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HOW WELL ARE WE AGING? CAPTURING THE COMPLEXITY OF HEALTH TRAJECTORIES OF OLDER ADULTS

Giola Santoni



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How well are we aging? Capturing the complexity of health trajectories of older adults

THESIS FOR DOCTORAL DEGREE (Ph.D.)

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Tibi

To the memories I forgot, I miss them dearly!

“Beware of wishes! They grant what you ask not what you want!” from The psychosocial function of wishes in the desire conundrum. Invisibilia Press, Feb 29th 1974

ABSTRACT

Despite its positive nature, population aging represents a public health challenge that could be alleviated by maintaining good health during older age. The aim of this thesis was to evaluate how well people are aging, taking the complexity of their health status into account. All four studies included data from the Swedish National Study on Aging and Care in Kungsholmen (SNAC-K). Study I also gathered data from the Kungsholmen Project (KP). The reference population consisted of the people living in the community or in an institution in Stockholm, Sweden. In the KP, they were aged 75+ in 1987, and in SNAC-K, aged 60+ between 2001 and 2004.

Study I. Between 1991 and 2010, both prevalence and incidence of disability remained steady with a tendency towards a gradual decline. In this period, survival increased in functionally independent people but remained constant in disabled people. Our findings suggest that we are living longer and healthier lives, at least in urban-dwelling non-impooverished societies with access to adequate health care and public health assistance.

Study II. We used four health indicators to characterize the health status of a population of adults aged 60+ living in Stockholm, Sweden: morbidity, physical impairment, cognitive impairment, and mild and severe disabilities. While multimorbidity and slow gait speed were already prevalent (>60% and >20%) among sexagenarians, both cognitive impairment and mild disability were low until age 84, and severe disability was nearly absent until 90.

Study III. The four health measures used in Study II were integrated in a health assessment tool (HAT) for assessing and following health changes in older adults. The HAT score ranges from 0-10 (poor-good health). HAT was reliable over time and accurately predicted adverse health outcomes (ROC area hospitalization: 0.78, 95% CI 0.74–0.81; mortality: 0.85, 95% CI 0.83–0.87). At baseline and follow-ups, at least 90% of participants aged 85 or younger were free of severe disability, and half were functionally independent despite some morbidity.

Study IV. A HAT score higher than the age-/sex-specific median was related to completion of the chair-stand test (OR: 2.6, 95% CI 2.1–3.3), better balance and grip test results (interaction OR: 1.2, 95% CI 1.1–1.3), and good self-rated health (OR: 2.2, 95% CI 1.8–2.7). HAT predicted social and medical care use better than did disability ($p < 0.001$) and morbidity (HAT better for hospital admission, formal care, and informal care; $p < 0.001$). HAT score can be computed with a flowchart, and the percentile curves help estimate individual health status.

Conclusions. The health status of this urban Swedish population was fairly good. Time trends in disability remained stable over 20 years (1991-2010), and at the same time, the increase in life expectancy during recent years appeared to be driven by the longer lives of functionally independent people. Studying the health status of older people using multiple indicators of health, we found that age 80-85 is a transitional period when major health changes take place, often following the co-occurrence of more than one negative health event. HAT, composed of relatively few items, may help assess and identify deviations from expected health trajectories at the individual level and determine medical, rehabilitation, or social care needs at the population level. Determination of individual-level deviations can be facilitated by creating reference health curves similar to the growth charts used by pediatricians. HAT is a reliable and valid health measure and is a good candidate for use in developing such geriatric health charts.

Key words: Cognition, gait speed, multimorbidity, physical function, disability, activities of daily living, temporal trends, health status, health assessment, geriatric charts, item response theory, Health Assessment Tool.

SAMMANFATTNING

Trots det positiva i en åldrande befolkning så medför den utmaningar ur ett folkhälsoperspektiv. Dessa utmaningar kan minskas genom bibehållande av god hälsa under åldrandet. Målet med den här uppsatsen var att utvärdera hur väl människor åldras, med hänsyn tagen till komplexiteten kring hälsostatus. Alla fyra studierna bygger på data från the Swedish National Study on Aging and Care in Kungsholmen (SNAC-K). Studie I bygger även på data från Kungsholmenprojektet (KP). Referenspopulationen bestod av de människor som lever i Stockholm, Sverige, (KP ålder 75+ 1987, SNAC-K ålder 60+, 2001-2004).

Studie I. Mellan 1991 och 2010 var både prevalens och incidens av funktionshinder stabilt, med en tendens mot gradvis minskning. Under den här perioden ökade överlevnad bland funktionellt oberoende personer men förblev densamma för funktionshindrade personer. Våra resultat tyder på att vi lever längre och hälsosammare liv, åtminstone den urbana välmående befolkningen med tillgång till bra vård.

Studie II. Vi använde fyra hälsoindikatorer för att karaktärisera hälsostatusen hos en befolkning av personer i åldern 60+ boende i Stockholm, Sverige; sjuklighet, fysisk nedsättning, kognitiv nedsättning samt milda och svåra funktionshinder. Medan multisjuklighet och långsam gång redan förekom (>60% och >20%) bland sextioåringar, så var både kognitiv nedsättning och mildt funktionshinder ovanligt fram till 84 års ålder. Svåra funktionshinder var nästan obefintliga tills nittioårsåldern.

Studie III. De fyra hälsoindikatorerna som användes i Studie II integrerades i ett hälsobedömnings-verktyg (Health Assessment Tool, HAT), för att bedöma och följa förändringar i hälsan bland äldre människor. HAT-poängsättningen sträcker sig från 0-10 (dålig-bra hälsa). HAT var reliabelt över tid och kunde förutsäga negativa resultat (ROC area för sjukhusvistelse: 0.78, 95% CI 0.74-0.81; dödlighet: 0.85, 95% CI 0.83-0.87). Vid baseline och uppföljning var åtminstone 90% av deltagarna i åldern 85 eller yngre fria från svåra funktionshinder, och hälften var funktionellt oberoende trots viss sjuklighet.

Studie IV. En HAT-poäng högre än den ålders- och könsspecifika medianen var relaterad till slutförande av chair stand test (OR: 2.6, 95% CI 2.1-3.3), bättre balans och greppstyrka (interaktion OR: 1.2, 95% CI 1.1-1.3), och bra självskattad hälsa (OR: 2.2, 95% CI 1.8-2.7). HAT förutsåg användande av socialtjänst och sjukvård bättre än vad funktionshinder gjorde ($p < 0.001$) och sjuklighet (HAT bättre för sjukhusintagning, formell vård och informell vård; $p < 0.001$). HAT-poäng kan kalkyleras utifrån ett flödesschema, och den procentuella kurvan kan användas för att bestämma en individs hälsostatus.

Slutsatser. Hälsostatusen hos den här urbana svenska befolkningen var ganska bra. Tidstrender för funktionshindrade var stabila över 20 år, och samtidigt verkar den ökande livslängden under senaste åren drivas av funktionellt oberoende individer. När vi studerade hälsostatusen bland äldre individer fann vi att 80–85-årsåldern är en övergångsperiod då stora förändringar inom hälsan sker, ofta följt av samexistens av flera negativa hälsohändelser. HAT, bestående av relativt få komponenter, kan vara ett verktyg för att hantera och identifiera avvikelser från förväntade hälsobanor på en individnivå och bestämma medicinska, rehabiliterings-, eller socialtjänstkostnader på befolkningsnivå. Fastställande av avvikelser på individnivå kan underlättas genom skapandet av referens-hälsokurvor liknande de tillväxtkurvor som används av barnläkare. HAT är ett reliabelt och validerat hälsoinstrument som är en god kandidat för att utveckla sådana geriatriska hälsokurvor.

Nyckelord. Kognitiv funktionellt, gång test, sjuklighet, fysisk funktionellt, funktionshinder, tidstrender, hälsostatus, geriatriska hälsokurvor, hälsobedömnings-verktyg.

RIASSUNTO

L'aumento della proporzione di anziani nella popolazione rappresenta un fattore che potrebbe destabilizzare i sistemi sanitari. Questo problema potrebbe essere alleviato facilitando il mantenimento di un buono stato di salute anche in età avanzata. L'obiettivo di questa tesi è di valutare come la complessità dello stato di salute nella popolazione anziana può variare durante il processo di invecchiamento. Gli studi presentati in questa tesi utilizzano dati dello Swedish National Study on Aging and Care in Kungsholmen (SNAC-K). Lo Studio I include anche i dati del Kungsholmen Project (KP). Tali progetti considerano come popolazione di riferimento quella residente a Stoccolma (Svezia), di età ≥ 75 anni nel 1987 per il KP, e di età ≥ 60 anni nel 2001 per lo SNAC-K.

Studio I. Fra il 1991 ed il 2010, la prevalenza e l'incidenza di disabilità si sono mantenute invariate. In questo periodo, il la durata mediana di vita per le persone funzionalmente indipendenti è aumentato, mentre è rimasto costante per le persone affette da disabilità. Questi risultati suggeriscono che la popolazione anziana in una società benestante e urbana con accesso ad un buon sistema sanitario vive più a lungo e con un migliore stato di salute.

Studio II. I seguenti indicatori sono stati usati per caratterizzare lo stato di salute di persone di età ≥ 60 anni: morbidità, performance fisica, stato cognitivo, e presenza di leggera e severa disabilità. Le prevalenze di multimorbidità e ridotta velocità di cammino si sono dimostrate rilevanti ($>60\%$ e $>20\%$) nei sessantenni, quelle relative alla presenza di limitazioni cognitive e di leggera disabilità si sono mantenute basse fino ad 84 anni, mentre la prevalenza di severa disabilità è risultata quasi assente fino ai 90 anni.

Studio III. I quattro indicatori usati nello Studio II sono stati integrati in uno score di salute (Health Assessment Tool, HAT) per poter monitorare i cambiamenti nello stato di salute delle persone anziane. L'HAT (range 0-10, cattiva-buona salute) ha dimostrato di essere affidabile nel tempo e di predire accuratamente eventi negativi legati alla salute (ROC area; ospedalizzazione: 0.78, 95% CI 0.74–0.81; mortalità: 0.85, 95% CI 0.83–0.87). Al basale ed ai follow-ups, almeno il 90% dei partecipanti di età ≤ 85 anni non presentava severa disabilità, mentre circa la metà era funzionalmente indipendente, pur con qualche morbidità.

Studio IV. Punteggi di HAT oltre la media specifica per età e sesso hanno dimostrato un'associazione positiva significativa con chair-stand test (OR: 2.6, 95% CI 2.1–3.3), equilibrio e prensione (interazione OR: 1.2, 95% CI 1.1–1.3), e stato di salute percepita (OR: 2.2, 95% CI 1.8–2.7). La capacità predittiva dell'HAT per l'utilizzo di assistenza sociale e di cure mediche è risultata essere migliore rispetto alle misure di disabilità ($p < 0.001$) e morbidità (HAT migliore per numero di ospedalizzazioni, assistenza sociale, ed assistenza familiare; $p < 0.001$). I punteggi dell'HAT possono essere calcolati con l'uso di una flowchart ed i percentili di tale score potrebbero aiutare a stimare lo stato di salute individuale.

Conclusione. Lo stato di salute della popolazione svedese urbana considerata è abbastanza buono ed il trend temporale di disabilità è rimasto costante negli ultimi 20 anni. Il recente aumento della speranza media di vita sembra essere legato prevalentemente a quello avvenuto nelle persone funzionalmente indipendenti. Lo studio dei diversi indicatori di salute ha mostrato che l'età tra gli 80 e gli 85 anni è un periodo di transizione in cui possono aver luogo consistenti cambiamenti di salute. HAT può essere utile sia per identificare deviazioni dalle traiettorie individuali di salute sia per determinare i bisogni della popolazione dal punto di vista medico, riabilitativo o sociale. Le curve geriatriche di riferimento per la salute, simili a quelle pediatriche, potrebbero facilitare la valutazione dello stato di salute degli anziani.

Parole chiave: stato cognitivo, velocità di cammino, multimorbidità, performance fisica, disabilità, trend temporali, stato di salute, health assessment, curve geriatriche.

LIST OF SCIENTIFIC PAPERS

- I. Angleman S, **Santoni G**, von Strauss E, Fratiglioni L. Temporal Trends of Functional Dependence and Survival Among Older Adults From 1991 to 2010 in Sweden: Toward a Healthier Aging. *Journals of Gerontology Series A: Biological Sciences and Medical Sciences*, 2015 Jun;70(6):746-52. doi: 10.1093/gerona/glu206. Epub 2014 Nov 13
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- IV. **Santoni G**, Calderon Larrañaga A, Orsini O, Fratiglioni L. Geriatric health charts for individual assessment and care needs prediction. *Manuscript*.

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LIST OF ABBREVIATIONS

ADL	Activities of daily living
CD	Chronic diseases
CI	Confidence interval
COOP	Charts of primary care practice
CORE-CARE	Comprehensive assessment and referral evaluation
DFLE	Disability free life expectancy
DSM-IV	Diagnostic and Statistical Manual of Mental Disorders, fourth edition
EuroQol	European Quality of Life Scale
HAT	Health Assessment Tool
IADL	Instrumental activities of daily living
ICD-10	10th revision of the International Statistical Classification of Diseases and Related Health Problems
KP	Kungsholmen Project
LE	Life expectancy
MICE	Multivariate imputation chained equation
MMSE	Mini-Mental State Examination
MPI	Multidimensional Prognostic Index
NA	Not available
NRm	Nominal response model
OARS	Older Americans Resources and Services multidimensional functional assessment
OECD	Organization for Economic Co-operation and Development
OR	Odds ratios
PAMIE	Physical and mental-impairment of function evaluation
QL	Quality of life
QWB	Quality of Well-being Scale
ROC	Receiver operating characteristic
RR	Relative risk
SELF	Self-evaluation of life function scale
SF-36	Short Form-36

SNAC-K	Swedish National study on Aging and Care
SRH	Self-rated health
TCC	Test characteristic curve
TIF	Test information function
TLE	Total life expectancy

1 INTRODUCTION

1.1 WHY AGING RESEARCH

1.1.1 Demographic transition

During the last half century, the world has experienced a demographic transition that is still ongoing: the global population is aging, and older adults are getting older.[1] The percentage of the global population aged over 60 years increased from 8% in 1950 to 12% in 2015.

Europe and Sweden experienced even higher rates of increase: 12% in Europe and 10% in Sweden (Figure 1 left). At the same time (between 1950 and 2015), the proportion of the global population aged 80 years old and older increased at a rate of 0.3% every decade. In Europe and Sweden, the rate was more than 0.7% per decade (Figure 1, left).

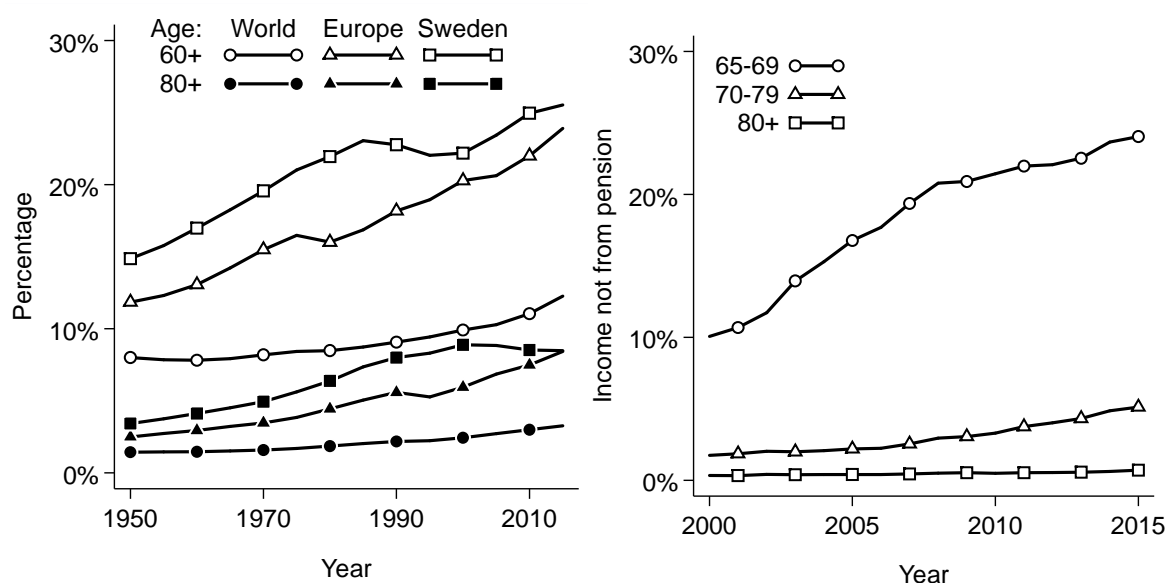


Figure 1. Left: percentage of people aged 60 and over (white symbols) or 80 and over (black symbols) in the world (circles), Europe (triangles), and Sweden (squares). Data source: United Nations, Department of Economic and Social Affairs, Population Division (2015). Right: percentage, by age group, of the total income between 2000 and 2015 that is not from pension. Age 65-69 (circles), 70-79 (triangles), and 80 years or older (squares). Source: Statistics Sweden.

The increase in the proportion and the number of people over the age of 60 years is the result of three major factors.[2] First, infant and child mortality rates have declined because public health conditions have improved; second, the fertility rate throughout most of the world and particularly in developed countries has declined; and third, life expectancy at birth and life expectancy at age 60 have both increased. The first two factors contribute to the increase in the proportion of older people in the population, and the third also contributes to the increase in the absolute number of older people.

1.1.2 Living longer: a positive development with some challenges

The positive achievement represented by the increasing number of people who survive beyond age 65 has led to a decrease in the potential support ratio (i.e., the number of working adults aged 15-64 years old per person aged 65 or older in the population) in most of

developed countries. In Sweden between 1960 and 2015, the potential support ratio fell from 5.6 to 3.2.[3] The aging population does not necessarily have to impose a large burden on society. Already, older people are contributing to society at many levels. Moreover, if more people can reach old age in good health, we may avoid or attenuate some of the most pessimistic scenarios, which are characterized by an unsustainable impact of older populations on public health systems.[1, 4] Furthermore, older people with better health are more likely to postpone retirement, alleviating their dependency on younger generations and reducing their need for health and social care services. It is noteworthy that in Sweden since 2000, the income of 65- to 69-year-olds that is derived from work has increased from 10% to 24% (**Figure 1**, right).

The extent to which the growing population of older adults has been able to maintain good cognitive and physical status into and throughout very old age remains uncertain. Better health could be achieved by promoting healthy lifestyles, minimizing health risk behaviors, decreasing vascular burden, and increasing psychosocial support.[5] Although many researchers agree on the factors and types of health support that could contribute to maximizing well-being in the population,[6, 7] there is still uncertainty about the ways those factors work together to influence several health outcomes and the real impact they have at the individual level.

Aging is a life-long process of progressive changes. The functional capacity of biological systems peaks in early adulthood and then progressively declines,[8, 9] but strong evidence indicates that health and functional status in older people are largely determined by lifelong exposures and actions.[10] Decades of research [11-18] have led to three major contributions that also represent the three major challenges in aging research today.

1. **Health in aging is a complex, multidimensional, and dynamic process.** Developing a disease may greatly affect health of an older person, but measures of morbidity alone are insufficient to capture the complexity of health; functioning must also be taken into account. Rather than merely being defined as the absence of diseases, health is a state of social, physical, and psychological well-being that allows people to live actively and in accordance with their needs and preferences. However, our current knowledge about health in aging concerns only single dimensions of health, and interpersonal differences obscure our understanding of intrapersonal changes. Further, little is known about variations in individual health. The assessment of health trajectories can significantly complement the conventional measures of health outcomes by providing information related to how health evolves over time.
2. **Health in aging is linked to multi-domain determinants.** Poor health is not a necessary consequence of surviving to older age. A number of contextual, biographical, and biological drivers lead to important variations in older people's health trajectories, such as exercise, nutrition, social engagement and support, stress levels, occupational experiences, and allostatic mediators. Strong evidence supports the hypothesis that single or aggregated determinants from biomedical, environmental (social and physical), and

psychological domains impact health in old age, but we still lack evidence about the interplay among the domains.

3. **Health in aging is the result of lifelong experiences and exposures.** We have ample evidence that as we age, our health status and risk for diseases are the outcomes of different life events starting at gestation and involving other periods of life, such as childhood, adolescence, and adulthood. The life-course approach has become well-established in social sciences and epidemiology, but knowledge on the interrelationships between social and biological factors over the life course is still largely insufficient.

The biological changes that lead to aging are neither linear nor consistent, and their association with chronological age is weak.[19] Some 70-year-olds may enjoy good physical and mental functioning, whereas others may be frail or require significant support in their daily life. Moreover, older people with similar health status at a certain time may later have different trajectories, and their needs will vary according to which trajectory they follow. Consequently, the health of the older population should be viewed as a continuum and should ideally be investigated longitudinally.[2] This intrapersonal and interpersonal variability in health is in part due to the randomness of many of the mechanisms of aging, but it is also partially attributable to the influences of environmental, behavioral, and biological factors. Some studies have suggested that whereas the level of physical and cognitive function reached in adulthood is in part genetically influenced, changes in both dimensions may be mediated by the social and physical environments and related health behaviors.[19-23]

In conclusion, if we want to achieve not only longer but also healthier lives, we need to increase our knowledge about health, health determinants, and individual health changes. To this end, it is important to explore health trajectories in aging in order to identify people at higher risk of severe negative health outcomes and predict care services utilization. We think that the starting point is to assess all dimensions of older adults' health, going beyond the clinical diagnosis of diseases and tracing the changes in those different dimensions of health with a composite and comprehensive assessment tool.

1.2 TIME TRENDS OF HEALTH AND DISABILITY

One of the main aims of epidemiological studies is to provide information on past, current, and future trends in population health. Such information can be used by policy makers to better develop and plan prevention and care policies aimed at improving the health and well-being of older adults.

An example of the contribution of epidemiological research to public health and of the use of epidemiological evidence to implement preventive actions is the recent trend in dementia prevalence. In recent years, several studies have reported that the prevalence of dementia has declined,[16, 24] and researchers have also found positive results regarding trends in dementia incidence.[16, 25] The positive changes in dementia trends have been achieved by increasing educational levels in the population, promoting beneficial lifestyle factors (physical activity, social engagement), and reducing excessive alcohol consumption and

smoking.[26] The positive changes are even more striking if we consider that the prevalence of multimorbidity (the presence of two or more chronic diseases) appears to have increased over the last decade (2001-2011).[27, 28]

For society and for individuals, a person's ability to be functionally independent is one of the most valued elements of health. From a sociological point of view, the need for informal care (care provided by relatives or friends) impacts not only the person who is receiving care but also the one who is providing care, as providing care requires both time and energy. Formal care (care provided by the state or private companies) requires careful planning from governmental agencies to allocate sufficient resources to provide cost-effective, high quality care.

The amount of care a person needs depends on the severity of their disability. The more severe the disability, the higher the cost of care and the more time and energy needed for the care. Severe disability is often measured as the number of activities of daily living (ADL) [29] that a person is unable to perform independently. Although functioning and disability can be measured with several different scales,[30-32] ADL dependence is the most common measure used in research and clinical settings. The tasks included in ADL, such as feeding and transferring, are less influenced by cultural and environmental factors than those included, for example, in the instrumental ADL (IADL) scale, which measures the ability to live independently in the community.[33] Moreover, ADL are also less functionally demanding than the Nagi scale,[30] which measures four types of physical activity, including pushing/pulling large objects and crouching. Basic ADL include the ability to bathe, eat, dress, use the toilet, and transfer independently and without difficulty. Independence in these tasks is highly valued by people as they age because the tasks represent the minimum functional requirements for maintaining independence in self-care.

Trends in ADL disability between the 1980s and the mid-1990s were consistent across countries and studies. In general, disability in older adults declined during this period in the United States [34-38] and in European countries.[39-41] Schoeni et al. [38] hypothesized that most of the gain in functionality was due to improvement in educational level, a proxy for socioeconomic status. Trends in disability after the mid-1990s have been less consistent,[38, 42-59] potentially because the prevalence of disorders relevant to disability (e.g., diabetes) increased, as did survival after disabling diseases (e.g., stroke).[38] A 2013 study from Denmark reported that the prevalence of physical and cognitive impairment in nonagenarians was lower in 2010 than in 1998,[48] whereas a study from Sweden reported that prevalence of ADL disability increased during the same period.[42] **Table 1** summarizes the literature on time trends in ADL; it includes those studies that covered at least until the first decade of 2000. The table shows considerably inconsistent results. It is important to note that although the studies included in the literature review measured disability with the same instrument (ADL), the formulation of the questions participants were asked, the number and type of activities included, and the method used to determine whether a person had disabilities (needed assistance or not, time frame) differed considerably. These methodological

differences make it difficult to compare results across studies, as removing an item or changing the formulation of a question can affect considerably the results. Most of the studies reported age and sex standardized or adjusted prevalence of disability in the population. However, some studies that reported increases in the prevalence of disability considered only crude results or large age strata; thus, the results could reflect changes in the population age structure more than changes in disability prevalence.[52, 55]

1.2.1 Knowledge gap

Studies of temporal trends are affected by many methodological factors such as study design (survey, population-based study), use of repeated cross-sectional or longitudinal sampling, number of measurement points, intervals between measurements, inclusion criteria (people living in the community vs. people living in an institution), use of proxy interviews, measures used (prevalence or incidence), and the representativeness of the data.[60] In particular, prevalence figures alone may be insufficient in the study of temporal trends. A steady prevalence may either be due to decreased incidence and decreased mortality in those with disability or to an opposite trend in these two measures. In a report from the United States examining the period 1984–2000,[49] a steady prevalence of ADL disability was found to be due to decreased incidence and decreased mortality. It is uncertain whether this is also the case in other countries where a steady prevalence has been reported in recent decades.[39, 48, 51-53] Because prevalence figures are insufficient to completely understand the temporal trends, prevalence, incidence, and mortality data should be reported together.

Table 1. Studies on time trends in ADL that included at least the first decade of the 2000s, ordered according to the main finding: declined (light green), stable (white), or increased (light blue) ADL.

Author, Year	Population	Period	Disability measure	Statistics	Results	Conclusions
Manton, 2008 Manton et al, 2006 [43, 44] USA	N=~25000 Age: 65+ Sex (F): NA All people Survey	1982, 1984, 1989, 1994, 1999, 2004/05	Screen. Seven ADL items, difficulties for 90+ days: bathing, dressing, toileting, transferring, grooming, continence, eating + IADL	Prevalence. Age standardized or stratified.	Decline 1982-2005: -1.5% per year, p<0.05. Decline 1999-2005: -2.2% per year, p<0.05. Decline also for severe disability (ADL alone).	Probably linked to better management of institutionalized people via: assisted living facilities, skilled nurse providing rehabilitation, and home- and community-based waivers.
Schoeni et al. 2008 [45] USA	N= 194973 Age: 70+ Sex (F): NA Non- institutionalized Survey	1982-2005	Self-reported ADL; because of impairment or health problem, not able or assistance in: bathing, dressing, getting around this home, or eating	Prevalence and OR. Age and sex adjusted.	Decline 1983-2005: Average annual rate of decline: 0.06%.	Declines in underlying difficulties and increase in use of assistive technology. Reduction (1997-2004) of diseases associated with disabilities (CVD, vision, and musculoskeletal)
Freedman et al. 2008 [46] USA	N=23229 Age: 75+ Sex (F) :~61% Non- institutionalized Cohort-study	1995-98 1998-00 2000-02 2002-04	Self-reported ADL; because of health or memory problems, any difficulty, can't, or don't do (lasting > three months): bathing or showering, dressing (include shoes and socks), using the toilet (up and down), walking across a room, getting in or out of bed	Prevalence: crude with sample weights; OR +age, sex, proxy adjusted for early- and mid- life influence.	Decline 1995-2004: -1.46% annual change in prevalence, p<0.01. Early-life adjustment: OR=0.99, p<0.05. + mid-life adjustment: OR=0.99, p>0.05. + late-life adjustment: OR=0.97, p<0.01.	Education, mother education, childhood health, and lifetime occupation + improved vision and increase wealth led to decline in ADL prevalence. Increase in number of chronic conditions reduced the gain.
Donald et al. 2010 [47] UK	N=9425 Age: 75+ Sex (F): NA Non- and institutionalized Survey	1998-2008	Elderly At Risk Rating Scale: 20 domains including ADL items washing, dressing, walking	Sex and age standardized prevalence and OR.	Decline in some domains (washing, dressing, nail care) stable in others.	The onset of significant disability in ADL may be delayed by four years.

Table 1. (Continued). Studies on time trends in ADL that included at least the first decade of the 2000s, ordered according to the main finding: declined (light green), stable (white), or increased (light blue) ADL.

Author, Year	Population	Period	Disability measure	Statistics	Results	Conclusions
Christensen et al. 2013 [48] Denmark	N = 3846 Age = 92-95 Sex (F): ~26% All born 1905 and 1915 Cohort study	1998, 2010	ADL, with or without aids able to: get up from a bed, get up from a chair, walk around in the house, go to the toilet.	Mean number of ADL. Total and sex stratified.	Decrease: 0.2 points, p<0.001.	Improvements due to better cognitive functioning and aids. "The success-of-success outweighs the failure-of-success."
Crimmins et al. 2009 [49] USA	N=30460 Age: 70+ Sex (F): NA Non-institutionalized Two longitudinal surveys	1984-2000	ADL, unable to perform: bathing, dressing, toileting, getting in/out of bed or chair, eating.	Transition probabilities with logistic regression.	Delayed onset. Decline in incidence. Increased recovery. Increased disability-free life expectancy.	LE unchanged; disability-free LE increased. Decreased incidence.
Zimmer et al. 2015 [50] China	N=31263 Age = 65+ Sex (F): 57% Two longitudinal samples	2002, 2008	Katz ADL, able without assistive devices: bathing, dressing, toileting, getting up from a bed/chair, eating.	Total life expectancy (TLE). Disability free life expectancy (DFLE) DFLE/TLE.	Decline in mortality rates and disability prevalence. Increase in TLE, DFLE, and DFLE/TLE, especially for women.	Compression of morbidity. Positive effect of socioeconomic changes in China.
Van Gool et al. 2011 [51] Netherland	N=66539 Age = 55-84 Sex (F): 53% Non-institutionalized Five surveys	1990-2007	Difficulties in: climbing stairs, walking, dressing. From OECD or/and SF-36.	Survey-specific weighted prevalence. Meta-analysis of OR.	Stable except increase in moderate OECD limitations in stair climbing and getting dressed.	Not declining prevalence in the period. The decline in people living in institution promoted in the 1980s can be a cause.

Table 1. (Continued). Studies on time trends in ADL that included at least the first decade of the 2000s, ordered according to the main finding: declined (light green), stable (white), or increased (light blue) ADL.

Author, Year	Population	Period	Disability measure	Statistics	Results	Conclusions
Hashimoto et al. 2010 [52] Japan	N=~3750000 Age = 0+ Sex (F): NA Random: population + hospital patients. Survey	1995, 2004	Self-reported. “Is your daily life affected by health problems?”, if yes ask ADL: bathing, dressing, rising, eating, going out + other activities.	Prevalence: sex and age specific (0-64, 65+).	Age 65+: Increased in women. Stable in men.	Increase in the duration of life lived with light or moderate disability during the period. Note: no age standardization in the large age groups.
Lin et al. 2012 [53] USA	N=218 955 Age = 70+ Sex (F): 60% Non-institutionalized Survey	1982-2009	Self-reported ADL, because of impairment or health problem, need assistance in any: bathing, dressing, getting around this home, eating.	Prevalence and fitted probabilities: age adjusted and not. Period, cohort, and age analyses.	Period: stable 1982-2009. Cohort: increase 1885-1940 but not significant. (Adjusted).	Younger cohorts are more disabled than older ones. Not linked to obesity or socioeconomic factors, only age. Note: cohort analysis: age ranges in each cohorts are quite different.
Parker et al. 2008 [42] Sweden	N=~3000 per year Age: 65-84 Sex (F): NA Random sample population Survey	1980-2005	Self-reported ADL, not able or assistance in any: bathing or showering, dressing, personal hygiene, getting up and going to bed, eating.	Prevalence: age standardized.	Decline 1980-96: -1% per year, p<0.001. Increase 1996-2005: Men +0.47% per year, p<0.05; women +0.89% per year, p>0.05).	Later increase maybe due increase in prevalence of CVD between 1980s and late 1990s.
Freedman et al. 2016 [54] USA	N=43720 Age = 65+ Sex (F): NA All people. longitudinal studies	1982, 2004, 2011	ADL – IADL, one or more: bathing, dressing, getting to the bathroom or using the toilet, walking around inside, getting in/out of bed, getting in/out of chair, eating, going outside + IADL.	Prevalence and remaining years lived with disability.	Decreased 1982-04; increased 2004-11 especially for women. Decrease % of expected years lived without disability in men (from 78 to 81%), stable in women (70%).	Mortality rate and postponement of disability onset can play an important role. These are the elements that explain the increasing gap between men and women.

Table 1. (Continued). Studies on time trends in ADL that included at least the first decade of the 2000s, ordered according to the main finding: declined (light green), stable (white), or increased (light blue) ADL.

Author, Year	Population	Period	Disability measure	Statistics	Results	Conclusions
Fuller-Thomson et al. 2009 [55] USA	N=>2000000 Age = 65+ Sex (F): NA Population non and institutionalized Survey	2000, 2001, 2002, 2003, 2004, 2005	Self-reported ADL; physical, mental, or emotional condition lasting six months or more that made difficult to: bathe, dress, walk inside the home.	Crude prevalence.	Increased 2000-05. Annual increase: 0.16%, p<0.05 in the community; 0.76%, p>0.05 community + institutionalized.	Increasing rates might be due to changes in the age structure of the population with a higher proportion of 80+ in 2005. Note: estimates are crude.
Yu et al. 2016 [56] China	N=54808 Age = 65+ Sex (F): 64% Non-institutionalized Cohort study	2001-12	ADL, unable to perform (1,2,3): bathing, dressing, toileting, getting from a bed to chair, grooming, walking across a small room, eating	Predicted probabilities. Age, period, cohort adjusted + other variables.	Increase 2001-2003: significant both adjusted and unadjusted. No cohort effect.	Due to decreased mortality with increased number of chronic diseases; growing long-term care waiting list (more people in the community than in institution).
Sjölund et al. 2014 [57] Sweden	N=709 Age = 78+ Sex (F): ~59% Non and institutionalized Two cohort studies	1995-98, 2001-03	Katz ADL: bathing, dressing, going to the toilet, transferring, eating, continence	Logistic regression (adjusted), Kaplan Meier.	OR disability in later period = 1.82 (1.0-3.10). No difference in mortality.	Higher prevalence of disability in the second period, mostly due to increase in prevalence of disability in women.
Steiber 2015 [58] Germany	N=5536 Age = 50-90 Sex (F): 52% Non-institutionalized Survey	2006, 2012	SF-12 and symbol-digit test	Repeated cross-sectional analyses of mean.	Decline in physical health only in those 50-64 years old. Improved cognitive functioning.	Diverging trends in the level of functioning maybe due to longer time in the work force and less physical activity.

ADL = Activity of daily living; LE = Life Expectancy; NA = Not Available; OECD = Organization for Economic Co-operation and Development

1.3 HEALTH AND AGING

1.3.1 What is health in older age?

Because health frequently declines with age, aging is often viewed as a sort of disease that everyone will eventually contract.[61] However, clearly the basic characteristics of aging make it distinct from disease. Aging is universal, intrinsic, progressive, and deleterious in nature,[62] a combination of characteristics that is not typical of any disease.

Although every human ages, the older population is extremely heterogeneous.[63-65] Such vast variation in health status of older adults suggests that multiple genetic and contextual factors are relevant to longevity, which can be achieved through a variety of pathways.[6] Health is a dynamic and multidimensional process, and this is especially evident in aging, in which health changes occur more frequently and rapidly as people grow older. Morbidity, physical and cognitive impairment, and disability are fundamental indicators of health in the older population.[66, 67] Although distinct from each other, these indicators are highly interrelated.[19, 67-69]

1.3.2 Indicators of health

According to the most recent aging theories, specific diseases are not the driving forces in aging; instead, aging itself is one of the determinants of body failure.[70-72] As people age, they will progressively experience changes in molecular structure and eventually failure in several organ systems. As we get older, multimorbidity and/or functional limitations and disabilities become very common, and the variation in health status increases.[73] For these reasons, researchers and clinicians agree that one indicator of health is not sufficient to capture the health complexity of older adults.[74, 75] If we exclude perceived health and well-being, most of the current indexes that measure the general health status of older adults include (**Table 2**): physical and cognitive functioning, morbidity, and disability.[76]

Physical functioning

Objective measures of physical functioning are critical indicators of the health status of older adults.[77] Good physical functioning is a prerequisite for carrying out basic activities of daily living, and its deterioration is probably the first sign in the pathway to disability.[78] Impaired functional mobility is an important predictor of disability in old age,[79-86] even in high-functioning older adults.[87] Moreover, physical performance, either at midlife or later, predicts both survival,[88] cognitive decline, and dementia.[89, 90]

One of the different measures of physical functioning, gait speed is increasingly used in research, as it is a good predictor of subsequent adverse outcomes,[91-97] such as death, hospitalization/institutionalization, and decline in mobility. On average, preferred walking speed; i.e., the speed at which a person choose to walk, is almost constant through adulthood and starts to decline around age sixty both in men and women. Whereas other measures of physical functioning, as grip strength, are strongly correlated with a person's strength, usual gait speed requires only a minimal amount of strength.[98] Nonetheless, walking speed has

been termed as the “sixth vital sign” [77] and the almost “perfect measure” of physical functioning because it is reliable, sensitive, and specific. Walking speed per se is not an indicator of a specific health problem, but it is a general indicator of several negative factors. Lastly, walking speed is a simple measure. No special equipment is needed to test it, walking speed tests are quick to perform, and test of walking speed are generally safer than other functional tests.

Cognitive functioning

Cognitive decline is one of the typical aging phenotypes and measures of cognitive decline can therefore contribute to better capturing the complexity of health in the older population. Cognitive functioning can be assessed with extensive cognitive batteries or with global measures of cognition. The Mini-Mental State Examination (MMSE) is a global measure of cognition,[99] commonly used as a screening tool for cognitive impairment and dementia. Although there is a multifaceted relationship between cognitive and physical functioning,[100, 101] MMSE scores seem to be associated with longitudinal changes in grip strength [100] and hence to be a different measure of the same process.

Morbidity

During aging, chronic diseases (e.g., cardiovascular disease and dementia) become increasingly common and often lead to functional dependency, poor quality of life, intense health service use, and mortality.[102] Seven out of 10 older adults have chronic multimorbidity,[103] an accumulation of multiple chronic diseases. The impact of multimorbidity is higher than the sum of the effects of individual diseases.[104, 105] Multimorbidity enhances the detrimental effects of individual diseases [69] and is the main driver of disability and frailty; it drives disability and frailty more than any single disease.[106] A large proportion of people have steady levels of health throughout older age without any multimorbidity. Others cope well with multimorbidity and do not develop disability, whereas still others with multimorbidity deteriorate and become disabled and/or die early.[107]

Severe and mild disability

Physical functioning is an important component of older adults’ health that can also help better define their need for social care and rehabilitation. Declines in functioning can be captured by considering disability in ADL (severe disability) and IADL (mild disability). Individual-level ADL and IADL evolve over time following a no-decline, moderate-decline, or sharp-decline course, depending on the underlying causes.[108, 109] Decline in physical and cognitive function after age 65 is a strong predictor of late-life disability,[108, 110] and disability is related to negative health outcomes such as reduced quality of life and mortality.[111]

This short review on physical and cognitive functioning, morbidity, and mild and severe disability shows that they are indicators of reduced health in older adulthood. Each one contributes differently to the measurement of health in older age. Some are more sensitive to

changes in younger older adulthood, and others are more useful in characterizing health in very old people. Each of these five measures provides valuable information on a person's health, and they complement each other by providing different information on a person's health needs.

1.3.3 Measuring health

Objective measurement of something as complex as health in older people could have several beneficial applications. As we age, it becomes critical to monitor changes in health to capture deviations from normal ranges early. Public health initiatives to improve older people's health should be based on individuals' health trajectories, since different points in the trajectory will require different responses from health care systems. During the period of life in which health is usually good and stable, public health actions should be aimed at promoting healthy behaviors, preventing diseases, and detecting chronic conditions or physical decline early. In the stage of life where health starts to decline, improvements can be achieved by removing barriers that limit participation and by finding strategies that reverse or slow the decline in capacities. Finally, when the loss of good health starts to be significant, public actions should support interventions to compensate for the loss of capacity and ultimately provide palliative care.[2] A prerequisite for this public-health framework for healthy aging is the ability to measure individual health status and trace health status trajectories.

Measuring health in older adults is not an easy task, although it is essential in order to identify health determinants and care needs. Health can be considered a latent measure that cannot be measured directly but can be derived from observable variables. Much effort has been devoted to capturing the complexity and variability of health by developing comprehensive instruments. Many of these have been developed for specific groups of people (e.g., chronically ill patients), for specific clinical settings, or for nursing homes (**Table 2**).[76, 112] Furthermore, other concepts such as successful aging [113] and frailty [114] have been developed to characterize the healthier or sicker parts of the older population, and still others to predict short or long-term survival (i.e., the multidimensional prognostic index [MPI]).[115] Finally, there are several indexes (**Table 2**), such as the short-form surveys SF-36 and SF-12,[31, 116] that have been mostly used for research purposes. Both instruments measure overall physical and mental health and rely on self-reported measures of health and well-being. Several of the indexes already available in the literature (**Table 2**) include objective and subjective measures of health (perceived health, emotional health, and health perception). Subjective measures might improve our ability to capture the characteristic complexity of health in older age. However, their inclusion may preclude future research on the association between objective measures and subjective measures and on assessing what determinants of health are better suited to improve either objective or subjective health. Other indexes include indicators that may simultaneously be determinants and consequence of a decline in health status (i.e., financial or social factors, symptoms, mood).

Table 2. Scales and questionnaires commonly used to asses health in older adults.[76]

Index	Settings	Dimensions	Restrictions
Physical and mental-impairment of function evaluation (PAMIE)	Clinical	Physical, psychological, social disability	Chronically ill Institutionalized
Charts of primary care practice (COOP)	Primary care	Self-rated health, functioning, social support, feelings	None
Duke health profile (The DUKE)	Primary care	Physical, mental, social, perceived health, self-esteem	None
Older Americans Resources and Services multidimensional functional assessment (OARS)	Research	Functional status, social and financial resources, service use	None
Comprehensive assessment and referral evaluation (CORE-CARE)	Service	Psychiatric, medical, nutritional, financial, and social problems	Living in the community
Self-evaluation of life function scale (SELF)	Research	Physical, psychological, social functioning	People aged 60+
McMaster health index	Service evaluation, clinical research	Physical, emotional, social function	Living in the community
Quality of Life Index (QL Index)	Clinical	Well-being	Terminally ill
Nottingham health profile	Primary care	Physical, social, emotional health	None
Short Form-36 (SF-36)	Population surveys	Eight dimensions including physical functioning, pain, emotional problems, and health perceptions	None
Quality of Well-being Scale (QWB)	Clinical	Mobility, physical and social activity, symptoms	None
European Quality of Life Scale (EuroQol)	Policy research	Mobility, self-care, activity, pain, mood	None

1.3.4 Knowledge gap

Studies on health in older people have mostly focused on defining a “dream scenario” of healthy aging rather than on constructing a practical definition based on objective and subjective measures of health. A person’s health can be defined in several ways: as the absence or presence of diseases (morbidity, often described in terms of medical diagnoses); as the ability to perform daily activities (physical and cognitive functioning, including a range of alterations from simple impairment to disability), and as the subjective perception of one’s own health. Most of the literature to date has taken into account only single dimensions of

health, and if complex dimensions were considered, they usually included self-rated health or subjective measures of health. To study inter- and intra-individual differences and monitor health changes in the general population of older adults, we need an instrument that is broad, objective, and covers multiple domains. Health changes are continuous and gradual. They result from a process that begins with the development of symptoms related to underlying biological changes and that continues to the onset of disorders and diseases, functional loss and disability, and ultimately death. To capture the vast heterogeneity characteristic of health in older age, the health assessment instrument should be able to measure health in people at various points on the spectrum and differentiate between these people.

2 AIMS

2.1 GENERAL AIM

The general aim of this thesis is to evaluate and predict how well people are aging, taking the multi-faceted complexity of their health status into account.

2.2 SPECIFIC AIMS

The specific aims addressed in the four studies are:

1. To verify temporal trends of disability in older Swedish adults between 1991 and 2010, taking into account occurrence of disability, number of years of life lived with disability, and age at onset of disability. (Study I)
2. To describe the four major dimensions of health (physical function, cognitive function, morbidity, and disability) in older adults and to estimate the prevalence of their most frequent patterns of aggregation. (Study II)
3. To develop a health assessment tool (HAT) for older people by using five clinical indicators and to detect age-related variation and individual health trajectories over time. (Study III)
4. To study a novel approach to monitoring changes in older people's health by proposing reference health curves that can help delineate ad-hoc public health and care actions. (Study IV)

3 MATERIAL AND METHODS

3.1 POPULATIONS

The data in this thesis came from the Kungsholmen Project (KP) and the Swedish National study on Aging and Care in Kungsholmen (SNAC-K).

3.1.1 Kungsholmen Project

The KP [117] is a longitudinal, population-based study on aging and dementia started in 1987 by the Stockholm Gerontology Research Center in collaboration with Karolinska Institutet. In October 1987, all people over 75 years who were living in the Kungsholmen district of Stockholm were invited to participate. A total of 1810 people (1810/2368, 76.4%) agreed to participate in the baseline data collection between 1987 and 1989. Participants were then invited to follow-up data collection every three years. A total of five follow-ups are available in the KP. The last one took place between 1999 and 2000, 12 years after baseline data collection.

Data from KP were used for the analysis of disability trends in Study I. Only the last four phases (Phase III, 1991-1993 to Phase VI, 1999-2000) were included because disability status was assessed differently during the previous phases. The KP participants are described in **Figure 2**.

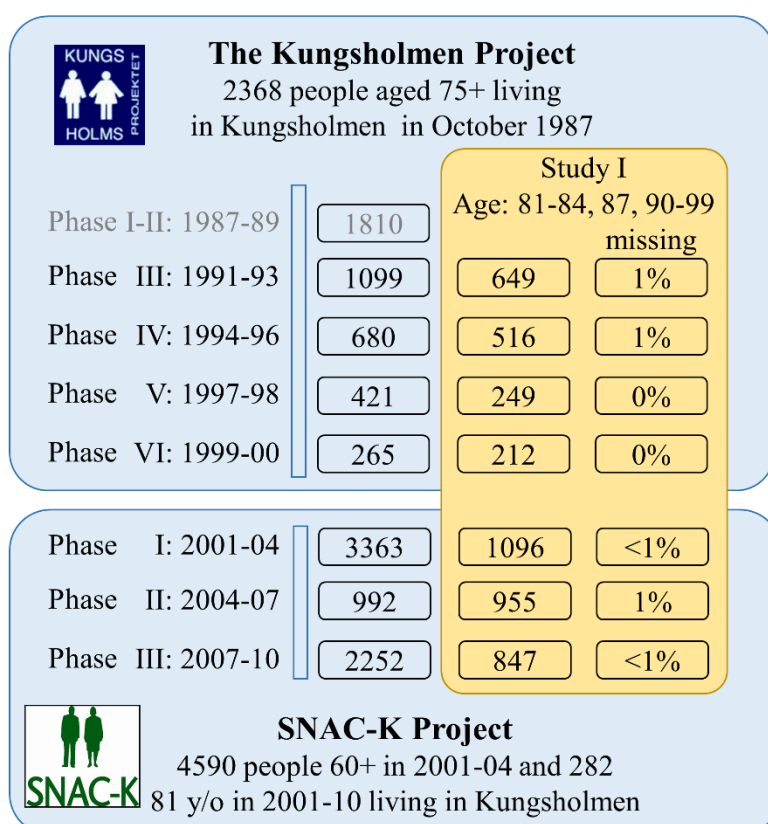


Figure 2. Kungsholmen Project and SNAC-K project study populations, participants, and samples in Study I.

3.1.2 The SNAC-K study

The SNAC-K [118] is a population-based longitudinal study on the aging and health of the general population in central Stockholm.

The SNAC-K study population consists of a random sample of people aged 60+ living either at home or in institutions in the Kungsholmen district of Stockholm between March 2001 and June 2004. The sample was stratified by age cohort and year of assessment. Eleven age-specific cohorts were chosen, with a six-year interval between the younger cohorts (60 to 78 years) and a three-year interval between the older cohorts (78+ years). Of the 4790 eligible people invited to participate, 1227 (1227/4790, 26%) declined to participate and 200 (200/4790, 4%) died before being called, leaving a study population of 3363 (a participation rate of 3363/4790, 70%) (**Figure 3**). In Study I, the new sample of 81-year-olds was included from the population living in Kungsholmen between 2007 and 2010 (**Figure 2**); of the 282 eligible participants, 194 agreed to participate (participation rate 194/282, 69%).

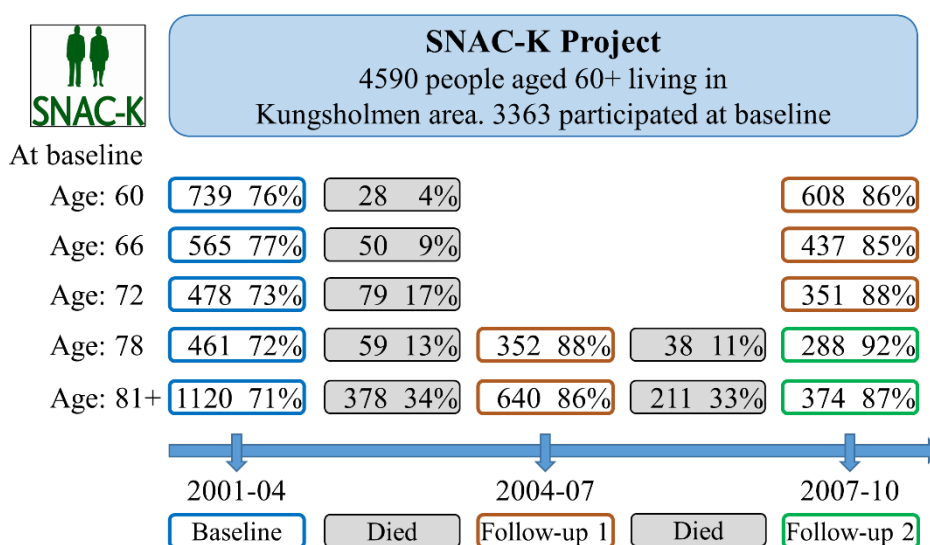


Figure 3. SNAC-K Project study population for Studies II, III, and IV. The figure shows the number of participants at baseline, follow-up 1, and follow-up 2 and the percentage of the people alive and eligible at the time of assessment who participated. The grey boxes report number and percentage of people who participated in the previous assessment but died before the next assessment.

3.2 HEALTH ASSESSMENT

The KP study and the SNAC-K study followed similar protocols for data collection: nurses collected data on personal and family history and doctors conducted a clinical examination of the participants following a structured protocol.

3.2.1 Disability

Activities of Daily Living (Studies I-IV). Severe disability was measured as difficulty with basic ADL (**Table 3**). In KP and in SNAC-K, nurses assessed the ADL ability of the participants using the Katz scale.[119] Five ADL abilities were included in all the studies: bathing, dressing, using the toilet, transferring, and feeding oneself. Continence was excluded as it is a condition more than an ability a person is able to perform.

Table 3 shows the criteria used to determine whether participants had an ADL disability. Participants who reported problems with at least one of the ADL were considered to have disability.

Table 3. Criteria used to determine difficulties in activities of daily living.

ADL item	Difficulty if:
Bathing	Not able to take a bath or shower by themselves.
Dressing	Not able to dress and undress themselves.
Using a toilet*	Not able to use the toilet. Able to use the toilet but need some help (i.e., to get to the toilet or/and on the toilet, or wiping or/and dressing themselves afterward).
Transferring from the bed to a chair	Not able to transfer or need a lot of help. Able to transfer but need some help. Cannot sit up from the bed.
Feeding oneself	Not able to feed self. Able to feed self but needs some help (i.e., to cut meat or open food containers).

ADL = activities of daily living.

* Note: Participants were not considered to have difficulty if they responded that they had difficulty but used a walker or wheelchair to get to the toilet or used a chamber pot that they later emptied by themselves.

Instrumental Activities of Daily Living (Studies II-IV). In SNAC-K, at baseline and at follow-up, moderate disability was measured as difficulty with IADL (**Table 4**). To avoid tasks that may be performed more frequently by one gender in this group of participants (i.e., cooking, light housework, heavy cleaning, and laundry),[120] only four tasks were included in the analyses: grocery shopping, managing money, using the telephone, and using public transportation. People who lived in nursing homes were considered unable to buy food.

3.2.2 Physical functioning (Studies II-IV)

Physical functional status was measured as gait speed. At baseline and follow-up, SNAC-K participants were asked to walk 6 m. However, if the participant reported walking quite slowly or if the interview was performed at a home or institution, the participant was asked to walk 2.4 m. If the participant was unable to walk or attempted unsuccessfully to walk, a value of 0 m/sec was recorded.

3.2.3 Cognitive functioning (Studies II-IV)

Cognitive functional status was assessed with the MMSE [99] at baseline and follow-up in the SNAC-K study. The MMSE is commonly used as a screening test for dementia. It measures global cognitive decline and encompasses basic cognitive domains such as orientation, memory, attention, language, visuospatial functioning, and executive functioning. MMSE scores range from a maximum of 30 (good cognitive status) to a minimum of 0 (poor cognitive status).

Table 4. Criteria used to determine difficulties in instrumental activities of daily living.

IADL item	Difficulty if:
Grocery shopping	Not able to go grocery shopping on their own. Needs food delivered. Goes shopping with someone else.
Managing money	Not able to manage money or needs help for regular transactions.
Using the telephone	Not able to. Able to answer the telephone but not able to make a call (apart from using speed dial numbers).
Using public transportation	Not able to use public transportation. Uses only taxis. Needs help to enter and exit the vehicle. Needs to be transported by ambulance.

IADL = instrumental activities of daily living.

3.2.4 Morbidity (Studies II-IV)

In SNAC-K, physicians assessed the general health status of participants and made clinical diagnoses on the basis of their assessments, laboratory tests, and hospital records. At baseline, they recorded current and past health status, whereas at follow-up they only evaluated current health status.

A team of experts based at the Aging Research Center, Karolinska Institutet and Stockholm University (internists, geriatricians, neurologists, and epidemiologists) worked together to derive guidelines for the definition of chronic diseases to be used in this and other projects. They compiled a list of diseases that met the definition of chronic diseases in the International Classification of Disease revision 10 (ICD-10). After compiling this list and taking the results of previous reports into consideration,[69, 121] the team chose to define a disease or a condition (i.e., the residual disability after an acute disease) as chronic if the disease or condition met one or more of the following criteria: 1) was prolonged in duration; 2) left residual disability; 3) worsened quality of life; or 4) required a long period of care, treatment, or rehabilitation.

Diagnostic criteria were derived from the ICD-10 for all diseases except dementia, which was diagnosed in accordance with the Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSM-IV);[122] diabetes, which was diagnosed on the basis of information from the medical examination, information on treatment for diabetes, and laboratory data on levels of glycated hemoglobin; and depression, which was diagnosed (ICD-10 in Study II and DSM-IV in Studies III and IV) after excluding those who were bereaved or had untreated thyroid, bipolar, or psychotic disorders.

3.3 ADDITIONAL VARIABLES

Age (Study I). The two studies (KP and SNAC-K) had different study designs and the age structures of the sampled population were different. The age categories in Study I were constructed to maximize comparability in age (see **Figure 2**). KP selected participants across a continuous range of ages (in KP 1991-93, participants were aged 77 and over), whereas SNAC-K selected participants in specific age cohorts (i.e., 60, 66, 72, 78, 81, 84, 87, 90, 93, 96, and 99+). The age categories used in Study I were thus largely driven by the SNAC-K age structure. This resulted in three comparable categories: 81-84, 87, and 90-99.

Other measures of **physical functioning (Study IV)** included balance, grip strength, and chair-stands. *Balance* was measured as the time (seconds) a participant could stand on one leg up to 60 seconds. *Grip strength* was measured with a dynamometer and converted to kilograms. The results of the *chair-stand* test were dichotomized; participants were divided into those unable to successfully complete the test and those able to successfully complete the test.

Self-rated health (Study IV) was assessed with the question, “In general, how would you say your health is?” Responses of very good and excellent were considered indicators of very good self-rated health.

Socioeconomic status and lifestyle (Study IV). With the exception of physical activity, the socioeconomic and lifestyle variables were collected during the nurse interview at baseline. Information on physical activity was gathered in a self-administered questionnaire. *Educational level* was dichotomized into low educational level (less than 9 years) and high educational level (9 or more years). *Civil status* was divided into married (including cohabiting), widowed/divorced, and single. *Financial level* was rated as low if the participant was unable to manage unplanned expenses. Participants were divided by *smoking* habits into never, former, and current smokers and by *alcohol consumption* into moderate drinkers (less than four glasses per week for men and less than two glasses per week for women), and never/heavy drinkers (a glass per month or less for men and women; more than five glasses per week for men and more than three glasses per week for women). *Physical activity* was divided into never and light/intense.

Outcomes regarding formal and informal care (Study IV). At baseline and at the three-year follow-up, nurses reported whether the participants needed formal and/or informal care. Formal care is service (household chores), personal care, or medical care provided by the municipality or the county (in this case, Stockholm County), even if the care is provided through a private company. Informal care is service or care provided by relatives, friends, neighbors, or volunteer/non-profit organizations.

For both formal and informal care, the amount of care needed was recorded as hours per weeks and weeks per month. For the analyses, the two measures were combined and the total number of hours per month (calculated as hours per week multiplied by weeks per month) was used in the analysis.

3.3.1 Mortality data (Studies I and III)

Date of death was available both by direct report to the data collection staff (via relatives or institutional staff) and from the Swedish Death Registry until December 1, 2012. Death dates were available for both participants and non-participants, although not for those who moved out of Sweden, or for non-participants who moved out of Kungsholmen.

3.3.2 Inpatient and outpatient registers (Study III and IV)

Inpatient and outpatient registry data were taken from the Stockholm County Council Inpatient Registry for the period 2001 to 2011.

Hospital use. Two outcome variables were computed for each participant: 1) number of hospital admissions in the three years after baseline assessment (data available for 3310 people) and 2) number of hospital admissions in the year after baseline.

Outpatient care use. The outpatient registry specifies not only the date of outpatient visits but also the specialty. We divided these data into primary care visits (codes 100s, paramedical professionals, and 800s, nurses and general practitioners) and specialty visits.

3.4 STATISTICAL ANALYSES

For most of the analyses, we accounted for the sampling design either by stratifying or adjusting by age.

3.4.1 Study I

After merging data from KP and SNAC-K, seven assessments were available for the period 1991 to 2010. Point prevalence in participants was calculated by age category and assessment. Sex-adjusted estimates of prevalence and tests for trends were derived from logistic regression models controlled for sex and assessment period and stratified by age. As a sensitivity analysis on the impact of nonparticipation, the same analysis was repeated on the whole population at each assessment (participants and non-participants). The ADL status of non-participants was imputed through multiple-imputation methods. The age, sex, and date of death of participants and non-participants was used to derive 100 complete datasets.

Cumulative incidence was calculated by age category for the six-year intervals 1991-93 to 1997-98 and 2001-04 to 2007-10. Only participants without any ADL difficulties at the first assessment and who participated in both assessments were included in the analysis.

Cumulative incidence was calculated by dividing the number of incident ADL disability by the number of non-disabled participants at the beginning of each interval.

The change in the odds of dying within three years during the period 1991-2010 by ADL disability status was computed with logistic regression models. Covariates were time of assessment (continuous variable), ADL status, and the interaction term between assessment time and ADL status. All analyses were controlled for sex and age. A model was computed for the overall sample (with mixed effect) and for each of the three age strata (81-84, 87, 90+). For the last assessment in 2007-2010, people with an assessment date after November

30, 2009, were excluded from the analysis because mortality data was complete only up to December 1, 2012.

The sex-adjusted median time lived with and without incident ADL disability was calculated with the Laplace regression [123] for censored data stratified by age group. This analysis included participants in KP Phases III or IV and SNAC-K Phases I or II. At each initial assessment A (any one of the four assessments) participants free from disabilities (green circle in **Figure 4**) were divided into participants with (orange circle) and without ADL disability at the subsequent assessment (B). Participants were then followed for six years starting from the mid-point between assessments A and B (white circle) to verify their vital status.

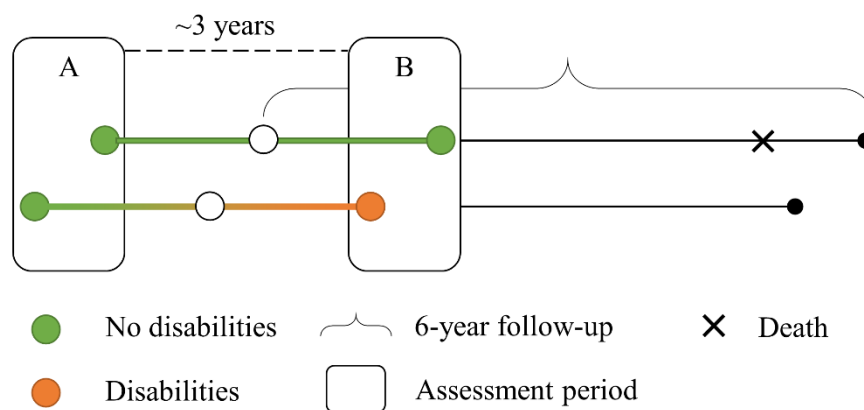


Figure 4. Schematic representation of the analysis of median time lived with and without disabilities.

3.4.2 Study II

Differences in health status between SNAC-K participants and dropouts were analysed with Fisher’s exact test. Risk ratios of death after baseline were derived from multinomial logistic models adjusted by sex, age group (divided into 60-69, 70-79, 80-89, 90+), participation status, and the interaction term between age group and participation status.

The association between age and each health indicator (number of chronic diseases [CD], gait speed, MMSE score, IADL, and ADL) was computed with the logistic quantile regression [124] for bounded outcomes, adjusted by sex. The probability of poor health status across age, adjusted by sex, was instead derived with logistic regression. Several indicators of poor health status were considered: 1+ CD, gait speed < 1.2 m/sec, [125, 126] MMSE < 27, MMSE < 20, 1+ IADL disabilities, and 1+ ADL disabilities. To explore the aggregation of different health indicators, we categorized each health measure into two to three groups. Sixty-three different health combinations (“health states”) were present. To estimate the prevalence of each health state, we ran a linear regression model (adjusted by sex and stratified by age) and plotted the health states with a prevalence of >5%. A sensitivity analysis of the effects of missing values was tested on ten new datasets imputed with multivariate imputation chained equation (MICE).[127]

3.4.3 Study III

The HAT was developed with the nominal response model (NRM). The NRM belongs to the item response theory frame [128] and is equivalent to a generalized mixed model with family multinomial and link logit. The NRM regresses the nominal variables (in our case, the health indicators) against a latent variable (in our case, health status). The variables in the NRM regression are allowed to have different numbers of categories, and no *a priori* order is given to the categories. The performance of all models was evaluated by checking two parameters, difficulty and discrimination, derived from the output of the NRM. Difficulty indicates the level of the latent trait when the probability of a certain answer is 50% (binary variable) or the probability of choosing one category is the same as the probability of choosing the next category (categorical variable). Discrimination measures how fast the probability of a certain answer changes across the latent variable. Higher values of discrimination indicate faster transitions from, for example, answering no to yes to a given question. For a mathematical description, see Section 3.5. Good models have difficulty values that cover the largest range of latent values (the latent variable has a mean of zero and a standard deviation of one) and discrimination values ideally above one.

To obtain the NRM with the best parameters (difficulty and discrimination), we tested different models with health-indicator categories defined in different ways in each model (**Table 5**). Most of the cut-offs chosen for the categories were derived from the literature.

Table 5. Categorizations of the health indicators tested in the nominal response models.

Variable	Categories			
ADL	0	1+		
IADL	0	1+		
ADL+IADL	0	1	2	3+
MMSE	30-27	26-24	23-0	
	30-27	26-20	19-0	
	30-29	28-20	19-0	
	30	29-28	27-20	19-0
	30	29	28-20	19-0
Gait speed	≥ 1.0	1.0 - ≥ 0.4	< 0.4	
	≥ 1.2	1.2 - ≥ 0.8	< 0.8	
	≥ 1.2	1.2 - ≥ 0.4	< 0.4	
	≥ 1.5	1.5 - ≥ 1.0	1.0 - ≥ 0.4	< 0.4
	≥ 1.5	1.5 - ≥ 1.0	1.0 - ≥ 0.6	< 0.6
Chronic diseases	0	1	2+	
	0	1-2	3+	
	0	1+		
	0-1	2	3+	
	0-1	2+		
	0-2	3+		

ADL = activities of daily living; IADL = instrumental activities of daily living; MMSE = Mini-Mental State Examination.

Each model's internal consistency was verified by running the model on ten samples (N=3363) drawn randomly with replacement from the study population. Three hundred models were tested; the final model was chosen on the basis of *a priori* criteria reported in **Table 6**.

Table 6. *A priori* criteria and actions performed to select the final model.

A priori criteria	Actions performed
1. Difficulty values for variables with two or more cutoffs in the expected order.	Removed models with unordered difficulty levels in at least one of the samples.
2. Difficulty levels as evenly spread across the latent variable trait as possible. 3. High discrimination among people of similar levels of health.	a) Calculate the distances between the different difficulty levels in a model. b) Keep models for which, in all samples, the mean distance, the minimum distance, and the standard deviation of the distances are greater than the respective mean of all models. c) Keep models with at least 30% of the difficulty values below zero (mean level of latent trait).
4. High precision over a large range of the latent trait.	Keep models with the largest total area of the test information function (TIF), largest area per unit height of the TIF, or largest health range for TIF above or equal to one.

Health Assessment Tool. Difficulty and discrimination values were used to compute the test characteristic curve (TCC); that is, the expected test score. HAT scores were derived from the linear regression of TCC with the variables used in the final NRM. To account for the high discrimination power of both IADL and ADL, the linear regression was stratified by having no IADL or ADL impairment, at least one IADL impairment, and at least one ADL impairment. The coefficients of the three regressions were used to derive the HAT scores. We tested for interactions between the variables and included those with the largest effects in the model.

We reported the median and inter quantile range per unit of HAT score for each health indicator in HAT. The reliability of HAT was checked by comparing the sex-adjusted distribution of HAT score at baseline with the corresponding values at the three-year and six-year follow-ups. Cross-sectional change in HAT scores by age and stratified by sex were computed with a linear quantile regression model; longitudinal changes (changes over six years) by age and adjusted for sex were computed with a linear quantile mixed-effect model.[126] Finally, the ability of HAT to accurately predict death in the five years after baseline and two or more hospital admissions (among community-dwelling people) in the year after baseline were determined by computing the area under the receiver-operating characteristics (ROC) curve.

3.4.4 Study IV

To validate the HAT score, we assessed the association between HAT score above the age- and sex-specific median and self-rated health and physical tests not included in the index (grip test, balance test, and chair-stand test) with logistic regression. In this analysis, the continuous variables gait strength and balance were transformed into z-scores to facilitate comparison. Chair-stand test results were dichotomized into able to rise five times from a chair without the help of hands (test passed) and not able to rise five times or used hands (test not passed). Self-rated health was dichotomized into poor, fair, or good health and very good or excellent health. The analysis was adjusted by socioeconomic status (education, financial level, and civil status) and lifestyle factors (smoking habits, alcohol consumption, and physical activity). Missing covariate values were imputed with MICE,[127] creating 50 new datasets. We included all the variables from the logistic model plus age at death and institutionalization status. The imputation was stratified by sex, mortality status during 13 years of follow-up, and outcome. A total of 1000 people (32%) had one or more missing covariate value.

The ability of HAT to predict several negative health outcomes in the three years after baseline was compared to that of morbidity status (i.e., number of chronic diseases) and disability measured as total number of ADL and IADL impairments. The predictive ability of each measure was estimated by computing the area under the ROC curve and their difference was tested to evaluate whether HAT had better predictive ability. The negative health outcomes considered were at least one hospital admission, more than ten primary care visits (median value), more than five specialty care visits (median value), and receiving formal or informal care. Only people living in the community at baseline were included in the sample because people living in institutions receive most of the care in the institution where they reside.

A flowchart, composed of three subgroups, was created to compute HAT scores for any person. Each flowchart subgroup represents one of the regression models between the TCC and the health indicators included in HAT and is constructed to take the interaction terms present in the models into consideration.

Finally, the change in the sex-specific reference curves of HAT by age were derived with logistic quantile regression. Seven percentiles were computed for each sex: 5th, 10th, 25th, 50th, 75th, 90th, and 95th. The computation of HAT score for any person was facilitated by the online HAT we have developed; upon entering a person's sex, age, and the values of their health indicators, the online HAT computes the score and plots the person's score and percentile on the reference curves (showing how the person's data compares with that of the SNAC-K population at baseline).

All statistical analyses (Studies I-IV) were performed using Stata[®] version 13 or 14 (StataCorp, TX, USA).

3.5 MATHEMATICAL FORMULATION

Difficulty and discrimination parameters

Binary items

Let us consider the IRT case with only binary indicator variables (or items). The logistic regression model $\text{logit}(p) = \beta_0 + \beta_1\theta$ can be rewritten as $\text{logit}(p) = a(\theta - b)$ where $a = \beta_1$ is the discrimination parameter and $b = -\beta_0/\beta_1$ is the difficulty parameter, θ is the latent variable, and p is the item characteristic function. The probability function is equal to $p = 1/[1 + e^{-a(\theta - b)}]$. Note that if $\theta = b$; i.e., the difficulty value, the probability p is equal to 50% (**Figure 5a**). The first derivative of the probability function with respect to θ is

$$\frac{\partial}{\partial\theta} p(\theta) = \frac{ae^{-a(\theta-b)}}{[1 + e^{-a(\theta-b)}]^2}$$

for $\theta = b$, the derivate is equal to

$$\frac{\partial}{\partial\theta} p(b) = \frac{a}{4}$$

Hence the discrimination parameter a is equal to four times the tangent to the probability curve for probability equal 50% (**Figure 5a**).

Categorical items

Consider a categorical item with K categories ($k = 0, 1, \dots, K$), base category 0. The multinomial logistic regression for the k th category is

$$\text{logit}(p_k) = \ln \frac{P_{k-1}(\theta)}{P_0(\theta)} = \beta_{0k} + \beta_{1k}\theta,$$

where θ is the latent trait. For two categories k and $k-1$ the multinomial logistic regression can be written as:

$$\left\{ \begin{array}{l} \ln \frac{P_{k-1}(\theta)}{P_0(\theta)} = \beta_{0k-1} + \beta_{1k-1}\theta \\ \ln \frac{P_k(\theta)}{P_0(\theta)} = \beta_{0k} + \beta_{1k}\theta \end{array} \right.$$

Solving for $P_0(\theta)$ and rearranging we obtain:

$$\left\{ \begin{array}{l} P_0(\theta) = \frac{P_{k-1}(\theta)}{e^{\beta_{0k-1} + \beta_{1k-1}\theta}} \\ \ln \frac{P_k(\theta)}{P_{k-1}(\theta)} = a_k(\theta - b_k) \end{array} \right.$$

Where the difficulty parameter $b_k = -(\beta_{0k} - \beta_{0k-1})/(\beta_{1k} - \beta_{1k-1})$, and the discrimination parameter $a_k = \beta_{1k} - \beta_{1k-1}$. If $\theta = b$; i.e., the difficulty value, $P_k(b) = P_{k-1}(b)$ and the two probability curves intersect (**Figure 5b**). The discrimination parameter

a_k measures the total angle between the two categories (**Figure 5b**). Note that the difficulty item parameter for category 1 is $b = -\beta_{01}/\beta_{11}$. If covariates x_j are present b_k is equal to:

$$b_k = -\frac{\beta_{0k} + \beta_{2k}x_2 + \dots + \beta_{nk}x_n - (\beta_{0k-1} + \beta_{2k-1}x_2 + \dots + \beta_{nk-1}x_n)}{\beta_{1k} - \beta_{1k-1}}$$

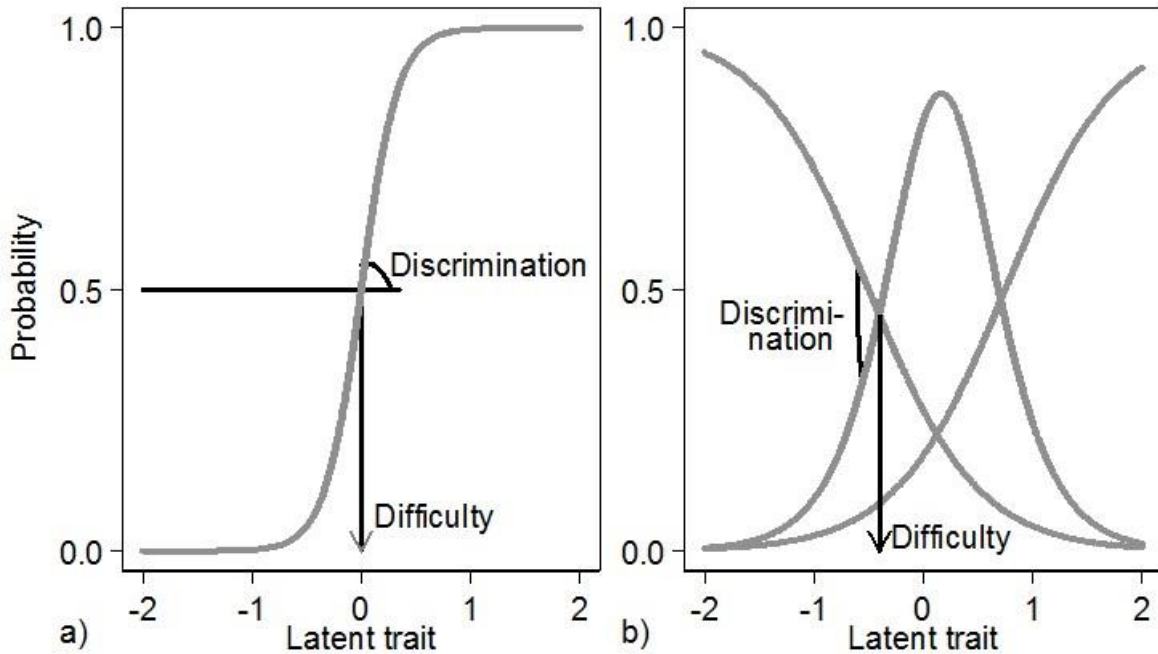


Figure 5. Discrimination and difficulty for a) binary items and b) categorical items.

Information function

From Muraki E. “Information Functions of the Generalized Partial Credit Model,” Applied Psychological Measurement, 1993, pp 351-363.[129]

Consider the case of a categorical item with K categories. The probability of selecting the k th category over the $k-1$ st category in a multicategory IRT governed by the logistic dichotomous response model; that is:

$$P_{jk|k-1}(\theta) = \frac{P_{jk}(\theta)}{P_{jk-1}(\theta) + P_{jk}(\theta)} = \frac{e^{Da_j(\theta-b_{jk})}}{1 + e^{Da_j(\theta-b_{jk})}}$$

Where $k = 2, 3, \dots, K_j$, with K_j is the number of response categories for item j , D is the scaling constant ($D=1.7$), a_j is the slope parameter, and b_{jk} is an item-category parameter.

The equation above can be rewritten for the case of multinomial logistic response as:

$$P_{jk}(\theta) = \frac{e^{Da_{jk}(\theta-b_{jk})}}{\sum_{c=1}^{K_j} e^{Da_{jc}(\theta-b_{jc})}}$$

The item information function is defined:

$$I_j(\theta) = \sum_{k=1}^{K_j} P_{jk}(\theta) \left[-\frac{\partial^2}{\partial \theta^2} \ln P_{jk}(\theta) \right]$$

Note that

$$\frac{\partial}{\partial \theta} \ln P_{jk}(\theta) = \frac{1}{P_{jk}(\theta)} \frac{\partial}{\partial \theta} P_{jk}(\theta)$$

and

$$\frac{\partial^2}{\partial \theta^2} \ln P_{jk}(\theta) = \frac{1}{P_{jk}(\theta)} \frac{\partial^2}{\partial \theta^2} P_{jk}(\theta) - \frac{1}{[P_{jk}(\theta)]^2} \left[\frac{\partial}{\partial \theta} P_{jk}(\theta) \right]^2$$

We have, after some rearranging

$$\frac{\partial}{\partial \theta} \ln P_{jk}(\theta) = D \left(a_{jk} - \sum_{c=1}^{K_j} a_{jc} P_{jc}(\theta) \right)$$

and

$$\frac{\partial^2}{\partial \theta^2} \ln P_{jk}(\theta) = -D^2 \sum_{c=1}^{K_j} a_{jc}^2 P_{jc}(\theta) + D^2 \left(\sum_{c=1}^{K_j} a_{jc} P_{jc}(\theta) \right)^2$$

Substituting the two derivatives in the equation of the item information function:

$$I_j(\theta) = D^2 \sum_{k=1}^{K_j} P_{jk}(\theta) \left[\sum_{c=1}^{K_j} a_{jc}^2 P_{jc}(\theta) - \left(\sum_{c=1}^{K_j} a_{jc} P_{jc}(\theta) \right)^2 \right]$$

For the j th binary variable we obtain:

$$I_j(\theta) = D^2 a_{j2}^2 P_{j1}(\theta) P_{j2}(\theta)$$

Where $1 - P_{j2}(\theta) = P_{j1}(\theta)$ and $a_{j1} = 0$.

For the j th variable with K categories we obtain:

$$I_j(\theta) = D^2 \sum_{i=1}^{K-1} \sum_{l=i}^K (a_{ji} - a_{jl})^2 P_{ji}(\theta) P_{jl}(\theta)$$

Where $\sum_{i=1}^K P_i(\theta) = 1$ and $a_{j1} = 0$. The item information function is a function of the discrimination parameter.

3.6 ETHICAL CONSIDERATIONS

Both the KP and SNAC-K received ethical permissions (**Table 7**) for baseline and follow-ups from the Ethics Committee at Karolinska Institutet and the Regional Ethics Review Board in Stockholm.

Table 7. List of ethical permits for the Kungsholmen Project and the Swedish National study on Aging and Care - Kungsholmen.

Kungsholmen Project	Dnr
Phase I and II – baseline	87:148 and 87:234
Phase III – 1 st follow-up	90:251
Phase IV – 2 nd follow-up	94:122
Phase V – 3 rd follow-up	97-413
Phase VI – 4 th follow-up	99-308
SNAC-K	Dnr
Phase I – baseline	01-114
Phase II – 1 st follow-up 78+	04-929/3
Phase III – 1 st follow-up 60-72, 2 nd follow-up 78+	Ö 26-2007
Registries	Dnr
Death certificate	99:025
Inpatient register data	01:020
SNAC-K permit for register data	2009/595-32

SNAC-K and KP data collection have two main ethical aspects. First, a considerable amount of time is required from the participants to answer interview questions and fill in all the questionnaires. Second, private and sensitive questions are asked. In both projects, participants were informed both in person and in writing about the purpose of the study and the interview process. Participants were informed that they could drop out from the study at any time without an explanation. If a participant was cognitively impaired, informed consent was provided by a proxy (family member or caregiver). Participants received a letter of invitation two weeks before the visit; a nurse telephoned those participants who had agreed to participate to schedule an appointment. A letter with the date and time of the appointment was then sent for confirmation. Participants provided both oral and written consent to participate. The studies followed the ethic principals that are described in the Swedish Council for Research in the Humanities and Social Sciences (Humanistiskt-Samhällsvetenskapliga Forskningsrådet).

Completed questionnaires are kept in locked drawers. Data are entered into the database system by the database group and saved in accordance with the rules for security and privacy. Researchers who want to work with data from either of the two longitudinal studies must receive permission from the PI of the KP and SNAC-K studies. Researchers obtain anonymized data where each patient is identified by a coded number without any reference to the person's name or personal identification number (*personnummer*).

4 RESULTS

4.1 TEMPORAL TRENDS IN FUNCTIONAL DEPENDENCE (STUDY I)

The KP sample had a higher prevalence of women than the SNAC-K sample even when stratified by age. For this reason, all analyses were adjusted by sex. On the other hand, mean age did not differ significantly within age categories for any of the seven assessments.

Prevalence. The sex-adjusted point prevalence of ADL disability remained steady between 1991 and 2010 in each age category (Figure 1 in Study I), although the prevalence in nonagenarians declined significantly when non-participants were included in the analysis (OR reduction of 7% per period, 95% CI 11% – 1%). Across gender, age, and time of assessment, difficulty with bathing/showering was the most prevalent individual ADL dependency item. This was most often followed by difficulty dressing oneself; there were a few exceptions in which either difficulty using the toilet or difficulty feeding oneself was the second most prevalent ADL difficulty. Having difficulty transferring oneself in and out of bed or from a bed to a chair was consistently the least common ADL dependency. Results were similar in a repeated analysis that included both participants and imputed values for non-participants.

Incidence. The sex-adjusted cumulative incidence of ADL disability remained steady in each of the age categories (**Figure 6**) between the two intervals. That is, there were no significant differences between the earlier time interval (1991-93 to 1997-8) and the later one (2001-04 to 2007-2010). However, the point estimates of the cumulative incidence were smaller in the later period (white bars) than in the earlier period (black bars).

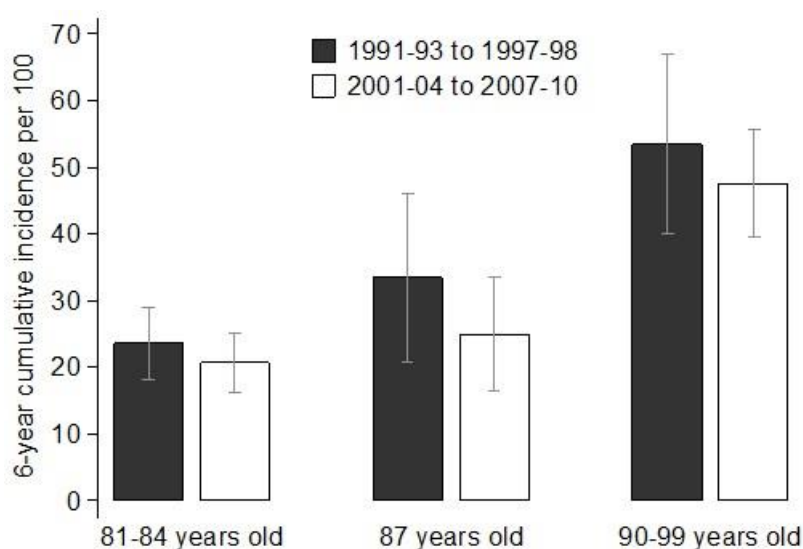


Figure 6. Sex-adjusted six-year cumulative incidence of functional disability per 100 people during two study intervals (1991–1993 to 1997–1998 and 2001–2004 to 2007–2010).

Mortality. The OR of death within three years (**Table 8**) declined between 1991 and 2010 for participants with no disability (OR = 0.93, 95% CI 0.88 – 0.98) and remained steady for participants with disabilities (OR = 1.00, 95% CI 0.94 – 1.07). Results were similar in the

three age subgroups. Sex-adjusted three-year mortality was higher in participants with disabilities than in those without disabilities. Even the youngest group of participants with disabilities had higher three-year mortality than nonagenarians without disabilities (Figure 2 in Study I).

Table 8. Age- and sex-adjusted odds ratios of death in relation to different times of assessment between 1991 and 2010. Results are presented by disability status for the whole sample and each age group. Time of assessment was entered in the logistic regression as a continuous variable with first assessment as reference.

	No disability	Disability
	OR (95% CI)	OR (95% CI)
All	0.93 (0.88; 0.98)	1.00 (0.94; 1.07)
81-84	0.91 (0.86; 0.96)	1.02 (0.91; 1.15)
87	0.95 (0.86; 1.05)	1.11 (0.95; 1.30)
90-99	0.93 (0.87; 1.00)	0.94 (0.85; 1.04)

Median survival time with and without incident disability. The median estimated years lived with ADL disability was steady between the two examined time intervals (**Figure 7**, black bars vs. white bars). In contrast, in participants younger than 90 years, the median estimated survival without ADL disability was longer in the 2000s than in the 1990s (81-84: difference in years 1.3, 95% CI 0.4 – 2.2; 87: difference in years 1.3, 95% CI 0.1 – 2.6.).

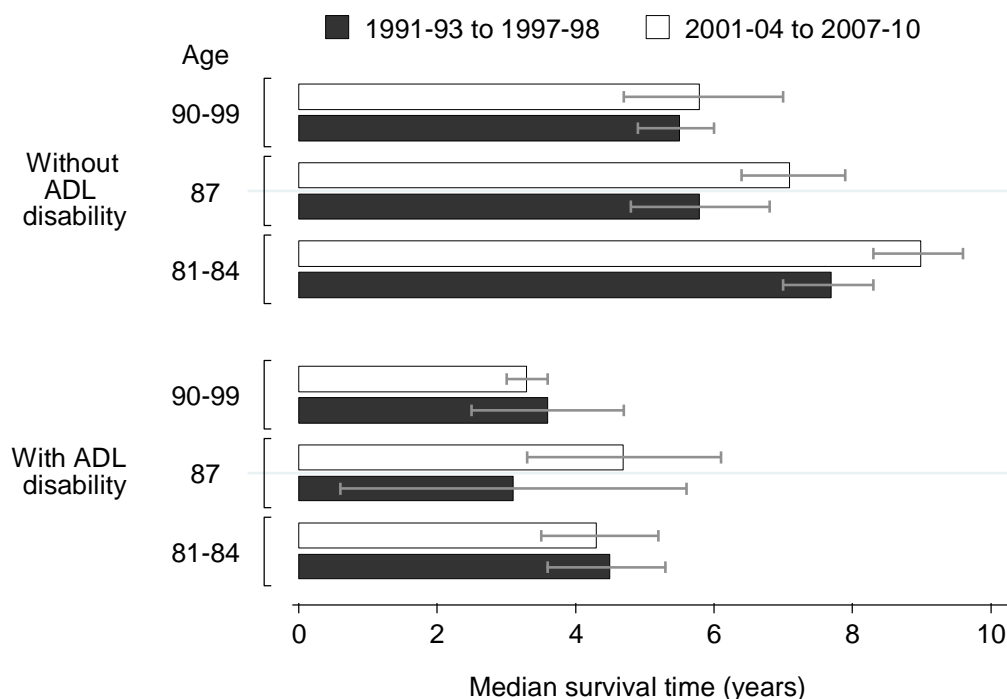


Figure 7. Median estimated time lived either with or without disability during two study intervals (1991–1993 to 1997–1998 and 2001–2004 to 2007–2010).

4.2 DIFFERENCES IN HEALTH STATUS BETWEEN PARTICIPANTS AND NON-PARTICIPANTS IN SNAC-K (STUDIES II-IV)

The SNAC-K participation rate was substantially steady across age and gender (above 70% in almost all assessments); however, women constituted a significantly higher proportion of the sexagenarians than men (60 or 66 years old: 77%, 95% CI 74% – 79%, Table 1 in Study II). Non-participants were more likely than participants to die within two years of the start of the study than after six years (**Figure 8**, white bars), for all age cohorts (grouped by decade) except nonagenarians. Sexagenarian and octogenarian non-participants were also more likely than sexagenarian and octogenarian participants to die between two and six years after the assessment than later on (**Figure 8**, black bars).

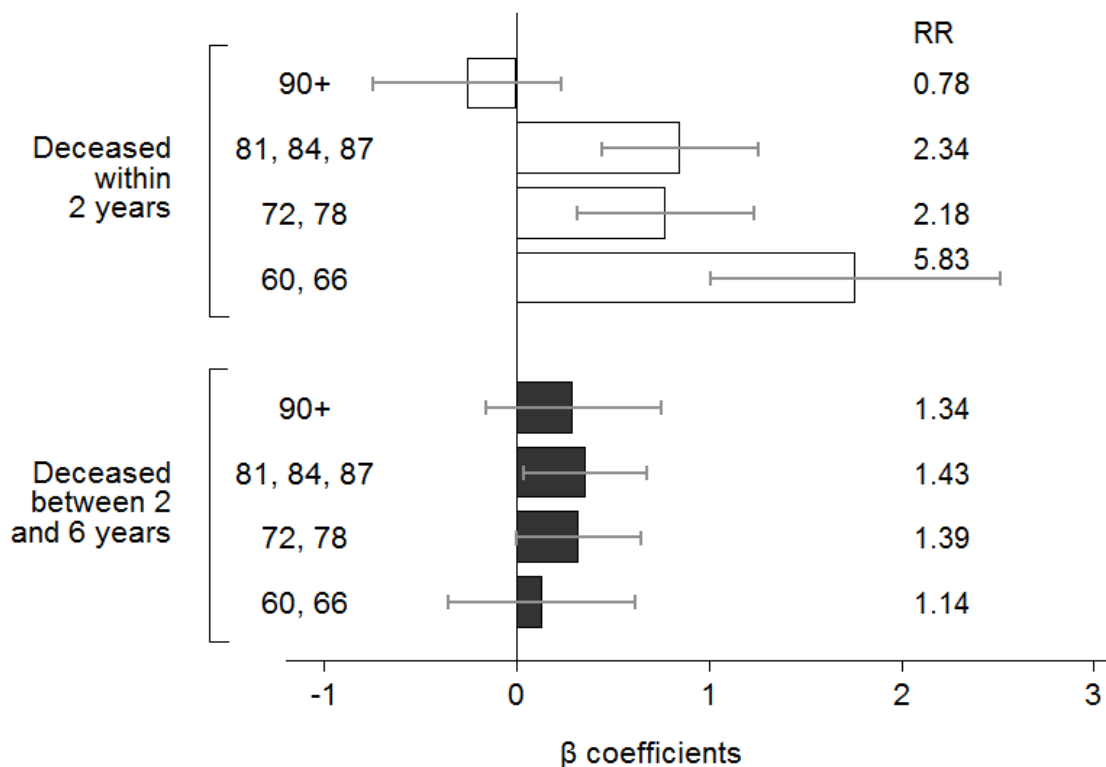


Figure 8. Relative risk ratios (RR), β coefficients from the regression [$\log(\text{RR})$], and 95% CI of dying within two years and between two and six years of baseline in non-participants (reference exposure group: participants; reference outcome: alive: after six years).

4.3 AGE RELATED VARIATIONS IN MEASURES OF HEALTH (STUDY II)

In Study II, 3080 participants had complete information on all variables. The 283 participants excluded from the main analyses because of missing information were significantly older, more likely to be women, and had a lower educational level than those with complete data.

Both the analysis of the distribution of the health indicators across age (Figure 1 in Study II) and the analysis of the prevalence of impairment in each indicator (Figure 2 in Study II) revealed similarities among indicators. In particular, the distribution of the MMSE score, the number of IADL and of ADL impairments had the same features at any age (i.e., narrow distributions in participants younger than 80 years and greater heterogeneity in participants older than 80 years). Similar age-related changes were detected between the curve of IADL

impairment and the curve of MMSE < 27 as well as between the curve of ADL impairment and the curve of MMSE < 20.

Figure 9 illustrates the sex-adjusted prevalence of health states (combinations of the five health indicators) with prevalence figures over 5%, stratified by age group. The best health status was characterized by no chronic diseases, gait speed ≥ 1.2 m/sec, MMSE ≥ 27 , no IADL impairments, and no ADL impairments. The prevalence of healthy people decreased with age, from 29% (95% CI 36.94 – 31.91) among the sexagenarians to 3% (95% CI 1.48 – 4.27) among the octogenarians, while no nonagenarians had this health status.

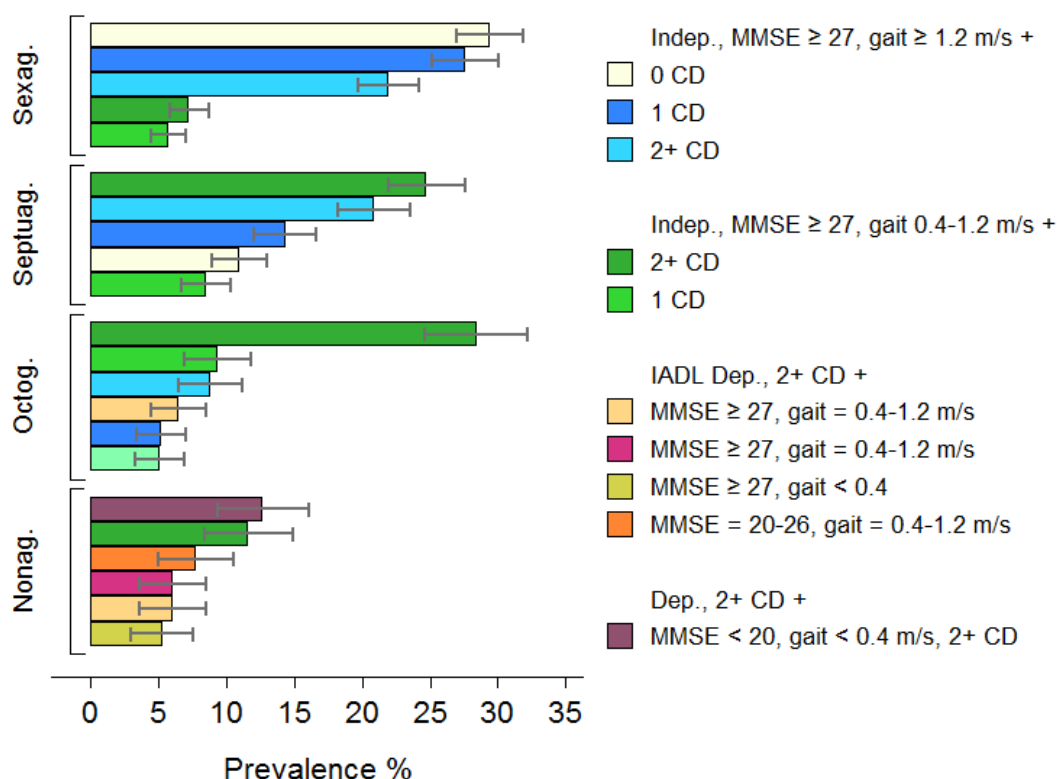


Figure 9. Sex-adjusted prevalence per 100 persons and 95% confidence intervals of health indicators, aggregated by age. Only the most common (over 5%) indicators or their aggregations in each age group are reported. CD = number of chronic diseases, Indep. = ADL and IADL independent, IADL Dep. = dependent in IADL, Dep. = dependent in ADL and IADL, Sexag. = sexagenarians, Septuag. = septuagenarians, Octog. = octogenarians, Nonag. = nonagenarians.

In the octogenarians, the most prevalent health status represented a transition from the independent and good cognitive functioning of the septuagenarians to the physical and cognitive dependence of the nonagenarians. Six percent (95% CI 4.43 – 7.52) of the octogenarians had some IADL limitations, along with medium gait speed and multimorbidity. In the nonagenarian age group, most of the combinations included low MMSE score and ADL or IADL impairment; however, the second most prevalent category (12%, 95% CI 8.35 – 14.85) was composed of functionally independent people with medium gait speed and multimorbidity.

4.4 HEALTH TRAJECTORIES (STUDY III)

In Study III, we used the indicators of health described in Study II to derive HAT. All 3363 baseline participants were included in the analysis. Three hundred models, each characterized by a different categorization of the indicators, were tested. The discriminant and difficulty levels from the selected NRM are reported in **Table 9** and a visual representation is presented in **Figure 10**. The latent trait health status is assumed to be normally distributed with a mean of zero and a standard deviation of one. The location of each point on the latent trait axis in **Figure 10** represents the value of difficulty, and the height of a point represents the discrimination value.

Table 9. Discrimination and difficulty parameters (95% confidence intervals) derived from the nominal response model for different categories of the five health indicators.

	Discrimination		Difficulty	
ADL				
No vs. 1+	11.0	(5.57; 16.5)	1.43	(1.36; 1.49)
IADL				
No vs. 1+	6.79	(5.10; 8.49)	0.85	(0.80; 0.90)
Gait speed				
≥1.5 vs. 1.49 to 1.0	1.13	(0.74; 1.51)	-1.20	(-1.40; -1.01)
1.49 to 1.0 vs. 0.99 to 0.4	3.97	(2.67; 5.28)	0.23	(0.18; 0.28)
0.99 to 0.4 vs. <0.4	4.59	(3.33; 5.85)	1.19	(1.13; 1.26)
MMSE				
30 vs. 29	0.45	(0.30; 0.59)	-0.08	(-0.30; 0.14)
29 vs. 28-20	1.16	(0.58; 1.73)	0.08	(-0.02; 0.17)
28-20 vs. 0-19	3.91	(2.74; 5.08)	1.54	(1.46; 1.63)
Morbidities				
No vs. 1-2 morbidities	0.75	(0.62; 0.89)	-1.49	(-1.72; -1.26)
1-2 vs. 3+ morbidities	0.59	(0.13; 1.05)	1.28	(1.05; 1.51)

ADL = activities of daily living, IADL = instrumental activities of daily living, MMSE = Mini-Mental State Examination.

The two measures of disability had the highest discrimination values (black dot: ADL = 11.0, 95% CI 5.57 – 16.5; black circle: IADL = 6.79, 95% CI 5.10 – 8.49), which indicates that each of the two indicators divides the population in two distinct groups. The probability of experiencing limitations in ADL changed from low to high around latent trait 11.0. On the other hand, number of chronic diseases (blue diamonds) had very low discrimination values, but at the opposite end of the health status spectrum, indicating that having no diseases or one or two diseases coincided with a large range of health status. Gait speed (green triangles) had both high discrimination values and a large range of difficulty levels, which shows that this measure differentiated different groups of people over a large spectrum of health status.

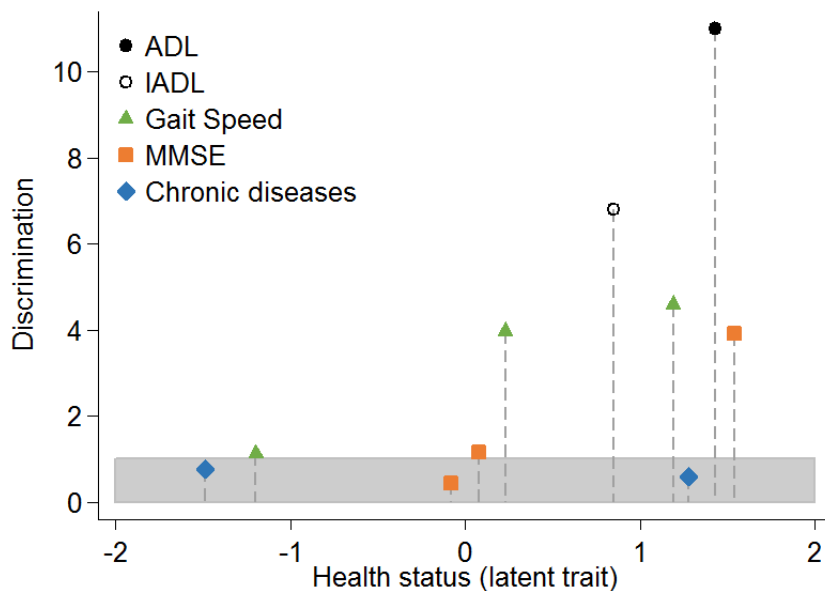


Figure 10. Distribution of the difficulty parameters on the latent trait and values of the discrimination parameters derived from the nominal response model. ADL = activities of daily living, IADL = instrumental activities of daily living, MMSE = Mini-Mental State Examination.

The final model included two categories of both IADL and ADL (0, 1+ impairments), five categories of MMSE scores (30, 29, 28-20, 19-0), four categories of gait speed (1.5 m/sec or above, below 1.5 to 1 m/sec, below 1 to 0.4 m/sec, below 0.4 m/sec), and three categories of number of chronic diseases (0, 1-2, and 3+ diseases). The TCC (expected score) ranged from 0 to 10. The TCC was more precise for people whose health status was above average (positive values of the latent trait), and the relationship between score and health status was not linear. The coefficients of the linear regression models between TCC and the health indicators are reported in **Table 10**.

The HAT score ranged from 0 (bad health) to 10 (good health). Each HAT score was characterized by a different clinical significance of the health status of a person (**Figure 11**). Scores below three indicated people with severe disability, physical impairment, and wide range of MMSE scores from very low to medium values. HAT scores between three and five differentiated between people with mild disability and different levels of physical functioning and multimorbidity. People with HAT scores above five were not disabled but had different levels of physical and cognitive functioning and multimorbidity.


The ROC curve analysis showed that HAT had a good ability to predict death within five years (area = 0.85; 95% CI 0.83–0.87) and two or more hospital admissions within two years (area = 0.78; 95% CI 0.75–0.81). HAT performed significantly better than the single items included in the tool except for walking speed, which performed similarly. HAT also performed better than the Multidimensional Prognostic Index and self-rated health (p-value <0.05 for both tests). The distributions of HAT at baseline and at the first and second follow-up were equivalent (Figure 1 in Study III), which indicates that HAT is reliable over time.

Table 10. Regression coefficients relating the single health indicators to HAT.

	No ADL or IADL impairment	Any IADL impairment	Any ADL impairment
IADL			
Any vs. no			-1.7
Gait speed			
≥1.5	Ref.	Ref.	Ref.
1.49 to 1.0	-0.6	-0.3	0
0.99 to 0.4	-2.4	-1.5	-0.9
<0.4	-3.9	-2.5	-2.0
MMSE			
30	Ref.	Ref.	Ref.
29	-0.2	-0.1	-0.1
28-20	-0.8	-0.4	-0.4
19-0	-1.5	-1.3	-1.3
Morbidity			
None	Ref.	Ref.	Ref.
1-2	-0.4	-0.2	-0.2
3+	-0.6	-0.3	-0.3
MMSE x gait speed			
29 x 1.49 to 1.0	0.0		
x 0.99 to 0.4	0.0		
x <0.4	0.1		
28-20 x 1.49 to 1.0	0.0		
x 0.99 to 0.4	0.2		
x <0.4	0.3		
19-0 x 1.49 to 1.0	-0.8		
x 0.99 to 0.4	-0.3		
x <0.4			
Constant	10.0	6.7	5.3

All p-value <0.001. ADL = activities of daily living, IADL = instrumental activities of daily living, MMSE = Mini-Mental State Examination.

HAT	ADL	IADL	Gait	MMSE	CD
9.5-10	0	0	1.5 (1.5-1.5)	30 (30-30)	0 (0-1)
9.0-9.4	0	0	1.2 (1.2-1.5)	30 (29-30)	1 (0-2)
8.0-8.9	0	0	1.2 (1.0-1.2)	29 (28-29)	2 (1-3)
7.0-7.9	0	0	0.8 (0.6-0.8)	30 (29-30)	2 (1-2)
6.0-6.9	0	0	0.6 (0.5-0.8)	28 (27-29)	3 (2-4)
5.0-5.9	0	0 (0-1)	0.3 (0.3-0.8)	28 (27-29)	2 (1-3)
4.0-4.9	0	1 (1-2)	0.5 (0.4-0.6)	28 (25-29)	3 (2-4)
3.0-3.9	0	3 (1-2)	0.2 (0.0-0.3)	27 (23-29)	2 (1-4)
2.0-2.9	1 (0-1)	3 (2-3)	0.4 (0.0-0.5)	21.5 (17-27)	2 (1-3)
1.0-1.9	1 (1-3)	3 (2-3)	0.2 (0.0-0.3)	25 (20-28)	2 (1-2)
0.0-0.9	5 (2-5)	4 (3-4)	0.0 (0.0-0.0)	6 (0-18)	3 (1-4)



Better

Worse

Figure 11. Median (inter quantile range) of each health indicator by score of the health assessment tool (HAT). ADL = activities of daily living, IADL = instrumental activities of daily living, Gait = gait speed, MMSE = Mini-Mental State Examination, CD = chronic diseases.

The longitudinal change in HAT score over a six-year period showed small cohort effects in the score (**Figure 12**). The median HAT score was above the disability level (HAT = 5) up to age 89; after age 85, at least 10% of the participants were severely impaired (HAT < 3). The upper decile (nine) declined slowly before age 85 and rapidly thereafter. The distribution of HAT score across age differed between men and women (Figure 2 and 3 in Study III). Older women had lower HAT scores than men of the same age; the difference appears at a younger age for the lower percentiles of the distribution.

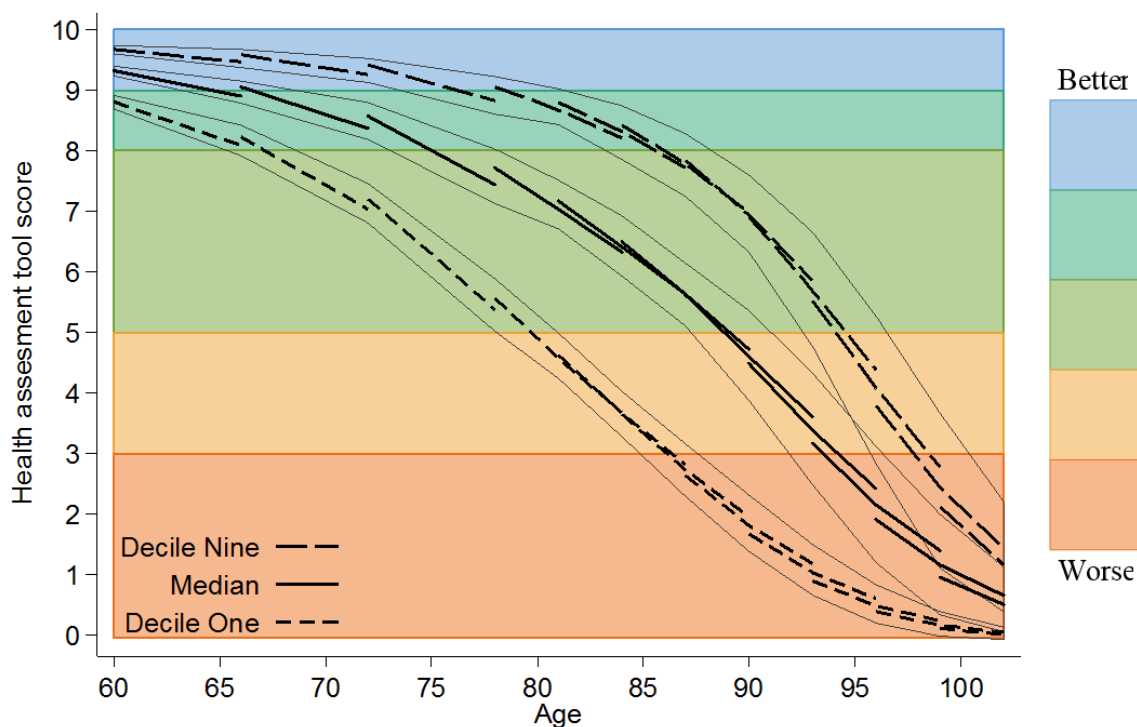


Figure 12. Sex-adjusted six-year longitudinal change in health status. Each line segment represents a birth cohort. Solid lines = median, long dashed lines = decile nine, dashed lines = decile one.

4.5 GERIATRIC CURVES TO MONITOR AND PREDICT CARE NEEDS (STUDY IV)

Analysis of the cross-sectional association between HAT and other indicators of health showed that very good or excellent self-rated health and being able to perform the chair-stand test were associated with a good HAT score above the median level (OR very good/excellent self-rated health: 2.19, 95% CI 1.77 – 2.71; OR passed chair test: 2.62, 95% CI 2.07 – 3.31). A combination of good balance and good grip strength was associated with better HAT scores (OR balance X grip strength: 1.15, 65% CI 1.05 – 1.25) (**Figure 13**).

The ability of HAT to predict hospital admissions and use of informal or formal care over three years was significantly greater than that of the count of morbidities (all p-values <0.001) and of the count of disabilities (all p-values <0.001) (**Figure 14**). HAT was better able to predict whether participants made over ten primary care visits and over five specialty care visits (ROC curve areas 0.70 and 0.63) than disability count (ROC curve areas 0.56 and 0.52; all p-values <0.001). However, HAT was neither better nor worse than a count of

morbidities in predicting number of primary care visits (ROC HAT = 0.70; ROC morbidity = 0.69; p-value = 0.07), and the count of morbidities outperformed HAT in predicting specialist visits (ROC HAT = 0.63; ROC morbidity = 0.66; p-value <0.001).

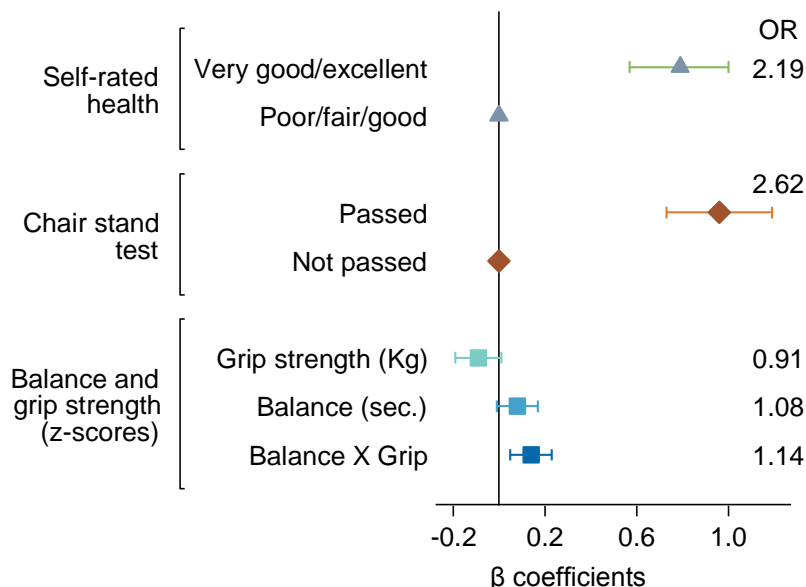


Figure 13. β coefficients, 95% confidence intervals, and odds ratios (OR) of having a HAT score above the age- and sex-specific median with respect to being below by other indicators of health. Adjusted for educational level, civil status, smoking habits, alcohol consumption, and physical activity.

Figure 15 shows the HAT score reference curves for men and women and for four individual people with the same health characteristics. The HAT scores for the four people were derived through the flowchart depicted in Figure 1 of Study IV. All four people have a HAT score of seven; however, their percentile values are different. The 80-year-old man had a percentile of 70, indicating that 70% of the men of his age have better HAT score than he does. The 80-year-old woman has a lower percentile, 64, indicating that 64% of the women her age have a better HAT score than she does. The 87-year-old man's percentile is 50 (half the men his age have better health), and the 87-year-old woman's is 32 (a third of the women her age have better health).

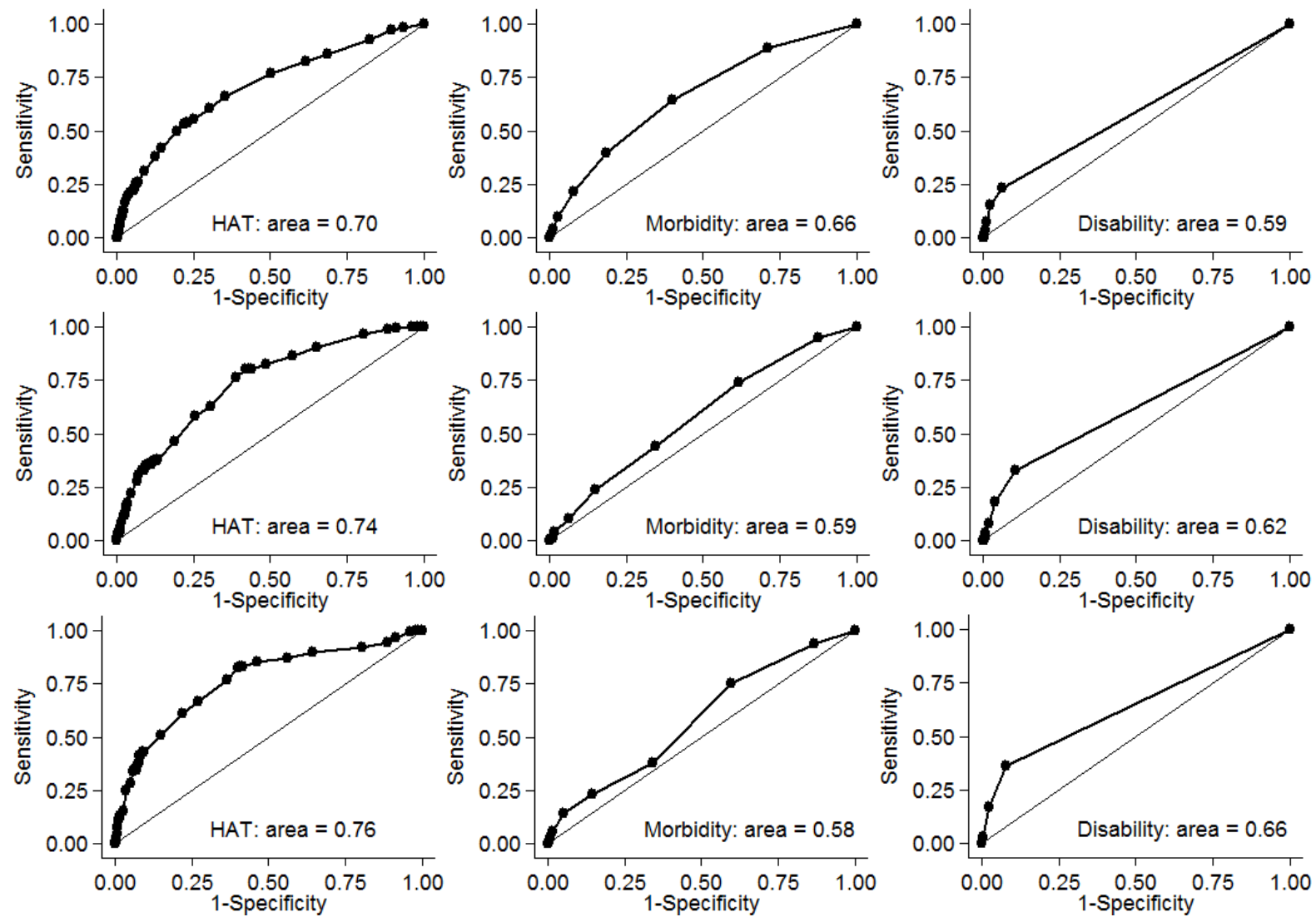


Figure 14. The ability (ROC curve) of each health measure to correctly predict three different care needs over three years. First row: at least one hospital admission, second row: informal care use, third row: formal care use.

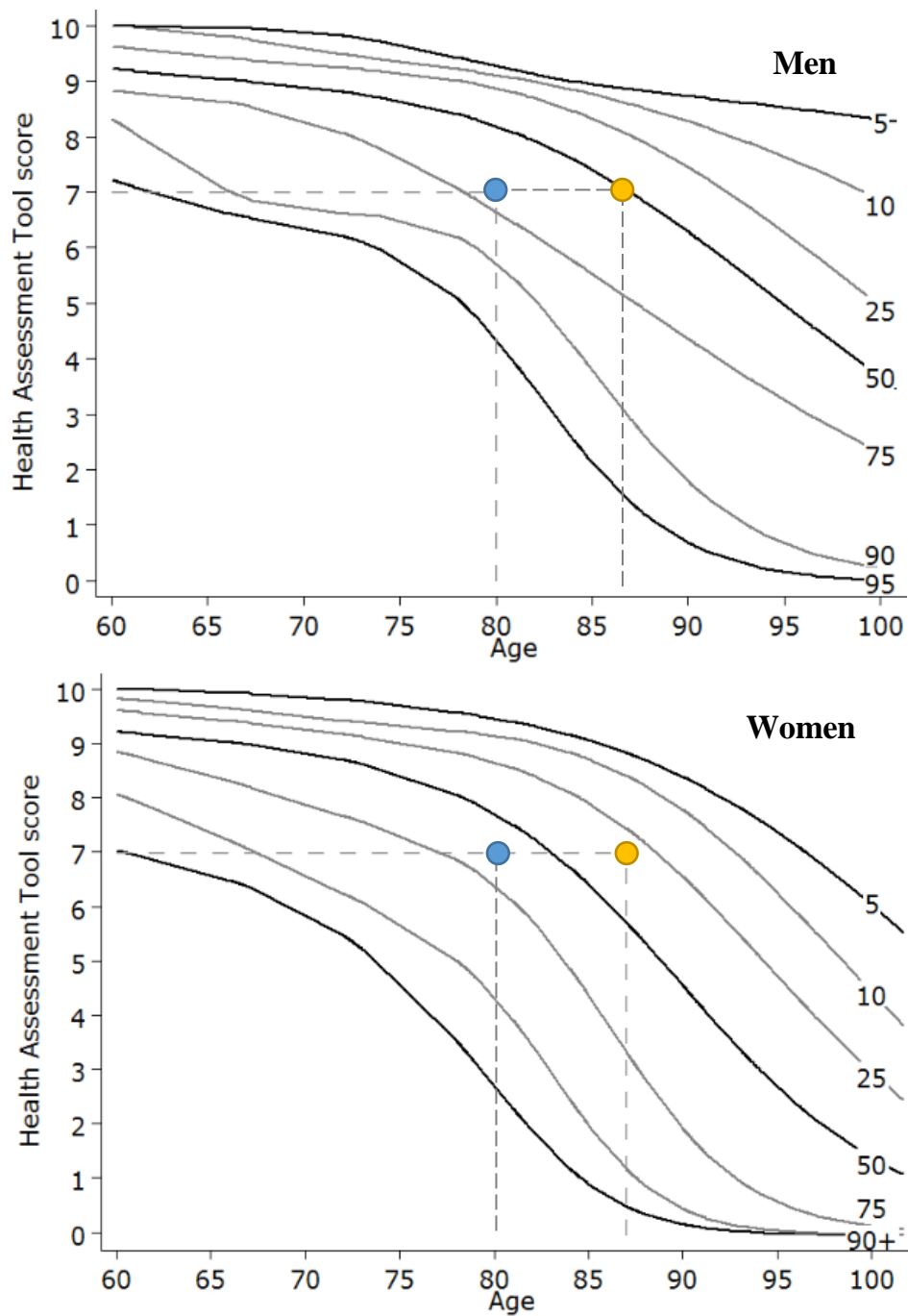


Figure 15. References curves for men and women. Health characteristics: no ADL or IADL impairments, MMSE score 28, gait speed of 0.9 m/sec, two chronic diseases. Four people (two men and two women) with the same HAT score are indicated by age. Blue dots = 80 years and yellow dots = 87 years. The reference population was SNAC-K participants at baseline. ADL = activities of daily living, IADL = instrumental activities of daily living, Gait = gait speed, MMSE = Mini-Mental State Examination.

5 DISCUSSION

5.1 MAIN FINDINGS

5.1.1 Time trends of disability

Between 1991 and 2010, both the prevalence and incidence of ADL remained substantially steady in the urban Swedish population studied in this project. Life expectancy increased for people without disability but did not change for people with disability. People with disability had high levels of mortality over the entire 20-year period.[130]

These results from Study I are consistent with those of other studies, which have also found a steady level of disability prevalence during a similar time period.[39, 51, 53] Despite some methodological differences from our study, a Dutch meta-analysis by van Gool et al. reported a steady level of disability in older adults from 1991 to 2007. They used different indicators of disability based on items from the OECD and SF-36 questionnaires [51] such as self-reported difficulties in climbing stairs, walking, and dressing. Moreover, their study sample was younger (aged 55-84 years) and had a higher proportion of men than ours. Their samples were also restricted to adults who were not living in an institution, whereas Study I included both adults who lived in institutions and those who lived at home. Lin et al. [53] used survey data on non-institutionalized people in the United States to study the prevalence of ADL. Their study had a lower proportion of women than our study but a similar age range (70+). Despite some methodological differences (Lin et al. examined only four ADL items but over a longer time period), they also concluded that the prevalence of ADL disability remained quite stable over the last three decades. The study by Parker et al. [39] had several similarities to our Study I. It included people from Sweden, people who lived in institutions and in the community, and used the same ADL measurements. However, they used survey data that was nationally representative of the population aged 77+, as opposed to our study, which included data representative of an urban district in the capital city of Stockholm. Their conclusion that the prevalence of disability in ADL remained stable from 1992 to 2002 was in agreement with our findings.

However, the findings in Study I are in conflict with the findings of other studies that report a significant decline [43, 45-50] or an increase [35, 42, 52, 54-58] in ADL disability.

Differences in design or analyses may explain part of these inconsistencies in findings. Many of the studies in question did not include people who lived in institutions, some analyzed survey data, some used data from longitudinal studies, and others compared cohort studies at different times. The wording of the question asked to assess disability, the scale used, and the items included were similar but not identical. Some studies defined a person as disabled only if the disability had lasted more than a certain period.[43, 46, 55] Other studies specified that impairments were caused by health problems;[45, 52, 53] health or memory problems;[46] or physical, mental, or emotional conditions.[55] Others did not specify cause. Most of the analyses reported calculated either age- and sex-standardized prevalence or adjusted odds ratios. A few reported crude measures that showed an increase in disability that could be

linked more to a different age distribution in the samples at different points in time rather than to an increase in the prevalence of disability over time.[52, 55]

Only a few studies on time trends of disability have included analyses of prevalence, incidence, and mortality at the same time. Steady levels of prevalence could be a result of incidence and mortality moving in opposite directions. Decreased incidence of ADL disability and increased recovery from disability, together with decreased mortality, could manifest as a steady prevalence of ADL disability over time, as it was observed in a U.S. study of the period 1984 to 2000.[49] The effect of recovery from ADL disability was minimal in Study I, as very few participants changed from being disabled to be non-disabled. Mortality among those with ADL disability and incidence of ADL appeared to remain constant throughout the study period. These two factors could contribute to the steady prevalence of ADL that was found in Study I. The incidence of ADL in the study could have been underestimated, as the analysis was based on assessment of ADL approximately every three years, and some participants may have developed ADL disability at some point between assessments and subsequently died before being assessed. The gradual tendency toward decline in disability prevalence suggested by the results of Study I might be explained by two simultaneous factors. The first is a high three-year level of mortality in participants with ADL disability, which would mean that these participants tended to die before the next assessment (three years is the approximate time between study assessments). The second factor would be the presence of lower mortality in participants without disability especially in the second period.

Unlike many studies, the analyses in Study I provide ADL prevalence data by narrow age strata, since age is the most important risk factor for ADL disability. Moreover, all the information available (date of birth, gender, and date of death) for the entire invited population—not only participants—was used in the analyses to ensure that differences in study participation did not influence the findings.

Numerous personal and environmental factors affect risk for, development of, and consequences of disability. Differences in the distribution of these factors could be the reason for the increases or decreases in disability observed in other populations. Disability or functioning in general is made up of the “intrinsic capacity” of the person, the environment in which the person lives, and the interaction between these two factors.[2] A person’s “intrinsic capacity” involves their health characteristics (which are subject to change over time) and all their physical and mental capacities, which can be fixed (i.e., sex, ethnicity) or variable (i.e., wealth, gender). Their environment includes all the factors that characterize the context in which they live. At the micro level, this can include the person’s physical environment and interpersonal relationships, and at the macro level, it can include health and social policies and services. As many factors are related to disability, a person with a certain functional limitation may not be dependent in an ADL because of a technology that allows that person to remain independent. It is also possible for a person to have a level of resilience that allows them to maintain or improve functionality in the presence of adversity over time.

Improvements in the management of chronic conditions could also result in a lower prevalence of disability. For example, in the United States, most of the disability decline observed between the 1980s and 1990s has been attributed to the changing prevalence of and better treatment outcomes for cardiovascular, vision-related, and musculoskeletal diseases.[45] However, later gains due to changes in chronic conditions have been less obvious, and some conditions, such as dementia and stroke, are still the leading contributors to disability, which could contribute to the stable prevalence findings of Study I. The higher proportion of women in the second period of Study I could also help explain our findings, since older women experience a higher level of disability than older men; this association is complex and most likely linked to socioeconomic, biological, and psychological factors.[46] Moreover, early- and mid-life conditions affect late-life disability, especially the onset of disability.[46] Mid-life and late-life behaviors are especially important in the early development of disability. A more sedentary life could contribute to a decline in physical health, as recently shown in Germany,[58] and if obesity levels increase, the risk of disabling chronic conditions (i.e., diabetes) could also increase.[33]

Autonomy, or being independent, is among the elements of life that older people value the most.[2] The findings of Study I provide a message that is positive both for the individuals and for society, since the prevalence of disability has remained steady in the last two decades or even tended to decline, particularly in nonagenarians. Life expectancy has increased for people without disability, which indicates that people are living longer without functional limitations and hence retain autonomy for a longer time. On the other hand, mortality rates for people with disability have not improved recently, and the clear decline in ADL prevalence consistently found between the 1980s and 1990s is no longer present.

5.1.2 Older people's health

Human health and its relation with risk/protective factors can be compared to the stress-strain curve in metals. The stress-strain curve of metals is composed of three main regions. The first is the elastic region. If the object is deformed in this region, once released, it completely recovers its original shape without any damage or permanent modification. The second is the plastic region. Beyond the yield point, any deformation will leave some modification even if most of the original shape is recovered. In this region, even a small amount of stress produces large deformations. The last region is the one beyond the ultimate stress or fracture point. If the amount of strain increases, the metal object already in the plastic region continues to deform until it cannot sustain any further strain, and ultimately it breaks. The stress-strain curve of a metal, along with the object design and production method define the intrinsic capacity of the object; environmental exposure during the life of the object changes both the length of the elastic and plastic regions and the amount of strain an object can withstand before reaching the yield point or breaking. Resilience is the area of the first region that is determined by the strain-stress curve and environmental agents.[131]

However, human health is much more complex than the stress-strain curve of metal objects, and for obvious reasons it is not possible to experimentally study the intrinsic characteristics

of people and the effect of environmental exposures. Thus, human health is often studied via observation of the manifestations of health in people's lives. In Study II and Study III, in order to assess the health status of people 60 years old and older, we studied the individual and combined distribution of five indicators of the underlying physiological changes that may occur during aging.

Health assessment with five indicators

In Study II, we identified two transitional periods during which most health changes occur: 1) age 81 to 84, when people experienced a gradual decline from relatively good functional health to multimorbidity, lower cognitive functioning, and some disabilities in IADL and 2) age 84 to 87, when severe cognitive and physical impairment gradually lead to disability in ADL. The first transitional period seems to represent the passage from the third to the fourth age (i.e., from a period of personal fulfillment to a period of dependency and death), and the second transition period can be considered the beginning of the fourth age.[74, 132, 133]

In our study population, mild impairment in walking speed and morbidity were already present in more than 20% of sexagenarians. This finding is consistent with findings in the literature,[121, 134, 135] which show that the association between limitations in physical functioning and chronic diseases is less evident in the oldest old than in younger old adults. A tandem-slope pattern was present between any cognitive impairment (MMSE <27) and IADL disability and between severe cognitive impairment (MMSE < 20) and ADL disability. In line with our results, other studies have found a specific pattern of age-related increases in cognitive and physical decline that roughly parallels an increase in disability.[89, 136-138] The findings of Study II confirm that IADL disabilities are good indicators of initial cognitive impairment and that ADL disabilities are strongly related to dementia.[139]

The health heterogeneity typical of older people was made evident by the 63 different health patterns observed when assessing the different combinations of the five indicators in the whole cohort. Heterogeneity increased with age; the health states that had a prevalence of 5% or more in each age group represented 92% of sexagenarians and 80% of septuagenarians but only 63% of octogenarians and 49% of nonagenarians. Nonagenarians are an "elite group" of people who have survived beyond the average life expectancy of their birth cohort,[63] and one might therefore expect that the selection would result in more homogeneity in their health. However, in previous studies, we have shown that several factors, both genetic and contextual, are relevant to longevity, which suggests that there may be a variety of pathways to longer survival.[6]

It is reassuring that the combination of multimorbidity accompanied only by slow gait speed was the second most prevalent health condition among nonagenarians and the most prevalent among nonagenarians who lived in the community. This lack of physical or cognitive disability means that although the need for medical care increased from age 60 to 90, the need for social assistance, including institutionalization, became prevalent only at very advanced ages. The striking increase in heterogeneity in health among older people also has important implications for the health care system. Hospital, primary, and social care personnel should

be prepared to encounter a much broader spectrum of diversity in abilities and needs in the oldest old than in younger old people. To provide a healthier life for older people in the future, prevention of multimorbidity and physical impairment should be the top priority when people are in their 60s and 70s, whereas postponing functional dependence and using more efficacious pharmacological and non-pharmacological treatments for chronic disorders is a great challenge during the entire aging period.

The health assessment tool

In Study II, we found that each health indicator provides a partial picture of the health status of a person. To study trajectories of health in Study III, we derived a health assessment tool that is easy to use and informative about a person's health needs. HAT includes the clinical measures of health that were analyzed in Study II: number of chronic diseases, physical and cognitive functioning, and mild and severe disabilities. In developing HAT, we aimed to create a continuous measure that could minimize the floor or ceiling effect present in some of the indicators and that could differentiate health status in a large age range of people with a wide spectrum of health.

To determine the cross-sectional relationships among the five health measures and to create HAT, we used the NRM (section 3.4.3).[128] HAT scale ranges from poor health (score = 0) to good health (score = 10). Better HAT scores are mostly characterized by changes in the number of chronic diseases and physical and cognitive functioning, whereas worse HAT scores are defined by mild or severe disability. Hence, higher HAT scores indicate mostly the need for medical care, and lower scores indicate the need for social care. In line with results of a previous report,[66] the NRM identified the two ADL measures and the MMSE score as the indicators that best discriminated when health starts deteriorating in people who belong to the heterogeneous 60+ old group. On the other hand, gait speed was informative over a large range of health status. Indeed, gait speed is associated not only with survival and functioning, but also with the well-being of older adults.[91, 98, 125, 140, 141] Number of chronic diseases was the least informative variable, although it was still useful in people with relatively good functioning.

HAT was better able to predict adverse health outcomes than other indices used in hospital setting, and improved the predictive ability of the single health indicators included in it. The strength of HAT derives from optimizing the information about health status provided by the interaction of the single measures. For example, a count of chronic conditions is not sufficient to capture the health status of a person.[2] A chronic disease may be disabling for some people but may just partially limit the physical or/and cognitive functioning of others. In HAT, the number of diseases is correlated to the associated functional status, and because of the other indicators included in HAT, people with the same count will probably have different HAT values depending on the severity of the diseases. Similarly, a given level of physical functioning might result in a higher or lower HAT score depending on the status of the other indicators, such as a person's cognitive status.

HAT's main advantage over to other measures already in use is its relatively quick and easy implementation, which might allow HAT to be used in clinical settings. Moreover, HAT could allow researchers to further investigate the association between health status and subjective and social/emotional components of health.

5.1.3 Health curves and health trajectories

The inter- and intra-individual trajectories of health measured with HAT retained most of the age-related changes in health found when we investigated the single measures. However, it allowed us to more reliably determine health status in the study population. There was a consistent part of the population of any age between 60 and 87 years (10%) that maintained relatively good health with high levels of physical and cognitive functioning and few chronic diseases. At least half of the people younger than 87 had no disabilities, even though they were affected by chronic diseases and functional impairments. It was only among the oldest old, 95 and older, that severe disability affected half or more of the sample.

The cross-sectional and longitudinal distribution of HAT scores across age confirmed that the heterogeneity of health increases with age, especially after age 70. The picture of the health of older people after age 60 that is shown by HAT trajectories is relatively positive. However, there is great variation in the health distribution at any age. For this reason, in most of our analyses, we did not focus on the mean change in the health measures. Instead we looked at three specific percentiles (10th, 50th, and 90th) to obtain a more complete picture of the change in health distribution with age. As in the *stress-strain curve* for metals, health during the latter part of the life course can be divided into three typical periods: a period of relatively good and stable health, a period of declining health, and a period of significant loss of health.[2] These periods are not defined by chronological age and can differ considerably from one person to another. By looking at the health distribution, it may be possible to develop interventions better tailored to people in each stage of health.

5.1.4 Geriatric health charts

Public health and medical care initiatives designed to improve older people's health should be based on individuals' health trajectories, since different points in the trajectory will require different responses from health systems. During the period of life in which health is good and stable, the goal would be to detect chronic conditions and physical decline early and to promote healthy behaviors. In the stage of life when health starts to decline, improvements can be achieved by removing barriers that limit participation and by finding strategies that reverse or slow the decline in capacities. Finally, when health starts worsen significantly and people become functionally dependent, health systems may intervene to compensate for the loss of capacity or, at the end of life, to support palliative care.[2] A fundamental prerequisite for this social and medical care delivery framework is the ability to measure health status at the individual level and to measure trajectories in a pragmatic but comprehensive way. As we age, it becomes critical to monitor health changes in order to capture deviations from normal ranges early.

In Study IV, we presented a novel approach to monitoring change in older people's health using reference health curves that can help delineate ad-hoc clinical and public health actions. The focus of public health strategies is to maintain and prolong people's mental and physical capacities as long as possible, by acting in a timely and proper manner. To this end, health systems need to detect and control health changes at the right time and in the right care setting. In Study III, we showed that HAT is a good candidate for developing such geriatric health charts. Although only five health indicators are included in the tool, HAT predicts care needs better than the single count of morbidities or disabilities, both of which are considered major determinants of poor health in aging.[2, 142] Of the physical tests typically used to measure health in older people, we included only the test of walking speed, as it is quick and easy to perform. Other objective measures of physical functioning (balance, grip strength, and the chair-stand test) are also good indicators of health status,[88] and the age- and sex-specific HAT score showed a good correlation with those indicators, even after adjustment for lifestyle factors and socioeconomic status. The age- and sex-specific HAT score was also associated with self-rated health, a powerful proxy of objective health.[143]

All these properties make such composite measures suitable for creating reference percentile curves, similar to the growth charts used by pediatricians to illustrate the distribution of selected body measurements in children. Several health indices, already available in the literature, also include more subjective measures of health and measures of well-being.[76] Although both components contribute unarguably to the person-centeredness of health definitions and care provision, our aim was to create an easy-to-use more objective measure of health with clear clinical significance and applicability. The reference curves allow for the interpretation of individual scores, which can be contextualised by taking into account the individual's age and sex. A score of 4.5 in a 60-year-old man should be considered a clear sign of compromised health (96% of 60-year-old men had better HAT scores), whereas the same HAT score in a 90-year-old woman could be considered acceptable (4.5 is the median score for 90-year-old women). The reference curves not only provide information about the present health status of older adults, but they also provide information on future trajectories and changes. This can be useful information for health care providers and family members when planning social care. Lastly, the HAT index can be useful in research in order to better describe the process of aging and to better understand the diverse pathways from determinants to intrinsic capacity and functional ability.

5.2 METHODOLOGICAL CONSIDERATIONS

5.2.1 Study design

All the studies included in this thesis used data collected from community based observational studies. Apart from the requirement of being 60 years old or older in the SNAC-K or 75+ in KP, both studies had few exclusion criteria (e.g., inability to speak Swedish), and the random samples selected to participate represented the population living in Kungsholmen at the time of data collection. As most studies, observational or not, the final sample included at baseline represented the healthier part of the population.

5.2.2 Sources of error

Random error

In any kind of research study, there are two types of random errors: one linked to the sample variance and the other to measurement error.

When a sample is randomly extracted from a population, the sample statistic (either mean, median, or any other measure) is not exactly equal to the population statistic because of the heterogeneity in the population. All studies are subject to this type of error, and statistical methods can be used to determine how distant the sample measure is from the true population statistic. Larger samples and/or higher homogeneity of the measure in the population help in minimizing the random variation and increasing the precision of the estimate.

Measurement error is the nonsystematic error that is introduced by random variation in measurement. As an example, walking speed was tested once for each participant at each assessment. If the test would have been repeated several times per assessment, most likely several different values would have been recorded. Repeated measures per person at every assessment could reduce this type of error. As for sample variability, if the measurement error is random, then the effect on the measure would be an increase in variability and a decrease in precision. In our analyses, we made no distinction between the two errors because there were no repeated data available per assessment. However, the error introduced by the lack of repeated measurement of gait speed should be minimal, as this measure has proven to be reliable even for people affected by stroke.[144]

Systematic error

Systematic error is problematic in all types of research studies because unreliable measures compromise the quality of studies. To reduce this type of error, study nurses and doctors underwent training prior to data collection to ensure that they followed the same procedures during the interviews. We also used standardized study protocols, procedures, and diagnostic criteria; the data collection staff turnover was low; and great effort was put into reducing sample selection and attrition.

Measurement error. ADL, IADL, and number of chronic diseases could have been affected by false recall from the participants. In the case of ADL, after the participant reported their ADL status, the nurse also reported whether he/she agreed with the participant's ADL assessment. If the nurse was unsure about the participant's judgment, if possible he/she consulted with a proxy for the participant before making a final decision. This was especially important for participants with impaired cognitive ability. IADL was self-reported without any nurses' evaluation and could be subject to systematic error, as people with problems in cognition might overestimate their abilities. Moreover, people living in institutions were not asked if they were able to buy groceries; in the analyses they were considered as unable. This could have led us to overestimate the number of people with one or more IADL impairments; however, this error should be small, as only 11 people living in nursing homes (5% of those in nursing homes, 0.3% of the sample) had one IADL limitations. The count of chronic

diseases relied on a non-predefined list compiled by doctors after an in-person clinical exam. Moreover, doctors checked laboratory data, drug use, and clinical records (when available) to reduce the error in the measure. However, in another study,[145] we showed that the count of diseases used in SNAC-K resulted in a lower prevalence of multimorbidity than when we also included data derived from the Swedish National Patient Register.

Walking speed was measured with a standard procedure. The main source of systematic error could be the difference in walking distance between those who reported that they walked fast (6 m) and those who reported that they walked slowly (2.4 m) (section 3.2.2). However, the results of the two tests are comparable,[146] so if systematic error was introduced, it should have been minimal.

Nurses asked the MMSE test questions to participants. Instructions on how to ask the questions and on the number of times a question could be repeated were clearly written on the MMSE questionnaire. Physical limitations (such as deafness or physical impairment) could prevent the successful completion of the test. Nurses clearly recorded whether the participant was not able to perform the test because of physical impairment. These people were considered to have missing in MMSE data.

Sample selection. Any inference is correct and represents a good estimate of the population that the sample represents. The problem arises from uncertainties regarding what population the sample at hand represents. There are two stages of selection in any type of study. The first involves the people that are randomly selected and that decline to participate. This selection is common to all studies that analyze data from the same database. The second selection is introduced by the missing values for each variable included in the analyses; different studies on the same data will lead to different sample sizes and hence different populations of origin. A big advantage of observational studies is that both stages are easily quantifiable, and it is still possible to obtain a clear definition of the representative population.

The representativeness of the KP sample has been described in previous research articles.[6] The personal characteristics of those who participated and those who declined to participate or moved were similar. On the other hand, people who died before participating (7.6% of the sample) were older and more often men than were the participants. In Study II, we observed that time to death in nonagenarians that participated in SNAC-K seemed to be similar to time to death in those who did not participate, whereas in the other age groups, the difference in this variable was significant. The sample selection could lead us to underestimate the prevalence of ADL limitations in Study I; however, the imputed analysis of non-participants in this study indicated that if an underestimation was present, it should be minimal. We tried to overcome the problem of sample selection by imputing disability status for those people who did not participate. As for the other three studies, sample selection could have given a healthier picture of the population than was really the case. When possible, selection due to missing values was investigated by conducting similar analyses on imputed data. All 3363 study participants contributed to the analyses that were used to derive HAT.

Attrition. All longitudinal studies are affected by attrition. Attrition is the longitudinal reduction in number of participants because participants die or decline to participate further. As with sample selection, attrition changes the population of reference and introduces more uncertainty into its definition. In Study I, longitudinal data from KP and SNAC-K were treated as cross-sectional random samples of the population at the time of the assessment. It should be noted that the new cohort of 81-year-olds invited to participate between 2007 and 2010 were also included in the analyses. The difference in the probability of participating in the study did not change over time from 1991 to 2010 among the 81- and 87-year-olds, whereas the proportion of 90+ year-old who participated decreased of 12 percentage points. There was more attrition that could have led to an underestimation of the true prevalence of disability in the population in the oldest participants than in younger participants. Moreover, Study I could have missed those people whose ADL limitations began between assessment periods and who died before the next assessment. However, for population-based longitudinal cohorts that involve such a comprehensive assessment, follow-up more frequent than three years is not very feasible. For the two younger age categories, this potential underestimation of ADL limitations would likely not be a great concern, as the mean time until death for those without disability was approximately 7.5 for those aged 81-84 and six years for those aged 87. It was approximately four years for people with disability aged 81-84 and slightly over three years for 87-year-olds with disability. However, in those 90-99 years, the mean time to death for participants with disability was only approximately two years (approximately 4.3 years for those without disability), so it is conceivable that the calculated incidence was underestimated in this age category.

Reliability and validity. A reliable assessment tool produces stable and consistent results. We did not directly test HAT's test-retest reliability on the same individuals, but we checked HAT's consistency across time by comparing the HAT distribution when assessed at three different points in time. The Cronbach's alpha reliability was 0.77 at baseline, 0.73 at the three-year follow-up, and 0.75 at the six-year follow-up, which indicates good internal consistency.

A valid assessment tool measures what it is supposed to measure. We assessed the validity of HAT by checking its ability to predict several negative health outcomes, including use of health service, hospital care, and social care. The predictive ability of HAT was good and even better than that of other measures usually used in clinical practice (i.e., morbidity and disability). However, we acknowledge that HAT was not tested in other populations but only in the one used to develop the assessment tool.

Confounding. Confounders are factors that explain or produce all or part of the association between the independent variable of interest and the outcome yet are not on the causal path of association. Potential confounders are risk factors for the outcome, are associated with but not surrogates of the independent variable of interest, and precede (temporally) the independent variable of interest. The type of confounding depends on the population of reference and may change with time.[147] Only when the relevant factors are measured and properly taken into

consideration in the regression modeling, can inference be extended to any other population.[148]

In the study on the temporal trends of disability, we stratified all the analyses by age (and adjusted for age when more than one age cohort was included in a strata) and adjusted them by sex. Primary analyses were not stratified by sex because the sample size was small. Time trends of disability can be affected by several other factors, such as early life conditions, present socioeconomic status, behaviors, genetics, and personality. All these factors can also be considered if the aim of the study is to determine how time trends change in specific strata of the population by risk factors for disability or if it is to determine what factors could be used to develop interventions. This was beyond the scope of this study and beyond the power allowed by the size of this study population. However, for health care and public health resource planning, it is helpful to predict age- and sex-specific trends in the prevalence of people with disability who will need care and support. In Studies II and III, we did not consider how other factors, apart from age and sex, could affect the characteristics of health and the health trajectories. However, because the distribution of the indicators of health considered in the studies varied considerably across age and sex, age and sex were always used either for stratification or adjustment in the analyses.

5.2.3 Generalizability

Generalizability is the validity of the results with respect to the people outside the sampled population. The reference population of the two studies included in this thesis was the population living in a large urban area in Sweden at the time of the assessment. The population of this area is characterized by a relatively higher educational status, a relatively higher proportion of women, and a relatively higher proportion of people with office-related occupations than the rest of Sweden.[149] In general, we can expect that the prevalence of chronic diseases, functional impairments, and disabilities would be lower in the study reference population than in the general population. Caution must therefore be used before generalizing these results to other populations, although the results might be valid for populations with similar socioeconomic standards and public health systems.

6 CONCLUSIONS

1. Between 1991 and 2010, both prevalence and incidence of disability remained stable in the urban Swedish population, with a trend toward a slow decline. At the same time, mortality remained steady in disabled people but decreased in persons without disability, which suggests that increased life expectancy during the last two decades may be essentially be driven by longer lives of functionally independent people.
2. Health is well-described by five indicators that provide a clear picture of the complexity and heterogeneity in health status of adults 60 and older. Until age 80, most people do not have functional impairment or disability despite the presence of morbidity or even multimorbidity. Disability becomes common only after age 90. Age 80 to 85 is a transitional period when major health changes often take place, often following the co-occurrence of more than one negative health event. This implies that the need for medical care increases after age 70 and that the need for social care, including institutionalization, becomes prevalent only at very advanced ages.
3. The Health Assessment Tool (HAT) uses relatively few items that capture both health and functioning, and could be a good tool for identifying deviations from expected health trajectories at the individual level and for determining medical, rehabilitation, or social care needs at the population level. We used HAT to study the health of older adults in Sweden (a western urban society) and found it to be fairly good. Despite the large heterogeneity detected in both cross-sectional and longitudinal analyses, the longitudinal analyses confirm that more than half of the population have no severe disability up to age 95.
4. Public health initiatives to improve older people's health should be based on individuals' health trajectories. A fundamental prerequisite to this public-health framework for healthy aging is the ability to measure the individual's health status and trajectory. This could be achieved by creating reference health curves similar to the growth charts used by pediatricians. Although further testing in other population is still required, HAT has proved to be a reliable and valid health measure, and could be a good candidate for use in developing such geriatric health charts.

7 RELEVANCE AND IMPLICATIONS

Older people are an invaluable asset to any society, and getting older is an achievement of which people are and should be proud. During the aging process, people may experience physical and functional decline, and it is the aim of aging research and of society to find strategies to prevent such declines and to preserve not only people's autonomy and ability to contribute to society, but also their well-being. At the same time the reduction in capabilities with age is inevitable, and it is the responsibility of the public health and care systems to find means to alleviate the burden of these changes on older people and their caregivers.

A simplistic conceptualization of health as the absence or presence of chronic conditions does not provide a holistic representation of health that enables 1) researchers to find the best strategies to prolong, reverse, or help people cope with health changes and losses and 2) public health providers to promote actions to foster the health and well-being of older adults.

Our findings are encouraging, as they clearly show that the prevalence of disability is not increasing, but instead is remaining stable or even tending to decline. This positive picture was persistent even when we analyzed health indicators separately and in combination using the HAT index. However, the shorter longevity of the disabled people in our study population warns us that there is room for further improvements. We envision the possibility for health care providers and policy makers to more reliably assess with the geriatric health charts the needs of people for health and social care. A prompt and well-targeted response to the health needs of a population is vital for a society where older people are viewed as a resource and aging is experienced as positive.

8 FUTURE DIRECTIONS

Health plays a central role in human life and especially in aging. Good health may not be enough to guarantee high quality of life, but it makes a significant contribution. Currently, the possibility of efficacious interventions is hampered by limited knowledge of biological mechanisms and determinants of aging and aging-related health problems. Prevention, both primary and secondary, is crucial, yet effective preventive actions are still very few.

This thesis proposes an index to assess and follow up both health and functioning in community-dwelling older adults. We believe that HAT could facilitate the timely identification of deviations from expected health trajectories at the individual level. HAT may also be useful from a public health perspective as a means to better respond to medical, rehabilitation, or social care needs at the population level. One of the first steps needed to make HAT more useful is to validate its construct in other populations.

HAT could help us plan for the future health and long-term care needs of the population by indicating what part of the population consumes more health care resources and needs more formal and informal long-term care. The ultimate aim would be to identify subgroups of older adults suitable for interventions aimed at cost containment and prevention of negative health care outcomes.

Moreover, in the past decade, convincing evidence has shown that biological traits, environmental factors, and health are intertwined in complex relationships that define health pathways over the lifespan—pathways that may substantially differ from individual to individual. Thus, a life course approach to determinants of healthy aging is an important future research field. Together with others, I would first like to study the combined effects of multiple determinants in different categories (social and physical environment, health behaviors and lifestyles, and biomedical events) on the health of older adults. Then, taking advantage of other Swedish databases, such as SWEOLD, we could explore multiple exposures and verify their effects at different time periods during the life course.

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11 APPENDIX

11.1 ADDITIONAL PUBLICATIONS

Only epidemiology articles.

- I. Rizzuto D, Mossello E, Fratiglioni L, **Santoni G**, Hui-Xin W. Personality and survival in older age: the role of lifestyle behaviors and health status. *American Journal of Geriatric Psychiatry*. 2017. (Accepted)
- II. Calderón-Larrañaga A, Vetrano DL, Onder G, Gimeno-Feliu LA, Coscollar-Santaliestra C, Carfi A, Pisciotto MS, Angleman S, Melis RJF, **Santoni G**, Mangialasche F, Rizzuto D, Welmer AK, Bernabei R, Prados-Torres A, Marengoni A, Fratiglioni L. Assessing and measuring chronic multimorbidity in the older population: a proposal for its operationalization. *Journals of Gerontology Series A: Biological Sciences and Medical Sciences* 2016.
- III. Liang Y, Fratiglioni L, Wang R, **Santoni G**, Welmer AK, Qiu C. Effects of biological age on the associations of blood pressure with cardiovascular and non-cardiovascular mortality in old age: A population-based study. *International Journal of Cardiology*. 2016 Oct 1;220:508-13.
- IV. Marseglia A, Fratiglioni L, Laukka EJ, **Santoni G**, Pedersen NL, Bäckman L, Xu W. Early cognitive deficits in type 2 diabetes: A population-based study. *Journal of Alzheimer's Disease*. 2016. DOI: 10.3233/JAD-160266.
- V. Marengoni A, Angleman S, Meinow B, **Santoni G**, Mangialasche F, Rizzuto D, Fastbom J, Melis R, Parker M, Johnell K, Fratiglioni L. Coexisting chronic conditions in the older population: variation by health indicators. *European journal of Internal Medicine*. 2016 Jun 30;31:29-34.
- VI. Heiland EG, Welmer AK, Wang R, **Santoni G**, Angleman S, Fratiglioni L, Qiu C. Association of mobility limitations with incident disability among older adults: a population-based study. *Age and ageing*. 2016 Apr 28;afw076.
- VII. Shakersain B, **Santoni G**, Faxén-Irving G, Rizzuto D, Fratiglioni L, Xu W. Nutritional status and survival among old adults: an 11-year population-based longitudinal study. *European journal of clinical nutrition*. 2016 Mar 1;70(3):320-5.
- VIII. Shakersain B, **Santoni G**, Larsson SC, Faxén-Irving G, Fastbom J, Fratiglioni L, Xu W. Prudent diet may attenuate the adverse effects of Western diet on cognitive decline. *Alzheimer's & Dementia*. 2016 Feb 29;12(2):100-9.
- IX. **Santoni G**, Angleman SB, Welmer AK, Mangialasche F, Marengoni A, Fratiglioni L. Age-related variation in health status after age 60. *PloS One*, 2015; 10(3), e0120077.
- X. Angleman SB, **Santoni G**, Pilotto A, Fratiglioni L, Welmer AK, MPI_AGE Project Investigators. Multidimensional Prognostic Index in Association with Future Mortality and Number of Hospital Days in a Population-Based Sample of Older Adults: Results of the EU Funded MPI_AGE Project. *PloS One*, 2015, 10(7), e0133789.
- XI. Kalpouzos G, Rizzuto D, Keller L, Fastbom J, **Santoni G**, Angleman S, Graff C, Bäckman L, Fratiglioni L. Telomerase Gene (hTERT) and Survival: Results From Two Swedish Cohorts of Older Adults. *Journals of Gerontology Series A: Biological Sciences and Medical Sciences* 2014 Nov 30. Epub 2014 Nov 30.

- XII. Welmer AK, Liang Y, Angleman S, **Santoni G**, Yan Z, Cai C, Qiu C. Vascular risk factor burden, atherosclerosis, and functional dependence in old age: a population-based study. *International Journal of Behavioral Medicine*, 2013, 1-8.
- XIII. Xu WL, Caracciolo B, Wang HX, **Santoni G**, Winblad B, Fratiglioni L. Accelerated progression from mild cognitive impairment to dementia among APOE ε4ε4 carriers. *Journal of Alzheimer's Disease* 2013;33:507 – 515
- XIV. Weuve J, Proust-Lima C, Power MC, Gross AL, Hofer SM, Thiébaud R, Chêne G, Glymour MM, Dufouil C, MELODEM Initiative. Guidelines for reporting methodological challenges and evaluating potential bias in dementia research. *Alzheimer's & Dementia*. 2015 Sep 30;11(9):1098-109.

11.2 DISSERTATIONS FROM THE AGING RESEARCH CENTER AND THE STOCKHOLM GERONTOLOGY RESEARCH CENTER, 1991-2017

1991

Herlitz Agneta. Remembering in Alzheimer's disease. Utilization of cognitive support. (Umeå University)

1992

Borell Lena. The activity life of persons with a dementia disease.

1993

Fratiglioni Laura. Epidemiology of Alzheimer's disease. Issues of etiology and validity.

Almkvist Ove. Alzheimer's disease and related dementia disorders: Neuropsychological identification, differentiation, and progression.

Basun Hans. Biological markers in Alzheimer's disease. Diagnostic implications.

1994

Grafström Margareta. The experience of burden in care of elderly persons with dementia. (Karolinska Institutet and Umeå University)

Holmén Karin. Loneliness among elderly - Implications for those with cognitive impairment.

Josephsson Staffan. Everyday activities as meeting-places in dementia.

Stigsdotter-Neely Anna. Memory training in late adulthood: Issues of maintenance, transfer and individual differences.

Forsell Yvonne. Depression and dementia in the elderly.

1995

Mattiasson Anne-Cathrine. Autonomy in nursing home settings.

Grut Michaela. Clinical aspects of cognitive functioning in aging and dementia: Data from a population-based study of very old adults.

1996

Wahlin Åke. Episodic memory functioning in very old age: Individual differences and utilization of cognitive support.

Wills Philippa. Drug use in the elderly: Who? What? & Why? (Licentiate thesis)

Lipinska Terzis Beata. Memory and knowledge in mild Alzheimer's disease.

1997

Larsson Maria. Odor and source remembering in adulthood and aging: Influences of semantic activation and item richness.

Almberg Britt. Family caregivers experiences of strain in caring for a demented elderly person. (Licentiate thesis)

1998

Agüero-Eklund Hedda. Natural history of Alzheimer's disease and other dementias. Findings from a population survey.

Guo Zhenchao. Blood pressure and dementia in the very old. An epidemiologic study.

Björk Hassing Linda. Episodic memory functioning in nonagenarians. Effects of demographic factors, vitamin status, depression and dementia. (In collaboration with the Department of Psychology, University of Gothenburg, Sweden)

Hillerås Pernilla. Well-being among the very old. A survey on a sample aged 90 years and above. (Licentiate thesis)

1999

Almberg Britt. Family caregivers caring for relatives with dementia – Pre- and post-death experiences.

Robins Wahlin Tarja-Brita. Cognitive functioning in late senescence. Influences of age and health.

Zhu Li. Cerebrovascular disease and dementia. A population-based study.

2000

Hillerås Pernilla. Well-being among the very old. A survey on a sample aged 90 years and above. (In collaboration with H. M. Queen Sophia University College of Nursing, Stockholm, Sweden)

von Strauss Eva. Being old in our society: Health, functional status, and effects of research.

2001

Jansson Wallis. Family-based dementia care. Experiences from the perspective of spouses and adult children.

Kabir Nahar Zarina. The emerging elderly population in Bangladesh: Aspects of their health and social situation.

Wang Hui-Xin. The impact of lifestyles on the occurrence of dementia.

2002

Fahlander Kjell. Cognitive functioning in aging and dementia: The role of psychiatric and somatic factors.

Giron Maria Stella. The rational use of drugs in a population of very old persons.

2003

Jönsson Linus. Economic evaluation of treatments for Alzheimer's disease.

2004

Berger Anna-Karin. Old age depression: Occurrence and influence on cognitive functioning in aging and Alzheimer's disease.

Cornelius Christel. Drug use in the elderly - Risk or protection? Findings from the Kungsholmen project.

Qiu Chengxuan. The relation of blood pressure to dementia in the elderly: A community-based longitudinal study.

Palmer Katie. Early detection of Alzheimer's disease and dementia in the general population. Results from the Kungsholmen Project.

Larsson Kristina. According to need? Predicting use of formal and informal care in a Swedish urban elderly population. (Stockholm University)

2005

Derwinger Anna. Develop your memory strategies! Self-generated versus mnemonic strategy training in old age: Maintenance, forgetting, transfer, and age differences.

De Ronchi Diana. Education and dementing disorders. The role of schooling in dementia and cognitive impairment.

Passare Galina. Drug use and side effects in the elderly. Findings from the Kungsholmen Project.

Jones Sari. Cognitive functioning in the preclinical stages of Alzheimer's disease and vascular dementia.

Karp Anita. Psychosocial factors in relation to development of dementia in late-life: a life course approach within the Kungsholmen Project.

Nilsson Jan. Understanding health-related quality of life in old age. A cross-sectional study of elderly people in rural Bangladesh.

2006

Klarin Inga. Drug use in the elderly – are quantity and quality compatible.

Nilsson Erik. Diabetes and cognitive functioning: The role of age and comorbidity.

Ngandu Tiia. Lifestyle-related risk factors in dementia and mild cognitive impairment: A population-based study.

Jonsson Laukka Erika. Cognitive functioning during the transition from normal aging to dementia.

2007

Ferdous Tamanna. Prevalence of malnutrition and determinants of nutritional status among elderly people. A population-based study of rural Bangladesh. (Licentiate thesis)

Westerbotn Margareta. Drug use among the very old living in ordinary households-Aspects on well-being, cognitive and functional ability.

Rehnman Jenny. The role of gender in face recognition. (Stockholm University)

Nordberg Gunilla. Formal and informal care in an urban and a rural population. Who? When? What?

Beckman Gyllenstrand Anna. Medication management and patient compliance in old age.

2008

Gavazzeni Joachim. Age differences in arousal, perception of affective pictures, and emotional memory enhancement. (Stockholm University)

Marengoni Alessandra. Prevalence and impact of chronic diseases and multimorbidity in the aging population: A clinical and epidemiological approach.

Rovio Suvi. The effect of physical activity and other lifestyle factors on dementia, Alzheimer's disease and structural brain changes.

Xu Weili. Diabetes mellitus and the risk of dementia. A population-based study.

Meinow Bettina. Capturing health in the elderly population – complex health problems, mortality, and the allocation of home help services. (Stockholm University)

Agahi Neda. Leisure in late life. Patterns of participation and relationship with health.

Haider Syed Imran. Socioeconomic differences in drug use among older people. Trends, polypharmacy, quality and new drugs.

2009

Thilers Petra. The association between steroid hormones and cognitive performance in adulthood.

Masud Rana AKM. The impact of health promotion on health in old age: results from community-based studies in rural Bangladesh.

Paillard-Borg Stéphanie. Leisure activities at old age and their influence on dementia development.

Livner Åsa: Prospective and retrospective memory in normal and pathological aging.

Atti Anna-Rita. The effect of somatic disorders on brain aging and dementia: Findings from population-based studies.

2010

Fors Stefan. Blood on the tracks. Life-course perspectives on health inequalities in later life.

Keller Lina. Genetics in dementia. Impact in sequence variations for families and populations.

2011

Schön Pär. Gender matter. Differences and changes in disability and health among our oldest women and men.

Caracciolo Barbara. Cognitive impairment in the nondemented elderly: Occurrence, risk factors, progression.

Rieckmann Anna. Human aging, dopamine, and cognition. Molecular and functional imaging of executive functions and implicit learning.

2012

Haasum Ylva. Drug use in institutionalized and home-dwelling elderly persons.

Mangialasche Francesca. Exploring the role of vitamin E in Alzheimer's disease. An epidemiological and clinical perspective.

Lovén Johanna. Mechanism of women's own-gender bias and sex differences in memory for faces.

2013

Hooshmand Babak. The impact of homocysteine and B vitamins on Alzheimer's disease, cognitive performance and structural brain changes.

Rizzuto Debora. Living longer than expected: protective and risk factors related to human longevity.

2014

Sjölund Britt-Marie. Physical functioning in old age: Temporal trends and geographical variation in Sweden.

Wastesson Jonas. Unequal drug treatment: age and educational differences among older adults.

2015

Sköldunger Anders. Dementia and use of drugs: Economic modelling and population-based studies.

Craftman Åsa Gransjön. Medicine management in municipal home care; delegating, administrating and receiving.

Svärd Joakim. Emotional facial processing in younger and older adults.

Wang Rui. Cardiovascular risk factors, brain structure, and cognitive decline in old age.

Pantzar Alexandra. Cognitive performance in old-age depression.

2016

Kelfve Susanne. Gotta survey somebody: methodological challenges in population surveys of older people.

Heap Josephine. Living conditions in old age: Coexisting disadvantages across life domains.

Håkansson Krister. The role of socio-emotional factors for cognitive health in later life.

Shakersain Behnaz. Impact of nutritional status and diet on cognitive decline and survival.

Bellander Martin. Plasticity of memory functioning: genetic predictors and brain changes.

2017

Ferencz Beata. Genetic and lifestyle influences on memory, brain structure, and dementia.

Köhncke Ylva. Lifestyle, cognitive aging, and brain correlates.