Understanding health dynamics among the oldest-old

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To my grandparents. I thought about you the whole time I was writing.

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English summary

In most developed countries, the proportion of oldest-old has increased during the last decades as a consequence of the decline in old-age mortality. An increasing number of oldest-old people will pose challenges for the health-care and economic systems of modern societies but it could be transformed into an opportunity from a social and economic perspective if those people succeed in aging healthily. Evaluating the health condition of the oldest-old is not straightforward as, especially for people in this stage of life, health requires to be analyzed by simultaneously considering multiple dimensions of health. For instance, health-care needs may be the result of a complex system of diseases, syndromes or other characteristics that is not satisfactorily described by a single aspect of health. Considering health holistically, by jointly analyzing several health measures, helps identifying health profiles that would allow to a better evaluation of the needs and a more efficient use of the resources. On the other hand, analyzing single objective health measures has the advantage of deepening the existing knowledge on the dynamic relationships between major health aspects, their deterioration and which factors are related to this process. The increasing presence of oldest-old people in modern societies implies a growing need of statistical information and indicators capable of monitoring the health conditions of those individuals. Over the last years researchers have tried to overcome the problem of scarce data availability on the health of the oldest-old by conducting specific surveys to reach those (not anymore) exceptionally old individuals to better understand the characteristics and dynamics of health among long-lived individuals. Self-rated health (SRH) is the most widely used indicator for assessing the general health status of a person: nowadays its related question is often included in general surveys and it has been harmonized to allow international comparisons. Understanding the mechanism that underlies the process of self-assessment of health is of great interest. It has been investigated both at the general population level and specifically on elderly individuals, however research on the oldest-old is still lacking. No matter which health dimension is analyzed, the socioeconomic status is always the first factor considered to explain health differences. Socioeconomic inequalities in health are well-known among the general population and the elderly. However, there is growing evidence that a socioeconomic gradient in mortality persists also at very old ages suggesting the need for further research to verify whether socioeconomic differences in health persist among the oldest-old.

The aim of this PhD thesis is to contribute at partly filling the gaps in oldest-old research by investigating (a) the health conditions in which people reach very old ages especially if considering health holistically; (b) the dynamic relationship between two major health aspects such as physical ability and cognition, their deterioration and which factors are related to this process; (c) the mechanism underlying the self-assessment of health; and (d) whether socio-economic health inequalities persist among nonagenarians. Each of the first three research questions (a, b and c) corresponds to a chapter of the thesis while the fourth one (d) is investigated across all of them.

Different data sources were used in the PhD thesis. Data from the Mugello Study were used to answer research questions (a), (c) and (d) and data from the 1905 Danish Cohort Study were used to answer research questions (b) and (d). Each of the research questions were addressed by performing the most appropriate methods to address specific issues.

Considering health holistically, by analyzing several health dimensions, allowed us to identify heath profiles that are expected to have different health-care needs. Moreover, individuals with certain demographic and socioeconomic characteristics were more likely to be characterized by one or another health profile. Analyzing the deterioration of specific dimensions of health, as physical ability and cognition, resulted in finding a dynamic relationship between two important aspects of health. Their deterioration process does not follow the same path, even though the socioeconomic and lifestyle factors related to both measures are similar. Self-rated health among the oldest-old seems to have a similar hidden structure compared to the one of elderly people. Functional and emotional health play an important role, while socioeconomic characteristics only affect the process of self-assessment of health indirectly via the functional component. Overall, socioeconomic inequalities in health persist among the oldest-old independently on the way health is measured.

More studies on the health conditions of oldest-old people, a growing segment of the population in developed country, are necessary to shed lights on many important aspects of health and the health-related factors. In a context of resources that are becoming scarcer and scarcer, this could help policy makers to drive their interventions to the most stringent issues and face them on time to adopt better strategies to cope with the challenges posed by the greater presence of oldest-old in the societies.

Sommario in italiano

Nella maggior parte dei paesi industrializzati, la proporzione di persone molto anziane è aumentata negli ultimi decenni a seguito principalmente del declino della mortalità in età avanzata. Il loro crescente numero costituisce una sfida per i sistemi sanitari ed economici delle società moderne ma potrebbe trasformarsi in una opportunità, sociale ed economica, se tali persone invecchiassero in buona salute. Valutare le condizioni di salute delle persone molto anziani non è affatto semplice in quanto è necessario considerare simultaneamente diversi aspetti. Infatti, il complesso sistema di patologie e condizioni tipico delle persone molto anziani, che ne determina le cure sanitarie richieste, non può essere descritto facendo ricorso ad un solo aspetto della salute. Considerare la salute in maniera olistica, analizzando simultaneamente diversi aspetti della stessa, aiuta a identificare dei profili di salute che permettano di valutare al meglio le effettive necessità dei singoli individui e di utilizzare in maniera più efficente le risorse sanitarie. D'altro canto, analizzare separatamente singoli indicatori di salute ha il vantaggio di poter studiare più a fondo le relazioni dinamiche che esistono tra diversi aspetti della salute, il loro deterioramento nel tempo e quali sono i fattori associati a tale processo. Il crescente numero di persone molto anziane nelle società moderne implica una maggior necessità di informazioni statistiche e di indicatori utili a monitorarne la salute. Nel corso degli ultimi anni, molti ricercatori hanno cercato di ovviare al problema della scarsa disponibilità di dati sulle condizioni di salute dei molto anziani, conducendo indagini sulle persone che (ormai non più) eccezionalmente raggiungono le età più avanzate. L'indicatore di salute percepita, Self-Rated Health (SRH), è il più utilizzato per valutare la condizione generale di una persona. La domanda ad esso associata è presente in molte indagini sulla popolazione ed è stata armonizzata per permettere confronti internazionali. Comprendere il meccanismo con cui si valuta la propria condizione di salute è sicuramente di grande interesse scientifico. Alcuni studi sono stati condotti su tutta la popolazione e altri specificatamente sugli anziani, ma la ricerca sui soli molto anziani è ancora limitata. Indipendentemente da quale dimensione della salute si analizzi, lo stato socioeconomico è sempre il primo fattore considerato come determinante delle disuguaglianze di salute. Questa relazione è ben nota nella popolazione generale e, in particolare, tra quella anziana. Sembrerebbe che persone con diverse caratteristiche socioeconomiche sperimentino diversi livelli di mortalità anche tra i molto anziani, suggerendo la necessità di condurre studi che considerino la salute in relazione allo stato socioeconomico anche per questo segmento di popolazione.

Questa tesi di dottorato ha lo scopo di contribuire a colmare alcune delle lacune presenti nella letteratura sulle persone molto anziane investigando: (a) le caratteristiche di salute, valutate in maniera olistica, con cui si raggiungono età molto avanzate; (b) la relazione dinamica tra salute fisica e mentale, valutando il loro deterioramento nel tempo e i fattori associati a tale processo; (c) il meccanismo che si cela dietro la valutazione della propria condizione di salute; e (d) l'importanza delle disuguaglianze socioeconomiche come spiegazione delle disuguaglianze di salute. Le prime tre domande di ricerca (a, b e c) sono state esaminate in singoli capitoli della tesi mentre la quarta domanda di ricerca è stata approfondita in ognuno di essi.

Nella presente tesi di dottorato sono stati impiegati dati provenienti da diverse fonti. I dati del Mugello Study sono stati utilizzati per rispondere alle domande di ricerca (a), (c) e (d), mentre i dati del 1905 Danish Cohort Study per le domande di ricerca (b) e (d). Diverse metodologie statistiche sono state impiegate per rispondere a ognuna delle domande di ricerca.

Valutare la salute in maniera olistica, ovvero considerando simultaneamente più aspetti della stessa, ha permesso di identificare diversi profili di salute con differenti esigenze sanitarie. Inoltre, le caratteristiche socioeconomiche sembrano determinare il profilo di salute a cui gli individui appartengano. Al contrario, analizzando il deterioramento di singoli aspetti della salute, nello specifico fisica e mentale, ha permesso di scoprire una relazione dinamica tra le due dimensioni. Il loro processo di deterioramento sembrerebbe non seguire lo stesso andamento nonostante i fattori associati al deterioramento fisico e mentale siano pressoché gli stessi. La valutazione della propria condizione di salute tra i molto anziani sembrerebbe seguire gli stessi principi osservati tra i meno anziani. Sembrerebbe che la salute funzionale e quella emotiva influenzino direttamente la valutazione della propria condizione mentre lo stato socioeconomico ha una influenza indiretta sulla salute, tramite la dimensione funzionale.

Studi sulle condizioni di salute nei molto anziani sono necessari al fine di comprendere al meglio gli aspetti più importanti che caratterizzano la salute e i fattori ad essa associati.

La crescente presenza di individui in etá molto anziane rappresenta una sfida per le società moderne, i risultati di questa tesi di dottorato possono essere d'aiuto a chi si occupa di politiche sanitarie e pubbliche per fronteggiare tale sfida, soprattutto in contesti dove le risorse sanitarie ed economiche tendono a essere ridotte.

Dansk resumé

I de fleste ilande er andelen af de allerældste steget igennem de sidste årtier som en konsekvens af nedgangen i dødligheden af de allerældste. En stigende del af de allerældste vil i fremtiden være en udfordring for sundhedsvæsener og økonomiske systemer, der eksisterer i moderne samfund. Fra et socialt og økonomisk perspektiv kan denne udfordring forvandles til en mulighed, hvis de allerældste ældes uden helbredsproblemer.

At evaluere de allerældstes helbredstilstand er ikke ligetil, da sundhed, især for mennesker i denne livsfase, skal analyseres ved samtidig at tage forskellige sundhedsdimensioner i betragtning. Sundhed, for eksempel, beregnes ud fra et komplekst system af sygdomme, syndromer og andre egenskaber, der ikke kan beskrives ud fra et enkelt aspekt af sundhed på tilfredsstillende vis. At betragte sundhed fra et holistisk perspektiv ved at analysere flere sundhedsdimensioner hjælper med at identificere sundhedsprofiler, hvilket ville kunne føre til en forbedret evaluering af sundhedsvæsenets behov og dermed en mere effektiv anvendelse af ressourcer. På den anden side vil det at analysere ud fra en enkel objektiv sundhedsdimension have den fordel at uddybe den eksisterende viden om de dynamiske forhold mellem vigtige sundhedsaspekter, deres forringelse og hvilke faktorer, der er relaterede til denne proces.

Den forøgede tilstedeværelse af de allerældste i moderne samfund antyder et større behov for statistikker og data, der kan anvendes til at overvåge de allerældstes helbred. Igennem de sidste par år har forskere forsøgt at overkomme problemet med manglende data på de allerældstes helbred ved at udføre specifikke undersøgelser for at nå ud til dem som (ikke længere) er ekstraordinært gamle for bedre at forstå sundheden blandt dem, som lever allerlængst. Selvvurderinger (SRH) er den mest anvendte metode til at vurdere en persons helbredstilstand; i dag er spørgsmål om helbred ofte inkluderede i almindelige undersøgelser og spørgsmålene er standardiserede således, det er muligt at udføre internationale sammenligninger. Der er stor interesse i at forstå mekanismerne, der ligger bag processen for selvvurderinger af sundhed. Det er blevet undersøgt både på det generelle befolkningsniveau og specifikt på ældre individer, men research om de allerældste er knap. Uanset hvilken sundhedsdimension der analyseres, er den socioøkonomiske status altid den første faktor, der tages i betragtning, for at forklare forskelle i sundhed. Socioøkonomisk ulighed i sundhed er velkendt hos den generelle befolkning samt hos de ældre. Der er dog voksende beviser for at en socioøkonomisk gradient i dødelighed også

vedbliver i meget høje aldre, hvilket indikerer et behov for mere research, der kan verificere, hvorvidt socioøkonomiske forskelle varer ved hos de allerældste.

Formålet med denne afhandling er at bidrage med at udfylde de tomrum, der eksisterer indenfor research af de allerældste, ved at undersøge (a) hvilke helbredstilstande, der gør det muligt at nå aldersgruppen af de allerældste fra et holistisk perspektiv; (b) de dynamiske forhold mellem to vigtige aspekter af sundhed såsom fysiske færdigheder og kognitive evner, svækkelse heraf og hvilke faktorer, der er relaterede til denne proces; (c) de mekanismer, der ligger til grund for selvvurderinger af sundhed; og (d) hvorvidt socioøkonomisk ulighed vedbliver hos de allerældste i alderen 90-99.De første tre research-spørgsmål (a, b and c) svarer til et enkelt kapitel af denne afhandling mens det fjerde spørgsmål (d) behandles i alle kapitler. Forskellige kilder er blevet anvendt i denne afhandling. Data fra Mugello-undersøgelsen er blevet anvendt til at besvare spørgsmål (a), (c) og (d). Data fra The Danish Cohort Study 1905 er blevet anvendt til at besvare spørgsmål (b) og (d). Hvert enkelt spørgsmål er blevet besvaret med metoder, der er passende for hver enkel problemstilling.

At betragte sundhed fra et holistisk perspektiv ved at analysere flere sundhedsdimensioner gjorde det muligt for os at identificere sundhedsprofiler, som forventes at have anderledes sundhedspleje. Individer med særlige demografiske og socioøkonomiske træk var mest tilbøjelige til at blive karakteriseret ud fra én eller anden sundhedsprofil. Analyse af forværringen af helbred herunder fysiske færdigheder og kognitive evner viste, at der er et dynamisk forhold mellem to vigtige aspekter af sundhed. Forværringsprocessen peger ikke samme retning selvom socioøkonomiske og livstilsfaktorer, som er relaterede til begge sundhedsdimensioner, ligner hinanden. Selvvurderinger af helbred blandt de allerældste har en lignende gemt struktur sammenlignet med ældre mennesker. Funktionelt og følelsesmæssigt helbred spiller en vigtig rolle, mens socioøkonomiske træk kun indirekte påvirker selvvurderingsprocessen af egen helbred via den funktionelle komponent. Socioøkonomisk ulighed i helbred eksisterer fortsat hos de allerældste, uafhængig af hvordan sundhed bliver målt. Flere studier om de allerældstes sundhedstilstand er nødvendig for at skabe lys over mange vigtige aspekter omkring sundhed og sundhedsrelaterede faktorer.

Set i en kontekst, hvor ressourcer bliver mindre, kunne dette hjælpe politiske beslutningstagere med at gribe ind og udvikle strategier til at hamle op med de udfordringer, der kommer som følge af en voksende andel af de allerældste i samfundet.

Introduction

Background

Population aging cannot be described without referring to the demographic and epidemiological transitions. The first one was proposed by Notestein in 1945[1] who theorized that the changes in the population age structure of modern developed countries are a consequence of the decline in death rates followed by the decline in fertility rates. According to Coale (1984)[2], this stage of the demographic transition is known as the "second phase". Overall, improvements in living conditions and advances in medicine were the main drivers of the demographic revolution.

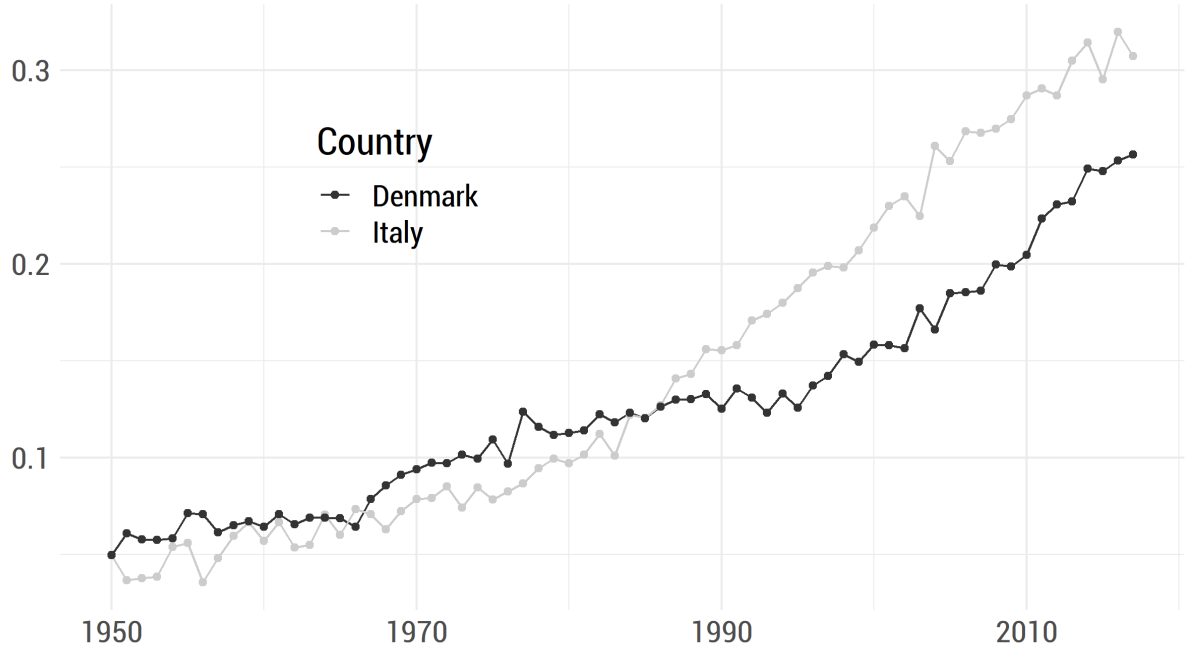
An additional theory was formulated in the second half of the 20th century: the epidemiological transition by Omran (1971)[3], extended twenty years later by Frenk and colleagues[4]. It emphasizes the changes in causes of death and occurrence of disease that accompanied the reduction of mortality.

What happened over the last centuries resulted in an older population age structure with a raise in the median age, namely the phenomenon of population aging.

During the last decades, the mortality improvements were mainly driven by the decline in old-age mortality[5–7]. This was possible thanks to major reductions of cardiovascular mortality and improvements in medical treatments[8,9]. As a result, the proportion of individuals reaching old ages increased significantly. Already in 1974, Neugarten suggested to differentiate between "young-old" and "old-old" for those who survived age 55 and were respectively younger and older than 75 years of age[10]. Some years later, this definition was updated by Laslett's definitions of third and fourth stages of life[11]. In more recent years, as the chance of reaching older ages increased, the interest of researchers moved to even older ages. The so called "oldest-old" were at first defined as people older than 80 and later as older than 85 years of age[12].

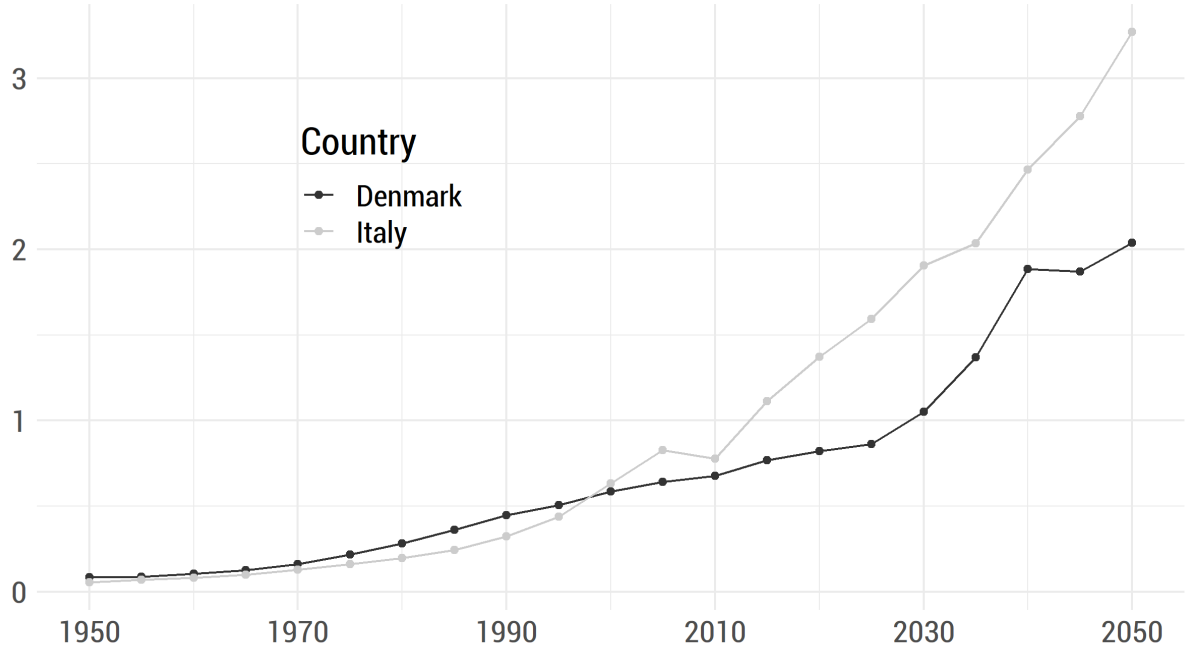
In this PhD dissertation, the focus is on people with 90 years of age or more. The probability of reaching age 90 has increased over the last decades by over six and five times respectively for Italy and Denmark. This is one of the reasons why the share of people aged 90+ that rose from 0.06% and 0.08% in 1950 to 1.37% and 0.77% in 2020 respectively for Italy and Denmark. These numbers are expected to increase in the next 30 years, according to World Population Prospects, to 3.27% and 2.04%[13].

Figure 1. Probability of reaching 90 years old for Italians and Danes from 1950 to 2015



Source: Own calculations on Human Mortality Database data

Figure 2. Share (%) of nonagenarians in Italy and Denmark from 1950 to 2020 and projections until 2050



Source: Own calculations on World Population Prospects data

Because of the increased average length of life, researchers started to question whether this was a good or a bad news for the societies from a social, economic and health

perspective. The consequence of population aging on health started to be discussed already in the late 1970s, when Gruenberg argued that the decline in chronic disease mortality might lead to an increasing prevalence of such diseases in the population: the “failure of success” theory. On the other hand, since the 1980s, Fries argued that the postponement of age at death might be accompanied by a postponement of the onset age of chronic illness[14]. The “compression of morbidity” theory that he proposed, suggests that morbidity might be compressed to the end of life similarly to what happened for death[15,16]. Since there is supporting evidence for both theories, there is no final answer to this issue and probably none of them is completely right or wrong[9,17]. Manton, in the early 1980s, proposed an intermediate view called the “dynamic equilibrium”[18]. According to his theory, it is not the occurrence of disease to be postponed together with age at death but its progression from light to severe. Since then, these three scenarios have been the hypothetical framework for research on health trends and dynamics[19].

Over the last decades, researchers focused on analyzing the consequences of the increased average length of life. The interest on population health substantially increased, as an increased proportion of individuals reaching very old age might translate into a challenge for the health-care and economic systems of modern societies[6,20]. However, it could and should be transformed into an opportunity, from a social and economic perspective, if those people succeed in aging healthy[14]. In order to achieve this ambitious goal it is important to measure population health properly and to understand its dynamics[21]. This would help increasing knowledge of health organizations, policy makers and societies and driving their attention on the right issues to target.

Health is a multidimensional concept that requires to be defined, measured and analyzed by taking into account its complexity. Already in 1948, the World Health Organization (WHO) recognized the need to include several aspects of health into its definition: “health is a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity”[22]. This definition, which is still the official one for health, was extremely modern at the time but also complex to operationalize[23]. This difficulty led many scholars, over the years, to propose alternative definitions. One of the arguments discussed by those researchers is that several decades have passed since the WHO formulated the definition. By then, as it is described in the first part of the Introduction, the demography of population health and the nature of disease has changed considerably. For instance, nowadays people can leave a perfectly active life with light functional limitations or chronic disease that could have led individuals to an early death, say, 50 years ago. For

this reason, Huber and colleagues, among the others, proposed to move the focus of the definition of health to the ability of adapting and managing social, physical and emotional challenges[23].

It is clear that when measuring people's health it is possible to focus on different dimensions and that none of them is completely unrelated with the others.

The health dimensions assessed in this PhD thesis are several: self-rated health (SRH), functional and physical ability, cognitive status and emotional health. Each dimension is measured with different instruments and results in one or more variables that are described in the Methods paragraph. They are analyzed as single indicators, in order to focus on a specific aspect of health, or combined, in order to obtain a multidimensional health profile. Each health dimension has different drivers and implications on a person's life. It is crucial to critically interpret the nature of every measure and what it means for a person to be unhealthy with respect to such aspect.

Oldest-old research comes out from research on aging in general. According to Wahl and Heyl (2015), there is only one study in which people aged 80+ were sampled before the Second World War[24]. From the 1950s some studies on aging were initiated in the US while it took another 10 years to have one in Europe. Those studies included people aged 70+, 80+ or even 90+ but they were not specifically focused on these age groups. The first study in Europe to exclusively sample the oldest-old was conducted in Lund in the late 1980s[25]. After that, many more studies were initiated in the 1990s and 2000s as the oldest-old was the fastest growing segment of the population, attracting the attention of social and health scientists[26–34].

Since the beginning, the topics in oldest-old research were various, with a strong focus on the psychological, medical and epidemiological aspects of aging. The first studies on the oldest-old were mainly focused on the biomedical parameters of people reaching very old ages[28,30,35]. Later, mainly in the last two decades, the focus moved to the social and external factors influencing healthy aging[36–38]. More recently, research on individual frailty and gene characterization of people succeeding to survive to exceptional ages is attracting a lot of interest too[39–42]. However, the last two arguments are not investigated and discussed in the present research project, as the aim of this PhD project is to assess the health conditions in which people reach very old ages and to understand the relationships that connect different aspects of health between them and with socioeconomic characteristics.

Many studies investigating the health conditions of people reaching age 85 or 90 were conducted in the last years to evaluate the level of heterogeneity in health among

them[29,37,43–45] and to understand whether there are successful agers between those individuals[46–48]. However, contrarily to what has been done for younger-old individuals[49,50], none of them considered health holistically by evaluating different aspects of health jointly and, in so doing, identifying groups of individuals.

As stated in the previous paragraph, no dimension of health is completely unrelated to the others. Health deterioration is very likely among frail individuals as the oldest-old are. This process does not necessarily follow the same pattern for different dimensions of health that, however, might be dynamically related with each other. Researchers over the last years focused on evaluating health and its deterioration among the oldest-old by considering single health dimensions[51–54]. However, the dynamic relationship between different aspects of health, such as physical ability and cognition, is highly recognized in the literature about elderly people[55] and should be also investigated among the oldest-old.

Furthermore, understanding how the oldest-old rate their health seems of great interest to fuel the discussion about health dynamics. The question about the perception of one's health, from which the indicator of SRH is obtained, is usually included in demographic and social surveys also when their main focus is not health. This measure is commonly used as a proxy of one's general health status but the knowledge about what it hides needs to be deepened[56]. While some researchers tried to disentangle the mechanism behind the self-assessment of health among the general and elderly populations[57,58] much more needs to be done among the oldest-old[59].

Finally, the socioeconomic gradient in health is well-known among the general population[60] but research on the oldest-old is still lacking, as of today there is only little evidence about it[61]. This could be investigated by assessing single dimensions of health but it should also be done when considering health holistically or while trying to disentangle the dynamics of health.

Research questions

The aim of the PhD dissertation is to contribute at partly filling the gaps in oldest-old health research by answering the following research questions:

a) What are the health conditions in which people reach very old ages especially if considering health holistically?
b) Is there a dynamic relationship between two major health dimensions as physical ability and cognition, how do they deteriorate and which factors are related to this process?
c) What is the mechanism underlying the self-rating of health of the oldest-old?
d) Do socio-economic health inequalities persist among the oldest-old?

Data sources

Different data sources were employed to answer to the research questions. Data from the Mugello Study were used to answer research questions (a), (c) and (d). It is a survey on nonagenarians living in 9 of the 11 municipalities of the Mugello area in Tuscany (Italy), aimed at evaluating the aging process by focusing on different health aspects. It comprised 504 non-selected individuals representing about 65% of all the nonagenarians living in that area in 2012. Participation rate was 69% after excluding potential participants who died before being interviewed and those who were not found[33]. Data from the 1905 Danish Cohort Study were used to answer research questions (b) and (d). This is a nationwide survey with no exclusion criteria: all the 1905-born living in Denmark have been contacted for taking part to the survey, resulting in 2262 participants (63%) at baseline in 1998 and 1086 (78%) in 2000. Information on several health dimensions as well as demographics, socioeconomic characteristics and health behaviors were collected within a panel setting[26]. Both data sources are described with more details and critically discussed in the following chapters of the thesis.

Methods

Each research question implies the analysis of different health dimensions. The first research question (a) was addressed by evaluating six different measures of health collected in Mugello Study survey. Self-Rated Health (SRH) together with the Mental and Physical Component Summary (respectively MCS and PCS) were collected via – or resulted from – the Short Form-12 questionnaire (SF-12). SRH measures one's perceived (general) health status with one single question. MCS and PCS result from the weighted combination of specific items included in SF-12 and measure the overall self-reported physical and cognitive status[62]. Cognitive health was also measured with the Mini-Mental State Examination (MMSE) which score indicates the level of cognitive impairment[63]. Emotional health was assessed with the Geriatric Depression Scale (GDS), higher scores suggest greater level of depression[64]. Functional health was measured according to the ability of performing six basic activities of daily living (ADL)[65]. For answering the second research question (b), MMSE was used, again, to assess the cognitive status of the Danish nonagenarians while the Chair Stand test (CS), which measures the ability to stand up from a chair with or without use of arms, was exploited for evaluating their physical ability[66]. Some of the health measures employed for addressing the first research question (a) were used to answer the third one (c), namely SRH and ADL. Within the sphere of functional health, sensory (sight and hearing) and motion impairment were also included in the analysis. Furthermore, some specific items from SF-12 were analyzed in order to build an indicator of emotional health: feeling lively, calm and sad. The number of chronic diseases was also measured among nonagenarians from Mugello. The way variables were categorized and a critical evaluation of the mentioned indicators are included in the chapters of the thesis.

Every research question was addressed by taking advantage of a specific method, suitable for the purpose, or by a combination of methods. The fourth one (d) was assessed with each of those methods. Latent Class Analysis (LCA) with covariates was used to identify groups of individuals according to their health characteristics, namely health profiles, among Italian nonagenarians (research question a) and to evaluate their association with the socioeconomic status (research question d)[67,68]. The latent class model is estimated by maximizing the log-likelihood function with the expected-maximization (EM) algorithm. Multi-State Model (MSM) for panel data was used to assess deterioration of physical and cognitive health, by computing transition probabilities from good to bad health and from both health conditions to death. The dynamic relationship between physical and cognitive health and factors associated with health

deteriorations were assessed within the same model, via Cox regression (research question b), including socioeconomic characteristics (research question d)[69,70]. In this case, the likelihood function comes from the transition probability matrix and it is optimized with a quasi-Netwon algorithm. Structural Equation Modelling (SEM) was used to evaluate the mechanism of self-assessment of health by analyzing simultaneously direct and indirect effects of observed variables and latent constructs (research question c), including socioeconomic status (research question d), validated via Confirmatory Factor Analysis[71,72]. Given the nature of the data, the Mean and Variance-adjusted Weighted Least Square (WLSMV) estimator was implemented. All the methods are described and discussed in details in the next chapters.

Thesis structure

The first three research questions (a), (b) and (c) are investigated in a separate chapter of the PhD dissertation (respectively 1, 2 and 3), the fourth one (d) is explored across all of them.

Chapter I: Strozza C. et al. *Health profiles and socioeconomic characteristics of nonagenarians residing in Mugello, a rural area in Tuscany (Italy)*. BMC Geriatrics 20, 289 (2020). doi.org/10.1186/s12877-020-01689-3

Abstract Health, as defined by the WHO, is a multidimensional concept that includes different aspects. Interest in the health conditions of the oldest-old has increased as a consequence of the phenomenon of population aging. This study investigates whether (1) it is possible to identify health profiles among the oldest-old, taking into account physical, emotional and psychological information about health, and (2) there are demographic and socioeconomic differences among the health profiles. Latent Class Analysis with covariates was applied to the Mugello Study data to identify health profiles among the 504 nonagenarians residing in the Mugello district (Tuscany, Italy) and to evaluate the association between socioeconomic characteristics and the health profiles resulting from the analysis. This study highlights four groups labeled according to the posterior probability of determining a certain health characteristic: "healthy", "physically healthy with cognitive impairment", "unhealthy", and "severely unhealthy". Some demographic and socioeconomic characteristics were found to be associated with the final groups: older nonagenarians are more likely to be in worse health conditions; men are in general healthier than women; more educated individuals are less likely to be in extremely poor health conditions, while the lowest-educated are more likely to be cognitively impaired; and office or intellectual workers are less likely to be in poor health conditions than are farmers. Considering multiple dimensions of health to determine health profiles among the oldest-old could help to better evaluate their care needs according to their health status.

Chapter II: Strozza C., Zarulli V., Egidi V. *Understanding Health Deterioration and the Dynamic Relationship between Physical Ability and Cognition among a Cohort of Danish Nonagenarians*. Journal of Aging Research, vol. 2020. doi.org/10.1155/2020/4704305

Abstract This study aims to determine how demographics, socioeconomic characteristics and lifestyle affect physical and cognitive health transitions among nonagenarians, whether these transitions follow the same patterns and how each dimension affects the transitions of the other. We applied a Multi-State Model for panel data to 2262 individuals over a 2-year follow-up period from the 1905 Danish Cohort survey. Within two years from baseline, the transition probability from good to bad physical health - ability to stand up from a chair - was higher than dying directly (29% vs 25%), while this was not observed for cognition (24% vs 27%) evaluated with Mini-Mental State Examination - a score lower than 24 indicates poor cognitive health. Probability of dying either from bad physical or cognitive health condition was 50%. Health transitions were associated with sex, education, living alone, Body-Mass Index and physical activity. Physical and cognitive indicators were associated with deterioration of cognitive and physical status respectively and with survivorship from a bad health condition.

We conclude that physical and cognitive health deteriorated differently among nonagenarians, even if they were related to similar socio-demographic and lifestyle characteristics and resulted dynamically related with each other.

Chapter III: Strozza C., Pasqualetti P., Egidi V. *Self-assessment of health: how socio-demographic, functional and emotional dimensions influence self-rated health among Italian nonagenarians*. In preparation for submission.

Abstract Self-Rated Health (SRH) is nowadays one of the most popular indicator of population health. SRH has shown its strong association with physical functioning, well-being and mortality across variety of populations and ages. Despite its wide use, the elements acting and interacting in the evaluation process of health are still not clear. Previous studies have explored the structure of SRH theoretically and empirically showing the direct and indirect effect of socioeconomic and health-related factors on SRH. However, much more research needs to be done among the oldest-old. Cross sectional data from the Mugello Study, including 504 nonagenarians interviewed and tested on their health status in 9 of 11 municipalities of the Mugello area in Tuscany (Italy), are suitable for filling this gap in the literature. The aim of this paper is to explore, by constructing a Structural Equation Model (SEM), direct and indirect effect of physical, functional and cognitive - as well as socioeconomic - status, on the good assessment of health among people in the last stage of their life. By applying Structural Equation Modelling (SEM), on Mugello Study data, we found a strong direct effect of emotional and functional health on SRH, confirming their important role in the process of self-assessment of health. Furthermore, we found indirect effects of socioeconomic status, presence of disease and functional health on SRH confirming previous findings on younger-old Italians.

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Chapter I

Health profiles and socio-economic characteristics of nonagenarians residing in Mugello, a rural area in Tuscany (Italy)

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Background

Currently, the world's population is aging, and the number of oldest-old people is increasing considerably[1,2]. For most developed countries, the share of nonagenarians in Italy increased by approximately 23 times in the last 70 years (from 0.06% in 1950 to 1.37% in 2020) and is expected to continue growing during the next several years, according to the World Population Prospects[3], reaching 3.27% in 2050. Consequently, a greater demand for medical care might be expected from this segment of the population. According to the Italian General State Accounting Department, people aged 65 and above had higher per capita medical expenditures in 2018[4]. For this reason, it is becoming increasingly important to be able to appropriately measure the health of elderly adults as well as that of the oldest-old people[5] and understand which factors are related to so-called “healthy aging”. This has been performed extensively among less older people in recent decades. However, as a consequence of the increasing number of oldest-old people in Western societies and their health characteristics and needs, it is only in recent years that studies focusing on the oldest-old have been conducted, aiming to understand the potential drivers of good health conditions at extremely old ages[6–10]. These studies have always focused on a specific dimension of health, such as cognition, physical and functional status or morbidities. However, health care needs are the result of a complex system of diseases, syndromes or health characteristics that cannot be described by a single dimension of health[11–14]. To consider the multidimensionality of individual health status, it is necessary to exploit a person-centered approach that is based not on the relationships among variables but rather on the characteristics of the individuals. This approach allows people to be distinguished into groups by taking only their individual characteristics into account[11,13].

To capture the heterogeneity of health status and evaluate the social disparities among individuals, researchers suggest the use of latent class analysis (LCA) as a person-centered approach[11–13]. LCA is a subset of structural equation modeling suitable for addressing multidimensional concepts, as in the case of health, to find groups of cases with similar characteristics in multivariate categorical data. The use of LCA in population health studies is extensive, with applications that vary from younger[15] to older individuals and elderly people[12–14,16–24]. Some scholars used this approach to identify profiles of health by considering functional, cognitive and psychological indicators[12–14,16,17,22], with some evaluating socioeconomic differences among the health profiles[12,13,17,22] and others predicting the health care expenditures of people belonging to different groups[14,16]. Other

researchers have applied a person-centered approach to identify profiles within a single aspect of health, such as morbidities[15,19,25], physical status[21], and depression[20], by considering several outcomes of the same health dimension. According to the existing literature, LCA could be used to identify groups of individuals requiring specific forms of health care and to predict their health care needs and expenditures. This approach could also help policymakers understand which groups of people to target with their interventions. The recent COVID-19 pandemic has again highlighted, especially in Italy, how vulnerable people are, such as the oldest-old and multichronic patients, which are groups that merit greater health policy focus[26].

It is also well documented that among elderly adults, demographic and socioeconomic characteristics influence health status and, consequently, health care needs and utilization[13,27,28]. Fewer researchers have evaluated this relationship among extremely old people, suggesting the persistence of social disparities in health, even in the last stages of life[29]. Gender, education and income were found to be associated with different health outcomes among the oldest-old individuals, prompting further investigation in this direction[6,29–32]. Evaluating the existence of a demographic and socioeconomic gradient in health among the oldest-old population could drive the attention of policymakers toward people who need interventions.

Despite the recognized advantage of using a person-centered approach for capturing the heterogeneity of health among elderly people, there is still not much evidence relating to health profiles among the oldest-old and the extremely-old populations[33]. To fill this gap in the literature, we analyzed data from the Mugello Study[34], which included 504 nonagenarians from a rural area in Tuscany (Italy) called Mugello. Our aim is to determine whether it is possible to classify oldest-old people according to their multidimensional health status, defined by physical, cognitive and psychological health, to help in choosing the best care needed by this growing segment of the population. Furthermore, we investigate whether there are demographic and socioeconomic differences among their health profiles, fueling the debate on social disparities in health in the last stages of life.

Methods

Study population and measures

The study population comes from the Mugello Study[10], which aimed to evaluate the aging process, focusing on different health aspects among nonagenarians living in 9 of the

11 municipalities of the Mugello area in Tuscany (Italy). It comprised 504 individuals representing approximately 65% of all nonagenarians living in that geographical territory in 2012. The participation rate was 69% after the exclusion of potential participants who died before being interviewed or who were not found. More information about the study design and survey methods is available in Molino-Lova et al.[10].

Much information about the individual health conditions of nonagenarians has been collected. For some of the health tests, it was not possible to assess the health status of several patients. Individuals who were not tested due to their (very) poor health conditions were categorized as non testable. Being non testable is considered the worst health condition for each of the variables, including this category. Variables have been categorized according to the existing literature. Cognitive function was measured according to the Mini-Mental State Examination (MMSE): the higher the score (0-30), the better the cognitive status is[35]. MMSE scores were divided into three categories to distinguish people with severe (0-17), mild (18-23), and no cognitive impairment (24-30)[36]. Functional status was assessed according to the ability to perform five of the activities of daily living (ADLs) (eating, dressing, bathing, toileting, transferring)[37]. The number of ADLs that people could manage independently was used to distinguish between the non- (0), semi- (1-4), and fully-autonomous (5) oldest-old individuals[38]. Mugello's nonagenarians were classified as disease-free (0), single-disease (1), and comorbid (2+) according to the number of chronic diseases (cardiovascular, neurological, pulmonary, connective tissue, gastroenterological, endocrine, renal, oncological, immunodeficiency syndrome) reported. The Geriatric Depression Scale (GDS) was used to evaluate depression status: the higher the score (0-15), the higher the level of depression is[39]. GDS scores were divided into three categories to distinguish nondepressed (0-4), depressed (5-15), and non testable individuals[40]. Self-rated health status was assessed using the Italian version of the Short Form-12 questionnaire (SF-12) from which it was possible to obtain the two synthetic indicators combining the 12 items together: the Physical and Mental Component Summaries (PCS and MCS)[41]. The PCS and MCS were divided into three categories: those who scored higher (or equal) than the average were considered to be in good health, those who scored lower than the average were considered to be in poor health, and non testable individuals were considered to be in the worst health. It was also possible to obtain the global self-rated health (SRH) of the individual from the SF-12, according to the first item of the questionnaire (in general, you would describe your health status as…). It was divided into three categories to

distinguish among nonagenarians declaring excellent/very good/good health, declaring acceptable/poor health and being non testable.

The results are controlled for age (90-91, 92-94, 95+), gender, education (0-2, 3, 4-5, 6+ years of education), and main occupation during the working lifespan defined according to the Italian National Institute of Statistics (ISTAT) classification of jobs[42]: farmer; housewife; and low-skilled (laborer or unskilled worker) or medium-skilled (office, industry or intellectual worker) work.

Statistical analysis

Health is a complex state involving different aspects or dimensions. To capture the heterogeneity of the health status among the oldest-old individuals, we supposed that Mugello's nonagenarians could belong to unobserved or latent classes according to their health characteristics. For this purpose, we chose LCA, which aims to group individuals into classes according to their indicator patterns. Each class includes individuals with similar characteristics that nonetheless differ from the characteristics of those in other classes.

LCA was used to identify different health profiles according to the health condition through the variables described in the previous paragraph, controlling for demographic and socioeconomic characteristics. LCA with covariates is an extension of the basic LCA, permitting the inclusion of covariates to predict an individual's latent class membership[43,44].

We performed the LCA twice, including the same variables: once on the whole study population and once on the subsample of testable individuals. Since we expected to obtain in the first analysis a group populated by only non testable individuals, we excluded those people in the second analysis to capture more heterogeneity in health status for the remaining oldest-old individuals. The effect of the covariates has been estimated with the "one-step" technique to obtain less biased coefficients: they are estimated simultaneously as part of the latent class model[45,46].

Suppose a latent class model with *C* classes is to be estimated according to *m* categorical variables and a covariate *x*. Let $Y_i = (Y_{i1}, \dots, Y_{iM})$ be the vector of an individual's response to the *M* variables, where $Y_{im} = 1,2, \dots, r_m$. Let $c_i = 1,2, \dots, C$ is the latent class membership of the individual to the class; let $I(y = k)$ be the indicator function that is 1 if *y* is equal to *k* and 0 otherwise; and let λ be the probability of membership in each latent class. Then, the latent class model can be expressed as follows:

$$P(Y = y|x_i) = \sum_{c=1}^{C} \lambda_c(x_i) \prod_{m=1}^{M} \prod_{k=1}^{r_m} \rho_{mk|c}^{I(y_{im}=k)}$$

where $\lambda_c(x_i) = P(C_i = c|x_i)$ is a standard baseline category for the multinomial logistic model. In the case of one covariate, λ can be expressed as the following:

$$\lambda_c(x_i) = P(C_i = c|x_i) = \frac{\exp\{\beta_{0c} + x_i\beta_{1c}\}}{1 + \sum_{j=1}^{C} \exp\{\beta_{0j} + x_i\beta_{1j}\}}$$

for $c = 1, \dots, C - 1$, where *C* is the reference class in the logistic regression. As a result, the log-odds of an individual falling into latent class *c* relative to the reference class *C*, giving x_i as the value for the covariate, is the following:

$$\log\left(\frac{\lambda_{c|c}(x_i)}{\lambda_{C|c}(x_i)}\right) = \beta_{0c|c} + \beta_{1c|c}x_i$$

Multiple imputation was necessary to address missing values (missing at random (MAR)) to avoid a loss of precision in the analysis. The K-nearest neighbor imputation method has been used for its high performance with survey data[47]. To obtain unbiased results, neighbors are found considering all the variables available in the dataset except those that are included in the models. Five neighbors were considered to calculate the aggregated values to impute. Education, main occupation during the working lifespan, MMSE score, ADLs performed, number of chronic diseases, PCS and MCS were imputed. None had more than 7% missing values. More information about data imputation is included in Table 1 in Additional File 1.

Statistical analysis was performed using R version 3.5.0[48], VIM[49], and the poLCA package[46].

Results

The 504 participants included a high number of women (369); the female/male sex ratio of 2.73 confirms the higher longevity of women. The mean age $\pm$ standard deviation was 93.1 ± 3.3 in the whole study population: the men's mean age (92.5) was lower than the women's mean age (93.3; t-test $p = 0.01$). Men were more educated (64.5% of males vs 46.1% of females completed more than 3 years of school) but performed more physical jobs: 80% of males vs 52.6% of females were farmers or low-skilled workers. Overall, men had better scores on all the health measures considered in the analysis. This result is partially explained by the sex-specific age structure of the study population. Large gender differences were found in cognitive and functional status (60.7% of males vs 37.1% of females were not cognitively impaired; 61.5% of males vs 43.6% of females were autonomous). The gap in the remaining health measures is mainly due to the larger number of non testable women (Table 1).

Three latent classes were found when both the whole study population and the subsample of testable individuals were considered. This number was chosen according to the "meaning" of the classes, together with the Akaike Information Criterion (AIC) and the Bayesian Information Criterion (BIC), whose values are shown in Table 2. Every latent class has been labeled according to the posterior probabilities (λ) of finding a certain characteristic in the class, as shown in Table 3.

Table 1: Baseline characteristics of the nonagenarians from Mugello (2012)

Characteristics	Gender						p*
	Male		Female		Total		
	n	%	n	%	n	%	
Study population	135	26.8	369	73.2	504	100	
Age (m. sd)	92.5	2.8	93.3	3.4	93.1	3.3	<0.001
Education (years)							
0 2	16	11.9	49	13.3	65	12.9	<0.001
3	32	23.7	150	40.7	182	36.1	
4 5	63	46.7	142	38.5	205	40.7	
6+	24	17.8	28	7.6	52	10.3	
Work (level#)							
farmer	88	65.2	163	44.2	251	49.8	<0.001
housewives	0	0.0	95	25.7	95	18.8	
low	20	14.8	31	8.4	51	10.1	
middle	27	20.0	80	21.7	107	21.2	
Self-rated health							
Excellent/very good/good	84	62.2	191	51.8	275	54.6	<0.001
acceptable/poor	34	25.2	85	23.0	119	23.6	
non-testable	17	12.6	93	25.2	110	21.8	
Mini-Mental State Examination							
24 30	82	60.7	137	37.1	219	43.5	<0.001
18 23	24	17.8	75	20.3	99	19.6	
0 17	29	21.5	157	42.5	186	36.9	
Activities of Daily Living							
5	83	61.5	161	43.6	244	48.4	<0.001
4 1	44	32.6	158	42.8	202	40.1	
0	8	5.9	50	13.6	58	11.5	
Geriatric Depression Scale							
< 5	77	57.0	141	38.2	218	43.3	<0.001
≥ 5	40	29.6	130	35.2	170	33.7	
non-testable	18	13.3	98	26.6	116	23.0	
Physical Component Summary							
≥ average	75	55.6	130	35.2	205	40.7	<0.001
< average	43	31.9	146	39.6	189	37.5	
non-testable	17	12.6	93	25.2	110	21.8	
Mental Component Summary							
≥ average	66	48.9	136	36.9	202	40.1	0.005
< average	52	38.5	140	37.9	192	38.1	
non-testable	17	12.6	93	25.2	110	21.8	
Chronic diseases (number)							
0	17	12.6	25	6.8	42	8.3	0.112
1	31	23.0	90	24.4	121	24.0	
2+	87	64.4	254	68.8	341	67.7	

*Male vs Female from Pearson $\chi 2$ test or t-test as appropriate

#low: laborer or unskilled worker; medium: office, industry or intellectual worker

Table 2: Model fit statistics for 2- to 6-class models

N. classes	2	3	4	5	6
Whole study population (n=504)					
AIC	5212.18	**4861.80**	7174.00	7145.64	7229.17
BIC	5372.64	**5123.59**	7537.14.	7610.12	7794.99
Testable subsample (n=385)					
AIC	3696.26	**3652.69**	3627.05	4113.39	4168.96
BIC	3814.86	**3850.35**	3903.77	4469.18	4603.81

Note: AIC: Akaike Information Criterion; BIC: Bayesian Information Criterion

LCA performed on the whole study population resulted in three health profiles. The first class is characterized by a high probability of being autonomous ($\lambda = 0.89$), not depressed ($\lambda = 0.81$), not cognitively impaired ($\lambda = 0.78$), perceiving good SRH ($\lambda = 0.92$), and having values of PCS and MCS higher than or equal to the average (respectively, $\lambda = 0.73$ and 0.65). This class, labeled the "healthy group", includes 215 individuals (42.9% of the whole study population). The second class is characterized by a high probability of being semi-/not autonomous (respectively, $\lambda = 0.47$ and 0.44), cognitively impaired ($\lambda = 0.97$), and not testable for depression ($\lambda = 0.97$) and SRH ($\lambda = 1$); consequently, PCS and MCS were not testable ($\lambda = 1$ for both indicators). This class has been labeled the "severely unhealthy group". It includes 110 individuals (21.8% of the whole study population), which encompassed almost all non testable nonagenarians according to the scales in analysis that included this category (SRH, depression, PCS and MCS). The third class includes nonagenarians with a high probability of being semiautonomous ($\lambda = 0.72$), mild/severely cognitively impaired (respectively, $\lambda = 0.32$ and 0.40), depressed ($\lambda = 0.74$), and having PCS and MCS scores lower than the average (respectively, $\lambda = 0.74$ and 0.66). Despite how they performed in the objective health measures, they frequently declare a better health status: $\lambda = 0.43$ for declaring good SRH conditions is relatively high (poor SRH: $\lambda = 0.57$). For this reason, the last class, composed of 179 (35.3%) individuals, has been labeled the "partially satisfied unhealthy group".

LCA performed on the subsample of testable individuals also resulted in three health profiles. The first class is characterized by a high probability of being autonomous ($\lambda = 0.88$), not depressed ($\lambda = 0.82$), not cognitively impaired ($\lambda = 0.83$), reporting good SRH ($\lambda = 0.91$), with PCS and MCS scores higher than or equal to the average (respectively $\lambda = 0.71$ and 0.67). This class has been labeled the “healthy group”. It includes 202 individuals (53% of the testable subsample) who were almost the same individuals populating the “healthy group” resulting from the first analysis. The second class is characterized by a high probability of being semiautonomous ($\lambda = 0.7$), depressed ($\lambda = 0.81$), and reporting poor SRH ($\lambda = 0.74$), with PCS and MCS scores lower than the average (respectively $\lambda = 0.91$ and 0.65). This group of 128 individuals (33.3% of the testable subsample) has been labeled the "unhealthy group". The third group is characterized by a high probability of reporting good SRH ($\lambda = 1$) and being semiautonomous ($\lambda = 0.60$), mild/severe cognitive impairment (respectively $\lambda = 0.43$ and 0.48), with MCS scores lower ($\lambda = 0.74$) but PCS scores higher than or equal to the average ($\lambda = 0.88$). Posterior probabilities for depression are similar: $\lambda = 0.43$ not-depressed vs $\lambda = 0.57$ depressed. This group was labeled "physically healthy with cognitive impairment". It included 55 nonagenarians (13.7% of the testable subsample). All the posterior probabilities are reported in Table 3.

Table 3: Health status indicator probabilities (λ) per health status profile resulting from the two LCAs

Variable	Item	Whole study population (n=504)			Testable subsample (n=385)		
		Latent class			Latent class		
		1	2	3	1	2	3
n	(%)	215(42.9%)	110(21.8%)	179(35.3%)	202(53%)	128(33.3%)	55(13.7%)
Activities of Daily Living	autonomous	0.89	0.09	0.22	0.88	0.23	0.38
	semi-autonomous	0.11	0.47	0.72	0.12	0.70	0.60
	non-autonomous	0.00	0.44	0.06	0.00	0.07	0.02
Geriatric Depression Scale	not depressed	0.81	0.03	0.23	0.82	0.20	0.43
	depressed	0.18	0.00	0.74	0.18	0.80	0.57
	non-testable	0.01	0.97	0.04			
Mental Component Summary	≥ average	0.65	0.00	0.34	0.67	0.35	0.26
	< average	0.35	0.00	0.66	0.33	0.65	0.74
	non-testable	0.00	1.00	0.00			
Mini-Mental State Exam.	24 30	0.78	0.01	0.28	0.83	0.32	0.09
	18 23	0.18	0.02	0.32	0.15	0.33	0.43
	0 17	0.04	0.97	0.40	0.02	0.35	0.48
Number of chronic diseases	0	0.11	0.13	0.02	0.10	0.02	0.04
	1	0.27	0.23	0.21	0.27	0.23	0.19
	2+	0.62	0.65	0.77	0.63	0.75	0.77
Physical Component Summary	≥ average	0.73	0.00	0.26	0.71	0.09	0.88
	< average	0.27	0.00	0.74	0.29	0.91	0.12
	non-testable	0.00	1.00	0.00			
Self-Rated Health	excellent/very good/good	0.92	0.00	0.43	0.91	0.26	1.00
	acceptable/poor	0.08	0.00	0.57	0.09	0.74	0.00
	non-testable	0.00	1.00	0.00			

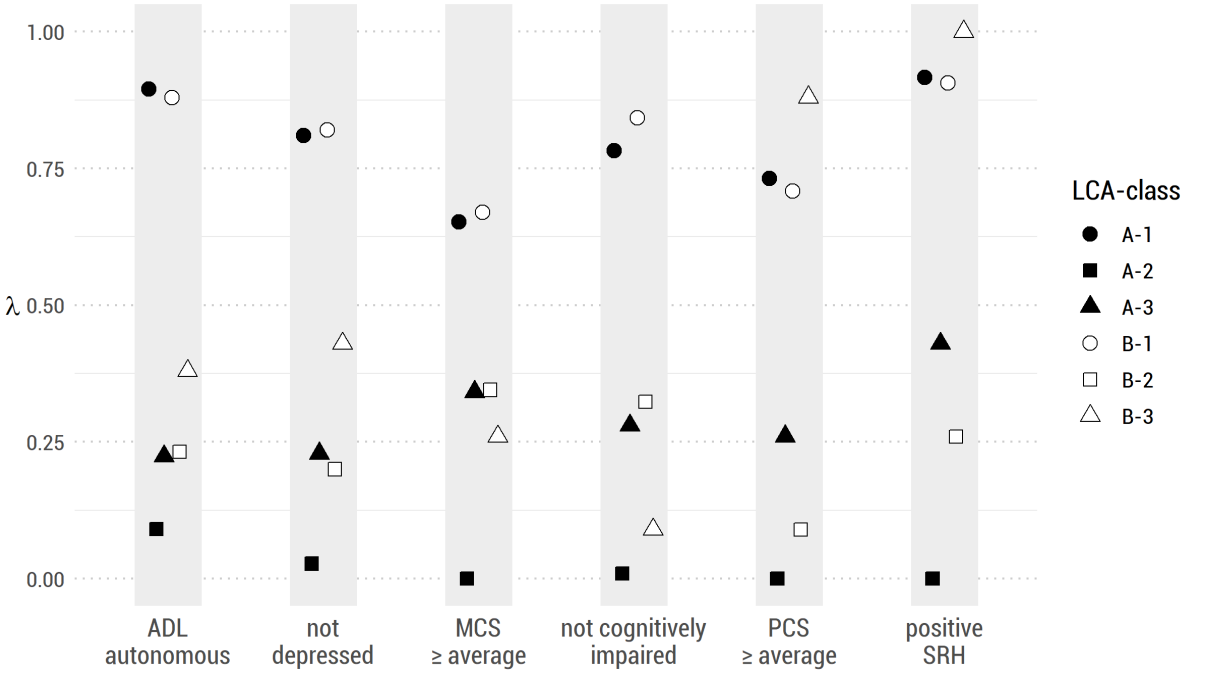
Empty items are due to the subsampling: non-testable individuals are not included in the second analysis

For both analysis 1: "healthy group"; respectively 2: “Severely unhealthy group” and “Unhealthy group”; and respectively 3: "Partially satisfied unhealthy group" and "Physically healthy with cognitive impairment group"

The first class has been labeled the "healthy group" in both analyses: posterior probabilities followed a similar pattern, especially in terms of (good) health status items, as shown by the black and white circles in Figure 1. The second class of the analysis on the whole study population was named the "severely unhealthy group" (see black squares in Figure 1). It was composed of almost all the non testable nonagenarians: individuals in the worst health conditions. Excluding the non testables for the second analysis, many individuals populating the third class moved to the second, resulting in an "unhealthy group" with less *extreme* health characteristics. The consequence of this exclusion was more evident for the last (third) class obtained in both analyses. When considering all nonagenarians, we obtained the "partially satisfied unhealthy group", i.e., people mainly in poor health conditions but not always declaring poor SRH. When excluding the non testable nonagenarians, some of the individuals populating the third group obtained in the previous analysis moved to the second group in the second analysis. As shown in Figure 1, the "partially satisfied unhealthy group" (first analysis) and the "unhealthy group" (second analysis) had similar posterior probabilities for the (good) health status indicators, especially in terms of functional and cognitive status. Within the second analysis, 55 out of the 385 nonagenarians composing the "physically healthy with cognitive impairment group" had a higher probability of declaring good SRH and obtaining a high PCS score than the "healthy group", but they had poor cognitive health, sometimes had depression and were mainly semiautonomous nonagenarians.

The results are controlled for age, gender, education, and main occupation during the working lifespan (Table 4). In the analysis on the whole of Mugello's nonagenarians, older individuals and housewives are more likely to be part of the "severely unhealthy group" instead of the "healthy group" (92-94 vs 90-91: odds ratio (OR) = 2.69; 95+ vs 90-91: OR = 7.25; housewives vs farmers: OR = 2.19), while being more educated reduces these odds (4-5 vs 3 years of education: OR = 0.49; 5+ vs 3: OR = 0.08). Being older also increases the odds of being in the "partially satisfied unhealthy group" instead of the "healthy group" (95+ vs 90-91: OR = 5.1), while both being male and a middle-level (qualified office) worker reduces it (male vs female: OR = 0.40; middle-level worker vs farmer: OR = 0.43).

Figure 1: (Good) health status item probabilities (λ) per health status resulting from the two latent class analyses (LCAs)



Note 1: Class 1: “Healthy group”, for both first (A) and second (B) LCAs; Class 2 for LCA-A: “Severely unhealthy group”, for LCA-B: “Unhealthy group”; Class 3 for LCA-A: “Partially satisfied unhealthy group”, for LCA-B: “Physically healthy with cognitive impairment group”
Note 2: ADLs: Activities of Daily Living; MCS: Mental Component Summary; PCS: Physical Component Summary; Positive self-rated health: excellent/very good/good self-rated health

In the analysis on the subsample of testable individuals, as for the last class of the previous analysis, being older increases the odds of being in the "unhealthy group" instead of the "healthy group" (95+ vs 90-91: OR = 5.37), while both being male and a middle-level (qualified office) worker reduces it (male vs female: OR = 0.44; middle-level work vs farmer: OR = 0.45). Finally, being both older and less educated increases the odds of being in the "physically healthy with cognitive impairment group" instead of in the "healthy group" (92-94 vs 90-91: OR = 4.62; 95+ vs 90-91: OR = 9.03; 0-2 vs 3 years of education: OR = 8.02).

Table 4: Odds ratios of demographic and socio-economic characteristics for the health profiles

LCA		Whole sample (n=504)					Testable subsample (n=385)				
Variable	Item	Coefficient	OR	Std. error	t value	Pr(>|t|)	Coefficient	OR	Std. error	t value	Pr(>|t|)
		2 vs 1					***2 vs 1***				
	(Intercept)	-0.88	0.41	0.33	-2.64	0.01	-0.29	0.75	0.33	-0.87	0.38
Age class (ref. 90 91)	92 94	0.99	2.69	0.34	2.92	0.00	0.10	1.11	0.38	0.27	0.79
	95 +	1.98	7.25	0.37	5.38	0.00	1.68	5.37	0.37	4.55	0.00
Sex (ref. female)	male	-0.85	0.43	0.38	-2.24	0.03	-0.82	0.44	0.35	-2.32	0.02
Education (ref. 3 years)	0 2	-0.60	0.55	0.46	-1.31	0.19	0.49	1.64	0.52	0.94	0.35
	4 5	-0.72	0.49	0.32	-2.24	0.03	-0.31	0.74	0.34	-0.89	0.37
	> 5	-2.59	0.08	0.98	-2.65	0.01	-0.99	0.37	0.74	-1.33	0.19
Work (ref. farmer)	housewives	0.78	2.19	0.39	2.00	0.05	-0.20	0.82	0.50	-0.41	0.69
	low level	0.05	1.05	0.50	0.10	0.92	0.08	1.08	0.44	0.17	0.87
	middle level	-0.09	0.92	0.40	-0.22	0.83	-0.79	0.45	0.42	-1.89	0.06
		3 vs 1					***3 vs 1***				
	(Intercept)	-0.14	0.87	0.31	-0.45	0.65	-2.44	0.09	0.70	-3.51	0.00
Age class (ref. 90 91)	92 94	0.21	1.24	0.33	0.66	0.51	1.53	4.62	0.66	2.32	0.02
	95 +	1.63	5.10	0.34	4.83	0.00	2.20	9.03	0.68	3.25	0.00
Sex (ref. female)	male	-0.92	0.40	0.32	-2.88	0.00	-0.50	0.61	0.73	-0.68	0.49
Education (ref. 3 years)	0 2	0.30	1.35	0.42	0.71	0.48	2.08	8.02	0.74	2.82	0.01
	4 5	-0.24	0.79	0.31	-0.77	0.44	-0.65	0.52	0.63	-1.03	0.30
	> 5	-0.46	0.63	0.54	-0.85	0.40	0.89	2.43	1.06	0.84	0.40
Work (ref. farmer)	housewives	0.11	1.12	0.40	0.29	0.78	0.97	2.65	0.63	1.54	0.12
	low level	0.06	1.06	0.42	0.14	0.89	-0.80	0.45	1.09	-0.73	0.47
	middle level	-0.85	0.43	0.38	-2.26	0.02	-1.15	0.32	0.94	-1.22	0.23

For both analysis 1: "healthy group"; 2; respectively 2: “Severely unhealthy group” and “Unhealthy group”; and respectively 3: "Partially satisfied unhealthy group" and "Physically healthy with cognitive impairment group"

Discussion

To identify health profiles among nonagenarians from Mugello (Tuscany - Italy), LCA was performed twice: first on the whole study population and then on the subsample of testable individuals, with nonagenarians in the "extreme" (worst) conditions having been excluded from the analysis. Removing these individuals from the analysis allowed us to capture more heterogeneity of health among the remaining oldest-old, especially among those with poor health that were hidden by the non testable individuals.

In both analyses, three classes were identified, resulting in a total of four different health profiles within the two LCAs performed, each labeled according to the posterior probabilities of finding certain health characteristics in them. Other researchers who looked at health profiles among elderly people by considering their physical, cognitive and psychological status found two to six classes[11–13,17,22]. In particular, other researchers could distinguish between a larger number of classes (four to six)[11,13,17,22], except for Ng et al. (2014), who identified only two profiles[12]. The fact that we found four health profiles within the two analyses means that, even at extremely old ages, there is still heterogeneity in the health conditions of the individuals. LCA allowed us to take into account the multidimensionality of health by including several health measures in the analysis. Having a larger study population could have helped to find the four profiles within a single LCA.

The "healthy group" (a), identified in both analyses and composed of almost the same individuals, and the “unhealthy group” (c), resulting from the second analysis, are consistent with other scholars’ findings among younger adults, including information on sensory health and specific chronic diseases[11,16] or quality of life and wellbeing [17]. Additionally, among nonagenarians, it was possible to find the two extreme groups of people in overall good and poor health. The “severely unhealthy group” (b), resulting from the first analysis, confirms that non testable individuals are a stand-alone group of people who, because of their extremely bad health conditions, cannot be tested on their health status. The "physically healthy with cognitive impairment group” (d), i.e., individuals with good self-rated health and physical condition but bad cognitive status, is similar to what Lafortune et al. (2009) called the “cognitively impaired group” in their paper on the Canadian elderly, where the authors did not include information on the perception of health[11]. However, this result is at odds with what Zammith and colleagues

found in 2012, in terms of self-perceived health, among the Lothian Birth Cohort 1936 “good fitness/low spirit group”[11,17]. It is known that one of the factors influencing the assessment of health among Italian elderly people is their physical status[50]. It is possible that, even at extremely old ages, physical health plays an important role in the self-assessment of health status. However, this could also be the result of the poor cognitive status of individuals populating the “physically healthy with cognitive impairment group”.

Certain demographic and socioeconomic characteristics were found to be associated with being part of some of the latent classes found. In this study, it is not possible to evaluate the health deterioration itself, but even at extremely old ages, being older results in having a higher probability of being in worse health. This suggests the need for further investigation on the health deterioration process among the oldest-old as it is commonly performed on the younger-old[51–53]. Males have a lower probability of being in worse general health conditions, confirming the so-called "gender paradox" also exists among the oldest-old: men are healthier than women at older ages[6,29,54,31]. The level of education is known to be associated with cognitive health in later life. Researchers analyzing English and Finnish nonagenarians show how this relationship still persists at extremely old ages[29,32,55]. In the present study, more educated nonagenarians are less likely to belong to an “unhealthy group”, while being less educated increases the probability of being among the cognitively impaired. These results are similar to those found in younger-elderly profiles[12,13]. Working experience is also associated with health conditions, showing different results. In line with the existing literature, a person who was a nonmanual (office) worker had a lower probability of being in bad health condition at older ages compared to someone who worked as a farmer[56,57]. Housewives were more likely to be in the worst health conditions, similar to study findings among Finnish nonagenarians[29].

This study has public policy implications that need to be noted. Even among nonagenarians, individuals are heterogeneous in terms of health. To capture this heterogeneity by taking into account several dimensions of health, it is necessary to apply a suitable methodology. LCA has been widely used for this purpose, and policy makers should take advantage of it to identify heterogeneous groups of individuals to target with their interventions[11–14]. Analyzing different health dimensions at the same time allowed us to distinguish between the most vulnerable individuals with several health problems and those individuals with dimension-specific health deficits. According to our results, it is likely that people with poor physical health also have cognitive impairment, resulting in complex care needs. However, cognitively deteriorated

individuals may be in good physical and functional status, requiring a different (specific) type of health assistance. Furthermore, health profiles were associated with socioeconomic status, showing that even among the oldest-old, the well-known socioeconomic gradient of health persists. As pointed out by Ng et al. (2014), this should suggest policy makers drive their interventions to the less advantaged groups of the population[12]. Other researchers evaluated the health care needs and expenditures among Taiwanese elderly people[14,16], showing how they differ among the health profiles that they identified. Being able to distinguish between groups of people with different health care needs is extremely important for reducing the excess of health expenditure that may result from not considering it holistically[11].

This study has limitations that need to be noted. It is based on a cross-sectional dataset: health characteristics have been collected only once. For this reason, we were not allowed to study the causal relationship between sociodemographic characteristics and health status and profiles. Furthermore, much of the information about health status is self-reported, and cutoff points - chosen according to the existing literature - did not equate to a clinical diagnosis. Thus, it would be useful to verify their veracity with objective measures. Finally, it is important to remark that Mugello's nonagenarians are a selected group of individuals in terms of health and mortality. Living in a rural area and following a Mediterranean diet is, for instance, something that affects this selection.

Conclusions

Large samples of nonagenarians, for which much information has been collected about their health status, are still rare to find. Considering health as a multidimensional concept by identifying health profiles could help to better evaluate the care needs according to the different health profiles of each person, even among extremely old individuals[16,58]. The demographic and socioeconomic gradient of health resulting from the analysis suggests that policy makers focus their interventions on specific groups of individuals at younger ages to prevent an excess of health care expenditure later on.

Supplementary material

Table 1: Marginal distribution pre- and post-missing values imputation of characteristics of the study population. Absolute values, percentages and differences

Characteristics	Pre-imputation		Post-imputation		Difference (%)
	n	%	n	%	
Education (years)					
0 2	65	13.5	65	12.9	-0.6
3	166	34.5	182	36.1	1.6
4 5	198	41.2	205	40.7	-0.5
6+	52	10.8	52	10.3	-0.5
total	481	100.0	504	100.0	
Work (level)*					
farmer	245	49.4	251	49.8	0.4
housewife	93	18.8	95	18.8	0.1
low	51	10.3	51	10.1	-0.2
middle	107	21.6	107	21.2	-0.3
total	496	100.0	504	100.0	
Mini-Mental State Examination					
24 30	213	43.8	219	43.5	-0.4
18 23	95	19.5	99	19.6	0.1
0 17	178	36.6	186	36.9	0.3
total	486	100.0	504	100.0	
Activities of Daily Living					
5	235	47.6	244	48.4	0.8
4 1	201	40.7	202	40.1	-0.6
0	58	11.7	58	11.5	-0.2
total	494	100.0	504	100.0	
Physical Component Summary					
≥ average	187	39.1	205	40.7	1.6
< average	181	37.9	189	37.5	-0.4
non-testable	110	23.0	110	21.8	-1.2
total	478	100.0	504	100.0	
Mental Component Summary					
≥ average	182	38.1	202	40.1	2.0
< average	186	38.9	192	38.1	-0.8
non-testable	110	23.0	110	21.8	-1.2
total	478	100.0	504	100.0	
Chronic diseases (number)					
0	42	9.0	42	8.3	-0.7
1	111	23.9	121	24.0	0.1
2+	312	67.1	341	67.7	0.6
total	465	100.0	504	100.0	

*low: laborer or unskilled worker; medium: office, industry or intellectual worker

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Chapter II

Understanding health deterioration and the dynamic relationship between physical ability and cognition among a cohort of Danish nonagenarians

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Introduction

The proportion of the oldest old has increased during the last decades as a consequence of the decline in old-age mortality[1–3]. The share of nonagenarians in Denmark increased from around 0.08% in 1950 to 0.82% in 2020 and is expected to further grow during the next years, reaching 2.03% in 2050[4]. This phenomenon is taking place in most developed countries, fueling a growing interest on the health conditions of oldest-old[2]. Health transitions at older ages are of particular interest as deterioration of both physical and cognitive health conditions is very likely[5,6].

Physical and cognitive health decline have been investigated, in order to understand whether they can be partially explained by other health characteristics[7]. A systematic review of the relationship between physical functioning and cognition was published by Clouston et al. in 2013[8], which found that physical functioning at baseline was associated with longitudinal changes in cognition but the opposite relationship was inconsistent. Physical mobility and functioning dynamically interact between healthy and unhealthy states[5,9–11]. Cognitive health declines with age more linearly, even though this decline can cover a more complex pattern[6,12,13]. It is therefore crucial to investigate further how the physical and cognitive deteriorations evolve and whether they follow different patterns. The relationship between the two dimensions of the health status has been widely investigated. However, the literature lacks studies on the oldest old and this is why in this study we focus on individuals aged 90+. With this analysis we aim at investigating (1) how demographic and socioeconomic characteristics and life style habits affect transitions in physical and cognitive health; (2) whether these transitions follow the same patterns and (3) how does each dimension (physical or cognitive) affect the transitions of the other dimension. To our knowledge, this is the first study that analyzes the relationship between physical and cognitive decline and the determinants of transitions in these two health dimensions (physical and cognitive) among nonagenarians.

Methods

Study population and measures

The study population comes from the 1905 Danish Cohort survey, which contains many individual level information on the members of the cohort born in Denmark in 1905 interviewed and tested for physical and mental health in their home by a survey agency. It is a longitudinal multi-assessment survey conducted from 1998 to 2005 with four waves realized every 2-3 years. Detailed information about the study design are available in Nybo and colleagues[14]. In this work we use the first two waves of the Danish 1905 Cohort Survey, collected in 1998 and 2000, when the oldest-old were respectively 93 and 95 year old. The initial population, corresponding to the study population, was composed of 2626 individuals. They represent 62.8% of the potential participants: individuals born in 1905 and living in Denmark. At the second data collection in 2000, 874 were found to be dead (38.6%) reducing to 1388 individuals the number of potential participants to the second wave of the study. The final population interviewed in 2000 was composed of 1086 individuals (78.2% of the potential participants).

The cognitive function was measured with the Mini-Mental State Examination (MMSE): the higher the score (0-30) the better the cognitive status[15]. We grouped it into three standard categories, in order to distinguish people with severe (0-17), mild (18-23) and no cognitive impairment (24-30) based on the most frequently used categorization in literature[16,17]. The physical function was assessed by the Chair-Stand Test: elderly who can stand up from a chair have better functional status than who needs to use hands or cannot do it. This test was found to be a good predictor of disability and mortality among the elderly other than a proper instrument to measure lower body strength[17–20].

We dichotomized both health indicators, in order to create two categories: healthy and unhealthy oldest-old. Regarding cognitive health: individuals were considered cognitively impaired when reporting a MMSE score from 0 to 23 and not cognitively impaired when the score was between 24 and 30. Regarding physical ability: individuals who were not able to stand up from the char, even with aids, were considered in bad physical health while individuals able to stand up from the char, with and without use of aids, were considered in good physical health.

Demographic and socioeconomic characteristics (sex, education and living conditions), critical events (loss of a close relative or friend), health characteristics and behaviors (self-rated health and depression, smoking habits, body mass index (BMI), physical activity and use of medications) were considered as confounders and controlled in the analysis. Education was used to measure the socio-economic situation of the participants. It was grouped into three categories: (1) elementary school; (2) vocational and (3) higher education. Living condition was divided into people living (1) alone and (2) with someone. The loss of a close-person, self-rated health and depression were used to assess the general health perception of the participant and the feelings related to it. The loss of a close-person was categorized into two classes: (1) lost someone (spouse, sons, close friends) and (2) no people lost due to death within the last five years. Self-rated health was assessed with the first question of Short Form 12 (SF12) questionnaire[21]: "How do you consider your health in general?". It was grouped in three categories: (1) very poor or poor; (2) acceptable and (3) good or excellent. Depression was assessed using an adaptation of the depression section of the Cambridge mental disorders of the elderly examination[22]. It uses a scale from 17 to 52 and it was grouped into three equal-size categories: (1) 17-22; (2) 23-28 and (3) 29-52. Among the health behaviors, smoking habits was categorized into (1) never smoked; (2) past and (3) current smoker. BMI was calculated on the basis of the reported height and weight at the interview and categorized into three groups: (1) <22; (2) 22-28 and (3) >28. Physical activity was assessed by asking if they were performing light (light gardening, short walks or bicycle rides) or heavy (heavy gardening, long walks or bicycle rides, sports, gymnastics or dancing) exercises at the time of the interview. It was grouped into three categories: (1) never or not able; (2) light and (3) heavy physical activity. The number of medications (daily intake) was coded according to the Anatomical Therapeutic Chemical classification system and it was grouped into three equal-size categories: (1) 0-1; (2) 2-3 and (3) 4+.

The main reference for variable selection and classification is the Appendix S1 of the article by Thinggaard et al. (2016) that uses the same study population[17]. The proportion of dropouts is 13.4%. We performed a sensitivity analysis in order to check whether drop out was associated with bad health and we did we did not find any significant association with both health indicators.

Statistical analysis

We applied a Multi-State Model for panel data - with Markov chain assumption - [23,24] to assess the association between the many potential drivers measured on the Danish nonagenarians and the probability of transitioning from one health state to another (defined as transition probability). The possible transitions are from good to bad health status, from good health to death and from bad health to death.

The Multi-State Model we used is based on a stochastic multi-state process $(X(t),\ t \in T)$ with a finite state-space $S = \{1, \ldots, N\}$ where $T = [0, \tau]$, $\tau < \infty$ represents the time (discrete, for panel data). It is fully characterized through transition probabilities between states h and j:

$$p_{hj}(s,t) = P(X(t) = j | X(s) = h) \quad (1)$$

for $h, j \in S,\ t, s \in T$ or through transition intensities:

$$\alpha_{hj}(t) = lim_{\Delta t \to 0} \frac{p_{hj}(t, t + \Delta t)}{\Delta t} \quad (2)$$

representing the instantaneous hazard of progression to state j conditionally on occupying state h at the previous time. According to the Markov assumption, the probability of the next transition depends only on the state occupied at the time t.

The effect of the explanatory variables z_{it} on the transition intensity for individual i at time t is modeled using proportional intensities, replacing α_{hj} with:

$$\alpha_{hj}(z_{it}) = \alpha_{hj}^{0} \exp(\beta_{hj}^{T} z_{it}) \quad (3)$$

We conducted the analysis separately for physical and cognitive health, in order to be able to include the baseline status of each dimension (respectively cognitive or physical) as potential driver in the model for the transitions related to the other dimension.

States have been defined according to the MMSE, when assessing cognition; according to the Chair-stand test, when the focus was on the physical status. Based on both classifications, we divided participants into two groups based on their good or bad health condition.

Transitions between four states (good health, bad health, non-participant but alive and non-participant because dead) have been estimated through transition probabilities. We evaluated the effect of the covariates on the transition intensities only for the "worsening" transitions: from good to bad health condition, from good health condition to death and from bad health condition to death. As expected, only few people experienced "improving" transitions, as this is unlikely at very old ages.

Because of the relatively small number of individuals in analysis, we could only use the dichotomic classification of MMSE and Chair-stand test, as the sample size was too small to estimate the coefficients with a finer classification of the variables. We could not perform the analysis separately for men and women due to the small number of nonagenarian men in the sample.

We used methods of imputation with survey data[25] to deal with missing at random values. More information about the imputation method is available in Supplementary Text 12.

Statistical analysis was performed using R version 3.5.0[26].

Results

Descriptive results

Of the 2262 - 93 years old - baseline participants to the study, one fourth were men (25.8%) while the rest of the people were women (74.2%). Men had, on average, a higher education level than women, especially in terms of vocational education (32.9% of men vs 14.2% of women). Fewer men were living alone than women (50.5% of men vs 64.4% of women). More men experienced the loss of a close person (spouse, children, close friends) due to death during the last five years (71.7% of men vs 66.9% of women) but they reported lower rates of depression (39.0% of men vs 32.3% of women were not depressed) without declaring better health conditions than women (12.5 % of men rated their health as good or excellent while 14.2 % of women did it). In terms of health behaviors, except for the higher share of (past or current) smokers (78.8% of men vs 32.4% of women), men had higher BMI (73.1% of men vs 55.3% of women had a BMI higher than 22) and performed more physical activity (43.8% of men vs 28.9% of women perform some physical activity) than women. More details about baseline characteristics of the population are available in Table 1. Men scored better in terms of cognitive (48.5% of men vs 40.6% of women were not cognitively impaired) and physical (52.1% of men vs 41.5% of women were able to stand up from the chair without any aid) health than women as reported in Table 2.

Table 1. Characteristics of the study population in the first wave in 1998 when the individuals were 93 years old

Characteristics	Sex						p
	M		F		T		
	n	%	n	%	n	%	
Sample	584	25.8	1678	74.2	2262	100.0	
Education							
elementary	292	50.0	1254	74.7	1546	68.3	<0.001
vocational	192	32.9	238	14.2	430	19.0	
higher	100	17.1	186	11.1	286	12.6	
Living alone							
no	289	49.5	598	35.6	887	39.2	<0.001
yes	295	50.5	1080	64.4	1375	60.8	
Loss of a close person							
no	165	28.3	556	33.1	721	31.9	0.033
yes	419	71.7	1122	66.9	1541	68.1	
Self-rated health							
very poor or poor	307	52.6	886	52.8	1193	52.7	0.013
acceptable	204	34.9	553	33.0	757	33.5	
good or excellent	73	12.5	239	14.2	312	13.8	
Depression							
29-52	184	31.5	591	35.2	775	34.3	0.008
23-28	172	29.5	545	32.5	717	31.7	
17-22	228	39.0	542	32.3	770	34.0	
Smoke							
current smoker	144	24.7	171	10.2	315	13.9	<0.001
past smoker	316	54.1	372	22.2	688	30.4	
never smoked	124	21.2	1135	67.6	1259	55.7	
Body-Mass Index							
<22	157	26.9	750	44.7	907	40.1	<0.001
22-28	348	59.6	785	46.8	1133	50.1	
>28	79	13.5	143	8.5	222	9.8	
Physical activity							
none/irrelevant	328	56.2	1193	71.1	1521	67.2	<0.001
light	177	30.3	390	23.2	567	25.1	
heavy	79	13.5	95	5.7	174	7.7	
Number of medications							
4+	228	39.0	714	42.6	942	41.6	0.057
2-3	153	26.2	423	25.2	576	25.5	
0-1	203	34.8	541	32.2	744	32.9	

*Men vs Women from Pearson χ^2 test

Table 2. Health conditions of the study population in the first wave in 1998 when the individuals were 93 years old

Characteristics	Sex						p
	M		F		T		
	n	%	n	%	n	%	
Physical ability: Chair-Stand Test							
not able	70	12.0	293	17.5	363	16.0	<0.001
with use of hands	210	36.0	689	41.1	899	39.7	
without use of hands	304	52.1	696	41.5	1000	44.2	
Cognitive health: Mini-Mental State Examination							
0-17	124	21.2	472	28.1	596	26.3	<0.001
18-23	177	30.3	524	31.2	701	31.0	
24-30	283	48.5	682	40.6	965	42.7	

*Men vs Women from Pearson χ^2 test

Multi-state analysis results

We analyzed physical and cognitive health deterioration in two different models including respectively cognitive and physical baseline health status because the main aim of the study is to examine the dynamic relationship between these two health aspects and not because we considered them independent. This implies that part of the individuals in the different states of the two analyses are the same, resulting in similar transition probabilities and covariates associated to transition intensities.

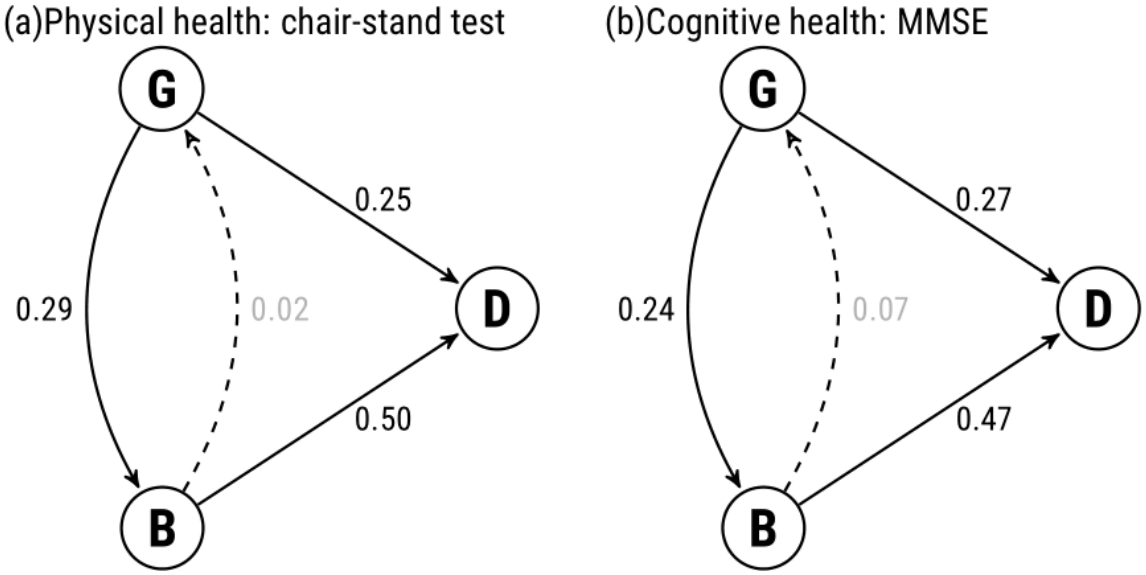
At baseline, 44.2% of the individuals were in good physical health while 42.7% were in good cognitive health. After two years, 38.6% of the study population died while 13.4% dropped out from the study.

The probability of moving from a good to a bad physical health condition within two years was higher than dying directly (29% vs 25%). People in bad physical health condition have a 50% probability of dying from a bad physical health status within two years.

When considering the cognitive health, the results showed a different pattern. The probability of worsening a good cognitive health condition was lower than experiencing death directly within two years (24% vs 27%), while individuals in a bad cognitive health have a 47% probability of dying from that condition in the next two years as shown in Figure 1.

The complete transition probabilities are available in Supplementary Tables S1 and S2.

Figure 1. Transition probabilities of the multi-state model where states are defined according to:



Legend: G: good; B: bad; D: dead

The effect of covariates on the transition intensities are reported in Figures 2 and 3 for the physical states and cognitive states respectively.

Full details about the two models are available in Supplementary Tables S3 and S4.

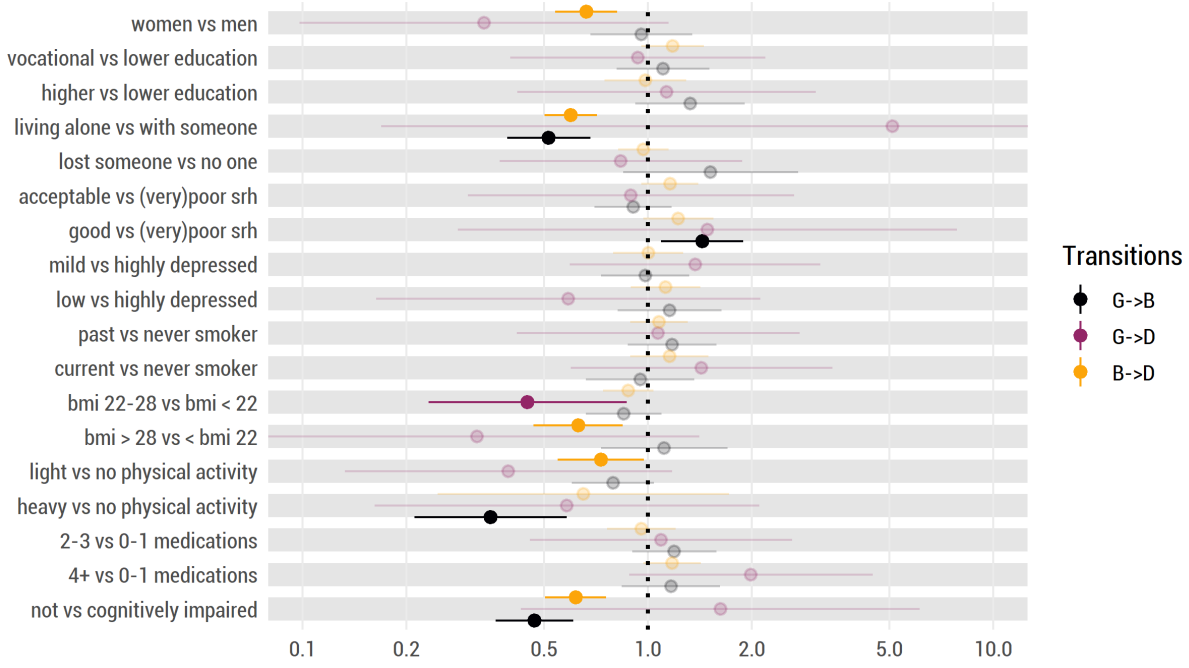
Physical health transitions

Being women was associated with lower probability of dying for people in bad physical health (female vs male HR = 0.66) as well as living alone (living alone vs with someone HR = 0.60). Living alone was also significantly associated with a lower probability of transitioning from a good to a bad physical health (HR = 0.52). Having a BMI higher than 22 statistically decreased the probability of dying, both from a good (BMI 22-28 vs <22: HR = 0.45) and a bad (BMI >28 vs <22: HR = 0.63) physical health. Performing physical activity lowered the transition probability from good to bad physical health (heavy vs no physical activity: HR = 0.35) and from bad physical health to death (light vs no physical activity: HR = 0.73). Finally, also being cognitively not impaired was statistically associated with a lower probability of worsening the physical health (HR = 0.47) and dying from a bad one (HR = 0.62).

Cognitive health transitions

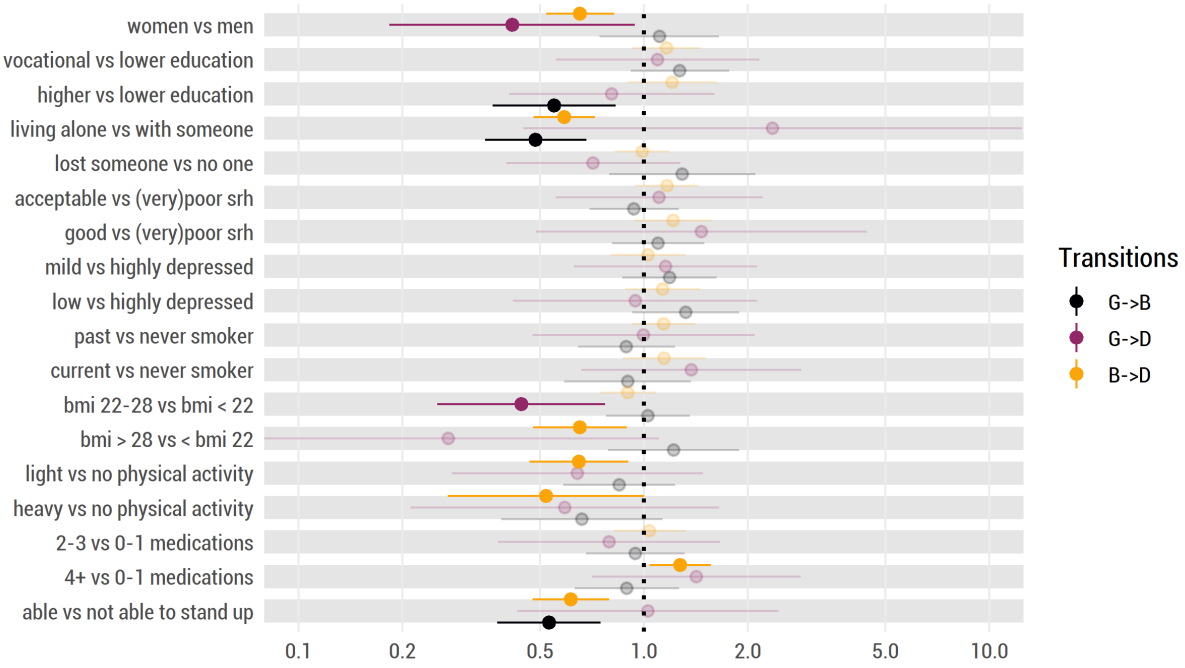
Being a woman was associated with a lower probability of death (from good health: HR = 0.42; from bad health: HR = 0.65). Having higher level of education decreased the probability of deteriorating the cognitive health (HR = 0.55) and well as living alone (HR = 0.49), which was also a protective factor against transitioning from bad cognitive status to death (HR = 0.59). BMI higher than 22 reduced the probability of dying from a good (BMI 22-28 vs <22: HR = 0.44) and a bad (BMI >28 vs <22: HR = 0.65) cognitive health. Doing physical activity was significantly related to lower transition rates from bad to death (light vs no physical activity: HR = 0.65, heavy vs no physical activity: HR = 0.52). As expected, using more than four medications per day was associated with higher probability of death when already in a bad cognitive health (HR = 1.27). Finally, being able to stand up from the chair without any aid was statistically associated with a lower probability of worsening the cognitive health (HR = 0.53) and dying from a bad one (HR = 0.61).

Figure 2. Multivariate predictions (hazard ratios) of transitions in physical health



Note 1: Highlighted hazards ratios are significant; G: good; B: bad; D: dead

Figure 3. Multivariate predictions (hazard ratios) of transitions in cognitive health



Note 1: Highlighted hazards ratios are significant; G: good; B: bad; D: dead

Discussion

The increasing proportion of the oldest old people in the last decades increased the attention of researchers and policy makers on this subgroup of individuals[2,3]. As physical and cognitive health are two dynamic processes and their deterioration is likely, especially at older ages, in the recent years it became a widely investigated topic[5,6,9,10,12]. Finding the determinants of physical and cognitive health changes and analyzing their longitudinal relationship are considered, nowadays, two of the major public health challenges[27,28]. However, only few studies analyzed such deteriorations among the oldest old[8,29]. Studying the determinants of physical and cognitive health transitions among very old people and analyzing the relationship between these two conditions will help to shed light on which are the most vulnerable groups. This study uses two waves of the 1905 Danish Cohort survey[14] to study the transitions in physical and cognitive health among individuals aged 93 at the baseline (1998) and 95 at the second wave (2000). Studies on this cohort showed that high level of disability and poor cognitive and physical performance are strong predictors of mortality in the oldest old[30,31]. More precisely, Thinggaad et al. (2016) found that being able to stand up from a chair and having a

good level of cognition increased the probability of surviving to age 100 for both women and men of the 1905 Danish Cohort Study[17].

Our results partially confirm the trends shown in the literature for both physical and cognitive health over the years among adults and younger elderly[7,9,11,29,32]. Even at very old ages, for individuals in good physical health conditions, the probability of dying directly was lower than the probability of first experiencing a health deterioration. This is what we called here a "one-step worsening pattern". However, this pattern was not observed for cognitive health in which the probability of deteriorating the level of cognition was lower than dying directly from a good cognitive status (24% vs 27%).

The analysis of potential drivers of the health decline showed similar results for physical and cognitive health, showing that the two dimensions of the health status follow somewhat similar patterns. However, it is important to point out that this might also partly be due to the overlap of individuals in good and bad state for both physical and cognitive health.

Demographic and socioeconomic variables in both cases resulted associated with health transitions. Not surprisingly, women had a lower probability of death [33–35]. However, by analyzing physical and cognitive dimension separately, we were able to uncover interesting dynamics. Being a woman did not affect significantly the transition from good to bad health. However, it was instead associated with a lower probability of dying from both good and bad cognitive status, but only lowered the probability of dying from a bad physical health condition. As expected, having a higher level of education decreased the probability of cognitive decline, confirming the results found among younger adults[12,32,36,37]. However, we found that the level of education did not affect the physical status, contrary to what has been found for a similarly aged (8 years younger) cohort of Canadian elderly[11,29]. Living alone is widely considered a predictor of physical [9,10,29] but not for cognitive health transitions. In our study, instead, we found that living alone affected both dimensions of the health status by decreasing the probability of deterioration. Anyway, it was not possible to disentangle the causal direction of the association (whether individuals in better health conditions are able to live alone, or whether living alone helps protecting the health condition).

Surprisingly, emotional characteristics did not have significant effect on any of the health transitions analyzed here, despite other scholars found that self-rated health and depression have an active role in explaining transitions in physical and cognitive health among old individuals[7,29,38,39].

For both health conditions, having a BMI higher than 22 (both categories “22-28” and “>28”) resulted in lower probability of dying both from a good and a bad health status, confirming previous findings on younger adults[40,41] and in mortality research[42]. Light to moderate exercise was significantly associated with lower probability of dying from both bad physical and cognitive status, while engaging in heavy physical activity was associated with a lower risk of deterioration of the physical health condition and a lower chance of dying when already in bad cognitive status. According to the instrument used by Nybo et al.[14], level of physical activity is related to the ability of performing Activities of Daily Living (ADL). Other studies reported this association in terms of physical frailty[5,9,10] for disability transitions while only little is known about the association between physical exercise and cognitive transitions[43]. As in the case of the living arrangement, it was not possible to distinguish the causal direction of the association between physical activity on physical health.

Conclusions

Our study sheds light on the dynamic relationship between physical and cognitive conditions among a cohort of nonagenarians, highlighting a "one-step worsening" pattern in physical health, which has not been shown before among nonagenarians. However, we did not observe the same pattern for cognition: individuals in good cognitive status at baseline are slightly more likely to die within two years than first experience deterioration of their cognition. The strengths of this study are the sample size and the extensive information available, which is rare to find given the age (93 years old) of the individuals under analysis. This made it possible to control for many covariates. The weakness of this study is that, even though the data set is longitudinal, it was not possible to clearly identify the causal relationship of some of the associations.

Transitions in both health dimensions were related to similar socio-demographic and behavioral characteristics, with some interesting exceptions, but, surprisingly, not to emotional factors. The two health dimensions resulted associated with each other in terms of transitions: being in a better health condition according to one of the two health measures lowered the probability of worsening the other health status or dying from a bad condition. This confirms what have been discussed by the extensive literature review by Clouston and colleagues[8] about the role

of the physical condition at baseline on the transitions in cognitive health and brings new evidence on the role of the cognitive status on the transitions in physical health for which the literature so far has not found consistent evidence.

Supplementary material

Supplementary text S1: missing data imputation

Multiple imputation was necessary to deal with missing at random values (MAR) in order to avoid loss of precision in the analysis. Following the literature on imputation with survey data, we used K-nearest neighbor imputation method (Chen & Shao, 2000). Taking advantage of all the variables available in the dataset except for the one analyzed, we considered five neighbors to calculate the aggregated values to impute.

*Supplementary table S1: Transition probabilities of the multi-state model where states are defined according to the physical health**

From/To	Good	Bad	Dropout	Dead
Good	0.34	0.29	0.13	0.25
Bad	0.02	0.34	0.14	0.50

*Health status according to Chair-Stand Test

*Supplementary Table S2: Transition probabilities of the multi-state model where states are defined according to the cognitive health**

From/To	Good	Bad	Dropout	Dead
Good	0.37	0.24	0.12	0.27
Bad	0.07	0.31	0.14	0.47

*Health status according to Mini-Mental State Examination

Supplementary Table S3: Multivariate predictions (hazard ratios) of transitions in physical health

Covariates	From	Good						Bad		
	To	Bad			Dead			Dead		
		HR	IC95%L	IC95%U	Dead	IC95%L	IC95%U	Dead	IC95%L	IC95%U
Sex (Ref. Men)	Women	0.96	0.68	1.34	0.34	0.10	1.15	0.66	0.54	0.82
Education (Ref. Lower)	Vocational	1.10	0.81	1.50	0.93	0.40	2.19	1.18	0.96	1.45
	Higher	1.32	0.92	1.91	1.13	0.42	3.07	0.98	0.75	1.29
Living alone (Ref. No)	Yes	0.52	0.39	0.68	5.11	0.17	154.80	0.60	0.50	0.71
People lost (Ref. No)	Yes	0.91	0.70	1.17	0.83	0.37	1.88	0.97	0.82	1.15
Self-rated health (Ref. Poor)	Acceptable	1.44	1.09	1.89	0.89	0.30	2.65	1.16	0.96	1.40
	Good	1.52	0.85	2.73	1.49	0.28	7.85	1.22	0.97	1.55
Depression (Ref. 29-52)	23-28	0.98	0.73	1.32	1.37	0.59	3.16	1.00	0.79	1.26
	17-22	1.16	0.82	1.63	0.59	0.16	2.11	1.12	0.89	1.42
Smoke (Ref. Never smoked)	Past	1.17	0.87	1.58	1.07	0.42	2.75	1.08	0.89	1.30
	Current	0.95	0.66	1.36	1.43	0.60	3.42	1.15	0.89	1.49
Body Mass Index (Ref. <22)	22-28	0.85	0.66	1.10	0.45	0.23	0.87	0.88	0.74	1.04
	>28	1.11	0.73	1.70	0.32	0.07	1.41	0.63	0.47	0.85
Physical Activity (Ref. None)	Light	0.79	0.60	1.04	0.39	0.13	1.18	0.73	0.55	0.97
	Heavy	0.35	0.21	0.58	0.58	0.16	2.10	0.65	0.25	1.72
Medications (Ref. 4+)	2 3	1.19	0.90	1.58	1.09	0.45	2.61	0.96	0.76	1.20
	0 1	1.17	0.84	1.62	1.99	0.88	4.47	1.18	0.97	1.42
Mmse (Ref. 0-23)	24-30	0.47	0.36	0.61	1.62	0.43	6.13	0.62	0.50	0.76

Supplementary Table S4: Multivariate predictions (hazard ratios) of transitions in cognitive health

Covariates	From	Good						Bad		
	To	Bad			Dead			Dead		
		HR	IC95%L	IC95%U	Dead	IC95%L	IC95%U	Dead	IC95%L	IC95%U
Sex (Ref. Men)	Women	1.11	0.74	1.65	0.42	0.18	0.94	0.65	0.52	0.82
Education (Ref. Lower)	Vocational	1.27	0.92	1.76	1.10	0.56	2.16	1.16	0.93	1.46
	Higher	0.55	0.36	0.83	0.81	0.41	1.60	1.21	0.90	1.62
Living alone (Ref. No)	Yes	0.49	0.35	0.68	2.36	0.45	12.45	0.59	0.48	0.72
People lost (Ref. No)	Yes	0.94	0.69	1.26	0.71	0.40	1.27	0.99	0.83	1.18
Self-rated health (Ref. Poor)	Acceptable	1.10	0.81	1.49	1.11	0.55	2.21	1.17	0.95	1.44
	Good	1.29	0.79	2.10	1.47	0.49	4.42	1.21	0.94	1.57
Depression (Ref. 29-52)	23-28	1.18	0.87	1.62	1.16	0.63	2.13	1.03	0.80	1.32
	17-22	1.32	0.92	1.89	0.94	0.42	2.13	1.13	0.88	1.46
Smoke (Ref. Never smoked)	Past	0.89	0.64	1.23	1.00	0.48	2.09	1.14	0.92	1.41
	Current	0.90	0.59	1.37	1.37	0.66	2.85	1.15	0.87	1.51
Body Mass Index (Ref. <22)	22-28	1.03	0.78	1.36	0.44	0.25	0.77	0.90	0.75	1.08
	>28	1.22	0.79	1.89	0.27	0.07	1.11	0.65	0.48	0.89
Physical Activity (Ref. None)	Light	0.85	0.58	1.23	0.64	0.28	1.48	0.65	0.47	0.90
	Heavy	0.66	0.39	1.13	0.59	0.21	1.65	0.52	0.27	1.00
Medications (Ref. 4+)	2 3	0.94	0.68	1.31	0.79	0.38	1.66	1.04	0.82	1.32
	0 1	0.89	0.63	1.26	1.42	0.71	2.84	1.27	1.04	1.56
Chair-Stand (Ref. Not able)	24-30	0.53	0.38	0.75	1.03	0.43	2.45	0.61	0.48	0.79

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Chapter III

Self-assessment of health: how socioeconomic, functional and emotional dimensions influence self-rated health among Italian nonagenarians

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Introduction

Self-rated health (SRH) is the most commonly used indicator to measure the general (or global) health status of an individual[1]. With a single and simple question: *"How is your health in general? Is it excellent, very good, good, fair or poor?"* respondents are asked to assess their own health condition. The aim of this question is to collect information on many dimensions of health (physical, functional, mental and emotional) summarized in one single answer. There are different variants of the question, the wording could be different depending on the context, and of the ratings, that can be more or less skewed to the good health. This could make cross national and over time comparisons of the resulting indicator (SRH) difficult to be interpreted.

SRH is known to be associated with several objective measures of health as well as to be a valid predictor of health care demand and mortality over different populations and ages[2–5].

Even though it is used extensively, it is still not clear which dimension of health plays an active role in the process of self-evaluation of health, whether the socioeconomic background is also involved in such process and how all those elements interact with each other. Many researchers, over the last decades, have tried to understand what influences SRH: demographic and socioeconomic characteristics, physical, functional and physiological health status, chronic conditions among the others were pointed out as possible determinants[6–14]. Jylhä in 2009 developed a conceptual model for SRH trying to explicit which factors could be involved in the cognitive process of self-evaluation of health[10]. The model is composed of two parts: first, it includes health-related factors such as medical diagnoses, current functional status and experienced bodily sensations and symptoms among the others; second, context-related factors are included such as age, comparison group, culture and so on.

In order to understand the structure of SRH, it is necessary to exploit a model that is able to evaluate simultaneously direct and indirect effects of observed and latent variables on the designed outcome. Since Structural Equation Modeling (SEM) has such characteristic, it has been chosen by several scholars as the right approach to address this issue[7,8,13–15].

Building up on Jylhä's model, among the more recent studies, Au & Johnston (2014)[12] highlighted the importance of vitality in the process of self-evaluation of health among Australians, while Golini & Egidi (2016)[13] found that the presence of chronic diseases plays a crucial role in this process on Italian elderly people.

The first study evaluating the mechanism of self-assessment of health among the oldest-old has been recently published by Lisko and colleagues[14] who analyzed a sample of Finnish nonagenarians. With the assumption that people lower their standards while getting older, understanding the process of self-rating health among the oldest-old, a growing segment of population in western societies, becomes extremely important. Given the higher prevalence of individuals affected by dementia among the oldest-old, Lisko and colleagues investigated whether a similar rating mechanism applies to the whole study population and to those who were affected by dementia[14]. On the other hand, they did not include any information on the socioeconomic status of the nonagenarians in their model, even though it has been shown that socioeconomic differences in health persist even among the oldest-old[16–19].

In this paper we extend the theoretical framework proposed by Golini & Egidi (2016) and Lisko et al. (2020) by including a socioeconomic construct in it to evaluate the process of self-assessment of health among Italian nonagenarians from Mugello, a rural area in Tuscany (Italy)[20]. By applying a SEM approach, we aim to evaluate the direct and indirect effect of socioeconomic status, presence of chronic diseases, and functional and emotional health on good self-rated health among Italian nonagenarians.

Methods

Study Population

The study population comes from the Mugello Study, carried out in 2012 in 9 of the 11 municipalities of the Mugello area in Tuscany (Italy), aimed to evaluate the aging process of individuals aged 90+. Demographic and socioeconomic information, as well as many health aspects, were collected by a trained physician at the patient's residence. 504 individuals were interviewed, representing about 65% of the whole nonagenarians living in that geographical territory in 2012. The participation rate was 69% after the exclusion of the nonagenarians who died before being interviewed or those who could not be reached. More information about the study design and survey methods are available in Molino-Lova et al. (2013)[20].

Structural Equation Modelling

Structural Equation Modelling (SEM) is suitable for evaluating conceptual frameworks that, in practice, include categorical and indicators of continuous latent variables. It allows estimating the direct and indirect effect of predictive variables on an observed or latent outcome[21].

In the present study the outcome is good SRH, expressed as a binary variable. All the observed indicators, used for identifying the latent variables, were also transformed into binary indicators, as described in the Measurement Model section. For this reason, the latent variables are linked to the observed indicators via probit regression models, as well as the outcome to the latent and observed variables.

SEM is characterized by two components: a measurement model that relates observed to latent variables and a structural model in which relations between outcome and observed or latent variables, as well as relations between latent variables, are expressed via regression models. The latent variables hypothesized in the conceptual framework are validated through Confirmatory Factor Analysis (CFA). The strength of the relationship between latent variables and observed indicators is indicated by factor loadings that are expected to be higher than 0.7 in order to provide convergent validity. Moreover, the estimated correlation between talent variables are expected to be lower than 0.9 in order to provide discriminant variability.

As recommended by Hu & Bentler (1998, 1999)[22,23], we reported some alternative indicators of model fit to the chi-squared statistic that is highly dependent on the sample size. In fact with a relatively high sample size, it tends to refuse the null hypothesis, indicating that the model represent the reality, too often. The authors suggest including the Standardized Root Mean Square Residual (SRMR), representing the portion of variance and covariance not explained by the model. This indicator is considered the most powerful to detect the adequacy of the model. They also recommend including at least one of the following indicators: the Root Means Square Error of Approximation (RMSEA), indicating the error made by approximating what we observe with the conceptual model; the Tucker and Lewis Index (TLI) and the Comparative Fit Index (CFI), representing the adequacy of the model compared to the null model where no relations among the variables are hypothesized.

Statistical analysis was performed in R version 3.6.3, using lavaan package[24].

Measurement Model

SRH was measured by the question “How is your health in general? Is it excellent, very good, good, fair or poor?” as part of the Short-Form 12 questionnaire (SF-12)[25]. Individuals reporting excellent, very good or good health were considered in “Good SRH” while individuals reporting fair or poor health were considered in “Poor SRH”. Some study participants could not be tested because of their poor health conditions. For this reason, they were considered “Non testable”[19]. These individuals were added to the “Poor SRH” class in the model, thus representing the counterpart of the “Good SRH”. The analysis was also performed excluding the “Non testable” individuals as a sensitivity check.

The measurement model assessed in this analysis is inspired by the framework proposed by Jylhä (2009)[10]. The author defined the process of self-assessment of health as a cognitive process that leads to answering to the SRH question. Building up on Jylhä’s framework and on the work by Golini & Egidi (2016)[13], the self-evaluation of health is assumed to depend on medical conditions (functional status and medical diagnosis) and sensations (feelings related to the status of the individual) but also on their socioeconomic condition. Other personal characteristics as age and gender are also included in the framework, potentially influencing the health perception. The health dimensions included in the model were summarized in two latent variables representing two of the three health dimensions that are assumed to contribute to the self-assessment of health: Functional Health (FH) and Emotional Health (EH). The third health component potentially involved and included in the model was directly measured on the patients: presence of Chronic Diseases (CD). Furthermore, the model includes a socioeconomic component summarized by the latent variable Socioeconomic Status (SES) that is supposed to play an active role in the process of self-assessment of health.

All the observed indicators were categorized as binary variables because of the small sample size of the study population. As the model assumed to represent the structure of SRH was based on assumptions that could not be simplified, the trade-off was to reduce the complexity of the variables. Furthermore, variables dichotomization makes the interpretation of the latent constructs easier and of the model results more straightforward. The indicators are always intended to represent the good dimension of each health domain (FH, EH and CD) and the highest socioeconomic status for SES. This choice is coherent with the one of other researchers investigating the structure of SRH among elderly and oldest-old[13,14]. Moreover, it allows to easily compare the results obtained in the present study and in the ones of Golini and Egidi on Italian elderly[13].

Functional Health (FH) represents the functional dimension of health that is assumed to be related to SRH and it was measured by three binary indicators. The functional limitations were evaluated by the ability to perform 5 Activities of Daily Living (ADL): eating, dressing, bathing, toileting, transferring. Individuals who could perform all the ADLs were considered "Autonomous" while individuals who were not able to perform at least one of the five activities were considered "Not autonomous"[26]. The sensory limitations were measured by the ability to hearing and seeing of the nonagenarians. Individuals with no sensory limitations, that is neither blind nor deaf, were considered as "Not impaired" while people reporting at least one of these problems were considered as "Impaired". The motion limitation of the nonagenarians was assessed by the question: "Is the patient: confined to bed; confined to the wheelchair; walking autonomously; walking leaning on the furniture; walking with help of people; walking with aids?". Individuals were distinguished between those who could walk autonomously ("Not impaired") and those who could only walk with help of people, aids or leaning on furniture and who were confined to bed or wheelchair ("Impaired").

Emotional Health (EH) represents the emotional and psychological dimension of health that are supposed to be related to SRH. The questionnaire used in the Mugello Study included the SF-12 questionnaire, which is also intended to evaluate mental and emotional aspects of health with three specific questions[25]. The three items used to represent the emotional health were assessed by the following questions: "In the last four weeks, how often did you feel calm?" (MH3); "In the last four weeks, how often did you feel sad?" (MH4); "In the last four weeks, how often did you feel full of energy?" (VT2). The possible answers to the three questions were: always; usually; often; sometimes; rarely and never. The items were dichotomized to emphasize the most severe or best condition depending on the question. For this reason, the cut-offs were chosen with reference to the frequency distribution of the observed variables, corresponding to the first or the third quartile of the distribution, depending on the implicit direction of the response range[13]. Individuals were considered calm when they answered always and usually while they were considered lively when they answered always, usually and often. Finally, individuals were considered sad when they answered always, usually, often and sometimes to the corresponding question.

Socioeconomic Status (SES) represents the social and economic latent dimension that is assumed to be related to SRH and it was intended to provide information about the influence of the level of education or type of living arrangement and main occupation performed during the working life on the perception of health at very old ages. The level of education was assessed by the number of completed years of education. It was dichotomized in order to

distinguish between people who had completed at most the first elementary degree (3 years of education or less) and people who continued to study after the first elementary degree (4 years of education or more). The main occupation performed during the working life was defined according to the Italian National Institute of Statistics (ISTAT) classification of jobs with 9 categories that were reduced to 2, as the resulting categories were found to be suitable for distinguishing people in good or bad health on the same study population[19]. Farmers, housewives and low skilled worker (laborer or unskilled worker) represented one category and medium skilled workers (office or, industry or intellectual worker) were the second one. The living arrangement was defined by where the interview was performed (home or institution) and by the question “If home, with whom do you live?” with four possible answers: alone; spouse; other relatives; other non-relatives. It was dichotomized in order to distinguish between people living alone and with someone or in nursing home. This distinction is often used by researchers investigating oldest-old health[18].

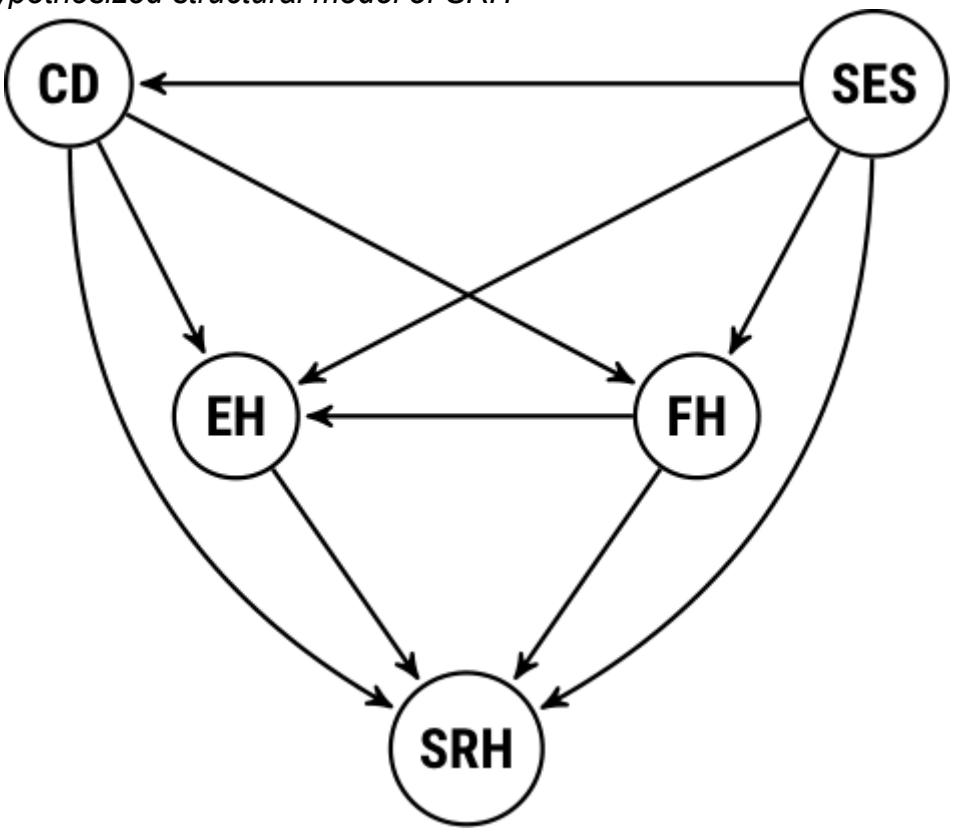
Structural Model

In the conceptual model proposed in this paper, good SRH is expected to be affected, directly and indirectly, by the socioeconomic status of the individual while presence of chronic diseases, functional and emotional health may have both an independent and mediating role. The model was designed following what Golini and Egidi proposed in 2016[13] but with the introduction of the effect of the socioeconomic status of the individuals as an active latent variable instead of a set of covariates. Socioeconomic variables seem to play a role in determining health in later life, even at very old ages[16,19,27]. The model follows the extension of Nagi’s model of disabilities causation proposed by Schultz et al. (2000)[28,29]. The causal chain goes from pathology to impairments, to functional limitations, to disability and finally to anxiety and depression. SRH is placed at the end of this causal chain, with the assumption that it is affected directly and indirectly by all these factors, as proposed by Jylhä in 2009. Moreover, the model proposed in this paper is coherent with the one proposed by Liang et al (1991)[30], in which the health structure is considered as the result of the interaction of different health factors. No reverse effect can be estimated because of the cross-sectional nature of the data. The model is represented in Figure 1 that includes the latent constructs and the observed variable, together with the hypothesized relationships.

In addition to the socioeconomic and health factors, age and gender were included in the model as covariates. Their influence on health perception is well known as it is their effect on other health factors that were assumed to influence SRH[31,32]. It was not possible to

analyze separately women and men because of the small number of the latter included in the dataset.

Figure 1. Hypothesized structural model of SRH



Note: SRH: Self-Rated Health; EH: Emotional Health; FH: Functional Health; CD: Chronic Diseases; SES: Socioeconomic Status

Results

Descriptive results

About three quarters of the nonagenarians from Mugello were women (73.2%), who were on average older than men (respectively 93.3 vs 92.5 years old). More than half of the nonagenarians rated their health as good (54.6%), almost one quarter of them rated their health as bad (23.6%) while the remaining were defined as non-testable (21.8%) because of their poor health condition.

Table 1 shows the distribution of the observed indicators measuring the latent variables. Half of the participants attended 4 or more years of education (51.5%). However, 68.1% of them worked as farmers or were housewives. Despite the old age, half of the study population was autonomous (52.6%) and almost two thirds of them did not have motion limitations (62.1%).

Table 1. Latent variables and distribution of the observed indicators in the nonagenarians from Mugello (2012)

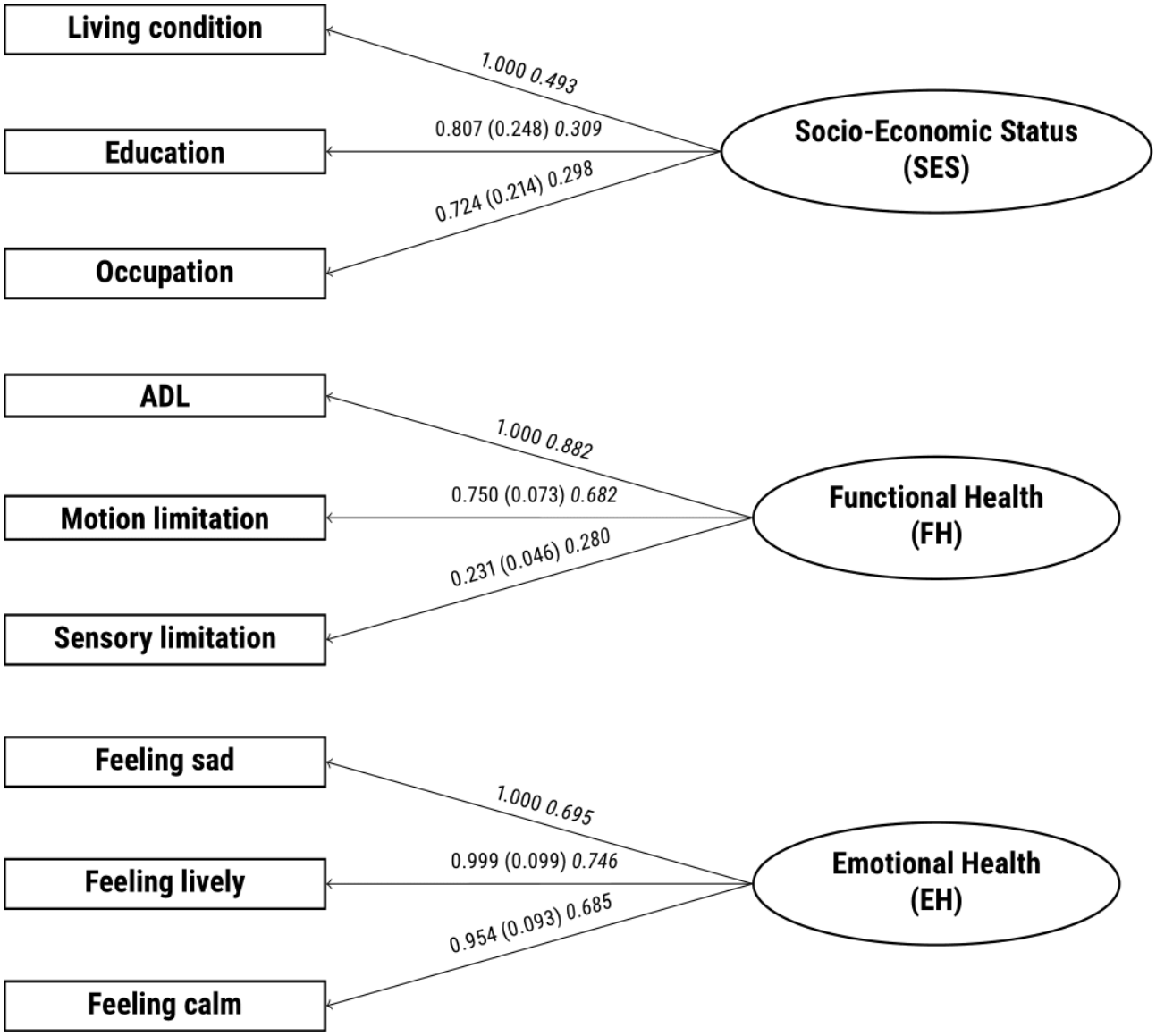
Latent construct	Observed indicator	Value	Counts	Proportions (%)
Socioeconomic Status (SES)	Years of education	0 = "0-3"	242	48.5
		1 = "4+"	257	51.5
	Main occupation	0 = "farmer/housewife"	338	68.1
		1 = "low-middle level worker"	158	31.9
	Living condition	0 = "with someone"	413	81.9
		1 = "alone"	91	18.1
Functional Health (FH)	Activities of Daily Living	0 = "non autonomous"	235	47.4
		1 = "autonomous"	261	52.6
	Motion limitation	0 = "no"	313	62.1
		1 = "yes"	191	37.9
	Sensory limitation	0 = "no"	425	84.3
		1 = "yes"	79	15.7
Emotional Health (EH)	Feeling calm	0 = "no"	359	71.5
		1 = "yes"	143	28.5
	Feeling sad	0 = "no"	340	67.7
		1 = "yes"	162	32.3
	Feeling lively	0 = "no"	376	74.6
		1 = "yes"	128	25.4

Model results

The hypothesized model fitted well the data: the value of the SRMR is 0.05, far below the empirical reference threshold of 0.08 suggested by Hu & Bentler (1998, 1999). The RMSEA is 0.05 (90% confidence interval 0.04-0.06). According to the previously mentioned authors, the value should be lower than 0.08 to be considered acceptable and below 0.06 to be considered good. CFI and TLI are greater or equal to the empirical threshold of 0.95: respectively 0.97 and 0.95[22,23].

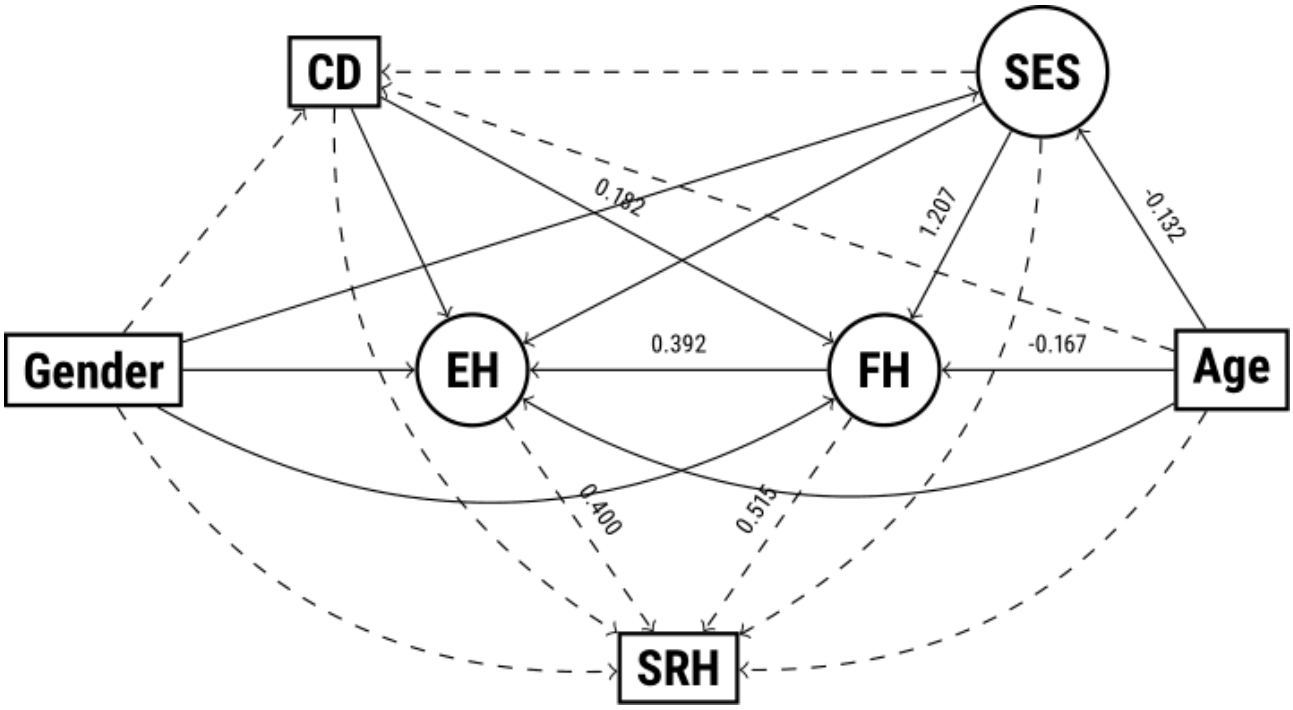
CFA verified construct validity of the three latent dimensions (SES, FH and EH) measured by the binary indicators described in Table 1. No factor cross-loadings were allowed: every indicator was assumed to have nonzero loading for the factor that it had to measure and zero factor loadings on all the others. Furthermore, measurement errors (e_i) associated with each indicator were assumed to be uncorrelated with measurement errors of the other indicators measuring the same latent variable and the latent variable itself. All the unstandardized factor loadings resulted statistically significant with a value greater than the recommended threshold of 0.7 (convergent validity) with the only exception represented by the Sensory limitation indicator. Unstandardized and standardized factor loadings, together with error variances, are presented in Figure 2. Moreover, the estimated correlations between latent variables were all lower than the recommended threshold of 0.9 (discriminant validity): 0.564 between SES and FH; 0.373 between SES and EH; and 0.520 between FH and EH.

Figure 2. CFA of the latent dimensions of SRH among nonagenarians from Mugello. Unstandardized (with standard errors in parenthesis) and standardized (in italic) factor loadings



Unstandardized probit and linear regression estimates are presented in Figure 3. Non-significant estimates are reported in Tables 2 and 3.

Figure 3. Hypothesized relationships between latent and observed health dimensions, covariates and Self-Rated Health (SRH) in the nonagenarians from Mugello



Note. Unstandardized linear and probit regressions are represented respectively by solid and dashed arrows.

The relationships among latent (and observed) health dimensions and between them and covariates are presented in Table 2. Being older (95 or more vs 90-94 years old) is strongly associated with having a worse socioeconomic status (SES) and worse functional health (FH). Higher SES and not reporting any chronic disease (CD) are positively associated with having a better FH. Finally, having a better FH is positively associated with a better emotional health (EH).

Self-rated health (SRH) is associated with both functional and emotional health with the first one showing a greater magnitude expressed by the standardized estimate, than the second one. No other associations were detected, as reported in Table 3.

Table 2. Relationships among latent and observed health dimensions and between them and covariates in the nonagenarians from Mugello

Model	Unstandardized estimate	Standard error	p-value	Standardized estimate
SES on				
Age (95+ vs 90-94)	-0.132	0.033	0.000	-0.313
Gender (men vs women)	0.029	0.032	0.369	0.067
CD on				
Age (95+ vs 90-94)	0.007	0.056	0.895	0.007
Gender (men vs women)	-0.002	0.050	0.969	-0.002
SES	0.287	0.230	0.211	0.118
FH on				
Age (95+ vs 90-94)	-0.167	0.062	0.007	-0.172
Gender (men vs women)	0.102	0.054	0.059	0.104
SES	1.207	0.345	0.000	0.526
CD	0.182	0.057	0.001	0.194
EH on				
Age (95+ vs 90-94)	0.075	0.041	0.069	0.097
Gender (men vs women)	0.054	0.041	0.185	0.069
SES	0.188	0.276	0.681	0.104
CD	-0.033	0.040	0.418	-0.044
FH	0.392	0.101	0.000	0.497

Table 3. Relationships between SRH and the latent and observed dimensions of health, socioeconomic status (SES) and covariates in the nonagenarians from Mugello

Model	Unstandardized estimate	Standard error	p-value	Standardized estimate
SRH on				
Age (95+ vs 90-94)	-0.037	0.048	0.477	-0.033
Gender (men vs women)	-0.047	0.046	0.298	-0.042
SES	-0.049	0.285	0.864	-0.018
CD	-0.053	0.045	0.236	-0.050
FH	0.515	0.122	0.000	0.449
EH	0.400	0.096	0.000	0.275

Discussion

The aim of our paper is to evaluate direct and indirect effects of socioeconomic characteristics and health-related factor on SRH among Italian nonagenarians. Based on the framework proposed by Jylhä in 2009[10] and on the extensions made by Au & Johnson (2014) first and Golini & Egidi (2016) afterwards, we propose an extra layer of complexity by including the socioeconomic status as a latent construct in the conceptual framework. Socioeconomic disparities in health are well documented among the elderly[33] and, in more recent years, evidence suggests that they persist at more advanced ages[16–19]. Therefore, we hypothesize that socioeconomic status could have a direct and indirect effect on the process of self-assessment of health among the oldest-old.

To pursue our aim, we exploit a SEM that allows the simultaneous evaluation of direct and indirect associations between latent or observed variables[21]. The SRH measure used in our analysis is obtained from the American version of the question: it is characterized by three positive items (excellent, very good, good) and two negative ones (poor, very poor). Comparing results to others obtained with the European SRH requires an appropriate rescaling of the health indicator[34]. In our study we collapsed all the good health categories into one to compare good to poor SRH. Since both versions of SRH have shown to be associated to the same demographic and health indicators and we only distinguish between good and poor health, it should be possible to indirectly compare our results with the ones of other studies following a similar analytical strategy.

We find a strong direct effect of emotional and functional health on SRH, the latter also having an indirect effect on good self-assessment of health through the emotional component. Socioeconomic status and presence of chronic disease have both an indirect effect on SRH via functional health. Being older has an impact on functional health while gender did not influence any of the construct included in the framework even if it has been observed that gender differences in health exist among nonagenarians from Mugello[31].

The psychological and emotional component has a double role in the process of self-assessment of health. It has a direct effect on SRH, as found by other scholars who analyzed emotional health as a single indicator[14,35,36] or as a latent construct[12,13]. At the same time, it mediates the effect of other health-related measures included in the process, confirming the importance of emotional health in the mechanism of self-rating health. This result is consistent with what has been found among Finnish oldest-old by Lisko and colleagues[14], who considered depression as a measure of psychological and emotional health. The same

double effect of emotional health in the process of self-assessment was also found among Italian elderly people by Golini & Egidi (2016)[13], who measured it with a similar latent construct.

Functional health also plays an important role in the process of self-assessment of health of the oldest-old. The direct effect is stronger than the effect of emotional health, indicating that being able to perform daily activities or not having motion impairments is very important for the oldest-old to positively rate their health. Even though it is not the strongest component of the mechanism, functional health resulted directly associated to SRH among Italian elderly as well as mobility among Finnish nonagenarians[13,14]. In accordance to what has been found by Golini and Egidi[13], functional health has also an indirect effect on SRH among Italian nonagenarians, confirming its importance in the process of self-assessment of health.

Chronic disease does not play a main (direct effect) role in the mechanism of self-rating health among Italian nonagenarians. This result is in contrast with what has been observed for less old Italians, for whom the presence of chronic disease was the main driver of poor SRH[13]. One possible explanation is that younger elderly are less used to living with chronic diseases than the oldest-old: the timing of occurrence might be the key factor here. An additional explanation could be that the diseases considered in this study are less strongly related to SRH than the ones analyzed by other scholars. Lisko and colleagues, for instance, included separately many different diseases in their model and found heart disease (direct), arthritis and dementia (indirect) to be related to SRH. They, in particular, considered dementia as a key factor in the process of self-assessment of health. For this reason, they analyzed the subsample of people affected by dementia, finding that dementia weakens both direct and indirect associations of observed and latent variables with SRH[14]. In the present study, excluding from the analysis non-testable individuals, those who are in the worst health conditions (mainly cognitive)[19], did not change the results obtained on the total population (see Supplementary material). However, it has not been possible to perform the same analysis on the subsample of non-testable individuals because of the small sample size.

Socioeconomic status does not have a direct effect on SRH, similarly to what has been found by Au & Johnston among Australian[12]. However, as for the presence of chronic disease, it has an indirect effect on SRH by influencing functional health, confirming that socioeconomic health disparities persist among nonagenarians[16–19]. This result suggests that socioeconomic status by itself does not influence the perception of health of the individuals, contrary to what one might think, that highly educated people or people living in

a better economic condition perceive their health differently from those who are less educated or wealthy. The association between socioeconomic status and SRH might be explained through other health factors that are directly influenced by the SES and that are associated to SRH. Further investigation is required in order to understand whether this result is confirmed among the oldest-old of other populations.

These results suggest that at older ages, oldest-old individuals with the same cultural background (Italian) share a similar mechanism of evaluation of their own health with the younger-old. This result is extremely important as it brings new evidence to the discussion of cross-age differences in SRH. It is known that, when growing older, the standards for considering one's health as good become lower. However, it is not clear whether the importance given to certain aspects of health when rating the own health conditions change. Lazarevič and Brandt, in a recent paper, investigated such difference in several countries, finding that between adults and elderly there were quite some differences in terms of health dimensions influencing SRH. However, they could not investigate differences between younger-old and oldest-old as the survey they did not include a sufficiently large group of very old people[32]. The results of this paper bring evidence on the cross-age comparison of SRH at older ages that was never explored before. Despite some questioning on the reliability of SRH as overall health measure at very old ages, European and American research shows that it remains a valid measure to capture objective health changes over time and to predict mortality as a consequence of health worsening[37–39]. Our results might suggest that even at very old ages, SRH is still sensitive to some objective health measures as functional health and presence of chronic diseases.

The present study has some strengths and limitations. The uniquely rich health data on nonagenarians (Mugello Study) and the use of a powerful statistical method as SEM are the two major strengths of this study. On the other hand, the cross-sectional nature of the data does not allow us to tackle the causal relationships between the latent and observed variables included in the model. Furthermore, we do not account for individual heterogeneity in the process of self-rating health. However, Hirve and colleagues (2014) showed that cultural background and individual-specific reporting behavior do not alter the mechanism of SRH[40].

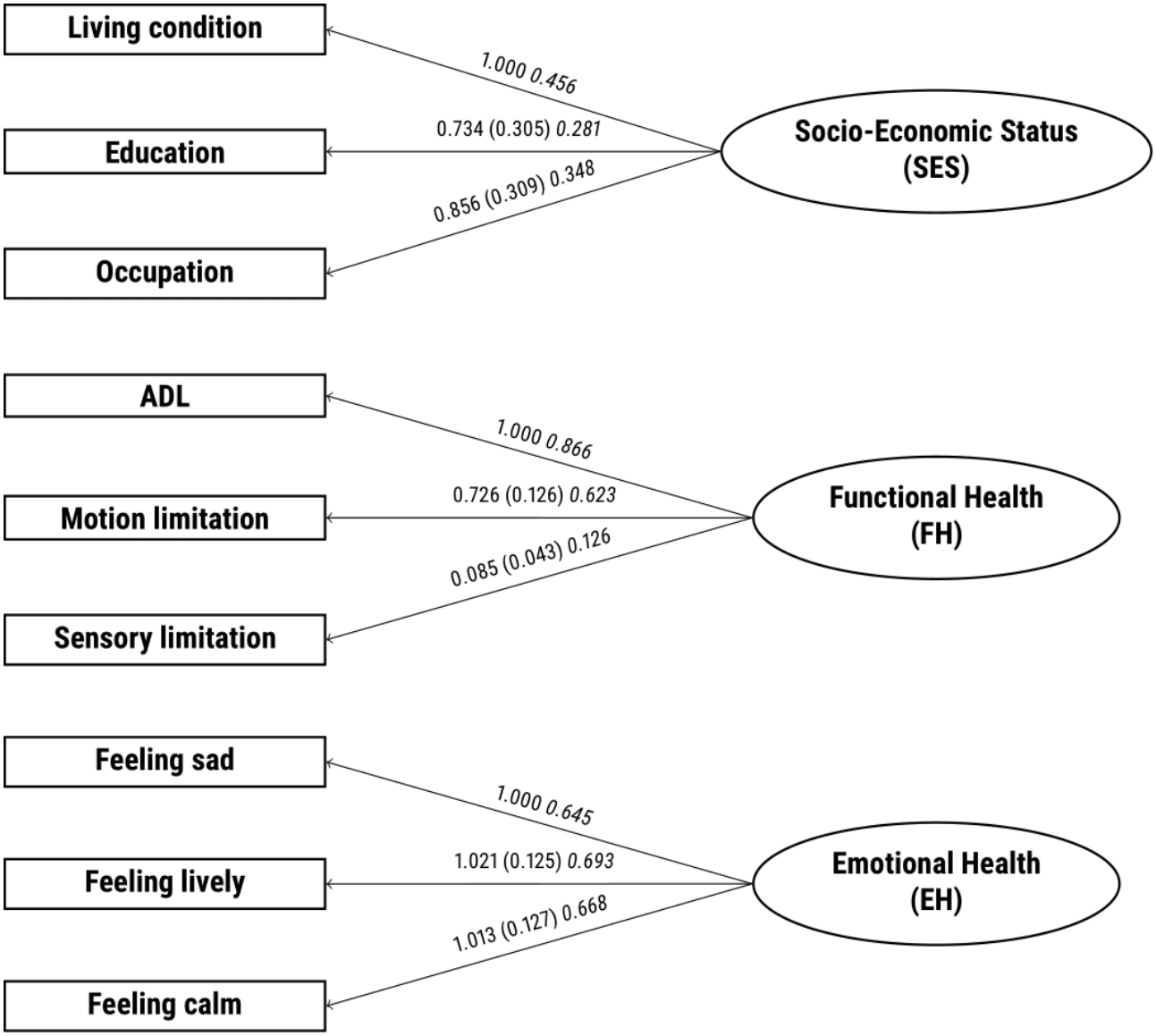
Conclusions

Overall, our study brings new evidence on the process of self-assessment of health among the oldest-old that, even though with some differences, it is coherent with the only other study on the topic we were able to find in the literature[14]. Our result suggests that self-assessment of health has the same structure among younger- and oldest-old for people sharing similar cultural background. To add important pieces of the puzzle, additional studies to compare different cultural contexts and different age groups, including the oldest-old, are necessary[32].

Finally, given the broad use of SRH, understanding the mechanism of self-assessment of health is crucial to correctly interpret the results obtained when SRH is used as an indicator of general health. Studies investigating the process of self-assessment of health at different ages, from young to old, and in different countries are present in literature. However, many more studies are necessary to disentangle such mechanism among older individuals. The oldest-old are the fastest growing portion of the population in the so-called "Western societies"[41]. As their participation to demographic and social surveys is increasing and it is expected to increase even more in the next years, future estimates of the health conditions of the oldest-old should become more reliable. Since SRH is commonly measured in general surveys, extending the knowledge on how long-lived individuals assess their own health becomes crucial. It could helps policy makers to better understand the needs of the older individuals populating modern societies.

Supplementary material

Supplementary Figure 1. CFA of the latent dimensions of SRH among testable nonagenarians from Mugello. Unstandardized (with standard errors in parenthesis) and standardized (in italic) factor loadings



Supplementary Table 1. Relationships among latent and observed health dimensions and between them and covariates in the subsample of testable nonagenarians from Mugello

Model	Unstandardized estimate	Standard error	p-value	Standardized estimate
SES on				
Age (95+ vs 90-94)	-0.129	0.040	0.001	-0.326
Gender (men vs women)	0.025	0.034	0.459	0.066
CD on				
Age (95+ vs 90-94)	-0.035	0.069	0.612	-0.032
Gender (men vs women)	-0.011	0.055	0.846	-0.010
SES	0.096	0.294	0.743	0.035
FH on				
Age (95+ vs 90-94)	-0.237	0.068	0.001	-0.248
Gender (men vs women)	0.036	0.056	0.520	0.040
SES	0.967	0.371	0.009	0.400
CD	0.227	0.054	0.000	0.256
EH on				
Age (95+ vs 90-94)	0.080	0.055	0.143	0.105
Gender (men vs women)	0.051	0.043	0.233	0.071
SES	0.239	0.312	0.443	0.124
CD	-0.018	0.049	0.717	-0.025
FH	0.301	0.103	0.004	0.376

Supplementary Table 2. Relationships between SRH and the latent and observed dimensions of health, socioeconomic status (SES) and covariates in the subsample of testable nonagenarians from Mugello

Model	Unstandardized estimate	Standard error	p-value	Standardized estimate
SRH on				
Age (95+ vs 90-94)	-0.094	0.064	0.146	-0.088
Gender (men vs women)	-0.069	0.050	0.165	-0.068
SES	0.093	0.307	0.763	0.034
CD	-0.026	0.053	0.621	-0.027
FH	0.305	0.119	0.010	0.274
EH	0.279	0.096	0.004	0.200

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Conclusions

The oldest-old are the fastest growing segment of the population in most developed countries[1]. The increasing number of individuals reaching very old ages is going to pose challenges for the economic and health-care systems of modern societies[2–4]. For instance, many countries are already facing the controversial problem of needing to raise the pension age to be able to face the cost of people surviving longer after retirement[5,6]. However, moving up the pension age is only feasible if people are able to work longer, which implies succeeding in aging healthy[7]. Furthermore, this change might give rise to additional fairness problems, if inequalities in health are not reduced[8]. As people aged 65+ are – by far – the most demanding in terms of health-care, having more people reaching old and very older ages in bad health conditions will result in an excess of health-care expenditures for the country[9,10]. On the other hand, if individuals do succeed in aging healthy, having more people at older ages could – and should – be transformed into an opportunity from both an economic and social perspective[3,4]. Of course, older people in good health can work longer and produce economic value for the society[8] but this should not be considered the only advantage of having more individuals actively aged[11,12]. Healthy people who can actively live their life at old ages can participate to the social life of their society by performing activities such as volunteering or taking care of their grandchildren[13,14]. This would generate a double advantage for both societies and individuals who will be engaged in such activities[15].

It is clear that, in the discussion about the consequences of having more people living longer in the societies, health plays a central role. The aim of this PhD thesis is to help understanding health dynamics among the oldest-old and bring new evidence in the field of health inequalities among long-lived individuals. It also aims at giving the right instruments to policy makers for better identifying the categories upon which focusing targeted interventions, when and how doing so.

As emerged from the results discussed in this PhD thesis, it is evident that there is noticeable heterogeneity in health among people reaching very old ages. This is visible either when considering single dimensions of health but also when considering health holistically. Being able to capture properly such heterogeneity is crucial for increasing our knowledge about health inequalities among the oldest-old and for giving to policy makers the right instruments to address urgent issues. Identifying health profiles among the oldest-old, by jointly analyzing multiple health dimensions within the same model, is especially helpful to assess health heterogeneity and to understand the appropriate care needs of the oldest-old[16–18]. It allows identifying the most vulnerable people but also individuals with dimension-specific health problems. According to the results showed in the first study of this PhD thesis, it is

likely that people with physical impairment are also affected by cognitive deterioration. However, individuals with cognitive impairment are not necessarily affected by physical or functional limitations. Researchers investigating these dynamics among the elderly showed that individuals characterized by different health profiles, according to their conditions in various health dimensions, require different kind or amount of care, thus resulting in higher or lower costs for the society[16,18,19]. Being able to classify the oldest-old within health profiles, by evaluating simultaneously many health dimensions, is crucial for avoiding any excessive use of human and economic resources by identifying the adequate care needed by each individual. Furthermore, as demonstrated by the results of the first study of the PhD thesis, which confirm the findings of previous studies, there are considerable socioeconomic differences between people characterized by different health profiles[20,21]. This result brings new evidence to the discussion of socioeconomic inequalities in health among the oldest-old. It is especially helpful for policy makers knowing which segments of the population to target for reducing socioeconomic disparities that will most likely result in health inequalities at older ages[22–24].

The health profiles emerged among Italian oldest-old suggest that different dimensions of health are related to each other. It does not mean that all the individuals experiencing poor conditions in a specific dimension of health are necessarily in poor conditions overall. Different health deficits might appear in distinct – and perhaps distant – moments in time with a probability that depends on other pre-existing conditions. In a longitudinal perspective, some people might experience, for instance, the occurrence of physical problems before reporting cognitive impairment or vice versa. As experiencing health deterioration is likely for people in the last stage of their life, evaluating the phenomenon of health deterioration in a cohort of oldest-old seemed of great interest. Furthermore, because different dimensions of health might follow different worsening patterns over time, analyzing two key aspects of health such as physical ability and cognition, and evaluating their dynamic relationship appeared of great scientific interest[25–28]. Literature on the dynamic relationship between physical and cognitive health is vast but studies investigating this phenomenon among the oldest-old are lacking[29].

According to the results presented in the second study, there is a dynamic relationship between different dimensions of health among the oldest-old. People in good physical health are less likely to experience cognitive deterioration and people with good cognition are less likely to have their physical ability deteriorated in the following 2 years. The results confirm the existing knowledge about the influence of baseline physical ability on cognitive

deterioration and bring new evidence about the role of baseline cognitive status on the worsening patterns of physical health[29]. The analysis of potential determinants of physical and cognitive health deterioration among the oldest-old, conducted in the second study, sheds light on key factors on which health and policy makers should focus their attention to enable more people to preserve their health longer. Among the others, the level of education, usually employed as proxy of socioeconomic status among long-lived individuals, which is known for being the main driver of cognitive health at older ages[27,30,31], still plays a major role in determining the cognitive status among the oldest-old. Moreover, engaging in healthy behaviors, such as performing physical activity or monitoring one's body mass index (BMI), is essential for staying healthy longer or preventing premature death[32,33]. Health organizations should insist in promoting healthy behaviors among people of every age, as their advantages are evident until the very last stages of life, but also make it possible for elderly and the oldest-old to engage in such activities.

The second study of the PhD thesis also confirms the presence of heterogeneity in the health conditions of people reaching very old ages. This heterogeneity makes it even more interesting to disentangle the mechanism behind the self-assessment of health among the oldest-old. Self-perceived health is the most commonly health indicator measured in demographic and social surveys. In a not-so-far future information on oldest-old will be collected in more and more surveys and understanding the complex cognitive mechanism that activates to answer the very simple question about one's health will become crucial. Over the last years the mechanism behind self-assessment of health has been theorized and investigated both at the level of the general population and specifically among elderly individuals to understand which factors are involved and how they interact[34–36]. However, at present, there is only one study that analyzed this complex mechanism among the oldest-old[37]. From the third study of this PhD dissertation emerged that Italian oldest-old seem to evaluate their own health by giving similar importance to certain aspects of health as younger-old do. In particular, emotional and functional health directly influence self-rated health while presence of chronic diseases and socioeconomic status indirectly influence it. This is the first study that finds such similarity between elderly and oldest-old people within the same context (country), bringing new evidence to the discussion of cross-age comparability of self-rated health. A recent comparative study of factors influencing self-rated health across different ages and countries showed that some factors differ between countries and among people of different ages[38]. However, they did not explore such mechanism among the oldest-old. Understanding what is hidden behind the indicator of self-

rated health allows to inform policy makers about the consequences of their past interventions but also to plan future ones as the needs of the population become clearer.

All the three studies presented in this PhD thesis included an analysis of the influence of socioeconomic factors on health among the oldest-old. Socioeconomic inequalities in health are well known among people of different ages and contexts[22,39–41]. However, much more research needs to be done among the oldest-old. Education is especially powerful at capturing disparities in cognitive health among elderly individuals[27,30,31] but also among the oldest-old as observed in the first two studies. The type of job performed during the working life emerged as good indicator to capture the health differences, especially when health is considered holistically, confirming the findings of previous studies[21,42]. Education and work were also included, together with living conditions, for defining a latent variable (socioeconomic status) that was found to be involved in the mechanism of self-assessment of health by indirectly influencing functional health. The results are clear: regardless of which aspect of health is considered and whether a single or multiple dimensions of health are analyzed, socioeconomic disparities in health persist even among the oldest-old[43–45]. The advantage given by belonging to a better socioeconomic group remains evident in the very last stages of life, not only in terms of surviving longer but also in terms of surviving healthier[23,43–45]. This growing evidence suggests that reducing socioeconomic disparities should be the main goal of policy makers if they want to reduce inequalities in health, even at older ages where most of the health-care resources are spent[46]. Making education more accessible to people is essential for fighting socioeconomic inequalities and allowing less advantaged people to continue their education will certainly help reducing inequalities in health later on.

The studies presented in this PhD thesis have limitations that need to be noted. The cross-sectional nature of Mugello Study data did not allow for evaluating respectively the causal relationship between socioeconomic characteristics and health profiles in the first study and between the latent and observed factors hypothesized to be part of the mechanism hidden behind the self-assessment of health. Even with longitudinal data, the causal mechanism behind some of the associations resulted in the second study were not disentangled as specific methodology would have been required. Moreover, some of the health measures employed in the studies are self-reported and the categorization according to cut-off points, even if chosen according to the existing literature, is not comparable to a medical diagnosis. It should be also noted that nonagenarians from Mugello, in Tuscany (Italy), are a selected group of individuals who live in a rural area with characteristics, as for instance dietary and lifestyle habits, that are not common to every other nonagenarian in Italy. The sample is

therefore not statistically representative of the health of the national population. Similarly, the 1905 Danish cohort health characteristics cannot be extended to the general Danish population as they are observed in a specific cohort. However, the relationships between different health outcomes and with other factors analyzed in the thesis were obtained controlling for the structural characteristics of the two study populations. This makes it possible to compare the specific results obtained in the three studies with others observed in populations with similar study settings but different characteristics, if those are controlled in the analysis. Given the very different nature of the data sources used in the chapters of the thesis, it was not intended to compare results obtained with Italian (Mugello) and Danish data. The analyses focused on different aspects of health to take fully advantage of the characteristics of the data.

Much more needs to be investigated among the oldest-old. For instance, since data on long lived individuals are becoming increasingly available, further research should focus on evaluating whether more recent cohorts of individuals are reaching the oldest ages in better or worse health conditions. This would fuel the debate on success or failure of the aging societies and drive policy makers interventions to promote healthy aging. Also, having more longitudinal studies allows to follow individuals reaching very old ages and to evaluate the evolution of their health status. This could help to better understand how health deteriorates with age and how different health dimensions influence each other resulting in the complex condition characterizing the individual's health status.

To conclude, assessing the health conditions of people reaching very old ages allowed bringing new evidence to the discussion of heterogeneity in health among long-lived individuals. It is clear that age cannot be considered a good indicator of health, given the amount of variability in health observed among the oldest-old. The contribution of this PhD thesis is extending to the oldest-old the existing knowledge about dynamics of health, intended both as interactions between different dimensions of health and as longitudinal changes of certain conditions. Moreover, understanding such health dynamics is essential for giving policy makers the appropriate instruments to evaluate past interventions and plan for future ones. Allowing more people to reach very old ages in good health should be the aim of modern societies. This is only possible if societies reorganize their structures and expenditures to address more efficiently the needs of the oldest-old: for healthy people, it means promoting activities they can be engaged with; for people with any kind of health impairment, it means breaking down barriers that are present in many societies for making their lives easier.

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