Chapter 8
Longitudinal Studies and Older Adults Cohorts

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Abstract Science never before faced such a complex, dynamic and time-dependent process as human aging. Longitudinal studies are a source of fundamental evidence of 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 older adults, 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 on aging, starting 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 taken from literature, which enable us to provide examples of scope and methodological implications, finally we suggested some strategies about strengthen the validity and generalization of results.

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 having less effect throughout the study.

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C. García-Peña et al. (eds.), *Aging Research - Methodological Issues*,
https://doi.org/10.1007/978-3-319-95387-8_8

Keywords Longitudinal studies · Longitudinal-research · Follow-up studies

8.1 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.

8.2 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].

The chapter will be limited to showing general aspects of observational longitudinal studies, experimental studies like clinical trials or quasi-experimental studies are discussed in Chap. 9.

All epidemiological studies may be classified according to the way the information search will be oriented. Considerable debate around a unique epidemiological studies classification has been present in the medical literature. Pearce for example, discusses that all epidemiological studies are bases on a specific population and during a specific period of time. Consequently, author argues that the fundamental

distinction is between studies of incidence and prevalence [4]. Truth is that there is not only one approach and we may to accept that more than one classification is needed depending on different purposes.

Related with longitudinal studies, also several perspectives had presented different classifications. 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. Caruana et al. [6] separate panel studies in three types: i) cohort panels, where some or all individuals with similar exposures or impacts are considered over time, ii) representative panels, where data are collected for a random sample regularly and iii) linked panels, where data collected for other purposes is tapped and linked to form individual-specific datasets.

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 must be given special consideration in studies on aging, where it happens more frequently, since the losses are related to events such as address change, 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 considered. 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 [7] 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 [8]. 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 [9, 10]. Like the other longitudinal studies, its objective is to describe the occurrence of time-dependent results [10], but the scope of this type of epidemiological study is related more to the incidence 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. Other cohort design studies worth to mention are case cohort design [11], integrates a selection of cases and a smaller set from an original cohort is and the nested case-control, within a cohort study, where cases and controls are selected from the cohort.

Retrospective cohort study or historical cohort occurs when the investigator accesses a historical roster of all exposed and non-exposed persons and then determines their current case/non-case status. The investigator initiates the study when the disease is already established in the cohort of individuals, usually long after the original measurement of exposure. 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.

In a prospective cohort design investigator begins by integrating a sample of participants, measure some characteristics that can predict an outcome and then follows these participants and measure them periodically [12].

It must be taken into account that older persons differ from other groups 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

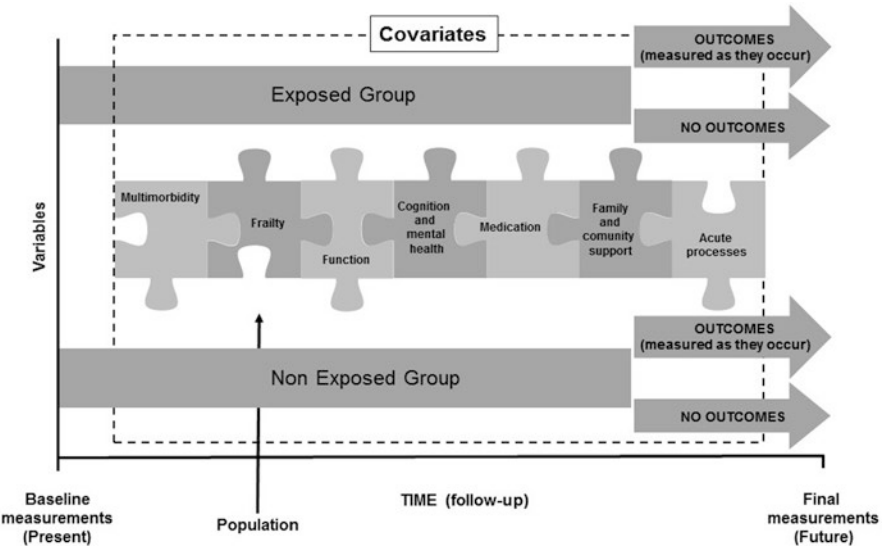

Fig. 8.1 Proposed outline of the scenario of a longitudinal study on aging

study of falls among old people [13] and the analysis of levels of complexity present in geriatric research among different populations of older people by Faes et al. [1].

Figure 8.1 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 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 [14, 15] (Fig. 8.1).

A clear example of the theoretical concept of this design is presented by the Canadian Longitudinal Study on Aging (CLSA). It [16, 17] 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.

8.3 Advantages and Disadvantages of Longitudinal Studies

Longitudinal studies present important advantages over other observational designs (Table 8.1). It makes it possible to evaluate the incidence of a particular illness or outcome and helps when investigating potential causes of a possible outcome, 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 [15].

Longitudinal studies with older 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, 18, 19].

On the other hand, longitudinal studies share the disadvantages of observational studies. The interpretation of causal relationships can always be limited by the presence of many confusing variables. However, longitudinal studies offer the best observational option for studying causal inference. 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 [9] 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 many 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

Table 8.1 Advantages and disadvantages of longitudinal studies [6]

Advantages	Disadvantages
Establishes cause-effect relationships in real time	No differential classification for lack of control in assigning of the exposure. Often requires large sample sizes
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, relative risk, excess risk.	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. Often very expensive

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 address, 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 [9, 20]. 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.

8.4 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 [21–24].

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 [24]. 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 [25, 26]. 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 are especially important.

8.5 Methodological Scopes and Implications of Longitudinal Studies on Aging

Longitudinal studies have made important contributions to understanding aging [24], 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 [27, 28].

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 [28], 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 8.2 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 8.3 of the original article. Despite the fact that the topics

Table 8.2 Topics related to longitudinal studies on aging [20]

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

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.

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 [29–42]. 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 8.3. 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 National Study of Health and Aging in Mexico (MHAS) [29] with four measurements over 14 years. 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, the fourth round was completed in 2015. Two more waves are prepared for 2018 and 2021.

Table 8.3 Longitudinal studies on aging

Study	Population	Follow-up	Objective
ENASEM-(MHAS in English) [29] Mexican study on health and aging in Mexico	n = 15,402 50 or more years of age	2001 2003 2012 2015	To obtain information on various characteristics of the objective population living in Mexico
ELSA [30] 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 deoxyribonucleic acid (DNA) to correlate the samples with epidemiological data
HRS [31] Health and retirement study	n= >37,000 50 years of age or more	1992-to present	To understanding interaction between health and social, economic, and psychological circumstances, particularly with the retirement decisions.
PREHCO [32] The Puerto Rican elderly: Health conditions	n = 4, 291 60 years of age or more	2002 2003 2006 2007	To provide quality data for researchers and policy makers about issues affecting the elderly population in Puerto Rico
CRELES [33] Costa Rican Longevity and healthy aging study	n = 2820 Born in 1945 or before	2005 2007 2009	To determine the duration and quality of life, and its causal factors, of the Costa Rican elderly
ELSI [34] The Brazilian longitudinal study of ageing	n = 10,000 50 years of age or more	2015-to present	To measure outcomes across a wide range of domains and to provide high-quality multidisciplinary data that can shed light on the causes and consequences of outcomes of interest.
SHARE [35] The survey of health, ageing and Retirement in Europe	n= >120,000 50 years of age or more	2004-to present	Micro data on health, socio-economic status and social and family networks, covers 27 European countries and Israel.
TILDA [40] The Irish longitudinal study on ageing	n = 8504 50 years of age or more	2010-to present	To provide and evidence base for addressing current and emerging concerns associated with aging population in Ireland
LASI [37] Longitudinal aging study in India	n = 60,250 45 years of age or more	2012-to present	To provide comprehensive longitudinal evidence base on health, social and economic wellbeing of elderly population in India.
CHARLS [36] China health and retirement longitudinal study	n = 17,500 45 years of age or more	2011-to present	To collect a high quality nationally representative sample of Chinese residents.
JSTAR [38] Japanese study of aging and retirement	n = 4200 Between 50 and 75 years of age	2007 2009 2011	Researchers can track the characteristics of the Japanese elderly population in terms of both their specificity and universality in the world.

(continued)

Table 8.3 (continued)

Study	Population	Follow-up	Objective
KLoSA [41]Korean longitudinal study of aging	n= > 10,000 45 years or older	2006 2008 2010 2012 2014	To create the basic data needed to devise and implement effective social, economic policies to address the trends that emerge in the process of population ageing
IFLS [42] Indonesian family life survey	n= > 30,000 26 years of age or more	2007 2008	The fourth wave was redesigned to collect data similar to those in the HRS and similar surveys.

The English Longitudinal Study of Aging (ELSA) [30] 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. 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.

The Health and Retirement Study (HRS) [31] was conducted for 25 years. The HRS is a national representative survey of subjects over 50 years of age in the USA, provides evidence of psychosocial content and policy changes in addition to the expansion into biomarkers and genetics that may affect individuals. The initial HRS Cohort (1992), included individuals born between 1931 and 1941 and their spouses of any age. In order to make the sample fully representative of the USA some new cohorts were enrolled through the years, the last was added in 2010 (Mid baby boomers born 1954–1959). The main survey occurs every 2 years, making 2016 the 14th follow up.

The PREHCO Project [32] investigated the characteristics of older non-institutionalized adults over 60 years of age in Puerto Rico, cross-sectional sample survey of target individuals and their spouses. The first round was between 2002 and 2003 (2167 variables and 4291 cases). At this moment has completed a second round to become a longitudinal study. The follow-up questionnaire included questions regarding the changing conditions of those individuals who participated in the first round, this second wave has 4291 cases and 2766 variables, those participants deceased or institutionalized were interviewed using a proxy.

Another survey distinguished by extensive measurement of health indicators as well as biomarkers is CRELES [33], also has linkages with the Costa Rican National Death Index in the follow up mortality events. First wave (2005) include participants who born in 1945 or before (2827 participants), the second wave in 2007 revisited the same participant group and the third wave was conducted in 2009 with 1855 surviving participants. Through these rounds different measurements were

made: fasting blood and overnight urine collection, DNA has been extracted for second and third cohort.

ELSI-Brazil [34] collects data relating to health and functioning, economic circumstances, social participation and networks, use of health services of adults aged 50 years or older. After the baseline information collection, the follow-up waves are biannual. This study has been planned to survey about 10,000 Brazilians every 2 years, new participants are added to refresh the different cohort age groups.

SHARE [35] is a multidisciplinary panel database of micro data on health, for more than 80,000 individuals in European population over 50 years of aged, this panel covers 27 European countries and Israel. From the first wave this database combined self-reports health with physical measurements reports. In wave four in 2010 were included dried blood spots samples, the relevance of this was that these blood spots were analyzed for C reactive protein, HbA1c and total cholesterol. In the future it will be possible to include vitamin D and inflammatory markers of the cytokine family.

TILDA [40] is a detailed study on ageing undertaken in Ireland. It involves detailed interviews of people aged 50 years and over, charting their health, social and economic circumstances over a 10-year period. As some of the previous international studies, TILDA also collected different important biomarkers.

LASI [37] is a study conducted in 30 states and 6 union territories of India, covering a panel sample size of 60,250 individuals aged 45 years and older and their spouses. This study adopts multi-stage clustering sampling design; three-stage sample design in rural areas and a four-stage sample design in urban areas. The main reason for adopting this four-stage sample is to make easier the selection of households because urban wards are quite large, making it difficult to list all the households.

CHARLS [36] is based on the HRS and related aging surveys such as the ELSA and SHARE. The pilot sample was a two-province sample collected in 2008 and followed up in 2012.The national wave of CHARLS was fielded in 2011and includes about 10,000 households and 17,500 individuals in 150 countries and 450 villages committees. These individuals will be followed up every 2 years.

JSTAR [38] is an interdisciplinary data resource on health, economic position, and quality of life in Japan. Like SHARE, HRS and ELSA this survey has the common aim to understand a variety of levels in aging, from individuals to countries, from an international perspective. The first wave of JSTAR took place in 2007, contains data on individual living circumstances of 4200 adults between 50 and 75 years of age. Three waves were conducted from 2007 to 2011.

In Korea: KLoSA [41] is sample of more than 10,000 persons at least 45 years of age that were interviewed among other topics, about information on work and income and health and disability. It was first conducted in 2006, with biennial follow-up waves since then. Topics include in this survey have an important impact on the economic and social activities of this group.

On the other hand, it is IFLS [42], a longitudinal survey representative of about 83 percent of the Indonesian population, containing more than 30,000 individuals in 13 in the country. First wave was conducted in 1993, it was designed as a household survey of individuals at least 26 years of age. For its fourth wave in 2007, it was

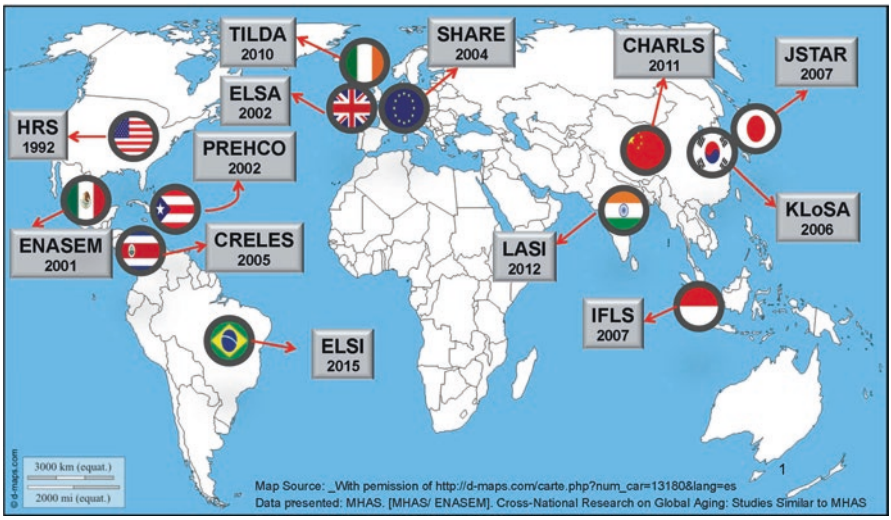

Fig. 8.2 Longitudinal studies on aging [43, 44]

redesigned to collect data similar to those in the HRS and similar surveys, including community survey and local conditions. Fig. 8.2 shows geographical location and starting year of the previously mentioned longitudinal studies on aging [43].

8.6 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 [25]. Most phenomena related to aging are time-dependent [24, 45], 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 [46, 47] 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 [48].

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 [47, 48].

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.

8.6.1 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.

8.6.2 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.

8.6.3 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 [47]. 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 [46, 49, 50].

8.6.4 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 cross-sectional weighting (within the same measurement time) or between subsequent measurements time zero vs. n times involved [31, 51].

8.6.5 Harmonization of Data

A very important effort was launched on 2015 by the RAND Corporation and the National Institute on Aging (NIA) which convened a meeting of the Network on the Harmonization of International Aging Studies with support from to facilitate cross-national comparisons [52]. The web page "Gateway to Global Aging Data" (www.g2aging.org) aims to promote harmonization and to serve as a repository of information about the HRS-family of studies. This web page presents comparative descriptions of the HRS-family of studies, harmonized variables and datasets, among other tools. Several longitudinal studies around the world are now present in this webpage.

8.7 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 multi-factor 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 must 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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