have been associated with extension life, but none of these was associated with longevity in the largest meta-analysis of 14 genome-wide association studies in European human [57, 58].

3.2.2 Human Models

It has been observed that in some humans the signs of aging are delayed, leading to increased life span. For this reason there have been multiple studies that compare individuals of 90–100 years and their families, which have helped to identify polymorphisms in genes associated with the longevity, among which are included *FOXOA3* and *APOE* [59]. However, the associations reported in humans occur in a small percentage of the population and/or have failed to be replicated in different populations [60]. It is important to consider that there may be variations even in the same individual, so they have used various tissues from biopsies or peripheral blood samples to study molecules and pathways involved in aging.

To try to identify molecular differences associated with aging in humans, an attractive approach has been the use of expression microarrays to identify genes showing changes with age (age-regulated genes). Changes in gene expression can lead to extensive tissue and functional changes associated with aging. Transcriptional profiles have been generated from various human tissues, among which brain, blood, eye, kidney, muscle and skin, among others. The major objective of these studies is the identification of new biomarkers that can be used as indicators of physiological age. The identification of genes and pathways associated with physiological age could reveal important processes in aging individual tissues [19].

Another approach to the study of the influence factors on longevity and aging in humans, is the study of genetic variants such as (GWAS) particularly aimed at identifying SNPs (single nucleotide polymorphisms) showing differences between individuals ≥85 years, compared to those <65 years of age. However, most human longevity GWAS have failed in identifying significant loci except for the case of locus *TOMM 40/APOE/APOC1* [61–63].

Furthermore, it has also been considered the study of individuals with premature aging syndromes (progeroid) as a useful complementary model and for identifying pathways involved in the aging process. The progeroid syndromes are classified according to the number of organs and tissues involved, in segmental (when expressed in multiple tissues and organs) and unimodal (when manifest mainly in an organ or tissue) [64]. Most progeroid syndromes are caused by a mutation in a gene involved in one or more processes of maintaining the integrity of the genome (including systems replication, repair, recombination and transcription of DNA) [65]. The best characterized segmental progeroid syndromes and have provided information on some of the genetic, biochemical and cellular bases of aging, are Hutchinson Gilford Syndrome (MIM ID # 176670) and Werner syndrome (MIM ID # 277700) [66, 67].

3.3 Examples of Relevant Biomedical Research in Aging

Examples of cross-sectional biomedical studies in humans are those that include comparisons of ancient families or families nonagenarian with average life expectancy; the description of expression profiles determined in a tissue or cell culture;

identifying SNPs associated with aging in diverse populations; comparing gene expression profiles in individuals of different age, etc.

An example of longitudinal studies include: repeated measurements of telomere length in cell culture under replicative senescence, comparisons of gene expression in the same individual under, cohort of individuals in which repeated measurements are used to determine how and when changes occur in the tissues as a function of chronological age and try to associate these changes with certain factors, SNPs, genes or pathways involved in the aging process [68–71].

Comparing gene expression profiles or a particular polymorphism in families with centenarian or nonagenarian regarding families with average life expectancy, compared gene expression in the aged group of individuals or organizations with respect to a young group, or compare a group of individuals with a given disease with respect to a reference group without disease [71, 72] are some examples of cohort studies developed in biomedical research.

An example of diagnostic test studies on aging, is the validation of a particular polymorphism in the DNA sequence, changes in gene expression at mRNA level (transcriptomics), changes in protein level gene expression (proteomics), or changes in molecules or metabolites (metabolomics) with its potential to predict life expectancy and disease susceptibility [3, 71, 73–76].

Experiment examples include the use of transgenic animal models, inhibitors of gene expression and microRNAs [77] and the use of drug candidates in animal models and cell cultures and in human [42, 53, 78].

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Chapter 4
Descriptive Studies

Mario Ulises Pérez-Zepeda and Lorena Jocabed Rocha-Balcázar

Abstract Descriptive studies are a group of designs that even they have a lot of limitations, in aging are particularly important to define the different conditions that affect older adults and are not well recognized or still are in very preliminary stages. There is a growing need of delimiting the dimension of conditions such as frailty, sarcopenia, cognitive decline among others; in order to alert both general public and in particular health professionals. On the other hand, smaller studies such as case series and case reports are needed in this age group to continuously describe diseases or other conditions that in the past were thought not to happen in older adults. Therefore this designs aid in increasing the recognition of health problems in older adults and the magnitude of them.

Keywords Descriptive-studies • Descriptive-research • Prevalence-studies • Ecological-studies

4.1 Introduction

There is a group of research reports that are very close to clinical practice and that are taken directly from daily practice, such as case studies and case series. Alternatively, and closer to epidemiology, are studies that look only at the frequency with which a phenomenon is present, most often illnesses in a fixed place and time, such as prevalence studies and ecological studies [1]. These studies may be derived either from new data or from databases, which in the hospital context are generally the patients' clinical records. The objective of this type of study is to observe and collect data about a given phenomenon in an individual or group of individuals [2]. Depending on the number of subjects and the presence of a reference group (or all

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of the subjects exposed to risk of suffering from the condition), these are divided into case studies, case series and prevalence studies. Only the latter contemplates taking an entire group of exposed subjects to learn the frequency with which the phenomenon of interest occurs in all of that population. They cannot yield data of causality, but they can suggest hypothesis.

4.2 Prevalence

One of the most important aspects of this type of study is the question of how representative a condition is within a given population. To have external validity, prevalence studies must start with a representative sample of the population to which it refers. However, this is not always possible in the case of older adults, since there are subgroups within this age group that are clearly differentiated from the rest, having a higher frequency of problems or illnesses, and the higher the age the higher will be the proportion with a particular illness. To this must be added the problem of survival, which could yield a false impression where a given condition has increased or decreased in frequency, depending on whether or not those who have died had the condition. When doing prevalence studies in older adults, not only the time and place of taking data must always be specified, but also the age group being referred to and whether there is a sampling strategy to avoid a misleading increase or decrease in groups of very advanced age. Knowing the type of place where the sample of older adults was taken is also very relevant in this age group because it is not the same to determine the prevalence of geriatric syndromes in residents of a personal care home as in ambulatory adults, since a larger prevalence of geriatric syndromes would always be found in the personal care home than in the ambulatory population [3].

One of the most common problems the researcher finds when developing prevalence studies in the senior citizen population is the lack of widely accepted definitions. Although this has been improving over time, as more consensuses are reached about the problems that concern the old, there is still a wide margin in the way in which geriatric processes are defined. One of the most common examples is frailty, where a multiplicity of definitions has been used, resulting in prevalence reports that differ enormously from one another, beyond the population variability itself [4].

Despite what these reports might contain arising from the records, many of the problems the researchers are trying to resolve might not be specified in the documents consulted, either because they are dealing with a recently defined condition or because the condition had a different name in earlier times. For example, in a 1990 article by Thorslund and collaborators, they were looking for the prevalence of protein energy malnutrition in older outpatient adults. However, the definitions used in this study make it almost impossible to compare the results with the current concepts. Worse, some of the criteria used for this condition might today be considered as part of frailty (inflammatory markers and skin test anergy) or sarcopenia (calorie and protein malnutrition). Even though it is an excellent study, its usefulness is questionable when trying to translate this knowledge to the present [5]. This example raises some of the problems described. There is no agreement on the definition of the term sarcopenia, and there are many definitions that might be found in the literature [6].

4.3 Case Study

This is the simplest design that can be made in clinical research where, from observation, a description is made from observation of an individual and of the clinical characteristics that are carriers of the phenomenon that is the object of the study. In general it is recommended that the classification be standardized and broadly accepted. In the case of studies of aging, an example is dementia, where many clinics would agree that it is appropriate to diagnose a subject with dementia using the DSM V criteria (even though new terminology of this edition changed). Most of these studies involve unusual cases that are not often seen in daily practice. However, especially in the case of old people, some illnesses are emerging that, while they might be considered common in younger groups, are uncommon in older adults. For example, a recently diagnosed case of Conn syndrome in an adult 95 years of age is a rare case in its own right, although the illness itself is not rare. Due to the increasing number of subjects of extreme age, the report of cases of different illnesses is useful for increasing available knowledge about the different manifestations that an older adult could present with an illness that is rare for this age group. Unlike prevalence studies, case studies may have a follow-up on the subject to learn the nature of the illness described; this aspect is shared in the case series design.

In the example chosen to illustrate a case study from the set of older adults, a case is described of systemic lupus erythematosus accompanied by primary biliary cirrhosis [7]. The illness in other age groups is not common, and much less so in older adults, so that in the description of the particular characteristics found, new knowledge from the case may be learned.

4.4 Case Series

This type of report groups similar cases that are presented during a fixed period of time. When similar cases of an illness are presented over a short time (days or weeks) they could raise an alert for an epidemic [1]. In the case of older adults a case series could be a substitute for clinical cohorts that require a larger number of subjects and that are difficult to put together in these age groups. As with the case study, definitions are very important; if no standard and accepted definition is available, the cases should be described completely instead of using a tag [8].

Both in this type of reporting and in the case studies, it is usual to review the available literature on the topic that supports the conclusions arrived at through the case or cases presented. These need not to be systematic reviews; however, they would provide a general overview of the topic being studied.

The case series do not report only illnesses; they might also report on the development of a new intervention or therapy, or adverse effects of these, as in the example shown below. In that report, six cases of infections of the joints following injections in the knee joint are presented [9].

4.5 Other Descriptive Studies

Some texts include within this type of descriptive studies what are called ecological and surveillance studies [1]. Ecological studies correlate phenomena in populations, not in individuals. In the example presented below, visits to an emergency room are correlated with environmental pollution; a positive correlation is found between the number of visits to an emergency ward and the level of pollution [10]. Monitoring studies describe the appearance of a given phenomenon. In the example presented, a system for monitoring falls is implemented, which enables researchers to learn the frequency of falls within a specific community. While it might appear as a study of cohorts, in monitoring studies the goal is only to try to describe a phenomenon in terms of frequency without putting forward specific hypotheses of causal exposures [11, 12].

4.6 Example Summaries of Descriptive Studies in Aging

Below are some summaries of case series and case studies, presented as examples of what is reported on older adults at present.

4.6.1 Prevalence

Sarcopenia is a problem that is increasingly identified among older people. An algorithm was recently developed to identify this condition. The objective of our study was to determine the prevalence of sarcopenia in a group of senior citizens in Mexico City, using the algorithm for sarcopenia of the European working group. A cross-sectional study was carried out on senior citizens in the community using a sample of 345 adults 70 years of age or older, during 2008. The data were obtained by a group of standardized interviewers. With the goal of determining the presence of sarcopenia, muscular mass and strength were measured as well as physical performance. Muscular mass was measured by the circumference of the calf, muscular force by the strength of the grip, and physical performance by the speed of walking. The cutoff points used were as those suggested in the same European algorithm. A total of 116 (33.6 %) of the subjects were found with sarcopenia, 75 (48.5 %) of them women and 41 (27.4 %) of them men, with higher prevalence in subjects 80 years of age or older (50.4 %). Sarcopenic obesity was found in five subjects (1.4 %), moderate sarcopenia in 21 patients (6 %) and severe sarcopenia in 94 subjects (27.2 %).

This study along many others on the topic of sarcopenia shows the actual difficulty that researchers and clinicians face when trying to define this entity, even that a clear definition was used, this is only one of about one dozen of definitions of this syndrome. Therefore, and appropriate description of how this algorithm was implemented is expected to be in the manuscript [6, 13].

4.6.2 Case Study

The report is of the case of a woman 69 years of age without a family history of autoimmune illness, only a history of hypertension. Over the previous 4 years she had presented transient arthralgia and arthritis. Later, she showed sensitivity to light, malar rash, and diffuse discoid lesions on her trunk and face, for which she was seeking medical attention. In addition, she reported a loss of weight of approximately 3 kg over the previous 3 months. The physical examination showed only synovitis of the wrists. The laboratory results were as follows: hyperglobulinemia (20 g/l), lymphopenia (850 cells/mm^3); with platelets, creatinine, and a general exam of urine normal. The immunology profile confirmed: positivity in the antinuclear antibodies (ANA) with titer 1:400 and anti-dsDNA 115 IU / ml, with serum complement normal. The following antibodies were negative: anti-La, anti-cardiolipin, lupus anticoagulant, anti-SM, anti-RNP, anti-SCL-70, anticentromere, rheumatoid factor, and anti-citrullinated peptide. With the foregoing, it was concluded that systemic lupus erythematosus (presence of 6 from 11 criteria of the American College of Rheumatology for lupus) was present.

One year later she developed liver dysfunction. The abdominal examination revealed hepatosplenomegaly, liver function tests found double the normal values. The antimitochondrial antibodies were positive (1:164), with anti-E2 positive fraction. Serology tests for the hepatitis B and hepatitis C virus were negative. The findings are consistent with the diagnosis of primary biliary cirrhosis so that, for testing and staging, a liver biopsy was carried out, which corroborated the diagnosis and was classified as being in stage 1. Treatment was given with 600 mg per day of ursodeoxycholic acid, normalizing liver function tests in a month.

Late onset of systemic lupus erythematosus is relatively rare, with a frequency of between 12 % and 18 %. Although the autoimmune mechanisms behind the association of these two autoimmune disorders are not completely understood, there are few cases reported for either illness. Moreover, the new onset of these diseases in older adults is still very rare, so descriptions found in clinical settings could aid at identifying them in daily routine work [7].

4.6.3 Case Series

Intra-articular injections of corticosteroids and hyaluronic acid in the knee are widely practiced as a conservative treatment for osteoarthritis. However, there are related side effects, in particular with the corticosteroids, mainly from infections. The microorganism most commonly encountered is Staphylococcus aureus, with the occasional participation of other organisms, including staphylococci and anaerobics.

In this report, the median age of the group was 75 years (64–87 years). Most of the patients had significant comorbidity. Three of the patients were treated with corticosteroids, and the other three with hyaluronic acid. All of the patients arrived in the emergency room 1–5 days after the injection. The main manifestations were pain, swelling of the extremities involved and difficulty walking. None of the subjects had fever at first.

The physical examination of the six patients revealed inflammation of the affected knee and pain with its movement (active and passive). Analysis of the synovial fluid revealed a lightly elevated white cell count (mostly neutrophils) in four of the patients; only two had positive Gram stain. Most patients had elevated erythrocyte sedimentation rate and C-reactive protein.

The resultant bacteria in the synovial fluid culture were staphylococcus or streptococcus. One patient had a sterile culture, probably because of oral antibiotic treatment before being admitted. Antibiotic treatment with cefazolin was started. It was adjusted according to the results of the culture. All of the patients were submitted to surgical treatment. In four of the patients the surgical intervention was carried out within the first 24 h. One patient, 64 years of age, refused surgery during the first 2 weeks of hospitalization and was initially treated only with antibiotics. Given that the condition did not improve, the patient finally consented and was intervened.

Three of the six patients were submitted to more than one surgery. Four patients were treated with formal arthrotomy and two with arthroscopy. The intraoperative findings in all cases were synovial congestion and purulent material. One patient, a man 86 years of age, was admitted to the intensive care unit following the operation after his second arthrotomy with progressive sepsis. Later he developed septic shock. He was again taken to the operating room for an urgent supracondylar amputation. He continued to deteriorate and finally died of septic shock.

Post-surgery, all the patients were treated in the same way: the antibiotics were administered for 4–6 weeks after surgery, the knees were immobilized for 3 days after surgery and were submitted to physiotherapy, drainage continued for several days. The median hospital stay was 22.5 days (9–40 days). The infection was finally resolved in five patients.

Intra-articular injection of the knee is not an inoffensive procedure and may be harmful and potentially fatal. In addition, its long-term benefit continues to be questionable.

This report shows rich information on septic arthritis secondary to intra-articular injections. This could give valuable information to clinicians on what to expect or bring up ideas to make new studies about the topic in researchers [9].

4.6.4 Ecological

The objective of this study was to investigate the effect of daily levels of air pollution (levels of carbon monoxide, nitrogen dioxide, ozone, sulfur dioxide and other particles with an aerodynamic profile $\leq$10 μm) in morbidity and correlation with the daily number of visits to the emergency rooms due to lower respiratory illness in persons older than 64 years of age in the city of Sao Paulo, Brazil between 1996 and 1998. Generalized Poisson additive regression models were used and adjusted for the long-term trend and the climate, the days of the week and the daily number of admissions. Ozone and sulfur dioxide were the pollutants associated with visits to emergency department in older adults. These results reinforce the idea that air contamination can promote adverse health outcomes in older adults.

In this example the interaction between pollutants and health conditions seem to be related. Even though it provides with information, the descriptive nature of the study precludes from having any conclusion, and further studies with other designs could evidence if the association is true [10].

4.6.5 Monitoring

Falls are the main cause of fatal and non-fatal injuries among older people in the United States. Despite the importance of injuries caused by falls, epidemiological studies of them among older persons have not identified either their causes or the means of preventing them. Therefore, a system of monitoring was established in the community in Miami Beach, Florida, as part of a study to evaluate falls among old people. A total of 1,827 events of injury from falls were produced in this community between July 1985 and June 1986. More than 85 % (1,567) of the persons who fell received attention in an emergency room (the main source of information). The other cases were identified from one of the three sources utilized: reports from firemen, medical registers of hospitalized patients or from the medical report of the doctor who first provided primary care. Most of the falls (97 %) were listed as accidental.

More than 100 persons sought medical assistance because of a fall every month. The moment of the injury was known by 68 % (1,244) of the persons who fell. Seventy-four percent of these falls (921) occurred during daylight hours. Fifty-four percent of the falls (986) occurred in or near the house, and 38% of them recorded the specific place in the home where the fall took place: 42 % occurred in the bedroom, 34 % in the bathroom, 9 % in the kitchen, 5 % on the stairs, 4 % in the living room and the other 6 % in other areas. This monitoring system will help us use the study to clarify the causes of old people's falls and identify and evaluate the efforts of appropriate prevention. It will also help other persons in the design and implementation of other injury monitoring systems.

This study describes the different features of falls on a specific community of older adults. More than establishing inferences, the main goal of these studies is just to describe what to expect of a certain phenomenon [12].

4.7 Conclusions

While this type of studies does not allow for conclusions or inferences of causality, it is useful for describing a phenomenon in its early stages. As well, these studies are of low cost and with few ethical implications. As with other age groups, what ensures fidelity of information for older adults is planning the study properly, taking into account the peculiarities presented by a study on aging.

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Chapter 5
Qualitative Research

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Abstract Qualitative studies have focused on giving an account of a broad range of topics on aging using strategies such as: case studies, of a single subject, focus groups and historical/comparative approaches. Among the topics this research has touched on are: the demography of aging, the relationship between the process of modernization and aging, the stratification of age, patrilineal families, formal/informal arrangements for living together, support systems, care of old people who live alone, the health/illness process, health care, disability, long-term care and death. There are also studies that focus on evaluating the impact on changes in the family, life satisfaction for retired people and their life conditions, care of old people, and reform of the retirement system and community services for people of advanced age. With this methodological proposal we try to increase the amount of information about age and aging to develop an integral and complete understanding of the context, while at the same time recognizing the presence of interdisciplinary elements that imply, among other things, values and the part they play in determining individual and collective circumstances of the people in this age group. In this chapter we approach qualitative research in the context of research on age and aging, with a proposal that takes elements from the theory of science in anthological, epistemological and methodological areas, and extracting those fundamental concepts to provide better understanding of the topic.

Keywords Qualitative research • Social gerontology • Psychogerontology

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5.1 Introduction

Research on aging leads to learn the patterns that regulate the last stage of life. Advances in quantitative methodology in knowledge creation have influenced this type of research. The key elements of this research method are: logical deduction, empirical observations, quantification and validation [1].

Research into aging has been frequently characterized by limiting these phenomena to quantifiable variables (specific and with set values), and this has led to reduction in the understanding of the phenomenon. Still, "reductionism" has been an advance in establishing a regular pattern, relationships or causal models, and descriptions of age and aging through quantitative research [2].

Qualitative studies have focused on giving an account of a broad range of topics on aging using strategies such as: case studies [3, 4], studies of a single subject [5], focus groups [6] and historical/comparative approaches [5]. Among the topics included in this type of research are: the demography of aging, the relationship between the process of modernization and aging, the stratification of age, patrilineal families[1], formal/informal arrangements for living together, support systems, care of old people who live alone, the health/illness process, health care, disability, long-term care and death [7, 8]. All are aspects that provide significant bases for understanding age and aging. There are also studies that focus on evaluating the impact on changes in the family, life satisfaction for retired people and their life conditions, care of old people, and reform of the retirement system and community services for people of advanced age [9–15]. All of these are located within the dimensions of the significance of the social processes associated with aging.

The qualitative perspective has also addressed other themes on aging such as social well-being and social security for older adults, physical and mental health, social and economic support, causes of and solutions to poverty among senior citizens, availability of income and financial resources for them, and the influence of public policy on quality of life and immigration [7, 11, 12].

Thus, qualitative research offers a diversity of contributions to a more complete understanding of the significance of various facts, and contributes to explaining the process of age, aging and the social environment in which it occurs in a broader and deeper way [15, 16]. With this methodological proposal we try to increase the amount of information about age and aging to develop an integral and complete understanding of the context, while at the same time recognizing the presence of interdisciplinary elements that imply, among other things, values and the part they play in determining individual and collective circumstances of the people in this age group. This approach to comprehension of the significance and social construction of the reality has contributed to improving the compilation and use of data, completing and complementing the most popular methods in positivist and empirical

[1] Patrilineal: adj. *Anthrop*. It means a social organization in which the paternal line predominates (adapted and translated from the Diccionario de la Real Academia de la Lengua Española, on-line version, consulted June 12, 2014).

frameworks [17], so that the qualitative approaches have been gaining an ever-larger space within the social research of aging.

In this chapter we approach qualitative research in the context of research on age and aging, with a proposal that takes elements from the theory of science in anthological, epistemological and methodological areas, and extracting those fundamental concepts to provide better understanding of the topic.

5.2 The Design of Qualitative Studies

One of the characteristics of qualitative studies stems from its versatility, which represents a shift from the orthodoxy of quantitative proceedings without losing the rigor needed to enable flows and recurrences to initial phases. In addition, contributions of the literature may always be incorporated at any time, and not just during the final interpretation of the results.

The main idea of the research is embedded in the very characteristics of the object being studied, its location in the reality from where it emerges, and especially the way it corresponds to the subjective, experiential, and representational dimensions of the subjects and society. Like all scientific approximation processes, having this basic idea could sustain itself in the experience of the researcher and in the practice of the scientific community, but that is not sufficient, and it needs to formulate abstractly a valid and creative questionnaire that expresses itself by posing the problem [18].

Figure 5.1 represents graphically the process of qualitative research in four phases. In each of these the researcher must choose options from the alternatives presented. If there is something in common among the different qualitative approaches it is the process of decision-making the researcher continually faces. It is possible to differentiate separate stages within each of the four phases. Normally, when the end of one phase is reached it yields some type of product. For example, the preparatory phase is comprised of the reflection stage, which in turn is made up of three basic tasks: formulating the problem, selecting the methodological strategy and choosing the context.

The different phases may be observed in Fig. 5.1 (start of the study, during the study, the end of the study, and the report), one after the other, without being lineal. If we look at the graphic representation, we see that each phase is superimposed over the preceding one and the succeeding one. It shows how subtly the qualitative research process develops. Before you have finished one phase you are already starting on next one. One can see this by looking at the graphical representation of the different stages that comprise each of the phases.

In the study's initial phase, the researcher, taking as a base his or her own education, knowledge and experiences of the phenomena, and of course their ideology, will set out to establish the theoretical framework conceptually, from where he or she embarks on the research and works on planning the activities to be carried out

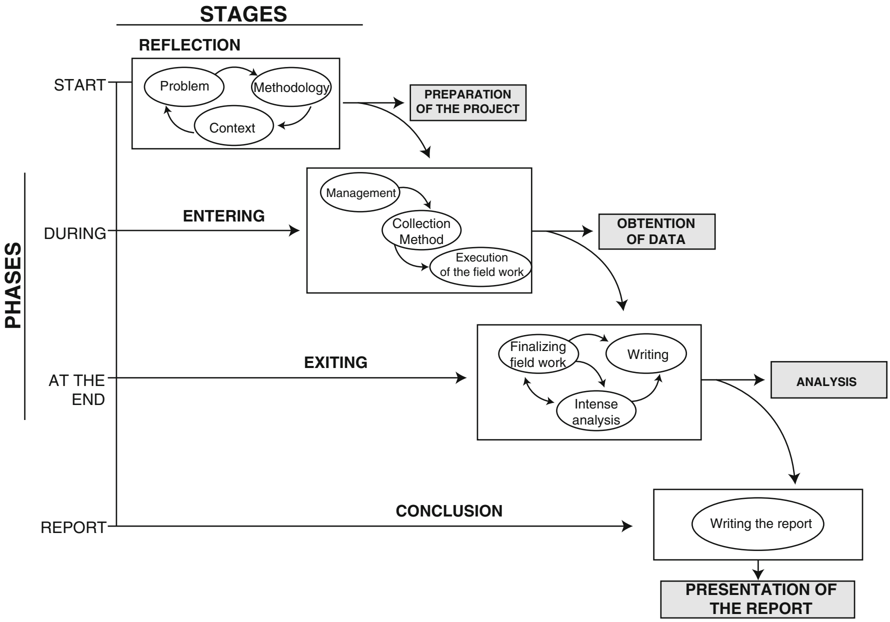

Fig. 5.1 The process of qualitative research

in the later phases. During the second phase, collecting the data from the field, the qualitative researcher will have to continue making a series of decisions, modifying, changing or redesigning the work. In the third phase, finalizing the study, the data analysis is considered to be a process with a certain level of systematization, which sometimes remains implicit in the activities undertaken by the researcher. Taking these inferences as a base, it is possible to establish a series of tasks or operations that constitute the basic analytical process common to most studies involving work with qualitative data, namely: finalizing the field work and obtaining results, analysis and conversion of the data, obtaining more results and writing the conclusions. These things are not always accomplished in order, and they might happen simultaneously [19]. The last phase culminates with the presentation and diffusion of the results. Thus the researcher not only arrives at a better understanding of the phenomenon that is the object of the study, but also shares it with others. The report should be a convincing argument; systematically presenting the data that supports the researcher's case and refuting alternative explanations. There are two basic ways to write the report: as if the reader were solving a puzzle with the researcher, or writing a summary with the principles discovered and the results that support the conclusions [19, 18].

5.3 Qualitative Methods

These methods have been used in research on the phenomenology of aging, illustrating the experiences and perspectives of senior citizens and their caregivers [20]. Phenomenological, psychoanalytical and feminist studies have taken the development of alternative theories on the impact of illness in seniors and on the quality of life of the individuals [16, 21]. Other qualitative studies have examined and evaluated health, focusing on evaluation of the ways of providing care [21].

The guidance and orientation, and therefore the choice of method used are deduced from the very nature of the research questions on the aging process.

Thus is thought that the method is the characteristic form of the research, determined by the substantive intention and the focus that directs it. The comparison carried out by Morse [12], shown in Table 5.1, classifies the methods used in quantitative research. In the first column of the table are the questions that direct the research, followed by the most appropriate method for addressing the question posed, then the discipline from which the method proceeds and the techniques of gathering the information that are used from that methodological focus, and lastly some relevant authors who have worked with each methodological option in age and aging [20, 22–39].

Ultimately, qualitative research seeks to learn the meaning the individuals give to their experience. The important thing is to learn the process of interpretation through which people define their world and act as a consequence [22]. A good way to learn the phenomenological method is through analysis of research that has been carried out in the context of aging using the same method.

Thus, before studying the impact of a nursing program designed for the care of an older adult, qualitative research would be interested in trying to understand the experience of becoming old through the experience of the persons who are aging, and the meaning this has for nursing practice. For example, before studying the quality of life of senior citizens in a retirement home, this research would be interested in what the experience is of being in these houses or what the experience is of a senior citizen being integrated with the family. To understand aging, qualitative research would investigate the perception of the seniors before looking into that of aging and death itself.

5.4 Data Analysis

According to Amezcua and Gálvez [40] the data analysis phase is the most complex part of qualitative research. On this point, Taylor and Bogdan [41] propose an analytical focus on progress based on three moments: discovery, codification and providing relevance, which are produced simultaneously with the compiling of data so that the researchers can develop an emerging understanding of the research on the questions asked. This interactive process of data collection and analysis leads finally

Table 5.1 Qualitative methods

Type of investigation	Méthod	Discipline of origin	Technique for obtaining the information	Studies in age and aging
Meaning: explain the essence of the experiences of the actors	Phenomenology	Philosophy (phenomenology)	Recordings, writing anecdotes of personal experiences	Da Graça da Silva [20]; Herrera [22]; Pérez-Dodoy [23]
Descriptive/interpretive: values, ideas, practices of the cultural groups	Ethnography	Anthropology (culture)	Unstructured interviews; participant observation; field notes	Vázquez Palacios [24]; Martínez [25]; Reyes Gómez [26–30]
Process: experience through time or change; might have stages and phases	Theory based	Sociology (symbolic interaction)	Interviews (recorded on tape)	Ferreira de Mello [31]; Curcio Borrero [32]; Veliz [33]
Centered on verbal interaction and dialog	Ethnomethodology analysis of the discourse	Semiotics	Dialog (recorded on audio and video)	Parales [34]; Hernández-Eloisa [35]; Rivera Navarro [36]; Treviño-Siller [37]
For improvement and social change	Research action	Critical theory	Miscellaneous	Rodrigues [38]
Subjective issues	Biography	Anthropology; sociology	Interview	Osotio [39]

to a point at which new categories or issues emerge. This is known as saturation, which indicates that the collection of data is complete [42]. This analytical strategy is directed toward seeking development of a deep understanding of the scenarios or persons being studied and requires a solid theoretical base and considerable experience. The diversity of proposed patterns also calls for seeking consensus [41]. This analytical strategy has been widely used in research on aging for the interpretation of the in-depth interviews, in particular through the focus on a theory-based and hermeneutic approach [8, 43–45].

5.5 Strengths and Weaknesses of Qualitative Methodology

The decision for or against using qualitative methods must be linked to matching the method with the problem under study and the research questions rather than being determined by fundamental considerations [46].

Qualitative research does not necessarily imply conflict with quantitative methods; rather, it could broaden and complement the knowledge generated from that type of study and point toward investigation of aspects and components that were also present in the object of the study but were avoided or not fully understood using quantitative methods –Mixed Methods chapter would explore this convergence of qualitative and quantitative methods. Methodological problems arise during any research, but a qualitative investigation involving older adults requires greater clarity. Ramos [47] describes three types of problems that could affect qualitative studies: the researcher-participant relationship, subjective interpretations of the data by the researcher, and the design. However, a well-designed research project must also take into account informed consent, confidentiality, the generation and analysis of data, the researcher-participant relationship, and notification of the final results [48].

In general there are three large categories of qualitative research of interest to researchers on age and aging: observational studies, studies with documented interviews, and textual analysis of various written records [49–51].

One of the main strengths of this methodology is that the findings derived from this approximation are amenable to specification, due to robust internal validity. In addition, the data derived from qualitative research provide information on the phenomena from a holistic perspective, leading to the propensity of this methodology to "communicate" with the subjects of the study, generating new research ideas not accessible to quantitative methods instead of confirming existing hypotheses.

The weaknesses of this methodology consist mainly in the following:

1. Research methods are not robust in terms of external validity
2. Difficult to summarize the findings
3. Large populations cannot be studied
4. Procedures are not established

5. Subjective reliability
6. Very time-consuming [52, 53]

In addition, it has been noted that studies developed using qualitative methodology might vary in the way they deal with data analysis, confusion of concepts, and more description than interpretation of results [40]. Examples of this type of methodological strategy as applied to research on age and aging are presented in Table 5.2.

There is no doubt that in the development of age-related research in recent decades, qualitative methodology has played an important role in the generation of information, knowledge, and especially understanding of this stage of life [10, 11]. However, it still has not been widely used, and it is necessary to understand that this methodology is complementary and possesses special characteristics that assist in the analysis and understanding of certain phenomena, permitting the resolution of problems and a diverse questioning in the field of research into age and aging.

5.6 The Rigor of Qualitative Research

The criteria commonly used to evaluate the scientific quality of a qualitative study, and thereby its methodological rigor, are reliability, internal and external validity, credibility and transferability [59, 60]. Reliability is established from the measure by which the results are consistent with time and account for what happened in the population under study. In addition, if the results could be reproduced with a similar

Table 5.2 Qualitative research on aging

Qualitative research	Strengths	Weaknesses
Experiences of the patients and their caregivers with pharmacological treatment administered to older adults	Understanding and knowledge of the process Concepts and contextual links	Lack of generalization
Experience of old people with health services	Knowledge of processes Action-oriented	Lack of generalization and foresight
Social representations of various illnesses in the senior citizen population	Transformation of data base Development of concepts	Too many data sources
Rating the stigma perceived by patients with dementia and their families	Practical relevance	Partiality
The emotions of aging and fear of death	Understanding, richness	Ethnocentricity
Mistreatment of old people	Interpretation, observations, richest selection of data	Partiality, lack of generalization

Sources: Donovan [54]; Cooper [55]; Campos-Navarro [56]; Nieto-Murillo [57]; Coutinho [58]; Reyes-Gomez [28, 29] methodology they will be considered reliable, while validity determines whether the research really states what is intended to be studied or as truths arising from the research [61]. The researchers determine validity by asking a series of questions, and often they look for the answers in the research of others [62]. In neither case is the magnitude expressed by a coefficient; it only verifies systematization in collection and the qualitative analysis [63]. Credibility is achieved when the results of a research project are true for the persons who were studied and for others who have experienced it or have been in contact with the phenomenon being researched, and thus make it possible to extend the findings. Not being able to establish a causal relationship does not invalidate the study, since its purpose is not rooted in generalization but in the intrinsic understanding of the process.

Transferability or applicability refers to the possibility of extending the results of the study to other populations. For this it is necessary to describe in detail the place and the characteristics of the persons where the phenomenon was studied. Therefore, the level of transferability is a direct function of the similarity between the contexts.

One could say that there is no magic research method that guarantees the validity of the findings. Pure methodological correction does not produce valid data. This leads to the belief that the truth is related to the significance (in an inter-subjective framework of references) and explicitly with the way in which the significant events of daily life are constructed.

5.7 Conclusion

Interest in qualitative methods of research on aging is growing, and offers unique opportunities to compensate for the loss of valuable information that often occurs with quantitative research, that could mean a scientific reduction.

Qualitative research enriches the understanding of aging with detailed data, unique approaches, and clear values, without losing sight of the fact that it is not a substitute for failing to provide data or not knowing statistical procedures, but is a specific way of proceeding with the research.

Studies on age and aging must incorporate qualitative methods and start seeing them in their many biological, psychological and sociological components. This is because neither the behavior of senior citizens nor their situation can be understood at the margin of their primary needs. It must be explained by interpretation of their own contexts, through multiple well-designed and rigorous qualitative methods consistent with their goals, objectives and results.

Lastly, it is essential to link qualitative research to the new technologies of information and communication, leaving behind the irreconcilable disputes about quantitative research, since in the end it is working together through the mixed approaches that make possible the advances in knowledge on what is happening in this population group.

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Chapter 6
Case–Control Studies

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Abstract In the planning phase of research related to age and aging, the quality of knowledge derived from epidemiological studies, depends heavily on the solidity of the methodological design and the strategies for collecting data designed to answer the research question. Case–control studies are a cost-effective alternative for providing a valid and reasonably precise estimate for identifying an association force of a hypothetical relationship cause-effect in studies related to older adults population. Recently case–control studies have been related directly to cohort studies, which enabled researchers to design new patterns for their development while obtaining major benefits. The case–control study is the appropriate choice and at times the only alternative for studying diseases of very low incidence in older adults. With this type of study it is possible to explore a broad range of related exposures to illness. Another important advantage is that they require smaller samples and are less costly than experimental designs or cohort studies. Among the disadvantages or drawbacks of this type of study is that it can only provide information about

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the event or target disease in the population that has been selected for carrying out the study.

Keywords Case–control study • Research-methodology • Cause-effect • Low-incidence studies

6.1 Introduction

Case–control studies are considered to be one of the advances in modern epidemiology. They are defined as an epidemiological, analytical, non-experimental procedure used to identify potential causal relationships between the presence of a specific event or illness and previous exposures [1, 2]. A case–control study is appropriate when the research question involves low frequency events and disease, such as car accidents [3] or Creutzfeldt-Jakob disease in older adults [4], diseases that feature long periods of latency like prostate cancer [5], and events or disease with multiple potential etiological factors, such as fractures due to falls [6]. A prospective cohort study might not be feasible due to the follow-up time required or for the loss of the subjects of the investigation –which is the case with older adults– usually due to death or migration.

This design might also be used when studying health problems where a relatively rapid treatment is required and the exposure or the prospective treatment might be ethically dubious, e.g. in the study of the therapeutic use of bisphosphonates for osteoporosis and its association with a higher risk for presenting ischemic stroke [7].

Thus, case–control studies are a cost-effective alternative that provides a valid and reasonably precise estimate of the strength of association of a hypothetical cause-effect relationship [8].

6.2 Theoretical Concept

The classic design of case–control studies identify older adults who have a specific outcome or disease (cases) and those who do not have it (controls), ideally from a random sample of the population in which the cases originated. Then, it is determined whether or not there is exposure to one or more factors, which are studied from a hypothetical cause-and-effect relationship, in other words, from the effect to the cause [9, 10]. Figure 6.1 presents the design of a case–control study.

Recently case–control studies have been related directly to cohort studies, which enabled researchers to design new patterns for their development while obtaining major benefits, mainly from cost of execution [8].

In this regard variants have been proposed: case-cohort studies, nested case–control studies or from an at-risk group, case-case studies and studies of proportional mortality.

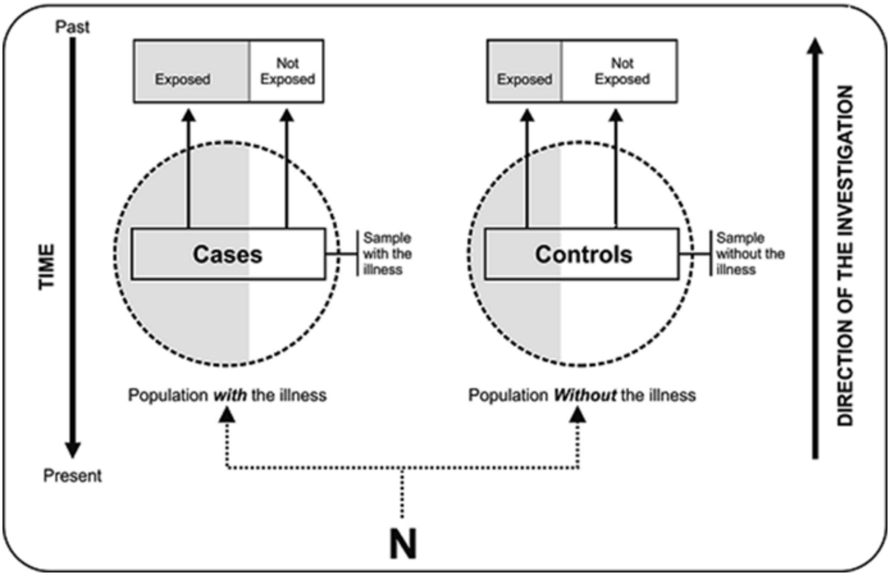

Fig. 6.1 Classical design of a case–control study

In case-cohort studies, the cases and controls are found nested within a fixed cohort that is well defined in time, space and place, estimating the cumulative incidence ratio, since all the cohort members have the same follow-up time. An example of this design, is depicted in a study where 100 patients consecutively submitted to a colon (n = 44) or rectal (n = 56) resection, the current practice of liquids being administered intravenously, as well as administration of sodium after the colon and rectal resection was assessed [11].

Nested case–control studies, or those of an at-risk group, use sample patterns known as the group at risk, in other words, the case that is chosen is found within the group of those exposed. This design is recommended for the study of infrequent illnesses, in dynamic cohorts in which determination of exposure and its changes through time in all members of the cohort could be very costly. An example of this is a study carried out in Denmark where medical records from the years 1989 to 2008 were examined, in which the effect of metformin on the risk of breast cancer was evaluated among pre- and post-menopausal women with type II diabetes mellitus [12].

Case-case studies serve to respond to what a particular individual was exposed to–in an unusual way– even before the disease or event has appeared. In this type of design, the individuals serve as their own control group. An example is a study that evaluated the development of acute myocardial infarction incidence according to the presence of intense anger two hours previous from a heart attack in two paired self-controls [8, 13].

In studies of proportional mortality, the cases are defined by the deaths, these are taken from a population source, while the controls are obtained from the deaths that occur in the population base but are not related to the exposure. In the study carried out by Freedman et al, death certificates were used to explore whether mortality due to multiple sclerosis was inversely associated with sunlight exposure [14].

6.3 Selection of Cases

It is necessary to have an operating definition of the event or illness to be studied before making the selection, in order to separate the cases that qualify in the category pre-defined [15].

An example of the case definition is that of sarcopenia in older adults. In the study by Baumgartner et al. older adults were considered to be sarcopenic if the value obtained was less than or equal to two standard deviations from the average of the appendicular muscle mass of a representative population of younger adults (18–40 years of age) [16]. However, there is an ongoing debate on how to define this entity.

Another option that may be used to define a case operationally is to use a commonly accepted definition –in the best scenario consensus. For example, the use of diagnostic criteria from the Diagnostic and Statistical Manual of Mental Disorders of the American Psychiatric Association, fourth edition (DSM-IV) to identify cases of severe depression disorder in older adults [17].

Once a definition is established there are several alternatives for selecting the cases. One of the best options is to include the cases according to how the event is presented or diagnosed, a strategy called "incident cases." This type of selection is similar to a cohort study, since it would include representation of all the events or illnesses of interest in the population from which they were obtained [18].

Another strategy is to choose older adults with the illness or existing event to be studied. These are called "prevalent cases." One disadvantage is that it will include episodes with higher survival, and it is possible that the risk factors of those older adults might not represent all of the old people with the illness or event being studied. Another drawback is the memory bias. Moreover this selection strategy makes it difficult to identify the population from which the cases come, and from which the control group will be obtained afterwards [8].

When records of a population on a particular event or illness are available is possible to draw the cases from this database. The most common way is to take a sample and not all of the cases, except for rare events or illnesses. In order to have enough cases of an illness or a rare event, it will be necessary to take both the incident as well as the prevalent cases, but they must be previously analyzed to ensure that both the prevalent and incident cases are from the same population; otherwise there would be a danger of obtaining erroneous conclusions [9].

It is possible to implement an strategy of case selection from a clinical setting, particularly if it is possible to ensure that all, or at least the majority of the older adults with the event or disease in the study are cared for in an specific hospital, and that the population from which they come from can be identified appropriately [19].

An example of a selection sample of a clinical setting is one reported by Suzuki et al., where the risk factors for hip fracture in older adults in Japan were studied. It was guaranteed that most of the hip fracture cases were diagnosed and treated in 21 hospitals included in the study, given that they covered 80 % of the Japanese population in 1989 [20], an essential feature when a clinical setting is chose for selecting cases.

It should be kept in mind that the validity of case–control studies resides in the condition that the cases included adequately represent the histories of exposure in all cases, in order to avoid selection bias, and that those histories of exposure have been recorded correctly to avoid information bias.

6.4 Selection of Controls

Before selecting controls it is necessary to identify the population from which the cases were drawn. It may be considered that the population is defined by all those older adults who have developed the event of interest, and would thus be seen as cases [9].

The selection of controls must be independent of whether or not they are exposed, to ensure that they adequately represent the population of origin. This could be achieved provided that the condition of exposure does not determine whether or not an older adult is included in the study as a control. This means the sample fractions must be the same for the exposed and non-exposed controls, which is complicated considering that most of the time these sample fractions are not known [8, 9].

The probability of a subject being selected for the controls should be proportional to the time the subject remains eligible for developing the event or illness being studied. In other words, if an older adult migrates or dies during the study he or she should no longer be eligible as a control. One way to cover this issue is to select a control from the eligible group each time a case is identified or selected; this is known as selection by at-risk group. Using this selection pattern ensures that the controls are at risk of developing the event at the time frame from which they are selected. This pattern also indicates that an older adult selected as a control at an early stage of the study might also be selected as a case in the later stages [8].

6.5 Advantages and Disadvantages of Case–Control Studies

The case–control study is the appropriate choice and at times the only alternative for studying diseases of very low incidence in older adults, such as systemic lupus erythematosus in men. This is due to the possibility of identifying most cases of a disease in a specialized hospital and subsequent research into its possible causes, which in this example could be due to the consumption of medications [21, 22].

In cohorts study it would be necessary to observe a very large number of older adult men to identify the few incident cases of systemic lupus erythematosus within a population. It could place the older adults at risk for consumption of medications, particularly those who consume ticlopidine [22], which could induce the development of systemic lupus erythematosus. This would make it very inefficient, since enormous resources and time are invested in the follow-up of older men adults who remain free of the illness.

In the case of diseases that, while not being rare, have a long latency such as the study of the risk of urinary tract cancer due to consumption of tea in older adults, is useful to design case–control studies. This is because the cases identified have already developed the illness and there is no need to wait for the time between the exposure (tea consumption) and the signs of the illness (cancer of the bladder and kidney), which could last for several years in a cohort study, and does not imply risk for older adults [23].

With this type of study it is possible to explore a broad range of related exposures to illness, such as risk factors for fractures from falls in older adults [6]. Another important advantage is that they require smaller samples and are less costly than experimental designs or cohort studies [8]:

It can also be used in the development of population-based procedures or interventions, as was the evaluation of clinical efficiency in older adults of an anti-pneumonia vaccine against pneumonia [24].

Among the disadvantages or drawbacks of this type of study is that it can only provide information about the event or target disease in the population that has been selected for carrying out the study.

Unlike the infectious processes, the causal agents are not known in many chronic illnesses, so diagnosis may be difficult and the difference between sick and non-sick is not straightforward. The long latency characteristic of chronic disease determines the interaction of many environmental and constitutional factors, so that defining the moment of exposure for any one of them with precision becomes a complex task [25]. Another factor that complicates cases identification (incidence) is that the moment of appearance of the clinical signs after exposure to the risk factor is not definitive, and also varies from one individual to another. This type of study presents higher chance for bias and erroneous inferences compared with other designs. Memory bias in classifying exposure is present when using the information the subject brings to the study, which in this case is of the older adult [8, 9]. It is fairly known that memory loss in older adults is produced by cognitive changes associated with normal aging [26]. It has the potential for memory bias by making use of the information that provided by older adults. One solution could be to use the help of a reliable informer (spouse, child, principal care giver) –also known as proxy interview, which is not free from flaws. Another disadvantage is not having a population base, so that incidence and prevalence cannot be estimated directly [2]. Table 6.1 presents a summary of the advantages and disadvantages of case–control studies.

Table 6.1 Advantages and disadvantages of case–control studies

Advantages
Studying uncommon events and illnesses, or those with a long latency period
When an estimator of prior risk is required for development of a prospective study
Faster to carry out
Lower cost
Fewer individuals required
Records as sources of information may be used: medical records, hospital discharges, morbidity statistics (potentially), specialized medical records (cancer, other chronic illnesses), records of epidemiological monitoring systems, death certificates or their equivalents
Pose no risk to individuals
Allows the study of multiple potential causes of the event or illness
Evaluation of procedures or interventions from a population base (screening programs, immunizations)
Health problems that require relatively fast treatment
When the prospective exposure or approach may be unethical
Disadvantages
Depends on the memory of individuals or records of information to determine past exposures (memory bias)
Data validation could be difficult or even impossible
Higher chance of selection and information bias
Not suitable for estimating prevalence and incidence of the event or disease
Time sequence between exposure and disease is not easily established
Unusual to achieve detailed study of the causal mechanisms

6.6 Conclusions

In the planning phase of research related to age and aging, the quality of knowledge derived from epidemiological studies, depends heavily on the solidity of the methodological design and the strategies for collecting data designed to answer the research question. Case–control studies are a cost-effective alternative for providing a valid and reasonably precise estimate for identifying an association force of a hypothetical relationship cause-effect in studies related to older adults population.

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Chapter 7
Longitudinal Studies

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Abstract The Science never before faced such a complex, dynamic and time-dependent process as human aging. Longitudinal studies are a source of fundamental evidence of the multi-factor changes over time, especially those that have contributed to understanding the aging process through research questions related to the course or prognosis of physical or cognitive functioning of the elderly, exposure to comorbidity, health conditions, and biological, environmental, social or emotional negative or positive factors, as well as other questions related to aging.

However these studies have major methodological challenges to keep the validity of information between standardized measurements and the generalization of the results, especially with the loss of participants due different causes. These difficulties motivated the realization of this chapter where we discussed the role of the longitudinal studies in the study of aging, beginning with methodological concepts, the importance of this design in geriatric research and the direction of new research questions, we present also a review of classic longitudinal studies from the literature, which enable us to provide examples of scope and methodological implications, and finally we suggested some strategies about strengthen the validity and generalizing of results.

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Longitudinal methodology represents a fundamental pillar in geriatric research. Its implementation always must to be supported by good planning that takes into account-standardized procedures as well as techniques that minimize the probable losses during the follow-up to minimize their effect throughout the study.

Keywords Longitudinal studies • Longitudinal-research • Follow-up studies

7.1 Introduction

The aging of the population is one of the most remarkable success stories in social development and human health. However, scientific understanding of the aging process has not developed at the same rate as the growth of the generations of older adults and their special health needs.

In this context longitudinal studies take on special importance, especially those that have contributed to understanding the dynamics of the aging process by analyzing physiological, psychological, social or environmental variables [1] that are time variant. These designs have yielded results on successful aging, longevity, frailty and other traits. Thus geriatric research has been nourished by a diversity of studies of an observational and especially a longitudinal nature, oriented to responding to the lack of knowledge about the latent changes in different generations of older adults, and posing new questions about exceptionally healthy old populations linked to the traits of robustness and functioning, in contrast to populations that are frail or disabled/dependent, with or without chronic degenerative illnesses [2].

The present chapter will be concerned with discussing the role longitudinal studies play in the study of aging. First it will analyze the theoretical concept of the longitudinal study, and then it will highlight the importance of this design in geriatric research and the direction of new research questions. In the second part we present a review of classic longitudinal studies from the literature, which will enable us to provide examples of scope and methodological implications, in order to offer some strategies to strengthen the validity and generalizing of results.

7.2 Theoretical Concept of Longitudinal Studies

The broadest notion of longitudinal studies refers to the analysis of a particular sample of individuals who show time-dependent patterns of change (variables of interest), which require the presence of three conditions: (1) that the data be collected during two or more distinct time periods; (2) that the sample elements (individuals) are comparable from one period to the other; and (3) that the analysis involves comparison of the data between two or more time periods [3].

Given that various types of both observational and experimental studies may be framed under these conditions, it is proposed to distinguish them according to the way in which the measurements are collected, the entry of the individuals into the study, the type of information desired [4], and how the differences in each design make them independent. Thus the present chapter will be limited to showing general aspects of observational longitudinal studies, since experimental studies like clinical or quasi-experimental trials form part of a review presented in another chapter.

Within the theme that concerns us, observational longitudinal studies may be classified according to the way the information search will be oriented. We present the way most studies related to aging have been conceived and that are worth mentioning in relation to their particular characteristics. Thus we find among others, those of the type panel, trends and cohort studies. The latter is considered to be the main longitudinal study for epidemiological research.

Given the different perspectives that exist for understanding the designs of the study, we present below the most frequently accepted structure and characteristics of each one:

Panel studies [5] obtain information by repeated measurements of the same group of individuals over fixed periods of time. This kind of study represents the conceptual base of a census or national survey carried out within the same population, with certain time periodicity to answer questions about the change of latent variables through time. It is also used to distinguish permanent characteristics from transitory ones of a specific phenomenon, analyze the life conditions of a group being studied, or differentiate intergenerational changes that are presented in a stage of life. These could be functional dependency, retirement from the labor force or characteristics of longevity in a population, as well as others.

One of its main weaknesses is that the sample responses could be subordinated to a "period effect," caused by an unexpected event or general circumstance (epidemic, climate change, or civil unrest, for example) at the time of the measurements, which could change the responses issued differentially among the subjects of the study. As well, the panel study could have a significant decline in the number of responses in each cycle of information collection, losses which would have a cumulative effect on the study's variables. This is related to the progressive loss of members of the sample during the course of the study [5], a phenomenon common to any longitudinal study. These losses have to be given special consideration in studies on aging, where it happens more frequently, since the losses are related to events such as change of domicile, death, hospitalization of the participant, or a decision to stop participating. It causes the sample to get smaller in each measurement period, a phenomenon called "panel fraying" or attrition. Given the importance of this possibility it will be described in more detail at the end of the chapter.

Trend designs [5] differ from panel studies because they analyze changes through time of different individuals in each evaluation period. With this characteristic, the data collected are analyzed collectively and not individually. Thus, as the name indicates, the information analyzed enables researchers to predict future trends about the individuals or the study universe, and the prediction variables may be evaluated through time. In this type of study unforeseen factors in the sample subjects are not considered, but the results may be easily influenced by other time-related variables not taken into account. For this reason, this type of design must be clearly delimited and the information collection strategies must be strictly replicated in each measurement period.

Lastly, the *cohort design* [6] is the longitudinal study most used on epidemiology and clinical research, since it is thought to be closer to experimental studies in terms of the search for causality and scientific evidence [7]. However, for the social and demographic sciences the cohort study represents the measurement of differences or changes in a population (or group) selected according to a common condition or experience where the main point is rooted in analysis, together with the population and the magnitude of the time-dependent change of events, which is often defined by the researcher [3]. This definition has a common denominator with other scientific areas, in that the longitudinal data are compiled in a time sequence that clarifies the direction as well as the magnitude of change in the variables. For epidemiological and clinical research, the cohort design makes it possible to check for a cause-effect association through time between the course of an exposure and an outcome of interest (event) that is produced over a period of time, where each subject makes an individual contribution [8, 9]. Like the other longitudinal studies, its objective is to describe the occurrence of time-dependent results [9], but the scope of this type of epidemiological study is related more to the incidence or occurrence of phenomena from the composition of the groups for an exposure variable that is present or absent among the subjects being studied. It follows through time in a prospective or retrospective manner up to the appearance of the event of interest. It should be mentioned that retrospective cohort studies are not discussed in this chapter. This is because, in relative longitudinal studies on aging, there are few variables that might respond to complex questions related to time changes, and the exposure events of interest occurred in the past, in other words before the study was begun. That is why the researcher does not have control over the nature and quality control of prior measurements or over data that could be important for a specific question and that were not gathered in the past. For that reason the study of diverse events in aging such as functioning, cognition, memory, depression, levels of physical activity, changes in body composition and others requires a prospective methodology that allows the researcher to include changes in the present time from their identification in repeated observations, for periods of time established by the researcher or until an outcome of interest is presented.

It must be taken into account that older persons differ from other types of populations in several ways. With this in mind, we present a proposal outline of scenarios that could be represented in a longitudinal study within the scope of research on aging. This outline was prepared taking as a reference the proposal of Fuller for the study of falls among old people [10] and the analysis of levels of complexity present in geriatric research among different populations of old people by Faes et al. [1].

Figure 7.1 starts by identifying variables to be evaluated in the study, both in the population of interest or group being studied and in the comparison group. At the start of the study (present time) initial measurements are made that enable the researcher to define the state or presence of specific variables, to show later the

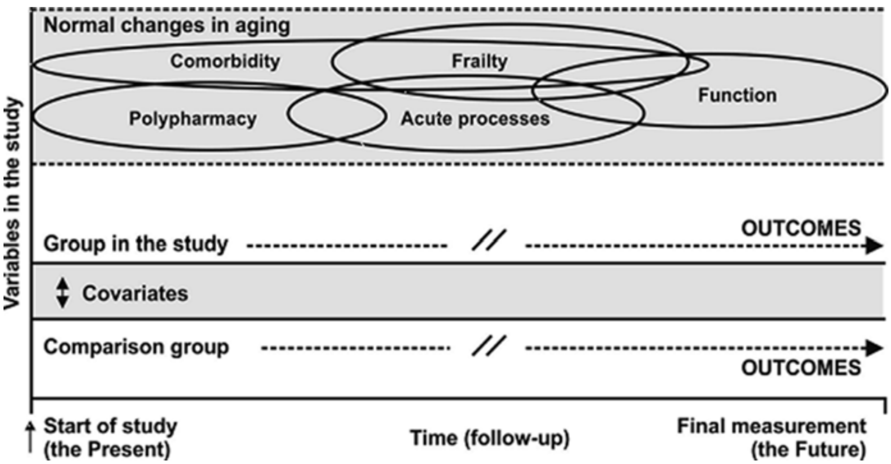

Fig. 7.1 Proposed outline of the scenario of a longitudinal study on aging

change of the variables of interest or new outcomes differentiated between the group being studied and the comparison group. This makes it possible to identify causal relationships between individuals with or without a specific risk factor (cause), and to attribute the changes related to the outcomes (effect). Different covariates or potential confusing factors that could interrelate among the groups in the follow-up are evaluated in parallel, as well as the presence of normal changes in the process of aging that are present and interconnected throughout the study in such a way that, if the perspective of aging in these studies were not considered, they could establish spurious and non-causal relations between the initial state of the variables of interest, their exposure, and their final outcomes [11, 12] (Fig. 7.1).

A clear example of the theoretical concept of this design is presented by the Canadian Longitudinal Study on Aging (CLSA) [13]. It is considered one of the most important studies in present and future geriatrics because it has the possibility of following up a representative sample of the Canadian population over 20 years, and will evaluate many medical and non-medical factors in the aging process (biological, psychological, social, lifestyle and economic). It will analyze how illness, health and well-being are influenced in older adults, and thereby achieve a better understanding of aging. The study began recruiting men and women between the ages of 45 and 85 years in 2010. Its Internet page announced in July 2014 that it has the first 40,000 subjects and its goal is to include a total of 50,000 participants to start the follow-up.

7.3 Advantages and Disadvantages of Longitudinal Studies

Longitudinal studies present important advantages over other observational designs (Table 7.1). It makes it possible to evaluate the incidence of a particular illness or outcome, and helps when investigating potential causes of a possible outcome,

Table 7.1 Advantages and disadvantages of longitudinal studies

Advantages	Disadvantages
Establishes cause-effect relationships in real time	No differential classification for lack of control in assigning of the exposure
Reduces the presence of biases between exposure and the event	Selection bias through losses during the follow-up (morbidity or mortality of the seniors)
Evaluates measurements of incidence of an event	Interdependence of time and variables related to the exposure and/or event
Observation of multiple results related to an exposure factor	Frequent use of key informants (proxies)
Efficient for unusual exposures	Complicated for infrequent events that are presented over a long period of time

whereby evidence is shown from the follow-up of exposed and non-exposed subjects at the moment they present an event being studied for the first time, or when it is modified by action of the exposure. In addition, it reduces bias between the exposure and the event when observing these sequentially. This type of design allows researchers to evaluate multiple results that could be related to the exposure factor [12].

Longitudinal studies in the senior citizen population have helped with the understanding of the many complicated relationships among primary and secondary risk factors and health outcomes. Given that older adults have an increasing risk of adverse outcomes (of death and disability, for example) compared with other age groups, and numerous physio-pathological processes can be almost simultaneous, longitudinal observation of the facts during aging is of great value for scientific research [1, 2].

On the other hand, longitudinal studies share the disadvantages of observational studies if they are taken as the gold standard in the search for causality in clinical trials. The interpretation of causal relationships can always be limited by the presence of many confusing variables. Other disadvantages are the lack of control in allocation of exposure (the realm of experimental studies), which could bring about differential biases in factors related to the occurrence of the event within the exposed and non-exposed group [8, 13] and lastly, the follow-up brings with it uncontrollable losses for the researcher.

In studies based on the older population, the final statistical power of the sample is often affected for a number of health-related reasons. These could include problems like mortality rates of up to 20 % per year if people older than 70 years of age are included, hospitalization and reports of illness, disablement and accidents, all of which commonly account for high rates of non-response and therefore losses for the study. As well, unlike what is likely to happen with other age groups, there may be causes of a social nature that could affect the quality of the information between measurements such as: changes of domicile, given that old people often move from one house to another since they depend on their support and care network, or frequent changes of a key informant with consequent difficulty in obtaining consistent and valid information.

The definition of "baseline evaluation" could also constitute a serious dilemma when dealing with old people. This is because of a complex interdependence with time and relationships among individual factors and measurements of results that could fluctuate even at time zero in a study, involving the exposure factor and the event being studied, along with other associations of change. These must be taken into account for an adequate interpretation of the results. Thus, when working with older populations the causal relationships are multiple and bi-directional, and the qualification of exposure must be identified with care, based on a solid theoretical framework.

The changes or modifications in the exposure factor or added variables that influence the exposure as much as the event of interest through time require broad and organized field logistics as well as more financial resources to maintain the cohort [8, 14]. Despite the advantage of being able to study several results, they could turn out to be difficult to analyze when one result produces a secondary one, and so on.

In some cases, the chain of causality is not clear or there is no conceptual consensus about certain topics, as is the case for issues like geriatric syndromes, frailty and the sequence between functioning and frailty. The inefficiency of longitudinal studies for studying "rare" or "low-frequency" events is an important point when discussing the senior citizen population. This means data collection requires extended periods of time during which the possibility increases of encountering correlated events that make it difficult to define the predictive factors. For that reason it is fundamental to analyze clearly the type of topic that can be evaluated using this methodology, as will be discussed later.

7.4 The Importance of Longitudinal Studies in Research on Aging

It is a fact that aging and its relationship with demographic, social and technological changes have created important knowledge needs at every level, especially in the area of health. An example of this is the longitudinal study of several pathologies with aging that break the classic patterns of its natural history compared with younger generations [2]. Another is the study of variables that have a positive impact on the health of senior citizens for achieving longevity or successful aging or failing to do so, and the presence of events such as loss of functioning, cognitive deterioration and frailty. These studies help to meet the need for understanding aging from different perspectives [15–18].

With respect to the evaluation of interventions, although controlled clinical trials provide most of the evidence for evaluating their effectiveness, this type of design faces important ethical and logistical dilemmas, especially when evaluating older populations [18]. The presence of cognitive deterioration, multiple morbidity, polypharmacy, and other factors are variables that often limit the inclusion of these participants in clinical trials, in addition to the difficulty encountered when using a proxy to obtain informed consent [19, 20]. For those reasons observational follow-up of interventions added to the normal care of old people represents a viable alternative to carrying out clinical trials, where longitudinal evaluations of programs is especially important.

7.5 Methodological Scopes and Implications of Longitudinal Studies of Aging

Longitudinal studies have made important contributions to understanding aging [18], with research questions related to the course or prognosis of physical or cognitive functioning of old people, exposure to comorbidity, health conditions, and biological, environmental, social or emotional factors both negative and positive. One point that has also attracted much interest is the scientific history of large-scale longitudinal studies in which groups from young populations have been included who are evaluated right through until they reach old age, thus providing evidence of latent changes over time and the multiple relationships with their environment. Those contributions base their knowledge about the course of life in the older population not only on the demographic evolution of the cohorts but on biological changes, roles and socio-cultural needs presented through time and dependent on the different stages of development of human beings from birth to death [21, 22].

To analyze the changes caused by aging over time and the relevant issues for that stage of life, a systematic review that included 51 longitudinal studies of aging was taken as a reference point [22], identified from the data base of longitudinal studies of the United States federal government's National Institute on Aging (NIA). This enabled the researchers to establish six non-exclusive topics of frequent interest. In 44 % of the studies questions were asked about cognitive function, 51 % on health and physical performance, 55 % on socio-economic status and 63 % of the cases analyzed predictors of multi-morbidity and mortality. However, it is interesting that areas considered important such as health costs or genetic factors were not reported among the most frequent themes.

The authors of this review postulate that the guidelines of the longitudinal studies on aging should be broader to provide strategic information on health systems for the care for old people. Table 7.2 summarizes the topics identified by the authors as being those most frequently considered in the studies didactically included in their review. For this chapter issues are included in place of variables or measurement scales as expressed in Table 7.3 of the original article. Despite the fact that the topics are analyzed relatively frequently, their relationship with other variables is reported less frequently. This is the case of the impact of cognitive decline in the results on health and the use of services, or the effect of social determinants on quality of life. As for clinical questions, what stood out was those biological variables that could become predictors of morbidity-mortality as metabolic, hormonal, immunological or other measurements that require time-dependent analysis.

Table 7.2 Topics related to longitudinal studies on aging [22]

Topics identified	Related sub-themes
Cognitive function	Age and mortality, cognitive deterioration, mortality and quality of life, use of services and results in health, social roles
Socioeconomic status	Relationship between functional condition and morbidity-mortality analysis among self-perception of physical health, age, sex and conditions of life
Health and physical performance	Functional association performance and decline of health condition, disability as a predictor of mortality, gait speed, grip strength and balance. Index of body mass associated with coronary illness, falls, cognitive deterioration, hospitalizations and mortality
Predictors of morbidity- mortality	Relationship of the state of health and mortality, as well as markers of Inflammation (CRP, IL-6) as predictors of morbidity-mortality
Costs of health care	Individual effects relative to social networks, association between illness and dependence, health care of the old person and its impact on frailty and mortality
Epigenetics	Genetic causes of aging, status of health and genomic sequence associated with the state of health, APOE and risk of dementia

CRP = C-reactive protein, *IL-6* = interleukin 6

Table 7.3 Longitudinal studies on aging

Study	Population	Follow-up	Objective
MHAS [23] Mexican Health and Aging Study	n = 15,402 50 or more years of age	2001–2003 2012	To obtain information on various characteristics of the objective population living in Mexico
BLSA [24] Baltimore Longitudinal Study of Aging	n = 1,200 Healthy subjects 20 years of age or more	1958-to present	To describe functional and physiological changes that occur in the aging process, predictor factors of healthy aging
ALSA [25] Australian Longitudinal Study of Aging	n = 2,087 70 years of age or more	1992–2010	Relationships between health, functioning, use of services, social networks and economic resources
ELSA [27] English Longitudinal Study of Aging	n = 11,391 50 years of age or more	2002-to present	Multidisciplinary approach related to health, well-being, financial and social resources, quality of life and DNA to correlate the samples with epidemiological data

DNA deoxyribonucleic acid

To exemplify the approach and methodology of longitudinal studies in aging, we present below a review of some of the projects that we believe to be representative of this type of study [23–27]. We should mention that the examples presented correspond to follow-up studies more than to the classic epidemiological cohort design that include the definition of an exposure. A brief summary of these studies is presented in table 7.3. The central themes are similar: identifying functional, social and environmental variables as predictors that change outcomes in aging. The average time of follow-up was 10 years. In Mexico the study with the longest follow-up is the Mexican Health and Aging Study (MHAS) [23] with three measurements over 11 years. The longest study is the Baltimore Longitudinal Study of Aging (BLSA) [24] at 54 years; it is also the longest of its kind in the United States. The Australian Longitudinal Study of Aging (ALSA) [25, 26] carried out a total of 11 measurements on its participants over a period of 18 years. With respect to the populations selected, only the English Longitudinal Study of Aging (ELSA) [27] and the MHAS took representative samples from their country of origin. The average age of the cohorts when they entered the study was 50 years, except for the BLSA, which included healthy volunteers of 18 years of age or more to recreate the normal course of aging over time, in contrast with the ALSA, which started with senior citizens 70 years of age or older.

As for methodological aspects, the ELSA included five measurements at two-year intervals, the first one in March 2002 with 11,391 subjects and their spouses (n = 708), chosen from the base of participants in the Health Survey of England (HES), a transversal survey carried out between 1998 and 2001. The criteria of eligibility were: having been born before March 1, 1952, participated in the HES, and lived in a private house at the time of the first measurement; the last measurement was done in 2011 with 10,317 subjects, with a response rate of 78 %. The lack of response was minimized from subsequent imputations. In the BLSA, the first transversal measurements were done in 1948, and ten years later it was integrated the first measurement of the cohort that started with 1,200 healthy volunteers 18 years of age and over; between 1958 and 1998 there were 2,264 participants. This study was conceived as an active cohort with transversal measurements every three years and the entry of new participants. Despite being the study with the largest biological data bank, its sample is not representative.

The ALSA is a classic example of longitudinal studies in adults 70 years of age or older in Australia, but despite the fact that the population was taken from a random sample from the electoral data bases and stratified by age and sex, the size of the sample was not representative of the population. This study included 11 measurements starting form a baseline measurement done in 1992 with 2,087 participants. The sample shrank over the time of the measurements and by the eighth measurement the population was 349 participants. Compared with the other studies analyzed, it had the largest attrition rate of response, with mortality being the most probable event for the subjects in the cohort.

Lastly, the MHAS is a panel study representative of the Mexican population of subjects born in 1951. The purpose of this study is to evaluate the aging process of the Mexican population, especially changes in morbidity, disability, intergenerational transference systems, migration and economy, for which measurements were carried out. In 2001, 15,402 interviews were completed, directly or with a proxy, with a response rate of 93 %. In 2003 the survey included 14,386 subjects, and in 2012 it included those interviewed in 2003 plus a new sample of persons born between 1952 and 1962, for a total of 18,465 persons, with one measurement more planned in 2015.

7.6 Strategies for Improving the Validity and Generalization of Longitudinal Study Results

One of the objectives of the longitudinal studies is to recreate, from an initial exposure or measurement, the natural history or trend of an illness or event at the time it occurs. To do that, measurement stages are established that enable the identification of changes in a particular group that is followed through time [19]. Most phenomena related to aging are time-dependent [18, 28], as much in their appearance as in their duration, so it is necessary to predict the changes over time or the cumulative effect of multiple associations with respect to the intervals of the measurements done, for example variables associated with functional or cognitive decline, or predictors of morbidity-mortality or frailty.

Another peculiarity of longitudinal studies in geriatric population is the speed of change of age-related variables that might be presented in cutoff periods or jump between subsequent measurements. Thus the basic threat to this design is centered on the study's losses from any number of causes. There is a lack of response in key variables [29, 30] before the presence of unexpected adverse events that could arise in the development of the longitudinal studies, such as death, hospitalization, disability of a participant or even changes in geographic mobility, for which the data are lacking, and so losses in longitudinal studies become a frequent challenge. For this reason, prior to the start of the study, strategies for containment of losses should be established, such as strategies of quality control and retention that minimize these problems and ensure the validity of the information.

This phenomenon of losses during the course of a study is known as attrition or wearing away. It affects the sample size and makes it difficult to calculate the estimators, such as making an adequate statistical inference. As well, it could result in selection bias when the participants who remain in the study present conditions different from those who were lost. The causes of attrition in studies of old people are often related to death, hospitalization or disability that occur when the participant cannot be evaluated during the measurement period. However, the participants might reappear in a third or fourth measurement, so that subsequent analyses could be more complex [31].

On the other hand, the missing data could be due to a general pattern when a participant refuses to participate. Or, it might follow specific patterns when the individuals fail to answer specific questions, or when the interviewer does not properly follow the steps for questioning, or the data capture process is wrong. For that it is necessary to analyze some variables that make it possible to contrast them with the sample in general, and could be estimated if the absence of data affects the internal validity of the study [30, 31].

There are strategies that could be planned and executed during fieldwork, such as home visits, telephone contact, or the incorporation of interviews with proxy informants such as primary care givers or the participant's spouse, who could provide responses close to what would have been given by the participant. Fieldwork could be enriched by using retention methods (positive messages, contact on important dates, information on the progress of the study, etc.) with the goal of minimizing the fatigue of staying in a follow-up over many years. A special element when working with older populations is offering the profile of interviewers, which demonstrates interest and empathy with the interviewees. It is thought to be useful in retaining subjects if the same interviewers are present during the different measurements, since that could create a climate of confidence with older adults and avoid rejection in subsequent measurements.

With the real possibility of failure to get information or sustaining losses during follow-up (whether they are occasional or constant), analytic strategies are required that reliably estimate the measurements made. However, it must be kept in mind how important it is to plan a study of this magnitude properly, especially in key sections that will be tied to the occurrence of losses, as well as including supervision strategies of data quality that enable later analysis to minimize the losses.

7.6.1 Sampling and Sample Size

It is crucial to make the right decision on how the sample in the first measurement will be set up, since errors committed in this phase will be very difficult to correct later. In this sense it must be ensured that each sample unit or individual is chosen randomly from the sample framework as a probability sample, to increase the precision of the study by being able to ensure that the samples are really independent right from the start of the study. As well, the sample size must in all cases take into account a percentage of real losses consistent with the theme of the study or area of influence of the participants. It is necessary to have a large enough number of observations, given that attrition tends to reduce the number of individuals over time, and so a size that will allow for the occurrence of said losses must be ensured. That way, the analysis may be carried out in the sub-groups of the population of interest without exposing the statistical power of the study at risk.

7.6.2 Standardization of the Measurements

As discussed earlier, longitudinal studies are based on the change of variables through time, for which the presence of random errors in the measurements represents a very complex problem, which could even overestimate the final results of the measurements. In this situation is especially useful to include not only previously validated and standardized instruments, but also to carry out exhaustive training of the field personnel, adding control questions that permit the analysis of differences at a given time and reduction of false data of change in the variables of interest, and carrying out a periodic calibration of the measurement equipment.

7.6.3 Imputing Lost Data

This requires the implementation of generalized equations, for which there are several statistical methods. In general, it is thought that in the first instance variables should be created that identify the data "without response or without measurement" in each measurement cut-off. This dichotomy of variables will serve as sub-groups within the study for the key variables, the reason for the imputation [30]. These variables must be compared between the defined times as losses (for example, an initial or baseline measurement vs. the second or third vs. the fourth measurement). This type of analysis considers the measurements between periods to be dependent, since they are from the same subjects, as happens in the case of the panel type study or the design of cohort study, so they must be seen as paired statistical tests, in order to establish whether or not there are statistically significant variations between the measurement times. If not, it will verify that the losses did not affect the behavior of the variables; otherwise, if it proves that the data do have variations between measurements, a multivariate probit model will be integrated that predicts the probability of attrition conditional on a set of variables measured in each cut-off during the study. This model identifies the common source of the data variation and is integrated as a possible response to the matrix model in seeking the most common responses. In any case it can mathematically predict the variability of the error, and if this does not have statistical significance, the data are presented as being free from error [29, 32, 33].

7.6.4 Data Weighting

This process is fundamental for an adequate estimate of the data. Reasons for the need to weigh the variables involved include the lack of responses, unequal selection of groups, adjustments in medication, and others.

Weighting involves giving each sample unit a numeric value that would be representative of its population being studied. Thus the weight of each variable in particular includes the relative value of the sub-sample it represents and the relationship between the size of the sample and the proportion of subjects interviewed. A process of statistical inference for each variable or time period involved is developed from these values. It should be mentioned that weighting in a longitudinal study could include transversal weighting (within the same measurement time) or between subsequent measurements –time zero vs. n times involved [31, 34].

7.7 Conclusions

Science had never before faced such a complex, dynamic and time-dependent process as human aging. Longitudinal studies are a source of fundamental evidence of the multifactor changes over time, which enables it to maintain the evaluation of interventions that have a timely and positive impact on the course of aging in the population.

Longitudinal methodology represents a milestone in geriatric research. Its implementation always has to be backed up by good planning that takes into account standardized procedures as well as techniques that minimize the probable losses during the follow-up and the consequent effect throughout the study. Finally, it will be expected that the results derived from the follow-up will reflect the evidence of a phenomenon present in the senior citizen population.

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Chapter 8
Clinical Trials

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Abstract Clinical trials are considered to be one of the main designs in health research and they are used primarily to test interventions in medicine. Aging research is no exception for this goal, and these kind of studies are used to test different interventions in older adults with a number of variations in this particular research. In addition to drugs, in older adults diverse non-pharmacological interventions are experimented for a wide-array of diseases and conditions that are particular for this age group. A careful design and sometimes adaptation of clinical trials is necessary to have accurate results and translate them into actions in everyday care of the older adult.

Keywords Randomized controlled trials • Clinical trials • Pragmatic trials • Sequential trials

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8.1 Introduction

Randomized clinical trials have been defined as "prospective studies that involve humans, evaluate the effectiveness of an experimental intervention when compared with a control group or standard intervention, or with two or more existing interventions; generally designed by recruiting several hundred persons and yielding evidence that could be sufficient to bring about a broad change in public health policies or in current standards of health care" [1]. Clinical trials are used for understanding the effects of interventions in human beings, such that a well-planned and managed clinical trial could be solid evidence for daily use in medicine [2]. Geriatrics is the specialty that deals with clinical care of the older adult, and is considered one of the most recently created medical disciplines [3]. That is why many interventions used in therapy for older people have been mainly empirical or derived from existing evidence from trials with younger adults. Only in recent years has the understanding of the problems and effective interventions in this age group started to be enriched through an increasing proportion of clinical trials that involve older adults, developing health care of senior citizens toward geriatrics based on scientific evidence. In addition, the range or variations that clinical trials acquire within the group of seniors enriches the possible approaches that could be made in experimental design that responds to a question being researched [4]. As well as its use in the clinic (mainly through geriatrics), other interventions could also be evaluated with these types of designs, and their application extends from the management of technology to improve the functioning, support groups, health services, and even complete systems [5].

In large part, "conventional" clinical trials in younger adults are often used to test a drug for the cure or control of a specific illness. Among old people the probability of suffering from "only" one illness is low, so they are often systematically excluded from pharmacological trials. In this age group, chronic illnesses and their different therapeutic options make them the principle users of medicines, and therefore of the data generated from these clinical trials [6]. New strategies for closing this gap should be sought in order to increase the quality of care of older adults. On the other hand, this type of design is used for evaluation of other non- pharmacology therapeutic options, such as exercise, nutritional interventions, support groups, technology (gerontechnology), education, and more [7–9].

Moreover, studies of senior citizens that evaluate complex interventions (with multiple components) are common, in contrast to conventional pharmacological clinical trials. Also, it is important to use variations of clinical trials (pragmatic trials) in this age group to evaluate existing health services (strictly speaking, this would be within complex interventions) and cost studies [4, 10]. Lastly, we must be sure to mention studies where interventions for the caregivers (above all of old people with dementia) are carried out that often have indirect repercussions on them, even if these do not apply directly to the sick persons [11].

Finally, having evidence-based treatments (either pharmacologic or non-pharmacologic), will improve the use of available interventions, diminishing the indiscriminate use of ineffective or marginally effective therapies that place older adults in a greater risk of having a deterioration of their health.

Below, we provide a general and schematic review of the theoretical concept of clinical trials and their variants, followed by examples of interventions and specific outcomes in research on older adults.

8.2 Theoretical Concept of Clinical Trials

In its simplest form, an intervention may be tested by noting the subsequent effect on the same group of persons, a design known as before-and-after (Fig. 8.1 (1)). This design has little validity due to various biases that could give a false impression of a change (regression to the mean, placebo effect, etc.). At the next level is application of a non-randomized intervention to two distinct groups (the control group

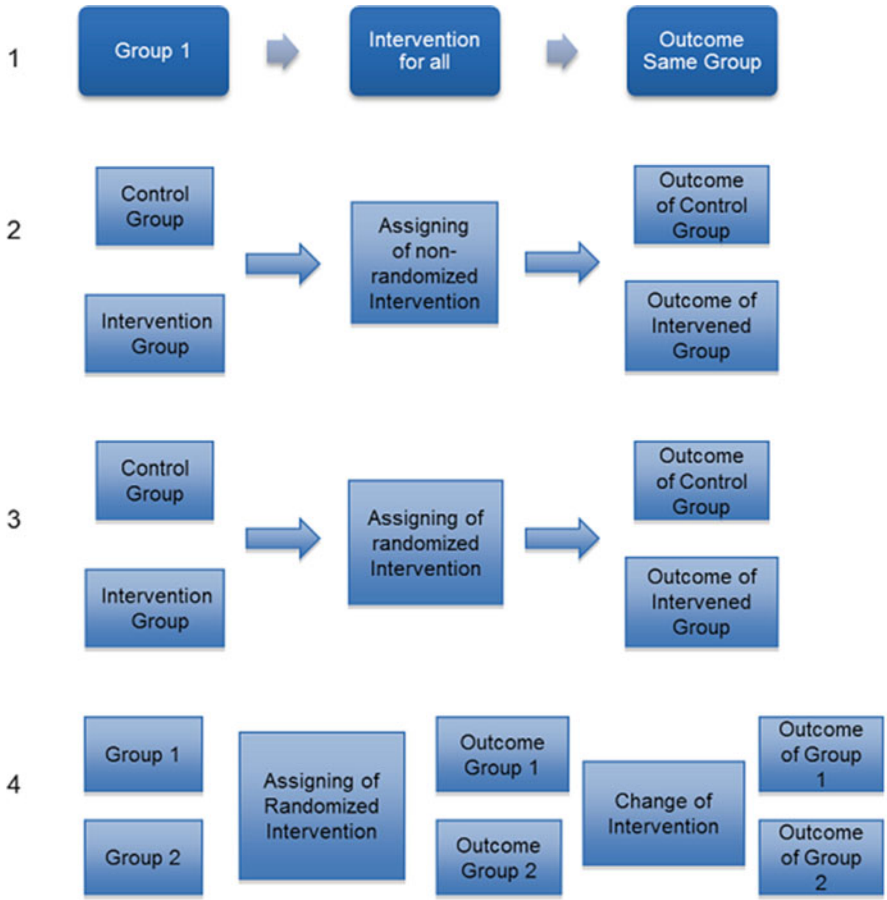

Fig. 8.1 Design scheme

and the intervened group). The main problem with this design is selection bias, since there is the option of choosing who will be given the new treatment (Fig. 8.1 (2)). The classic scheme of a clinical trial features randomized subjects for assignment of the intervention with different variants as to control of the intervention, blinding the administration of the intervention and the sequence of administration of the intervention (Fig. 8.1 (3)). This last characteristic is highlighted in the so-called crossed trials, in which all the subjects are administered the experimental intervention. One group is the study's control group at the start of the study, and in a second round it receives the intervention (in some cases with something known as the washout period, to lessen the effect of those who were submitted to the experimental intervention), and the outcomes at each of the times are measured (Fig. 8.1 (4)).

While it is thought that a clinical trial has more internal validity if the assigning of the intervention is randomized (the results generated are precise), the intervention is controlled throughout the process and the blinding is at the maximum. However, the external validity (generalization of the results at the population level) with such a rigid design could compromise it. To resolve this type of methodological problem clinical trials have been classified in two large groups: explanatory (internal validity) and pragmatic (external validity) [10]. In research on older adults, the use of pragmatic trials makes it possible to test interventions that are not possible with clinical trial; in addition, it may be possible to evaluate more extensive population groups (See Table 8.1).

8.2.1 Explanatory Studies

This is most commonly used in the pharmaceutical industry, with great internal validity but with critical difficulties at the time of large-scale implementation in population groups. Their intention is to ensure that the subject has the intervention constantly, and requires high levels of attachment to the treatment and comparison with a standard or a placebo. The assigning of a treatment is one of the fundamental points, as well as blinding of most of the participants in the study (the ill, care givers, researchers, etc.). Trials of this kind are more difficult to carry out in this age group, given that their characteristics are often associated with non-compliance with what was stated above, and therefore are not useful for preparing conclusions [12]. Although it has been used mainly for the evaluation of drugs, it can also be used in other types of interventions, such as nutrition, education, physical activity and others.

8.2.2 Pragmatic Studies

Among these studies are those with greater external validity and that imitate “real” conditions in which a therapy is implemented. Unlike explanatory studies, they are often most useful in evaluating interventions outside of the pharmacological field, such as complex interventions (multiple components that interact with each other), socio-medical, rehabilitation, physical activity, nutrition studies, etc. [13]. The evaluation of care systems is one of the main uses of this type of trial, since for a

Table 8.1 Differences between explanatory trials and pragmatic trials

	Explanatory trial	Pragmatic trial
Recruitment	Direct recruitment, in general does not consider the service provider	If randomizing is used for groups, the patients and the service providers are used. This involves having consent and baseline data from both
Selection criteria	Strict criteria to lower the probability of confusing factors that have an impact on the outcome (like illnesses)	Try to be as inclusive as possible to improve the possibility of generalizing the outcomes
Randomization	Randomizing by participant	Randomizing by groups is often necessary, especially for replicating real clinical scenarios
Blinding	Double blind is considered obligatory	Blinding must be done wherever possible, but the nature of the intervention generally doesn't permit it. Blinding the surveyors, analysts and baseline data collection before randomizing could lower the bias for lack of blinding
Intervention	Frequently a single simple activity (taking a medicine)	Frequently involves a complex activity of interaction between patient and doctor. The doctors need only a few light instructions to carry out the intervention.
Control	Usually a placebo	Usually standard care
Contamination	Avoided with blinding	The randomization of groups can lower its occurrence but not avoid it
Evaluation of attachment	High levels of attachment are required	Efforts to achieve attachment to the intervention are made; however, it should not exceed what would normally be done in the clinic. On the other hand, the attachment is analyzed as an outcome and could indicate that an intervention is not useful on a day-to-day basis
Size of the Sample	Standard statistical fixing	The effects of randomization in groups should be taken into account for the calculation. Consequently, a higher number of subjects is required to reach sufficient power
Outcomes	Frequently specific	Also very specific. Some secondary outcomes are used to try to explain the effect of the intervention.
Analysis	Univariant and multivariant analysis are standard	Take into account in the randomized analysis of the group, since the outcomes of a group could be similar for the medical effect
Potential dangers	The attempt to have purity	The attempt to reach a generalization could result unfeasible

particular system that is already established, it promotes the evaluation of what could be without having control over the intervention but rather with an evaluation of its process and the determination of its components to be able to learn the potential measurers of efficiency (or not) of the same on a determined outcome [14].

8.3 Interventions

8.3.1 Pharmacological

The use of medications in this group of population is well known, where some people routinely consume more than five medications and the average consume more than two. This, unfortunately, is generated with evidence from other age groups (Fig. 8.2).

As mentioned earlier, there are several ways to divide the group of senior citizens. However, the generation of new drugs must define the function of that division; in other words, medication for the chronically ill, for the disabled, and for those who are frail; and the second condition is the effect on each group of the medications on the chronically ill, the disabled and the frail.

There is evidence of exclusion of the older group from the clinical trials of the pharmaceutical industry [15] and in publicly funded trials. An example of the lack of balance between existing need and the creation of products for this need is the proportion of subjects with cancer, which in countries like the United States is as high as 63 %, while clinical trials have a representation of just 25 %. Table 8.2 shows some of these barriers and their potential solutions [16]. In a recent review of clinical trials for senior citizens, Lindley calls for the inclusion of frail subjects in all pharmacological clinical trials; however this always represents a risk, given the

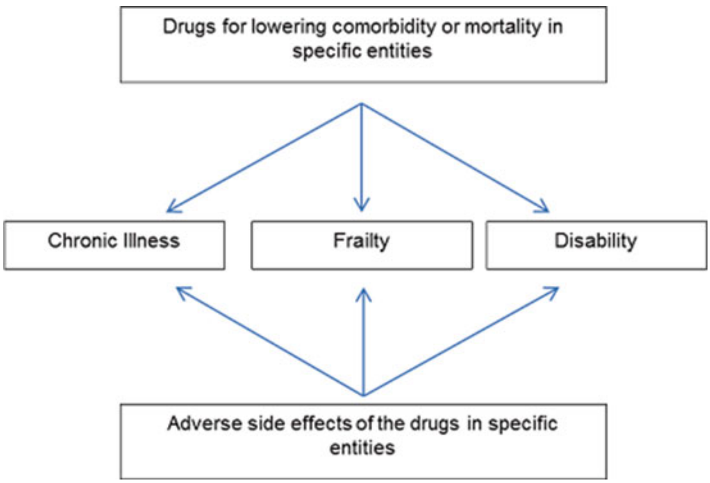

Fig. 8.2 Spectrum of pharmaceutical clinical research in old people

Table 8.2 Barriers and their potential solution for the participation of older people in pharmacological clinical trials

Barrier	Solution
Potential risk of commercial use	More financing by the government of pharmacological clinical trials in senior citizens
Exclusion of subjects with comorbidity	Include them but measure Do specific studies for old people with specific pathologies (cancer, frailty)
Limitation of access to the research site	Include home visits or transportation to the research center in the logistics
Family opposition to entering into a study	Invest resources and time in information sessions
High mortality rate	This could be an advantage in some cases, where any intervention could lower the rate. It could be a disadvantage for the high rate of losses attributed to mortality; it is necessary to make an estimate of an appropriate sample taking losses by mortality into account

nature of frailty, where a priori a high level of side effects can be expected. However, this same review suggests always doing the measurement of frailty, so that the condition of the subjects included in the study can be known [12] (Table 8.2.); this should be added to already well established characterization of older adults in clinical trials such as creatinine clearance or expected survival.

8.3.2 Pharmacological "Inverses"

Given the high frequency of side effects in old people, this type of trial is designed to stop a drug and compare it with subjects that continue to use it: a drug previously identified as potentially inappropriate is withdrawn and its use is compared "inversely" with subjects who continue with the treatment, in many studies continuing to give a placebo to the group that has left the drug in which it hopes for a better outcome. This has been tested in subjects with dementia, especially with the antipsychotics, which have seen a higher frequency of mortality due to cerebrovascular events in large population studies.

An example of this type of study is called DART AD (*Dementia Antipsychotic Withdrawal Trial)*, in which patients with Alzheimer's are randomized into two groups, one that continues using the antipsychotic medication, and in the other group it is replaced with a placebo. A reduction was found in the mortality of the placebo group compared with those who continued with the antipsychotic medication [17, 18].

8.3.3 Complexes

Complex interventions have a series of processes that cannot be totally controlled, and that often are not pharmacological. One classic study of these characteristics is from the Beswick group, where an intervention with many components was evaluated to learn its effect on the mobility in a group of ambulatory old people [13].

8.4 Outcomes

In this category there isn't much debate on which outcomes should be used as effect variables in clinical trials in other population groups. However, in the case of old people, mortality, one of the outcomes most broadly used for other groups, isn't very useful with the advanced age due to the increase in the probability of death, a phenomenon that often presents a plateau around 90 years of age, where mortality starts to be equalized, and that could be observed graphically on the Gompertz curve. Among the main outcomes to test the effectiveness of an intervention on them, as well as mortality, are found to be functioning, dependence, geriatric syndromes (falls, incontinence, delirium, etc.), quality of life and utilization of services.

8.5 Conclusions

Clinical trials in research on older adults are enriched by distinct possibilities that exist for evaluating an intervention. What is of special interest is to learn these options for carrying out clinical research in this age group, so that they can have an extended reference of what could be obtained by utilizing this design on this population group.

Regulatory agencies all over the world should start recognizing older adults as the larger group of therapies consumer (either pharmacologic or non-pharmacologic), and therefore start the application of rules for clinical trials where available or elaborate legislation where there is still lack of it.

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Chapter 9
Mixed-Methods Studies

Elías Vargas-Amezcua

Abstract Mixed methods represent an alternative to the dichotomy that has been established between quantitative and qualitative approaches. The complementarity between the two paradigms can grasp the complexity of social reality in which the processes of aging and current aging itself are happening; so that the articular mixed scaffolds in research design may account for various heterogeneous components involved in these processes. Mixed-methods are related to the theoretical contributions of the complex thought, and are also a tool for understanding research as a process that requires openness, creativity and flexibility by the researcher to recognize the scope and limitations of both approaches. This makes us think that in the development of various research questions it is necessary to use different methodological tools, either to obtain information or analyze it. This section seeks to provide elements that contribute to the discussion about the feasibility and importance of research with mixed-methods, and how they articulate and complement each other. The first section presents some debates on how there is a parceled knowledge and its consequences. Later, recognizing that reality is complex, we have tried to offer elements that serve to demonstrate that it is necessary and feasible to propose approaches sensitive and able to account for this complexity.

Keywords Research methodology • Geriatric research • Mixed-methods studies • Complexity • Health in older adults

9.1 Introduction

Over a period of time, when the author was attached to the gerontologist care department of a public institution which, among the various activities, attended to cases of older persons in situations of neglect, violence and care giver overload, he gave a battery of quantitative court tests and, by means of closed interviews, designed a complete systematic geriatric evaluation that made it possible to measure and obtain

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information about cognition and health, physical functioning, social support and care giver evaluation using the Zarit and Zarit Scale [1].

Among other things, the results obtained when applying the latter questionnaire to the family member identified as the primary care giver proved interesting. This is because, even though many visits for geriatric evaluation had been made in response to allegations of conflict and precariousness of the care of the older adult, responding to the 22 Likert-type reagents that comprise this questionnaire – which could be an indicator of emotional, physical, social and economic overload – yielded little information about the context in which the care was organized, from unequal sharing of care duties among family members, asymmetrical relationships to imposing the distribution of responsibilities. The questionnaire did not allow to inquire about the absence of institutions, programs and support actions from public and private sectors for the care of disabled older adults. Nor was it permitted to observe the experience of caring or of being cared for. Finally, the questionnaire didn't provide details about conflicts arising from care or about those that have been latent in familiar relationships but who got involve when the disabled older adult had to be cared for.

With unstructured interviews and observation came relevance, as they made it possible to identify and understand these conditions, as Goffman shows:

> […] there is no group […] in which a meaningful, sensible and normal life is not revealed once it is known from the inside; and a good method of learning something about any of those worlds is to submit oneself personally, in the company of family members, to the daily routine of minor emergencies to which they themselves are subjected [2].

Thus this example serves as a provocation to bring elements into the discussion about the relevance and need for mixed methods to approach the issues of age and aging. It must be mentioned that it is relevant to work in this problem-filled field, because we find ourselves at a time of opportunity, in which demographic conditions are more favorable for prevention of the troubled conditions that older adults could be facing. But this work requires methods capable of yielding information that takes into account the material, structural, political, epidemiological, cultural, psychological, symbolic and subjective conditions in which we find within persons of this age group.

Of course, reconciling all these dimensions is a challenge that could be met using mixed methods, although it must be recognized that reconciliation and complementarity between quantitative and qualitative approaches assumes that this method is not simple and requires dialog and creativity on the part of the researcher. Thus the present section seeks to bring elements to the discussion about the need for and relevance of developing research work that yield dividends in this way.

The mixed methods are linked here with the theoretical contributions of complex thought, such that they permit an understanding of research as a process rather than a systematized procedure in which various stages follow one another as if this work were possible without being affected by the reality itself. This forces one to think that in developing the research specific questions are going to appear that call for bringing in different methodological tools, whether for gathering information or for analyzing it, questions that in fact affect the stating of the problem and the presentation of the report.

Although the automatism acquired in the research methodologies make possible the economy of a permanent intervention, it is necessary to be careful with the belief that the subject of the scientific invention acts as an automaton that obeys the organized mechanisms of methodological programming once and always [3].

9.2 The Fragmentation of Knowledge: The Dichotomy Between the Qualitative Paradigm and the Quantitative One

Morin states that humanity has succeeded in acquiring unprecedented knowledge about the physical, biological, psychological and sociological worlds. However, it is announced here that error, ignorance, and blindness progress at the same time as knowledge. These conditions are due to the mutilating way knowledge is organized and incapacity to understand the complexity of what is real. This mutilation is guided by "super-logical" principles of organizing thought, or paradigms that are defined as hidden principles that govern our vision of things and the world without our being conscious of it [4].

At present we find ourselves within the paradigm of simplification which has driven the disjunctive thinking itself. This disjunction, among other consequences, has reduced knowledge to simplification. Simplification has come about through hyper-specialization, which has imposed arbitrary borders on reality, leading us to believe that the divisions are reality itself. As well, classic science has focused its rigor and operating method on measurement and calculation in such a way that what is thought to be reality is nothing more than formulas and equations that govern the quantified entities. This simplifying way of thinking is incapable of conceiving the union of the one with the many; rather it unifies by abstraction, nullifying diversity; although it also juxtaposes diversity without thinking of it as unity [4]. Methodologically it assumes disassociation among elements and as a result it also establishes the impossibility of engaging and reflecting on them. Thus we see how it has set up a polarization in knowledge creation among the different methodologies, which have deep roots in their own social imagery, and have imposed hegemony on perspectives that is based on positivism and the use of quantitative tools.

This fragmentation of knowledge and overvaluation of the quantitative has also been described in the report that Wallerstein, developed together with the Gulbenkian Commission for restructuring the social sciences. It showed that since the nineteenth century intellectual history has been marked by the disciplinization and professionalization of scientific knowledge divided into separate knowledge groups that is, for the creation of permanent institutional structures designed as much to produce new knowledge as for its players [5].

In this process of institutionalization, each discipline sought to define what sets it apart from the others. According to these authors, on one hand they turned to mathematics alongside the experimental natural sciences. At the other extreme were the humanities, with philosophy and the study of formal artistic practices. The study of social realities was left between the humanities and the natural sciences, with history (ideographic) and social science (nomothetic) closest to the natural sciences. Thus it came to be that since then, social sciences scholars were trapped in the middle and deeply divided about those epistemological problems. Most nomothetic social sciences emphasized their interest in general laws, the tendency to perceive phenomena that can be studied as cases (and not as individuals), the need to divide human reality into segments to analyze it, the possibility and preference for scientific methods (formulating a hypotheses that can be tested by means of strict procedures and quantified wherever possible), and data produced systematically with instruments that permit quantifying data and the controlled observations [5].

Another debate with its beginnings in polarization was the epistemology between the explanatory and comprehensive dimensions. This debate was revived by Dilthey by making evident the very character of comprehension, as distinct from the explanatory resources. According to Mier, for Dilthey, the "spirit sciences" could not dismiss the uniqueness of the event and avoid human capacity built on experience. Then, turning to Popper, he recognized that unlike the hard sciences, the field of social sciences was condemned to contingency and the impossibility of delimiting controllable conditions. Similarly, he recognizes that the field of study, being historical, is faced with the impossibility of descriptions and formulation of regularities, or of predictions. Lastly, making another point, he assumes that the intervention of memory and its role in the constitution of the experience makes experimentation non-viable. This route leads to recognizing that comprehension has the trait of being interpretative, as "part of the symbolic universe where the phenomenon occurs that is trying to explain the subject [6]." Also, the positivist explanatory method, which in its condition of factual science attempts empirical verification of its propositions, contrasts them with data obtained by experimentation, iteration or the use of statistical procedures, and thus bases the explanations of its object of study on that.

That was how a type of normal science was established which, in Kuhn's classic work *The structure of scientific revolutions*, is defined as "research based firmly on one or more past scientific achievements that a particular scientific community recognizes during a given time as the basis of its subsequent practice [7]." In other words, it is the kind of accepted research that only reproduces the existing theoretical and methodological frameworks. It is a kind of scientific activity that most scientists use almost all the time. It rests on the assumption that the scientific community knows how the world works and owes its success to the defense of the community with that assumption. As we have seen, this disjunctive and fragmented normal science has produced, among other things, the polarization between the quantitative and qualitative paradigms.

This opens up another problem, the political dimension of knowing what legitimization implies for the paradigms and what is expressed through their polarization, which appears at the moment when knowledge and relationships enter into conflict and try to put a value on their present and future status.

If we think that methodology always implies a series of decisions, we will have to recognize that legitimization is the process by which a standard is enunciated that introduces a set of rules and conditions to knowledge in order for it to be accepted as valid [8]. It is also the process through which, in its function as "legislator," what is taken by the representatives of the scientific community imposes conditions put together so that the research strategies could be held to account as correct. Then legitimization makes it evident that "knowledge and power are the two sides of the same question: who decides what knowledge is? and who knows what is suitable to decide?" [8] Of course this legitimization sets the limits, not only for legitimate knowledge but for the accepted ways of knowing, which is equivalent to instituting a form of "truth" and the one and only vision of what and how the world is, which attempts to imagine it as universal values that colonize knowledge. Feyerabend assumes that science has not achieved its hegemony due to its method or its results, but that it is a product of political pressures, and he says that "the traditions are neither good nor bad, but simply are […] (and) acquire positive or negative traits only when they are seen through the crystal of […] other traditions" [9]. Also, from the post-colonial proposals, with the notion of colonization of power, he says that techno-science tends to eliminate some kinds of knowledge and substitutes them with the one and only "truth" for knowing the world: as supplied by technical scientific rationality of modernity [10].

Therefore, it is also relevant to ask what effects this asymmetrical relationship could have on knowledge produced by the different methodologies since, if there is a conflictive relationship it could affect the process of research and recognition of the information produced by each of them, impeding collaboration between approaches as a result of a political and ideological confrontation rather than of the effectiveness of the tools. This is evident in the conflictive relationship among different ways of knowing and assumes that schools of thought compete to try to confirm their own and discredit, when it can't liquidate, the competing body of thought [11].

Legitimization is important because it contributes a standard of knowledge and the "correct" methodology. In our case, it would be assumed that it not only institutes certain methodological practices because they may be "good" or "effective," but it must have a "legitimization" that defines both "correct" and "incorrect" practices. Thus the researcher adheres to certain approaches, since "Legitimization not only indicates to the individual that he must carry out one action and not another; it also indicates why things are as they are" [11].

This polarization has generated a controversy that has been reflected in different postures about the complementarity of quantitative and qualitative methodologies, which goes from mutual rejection and negation to less radical positions that accept that some research problems require the different approaches; to others that assume that the interrelationship between the two methods depends on the topic and the moment when they are favored in research; and lastly, those who assume that the same problem could be seen through different approaches [12]. Thus, mixed methods have been enveloped in the controversy that leads to relationships of cooperation/rejection, symmetry/asymmetry, solidarity/competition or hegemony/subordination.

9.3 Opening the Investigation: The Mixed-Methods

Before this series of postures, where it would seem that the quantitative and qualitative methods are difficult to reconcile, we want to suggest a theoretical methodological system that enables it to be recognized as a dynamic framework in which they are in continuous interaction. These conditions are precisely a return to Wolf's thesis when he said that "humanity is comprised of a totality of multiple interconnected processes and that the efforts to take apart this totality, which cannot be put together again later, falsify reality." [13] Then he asks, "If we find connections everywhere, why do we try to convert dynamic and interconnected phenomena into static and disconnected things?" [13] Considering that the foregoing makes relevant certain contributions of Castoriadis [14] that could respond to Wolf's question, this philosophy shows that the domains of social activity are truly not separable. These domains, as he calls them, are not abstractions, correlations with the chosen site to observe the object, nor are the categories that are put into play for understanding. That is why, he says, these sites and categories only exist from and as a function of a particular historical-social institution. Thus it is assumed that if theory distinguishes the separate aspects of certain societies, in spite of what they themselves cannot distinguish, it is not due to the progress of knowledge or the refinement of reason, but to the fact that the society in which it lives has in reality instituted the differentiation of the categories. Thus it is the breaking up of quantitative and qualitative, among other opposing positions that appear to us to be so evident, is nothing but a social institution fad of the particular research of a series of societies, of which ours is one.

A clear example of the need to rethink the phenomena in a way that enables us to articulate the dimensions and methods before the fragmented institutionalization of knowledge has been the concept of disability. Today, disability is a generic term that includes deficiencies, limitations in activity, and restrictions in participation that indicates the negative aspects of the interaction between an individual with a health condition and his or her contextual factors [15]. However, this perspective of interaction between subject and context has had to broaden the previous notion in which for a long time it was thought that the limitations in activity and functioning were considered only from a biological perspective that breaks down both the contexts where it is opened and the subjective experience of persons who live with this condition. The foregoing conceptualization, established in the International Classification of Deficiencies, Disability and Handicaps of the World Health Organization, considers that the deficiency was the result of the illness in an organ, apparatus or system that conditioned the physical or psychological function of the individual; the disability arises from the restriction or lack of ability to carry out an activity; lastly, handicap would be a barrier in the individual, the product of the deficiency or disability that would avoid or impede the development of the hoped-for role of an individual in a "normal" situation. This model represented a linear sequence and is specifically centered on the individual and the illness without taking into account the social and cultural context where the deficiency is present. According to the review carried out by Putman on theories of aging, none of them were necessarily designed with the experience of physical aging-with-disability in mind, and emphasizes that disability is a complex construct. Thus, confronted with the complexity of disability, it has been necessary to open the question to contextual, social and subjective factors, so that disability is not inherent in the persons, but is a relationship of interaction between the environment and the person, to say the least [16].

Therefore this separation of dimensions which turns out to be more artificial than real forces us to consider empirical work that enables us to recognize the relationships and forms of coordination of the various sectors in play. Then, to be able to join these quantitative and qualitative paradigms, it is necessary to understand that the method is a process of synthesis that institutionalizes a way of "thinking" and "acting" on the objects of research, the problematic fields, the collection of information, the tools and analysis, for which it is possible to recognize in the methodological devices not only their functional dimension but also their historical and social character for which it is feasible to assume that they are capable of being transformed.

This transformation has been taking place with slow steps, but voices have finally emerged that have tried to break up the stagnant polarization of paradigms. For example, Blanco and Pacheco have synthetically described the path of the methodological debates between quantitative and qualitative approaches from the sociological proposals of Comte up to the 1960s, and especially in the 1970s, when there started to be systematic questions asked about the positivist postulations, among others the exacerbation of empiricism and the almost absolute domination of quantitative data [17].

One of the most obvious advances in this sense is that the criticisms that both positions mutually make are starting to be taken into account, and with that there is more interest in the themes that have opposed the positions, for example those that refer to validity, reliability, sample selection and the use of techniques for compiling information [17].

Once the issue began to be presented in this context, it opened the door to complementarity, and it was noted that if both approaches are interested for different questions, each has methods and instruments that enable them to get closer to distinct dimensions, which could make possible a division of labor that would necessarily be cooperative. Complementarity poses the combination of methods, techniques, instruments and sources in such a way that each approach is appropriate for achieving different ends that enable them, on one hand, to learn aspects that one vision alone cannot achieve, and on the other, that together they add depth and breadth to the analysis.

Entering the 1980s, these same authors said that the interest was focused on the meeting point between the macro and micro dimensions, recognizing that the former constitutes the framework of reference that defines the limits of the microprocesses, since they raise the issue of interaction and continuum between both levels. Then they passed on to the “interactive model” where the “interactive continuum” that maintains as its base the statement that qualitative and quantitative approaches are not mutually exclusive, but that there is a need to eliminate this dichotomy, focusing attention on the questions being investigated.

Cortés recognizes that with the step from logical empiricism to post-positivism, the frontiers between the qualitative and quantitative methods have been diluted, mainly in the traditionally controversial elements like the ontological, epistemological, and axiological foundations, causality versus interpretation, about the objectivity/subjectivity distinction and the generalization of their conclusions. However, he recognizes that the current technical differences that are still maintained are understood more as tactics than strategies, mainly in the construction of the concepts in the research problem, the hypothesis, the stock of information, and analysis. But he believes that complementarity must respond whether or not the approaches are able to answer some of the questions that arise throughout the study, since there are questions that can be answered only with difficulty by quantitative data, and questions that cannot be answered by qualitative means [12].

Based on the foregoing route, the possibility is recognized of developing research with approaches of mixed methods with an interdisciplinary perspective that ties together information obtained from quantitative and qualitative research methods, with the necessary power to break up the polarizing inertia and, through its complementarity, make it possible to generate information on the processes of age and aging in a broader and deeper way. It must be said that the basic reason for the use of this complementarity resource is that both paradigms not only are compatible but can enrich one another to achieve better quality in the final product [18]. Thus Hernández, Fernández-Collado and Baptista have defined mixed methods as “a process that collects, analyzes and links quantitative and qualitative data in the same study or series of investigations to respond to the problem posed.” [19]. In other words, the mixed method does not reduce the collection of information, but involves it differentially according to the design proposed.

In this sense it proposes to start a dialog between the paradigms that could be considered opposites, but as Ruíz clearly shows, “this dispute […] is more tribal than scientific” [18]. It is true that the basic epistemologies of explanatory and interpretive paradigms have deep differences, but by understanding the research itself as a process it is feasible to put together a collaboration that brings information from different visions, and in the end to show the different elements that conform to the complex reality in which older adults live.

To achieve this it is necessary to recognize the ranges and limits each paradigm has in the study of a problematic field so that, rather than reject an approach due to its limitations and weaknesses, an approach must take advantage of their ranges and thereby offer a more complete perspective on the field of study.

This is the place for a warning, since it must be recognized that research is only capable of understanding a part of the reality. To arrive at the totality is an enterprise that goes beyond from the purpose of research work because, as Kuhn says, no linguistic or conceptual system exists that is scientifically or empirically neutral. He sees this as a restriction, and consequently assumes the impossibility of having access to all of the possible experiences and all of the possible theories, so he states that “no theory ever solves all the puzzles that confront us at a given moment, nor are the solutions obtained very often perfect” [7].

This places us before the fact that in the same problematic field there will be different perspectives, ways of approaching and questioning, so that we are obliged to submit to complexity over completeness. This is so partly because the latter could bring with it a series of confusions to be understood as a pretension to explain the “essence” of a social fact (as if each phenomenon were to have a concept that enables it to be a particular example of a universal concept), although it is not the intent in this work to assume that it is possible to affirm a universal truth that avoids the particularities of the research theme. Thus, as Adorno says: “The social totality does not maintain a life of its own beyond the components that make it up and those that, in reality, are going to appear. It produces and reproduces itself by virtue of its particular moments” [20]; and as Morin says:

> […] one of the axioms of complexity is the impossibility, even theoretically, of omniscience. But it is also involves, as a principle, recognition of the links between the entities that our thinking must necessarily distinguish, not in isolation but together […] the complex thinking is encouraged by a permanent tension between aspirations for knowledge that is not fragmented, not divided, not reductionist, and the recognition of the unfinished and incomplete nature of all knowledge [4].

This has led us to rethink the fact that social science works with subjects and socially constructed realities which are produced historically in particular socio-cultural contexts; and on the other hand they also face the singularity in which the subjects live, as well as making precise the recognition of the conditions for entering the field of work, the tools and the planned strategies, and they must be reflected and adapted to uncontrolled, unrepeatable and uncertain conditions to achieve a productive relationship with the informants. In other words, the development of the research is always found to be situated in determined socio-cultural contexts, are produced historically, and are always designed for the singularities and the event, which can only be understood with difficulty by isolated statistical visions, and in the same way, they run the risk of focusing only on hermeneutic and interpretive methods that can avoid the conditions in which the symbolic and subjective universes of older people are produced and developed. The warnings of Lahire must be heeded. They reflect on sociological constructivism and show that in research work there is an uncritical, hyper-relativist, anti-realist and anti-objectivist tendency based on the reduction of the social world to its symbolic dimension and with that to “simple beliefs” or “simple representations” that the actors make of the social world. For the author, sociological constructivism is necessary to denature and stand back from the categories, but he assumes that this is not enough, and that it is precisely recognizing that they have history and conditions of possibility [21]. As

Sartre (S/a) states, historical situations vary, and what doesn't vary is the need of man to be in the world. The limits, understood as condition, are neither subjective nor objective, or rather they have both an objective and subjective face. They are objective because they are found in everything and are recognizable, and subjective because they are lived and are nothing if the man doesn't live them [22].

Instead of the fragmented approaches, mixed methods could be an alternative for research fields that present questioning similar to the foregoing. The critical anthropology of health could be a good example. One of its representatives, Nancy Scheper-Hughes, questions the alternative between the individualizing perspective, centered on the significant and the hermeneutics on one hand, and the collectivized, depersonalized view, on the other. Her questioning turns on the possibility of understanding the structures that explain things and the comprehension of the subjective contents of illness and its care as lived events [23]. This question not only has theoretical relevance, but is also based on the "mixed" vision in research methodology, so it is through complementarity that one can be aware of the interrelationship that exists between these dimensions.

A clear example in the area of health is the work of Bronfman, cited by Castro. He showed that Bronfman demonstrated first of all that conventional explanations of the relationship between socio-demographic variables and infant mortality faced very clear limits and a large part of the phenomenon was unexplained. Then he showed that the most powerful explanations of the problem were achieved based on the coordination of quantitative and qualitative approaches. This demonstration was achieved by linking the structural determination of infant mortality with interactional elements of the individuals, and showed that these played as central a role in both the generation of the problems that led to infant mortality and in the solution [24].

This interrelationship between approaches can also be observed in other works, which although they do not define themselves as mixed methods have used complementarity, for example in Durkheim's classic study on suicide, where he used qualitative data and techniques as well as statistics [25]. Also Bourdieu, who was faced with a series of opposing arguments in social sciences, uses and tests, as he says in his work, which is a research task inseparably theoretical and empirical, a range of methods of observation and of quantitative and qualitative measurements, statistics and ethnographics, macro-sociological and micro-sociological [26]. Another type of work where we find this tendency of cooperation between quantitative and qualitative approaches is in the area studies that were initially developed in the United States. These studies focused attention on geographic zones that had some cultural, historic and/or linguistic coherence. Their character was mainly defined by the interdisciplinary proposal, which was able to unite specialists from the different knowledge areas, not only from the social sciences but also from the humanities and natural sciences. Julian Steward recognizes that methodologically, these works, especially one of their modalities called community studies, which although it was predominantly qualitative, used ethnography as its main tool for collecting information. It also used quantitative sources and tools first to improve the information samples, and second to quantify some categories of the area studied [27].

It was also observed in the proposals of sociocultural epidemiology of Menéndez who posed the coordination and complementarity between epidemiology and medical anthropology. This proposal isn't far from the questioning and debates about complementarity and recognizes the difficulties of articulation, above all in the possibility of establishing generalizations, the reliability of the qualitative data and statistics, and the selection criteria of the informants. In spite of the strong polarization that might exist between the two disciplines, they sought to articulate them through problematizing the issues of health-illness-care, which includes putting in question the theoretical, technical and empirical proposals of the researchers themselves [28].

Sociocultural epidemiology is characterized, among other traits, by posing the necessity of including in the studies of the health-illness-theoretical processes not only the social aspects, but also the cultural and economic-political ones, together of course with the biological and ecological ones. In the second place, it proposes a type of work that really uses and articulates both statistical and qualitative approximations. Lastly, they gambled on the application of a relational approach that includes not only the different factors that operate with respect to a set problem, but also incorporates the uniting of significant social actors in the problem of research.

Summing up, one must say that the mixed methodological approach must assume that this relationship is a fabric, and so the strategy must note that if the researcher is to understand how the association between these various heterogeneous components works. This gamble tries to show the attachment, the connections and its legitimacy. It is not intended at any time to give value to the heterogeneous terms in a homogeneous element that promises a resolution in a unit or system, balanced and static. On the contrary, it is located precisely in the relationship between the distinct terms among those who act. Of course this implies understanding that research is not a succession or conglomeration of confusing events, but that it develops in a specific sequence of connection, from one event to the next. The interaction of these approaches is not homogeneous; on the contrary there is tension and at certain times they could be importantly determined or in conflict; what it doesn't signify is that the others are eliminated.

Lastly, it has to be said that setting out our mixed methodological strategy is based on the fact that scientific research is a process. Methodology is not simply the element that organizes and gives life to the research; we could say that it is a complex field that coordinates epistemological, theoretical, technical–instrumental, ethical, and strategies of incursion into the field to question the social life, which – from our conception of it – is in constant dialog. It is not like a more positivist approach that considers that the scientific method to be the definitive element of science and has a general character, as "a procedure that is applied to the entire cycle of the research in the framework of each knowledge problem" [29] and that the only thing that could vary, depending on the object being studied, is the strategy, that is to say the planning and use of methodological tool. Instead, this proposal assumes the idea of Adorno, when he says that: "Methods do not depend on the methodological ideal but on the thing" [20]. Then, the methods are constructed as a correlation of the problematization, the theoretical perspectives, the involvement of the researcher and the access conditions to the field of work. From our approach the question that problematizes the field of study presents more relevance in the development of the research, and so in agreement with Bachelard, the problems do not ask themselves, and it is these that sustain the character of truth to the scientific spirit and affirm that: "For a scientific spirit any knowledge is a response to a question. If there had not been a question there could not be scientific knowledge. Nothing is given. Everything is built" [30].

9.4 Conclusions

This section has sought to bring elements that contribute to the discussion about the viability and importance of research that uses the quantitative and qualitative paradigms, traditionally polarized by a normalized science that has instituted its dichotomy, which to us appears to be the result of being more ideological and political than real. Thus we have presented a synthesis of some of the debates that have fragmented knowledge and the tools for its construction.

Next, recognizing that reality is complex, we have tried to offer elements that demonstrate that it is necessary to propose approaches to sensitivity and capability to take this complexity into account. To be able to carry out this task it is necessary to open up the closed paradigms and ask not only about the functioning of the collection tools and analysis of the information, but in the same way about how scientists think about and understand reality.

The contributions of complex thinking have allowed for recognizing that research is a process that could offer information about the interactions between the dimensions that conform to reality; similarly, it insists on creative ability and the opening of dialog between opponents who think they are not reconcilable. By exemplifying some works and research approaches we have tried to demonstrate that coordination and collaboration is possible. However, the use of these methods is not free from difficulties that demand serious and responsible work to develop them. There is still very limited production of research of this type in terms of the issues of age and aging.

Lastly, it has to be said that at no time was it the intention of this work to distort any approach; on the contrary it has insisted that recognition of the strengths and weaknesses of each can be overcome by being able to propose mixed approaches, which among the main challenges that exist in the future is to break the inertia of polarization that for many institutional determinants and teaching still remains in effect.

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Chapter 10
Systematic Review and Meta-Analysis

Miguel Ángel Villasís-Keever and Mario Enrique Rendón-Macías

Abstract Systematic reviews and meta-analyses are proven tools for decision-making in health care, both for patients and for public policy. For example, nowadays they constitute a substantial part of evidence based clinical practice guidelines. However, the number of systematic reviews developed so far, and their use and application to improve the health of elderly has been somehow slow. This chapter describes in detail each of the steps necessary to conceptualize and conduct systematic reviews and meta-analysis. It begins with a description of the different uses these types of tools have today. Subsequently the differences they have with narrative reviews are given. With regard to the methodology to assemble them, it starts in the form of how the research question is formulated, which is the essence for the construction of each of systematic reviews. Then we continue with the selection of studies, first by searching in different electronic databases (e.g., Medline). Once studies are located, each of them should be reviewed thoroughly to determine if they comply strictly with the selection criteria. Finally, with the selected studies the next step is data extraction from each one, which eventually constitutes the results section of the systematic review. Noteworthy, in each of the steps we pointed out each of the aspects necessary to make the reviews with the highest quality. The last part of the chapter focuses on the different alternatives of meta-analyses and how they need to be carried out.

Keywords Systematic review • Meta-analysis • Methodology • Secondary research

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10.1 Introduction

Finding efficient and effective methods for the care of senior citizens is important. However, it's often the case that time, motivation or the necessary skills to find, evaluate critically and synthesize the information of published studies to integrate the results of the research to normal clinical practice are not available. In this context, several years ago systematic reviews and meta-analyses have been growing in numbers as a tool for making decisions in different areas of medicine, from the moment the doctor meets the patient through conception of a research project or the planning of health-care policies. However, its use has been slow to seep into every possible area, possibly due to lack of knowledge of its scopes, advantages and reliability [1].

In part, this type of research has emerged because the volume of information is growing every day, and this makes it necessary to make documents available that summarize in orderly fashion and under scientific criteria the state of knowledge of a given topic, in order to facilitate decision-making for health-care personnel, researchers, patients and those who implement health-related public policies.

From the start of the development of the process of an orderly summarizing or synthesizing and criticizing scientific evidence until arriving at what today is known as systematic review and meta-analysis, different terms have been used: review articles, synthesis of research, overview, etc. As well, various definitions have been developed, but one of the most widely accepted is the one proposed by Ian Chalmers and Douglas Altman – two of the main pioneers in this area – which establishes that: "a review is what has been prepared through a systematic process to minimize biases and random errors, which is documented in the material and methods section" [2]. With this definition, it is clear that a systematic review is a research project that includes studies from a single theme or topic [3]. Meta-analysis is the term used when a statistical analysis of the results of at least two individual studies obtained from a systematic review is carried out. Thus it is necessary to recognize that all meta-analyses are also systematic reviews.

Systematic reviews are also known as secondary investigations, since they deal with synthesizing the information from primary or original studies that have been done through the years on a particular theme. In other words, a systematic review concentrates all of the studies carried out on a specific theme using the scientific method [4].

Although earlier systematic reviews and meta-analyses focused on synthetizing studies on therapeutic interventions (like drugs or surgical interventions) described in controlled clinical trials to determine which were the most effective, over time the spectrum has broadened to include observational studies whose objectives are to learn the prognosis of illnesses, evaluate the best diagnostic tool, or establish causes or risk factors of illnesses [5].

10.2 Types of Reviews

In spite of the development and evolution this field of research has had in recent decades, not all "review" articles or publications are systematic reviews. Because of this, it is necessary to distinguish between systematic reviews and narrative reviews. Narrative reviews are documents that describe a specific theme or topic, which may be considered similar to what is usually presented in a chapter of a book, where historic aspects, epidemiology, signs and symptoms, or the clinical course of an illness are presented, as well as the process of making the diagnosis and even the therapeutic options [6]. In the case of systematic reviews, although they also deal with a particular illness, the approach is very specific; in other words, the synthesis of the information is centered only on the treatment, diagnosis, risk factors or the prognosis [7].

There are also differences in the process of including the various articles or references that support the authors' arguments; in a narrative review there is no selection process, even though it may be based on recent publications. For this reason it is thought that the information in these documents is directed specifically toward the concepts or proposals of the authors themselves, since the support documents only agree with what is described in the text and do not include everything published on the theme. For example, if the author of a narrative review has been distinguished for having carried out research on a specific drug, then possibly the information included in the article would be limited specifically to the findings that he or she has described, even if there may have been other studies with different results. In contrast, in systematic reviews where a search of all the available studies in world literature is carried out, it will include articles both in favor of and against the effectiveness of the drug, as well as all the adverse events. As well, if possible, a systematic review could include what is called gray literature, that is, the results of research not published in scientific periodic circulation journals, such as theses or works presented at medical conferences [8].

10.3 Uses of Systematic Reviews

Because systematic reviews synthesize research studies published up to the present, they are one of the basic tools in Evidence-Based Medicine (EBM) [8]. As we know, two of the principal steps of EBM refer as much to the search as to critical reading of the studies, which will support medical decisions for patients on aspects mainly related to the diagnosis, treatment or prognosis. By virtue of the fact that a research group has previously completed the task of identification and evaluation in the published studies, the use of systematic reviews and meta-analysis will be beneficial for the practice of EBM. For example, in the case where the review might have demonstrated the effectiveness of a drug for the treatment of arterial hypertension in patients older than 65 years of age, after reading a systematic review of controlled clinical trials published up to the present, the doctor, instead of reviewing and analyzing each clinical trial where a particular drug was analyzed, could direct his efforts toward determining the viability of giving this intervention to his patients (for availability, cost or the characteristics of the patients), or evaluating the result once the intervention is implemented [6].

Moreover, at present systematic reviews are essential for preparing evidence-based clinical practice guidelines. An example is where more than one option is available for aspects of diagnosis or treatment, in which case the recommendations of the guidelines will be based mainly on the results of the studies with the best quality of execution. In this context, as the treatment of arterial hypertension involves a therapeutic intervention, if a meta-analysis of controlled and randomized clinical trials is identified where it is shown that this intervention is effective and with few side effects for patients older than 65 years, then that information would be included in the guideline, and would form part of the recommendations [9].

Another use that has arisen in recent years, both of systematic reviews and meta-analyses, is in health-care policy, where they are becoming increasingly important as a reference point. For example, in making decisions on the incorporation of new drugs for a specific illness, whether for a hospital or health system, all of the alternative therapies available are considered, including the results of their clinical effectiveness and costs. In this latter category it must be emphasized for cost evaluation that compared with clinical studies, the carrying out and publication of economic studies is limited; still, for experts in health economics systematic reviews are extremely useful for identifying the impact of each of the interventions in health outcomes (therapeutic efficiency, morbidity, mortality, quality of life, to name a few), and this could serve to bring about cost-effectiveness, cost-utility and cost-benefit evaluations [5].

10.4 The Process of Preparing Systematic Reviews

Like all research, systematic reviews must start with the drawing up of a protocol. This protocol will describe the process for executing each of the steps with the smallest number of errors or biases. Figure 10.1 outlines the process.

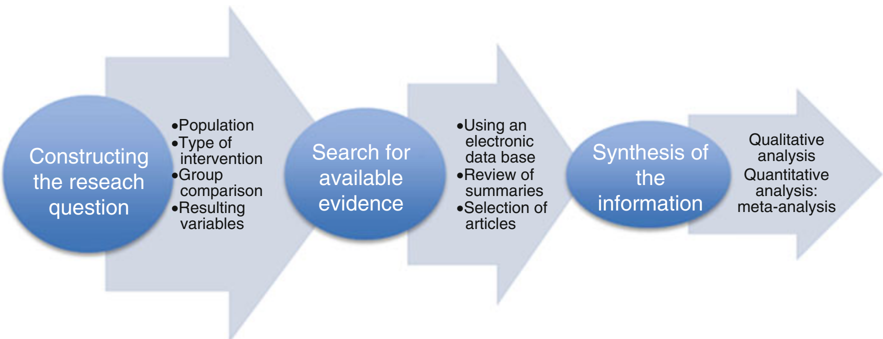

Fig. 10.1 The process for drawing up a systematic review

10.4.1 Preparation of the Research Question

The first step in doing a systematic review is to focus as much as possible on studying a single fundamental, answerable question by constructing one that determines the scope of the study [10]. The more concrete the question is the easier will be the review. To construct the question the following must be taken into account: (1) the population of the study, where it includes age (children, adults, seniors) and the illness to be studied; in other words, the illness itself or one or more of its complications; (2) the intervention to be evaluated, whether it be treatment, diagnosis, risk factors or prognosis; (3) the possible options for intervention; for example, two or more drugs, procedures, diagnoses, etc.; (4) the different results of the effect of the intervention, for example, if it is therapeutic, then the results to evaluate are to avoid complications or death; while if it is diagnosis, the capacity of one or more tests to confirm or rule out the illness being studied.

10.4.2 The Search for Articles

Once the research question has been defined, the next step is to start the search for studies that have been done on the theme. To begin this task, the researcher has to take into account each of the elements included in the question. To do this, electronic databases are used that concentrate the bibliography or publications on health care themes. The largest databases in the world are Medline and EMBASE, which use terms or text words to classify each publication. Other important sources could be the Cochrane Collaboration and CINAHL. There are now proven methods for obtaining the most efficient searches, in other words, which have the highest sensitivity for locating pertinent studies to resolve research questions [10]. However, one problem in this search is that in these databases, only the titles and the summaries of the publication are available, so it is necessary to read and scrutinize to choose the articles that would potentially serve for the systematic review and then get their full version. In a high-quality systematic review, the selection of titles and summaries is done by a peer-review process, which means that two or more researchers work together to discriminate and decide which studies meet the inclusion criteria. The goal in this phase is to choose only the articles where both researchers agree to include them; if there is disagreement, they could consult a third researcher, who could decide on whether or not to include it, or they could make a consensual decision [11].

When doing the search for summaries on these databases, articles in any language could be identified, so it is important to decide whether language restrictions will be included in the criteria. In this context, the reader of a systematic review should be aware of the possibility of biases about this. However, when the inclusion of studies is restricted to English, it is seen as a small error, since about 90 % of world scientific production is published in that language.

10.4.3 Selection of the Studies

After having chosen the titles and summaries, the next step is locating the published or complete versions of the studies selected. Once the studies are available the researchers proceed to review them for each of the components (especially in the methodology and results sections) to determine whether they effectively comply with each point identified in the research question. As one would expect, it is only at this time that it can be determined with certainty whether the studies contain enough and adequate information to be incorporated into the systematic review and subsequent analysis. This is another phase of scrutinizing, since a large proportion of the articles recovered will not contain the minimum elements necessary to be analyzed. For example, in systematic reviews of therapeutic interventions, in this phase not only must the section on material and methods be verified as to whether the study relates to a controlled and randomized clinical trial, but also whether there is enough information about the results the researchers are looking for. On this point, it should be mentioned that there are publications that refer to research protocols, reviews, or initial reports, but without data on that or the patient outcomes, and so these must be excluded from later analysis.

Added to the foregoing and with the goal of identifying a larger number of publications that would not have been located with the search strategy, in many systematic reviews the reviewers opt to review the list of bibliographical references of the studies included [10].

Lastly, the quality of this phase is again guaranteed when a peer-review process is carried-out, in the same way the summaries were selected.

10.4.4 Data Extraction

In this phase of the systematic review the researchers try to obtain useful information contained in each of the studies that will conform to the final analysis and that complies with the study's objectives. To do this, the researchers must set up data collection sheets on each variable, taking into account all the variables: outcomes and intervention, as well, as demographic data. Based on what is described in each of the studies included, these sheets will be filled with information on the general characteristics of each study, where (e.g., country or a hospital) it was done, the characteristics of the patients included (age, sex, selection criteria of the patients, number of participants, etc.), the intervention (for example, studies on therapy should specify doses, methods of administration, duration time of the intervention, co-interventions) and, of course, the results (*outcome measures*) of the way in which the original article shows them. If necessary they will have to include the definitions used in each study, since these could vary [8].

In this phase, too, it is recommended that the information be extracted and recorded by a peer-review process, as mentioned for the previous steps [5].

10.4.5 Analyses of the Results of a Systematic Review

This phase of the systematic reviews depends on the findings obtained in each of the previous phases. Thus, to determine the way the results will be described, it is necessary to know whether or not the studies included were similar. This is done by means of an individual analysis of each one, contrasting it with the others. It is important to evaluate the selection criteria of the patients, the intervention, and the method of measuring the variables of the results, whether they were similar among the studies [11]. If differences in each of these principal aspects are observed, it is considered that there is heterogeneity among the studies, and thus the results will be made only on the qualitative aspect. This could mean that the final report will be based on the description of the characteristics of each of the studies included. This is known as systematic review [2].

When the studies are considered to be similar, that is, there is homogeneity; a statistical analysis could be carried out combining the data on one or more variables of results when these come from at least two different studies. This procedure is known as meta-analysis. To do this it is necessary to consider the scales of measurement of the variables used by the authors of the studies included, since the relevant statistical method will be selected in accordance with their nature. For example, if the review deals with evaluating the therapeutic effect of a drug for systemic arterial hypertension, it is possible that the outcome variables have been established as disappearance of the hypertension (a variable with qualitative measurement scale) or modification of the blood pressure values (a variable with a quantitative measurement scale). Each variable will be analyzed with different estimates, which will be obtained by separate statistical procedures (see below). At present there are several statistical packages available, such as *RevMan* o *Metaanalyst*, for working with these specific data in carrying out a meta-analysis.

10.4.6 Final Report and Edited Recommendations

The last step in systematic reviews is the preparation of the final document, which, in addition to describing the entire process carried out, includes the results obtained from the qualitative or descriptive perspective and, if relevant, the quantitative results when the meta-analysis was done. It is important when preparing the final report to be objective and neutral on the findings, and to provide information on all the elements so that future readers can make their own decisions [4]. It is not rare to find systematic reviews where the authors indicate the existence of not enough evidence to achieve a definitive conclusion because of the poor quality of the published studies, or due to a small number of patients studied, or because the available studies have not shown obvious clinical benefits.

10.5 Meta-Analysis

To deepen the theme of meta-analysis, it should be mentioned that one of the most important reasons since its conception and development through the years, during the growth of systematic reviews, was to think about the possibility of increasing the number of subjects studied on a specific topic obtained by adding up the results of different studies. Thus it should be recalled that in a number of studies worldwide, it is common the authors recognize that due to the small size of their study, they did not dare to offer a solid conclusion about their findings, for example, whether a new intervention is better than the usual treatment. When a meta-analysis is done it is accepted that it will be equivalent to having done a single study but with a much larger sample size, in other words with more statistical power, since it combines the results from two or more studies to issue a more reliable conclusion. Taking this scenario into account, by increasing the number of participants it is more probable that it will demonstrate the true effectiveness of an intervention. If this assumption is true, it is feasible to make decisions based on studies that are already done without undertaking the task of doing a large-scale study. However, if there are still doubts despite these benefits of meta-analysis, nowadays it is preferred to do a study with a large sample size to determine the effectiveness of an intervention, since this ensures that all the participants in the study were exposed to similar maneuvers during the same time period [9].

Another point to consider in carrying out a meta-analysis, as was mentioned previously, is the method of reporting the results, that is, the scale of measurement of the variables of the outcomes. The five most used measures are, for quantitative variables: the weighted mean difference and the standardized mean difference (the latter is also known as size of the effect) (Fig. 10.2); and for qualitative variables: relative risk (RR), odds ratio (OR) and risk difference (Fig. 10.3) [12].

In general, there are two models for carrying out a meta-analysis, the fixed effects model and the random effects model. In the former it is accepted that the studies

	Present			Absent				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
Conter, et al.	41.8	8.1	38	86.9	0.9	1711	0.0%	-45.10 [-47.68, -42.52]
Escherich, et al.	53	15.5	11	85.4	1.5	566	20.0%	-32.40 [-41.56, -23.24]
Gaynon, et al.	45.5	7.2	63	86.9	0.8	2008	0.0%	-41.40 [-43.18, -39.62]
Kamps, et al.	42.9	18.7	7	83.7	1.3	460	8.8%	-40.80 [-54.65, -26.95]
Liang, et al.	71.1	12.8	16	82.6	1.7	716	42.7%	-11.50 [-17.77, -5.23]
Mitchell, et al.	43.9	7.6	43	78.1	1	1791	0.0%	-34.20 [-36.47, -31.93]
Moricke, et al.	39.5	7.5	43	88.6	0.7	1917	0.0%	-49.10 [-51.34, -46.86]
Pui, et al.	50	17.7	6	84.3	2.9	159	8.4%	-34.30 [-48.47, -20.13]
Salzer, et al.	34.8	4.3	128	87.3	0.5	522	0.0%	-52.50 [-53.25, -51.75]
Shmeigelow, et al.	78	14	9	89	1	228	20.1%	-11.00 [-20.15, -1.85]
Total (95% CI)			49			2129	100.0%	-20.06 [-24.16, -15.96]

Heterogeneity: $Chi^2 = 30.38$, $df = 4$ ($P < 0.00001$); $I^2 = 87\%$
Test for overall effect: $Z = 9.59$ ($P < 0.00001$)

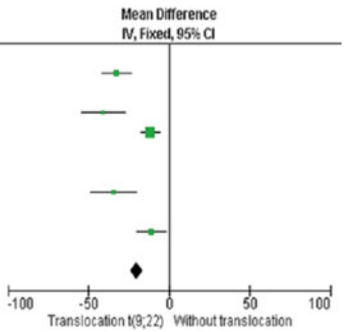

Fig. 10.2 Representation by *Forest Plot* of meta-analysis with quantitative variables through the use of weighted mean difference

	Intervention		Placebo			Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI
Barton, 2002	15	38	33	39	8.0%	0.12 [0.04, 0.35]
Bikhazi, 2004	5	41	26	44	8.9%	0.10 [0.03, 0.29]
Daniels, 2001	9	51	46	51	15.3%	0.02 [0.01, 0.08]
Desjardins, 2001	4	54	37	54	13.8%	0.04 [0.01, 0.12]
Hubbard, 2003	11	67	30	63	10.4%	0.22 [0.10, 0.49]
Malan, 2003	1	55	7	61	2.6%	0.14 [0.02, 1.20]
Mehlish, 2003	12	51	47	50	14.7%	0.02 [0.01, 0.07]
Snabes, 2007	18	204	64	194	24.2%	0.20 [0.11, 0.35]
Tang, 2002	2	17	6	18	2.1%	0.27 [0.05, 1.57]
Total (95% CI)		**578**		**574**	**100.0%**	**0.11 [0.08, 0.15]**
Total events	77		296			

Heterogeneity: Chi² = 24.29, df = 8 (P = 0.002); I² = 67%
Test for overall effect: Z = 13.33 (P < 0.00001)

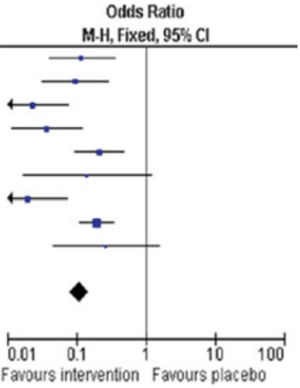

Fig. 10.3 Representation by *Forest Plot* of a meta-analysis with qualitative variables using the odds ratio (OR) calculation

included estimate the same “true” value of the effect, and that the differences observed among them are due to chance. In the random effects model it is assumed that the trials or studies included are only random samples from a “universe of studies,” and that their results are positioned randomly around a single central value [1].

For presenting the results of the meta-analyses it is always useful to include graphs, with the *forest plot* being the most commonly used one, where in addition to describing the individual results from each study included, it shows the global estimate, which is considered the truest one. As shown on the right side of Figs. 10.2 and 10.3, a vertical line divides the graph, where the left side usually shows the benefit of the experimental intervention and the right side the control intervention. As well, each horizontal line represents each of the studies; this line has two components: (1) the estimation point (square) and (2) the extremes of the interval of reliability (horizontal line). In the lowest part of the graph is shown the global synthesis of all the studies (indicated with a diamond).

As well, in all meta-analyses the differences between the studies from a statistical point of view are determined, which will indicate whether or not there is heterogeneity. The most frequent analyses for documenting this are the Breslow-Day, Q of Cochran, and Chi-squared tests. When a value of $p \geq 0.10$ (in these tests) is obtained it shows that there is heterogeneity, from which it can be inferred that there are important differences between the studies. This situation obtains possibly because the number of subjects among the studies is very different, or more often, because the effect of the intervention is not consistent among them (some studies indicate benefits and others do not). One strategy for resolving this is to select a meta-analysis model of random effects or to carry out a sensitivity analysis. The latter could be done by analyzing only data from the studies with the largest number of participants, or according to the quality of the studies [1, 12].

Lastly, one aspect that must be mentioned is the possibility of a “publication bias.” As one of the primordial objectives of systematic reviews and meta-analyses

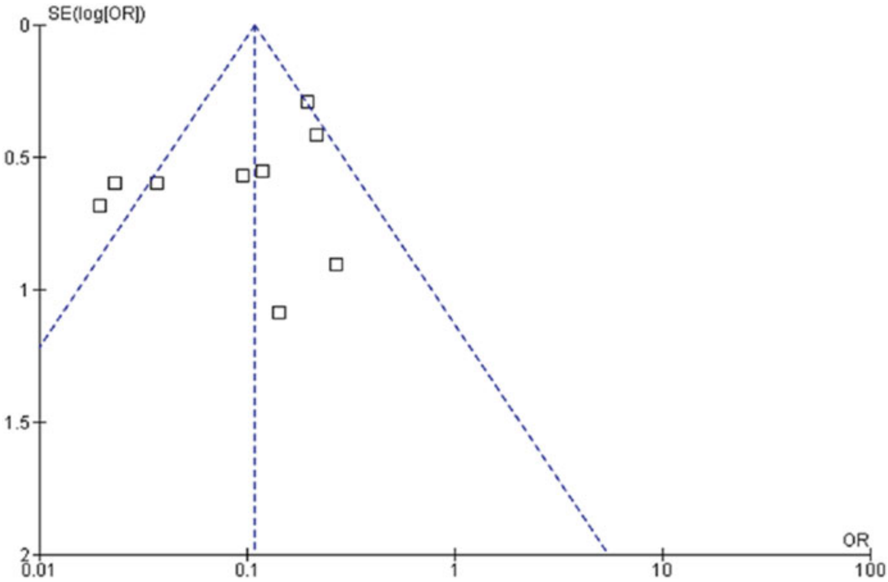

Fig. 10.4 Example of a *Funnel Plot*

is to look for and concentrate *all* the studies on a specific theme in one study, it is necessary to take into account the tendency to publish only the studies that show benefits toward a determined intervention or manoeuver. Therefore, it is more difficult to find studies where the findings go against the hoped-for effects "where no statistically significant differences are found." This has been named publication bias, since all meta-analysis should evaluate its possible existence [9]. The usual way of doing that is through graphic representation of this phenomenon. Graphs called funnel plots are the most commonly used to show the relationship between the size of the sample and the effect of the intervention from each study included. In this graph, each study is represented by a point. When there are no publication biases, the graph should appear as an inverted funnel which must contain all the points, but if parts of the funnel are lacking (absence of points or outside of the funnel), then publication bias might exist. If the later occur the results should be interpreted with caution. A funnel plot is shown in Fig. 10.4, which shows that there may be publication bias.

10.6 The Quality of Systematic Reviews

It should be mentioned that, like all research processes, systematic reviews could have problems during their execution, for which the readers of this type of document must determine their reliability. To facilitate their evaluation, some instruments or scales have been developed over time to evaluate the quality of systematic reviews. These scales are based on the analysis of each of the steps (phases) of the preparation of a systematic review. As well, efforts have been made in which the publications of the reviews follow a standard format, called QUORUM, and more recently PRISMA [2, 5] to help readers evaluate them. The items that evaluate these and other instruments are based on the good execution of the systematic reviews, most of which were mentioned above.

It should be said that independently of whether or not the reader knows the essential elements for establishing whether a systematic review is of high quality, there are organizations that prepare them on a state-of-the-art basis, and these are usually reliable. The largest organization, and the one that sets the standards of quality for systematic reviews at present, is the Cochrane Collaboration. The advantages of this organization is that it is non-profit, and so all the reviews are available for consultation free of charge, and in many cases in different languages, including Spanish (www.bibliotecacochrane.com).

Other organizations with reliable systematic reviews are those produced by the *Agency for Healthcare Research and Quality* (www.ahrq.gov) in the United States of America, or by *Health Technology Assessment Programme* in the United Kingdom (www.hta.ac.uk).

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Chapter 11
Technology and Aging

Jesús Favela and Luis A. Castro

Abstract Advances in Information Technologies have propelled the development of a diversity of solutions to assist aging. These range from service robots that help older adults perform activities of daily living to monitoring systems for early detection of clinical conditions such as frailty or dementia. The evaluation of these technologies imposes several challenges, due to issues such as the risk inherent in evaluating health outcomes and the nature of emerging technologies that could be unreliable, might be used at unpredictable periods of time, and support implicit interactions, that is, the technology is not at the center of attention of the user, but rather it peripherally supports the task at hand. This chapter describes some of these challenges, exemplified with different assistive technologies and shows how they can be evaluated at different stages of development. In addition, we describe how emerging computing technology can be used to support clinical research on aging. In particular, we show how mobile computing systems can be used to monitor clinical variables and health outcomes in interventions for aging. We illustrate the potential for these technologies with an example of a monitoring platform for mobile phones that can be used to measure parameters associated with frailty, and a videogame that uses a natural user interface to measure muscle strength while the user focuses on playing, and can be used for early detection of sarcopenia.

Keywords Technologies • Inventions for aging • Mobile computing systems • Videogame

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11.1 Introduction

Technology is becoming pivotal in aging research in at least two important ways. On the one hand, there is an active body of research and development on the design and evaluation of emerging technologies to support aging. These technologies can be as diverse as a voice recognition system in a service robot that assists elders in performing everyday activities, to videogames that track user performance and can provide early evidence of dementia, or sensing devices that assist caregivers by sending an alarm when a person who suffers from dementia exits the home. Assessing the effectiveness, usability, risks and adoption of these systems has become a major thrust of aging research.

On the other hand, advances in information technologies are impacting research on aging in numerous ways. One notable case is the use of sensing technologies to support epidemiological studies and clinical interventions in aging. Behavioral epidemiology studies how lifestyle and behavior relate to the occurrence of a disease and evaluates interventions aimed at changing unhealthy behaviors, such as overeating or smoking. Numerous diseases provide early evidence of their onset from changes in behavior, long before confirmed by clinical studies. In particular, mobile phones include a variety of sensors that can be used to gather data about users' behavior, such as the places they visit, their level of activity and how frequently and with whom they socialize. The collection and analysis of these data have been the focus of recent attention in a rising field known as mobile sensing and offers valuable data to aging research.

This chapter presents some examples of how technology can be used for supporting research on aging. Section 11.2 presents two case studies in which we illustrate the challenges associated with evaluating assistive technologies. Section 11.3 presents the use of novel Information Technology (IT) that can be used to collect information about patients in a more natural, frequent fashion, through the use of sensor technology implemented in their homes. We hope that the examples provided can help derive further interest and development in research projects on aging enhanced or supported by technology.

11.2 Evaluating Assistive Technologies for Aging

The proliferation of mobile devices, ubiquitous connectivity and natural user interfaces are making possible the development of novel assistive technologies for aging. These technologies can be used to assist older adults perform everyday activities, facilitate caregiver tasks, and encourage active aging. As these solutions proliferate, it becomes paramount to evaluate their effectiveness in order to guide further development in the area and inform users who could benefit from their adoption.

There are, however, several challenges associated with evaluating assistive technologies for aging. On the one hand, it is important to evaluate these technologies in the context in which they will be used. Although evaluations conducted in a controlled environment, such as a lab, can be useful at early stages of development, conducting interventions with actual users, in their residences where they normally perform the functions that the technology aims to assist, is crucial to assess adoption and the usefulness of the technology. Thus, the ecological validity of the intervention needs to be carefully planned. In addition, assessing the effects of the technological interventions often calls for evaluations that last for weeks or months. These interventions need to place careful consideration to technology maintenance and on deciding whether to incorporate innovations if they become available, or even if early results suggest improvements in the technology. This is of particular importance when evaluating emerging technologies that might be brittle and subject to failure. Long-term interventions of new and novel assistive technologies with high ecological validity are, of course, difficult to conduct with large populations, which favors the use of qualitative research methods, or mixed-methods that combine quantitative data gathered from the log of the use of the technology, as well as direct observation and interviews with participants.

We illustrate some of the challenges of evaluating technologies for aging with two case studies. The first one describes an intervention conducted in a geriatric residence to asses a mobile tool to assist professional caregivers to document their care activities. This study illustrates the use of mixed methods to evaluate technologies for aging. The second study describes a novel method, called naturalistic enactment, used to evaluate a mobile tool for geriatric nurses that participated in a long-term intervention to assess in-home elderly care. The method offers a balance between ecological validity and control in the intervention when evaluating ambient technologies.

11.2.1 Mixed-Methods to Evaluate a Mobile Information Management Tool for Caregivers in a Geriatric Residence

The aim of this study was to assess the effectiveness and ease of use of a mobile tool aimed at assisting caregivers in a geriatric residence document their activities and those of the residents. The design of this tool was informed by the results of a qualitative study aimed at understanding care, coordination and information management activities of the caregivers. From this study, it became evident that caregivers had a hard time keeping an updated record of their activities and those of the residents.

The solution proposed was a mobile app in a smartphone that can record the activities performed by each resident using Near Field Communication (NFC) tags on a single touch. The tags were placed around the residence. For instance, when a caregiver gave the medication to a resident, she would scan one of the tags in the wall besides the resident's bed to record this activity with minimal effort. The caregivers receive notifications on the device when activities, such as feeding a resident, need to be performed. The information is transmitted to a server where staff members can track activities and inventory, or schedule new tasks. The tool was aimed at replacing paper documentation.

The prototype was evaluated in-situ during 4 weeks in a geriatric residence, to validate the technical requirements, the feasibility of the implementation, and its usefulness. The tool was used daily by the caregivers for 5 months after the evaluation, demonstrating the need and usefulness of this kind of technology. Eleven caregivers and 12 residents participated in the intervention. Also, data was acquired by means of 12 h of observation, 11 interviews, 2 focus groups, and the usage logs of the system.

The experiences, comments and opinions from the interviews and focus group of caregivers, from the in-situ evaluation, were analyzed using open coding. One result from an initial analysis was that caregivers found frequent notifications to be a burden; even though during the requirement gathering phase they explicitly asked to be informed when new actions were recorded. This led to a reconfiguration of the tool during the intervention. That is, the technology being evaluated was modified during the intervention, a flexibility that would not be allowed when conducting a randomized clinical trial.

Results from the usage logs of the system showed a significant increase in the number of activities recorded per day, which almost doubled those recorded on paper. In fact, we had asked the caregivers to continue using the paper-based recording method for 2 weeks, while they became familiar with the mobile system, but after 10 days they stopped recording activities on paper, as they were clearly confortable with the new tool.

11.2.2 Evaluating Technologies for Aging in the Wild: Naturalistic Enactment

The work presented in this section was part of a study involving in-home elderly health care, which was aimed at comparing three different intervention schemes during a 9-month period [1]. The first scheme involved a group of 50 elders who continued with their conventional form of care i.e., they obtained a monthly medical checkup at the clinic they are assigned to. The remaining two groups were part of the intervention groups. That is, there was a group of nurses who visited them on a weekly basis in their homes for assessment. From those groups, one of them carries out the assessment using paper-based records, and the second one used electronic-based emergency nursing protocols (i.e., a mobile device).

As mentioned, there are several challenges associated with evaluating assistive technologies for aging. We developed an auxiliary technique for evaluating technologies in the wild called naturalistic enactment. This technique can become handy in situations where it may be difficult to carry out a hands-on evaluation due to the risk associated with having actual users. Consider the case of a belt to be worn by older adults which monitors falls at home, which can contact family members in the event of a severe fall. While it may be desirable to evaluate this technology with actual users in naturalistic settings (e.g., their homes), there are several inherent risks associated with those events, plus the uncertainty of when it may happen. Therefore, the use of techniques that can provide a good compromise between realistic conditions and minimizing risks can be desirable.

We used the naturalistic enactment approach for evaluating the introduction of a mobile phone aimed at assisting nurses attending emergency calls from elders [2]. In this particular case, the evaluation with nurses comprised the enactment of certain tasks under naturalistic conditions, reaching a good compromise between a controlled setting and high ecological validity, meaning that there was a high degree of user involvement and high levels of fidelity while performing the tasks in the evaluation. The part of the evaluation that provided control was the utilization of simulated patients. That is, instead of using actual older adults, we made use of actors who were previously trained and who acted as elderly callers who had been involved in an emergency situation. For the study, each nurse was allocated seven to eight elderly patients, who could call them at any time. Following the research protocol, designed jointly with a physician, the simulated patients contacted the nurses at particular times regarding four different afflictions (falling, food poisoning, heart attack, mild depression).

The electronic-based protocols were based on standard telephone triage protocols for nurses. These protocols are based on procedures for deciding who receives medical attention first, based on how seriously someone is injured [3]. The electronic-based protocols consisted of 27 protocols related to the most typical afflictions of geriatric patients. The electronic-based protocols consisted of an application for a mobile device (i.e., Apple's Ipod Touch), which provided a clear-cut interface where the names of the patients assigned to the nurse are presented in the first screen. When a nurse selected one of them, the contact information of a member of the elder's network became available. Then, the nurse selected the protocol that she considered to be the most appropriate based on personal criteria, professional experience, and the medical record of the patient. Next, a set of questions were presented related to the affliction of the patient. These questions were used to assess the severity of the patient's condition, to which the nurse had to respond with YES/NO answers. The first set of questions pertained to injuries or conditions that can put the patient at high risk such that urgent attention might be needed. The severity level decreased as the assessment process carries on. Should the nurse positively endorse one of the questions, a recommendation was displayed depending on the severity of the condition such as calling an ambulance. Ultimately, if the injury or condition was not life-threatening, a set of home care recommendations were provided (Fig. 11.1).

One of the advantages of using the naturalistic enactment (as opposed to controlled experiments in the laboratory) was that the system can contribute to providing the end user with an authentic user experience. In our case, the use of naturalistic enactment enabled the stimulation of participants such that at some point they were immersed in the conversations. In addition, the use of this technique allowed us to

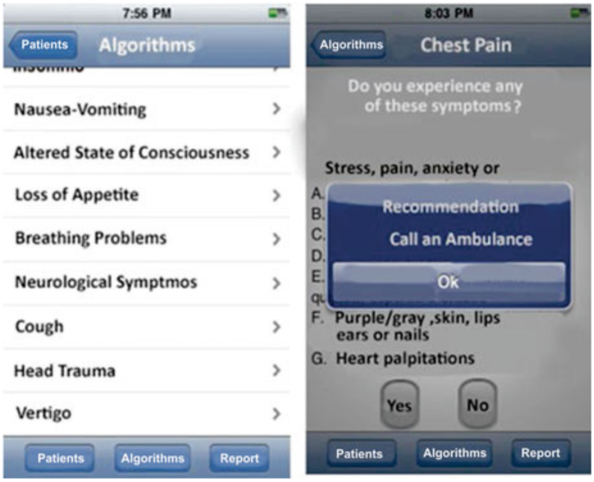

Fig. 11.1 Triage nursing protocols in the Ipod Touch (*left*). Final recommendation of the mobile application (*right*)

pinpoint situations that would have otherwise been overlooked, such as the interruption of activities.

As opposed to controlled experiments where the focus is on factors such as speed, efficiency, and effectiveness, during the naturalistic enactment, special emphasis was put on pragmatic aspects that are often made apparent only after the system has been used in realistic conditions. These are situations upon which we have no control but they reflect to a certain extent the potential of this technique to uncover a variety of matters and concerns embedded in the actual context of use. While the complexity of evaluating this type of technology may not be as high as in more sophisticated mobile systems, the high degree of ecological validity in this context seemed to pose interesting challenges not only to evaluate the actual experience but to assess the performance of nurses in real-world situations.

There are critical issues that need to be accounted for beforehand, like in any other method. One of the main downsides of using simulated patients during this evaluation was that nurses struggled to obtain a full perspective of the condition of the patient, perhaps due to the modest performance of some of the actors. They commented that diagnoses became challenging as other interrelated symptoms were not utterly communicated by the patients during the calls. For instance, the simulated patients were not actually suffering a heart attack and have probably never experienced one. Thus, the patients seemed to have rigidly stuck to the research protocol provided and overlooked apparently relevant related symptoms that nurses could have used to better diagnose the patients' condition.

To conclude, the naturalistic enactment technique is appropriate for scenarios that are not easily replicated in a laboratory setting and might cause risks to users or other stakeholders if used at a prototyping stage, as is often the case in the healthcare domain. One of the advantages of using evaluation technique of this sort is that several pragmatic aspects of the actual experience can be revealed that would have otherwise been difficult to bring about without proper stimuli. These issues would have been almost impossible to apprehend under a more controlled experiment. In this particular case, receiving emergency calls and operating the Ipod Touch within the actual personal space of nurses caused uncomfortable situations that were not apparent to the subjects before the intervention. Also, some nurses reported awkward situations when receiving these calls while attending other patients.

11.3 Using Novel IT to Support Research on Aging

Novel uses of information technologies have been emerging in the last few years. This new generation of technologies is enabling researchers in the medical fields to support patient diagnoses or prognoses by providing new ways of collecting patient-related information. In the realm of computer science, important advances are being made in approaches for detecting various forms of behaviors, mannerisms, or actions that are relevant to research on aging, such as coughing [4], anxiety [5], or socialization [6]. These advances are making possible the use of behavioral cues as the basis for novel computing systems that can be used to support medical work that range from early diagnosis, ambulatory assessment, inducing behavior change, disease management, continuous remote monitoring of patients, and dealing with problematic behaviors from people suffering from dementia.

In this section we illustrate how mobile sensing technology can be used to more reliably measure aspects of interest for functional assessment, which are traditionally obtained from self-report. Among the advantages of this method of assessment is that data can be gathered opportunistically as informants perform everyday activities through unobtrusive and ubiquitous sensors, such as mobile phones. This also allows for continuous monitoring rather than requiring patients to attend a clinic to complete surveys or be interviewed. We first present how mobile phones can be used to obtain behavioral data related to frailty, including data on mobility and activity. We then describe a videogame that uses a natural interface based on a pressure sensitive bar which measures muscle strength as the user plays. The game can be used to detect early signs of sarcopenia or fatigue.

11.3.1 Functional Assessment of Older Adults Using Mobile Sensing

Ambulatory assessment methods can make use of mobile phones to better understand the context in which certain biopsychosocial processes unfold. Taking measurements of certain aspects while the participant undergoes normal daily activities is desirable as they provide data capture methods that are ecologically valid [7]. Some of these methods include ecological momentary assessment, experience sampling, daily diary techniques, and the use of wearable devices, smartphones, and other technologies for the ambulatory monitoring of physiological function, physical activity, movement, among other parameters of interest.

Functional assessment often relies on self-report or is carried out in the doctors' office. Self-report refers to answers provided by the patient to questions related to her habits or symptoms. This approach has validity problems as patients may underreport or exaggerate symptoms. Also, patient assessment is based on physical tests performed in a laboratory setting, yet frequent measurements obtained in a naturalistic setting have more ecological validity. For instance, the Timed Up and Go test is frequently used to assess older adults' functional mobility, gait speed and risk of falling. Frenken et al. at OFFIS in Germany proposed an approach to perform an equivalent test using ambient sensors in a domestic environment without supervision [8]. The test can be performed continuously, given the physician a more reliable assessment of functional mobility than a test that is performed in a lab every few months, at best. Walk speed and fatigue are among the factors associated with the frailty syndrome [9]. Unobtrusively monitoring gait speed over a period of time, for instance in a route frequently walked by an individual, could provide early evidence of fatigue.

One aspect of interest for the functional assessment of older adults is the frailty syndrome. Frailty is a state of increased vulnerability to adverse health outcomes for people of the same age [10]. The frailty syndrome involves several aspects such as involuntary weight loss, exhaustion, muscle weakness, slow walking speed, and low physical activity [9]. Frail people are at high risk for major adverse health outcomes, including disability, falls, institutionalization, hospitalization, and mortality [11]. The clinical assessment of older adults is to a large extent based on retrospective accounts of incidents. This can be unreliable as patients often do not remember or try to hide or minimize negative incidents. For example, widely-accepted surveys to estimate frailty in older patients include questions such as "In the last week, in how many days you walked at least 10 min?" and "How frequently do you speak with your friends/spouse?" Often, responses to these questions are hardly precise, having older adults providing rather vague answers to questions of this nature. Therefore, mobile sensing represents an attractive approach for estimating some of those variables (e.g., physical activity, socializing with others) that could correlate to surveyed data of older adults pertaining to frailty.

Mobile sensing is mainly carried out with modern mobile phones, which have been augmented with several built-in sensors that can provide information relevant to health studies. Some of these devices include up to 15 hardware-based sensors such as accelerometer, gyroscope, magnetometer, GPS, microphones, proximity, light intensity, among others. These sensors can be used to derive certain user behaviors. For instance, the accelerometer can be used for estimating gait speed, step counting, or physical activity. There are several technological frameworks that can help rapidly deploy these types of studies such as Funf (http://www.funf.org) or InCense [12, 13].

Using InCense, we collected data to assess frailty in older adults and compare it with the results of the clinical assessment. We recruited 15 community-dwelling

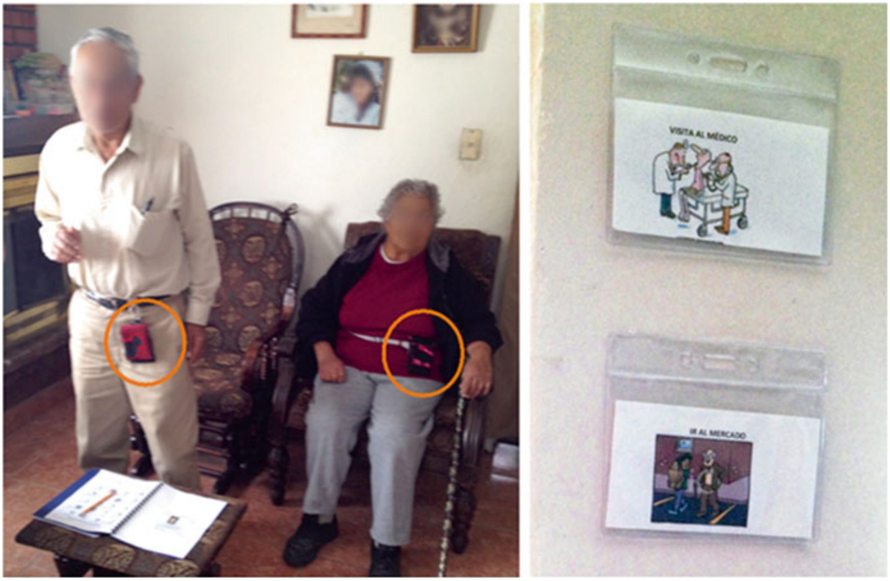

Fig. 11.2 Older adults carrying mobile sensing devices (*left*); NFC-enabled card describing frequent activities performed by older adults (*right*)

older adults, average age was 75.3 (SD = 1.8), to carry mobile phones in order to gather data from their activities and behaviors (Fig. 11.2). Four of our participants were classified as frail, based on the frailty index developed by Fried [9]. We collected data from several sensors in the mobile phones including location, audio, and others. The functional assessment of frailty in elders included standard inventories such as the ADL-KATZ [14], the SF-36 health survey [15], the Mini-Nutritional Assessment (MNA) [16], and the International Physical Activity Questionnaire (IPAQ) [17, 18].

From our results, which can be consulted at [13], we found that that sleeping time in frail participants was larger than for fit participants. Also, not surprisingly, frail participants went out of their households less often than fit participants. Also, we found that participants who were fit performed significantly more intense activity bouts than those who were frail. Finally, we were also able to estimate our participants' geographic life-space [19], which can be used to identify individuals in a community that may be at risk of not living a prosperous life [20] or to determine early functional decline in older adults with a reduced life-space [21]. Some of these results are not particularly astonishing from a medical point of view, but they were obtained through sensor data collected from their mobile phones. That is, in many cases, mobile phones can be used for some form of ambulatory assessment, which can be used to support research in this area, and provide more reliable data than self-report that is ecologically valid.

11.3.2 Using Videogames to Estimate Muscle Strength and Fatigue

Sarcopenia is recognized as a hallmark of aging and for years the term encompassed both the loss of strength and muscle mass. However, there is evidence that the loss of muscle strength is the critical factor in maintaining physical function, mobility and vitality [22] and a better predictor of disability and mortality [23]. Another important aspect related to frailty and physical decline is the sensation of fatigue. Muscle fatigue is defined as the ability to produce sustained muscle effort. Fatigue has also been closely associated with frailty [24]. In fact, it might be considered a better indicator of frailty than muscle strength since performing Activities of Daily Living (ADL) do not require a maximal effort but rather a sustained moderate effort over a period of time [25]. In addition, poor muscle fatigue resistance could explain the sensation of fatigue, which is considered a predictor of disability in pre frail subjects [26] and even mortality [27]. Muscle fatigue can be assessed using instruments to measure self-perceived fatigue [28], or through direct measurement. Hand grip performance has been found to be closely correlated to self-perceived fatigue, and a method has been proposed to measure muscle resistance with aged subjects utilizing the Maximum Voluntary Contraction (MVC) with a dynamometer [29]. Usually, these types of measurements are lengthy given that the muscle needs time to recover, thus verbal encouragement has been used to motivate the subject to obtain their maximum performance [30].

One alternative to measure muscle strength and fatigue is to use videogames, in particular "ambient games" that incorporate a new paradigm of interaction, which allows an embodied, physically active way of engaging with the game with the use of intuitive natural interfaces based on body movement. The continuous unobtrusive assessment performed while playing a videogame could be equal or more effective that the assessment performed in a clinical environment. The continuous use of the games may reveal a more complete picture of the measured strength and fatigue, motivating the patient to participate, eliminating the stress induced by these tests, while increasing the ecological validity of these measurements. While a clinical assessment in a controlled environment might provide more accurate measurements, their low frequency might fail to detect relative variations at a greater level of granularity.

To interact with the videogame, a device capable of measuring the user's grip strength as she or he plays the videogames was developed (Fig. 11.3) [31]. A Vernier Hand Dynamometer (http://vernier.com) was chosen as the core element of the interface along with additional electronic circuitry to augment the player interface such as an accelerometer and digital buttons. To measure muscle fatigue, we used the method described by Bautmans and Mets [29], in which the person is instructed to perform a MVC using a dynamometer, and then to hold this level of force for as long as possible. The time occurring between the maximum force and 50 % of the maximum force is the muscle fatigue resistance. Using the aforementioned method, we developed two videogames to measure muscle strength with a simple plot for inexperienced players that are not familiar with current videogames.

Fig. 11.3 A person playing the videogames

The first game requires the player to control the flight of a bird utilizing hand strength. When the player presses the controller, the bird will gain height and speed trying to avoid the planes flying randomly on the screen and, at the same time, enabling the player to collect items. If the bird collides with a plane an explosion will occur and the player will lose points. On the other hand, if the player collects the items (e.g., fruits) some points will be earned.

In the second game, the player controls a helicopter with the mission of suppressing an imminent wildfire. The player needs to suppress the fire of a group of burning trees as quickly as possible by collecting water from a nearby lake. The water collected needs to be carried while holding the dynamometer and retaining the initial force. As with a helicopter, the player can tilt the cyclic stick (i.e., dynamometer) to control the angle. Finally, the player has to pour the collected water over the fire area to prevent fire from spreading. As a way to make challenging for all types of players regardless of their muscle strength, the videogame has several scenarios that can be customized to account for different kinds of measures.

The games were played by five participants in 30 min sessions. We found that the device accurately measures grip strength and the games resulted entertaining and easy to learn by older adults, although the results revealed differences in perception about difficulty based on gender and past experiences. These games could be adapted automatically based on the signals received from the sensors to balance the difficulty presented with the skills perceived or the physical condition to provide better incentives for player engagement.

In this section, we have described two distinct approaches to measuring parameters of relevance to aging research. One involves the use of the sensing and processing capabilities of mobile phones that are becoming ubiquitous and are frequently worn by its users. These devices can be used to measure parameters associated with mobility, physical activity, and socialization. The analysis of this data over long periods of time can provide information about behavior patterns and how they relate to health variables. In addition, the devices can be used to persuade the user to adopt healthier habits or communicate with caregivers. We have also described a videogame and sensing device specifically developed to measure muscle strength and fatigue. Similar sensing systems could be embedded in living environments to enable opportunistic sensing. For instance, pressure sensors in beds can monitor sleep quality that can in turn be correlated to activities performed during the day or the mood of the subject the following morning. These technologies could give rise to new assessment methods that have the advantage of continuous monitoring with high ecological validity and will become an integral part of research on aging.

11.4 Closing Remarks

The works we presented are a few examples in which research on aging can be enhanced or supported by technology. We first presented how to evaluate in the wild the effectiveness and adoption of assistive technologies, and the challenges that are associated with this approach. In the second study, several aspects related to the functional assessment of older adults were obtained through mobile phones and videogames, making possible to envision the possibilities that this sort of technology can have for research on aging.

The emergence of these novel forms of information technologies offer unprecedented opportunities for scientists and practitioners to better understand and potentially influence patients and their contexts. These advances are being helpful in stepping up our understanding of human dynamics and contexts. Even more, a better understanding comes with an opportunity to provide adequate services to patients and potentially influence their attitudes and behaviors.

At the same time, these emerging technologies pose new challenges for well-established research methods as some of them have to be rethought, reshaped, or overhauled. Technologies that could provide a continuous data stream of measurements for researchers and physicians were unthinkable two decades ago. Modern mobile phones, coupled with their augmented capabilities and ubiquity, are indeed creating new opportunities for measuring behavior, conducting epidemiological studies and enacting interventions to change behavior. Mobile phones can boost medical studies by gathering data from larger populations, increasing the frequency of reporting and providing more reliable data based on the continuous monitoring of actual behavior rather than from sporadic interviews that rely on self-report. Analysis from larger populations, for instance, could result in findings that take into account differences in groups regarding gender, age, or upbringing, with results drawn rather rapidly and with higher ecological validity.

Finally, when comparing these emerging technologies to traditional approaches in research, there are stark differences between the types of data that can be collected (e.g., audio, video) as well as the frequency in which measurements can be taken (e.g., continuous), all of these with higher ecological validity. Nevertheless, there is plenty of work ahead to supplement current methods, rethink some of them, or perhaps create new methodologies that can take full advantage of the opportunities being offered by technology to aging research. Still, one of the big questions that will need to be addressed is whether revising current methods (and instruments) by increasing the frequency of measurements, increasing data quality, aggregating data from various sources, and having higher ecological validity will have, ultimately, medical significance. That is, if any improvements to current methods or new proposed methods will have an ultimate effect on the health outcomes of patients. Undoubtedly, incorporating these emerging technologies to research on aging will provide a different lens through which researchers, practitioners, and family members can scrutinize subtle changes in patient conditions and behaviors, perhaps before it is too late. Ultimately, what technology will surely provide, as it has been shown in other disciplines, is an increase of the scope, depth, and complexity in the design of much more comprehensive studies in the area.

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Chapter 12
Translation of Scientific Knowledge

Elizabeth Caro-López

Abstract Public policies are based on evidence of every day life. This derives from the need to make decisions in the shortest possible time and cost and likelihood of further quantitative and qualitative impact on the lives of individuals and the welfare of countries. To the everyday set of problems that require solving day to day one more global and local impact must be added: the aging of the population. The main challenge is to converge the research agenda and the agenda of government. A brief summary of what the process involves public policy and a proposal of what research can contribute to it occurs.

Keywords Public policy • Evidence-based policies • Policies for the older adults

12.1 Introduction

A public policy is not a single action of government in response to specific political circumstances or social demands of the moment. Many definitions have been created about public policy; for the purposes of this chapter I will use one of the most comprehensive: public policy is everything the government does, and its main objective is to match goals to the facts, purposes and mandates it receives from society through a process that unites resources, laws, organizations/institutions and programs [1].

The process of satisfying the needs that are thought to be in the public interest is complex. Each need must be clearly identified, recognized, and ideally it should have a minimum of social consensus to define an intervention by public institutions. There are aspects of social development for those that have absolute certainty as to the need for action, as is the case for procurement of public services, education, health, and public safety, among others. New areas of development have been included more recently in governmental action, such as the case of gender equality, promotion of a sustainable environment and, no doubt, the aging of the population.

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In today's societies there are increasing interests and needs to be attended to, and so the most recent discussions are about not only all the needs to be covered but principally the priority of their attention, as well as the forcefulness and immediacy with which they can and must intervene.

What priority does attention to age and aging have in the actions of the institutions? How many economic, material and human resources are assigned to them and how many should have to be assigned? What are the costs and the benefits? Are the interventions defined from the evidence? How are these interventions evaluated?

From these and other questions, public policy on a complex theme like the aging of the population requires development of two components: one political-normative that consists of understanding and attending to needs that are concordant with the legal framework; and the other one scientific-technical, based on having enough evidence to enable the government and its institutions to set priorities and act efficiently and effectively.

The development and implementation of evidence-based public policies is a challenge worldwide, since in general, public policies are not designed with enough evidence, or scientific-technical knowledge is not developed fast enough for the policy designers. More than a question of will, it is the need to analyze the process or cycle of the policy to identify why the political-normative and the scientific-technical components do not match.

It is timely to show that research agendas should focus on proper scientific interests, and therefore do not need to consider the formulation of public problems that later must be transferred to the institutions and executed by them. Generally, scientific research includes in its conclusions the need to formulate public policies that provide an outlet for the knowledge discovered. This configuration should be a premise of research per se, from the idea that the main question or hypothesis of public policy is: what are the problems that need to be solved?

12.2 The Process of Public Policies

As was stated, knowing the process of making public policies contributes in certain measure to identifying which part might have a convergence or divergence between public action based on law (plans, programs and actions of the institutions) and the use of scientific evidence.

12.2.1 Formation of the Public Agenda and the Government Agenda

The public agenda is shaped by the consensual expression of a group (which might be civil society, the academy, a private institution, etc.) or by all of society together, on a need for attention or a problem to solve. The government agenda is formed from the public agenda, but also from the diagnosis of needs from the national sphere identified to prepare the sectorial programs or needs expressed directly by the elected representatives and the legislators.

At present, the issues of population age and aging are on most public and government agendas both nationally and internationally. "The problems of the older adult population" are mentioned very frequently, as if they were dealing with a collective and static homogeneity. In addition, these issues do not have the same priority for all countries; even within a country the issue could be more or less important depending on the location. For the international community, represented by the United Nations (UN) and the World Health Organization (WHO), the issue is mainly of interest for its implications on health, social development and human rights. In recent years this interest has increased not only due to the growth of the population 60 years of age or older, but mainly for the conditions in which people are aging and the implications for the family, society and governments.

The UN has studied the issue of older adults since 1948, when the General Assembly approved resolution 213 (III) relating to the project of the declaration of rights of the aged. Since then the issue has been approached indirectly by the General Assembly and by the organisms interested in social issues [2]. It was not until 1977 when the problem was approached directly with emphasis on the need to organize a world assembly on older adults, and in 1978 it was agreed that this conference would take place in 1982. The second World Assembly took place in 2002 and from these came a large number of documents that suggest the way to approach the issue.[1] For WHO the issue has always been present, but especially after 2000 it began to create specific studies such as the Study on Global AGEing and Adult Health (SAGE). Another example of how the question has become more relevant is the fact that April 7, 2012, World Health Day, was dedicated to the theme of aging and health.

In Mexico, public policies for the older adult population were established in the 1940s through key institutions like the National Institute of Old Age (now the National Institute of Older Adult Persons), the Mexican Institute of Social Security (IMSS), the Institute of Social Security for State workers (ISSSTE), and the National System for the Integral Development of the Family (SNDIF).[2]

Now, is there or is there not a consensus among the various agendas, both public and government (federal and local) on how to understand and attend to age and

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[1] A comprehensive review of the documents is available on the following page:
http://www.un.org./esa/devagenda/aging.html

[2] For a broader reference to public policies for the older adult population in Mexico, see the following texts:

Caro, E. Gestión pública y envejecimiento: la gestión de programas para la población adulta mayor en México. Revista de Administración Pública No. 124. Volume XLVI, N°1 (January–April 2011). Pages 15–42. Available online at:
http://www.inap.mx/portal/images/REVISTA_A_P/rap124.pdf

Vivaldo, M. Martínez, Ma. de la Luz. La política pública para el envejecimiento en México. Historia, análisis y perspectivas, en Envejecimiento y Salud: una propuesta para un plan de acción. México, UNAM. 2012.

aging, and what the priorities are? The short answer is no, because the issue has more or less importance depending on the situation. For example, the importance the issue has in Mexico's Federal District, being the region with the largest older adult population, and where there are more actors active on it (organizations of civil society or institutions), is not the same as in the state of Chiapas, where the average age is less than 30 years and where public policy priorities are directed at ethnic, labor and frontier issues. Agendas required as a jumping-off point are discussed in the following point.

12.2.2 The Definition of the Issue

If there is one crucial aspect at the hour of defining a public policy it is the definition of the need or problem. For that, technical-scientific evidence is of vital importance. It would appear simple to make decisions about attention to it from knowledge about the issue of age and aging; in principle it is. In other words, there is a worldwide and local consensus that the population is aging and that this has implications in society. Now, to be able to define a public policy on this, it is necessary to agree on what is, for example, age and aging itself, and what are the preventive or care aspects to avoid situations like frailty, sarcopenia, disability, dependency or the geriatric syndromes. What are their dimensions and causes? Who is affected and how much? And, how will this develop if nothing is done about it?

At present in Mexico there is plenty of current information on each of the issues mentioned: statistical data, surveys, ethnographic studies, scientific studies, clinical trials, and more. Each study will have a specific weight in terms of the intervention for the design that is wanted. It is possible that the more variables that exist on the issue, the more complicated it becomes to be able to define or prioritize an intervention, but it also increases that probability of being more assertive. It should be mentioned that the use of the language is pivotal, so that the information generated by scientists the so-called stakeholders may use it to make decisions. What is clear to an expert in demography or medicine is not clear to the person in public administration, and vice-versa. The information could be the best in the world, but if it is not accessible and uses language not reasonably comprehensible for everyone, its use will be confined to a group of specialists on the topic.

Once the question is defined on some of the many facets of age and aging, the decision must be made to intervene, that is, to create a public policy, and to do that, the next stage is significant.

12.2.3 The Making or Formulation of Public Policy

This stage refers to building options to resolve the problem stated above. The decision to design an intervention to tackle a problem through public institutions depends, obviously, on deciding to do so, and is derived in part from the existing consensus – and what might turn into a true social pressure – such as the budget and resources available. Usually, time is an element that works against it. Economic, material and human resources are also scarce and there are many problems to deal with. Therefore, the formulation of a policy must be very clear and limited to the following elements:

- The objectives and priorities. For example it's not enough to say that it will improve the quality of life of older adults. It has to specify exactly what that means and in all aspects to be covered, which ones will be attended to first as a function of the characteristics of the community, and what the parameters will be to measure the better or worse quality of life.
- The existing alternatives. Research could contribute in large measure to tackling this aspect. Being aware of similar policies and programs in national and international settings would make it possible to optimize costs and maximize benefits of an intervention, and also to avoid duplication and promote inter-institutional and multidisciplinary work.
- The risks. All interventions have unwanted effects. For example, there will be some people whose characteristics will be included in a health program and others whose characteristics are not. There will be programs implemented without enough evidence and that demonstrate over time that the benefits are limited and that even have adverse effects. One such case was the use of vitamin E, which in some places is recommended on a daily basis as an "anti-oxidant," however recently a meta-analysis showed that even though it could prevent cardiovascular illnesses and cancer, in high doses could increase any cause of death [3].
- Maximizing the results. Because of the need to optimize health care expenditures given the scarcity of public resources, being able to ensure that an intervention is viable and favorable in cost-effectiveness terms often becomes a decisive factor. In general both medical and administrative personnel carry out this type of study. Ideally, they do it together since this will have the effect of overseeing the optimization of resources per se, but also of achieving health objectives with more benefits than costs.

Ideally these aspects should be considered (at least in a general way) in all research on age and aging. This also will move closer to the possibility that public policies or programs are based on technical-scientific evidence.

Research doesn't necessarily have to approach all the issues, but within the theoretical framework that exists, it is desirable to include at least one of these variables to contribute to formulating an intervention.

12.2.4 The Decision, or Choosing Among Options

There are three aspects to be taken into account here: technical viability, which generally considers economic resources, infrastructure and human capital; political viability, which includes the will of the various actors (public, social and private), as well as the participation of opinion leaders and communication media in general; and social viability, which may be understood as the possibility that communities will not only accept but also adopt the policy and be active agents in moving forward with it.

If one of these aspects is missing, it does not mean the intervention should be stopped, but it lowers the probability that what is done will be efficient and effective, and that at the end it might be something ephemeral and thus become an expense and not an investment. The gap that might exist between the technical-political and social areas could diminish or even disappear if the research has information derived from other similar programs. This aspect relates clearly to the evaluation phase.

12.2.5 The Evaluation

The evaluation of a public policy means, in general, a systematic process of collection and analysis of information for the purpose of showing the efficiency and effectiveness of the interventions. Thus, within the institution the cost-benefit (efficiency) is evaluated; as well as the objectives programmed vs. the goals reached (effectiveness), while outside of the institution, what is most important is to measure the effect achieved with the intervention (effectiveness).

Evaluations could be classified according to who carries them out, the purpose looked for, their content and the time they are applied. As shown in Fig. 12.1, an evaluation could be done by the same team that designs and implements the policy, by an external team, or by a mixed team. Regardless of who does the evaluation, the most important thing is to define the objective of the evaluation – whether it is for generating information or whether it is required for administrative control, to introduce reforms, to rationalize resources, or to systematize the knowledge.

It is highly desirable that the evaluation be considered from the beginning of the design of the public policy intervention, and that it even considers the pertinence of evaluating the design itself as a control mechanism of results; or else, evaluating the process of implementation and management; or the results and even the impacts of a policy. It will not seem strange to the reader to find that the evaluation always seeks to know the impact of the intervention; however, for that reason it is important to take into account the moment the evaluation is applied. An evaluation applied after the intervention (*ex post*) could propose the knowledge of the results and the impact of what is done, although this implies even more time and establishes clearly that it is considered as impact in an intervention. What impact is expected from a low salt diet? What would be the standards of measurement? What impact can be expected from exercising? What impact is expected from promoting ballroom dancing among older adults?

An intermediate evaluation or one during the intervention is focused on learning details of the implementation and management, in terms of cost-benefit. Lastly, an evaluation that is applied before the intervention enables us to learn the details of

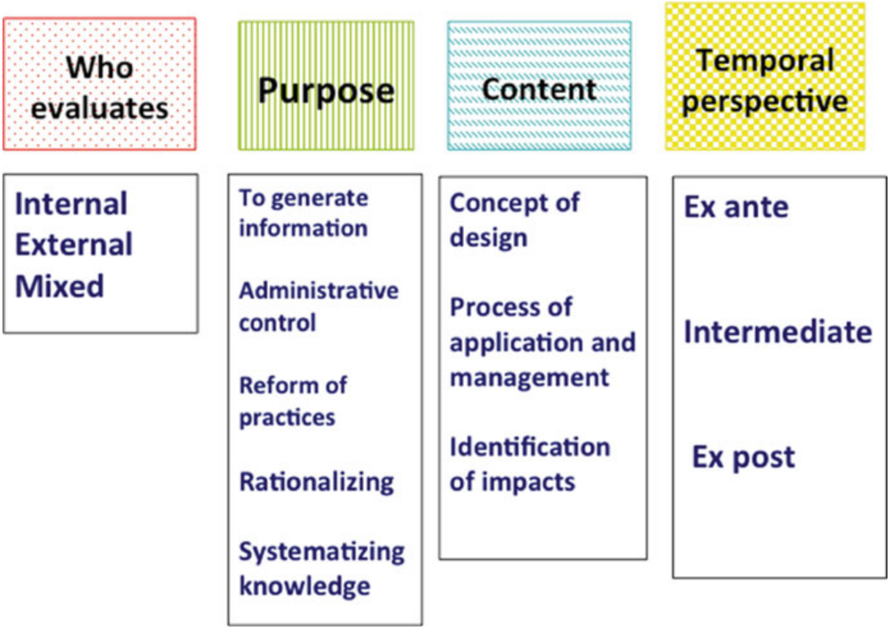

Fig. 12.1 Types of evaluation applied to public policy

the design of the entire intervention to thereby ensure or at least control the results or goals established.

Although many public policies are well designed and implemented, they do not necessarily solve the problem posed, or have unwanted effects, or turn out to be very expensive and therefore unsustainable. Evaluation has gradually become more relevant in the public policy process, although to tell the truth, it is not always considered in the design of the intervention, but rather at the end and seeking to learn only the impact. It's rare that sufficient economic and human resources are assigned to it and the results are not always used to change or even make a decision on whether to end or stop the intervention.

No doubt this is a space where scientific research could bring great added value into the process of public policy. Since objectivity is assured, newer and better evaluation methods would be applied and the backing of a research or academic institution could help decision-makers put forward arguments that are not only solid but that carry greater legitimacy as to whether to continue or suspend a public policy [4].

12.3 The Role of Researchers in Decision-Making

With the areas of scientific research and of public policies being so different, in a somewhat creative societal metaphorical exercise, one could say that the government is equivalent to the brain; the resources, what nourishes the body to enable it

Table 12.1 Interaction between the researcher and decision-maker, to be taken into account in the translation of knowledge

Needs of the decision-maker	What the researcher contributes
To solve problems	How is the question defined?
	Which are the dimensions and causes?
	Who is affected and how much?
	Which will be the consequences if there is no intervention?
To formulate alternatives	Options for tackling the problem
	Objectives and priorities
	Existing alternatives
	Risks, costs and benefits
	Maximizing results
To choose an alternative	Technical viability
	Political viability (social research)
	Social viability (social research)
To implement/intervene	Actors who should be involved
	Means of ensuring the results
To evaluate the intervention	Criteria of quantitative or qualitative evaluation
	Recommendations for improving or terminating an intervention

to function; the institutions are the main organs: heart, liver, lungs, kidneys, stomach, etc.; the legal framework constitutes the skeleton; the public and private actors, the muscles; and finally, the public policies the veins and arteries and the nervous system that connects and enables the body (society) to communicate and function using all its components.

Research could contribute to anticipating problems or identifying them in time, defining them, predicting changes during the implementation of an intervention that affects the stated objectives and especially, contribute to carrying out ever-improving evaluations from the best methodologies (Table 12.1).

12.4 The Bridge Between Research and the Creation of Public Policies

These bridges (communication channels, common language, discussion groups, etc.) would help to improve the links between the supply of scientific evidence and the demand for and use of evidence. They require, among other things:

- Knowing and understanding the agendas of the research and decision-making. The time necessary for an investigation contrasts with the immediacy of the policy decisions. Matching the agendas can facilitate decisions in which part of the public policy process will participate.

- The use of language. Effort is necessary on both sides. The researcher must consider using simple and accessible language for the general public; and the decision-maker must commit to doing or commissioning a specialist to do detailed studies on what they want to solve.
- Creating a larger number of "working groups" between researchers and decision-makers. An example is the initiative of *Nesta Operating Company*, (http://www.nesta.org.uk/). This foundation for innovation is located in the United Kingdom, where its objective is to offer investments and subsidies for researchers whose knowledge they believe should be applied, and to disseminate that knowledge through the permanent work of these groups and making technology become a useful tool [5].
- Maintaining the independence of both the researcher and the decision-maker. This is of critical importance to ensure the objectivity of the research and the intervention proposal. Researchers must not perceive it as doing an investigation only for the decision-makers, and that group must also take into account not only the knowledge but also the daily situation of the population.

Lastly, the person doing the research must not forget that public policies are always in permanent debate. What is hoped for are public policies that solve public problems at lower cost and with broad impact; that they achieve this through the consensus of a large number of actors; that they are sustainable (economically and socially), inter-institutional, and above all that the impact be absolutely measure-able, both quantitatively and qualitatively; and that they avoid duplication of programs or in the pattern of beneficiaries. As well, the way in which public policy is now done has changed in terms of the way the government and its organizations are structured, and this makes the problems ever more complicated to resolve.

Thus, age and aging are no longer an issue that relates only to the 60-and-over age group. It has become a challenge for all areas of human development. Like the concept of health as defined by the WHO, not only is it the absence of illness, but also the total state of physical, mental and social well-being. Similarly, geriatrics not only is the study of prevention, diagnosis, treatment and rehabilitation of illness related to age, but its goal goes beyond that and involves other disciplines to be able to attend to the many social-sanitary aspects that affect the process of aging, illnesses, exposure to risks, long-term care, research, the training of specialists, and more.

Far from thinking this is an adverse panorama, it is evident that the meeting points for translation of knowledge are continuing to broaden and at different times, as much in the process of research as in public policies. There are many examples where this is already a reality, but what is now required is that it be done systematically and that there is a formal registry of it.

Research and knowledge generation is a public good in its own right. It produces social value when it is translated into better technologies or methods of diagnosing illnesses that are increasingly complicated; when it leans toward the generation of models of prevention and replicable care, and no doubt when it contributes to those individuals having better knowledge about their health and how it improves their lifestyles and its quality and conditions. Therefore stakeholders should consider knowledge translation as an essential link in the generation not only of public policies but also of the generation of public value.

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