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TRENDS IN POPULATION HEALTH IN AN ERA OF INCREASING LONGEVITY

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TRENDS IN POPULATION HEALTH IN AN ERA OF RISING LONGEVITY

THESIS FOR DOCTORAL DEGREE (Ph.D.)

By

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Für meine Geschwister
Julian, Robin & Kira,

die genau wie ich ihren eigenen Weg gehen.

POPULAR SCIENCE SUMMARY

Populations in almost all countries worldwide are ageing. In Sweden, the number of older adults over the age of 85 increased by 75% since 1990 while the number of people over the age of 100 has almost quadrupled. Since older adults have a higher risk of many diseases and of care-dependency, population ageing is often portrayed as concerning and as a challenge for health and care systems. But populations are not only ageing; many other aspects, such as educational attainment or the number of foreign-born people in the population are rapidly changing. Some diseases have become far less common, while others occur more frequently. Survival chances, too, have changed and improved for many diseases. In light of the shifting population structure and the evolving disease panorama among older adults, the impact of population ageing on public health is not straightforward.

Composed of five scientific studies, this thesis investigates the changing disease and survival patterns among older adults in Sweden during the past three decades. Together with my co-authors, I examine potential differences between population groups, such as men and women or educational groups. Moreover, we take on a novel approach: To explore differences between people who have experienced one or more diseases and people without disease. Thereby, we aim to promote a better understanding of changing needs for health and geriatric care in ageing societies.

All five studies are based on Swedish population registers that have been linked using the unique personal identification number given to each person living in Sweden. Our data therefore includes all adults over the age of 60 in Sweden. Besides basic information such as gender, education, age, and date of death, we have access to information about hospital stays, disease diagnoses, geriatric home care, and care home residence. We investigate common and severe diseases, including myocardial infarction (heart attack), stroke, hip fractures, and different kinds of cancer. These include the most common causes of death in Sweden and globally. Three studies focus on hip fractures, an enormous public health problem in the Nordic countries. In Sweden, one in five women and one in nine men experience a hip fracture in old age and their prognosis is often poor.

Our results in Studies I and II show that life expectancy has increased faster among men and women who had a heart attack, a stroke, or cancer than it has in the general population. This implies that increasing life expectancy in Sweden has not merely been driven by healthier people. In fact, almost half of the total increase in life expectancy between 1994 and 2016 was a result of longer survival among heart attack patients. However, life expectancy did not increase among older adults who had a hip fracture.

In Studies III and IV we develop methods to measure hip fracture occurrence in Swedish registers and present time trends in hip fracture occurrence and survival after hip fracture. We found that, when eliminating the effect of population ageing, hip fractures have become less frequent between 1998 and 2017. We found declining hip fracture rates both in the total Swedish population and in all examined population groups, including both genders, different educational levels, and people born in different countries. Furthermore, hip fractures have become less frequent in healthy population groups, but also among those who had severe diseases other than hip fracture.

Twenty percent of women and 30% of men died within one year of their first hip fracture. Despite decreasing hip fracture risks, survival chances did not change over time. We found that increasing numbers of comorbidities, i.e., other diseases among hip fracture patients, explain part of the continuously high mortality rates.

Study V demonstrates that hip fractures are not only often fatal but that many patients begin to receive home care services or move to permanent care homes after their fracture. Nevertheless, we also found that hip fracture patients are less healthy and more often care-dependent than the average older person already before their fracture. These findings suggest that the increased care use among hip fracture patients is not merely the result of the fracture, but also the result of poorer health in general.

In conclusion, life expectancy increases were not limited to the healthy part of the population. Instead, longer life expectancy among older people with heart attack and stroke and some cancer types has contributed substantially to increasing life expectancy. Still, we found no improvements in hip fracture survival. Hip fracture patients – and especially men – are a vulnerable population group with increasing numbers of other diseases and high mortality risk.

POPULÄRWISSENSCHAFTLICHE ZUSAMMENFASSUNG

Bevölkerungsgesundheit in Zeiten steigender Lebenserwartung

Die Bevölkerungen fast aller Länder weltweit altern. In Schweden ist die Anzahl von Menschen über 85 seit 1990 um 75% gestiegen, während sich die Anzahl von über 100-jährigen fast vervierfacht hat. Da ältere Personen ein höheres Risiko für viele Krankheiten haben und häufiger pflegebedürftig sind, wird Bevölkerungsalterung oft als besorgniserregend und als Herausforderung für Gesundheits- und Pflegesysteme dargestellt. Aber Bevölkerungen altern nicht nur, sondern verändern sich rasant auch hinsichtlich vieler anderer Aspekte wie Bildungsniveaus oder ethnischer Zusammensetzung. Manche Krankheiten sind weitaus seltener geworden, andere hingegen treten immer häufiger auf. Auch die Überlebenschancen haben sich bei vielen Krankheiten zum Positiven verändert. Angesichts der sich wandelnden Bevölkerungsstruktur und des veränderten Krankheitspanoramas bei älteren Menschen sind die Auswirkungen der Bevölkerungsalterung auf die öffentliche Gesundheit nicht einfach vorherzusehen.

In fünf wissenschaftlichen Studien untersucht diese Dissertation die sich ändernden Krankheits- und Mortalitätsmuster unter älteren Erwachsenen in Schweden während der letzten drei Jahrzehnte. Dabei berücksichtigen wir mögliche Unterschiede zwischen Bevölkerungsgruppen wie Männern und Frauen oder Menschen mit unterschiedlichen Ausbildungsniveaus. Darüber hinaus verfolgen wir einen neuartigen Ansatz und untersuchen Unterschiede zwischen Personen mit schwerwiegenden Krankheiten und gesünderen Bevölkerungsgruppen. Damit möchten wir zu einem besseren Verständnis der sich ändernden Bedürfnisse an Gesundheitsversorgung und Altenpflege in alternden Gesellschaften beitragen.

Alle Studien basieren auf schwedischen Registerdaten. Mehrere Bevölkerungsregister wurden mithilfe der einzigartigen Personennummern, die jede in Schweden lebende Person erhält, verknüpft. Unsere Datensätze umfassen daher alle Erwachsenen über 60 Jahren in Schweden. Neben Grundinformationen wie Geschlecht, Bildung, Alter und Sterbedatum haben wir Zugriff zu Daten über Krankheitsdiagnosen, Klinikaufenthalte, über die Inanspruchnahme von Pflegediensten und über Pflegeheimaufenthalte. Wir untersuchen unter anderem Herzinfarkte, Schlaganfälle, und einige Krebsarten – die häufigsten Todesursachen in Schweden und fast allen anderen Ländern weltweit. Drei Studien untersuchen Hüftfrakturen, die ebenfalls ein enormes öffentliches Gesundheitsproblem darstellen, insbesondere in Skandinavien. In Schweden erleiden jede fünfte Frau und jeder neunte Mann eine Hüftfraktur im Alter.

Die Ergebnisse der Studien I und II zeigen, dass die Lebenserwartung bei Personen, die einen Herzinfarkt, Schlaganfall oder Krebs hatten, schneller gestiegen ist als in der Allgemeinbevölkerung. Tatsächlich konnte zwischen 1994 und 2016 fast die Hälfte des gesamten Anstiegs der Lebenserwartung auf das längere Überleben von Herzinfarktpatienten zurückgeführt werden. Im Gegensatz dazu ist die Lebenserwartung bei älteren Erwachsenen mit einer Hüftfraktur nicht gestiegen.

In Studie III entwickeln wir Methoden, um das Auftreten von Hüftfrakturen in schwedischen Registern zu messen. Darauf aufbauend zeigen wir in Studie IV, dass Hüftfrakturen zwischen 1998 und 2017 in Schweden seltener geworden sind, insbesondere wenn man die wachsende Anzahl alter Menschen im Rahmen der Bevölkerungsalterung statistisch herausrechnet. Wir fanden rückläufige Hüftfrakturraten sowohl in der schwedischen Gesamtbevölkerung als auch in allen untersuchten Bevölkerungsgruppen, einschließlich älteren Menschen mit mehreren anderen Erkrankungen.

20 Prozent der Frauen und 30 Prozent der Männer starben innerhalb eines Jahres nach ihrer ersten Hüftfraktur. Trotz einer Abnahme des Hüftfrakturrisikos änderten sich diese Sterblichkeitsraten im Laufe der Zeit nicht. Wir fanden heraus, dass eine zunehmende Zahl von Komorbiditäten, d.h. anderen schwerwiegenden Erkrankungen bei Hüftfrakturpatienten, einen Teil der anhaltend hohen Sterblichkeit erklärt.

Studie V zeigt, dass Hüftfrakturen nicht nur die Sterblichkeit erhöhen, sondern auch, dass viele Menschen nach ihrer Fraktur häusliche Pflege erhalten oder dauerhaft in Pflegeheime umziehen. Allerdings sind Hüftfrakturpatienten bereits vor ihrer Fraktur in schlechterem Zustand und häufiger pflegebedürftig als eine durchschnittliche gleichaltrige Person. Diese Ergebnisse legen nahe, dass die erhöhte Inanspruchnahme von Altenpflege bei Patienten mit Hüftfraktur nicht nur auf die Fraktur, sondern auch auf einen schlechteren Gesundheitszustand im Allgemeinen zurückzuführen ist.

Zusammenfassend lässt sich sagen, dass der Anstieg der Lebenserwartung seit den 1990ern nicht nur auf den gesunden Teil der Bevölkerung beschränkt war. Stattdessen hat die längere Lebenserwartung älterer Menschen mit Herzinfarkt, Schlaganfall und Krebs wesentlich zur Erhöhung der Lebenserwartung beigetragen. Dennoch fanden wir keine Verbesserung des Überlebens nach einer Hüftfraktur. Hüftfrakturpatienten – und insbesondere Männer – bleiben eine Bevölkerungsgruppe mit hohem Sterberisiko und einer zunehmenden Zahl anderer schwerwiegender Erkrankungen.

POPULÄRVETENSKAPLIG SAMMANFATTNING

Befolkningens hälsa i en tid med ökande medellivslängd

Befolkningen i nästan alla länder runt om i världen åldras. I Sverige har antalet personer över 85 år ökat med 75 % sedan 1990, medan antalet personer över 100 år nästan fyrdubblats. Eftersom äldre löper högre risk för många sjukdomar och oftare är i behov av vård, framställs åldrande befolkningar ofta som oroande och som en utmaning för vård- och omsorgssystemen. Men befolkningen åldras inte bara, de förändras också snabbt när det gäller många andra aspekter, såsom hälsa, utbildningsnivå och etnisk sammansättning. Vissa sjukdomar har blivit mindre vanliga, medan andra blivit vanligare. Chanserna att överleva har också förändrats till det bättre vid många sjukdomar. Sammantaget gör detta att åldrandets konsekvenser för folkhälsan är komplexa att förutspå.

I fem vetenskapliga studier undersöker denna avhandling de förändrade sjukdoms- och dödlighetsmönstren bland äldre vuxna i Sverige under de senaste tre decennierna. Vi undersöker eventuella skillnader mellan befolkningsgrupper som män och kvinnor eller personer med olika utbildningsnivå och studerar även hur befolkningsgrupper med och utan sjukdom har utvecklats. Med detta vill vi öka förståelsen över utvecklingen och för de förändrade behoven av hälso- och sjukvård och äldreomsorg i åldrande samhällen.

Samtliga studier är baserade på svenska registerdata och omfattar alla över 60 år i Sverige. Olika befolkningsregister har kopplats samman med hjälp av de unika personnummer som varje person som bor i Sverige får. Utöver grundläggande information som kön, utbildning, ålder och dödsdatum har vi tillgång till uppgifter om sjukdomsdiagnoser, sjukhusvistelser, användning av äldreomsorg och vistelser på äldreboenden. Vi undersöker hjärtinfarkt, stroke och vissa cancerformer - de vanligaste dödsorsakerna i Sverige och nästan alla andra länder runt om i världen. Tre studier undersöker också höftfrakturer, som även det är ett stort folkhälsoproblem, särskilt i Skandinavien. I Sverige drabbas var femte kvinna och var nionde man av en höftfraktur i hög ålder.

Resultaten från Studie I och II visar att medellivslängden har ökat snabbare hos personer som har haft hjärtinfarkt, stroke eller cancer, än i befolkningen i övrigt, även om den fortsatt ligger på en lägre nivå. Faktum är att nästan hälften av den totala ökningen av medellivslängden mellan 1994 och 2016 kan tillskrivas den ökande överlevnaden för hjärtinfarktpatienter. Däremot har den förväntade livslängden inte ökat hos äldre vuxna som drabbats av en höftfraktur. Detta resultat föranledde mer fokus på höftfrakturer i studierna III-V.

I studie III, som har fokus på metod, utvecklar vi algoritmer för att mäta förekomsten av höftfrakturer i svenska register. Med utgångspunkt i detta visar vi i studie IV att höftfrakturer blev något mer sällsynta i Sverige mellan 1998 och 2017, särskilt om man statistiskt räknar på det växande antalet gamla i befolkningen. Detta gällde i alla studerade befolkningsgrupper, inklusive äldre med flera andra sjukdomar, vilket är glädjande. Däremot är prognosen efter höftfraktur fortsatt dålig. 20 procent av kvinnorna och 30 procent av männen dog inom ett år efter sin första höftfraktur. Trots en minskning av risken för höftfraktur förändrades alltså inte dödligheten över tid. Vi fann att ett ökande antal komorbiditeter, det vill säga andra allvarliga sjukdomar hos patienter med höftfraktur, förklarar en del av den fortsatt höga dödligheten.

Studie V visar att höftfrakturer inte bara ökar dödligheten utan att den ofta innebär en utlösande faktor för att få hemtjänst eller flyttar permanent till äldreboende. Däremot visar vi att höftfrakturpatienter inte är jämförbara med den allmänna befolkningen i samma ålder. De har en sämre hälsa och kräver mer vård än genomsnittspersonen i samma ålder även innan frakturen inträffar. Dessa resultat tyder på att det ökade vårdbehovet hos patienter med höftfrakturer inte bara beror på frakturen, utan också på sämre hälsa generellt.

Sammanfattningsvis har ökningen av medellivslängden sedan 1990-talet inte varit begränsad till den friska delen av befolkningen. Tvärtom har den längre förväntade livslängden för äldre personer med hjärtinfarkt, stroke och cancer bidragit väsentligt till att öka medellivslängden. Vi fann dock ingen förbättring av överlevnaden efter en höftfraktur. Höftfrakturpatienter – och i synnerhet män – är fortfarande en befolkningsgrupp med hög risk för dödsfall och ett ökande antal andra allvarliga sjukdomar.

ABSTRACT

In Sweden, the number of older adults over the age of 85 increased by 75% since 1990 while the number of centenarians has almost quadrupled. Rapid population ageing is a global phenomenon and projected to continue in almost all countries worldwide, Sweden among them, throughout the 21st century. Since old age is generally associated with a high risk of disease and care-dependency, population ageing often evokes concern. However, population ageing is accompanied by changing disease patterns and by a changing sociodemographic population composition and its consequences for public health are thus not straightforward.

Highlighting heterogeneity in the population, this thesis aims to present changing mortality and morbidity patterns among older adults in Sweden during the past three decades. I thereby aim to increase the understanding of changing health and geriatric care needs in an ageing society and to explore how a changing population structure affects population health. The thesis is based on a linkage of several nationwide population registers covering all individuals over the age of 60 in Sweden. It integrates both epidemiological and demographical methods and focuses on some of the most common and severe diseases in old age. While Studies I and II additionally include cardiovascular diseases and cancer, the two most common causes of death globally, Studies III to V focus on hip fractures – an enormous public health issue in Sweden, where lifetime risks exceed 20% among women and 10% among men.

In Studies I and II, we use life table methods and decomposition techniques to show that remaining life expectancy in old age has increased faster among men and women with a history of cardiovascular diseases and cancer than it has in the general population. Almost half of the total increase in Swedish life expectancy during 1994 to 2016 can be attributed to improved survival among individuals with a history of myocardial infarction alone. As a result of longer life expectancy, disease prevalence increased. These two processes had counteracting influences on the development of life expectancy, but at least for cardiovascular diseases, the positive impact of improved survival far outweighed the negative one caused by rising disease prevalence. In contrast to all other diseases, life expectancy did not increase among older adults with a history of hip fracture.

In **Study III**, we found the Swedish Hip Fracture Quality Register and National Patient Register to be suitable to study nationwide hip fracture trends. Nevertheless, some patients dying shortly after their fracture were not included in the quality register, indicating a selection towards healthier patients. We further derive algorithms to operationalize first and recurrent hip fractures in the National Patient Register. **Study IV** shows that the age-standardized incidence of first and recurrent hip fracture has declined between 1998 and 2017 in the total population and in population strata defined by gender, education, comorbidity level, and birth country. Nevertheless, 20% of women and 30% of men died within one year of their first hip fracture and these risks remained essentially unchanged. The lack of mortality improvements could at least partly be attributed to rising comorbidity levels among hip fracture patients.

Study V demonstrates that hip fractures have an immediate negative impact on care trajectories of older patients. However, already before their fracture, older adults who sustained a hip fracture were frailer and more likely to receive geriatric care than the general older population. Our comparison to a health-matched control group suggests that the increase in care use among hip fracture patients might have also occurred in absence of the fracture, even if somewhat later.

In conclusion, life expectancy increases were not limited to the healthy part of the population. Rising life expectancy can at least partly be attributed to tertiary prevention enabling older adults who experienced severe diseases to survive longer. However, trends were not uniform across diseases. While we observed rising life expectancy among older adults with a history of cardiovascular diseases and cancer, hip fracture patients – and especially men – remain a vulnerable population group with increasing comorbidity levels and high mortality risk. Our findings also emphasize the importance of selection processes and the choice of adequate comparison groups when examining the consequences of disease.

Keywords: population ageing, population health, epidemiology, register-based research, life expectancy, hip fracture, myocardial infarction, stroke, cancer, comorbidity, ageing

SCIENTIFIC PAPERS INCLUDED IN THE THESIS

I. **Meyer AC**, Drefahl S, Lambe M, Ahlbom A, Modig K (2020) Trends in life expectancy: did the gap between the healthy and the ill widen or close? BMC Medicine; 18(1):41. doi:10.1186/s12916-020-01514-z

II. Ebeling M, **Meyer AC**, Modig K (2020) The rise in the number of long-term survivors from different diseases can slow the increase in life expectancy of the total population. BMC Public Health; 20(1):1523. doi:10.1186/s12889-020-09631-3

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IV. **Meyer AC**, Ek S, Drefahl S, Ahlbom A, Hedström M, Modig K (2021) Trends in Hip Fracture Incidence, Recurrence, and Survival by Education and Comorbidity: A Swedish Register-based Study. Epidemiology; 32(3):425-433. doi: 10.1097/EDE.0000000000001321

V. **Meyer AC**, Ebeling M, Drefahl S, Hedström M, Ek S, Sandström G, Modig K. The impact of hip fracture on geriatric care and mortality among older Swedes: Mapping care trajectories and their determinants [Under Review]

PUBLICATIONS NOT INCLUDED IN THE THESIS

I. **Meyer AC**, Sandström G, Modig K (2021) Nationwide data on home care and care home residence: presentation of the Swedish Social Service Register, its content and coverage. Scandinavian Journal of Public Health. [online ahead of print] doi:10.1177/14034948211061016

II. Brändström A, **Meyer AC**, Modig K, Sandström G (2021) Determinants of home care utilization among the Swedish old: nationwide register-based study. European Journal of Ageing. [online ahead of print] doi:10.1007/s10 433-021-00669-9

III. Ek S, **Meyer AC**, Hedström M, Modig K (2021) Hospital Length of Stay After Hip Fracture and Its Association With 4-Month Mortality—Exploring the Role of Patient Characteristics. The Journals of Gerontology: Series A; 8:glab302. doi:10.1093/gerona/glab302

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V. **Meyer AC**, Eklund H, Hedström M, Modig K (2021) The ASA score predicts infections, cardiovascular complications, and hospital readmissions after hip fracture - A nationwide cohort study. Osteoporosis International; 32(11):2185-2192. doi:10.1007/s00198-021-05956-w

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VII. **Meyer AC**, Modig K (2021) The role of having children for the incidence of and survival after hip fracture - A nationwide cohort study. Bone; 145:115873 doi:10.1016/j.bone.2021.115873

VIII. Modig K, **Meyer AC**, Ahlbom A. (2020) Re: Thirty-five–year Trends in First-time Hospitalization for Hip Fracture, 1-year Mortality, and the Prognostic Impact of Comorbidity. Epidemiology; 31(1):e4. doi:10.1097/ede.00000000000 01115 *[Letter to the editor]*

IX. **Meyer AC**, Brooke HL, Modig K (2019) The role of children and their socioeconomic resources for the risk of hospitalisation and mortality – a nationwide register-based study of the total Swedish population over the age 70. BMC Geriatrics; 19(1):114. doi:10.1186/s12877-019-1134-y

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CONTENTS

LIST OF ABBREVIATIONS

AHC	Ageing and Health Cohort
CCI	Charlson comorbidity index
CI	Confidence interval
CDR	Cause of Death Register
CVD	Cardiovascular disease
HR	Hazard ratio
ICD	International classification of diseases
IR	Incidence rate
LISA	Longitudinal Integrated Database for Health Insurance and Labour Market Studies (*Longitudinell Integrationsdatabas för Sjukförsäkrings- och Arbetsmarknadsstudier)*
NOMESCO	Nordic Medico-Statistical Committee Classification of Surgical Procedures
NPR	National Patient Register
OR	Odds ratio
PPV	Positive predictive value
RLE	Remaining life expectancy
SHR	Swedish Hip Fracture Register (*RIKSHÖFT*)
SSR	Social Service Register (*Registret över insatser till äldre och personer med funktionsnedsättning enligt socialtjänstlag*)
TPR	Total Population Register
WHO	World Health Organization

1 INTRODUCTION

The 21st century is an era of global population ageing. Virtually all countries worldwide have experienced increasing numbers of older men and women during the past decades and expect continuously growing numbers for decades to come. Although the substantial rise in life expectancy in recent history is arguably one of the biggest achievements of humankind, population ageing often evokes concern. It is portrayed as a challenge for modern health and welfare systems because old age is generally associated with a high risk of disease and care-dependency [1-6]. Measures such as the old-age dependency ratio imply that older men and women are sometimes seen as a burden to societies based on the assumption that most older individuals are not formally employed in the labour market while their health care, geriatric long-term care, and pensions are often costly [3,5,6]. Even though population ageing remains to be frequently described as challenging, the focus of ageing research has moved away from seeing old age as a period determined to poor quality of life. Instead, research has shifted towards acknowledging the diversity of older individuals and promoting "successful ageing" and health at higher ages [5,7-9].

Ageing research is today a flourishing and multidisciplinary field. While longevity and population ageing are central to demography, the promotion of health is a task that lies at the core of epidemiology and public health sciences. Whether increasing longevity entails improved health or a larger burden of disease is a question of utmost importance for epidemiological research. Originally put forward by Fries in 1980 [10], the compression of morbidity hypothesis has since been tested frequently but with varying results [11-14]. We know today that there is no simple answer to this question. Academic consensus has largely settled on the notion that longer lives are spent in both poor and good health, depending on the health indicator and the population under study.

Population ageing is accompanied by changing disease panoramas and mortality patterns in the population [15]. The pronounced decline in the incidence of and mortality from cardiovascular disease (CVD), the most common cause of death worldwide, is one of the most prominent examples of changing disease patterns in the past 50 years. This results in changing demands but also opportunities for the welfare state. Epidemiological research on trends in population health can guide policy makers who aim to allocate welfare resources fairly and efficiently. For instance, it is not yet fully understood to which extent declining CVD incidence can be attributed to improved prevention and treatment of risk factors or to changing health behaviours in later-born birth cohorts, and whether some population groups experienced larger improvements than others.

Investigating temporal trends in population health of ageing societies entails methodological challenges. Longitudinal, comparable data is not always available, and the measurement of health is not straightforward. In addition, ageing populations are not homogeneous. Previous research has suggested that a small part of the older population stands for a large share of health expenditures [5] and that rising life expectancy has been accompanied by growing lifespan variability within the population [16]. Disregarding such heterogeneity can lead to misleading conclusions about population health and conceal population groups that might benefit from targeted health policies or interventions.

Sweden is a country with extraordinary data on population ageing. Not only can some trends, such as the development of life expectancy be traced as far back as 1750 [1,17,18], but population registers including various health and sociodemographic indicators provide a rich database for researchers. This database covers virtually the entire population, even those in poor health who may be difficult to reach through surveys and fail to meet inclusion criteria of clinical studies.

Building upon national population registers, this doctoral project concerns the changing mortality and morbidity patterns in the ageing Swedish population. In five studies, I examine secular trends in disease incidence and mortality, as well as health care consumption among the old. Integrating both epidemiological and demographic methods, I emphasize heterogeneity within the population thereby exploring how a changing population composition can affect population health. The studies included in this thesis focus on CVD, hip fractures, and certain kinds of cancer – conditions that constitute a large part of the disease panorama among the Swedish old. Without intending to be exhaustive, the following literature review briefly presents major epidemiological and demographic research on this topic and the theoretical and empirical foundation of the present thesis.

2 BACKGROUND

2.1 LONGEVITY AND POPULATION AGEING

2.1.1 An inevitable shift in population structure

Human populations worldwide have been ageing for decades, some of them for centuries, and population ageing will likely continue in the future [6,7,19-21]. Between 2019 and 2050, the number of individuals over the age of 65 globally is expected to double while their share of the total population is projected to rise to 16%, up from 6% in 1990 [7]. A common measure of population ageing is the old-age dependency ratio, defined as the share of individuals in retirement age in relation to the work force [7,21]. This measure implies that older individuals above a fixed age threshold constitute a burden to society and has therefore been criticized.

More recently, alternative indicators have been developed that do not solely build upon people's chronological ages to delineate old age. These approaches, for instance the economic or prospective old-age dependency ratios, are based on the notion that a person aged 65 in contemporary Sweden is probably not comparable to a 65-year-old person living in the year 1950 or living in another country. Instead, these indicators take into account a person's health, their life expectancy, or their economic consumption and contributions irrespective of their chronological age [7,19-22]. Since life expectancy has been rising and the average retirement age continues to be postponed in many societies, these indicators often paint less pessimistic pictures of the increasing burden of ageing populations today and in the future [7,21,22]. Nevertheless, the United Nations estimates that all of these dependency ratios will inevitably increase in most countries in the future [7].

Sweden is no exception to these trends. During the past half century, population growth has been most pronounced among older adults – a trend projected to continue in the future (Figure 1). As a result, the total number of older individuals residing in Sweden has been rising dramatically and the old-age dependency ratio has increased [3,7,23]. While the total population increased in size by roughly 20% between 1990 and 2019, the number of older individuals over the age of 85 rose by 75% [23]. At the same time, the number of centenarians residing in Sweden grew exponentially and has almost quadrupled [23,24]. Irrespective of whether life expectancy continues to increase, population ageing will likely continue due to low fertility and the ageing of large birth cohorts born in the 1950s and 1960s (Figure 1).

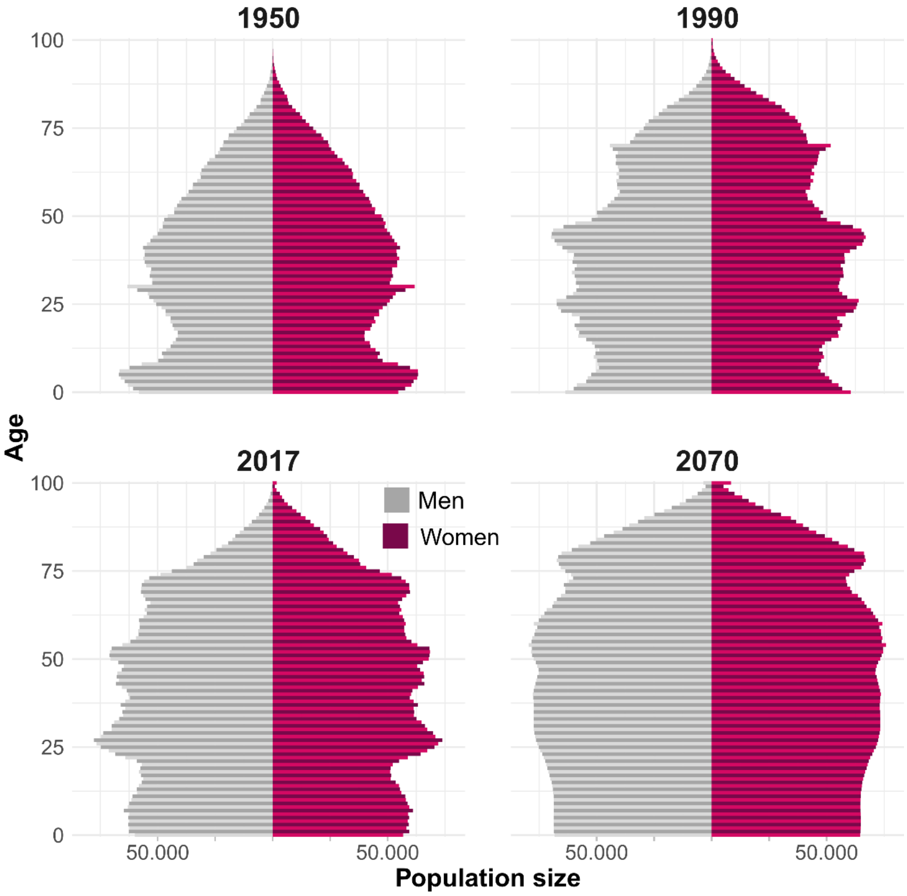

Figure 1: Population pyramids for the Swedish population 1950, 1990, 2017, and 2070
All ages above 100 are included in the highest age interval.
Data and projection from Statistics Sweden [23,25].

2.1.2 The importance of mortality improvements in old age for population ageing

Together with sinking fertility rates, declining mortality in old age is today the main driver of global population ageing. The demographic transition model is a (thus far) empirically well-supported model placing human populations on a continuum of progress ranging from a state with high mortality and high fertility to a state with low mortality and low fertility [26-29]. Most high-income countries, Sweden among them, are today in the latter stage of the demographic transition.

Historically, population ageing has been propelled by decreasing mortality at younger ages, primarily among infants and children. In the European and many other high-income countries, mortality in these age groups had already during the 20th century reached levels so low that they leave only limited room for improvements [30,31]. Old age mortality, on the other hand, continues to decline to the present day. Recent gains in life expectancy have been primarily driven by mortality improvements at older ages and even in most Western societies, old age mortality has not yet reached levels of today's vanguard populations in East Asia or Southern Europe (see also comparison of Swedish and Japanese survival curves in Figure 3) [30,32-34]. It is thus reasonable to assume that – at least in theory – mortality rates can be further reduced in the future.

2.1.3 Measuring mortality patterns in the population: Period and cohort perspectives

Mortality in a population can be measured and described in many ways. Epidemiological studies most often take on a cohort perspective, following a specified cohort over time. Survival curves, for instance the Kaplan-Meier estimator, can be used to visualize observed mortality patterns. Alternatively, survival proportions within defined time frames are often reported, for example during the first 30 days or the first 5 years of disease onset. These measures do not account for the age distribution of a population (or the distribution of other factors relevant for mortality such as sex) and, therefore, seldomly provide meaningful information when comparing different populations or when examining secular mortality trends. Stratification and standardization methods can be applied to facilitate comparisons between populations and to study secular trends, but still, these methods require to follow a study cohort over time. Especially when examining longevity and long-term survival, it is often not practical or feasible to observe a study cohort until all cohort members have died off.

Demographers often take on a period perspective to study population mortality. In contrast to observing a specific study cohort, the period perspective focusses on a population alive during a specific, cross-sectional time point. Figure 2 visualizes the difference between cohort and period perspectives in a Lexis diagram [28,35].

Period life expectancy – often simply called life expectancy – is a measure of population mortality that is calculated based on a period perspective. As such, it can be estimated even with short-term information, for instance data collected during a single year. Life expectancy therefore responds fast to external influences and can be used to describe very recent trends in population mortality, as has been done by several studies exploring the impact of the Covid-19 pandemic [36-38]. In addition, it is implicitly age-standardized and "translates" mortality rates into years of remaining lifetime – a measure that is easily interpretable even for lay people. Life expectancy is hence a frequently used indicator to describe trends in population mortality. Previous epidemiological research has also shown that period life expectancy can be used to estimate long-term survival chances of individuals with certain diseases, whereas observed survival rates in patient cohorts may provide an overly pessimistic scenario in times of steady mortality improvements [39-41]. However, life expectancy is also prone to being misunderstood because its estimation and underlying assumptions are not always known or understood by lay people, health scientists, or policy makers [42,43]. Most importantly, it is important to note that today's life expectancy does not represent the time people alive today are expected to live and it is neither the observed lifespan of a "real" historical cohort followed over time.

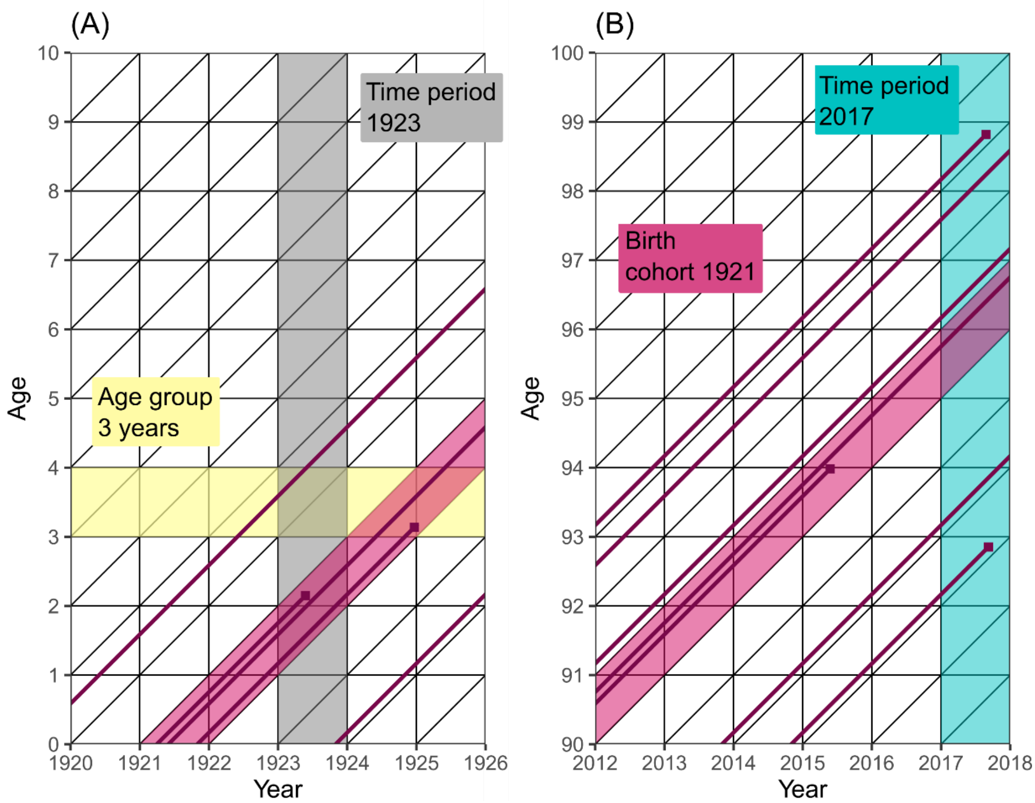

Figure 2: Period and cohort perspectives in the Lexis diagram
Lexis diagrams illustrate the relationship between calendar time (horizontal axis), age (vertical axis), and birth cohort (diagonal, moving through the diagram at a 45° angle) and are useful for understanding trends in incidence and mortality rates in a population.
Panel A depicts a Lexis diagram using the example of children aged 0-10 during 1920-1925. Five life-lines (purple) represent person-time contributed by five hypothetical individuals from their birth (intercept of x-axis) until they experience an event (denoted by diamonds) or until censoring (December 31st, 1925). **Panel B** shows a Lexis diagram for nonagenarians during 2012-2017. The birth cohort of 1921 is highlighted in both Panel A and Panel B (purple shading).
Period life expectancy is based on person-time at risk and events observed during a specific period (period life expectancy in 2017 is based on the area shaded in blue). Individuals contributing to life expectancy in 2017 are born at any time before 2017. The birth cohort of 1921 surviving until 2017 contributes person-time and events for the age groups 95-96 in 2017 (intercept of areas shaded in purple and blue).

Life expectancy is calculated using life table methods [44], a technique that also enables the calculation of a number of related indicators of population health. Lifespan variation is an indicator of the variability of ages at death in a population [16,45]. Lifespan variation increases if more individuals die at ages far below or far above life expectancy; it is thus a measure of inequality within the population. Years of life lost due to specific causes of death is another life table-based indicator, that is used to quantify the burden of certain diseases in the population [46-48]. Finally, indicators, such as healthy life expectancy, health expectancy, or disability-adjusted life expectancy, are summary indicators of both mortality and morbidity in a population [44,49,50].

2.1.1 Trends in mortality

2.1.1.1 Longevity and life expectancy

During the past century, life expectancy has increased by more than two years per decade in Sweden and in many other high-income countries [51-53]. During this time, increasing life expectancy was largely a result of decreasing mortality in younger ages; among children, in midlife, but recently also among the "younger old" (Figure 3).

Between 1990 and 2018, remaining life expectancy at age 65 in Sweden increased from 15.3 to 19.0 years among men and 19.1 to 21.6 years among women [51]. Nevertheless, few men and women continue to reach exceptionally high ages far above the average life expectancy [45,54,55]. Already in 1980 Fries noted that "the average length of life has risen from 47 to 73 years in this century, but the maximum lifespan has not increased" [10]. This has barely changed until today. Chances of survival among centenarians have remained fairly constant both in Sweden and globally although the number of centenarians has risen exponentially [55-57]. As a result, the age at death has become more homogeneous across the population resulting in declining lifespan inequality and a "rectangularization of the survival curve" (Figure 3) [16,45,54,55].

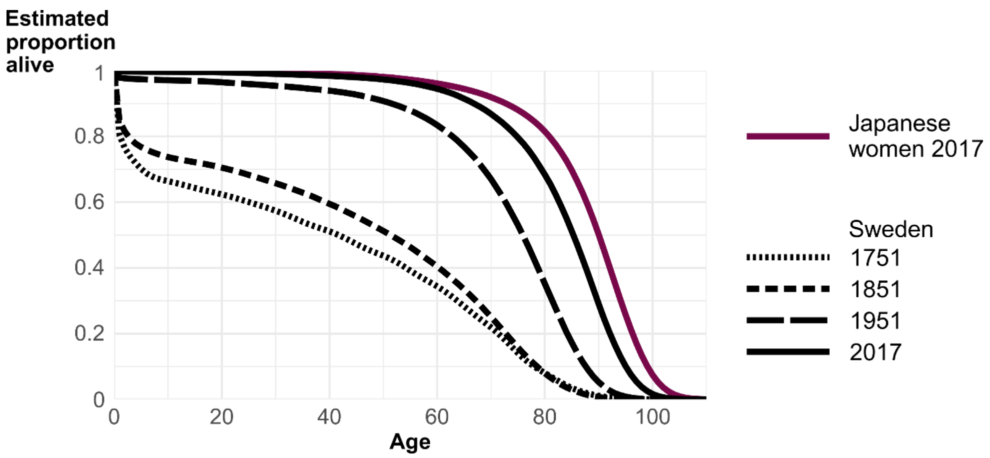

Figure 3: Secular trends in period survival in Sweden 1751 to 2017
Mortality rates were historically more evenly distributed across the life course. Today, almost the entire population is expected to survive beyond age 60 and the majority of deaths occur among octogenarians and nonagenarians ("rectangularization of the survival curve"). Japanese women shown as a low-mortality vanguard population.
Data from Human Mortality Database [58].

Life expectancy increases are projected to continue in large parts of the world including Sweden and most other high-income countries [33,46]. However, the practice to take continuous increases in life expectancy alongside declining lifespan variation for granted has recently been challenged. Covid-19 has hampered life expectancy gains at least temporarily [36-38] and it remains to be seen how the pandemic unfolds and how mortality patterns evolve during subsequent years. In some countries, most notably the United States and United Kingdom, life expectancy increases had already slowed down or even reversed during a few years before the pandemic [59-64]. To a large extent, these declines have been attributed to rising mortality among adults in working age and in early retirement age leading to increasing lifespan inequality in the population [16,59-64].

2.1.1.2 Subgroup-specific trends

Increasing lifespan variation prompts researchers to identify population groups that may be left behind as mortality improves. Gender differences are one prominent example of heterogeneity in the population. Women generally live longer than men [54,65], but the female survival advantage has decreased in many countries in recent decades including Sweden [66,67]. Numerous studies have also investigated the question of whether the increase in life expectancy has occurred at a similar pace across population groups distinguished by socioeconomic position, ethnicity, or geographical area [68-78]. Many of these found that socioeconomic disparities in life expectancy have indeed increased both in Sweden and other Western countries during recent years [68-74,76-78]. In addition, a few studies using data from the Nordic countries also indicated that inequalities may have increased even *within* some socioeconomic groups [16,79].

Fewer studies have moved beyond sociodemographic indicators to delineate population groups. However, the tentative finding of increasing lifespan inequality within socioeconomic groups suggests that inequalities in the population may be linked to characteristics that are more difficult to observe than education or income, such as underlying biological and health profiles or more intricate factors associated with one's socioeconomic position. A few previous studies suggested that improvements in health have been driven by advances at the upper end of the health distribution while other parts of the population have lagged behind [80-82]. Some studies have also explored trends in life expectancy among population subgroups who had experienced specific diseases in comparison to life expectancy trends in the general population. These studies yielded mixed results; while some found narrowing gaps between life expectancy in the general population and among subgroups with a history of disease [83-85], others reported persistent gaps for subgroups with diseases such as type 1 diabetes, schizophrenia, or lung cancer [48,84,86].

2.1.1.3 Cause-specific mortality and disease survival

The most common causes of death in Sweden during the past 30 years were CVD and cancer which in the year 2000, for instance, accounted for 70% of all deaths in Sweden [34,87,88]. Improvements in survival with CVD and many kinds of cancer during this time frame have been well documented in Sweden and in other high-income countries [89-96]. Many studies demonstrated that these improvements were not limited to case-fatality or short-term survival [90,92,93,95-98]. Allemani et al. showed in *The Lancet* that 5-year survival proportions increased between 1995 and 2014 for most types of cancer including colon-, rectal-, female breast-, cervical-, prostate-, lung-, pancreatic-, liver-, and brain cancer both in Sweden and many other countries globally [89]. As a result, declining mortality rates from cancer and CVD were among the primary contributors to rising life expectancy worldwide [32,34,99,100].

While mortality rates improved significantly for CVD and cancer, other causes of death became more common. In Sweden, age-standardized mortality from neurodegenerative diseases, chronic respiratory conditions, and fall injuries has increased since the 1990s [87]. These increases are probably partly promoted by the substantially declining mortality rates from the most common cause of death, CVD, which is an important competing risk for deaths from other conditions. This suggests that trends in cause of death statistics might not necessarily correspond to patient survival. In fact, survival with neurodegenerative diseases such as dementia has increased in Sweden [101]. On the other hand, survival after hip fracture has remained remarkably stable during the past decades despite increasing life expectancy [102-106]. Hip fractures are one of the most severe fall injuries among the old and mortality remains high with up to 30% of patients dying within one year of sustaining a hip fracture [107-109]. A number of studies have attributed the persistently high mortality rates among affected individuals to increasing comorbidity levels [102-105]. However, this raises the question of why survival rates have increased markedly for other conditions, such as myocardial infarction and stroke, for which rising comorbidity levels have been reported [93,95,98], but not for hip fractures.

2.2 HEALTH AND MORBIDITY IN THE AGEING POPULATION

2.2.1 Measuring health and morbidity

Since health is more than the absence of disease, a variety of indicators can be employed to describe a person's health status [7,110]. Besides the presence of disease, these include, but are not limited to, functional limitations in daily life, care-dependency, frailty, self-rated health, or quality of life [111]. In addition, there are numerous indices that combine different risk factors, diseases, or other health-related measures into a single indicator. Two examples are the Gilbert frailty index and the Charlson comorbidity index (CCI) [112-116], both of which are weighted indices of a number of specific diseases identified in routinely collected hospital admission data.

Owing to the diversity of indicators to measure individual health, there are also numerous measures that can be used to describe morbidity on the population level. These indicators include incidence rates, cumulative incidence, or the prevalence of diseases, disabilities, frailty, or multimorbidity in the population. Health expectancy and disability-adjusted life expectancy are further morbidity measures that are based on life table techniques. Depending on the studied measure, trends in disease occurrence sometimes point in different directions and the choice of outcomes can thus support different conclusions about population health. For example, the increasing prevalence of a type 2 diabetes in Sweden [117-119] could be brought forward as evidence for increasing morbidity. Yet, diabetes incidence has declined [117,119] and the rising prevalence is hence the result of improved survival with diabetes. Some individuals may also perceive themselves as healthy even though they live with several well-controlled chronic diseases. Therefore, different measures of disease frequency should be used in conjunction to present a comprehensive picture of changing morbidity patterns in the population.

2.2.2 Trends in population morbidity

2.2.2.1 Disease occurrence

Although trends in the prevalence of specific diseases vary, some researchers conclude that disease prevalence among the old is increasing in high-income countries [30,120]. It is assumed that this increase partly reflects actual changes in the prevalence of chronic conditions but also improved diagnostic sensitivity and awareness leading to an increased or earlier detection of disease [30]. In Sweden, increasing prevalence has been reported for many types of cancer – a logical consequence of increasing incidence rates and improved survival [89,121-125]. Even though the evidence is not unanimous, dementia incidence seems to decline in several Western countries in recent decades [126,127]. In Sweden, one study suggests decreasing incidence and stable prevalence between 1987 and 2004 based on data from repeated cross-sectional measurements [101]. Other survey-based studies found a decreasing prevalence of dementia during the same time period [128,129]. Yet another study analysed data from the Swedish National Patient Register and found increasing incidence rates of dementia diagnoses between 1987 and 2011 and a moderate decline thereafter [130]. These examples illustrate the importance of data sources used to estimate disease incidence and prevalence.

The incidence of two of the most severe manifestations of CVD, myocardial infarction and stroke, declined substantially during the past decades with up to 50% in some age groups [93,96,97,123,131-135]. These declines have even been large enough to considerably reduce the yearly number of myocardial infarctions and strokes occurring in Sweden despite an ageing and growing population [123,132,134,135]. Hip fracture incidence, too, has declined in Sweden and in many other countries albeit to a smaller extent [102,136-142]. As a consequence of population ageing, many researchers still expect growing numbers of hip fractures in the future [137,139,143,144]. In contrast, the incidence of many common kinds of cancer, including prostate-, colon-, and skin cancer, as well as lung- and breast cancer among women, has increased which – together with improved survival – naturally results in increasing cancer prevalence [121-124].

2.2.2.2 Multimorbidity and disease recurrence

Longer lives and improved survival with many diseases likely result in a higher risk of attaining more than one long-standing illness. Multimorbidity, the presence of several diseases at the same time, is an increasingly common issue in ageing societies. Multimorbidity is usually defined as the co-occurrence of at least two chronic conditions, but operationalizations vary between studies [145]. The choice of data sources, too, impacts the prevalence of multimorbidity reported in studies [145-147]. As a result, prevalence varies greatly between studies, but it is likely that the majority of older individuals in Sweden can be classified as multimorbid [148-150].

Changing diagnostic criteria and procedures further limit the comparability of multimorbidity assessments over time [151]. Nevertheless, a large number of studies provide strong evidence for an increasing prevalence of multimorbidity among the old in several Western countries since the 1990s [150-159], Sweden among them [150,155,159]. However, one Swedish study suggests that the prevalence of multimorbidity, albeit rising until 2002, stabilized between 2002 and 2011 [159].

Increasing risks of recurrent acute disease events are another potential consequence of improved survival with disease. However, several studies show declining recurrence rates for stroke, myocardial infarction, and other coronary heart events in the past 30 years [132,160,161]. Evidence on trends in the incidence of recurrent hip fractures is sparse and hence less conclusive. One Norwegian study examined the incidence of second hip fractures between 1999 and 2008 and found a stable incidence of second fractures during this time frame [162] while Melton et al. observed somewhat declining incidence rates of second hip fractures between 1980 and 2016 in the United States [163]. So far, there is, to my knowledge, no evidence on trends in recurrent hip fracture risks in the Swedish setting. However, since recurrent events can have debilitating consequences and may in many cases be avoidable through targeted tertiary prevention programs, monitoring and understanding patterns in disease recurrence should be one objective of epidemiological research on population ageing.

2.2.2.3 Subgroup-specific disease trends

Changes in morbidity indicators do not necessarily occur at the same pace – or in the same direction – across different population groups. The example of hip fracture incidence, for instance, highlights the need for considering heterogeneity within the population. While the incidence of hip fractures has declined throughout the past decades, improvements were less pronounced among men than among women [104,109,139,141,142,144,162,164-171]. In fact, some studies indicate that men did not experience any declines in hip fracture incidence in the Nordic countries [104,109,171]. Most, but not all, studies also suggest that hip fracture incidence has decreased most considerably in younger age groups while older men and women have not experienced such progress [141,143,167,169,172,173]. A similar pattern has been reported for stroke incidence in Sweden, where improvements were found among younger age groups but not among the oldest old over the age of 90 [132].

Previous research distinguished most commonly between population strata defined by gender, socioeconomic position, geographical area, or ethnicity. For instance, although mortality is lower among women, several studies have reported higher a prevalence of many diseases, multimorbidity, and disability among older women than among older men [30,53,101,122,149,157,159,174-180]. Socioeconomic position has been associated with a wide range of morbidity outcomes in old age such as self-rated health [181], age at first hospital admission [182], cardiovascular morbidity [183] or fracture risk [184] and some studies suggest that these inequalities persisted throughout the past decades and exist even in the Nordic countries in which socioeconomic disparities are comparatively small [181-183,185].

The impact of heterogeneity with regards to latent characteristics on trends in population level outcomes has been studied less frequently. As mentioned earlier, several studies indicate that the persistently high mortality after hip fracture can be attributed to rising comorbidity levels among patients [102-105]. These studies further suggest that mortality after hip fracture has declined when adjusting for patients' higher comorbidity levels. This illustrates how a changing population composition, in this case increasing shares of individuals with comorbidities, may influence trends observed in the total population.

2.2.3 Compression or expansion of morbidity?

Already in 1977, Gruenberg published the failure of success hypothesis suggesting that medical progress has enabled increasingly frail individuals to reach higher ages [186]. As a counterpoint, Fries proposed the compression of morbidity hypothesis, arguing that increasing life expectancy is accompanied by a postponement of disease onset and, therefore, shorter durations spent in compromised health [10]. The multidimensionality of health and complexity of measuring morbidity do not allow to draw conclusions about whether morbidity has been compressed or not. Instead, it is likely that the increasing life span has been accompanied by both expansion and compression of morbidity, depending on the specific disease and morbidity measure under study.

While studies on disease prevalence and multimorbidity often point towards increasing durations spent with disease, morbidity compression can be found for other health indicators [11,12,82,120,152,155,187-190]. Studies from Sweden, for example, suggest that self-rated health has become better and that the number of functional limitations and disabilities among the Swedish old has declined over time [80,81,155,191], although one study found a stable prevalence of disability between 1991 and 2010 in octogenarians and nonagenarians in Stockholm [82]. Some of these studies also reported trends towards better subjective health despite increasing numbers of chronic diseases or long-term health problems [80,155] as well as progress in perceived age of older individuals [111]. This highlights the distinction between perceived and objectively measured health when interpreting time trends in morbidity. Modern treatments and assistive aids may have, in many instances, improved individuals' perceived health and independence despite the presence of certain diagnoses.

2.3 GERIATRIC CARE USE

2.3.1 Long-term care for older individuals in Sweden

Care for older individuals is an important aspect of population health in ageing societies. Not only can population ageing put increasing pressure on publicly funded geriatric care systems, the provision of adequate care is also of utmost importance for older individuals' wellbeing and the wellbeing of their close kin. In Sweden, long-term care provided by the municipalities constitutes more than 90% of formal geriatric care [192-194] and is used by the majority of Swedes at the end of their life [195]. Publicly funded care resources are allocated based on needs and heavily subsidized [193,196-198]. Depending on their financial capacity to contribute, older individuals contribute small fees that are deemed affordable or receive care free of charge. To allow older individuals to "age in place", care is preferably provided in the form of home care services. Only when a person's needs can no longer be met in their own home, they are transferred to care homes. Although the uptake of privately paid elder care has been increasing, so far, few older individuals purchase services on top of publicly financed care [192-194,199].

2.3.2 Trends in care use among the Swedish old

In Sweden, population ageing is paralleled by structural changes in health and elder care [192-194,196,199-203]. A growing proportion of older individuals lives at home rather than in institutions, and hospital stays have become fewer and shorter [192-194,196,200-203]. The age at first hospital admission has become higher [188] and the proportion of individuals without any hospital admission in the older population has increased [187]. This may indicate declining care needs or that treatments and care processes have become more efficient. In some instances, however, reductions in care may also have serious consequences including a higher risk of death among patients [204,205].

Even though functional status has improved among the old, several studies have shown that that publicly provided home care cannot completely compensate for the lack of care previously provided in institutions. As a result, family members take on increasing amounts of care for their ageing relatives [192,193,196,200]. This implies increased pressure for family members and a potential care deficit among older men and women without close kin. Since social isolation and loneliness are well-established risk factors for mortality [206-209], and living alone as well as childlessness are becoming more common, older men and women without close family may require more support today and in the future. This stands in contrast to an increasing shortage of staff in Swedish health and elder care [210,211].

Little is known about the distribution of geriatric long-term care in the older Swedish population and about the health determinants of care utilization. However, the distribution of such care and its consequences are of utmost importance for older individuals, their families, for health and care workers and for policy makers alike. Although publicly funded municipal care represents the vast majority of geriatric care in Sweden, it has only been recorded since 2007 in the Swedish Social Service Register (SSR). It is known that data quality was poor in the early years of the register but has improved more recently [195,212,213]. Thus far, only few studies have used its data and because of this, evidence on secular trends of geriatric care use in the ageing population is largely limited to survey data. Such data may not always be representative and is oftentimes restricted to specific population groups, for example community-dwelling individuals [199].

2.4 DETERMINANTS OF HEALTH IN AGEING POPULATIONS

2.4.1 Dahlgren and Whitehead’s model of health determinants

Epidemiology has linked a plethora of factors to individuals’ health and mortality. Dahlgren and Whitehead’s model of social determinants of health summarizes many of these factors in a comprehensive manner [214,215]. Shown in Figure 4, the model illustrates that individual health is shaped by several layers of determinants ranging from individuals’ characteristics and their behaviours on the micro level to overarching societal and environmental conditions on the macro level. Its "rainbow" shape depicts how some layers are embedded in others. Socio-cultural, economic and environmental factors shape living and working conditions. Individual behaviors are embedded in social networks, which in turn are influenced by education, working conditions, access to resources, housing, and the greater environmental context [215]. Dahlgren and Whitehead emphasize that – while age, sex, and individual factors such as genetics at the center of their model are largely fixed – other health determinants are modifiable through policies and interventions [215,216]. As such, research on these factors may contribute to developing public health measures that promote health and reduce social inequalities in the population.

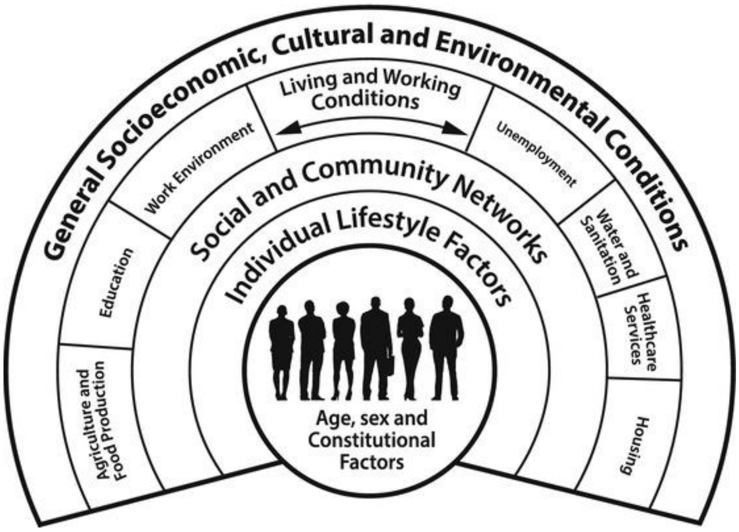

Figure 4: Social determinants of health
Source: Dahlgren and Whitehead 1991 [214].

2.4.2 The life-course perspective

Health and mortality risk in advanced age are shaped during the entire life-course [9,217-226]. The present project includes studies on hip fractures, CVD, and cancer. All of these diseases do not occur spontaneously; osteoporosis, ischemic heart disease, and cancer risk typically develop over the course of decades. Epidemiologists acknowledge the importance of critical and sensitive periods in life, that is, ages at which exposures may have a disproportionately large impact on later health outcomes [9,217-220,222-225]. These periods may predate the manifestation of disease by decades. For instance, adolescence as well as reproductive periods have been linked to bone mineral density in later life and may hence be particularly important life stages determining fracture risk in older women [227-230].

Circumstances and achievements in early life affect lifelong health trajectories. Even though education is usually attained in early adulthood and thereafter fixed, it may launch the accumulation of risk factors throughout the whole life course [224,231]. Higher education may not only have a direct effect on individual health through greater knowledge about risk factors or health literacy but is also associated with life-long income, living and working conditions, and access to resources through wealthier social networks which can all exert a positive influence on health. Higher educational attainment in adolescence and young adulthood may thereby manifest as cumulative advantage throughout the life-course [224,231].

Investigating health in old age thus requires taking on a life-course perspective and taking into account historical developments during older individuals' entire life span. Environmental and political factors, societal norms, access to information, and healthcare are constantly evolving and influence individuals' health and behaviors in the process. Marital status among todays' 80-year-olds is partly determined by economic conditions, political systems, and cultural norms since the mid 19-hundreds. Educational achievement is a result not only of one's own ambition as a young adult but also access to education and social or economic incentives associated with it. Owing to the substantial educational expansion throughout the past century the effect of a given educational level on health outcomes may hence differ between birth cohorts.

2.4.3 From individual to population-level health

Dahlgren and Whitehead's model of health determinants and the life-course perspective are valuable tools to understand individual health outcomes in old age. However, the relationship between individual health outcomes and observations on the population-level is not always straightforward. Since the composition of the ageing population is constantly changing, this relationship is important to consider when studying temporal trends in population health.

Most diseases are more common among some population groups than among others. As a result, a changing population composition affects morbidity and mortality patterns observed in the total population [232]. One example is the shifting gender distribution among older individuals. In Sweden and many other countries, the number of older men is currently growing faster than the number of older women because male life expectancy is improving at a faster pace than that of women [233]. At the same time, the educational expansion and shifting migration patterns have also altered the sociodemographic population composition. Changes with regards to observable factors are accompanied by changes in unobservable heterogeneity, for example with regards to latent biological and risk-profiles that differ between individuals [234,235]. Some examples are a genetic predisposition for certain health outcomes, malnutrition, or the prevalence of other risk factors such as high blood pressure and osteoporosis.

Identifying underlying mechanisms behind health trends observed in the general population entails the methodological challenge to disentangle age, period, and cohort effects. Medical advances in treatment and prevention, epidemics, or heat waves are exposures affecting the entire population alive at a specific time (period effects). However, certain birth cohorts may also experience such events or other environmental circumstances during sensitive periods of their life (cohort effects). Statistical methods have been developed to solve the so-called identification problem of age-period-cohort analyses that arises due to the perfect correlation between age, time period, and birth cohort [236,237]. However, these methods are not always applicable. Considering both cohort and period perspectives to population health may be particularly valuable when monitoring population health despite the dynamically changing population composition.

2.5 RESEARCH GAPS

This thesis addresses a number of gaps in ageing research that have been outlined in the sections above. While the rise in life expectancy during past decades is well-documented, most epidemiological studies estimate survival rates following a *real* cohort of patients, and only a few utilize period life table techniques. This results in limited comparability with life expectancy in the total population and a limited ability to capture recent trends in disease survival beyond the acute phase. A few studies have estimated trends in remaining life expectancy with certain diseases but none have, to my knowledge, examined trends in remaining life expectancy for populations with a history of hip fracture, CVD, or many kinds of cancer – at least in the Swedish setting. However, these diseases constitute a large part of the disease panorama among the old [34,143].

Changing patterns of disease incidence, prevalence, and survival also raise the question of how individuals who experience these diseases contribute to trends in life expectancy on the population level. On the one hand, improved survival with disease may have a positive effect on life expectancy. On the other hand, increasing survival of individuals with disease could also have a negative impact on life expectancy in the total population.

Comprehensive pictures of disease incidence and survival in the total older population and in different population strata have also not been presented for many conditions. This thesis focuses on hip fractures specifically, an enormous threat to public health in the Nordic countries, where one in five women is expected to sustain a hip fracture during their life [143]. Hip fracture incidence differs between ethnic as well as socioeconomic groups [140,184,185,238-251] but little is known about secular trends in these population strata or in population strata defined by health status. Yet, it is known that comorbidity levels among hip fracture patients are rising. Exploring hip fracture risk and survival among groups with different comorbidity levels may hence provide valuable insights into hip fracture epidemiology today and in the future [109,252,253]. In addition, few studies have examined trends in hip fracture recurrence rates, perhaps partly since large-scale representative data is often not available and recurrent disease events may be challenging to assess in secondary data. Finally, little is known so far about the distribution of geriatric long-term care in Sweden, its determinants, and its utilization across population groups.

3 RESEARCH AIMS

Building upon national population registers, this doctoral project concerns the changing mortality and morbidity patterns in the ageing Swedish population during the past 30 years. It focuses on ageing on the population level, integrating both epidemiological and demographical approaches. Together with my co-authors, I examine secular trends in disease incidence and mortality, as well as geriatric care among the old while highlighting heterogeneity within the population and thereby exploring how a changing population composition may affect population health.

In five studies, this project aims to

(i) examine whether the remaining life expectancy of older adults who have experienced common and severe diseases has improved at a pace similar to that of the general population and whether trends varied across individuals with different educational or comorbidity levels (Study I).

(ii) investigate how improved survival for major diseases has contributed to gains in general life expectancy in Sweden, and whether these gains have been offset by increases in disease prevalence (Study II).

(iii) compare the Swedish Hip Fracture Register (SHR) and hip fracture data in the National Patient Register (NPR) regarding coverage, agreement and representativeness thereby gaining insights into how to measure disease incidence and recurrence in administrative population registers (Study III).

(iv) present secular trends in hip fracture incidence and mortality and explore whether trends have developed in a similar pattern among individuals with different educational and comorbidity levels, as well as among individuals with migration background (Study IV).

(v) examine the impact of hip fractures on long-term geriatric care, living arrangements, and mortality and to explore the association of several factors with care use, living arrangements, and mortality among hip fracture patients (Study V).

4 MATERIALS AND METHODS

4.1 DATA

4.1.1 Swedish population registers

Sweden has a long history of civil registration dating back for more than 250 years [254]. Today, there are a variety of Swedish administrative population registers providing a rich pool of data that is accessible for research [254,255]. Owing to the unique personal identification numbers assigned to each resident in Sweden, all population registers can be linked to each other and to many other databases and surveys. Any person who legally resides in Sweden for at least one year receives a personal identification number and is thereby included in population registers regardless of their citizenship [255]. Record linkage is conducted by Statistics Sweden and data is handed out to researchers after ethical vetting and in pseudonymized form.

Population registers are invaluable for research on trends in population ageing because they cover virtually the entire population. Since administrative population registers are not created for research purposes, however, they have some limitations. While some diseases can be studied exceptionally well with administrative registers, others are more difficult to examine [256,257]. Furthermore, many “softer” health indicators, such as self-rated health or functional limitations in daily life, cannot be assessed in administrative data. Population registers also lack detailed medical information necessary for many research questions. Because of this, several disease-specific quality registers containing more comprehensive medical information and health indicators have been established. These quality registers contain individualized data about patients’ characteristics, medical treatment, and procedures. Today, there are more than 100 national quality registers in Sweden [258]. In contrast to administrative registers, reporting to quality registers is not mandatory. Clinicians or hospitals can choose not to report to the quality registers, and patients can opt out of being registered. Therefore, quality registers vary in degree of coverage and generalizability [259,260].

4.1.2 The Ageing and Health Cohort

All studies in this thesis are based on the Ageing and Health Cohort (AHC), a comprehensive cohort created through linkage of several Swedish population registers. The AHC contains data on all men and women born between 1890 and 1950 who legally resided in Sweden at any point after their 60^{th} birthday regardless of their birth country or citizenship (index persons). In addition, the AHC includes spouses and children of index persons. Although this does not encompass the entire Swedish population born after 1950, the AHC even covers the majority of the population born after 1950 because most are either a spouse or a child of an index person. The AHC today includes data on more than ten million people with follow-up information until the end of 2017 except for data in the Cancer Register, which was available up to the end of calendar year 2016. Table 1 displays the registers used in each study and the variables retrieved from each register. A more detailed description of the registers central to this thesis is given in the following section.

Table 1: Data sources and variables used in Studies I to V

	Measurement interval	Variables	Study I	Study II	Study III	Study IV	Study V
Total Population Register (RTB)	yearly, monthly or daily (depending on variable)	• birth date • gender • migrations • birth country • civil status	Studies I – V				
National Patient Register (NPR)	daily	• disease diagnoses: hip fracture, myocardial infarction, stroke, dementia • Charlson comorbidity index • Gilbert frailty index • mode of hospital admission	Studies I – V				
Cause of Death Register (CDR)	daily	• date of death • cause of Death	Studies I – V				
Cancer Register	daily	• cancer diagnoses: Breast-, colon-, lung cancer	Studies I + II				
Social Service Register (SSR)	monthly	• home care hours • care home residence					Study V
Swedish Hip Fracture Register (SHR)	daily	• hip fracture diagnoses			Studies III – V[a]		
LISA	year	• education	Study I			Studies IV + V	
Population and Housing Censuses	5-year intervals	• education	Study I			Studies IV + V	
Dwelling Register	yearly	• cohabitation					Study V

[a] used in sensitivity or additional analyses but not in final paper of Studies IV and V.
LISA: Longitudinal Integrated Database for Health Insurance and Labour Market Studies.

4.1.2.1 Total Population Register

The Total Population Register (Registret över Totalbefolkningen, TPR) was established in the 1960s and has since recorded data on all individuals registered in Sweden [255]. The register includes information on each person's sex, birth date, birth country, civil status, place of residence, and migrations [255,261]. For this project, dates of immigration and emigration were available on a daily basis, birth dates on a monthly basis, and all other variables in the TPR on a yearly basis reflecting the population as of December, 31st.

The coverage and data quality of the TPR is estimated to be high and basic quality control measures, for instance the identification of missing or contradictory data, are in place at Statistics Sweden [255,261]. However, some limitations have to be considered when studying migrants [255]. Unregistered immigrants or individuals staying in Sweden for shorter time periods are not included in the registers, but these represent a presumably small part of the old-aged population. Over-coverage of migrants may be a somewhat larger issue for epidemiological research on older people. Individuals who do not report emigration to authorities are retained in the TPR and thus contribute person-time but their deaths, hospitalizations, or other outcomes are not registered. As a result, these individuals may appear immortal and healthier than they are. Swedish authorities audit each person over the age of 100, but these audits are not conducted on a continuous basis [255]. It is estimated that over-coverage due to emigration is approximately 0.1% among individuals born in the Nordic countries but substantially higher among those born elsewhere [255]; in total, Statistics Sweden estimated an over-coverage of 0.6% in 2018 [261]. Finally, although ten-digit personal numbers are unique among individuals who are alive, they are sometimes re-used, for instance for immigrants, after an individual has died. The TPR specifies whose personal number has been re-used so that these people can be excluded of studies if necessary. These limitations should be kept in mind when examining migrant health specifically.

4.1.2.2 National Patient Register

First established in the 1960s, the National Patient Register (NPR), contains data on all hospitalizations within Sweden since 1987 [256]. Reporting to the NPR is mandatory for all hospitals and the register collects data on hospital admission and discharge dates, surgical procedure codes, primary and secondary diagnosis codes for each admission assigned by physicians, as well as some other variables [256]. Diagnoses are coded according to the ninth revision of the Swedish international classification of disease system (ICD-9) from 1987-1996 and according to the tenth revision (ICD-10) from 1997 onwards. Surgical procedure codes are registered according to the Swedish version of the Nordic Medico-Statistical Committee Classification of Surgical Procedures (NOMESCO) [262] since 1997.

Depending on the disease under study, the completeness and validity of diagnoses in the NPR ranges from poor to excellent [256]. The register provides high coverage for diseases that almost always require hospitalization and are often accurately diagnosed. Estimating disease incidence and survival rates requires reliable information on the date of disease onset. Admission dates in the NPR correspond well with these dates for diseases that are acute and require immediate hospital care. Hip fracture, myocardial infarction (MI), and stroke are examples for diseases that can be studied exceptionally well in hospital discharge registers [256,257,263]. In accordance with this, the sensitivity and validity of these diagnoses in patient registries of other Nordic countries have been shown to be high [257,264-270]. Previous research has also estimated positive predictive values (PPV) exceeding 95% for stroke, myocardial infarction and hip fracture diagnoses in the Swedish NPR specifically [256].

4.1.2.3 Cause of Death Register

Sweden has registered causes of death since 1751. Digitalized death records are available in the Cause of Death Register (CDR) from 1952 onwards [18,254]. The CDR contains data on date and cause of death for all individuals registered in Sweden [18]. Causes of death are coded according to ICD-9 during 1987-1996 and ICD-10 from 1997. In contrast to the NPR, the CDR uses the international rather than Swedish versions of the ICD classification, but both versions are largely similar [18]. Deaths of individuals registered in Sweden that occurred abroad are also included in the CDR. In addition, even if no death certificate was completed, all deaths reported to authorities are included in the CDR. It is therefore considered virtually complete and underlying causes of death are missing only for a negligible proportion of records [18].

The validity of assigned causes of death, however, depends on clinicians and on resources, for instance to conduct autopsies. Especially among the old, reported causes of death do not always correspond with causes that would have been assigned through gold standard methods [18,271]. A Swedish study found a general accuracy of death certificates of 77% in 1995. However, this study was not based on a random sample but on a selection of individuals with discrepant hospital and death records, therefore probably underestimating accuracy to a large extent [271]. Regardless of whether or not this number may be generalizable to the entire Swedish population, the validity of data has been shown to be higher for some causes of death including heart disease and cancer than for others, such as chronic obstructive pulmonary disease or pneumonia [271].

4.1.2.4 Cancer Register

The Swedish Cancer Register, founded in 1958, is a nationwide register recording all malignant as well as certain benign tumors [272]. Because reporting to the Swedish Cancer register is mandated by law, the register has an estimated completeness exceeding 95% [272]. All cancers including their tumor characteristics diagnosed through clinical examinations, laboratory tests, and autopsies are reported to the register. Since 1993, the Cancer Register records tumors using International Classifications of Diseases for Oncology (ICD-O), an extension of the ICD framework to include tumor characteristics [273]. In addition, in order to increase comparability of data over time, the cancer register includes ICD-7 codes from its establishment in 1958 to the present day [273]. Owing to lags in reporting and quality assurance, the Cancer Register was available until the end of 2016 in contrast to all other population registers which were available until the end of 2017.

4.1.2.5 The Social Service Register

Each municipality in Sweden is legally obligated to provide care for all older individuals in need according to the Social Service Act. The Register for Municipal Care of the Old and Functionally Impaired (*Registret över insatser till äldre och personer med funktionsnedsättning enligt socialtjänstlag*), in short Social Service Register (SSR), contains data on such care. The register records information on older individuals' care home admissions as well as publicly funded home care and home help services on a monthly basis since 2012 [197,213]. Available information includes care home residence, the number of granted home care hours and the kind of support provided by home care services. The SSR covers all publicly funded care, regardless of whether home care or care homes are operated by the municipalities themselves or by private contractors. Care paid entirely out-of-pocket is not included in the SSR. Basic quality control measures, for instance the identification of missing or contradictory data, are in place at the National Board of Health and Welfare and municipalities are contacted to complete or correct their data if necessary. However, previous research has shown that not all municipalities reported to the register consistently [197,213]. Thus, depending on the study period and research question, researchers should consider excluding some municipalities when using SSR data.

4.1.2.6 The Swedish Hip Fracture Register

Sweden was the first country to implement a national quality register for hip fractures in 1988 [274]. Today, the Swedish Hip Fracture Register (SHR), RIKSHÖFT, contains data on more than 300,000 hip fractures, including patients' health status, fracture type, surgery method, and outcomes at a follow-up assessment four months after the fracture [274]. Even though the SHR has been used frequently in hip fracture research, no study has thoroughly assessed its data quality. The National Board of Health and Welfare reported that in 2015, approximately 97% of hip fractures in the SHR could be found in the NPR [275]. Vice versa, 87% of fractures in the NPR also occurred in the SHR [275]. While this indicates an excellent degree of completeness in the NPR, it is not known whether patients who are registered in the SHR differ from those who are not, for instance regarding their sociodemographic characteristics, fracture types, or survival chances.

4.1.2.7 Other population registers

Data on education was retrieved from the Longitudinal Integrated Database for Health Insurance and Labour Market Studies (*Longitudinell Integrationsdatabas för Sjukförsäkrings- och Arbetsmarknadsstudier*, LISA), which contains data on education, income, civil status and other sociodemographic variables on a yearly basis since 1990 [276]. Since educational levels in LISA are not recorded for some retired individuals, highest attained education was also identified in the population and housing censuses (*Folk- och bostadsräkning*; FoB) conducted in 5-year intervals between 1960 and 1990. Education in LISA and the censuses is coded according to the SUN2000 nomenclature (Svensk utbildningsnomenclature) which can be translated to the International Standard Classification of Education (ISCED). The Dwelling Register was used to identify cohabiting individuals. It is available on a yearly basis since 2011 and allows to identify all individuals who are registered in the same household.

4.2 STUDY BASE

4.2.1 Study I

Study I included all individuals over the age of 65 in the AHC who were alive and residing in Sweden at any point during the 20-year period between 1998 and 2017. This allowed for a minimum of 11 years since the nationwide implementation of the NPR in 1987 to trace back a person's disease history. Individuals entered the study at their 65th birthday and were followed until death, emigration, until they were lost to the registers (i.e., until they could no longer be found in the annual registers although no death or emigration was recorded), or the end of follow-up on December 31st, 2017, whichever came first. Individuals migrating internationally after their 60th birthday were censored at the date of their first migration since it was not possible to observe their complete disease history.

In addition to the total population, several disease-specific subpopulations were examined in Study I. Based on diagnoses in the NPR and Cancer Register, we identified populations with a history of seven different diseases: Myocardial infarction, ischemic stroke, hemorrhagic stroke, hip fracture, colon cancer, lung cancer, and breast cancer, the latter being examined among women only. Individuals entered these disease-specific subpopulations at the date of their first disease occurrence in the NPR, Cancer Register, or CDR, even if dating back further than 1998. Each disease was selected separately, meaning that individuals could belong to more than one disease group. The total population included all individuals registered in Sweden regardless of whether or not they experienced any of the included diseases. As such, each disease-specific subpopulation was part of the total population.

4.2.2 Study II

Study II included all individuals over the age of 60 in the AHC who were alive and residing in Sweden in 1994 or 2016. This study period allowed for a washout period of at least 7 years with nationwide coverage of the NPR in order to identify previous disease diagnoses. While in Study I, life expectancy was estimated for each year during the study period, Study II conducted decomposition analyses comparing the single years 1994 and 2016. To facilitate comparisons of cancer – for which data was available until 2016 – with other diseases, we did not use data from the year 2017 in Study II.

Study II distinguished between five diseases: myocardial infarction, stroke, hip fracture, colon cancer, and breast cancer, the latter being examined among women only. Unlike in Study I, ischemic and hemorrhagic strokes were grouped together, since the diagnostic accuracy of assigning stroke subtypes increased substantially over time. For the methods used in Study II, a reliable measurement of prevalence in the population is essential. Since diagnoses of "unknown stroke subtype" were more common in 1994 than in 2016, the prevalence of ischemic and hemorrhagic strokes is probably underestimated in earlier years. Furthermore, owing to the small number of individuals with a history of lung cancer, we excluded lung cancer from Study II.

For each of the five diseases, we distinguished three further subpopulations: Recent cases, distant cases, and the disease-free. Individuals contributed person-time to the disease-free population until their first disease diagnosis in the registers. For myocardial infarction, stroke, and hip fracture, individuals contributed person-time to recent cases for three years after their first diagnosis in the NPR and thereafter entered the population of distant cases. For the cancer populations, recent and distant cases were defined as individuals with their first cancer diagnosis up to five years ago and those with their first diagnosis further back in time. Disease populations were studied independently from each other; one person could, for instance, belong to the recent cases of stroke, distant cases of colon cancer and the hip fracture-free population at the same time. Individuals were followed until death, emigration, loss to follow-up, or the end of the study period, whichever came first.

4.2.3 Study III

Study III included all individuals over the age of 60 in the AHC between 2008 and 2017 and compared groups of hip fracture patients identified in the NPR to records in the SHR using various further inclusion criteria.

4.2.4 Study IV

Study IV included all individuals over the age of 60 in the AHC living in Sweden at any point between 1998 and 2017 excluding those with prior hip fracture since 1987 in the NPR. The total population (without prior hip fracture) was followed to measure incidence rates of first hip fracture. To measure the incidence of recurrent (i.e., second) hip fractures, individuals were followed from 14 days after hospital admission for their first hip fracture. We also followed all individuals with hip fracture to measure mortality. Survival proportions were assessed at 30 days and at 365 days after hospital admission for the first hip fracture. All individuals were followed until the outcome (first hip fracture, recurrent fracture, or death), emigration, loss to follow-up, death or the end of follow-up on December 31st 2017, whichever came first.

4.2.5 Study V

All individuals in the AHC aged 65 and older with their first hip fracture during 2014 and 2015 were identified in the NPR, excluding those with prior hip fracture since the introduction of ICD-10 in Sweden in 1997. In addition, we excluded individuals residing in municipalities that did not report consistently to the SSR or reported potentially unreliable data in any month during the study period [213]. In total, 197 of 290 municipalities – home to 77% of the Swedish population over the age of 65 – were included in Study V. We identified two matched control groups that were randomly drawn from the AHC. Both hip fracture patients and control groups were identified in municipalities that reported consistently to the SSR. Individuals who migrated internationally after their 60th birthday were excluded and all groups were followed for two years after their hip fracture.

4.3 VARIABLES AND DEFINITIONS

4.3.1 Diseases and disease indices

Disease occurrence was measured through diagnoses in the NPR (Studies I to V) and SHR (Study III). Table 2 shows the ICD and NOMESCO codes used for each study. Definitions were based on previous register-based research and validation studies [131,135,257,264,268-270,277,278]. Hip fracture subtypes included in in Study III were intracapsular, pertrochanteric, and subtrochanteric fractures. Due to their different etiology and survival chances, we did not include pathologic hip fractures in any study.

The CCI [115,116] was used as a comorbidity measure in Studies I, III, and IV. The original CCI was developed already in the 1980s as a weighted index of 19 comorbidities associated with mortality risk but has since been modified frequently and adapted for different purposes [112,279-281]. The version of the CCI used in this thesis was modified by Brusselaers et al. [279] for contemporary register-based research and includes 14 relevant comorbidities. In Study V, we calculated a hospitalization-based frailty index using the algorithm developed by Gilbert et al. [113]. The Gilbert frailty index is a weighted score of 109 diagnoses and was developed to capture frailty in routinely collected hospital admission data.

The lookback periods used in each study were based on the distribution of comorbidities in the study population. For example, comorbidity scores based on inpatient records are naturally higher in populations in which each person has been hospitalized at least once, such as in Study III. Study IV, on the other hand, included all men and women over the of 65 who often had few – if any – prior hospitalization in the NPR resulting in a vast majority of individuals classified as having no comorbidities. Study III, therefore, included all diagnoses made during the index hospitalization for hip fracture to calculate CCI scores, while Study I additionally considered diagnoses made during one year before index hospitalizations and Study IV had an extended lookback period of ten years. Likewise, the Gilbert index in Study V was based on diagnoses in the NPR during 10 years before baseline (Table 2).

The categorization of these indices was determined by the data. Since the distribution of index score values varies depending on the study population, e.g. depending on the included age groups, categories proposed in previous research are not necessarily transferable to our work. For each study, we thus considered the size of the population as well as the specific distribution of index scores and chose categories that allowed us to divide study populations into groups of sufficient size to maintain statistical power and represent a sizable proportion of the population. We distinguished between no comorbidities (CCI score 0), mild comorbidities (CCI score 1), and severe comorbidities (CCI score >1), but the groups of mild and severe comorbidities were collapsed into one category in small disease populations in Study I.

Table 2: ICD and NOMESCO codes used to identify diseases in Studies I to V

	Study I	Study II	Study III	Study IV	Study V
Hip fracture[a]	820 (ICD-9) and S72 excluding codes S72.3, S72.4, S72.9 (ICD-10) *Primary diagnoses*		All HF: 820 (ICD-9) and S72.0-S72.2 (ICD-10); Intracapsular HF: S72.0 (ICD-10); Pertrochanteric HF: S72.1 (ICD-10); Subtrochanteric HF: S72.2 (ICD-10); *Primary and secondary diagnoses* HF surgery: NFB* and NFJ* (NOMESCO [253])	820 (ICD-9) and S72.0-72.2 (ICD-10) *Primary diagnoses*	
Myocardial Infarction[a]	410 (ICD-9) and I21-22 (ICD-10) *Primary diagnoses*				
Stroke[a]	Ischemic: 433-34 (ICD-9) and I63 (ICD-10); Hemorrhagic: 431-32 (ICD-9) and I61-62 (ICD-10) *Primary diagnoses*	Any stroke: 431, 434, 436 (ICD-9), I61, I63, I64 (ICD-10) *Primary diagnoses*			
Cancer[b]	Colon: 153 (ICD-7) and C18 (ICD-10) Lung: 162-63 (ICD-7) and C33-34 (ICD-10) Female breast: 170 (ICD-7) and C50 (ICD-10)	Colon: 153 (ICD-7) and C18 (ICD-10) Female breast: 170 (ICD-7) and C50 (ICD-10)			
Other diseases and disease indices[a]	CCI: Algorithm by Brusselaers et al. [115, 116, 272] *Primary and secondary diagnoses during and 1 year prior to index hospitalization*		CCI: Algorithm by Brusselaers et al. [115, 116, 272] *Primary and secondary diagnoses during index hospitalization*	CCI: Algorithm by Brusselaers et al. [115, 116, 272] *Primary and secondary diagnoses during 10 previous years*	Frailty: Gilbert index [113] Dementia: F00-F03 and G30 (ICD-10) *Primary and secondary diagnoses during 10 previous years*

[a] Data from NPR and CDR.
[b] Data from Cancer Register.
CCI: Charlson comorbidity index; HF: Hip fracture; ICD: International classification of diseases; NOMESCO: Nordic Medico-Statistical Committee Classification of Surgical Procedures; NPR: National Patient Register.

In Study V, the study population was divided into four frailty groups: Gilbert frailty scores of 0, 0.1 to 1.9, 2.0 to 7.9, and 8 or more. To enable comparability of hip fracture patients with the control group, diagnoses that occurred for the first time during the hospitalization for the index fracture were not considered for the variables used during the propensity score matching process (Gilbert frailty index and dementia). However, diagnoses made during the index hospitalization were included when creating frailty and dementia variables for the multistate analyses, since these analyses were restricted to hip fracture patients only.

4.3.2 Definition of recurrent hip fractures

Study IV estimated the incidence of recurrent hip fractures based on data in the NPR. Hospital records, however, do not indicate whether repeated hospitalizations result from new incident fractures or from previous ones. In Study III, we investigate whether and how recurrent hip fractures can be identified in the NPR. Based on these results, a hospitalization with a primary hip fracture diagnosis at least 14 days after a previous hospital admission for hip fracture was considered a recurrent event. Thus, for the estimation of recurrent (i.e., second) hip fracture incidence, individuals were at risk from 14 days after their first hip fracture. In order to reduce the risk of misclassifying hospitalizations due to complications of a previous fracture as incident recurrent fractures, we conducted sensitivity analyses increasing the time from which a person begins to be at risk for a recurrent fracture from 14 to 90 days. However, it should be noted that this strategy may instead lead to an underestimation of recurrent fracture incidence since many recurrent fractures occur within the three months after the first. In sensitivity analyses, a comparison with the SHR, which includes clinically confirmed fractures only, found that approximately 10% of second hip fractures occurred within 90 days after the first fracture, while roughly 1% occurred within the first 14 days.

4.3.3 Operationalization of other variables

We distinguished between two levels of highest attained education: compulsory education (up to 8-9 years, depending on the birth cohort) and more than compulsory education. Birth country was divided into three groups: Sweden, the other Nordic countries (Denmark, Finland, Iceland, Norway), and other countries. Cohabitation was considered as a binary variable distinguishing between individuals who were registered with at least one other person in the same household in the Dwelling Register and those living alone.

Hospital size was operationalized according to the number of hip fracture patients treated during the study period. As such, our definition of hospital size reflects the volume of hip fracture patients which is likely more relevant for hip fracture management and registration routines than the absolute hospital size. Mode of admission was retrieved from the NPR and comprised three categories: admitted from own home, institutional housing, or another hospital.

Care states examined in Study V were categorized into five states: No care, home care with less than 40 hours per month, home care with 40 or more hours per month, care home residence, and death. The 40-hour threshold was chosen based on sensitivity analyses comparing different cut-off values as well as the distribution of home care hours in the population [213]. If an individual received both home care and resided in a care home, they were categorized as care home residents.

4.4 STATISTICAL ANALYSES

4.4.1 Estimation of trends in life expectancy (Study I)

Remaining period life expectancy was estimated as the area under the Kaplan-Meier product limit estimator [44]. This procedure is equivalent to the period life table technique used by the World Health Organization (WHO) [44], but takes advantage of the daily information available in Swedish registers. Person-time and deaths observed during a limited time period, in our case one year, can be used to estimate the non-parametric Kaplan-Meier product limit estimator [44]:

$$\hat{S}(t) = \prod_{i:t_i \leq t} (1 - \frac{d_i}{n_i})$$

with d_i representing deaths occurring at age i and n_i denoting the number of individuals remaining in the study population at time age i. Taking on the period perspective (as discussed in section 2.1.3), the Kaplan-Meier estimator represents the survival curve of a hypothetical cohort. Adopting the notation used by Preston et al. [43], it can then be used to estimate period life expectancy at age 65:

$$e_{65}^{0} = \int_{65}^{\infty} \hat{S}_y dy \quad .$$

Remaining period life expectancy at age 65 during 2017 can be interpreted as the expected mean survival length of a person at age 65 if prevailing mortality rates at all ages above 65 that were observed during 2017 remained constant throughout the rest of his or her life. Remaining life expectancy at age 65 was estimated for all calendar years between 1998 and 2017 separately for the general population and for each subpopulation of individuals with disease history. To compare life expectancy between subpopulations and the general population, absolute differences in years were calculated. Disease populations were examined independently of each other; each person could belong to several disease populations if they experienced more than one of the included diseases.

For each disease, remaining life expectancy was further estimated separately for individuals with compulsory and higher education, and for individuals with no, with mild, and with severe comorbidities at the time of disease onset. To ensure a sufficient number of individuals in each group, the study period was aggregated into five calendar-year groups for the estimation of remaining life expectancy stratified by educational and comorbidity level. Sensitivity analyses were conducted excluding those who died within 28 days after disease onset, estimating remaining life expectancy at other ages than 65 (60, 75, and 85 years), and holding the age at disease onset constant across all individuals and throughout the study period.

4.4.2 Decomposition of changes in life expectancy (Study II)

For each disease separately, we calculated the age-specific proportion of person-years in the population lived by individuals without disease, by individuals with recent disease onset, and by those with distant disease diagnosis in 1994 and in 2016. As in Study I, individuals could belong to more than one disease population if they experienced more than one of the included diseases. The proportions of total person-time lived by individuals with recent disease onset and by individuals with distant disease onset were labeled prevalence of recent cases and prevalence of distant cases, respectively. We also measured the number of deaths observed in each of these groups and calculated death rates smoothed over age and time with a two-dimensional smoothing procedure [282].

Since individuals with disease are part of the total population, overall life expectancy can be seen as a weighted average of mortality among individuals with recent, distant, and without disease history [232]. Individuals with disease history contribute to life expectancy in the total population through two mechanisms; (i) the larger the prevalence of a disease the larger its impact on life expectancy and (ii) the larger the excess mortality among those affected by disease the larger its impact on life expectancy. Using a general decomposition algorithm [283], we distinguished the contributions of these two mechanisms and quantified how much (i) changes in prevalence and (ii) changes in disease-specific mortality rates contributed to changes in remaining life expectancy at age 60 in the total Swedish population. In this study, remaining life expectancy at age 60 was approximated by partial life expectancy between ages 60 and 104 due to methodological limitations. However, because only few individuals reach ages above 104 and life expectancy is short at that age, remaining life expectancy and partial life expectancy are virtually identical.

4.4.3 Comparison of hip fractures in the NPR and SHR (Study III)

4.4.3.1 Coverage and agreement

The coverage of the SHR was estimated by calculating the proportion of first hip fractures (as primary cause of hospitalization) in the NPR that had a matching record in the SHR within ±7 days of the hospitalization date. The agreement between fracture types in the SHR and the NPR was compared among patients with matching records using Cohen's kappa. In order to assess the agreement between dates, we compared the admission dates in both registers among all patients with matching records within ±30 days.

4.4.3.2 Using ICD-codes to identify hip fractures in the NPR

Previous studies employed different algorithms to identify incident hip fractures in inpatient registers [256,264-266,269,284]. In order to identify the optimal operationalization of incident hip fractures in the Swedish NPR, we compared three different definitions in the NPR to diagnoses in the SHR. First, we defined hip fractures as any hip fracture diagnosis in the NPR, considering both primary and secondary diagnoses. Second, we excluded patients without a surgical procedure code for hip fracture surgery. Third, we defined hip fractures through primary diagnoses in the NPR only. The proportion of hip fractures in the NPR with a matching record in the SHR was calculated for each of these definitions.

4.4.3.3 Potential over-coverage when estimating fracture recurrence in the NPR

Hospital records in the NPR do not indicate whether repeated hospitalizations result from new incident fractures or from complications or other reasons related to a previous fracture. In order to determine whether the incidence of recurrent fractures can be studied using the NPR, we compared the coverage of the SHR for first fractures, recurrent fractures, and all fractures in the NPR. All hip fractures occurring at least 14 days after discharge from a previous hip fracture were considered incident hip fractures in the NPR.

4.4.3.4 Representativeness of patients registered in the SHR compared to the NPR

Characteristics of patients registered in both the SHR and NPR were compared to characteristics of patients who were not registered in the SHR using logistic regression for each variable separately and in a model adjusted for all other covariates. Survival during different follow-up periods was examined using Kaplan-Meier curves and Cox proportional hazard regression using age as the underlying time variable.

4.4.4 Hip fracture incidence and survival (Study IV)

Incidence rates of first and recurrent hip fractures were calculated as the number of hip fractures divided by person-years at risk. We estimated all rates as an average of four-year-intervals, i.e. for 1998-2001, 2002-2005, 2006-2009, 2010-2013, and 2014-2017. Survival during the first 30 days and the first year after hip fracture was calculated as the proportion of hip fracture patients alive at 30 days or one year after their fracture, respectively. We age-standardized incidence rates and survival proportions using direct standardization. Since well-established standard populations used in epidemiological research are hardly comparable to the population of older hip fracture patients in Sweden, we used our own data as a standard population. The total Swedish population in the middle of the study period (2008) was used as the standard population for the incidence of first fractures. For the calculation of recurrent fracture rates and survival proportions, the population of patients with first hip fracture in 2008 was used as standard population. We estimated 95%-confidence intervals using the normal approximation method.

In order to examine how trends in survival after hip fracture in the general population were influenced by changes in health status of hip fracture patients over time, we estimated time trends in mortality risk after first hip fracture using Cox proportional hazard regression with age as the underlying time scale and categorical coefficients for calendar time. In these analyses, health status was defined as the CCI score at the time of the fracture. The proportionality of hazards assumption was tested through Schoenfeld residuals and log-log plots.

4.4.5 Matching (Study V)

For each hip fracture patient, an age-and-sex matched control was randomly selected among individuals in the general population who were alive and hip fracture-free up to that age, hereafter referred to as general population control group. Age was matched in yearly and hip fracture occurrence in monthly intervals because care status was recorded on a monthly basis. For example, a woman born in 1920 experiencing a hip fracture in May 2014 was matched to a woman born in 1920 without hip fracture before or during May 2014. Controls were selected with replacement and allowed to experience a hip fracture at any time after their matching date. Individuals born 1914 or earlier were categorized into one open-ended age-category to allow matching among the oldest old (age 100 years or older; 0.5% of individuals).

In addition to the age-and-sex-stratified matching, we employed propensity score matching to generate a control group with characteristics similar to hip fracture patients, especially in terms of health and care status at baseline. Propensity scores were based on a logistic regression model including age, sex, education, cohabitation, birth country, dementia, and frailty score. Age was included as a continuous, quadratic variable to allow for a curvilinear association between age and fracture risk. The regression model was further stratified by care state at baseline to assure a balanced distribution of initial care states which are likely among the strongest predictors of later care trajectories. Based on the estimated propensity score, each hip fracture patient was matched to the closest hip fracture-free person alive (nearest neighbor) or, in case of several potential matches, a randomly selected person among the nearest neighbors. The propensity score matched control group is hereafter referred to as health-matched control group.

4.4.6 Multistate modeling (Study V)

Factors associated with different types of care trajectories among hip fracture patients were explored using multistate models [285]. This technique allowed us to estimate transition rates between care states while taking into account their interdependence and competing risks. For example, moving into care homes, receiving home care, and dying are three competing events for community-dwelling individuals without care. To reduce complexity, our multistate models focused on the time period up to three months after the fracture, the two home care states were collapsed into one state, and rare transitions were omitted. The model thus contained four states and six transitions (Figure 5). Individuals who experienced other, rare transitions (e.g. moved from care homes to their own home) were assumed to remain in their occupied state until they experienced another transition or until the end of follow-up. These restrictions were based on the observed care trajectories as well as previous research showing that most of the changes in functional abilities among hip fracture patients take place within few months of the fracture [286].

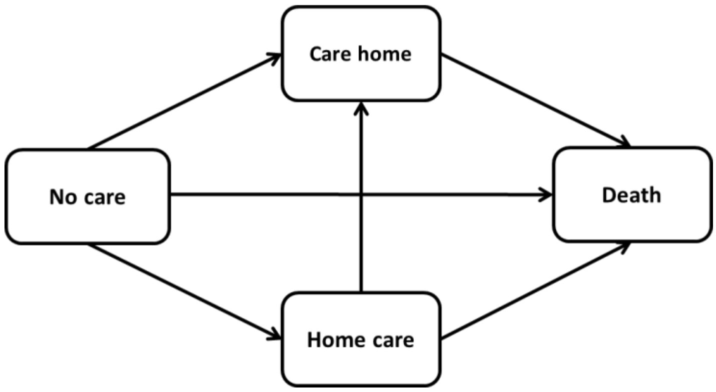

Figure 5: Multistate model for transitions between care states after hip fracture

Potential predictors included in the multistate model were age (categorized in five categories; 65-74 years, 75-79 years, 80-84 years, 85-89 years, 90+ years), sex, cohabitation, educational level, birth country (Sweden vs. other), dementia, and frailty score. Average frailty scores are higher among hip fracture patients than in the general population and therefore, we used a different categorization of the Gilbert frailty score in our multistate model. We calculated quartiles of the distribution of frailty scores among hip fracture patients and assigned each person to one of four frailty categories. Cox regression was used to estimate Hazard ratios (HR) with 95%-confidence intervals for the impact of each covariate on each of the six transitions of interest. Estimation was conducted using the packages mstate and survival in R version 3.6.2 [287].

4.5 ETHICAL CONSIDERATIONS

Swedish authorities routinely collect and store a large amount of personal and sensitive data. We strive to use these data for the benefit of the greater good by conducting research that is of high scientific quality, reproducible, and unbiased [254]. Our research aims to monitor trends in population health and explore potential disparities, for instance between genders, between educational groups, or between population groups with disease history. We ultimately aim to identify strategies to promote health and reduce inequalities in the entire Swedish population and in populations of comparable countries. We provide the public and scientific community access to our results by actively presenting our work to other researchers and by publishing our work open access in peer-reviewed journals.

All studies in this doctoral project fall into the project "The ageing population: An epidemiologic approach to a fundamental public health issue". The project was approved by the regional ethics committee in Stockholm which considered that the scientific value outweighs its harm and waived the need for patient consent. The linkage between data sources was conducted by Statistics Sweden and we received a pseudonymized data set. Since authorities hold a key that can be used to link the pseudonyms to specific individuals, however, data cannot be considered anonymous [288]. Data on health and disease are sensitive personal information and should be handled and results should be communicated carefully in order to maintain the integrity of each person [254]. We analyze and store data in a secure environment at Karolinska Institutet which is accessed through a remote desktop program. No sensitive data is handled outside of this environment.

Even though researchers have no access to names or personal numbers, the identification of specific individuals is possible through the detailed information available in the registers and hence, there remains a risk to violate personal integrity. We assured not to publish or report elsewhere detailed individual data that allowed the identification of specific individuals.

In order to prevent scientific misconduct, research should be reproducible and ideally, data and code should be shared with other researchers. However, data sharing is not possible with Swedish register data. While this may reduce the risk of violations of personal integrity, it may increase the risk of scientific misconduct. We aim to store our data in a well-organized way for at least 10 years in order to allow colleagues and other researchers to reproduce the study in the future, even in absence of the original author.

5 MAIN RESULTS

5.1 STUDY I

Remaining life expectancy at age 65 rose by 1.5 years among women and 3 years among men between 1998 and 2017, reaching 21.5 years for women and 19.2 years for men in 2017. As illustrated in Figure 6, life expectancy remained lower in population groups with a history of disease than in the general population but increased over time in all groups, except for women who had experienced a hip fracture. Life expectancy rose faster among women and men with a history of myocardial infarction, both stroke subtypes, colon cancer, and breast cancer than it did in the general population.

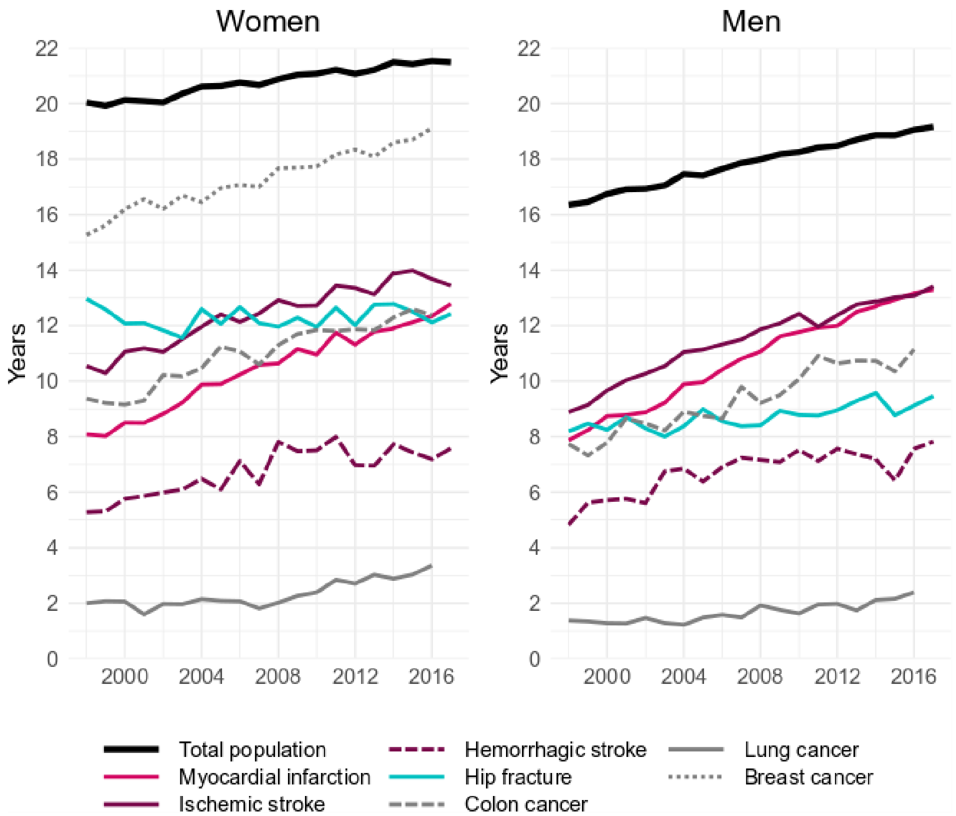

Figure 6: Trends in remaining life expectancy at age 65 for subpopulations with a history of disease and the general Swedish population, 1998-2017

The gaps in remaining life expectancy between subpopulations with disease history and the general population declined most notably for older adults who had experienced a myocardial infarction or ischemic stroke, and for women with a record of colon- or breast cancer but less so among women and men with a history of hemorrhagic stroke and among men who had a record of colon cancer (Figure 7). The difference in life expectancy among women with a history of myocardial infarction and the general female population was 3.3 years smaller in 2017 than in 1998. On the contrary, the gaps in remaining life expectancy compared to the general population widened for older adults with a history of lung cancer and hip fracture.

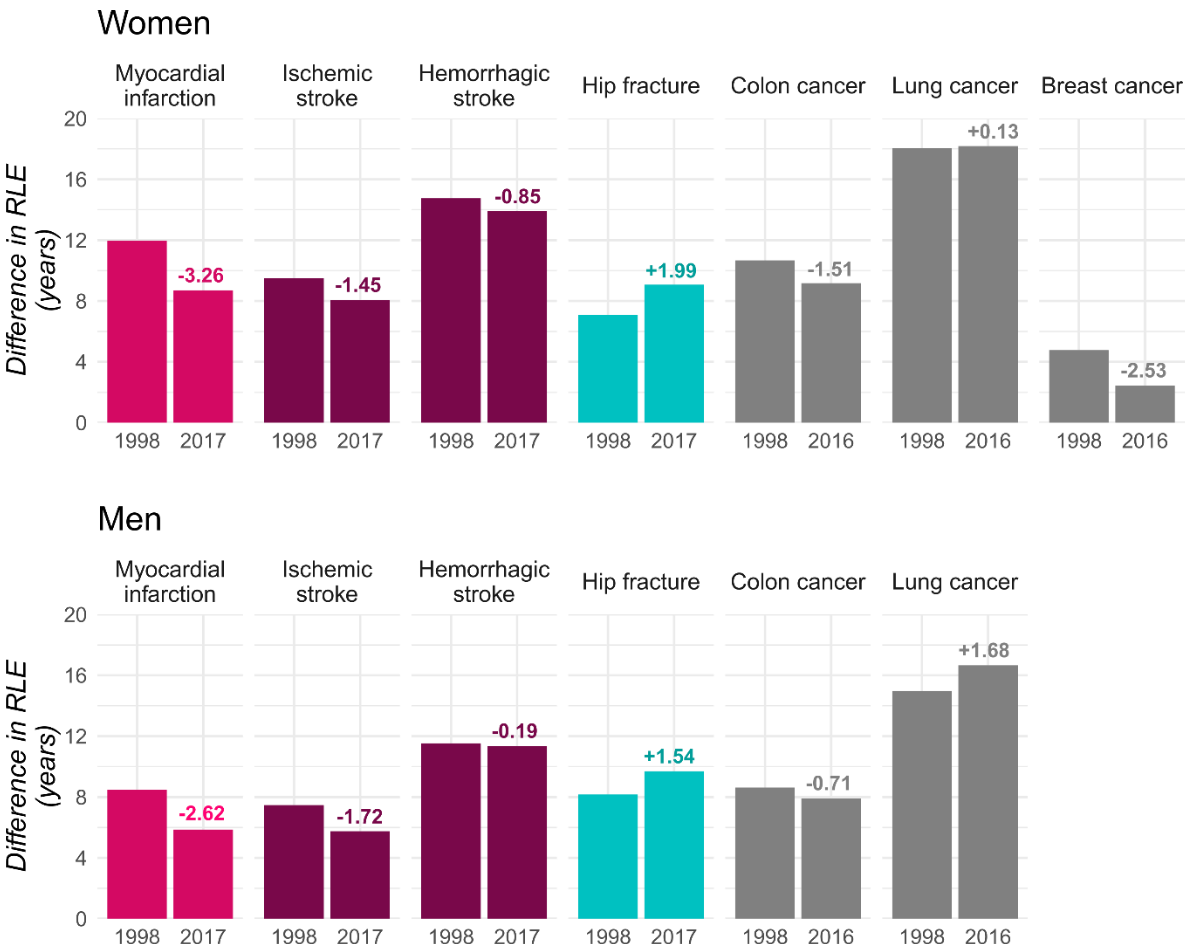

Figure 7: Differences in remaining life expectancy (in years) between populations with a history of disease and the general population, 1998 and 2017
Changes from 1998 to 2017 displayed above bars.
RLE: Remaining life expectancy.

Among all subpopulations who had a history of disease, except for those with hip fracture, gender differences in remaining life expectancy were smaller than in the general population. For CVD specifically, women did not have a higher life expectancy than men. Remaining life expectancy was generally lower among men and women with basic education than it was among those with higher education but increased at a similar pace among both educational levels.

A high comorbidity burden was also consistently associated with shorter life expectancy. In 2013-17, women and men with a history of myocardial infarction and a CCI score of zero reached a remaining life expectancy of more than 16 years, while those with severe comorbidities had a life expectancy of about four years. Still, remaining life expectancy rose across all subgroups distinguished by CCI score, and for all diseases. While we detected no increases in life expectancy among women with a history of hip fracture and only minor improvements among men, stratification by comorbidity level revealed upward trends in remaining life expectancy among individuals with both low and high comorbidity levels. The pace of life expectancy improvements did not differ between groups with higher comorbidity levels and those with no record of comorbidities.

5.2 STUDY II

Between 1994 and 2016, remaining life expectancy at age 60 increased by 3.4 years for men and 1.9 years for women. Figure 8 illustrates increases in remaining life expectancy as well as the contribution of five different diseases to these trends among men and women. Our decomposition shows that mortality improvements have positively contributed to life expectancy trends for all diseases under study. Both among men and women, almost half of the observed increase in remaining life expectancy can be attributed to prolonged survival among those who experienced a myocardial infarction. Improvements in survival among those with stroke, too, contributed substantially to increasing life expectancy, while contributions were smaller for hip fracture, colon cancer, and breast cancer.

At the same time, the proportion of person-years lived by people with a history of many diseases in the Swedish population increased. Figure 8 shows that increasing prevalence of stroke, and colon cancer among both genders, and breast cancer as well as myocardial infarction among women had a negative impact on remaining life expectancy in the total population. However, for myocardial infarction and stroke, this negative impact is far outweighed by the positive contribution of improved survival.

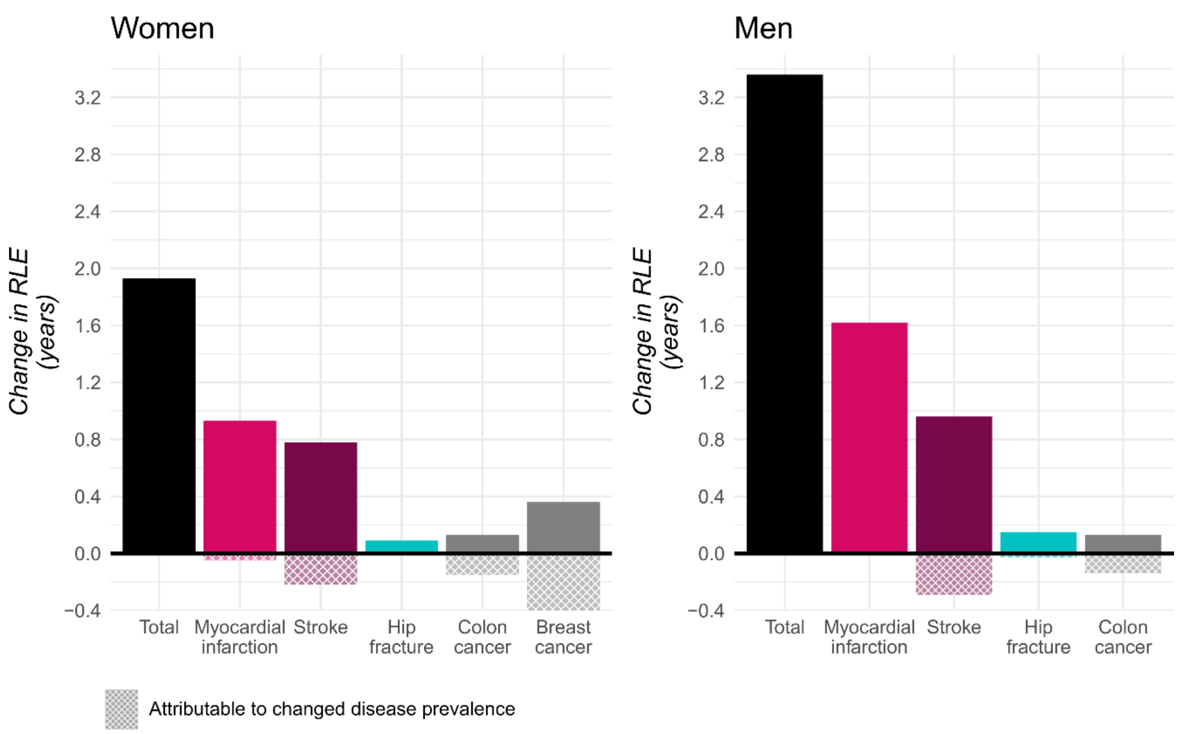

Figure 8: Decomposition of change in remaining life expectancy at age 60 between 1994 and 2016. Contributions of changing disease prevalence and improved survival
Solid areas represent increasing life expectancy attributable to improved survival chances. Checked areas represent changes in life expectancy attributable to improved survival chances.
RLE: Remaining life expectancy.

Figure 9 illustrates the results of a second level of decomposition, additionally distinguishing between the contribution of individuals with recent disease onset and the contribution of individuals with a disease onset dating further back in time. For both recent and distant cases and for all diseases, survival improved and contributed positively to life expectancy increases. The declining prevalence of having a recent disease diagnosis had positive effects on total life expectancy for CVD and hip fractures but not for colon and breast cancer, for which increasing prevalence contributed negatively to changes in life expectancy. Growing proportions of long-term survivors (increasing prevalence of distant cases) contributed negatively to changes in life expectancy for all diseases among both men and women. This negative effect on life expectancy was most notable for myocardial infarction, stroke, and female breast cancer.

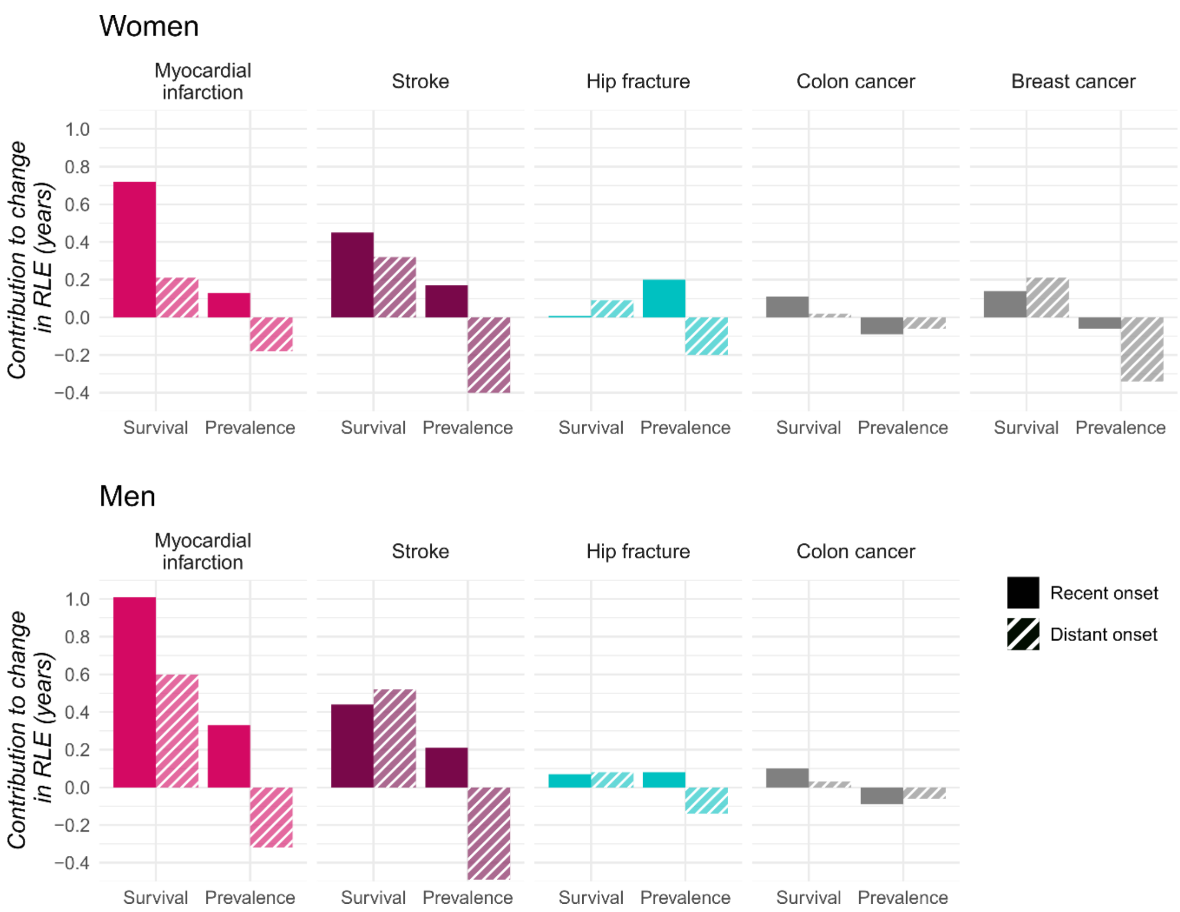

Figure 9: Decomposition of change in remaining life expectancy at age 60 between 1994 and 2016. Contributions of changing disease prevalence and improved survival of five major diseases stratified by time since disease onset
Recent disease onset defined as onset within the past 3 years (myocardial infarction, stroke, hip fracture) or 5 years (colon and breast cancer).
RLE: Remaining life expectancy.

5.3 STUDY III

We identified 140,724 patients with first hip fractures between 2008 and 2017 in the NPR. The proportion of these individuals that had a matching record in the SHR is shown in Figure 10. In total, 81.2% of patients had a matching record in the SHR. During the study period, coverage increased to a maximum of almost 90% in 2014 and since declined to approximately 80%. The decline observed after 2014 could be attributed to five hospitals in Sweden that ceased to co-operate with the SHR. Coverage was somewhat lower for patients with diagnoses of subtrochanteric fractures in the NPR than for patients with diagnoses of intracapsular and pertrochanteric fractures. The coverage of the SHR was also lower for recurrent fractures identified in the NPR. Our comparison suggests that the over-coverage of recurrent hip fractures amounts to approximately 13%.

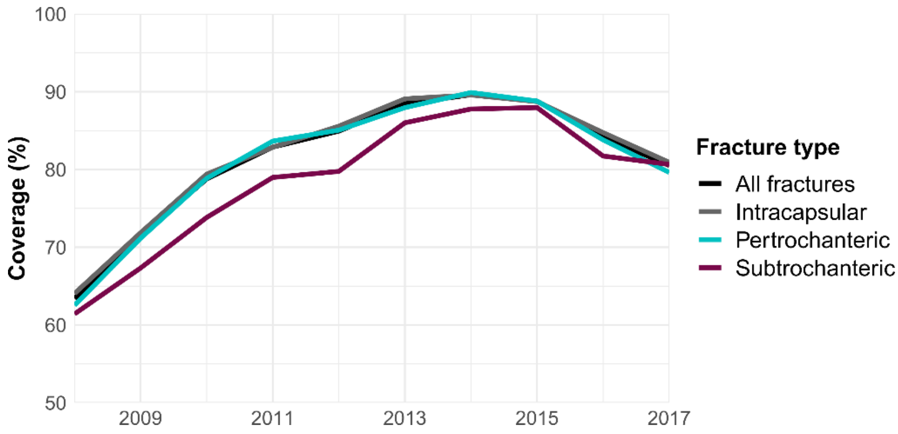

Figure 10: Coverage of first hip fractures in the SHR by diagnosis in the NPR, 2008-2017 (N=140,724)

Our comparison indicates an excellent coverage of hip fracture diagnoses in the NPR. Almost all patients in the SHR (95.8%) had a matching record with a primary hip fracture diagnosis in the NPR. However, only two thirds of these patients additionally had a procedure code for hip fracture surgery in the NPR. The agreement between fracture dates was excellent; 89% of of patients included in both registers were recorded on the same day and only 1% of records were registered more than 7 days apart. Furthermore, the agreement between fracture types was high (Cohen’s kappa = 0.87) albeit somewhat lower for subtrochanteric fractures; one fifth of subtrochanteric fractures in the SHR were classified as pertrochanteric fractures in the NPR.

Patients who were included in both registers were similar to patients who had a record in the NPR, but not the SHR, with respect to education, birth country, and comorbidity level (Table 3). However, patients recorded in both registers were more likely to be older, treated in larger hospitals, more often lived in the community, and survived longer after sustaining their hip fracture (Table 3). The survival advantage was most pronounced shortly after the fracture (Table 3, Figure 11). During the first 30 days after their fracture, patients who were recorded in both registers experienced a 30% lower mortality risk than patients with a record in the NPR only. Patients who died within one day of sustaining a hip fracture had 79% reduced odds to be registered in the SHR even when adjusting for age, fracture type, and CCI score (Table 3).

Table 3: Odd ratios and 95%-confidence intervals for registration in the Swedish Hip Fracture Register among hip fracture patients identified in the National Patient Register, 2008-2016 (N=125,605)

	Odds of registration in SHR	
	Crude Analyses[a]	Multivariable Analyses[b]
	OR [95% CI]	OR† [95% CI]
Fracture type in NPR		
Intracapsular	1.00 [1.00-1.00]	1.00 [1.00-1.00]
Pertrochanteric	0.97 [0.94-1.00]	0.93 [0.90-0.96]
Subtrochanteric	0.81 [0.77-0.85]	0.77 [0.73-0.81]
Unclear (several)	0.63 [0.56-0.71]	0.62 [0.54-0.70]
Hospital size		
Small	0.45 [0.43-0.48]	0.45 [0.43-0.48]
Medium	1.00 [1.00-1.00]	1.00 [1.00-1.00]
Large	1.29 [1.23-1.34]	1.32 [1.26-1.37]
Largest	1.41 [1.36-1.46]	1.40 [1.34-1.45]
CCI score		
0	1.00 [1.00-1.00]	1.00 [1.00-1.00]
1	1.02 [0.99-1.05]	0.95 [0.92-0.99]
2+	0.92 [0.89-0.96]	0.84 [0.81-0.88]
Survival length,		
0-1 day	0.22 [0.19-0.26]	0.21 [0.18-0.25]
2-7 days	0.63 [0.58-0.68]	0.64 [0.59-0.70]
8-30 days	0.87 [0.81-0.93]	0.90 [0.84-0.96]
31-365 days	0.91 [0.88-0.93]	0.92 [0.88-0.96]
>365 days	1.00 [1.00-1.00]	1.00 [1.00-1.00]

[a] Crude analyses adjusted for fracture year.
[b] Adjusted for all co-variates and for fracture year, age, gender, birth country, education, and mode of hospital admission.
CCI: Charlson comorbidity index; CI: Confidence interval; NPR: National Patient Register; OR: Odds ratio; SHR: Swedish Hip Fracture Register.

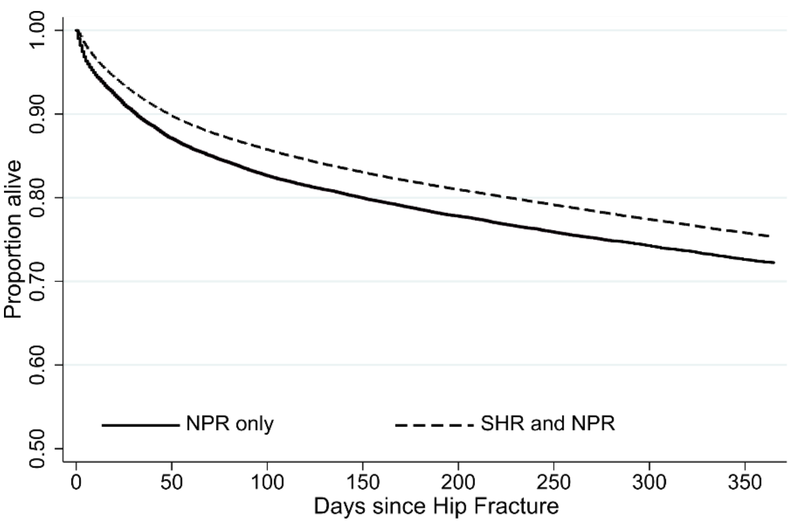

Figure 11: Survival during one year after first hip fracture for patients registered in the Swedish Hip Fracture Register and the National Patient Register, 2008-2016 (N=125,605)
Kaplan-Meier survival estimates**.**
NPR: National Patient Register; SHR: Swedish Hip Fracture Register.

5.4 STUDY IV

Approximately 20% of women and 30% of men died within one year of experiencing their first hip fracture (Figure 12). While age-standardized survival proportions remained largely unchanged in the general population, within educational groups, and within population groups defined by birth country, one-year survival improved within groups defined by CCI score among both genders during the study period. In age-adjusted Cox regression models, the hazards of dying within the first year of sustaining a hip fracture were 13% and 21% lower among women and men in 2013-2017 compared to 1998-2011.

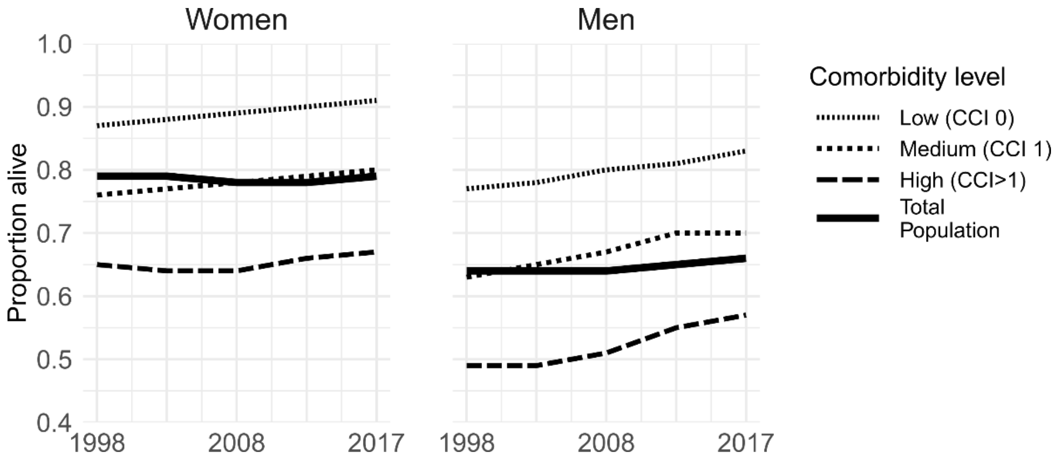

Figure 12: Age-standardized proportion of patients with first hip fracture surviving 365 days by comorbidity level, 1998-2017
CCI: Charlson comorbidity index.

While survival chances remained stable, the total number of annual first hip fractures in Sweden decreased between 1998 and 2017 among women but increased among men. Figure 13 shows age-standardized incidence rates of first and recurrent fractures in the total population and in different population groups. The age-standardized incidence of first hip fractures declined by approximately 20% and declines occurred at a similar pace in all examined strata. The age-standardized incidence of recurrent fractures was higher than the incidence of first fractures but declined faster than the incidence of first fractures. During the study period, the age-standardized incidence of recurrent hip fractures decreased by 48% among men and 46% among women.

Comorbidity level was the strongest predictor for fracture risk; age-standardized incidence rates of first hip fractures were more than twice as high among men and women with severe comorbidities than among those with a CCI score of zero. Male gender, higher education, and being born outside of the Nordic countries were also associated with lower incidence rates of first hip fractures. The incidence recurrent fractures was similar between population groups defined by gender, educational level, and birth country. However, patients with higher comorbidity level at the time of their first hip fracture were at elevated risk of sustaining a recurrent fracture.

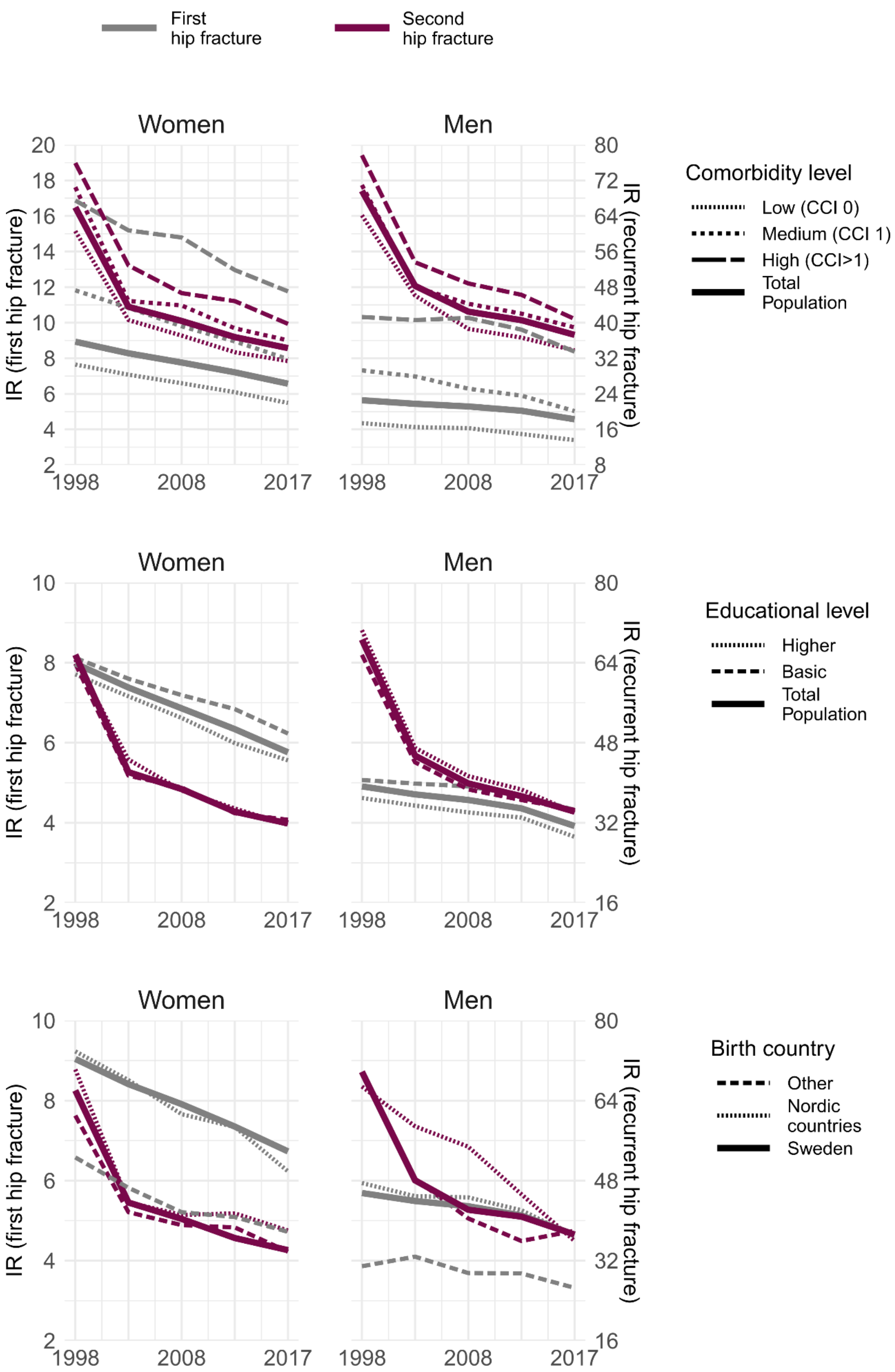

Figure 13: Age-standardized incidence rates per 1000 person-years of first and recurrent (second) hip fractures by comorbidity level, educational level, and birth country, 1998-2017
Note: Incidence by educational level restricted to individuals up to 90 years.
CCI: Charlson comorbidity index; IR: Incidence rate.

5.5 STUDY V

Study V included 20,573 individuals with a first hip fracture during 2014 and 2015. The mean age at hip fracture was 83.6 years and two thirds of hip fracture patients were women. Figure 14 shows trajectories of long-term care among hip fracture patients as well as among the general population and a health-matched control group. The left panels illustrate longitudinal trajectories from baseline, i.e., the last time point before the fracture or the matching date (T1), until 24 months later (T4) among all individuals, while the right panels present the prevalence of states at each time point restricted to individuals who survived (i.e., excluding individuals who died).

Experiencing a hip fracture was associated with considerably higher mortality and higher transition rates to receiving care. Almost half of hip fracture patients without care before their fracture received municipal care 3 months later (47.1%) and less than a quarter of those (23.8%) returned to living without care during the follow-up. However, at the end of follow-up the distribution of care states among hip fracture survivors was virtually identical to survivors from the health-matched control group (Figure 14). This suggests that part of the long-term increase in care use among hip fracture patients might have occurred even in absence of the fracture.

Table 4 shows baseline characteristics of hip fracture patients in comparison to the general population. More than half of hip fracture patients but only one third of the control group received either home care or lived in care homes. In comparison to the general population, hip fracture patients also had higher frailty scores. Diagnosed dementia was 2.4 times as likely among women and 3.1 times as likely among men with hip fracture compared to women and men in the age-matched control group.

Table 4: Health characteristics of patients with first hip fracture in 2014-2015 and age-matched controls from the general population (N=41,146)

	Women		Men	
	Age-matched controls (N=14,010)	Hip fracture patients (N=14,010)	Age-matched controls (N=6,563)	Hip fracture patients (N=6,563)
Care status at baseline (%)				
No care	66.0	47.4	77.4	53.2
Home care <40h	13.7	17.8	9.7	16.9
Home care 40h+	7.9	13.3	5.1	12.1
Care home	12.4	21.5	7.7	17.8
1-year mortality (%)	8.1	20.7	7.8	28.7
2-year mortality (%)	15.4	31.3	16.5	40.3
Dementia diagnosis [a] (%)	4.7	11.4	4.0	12.3
Frailty score [a] (%)				
0	54.0	38.2	53.9	29.3
0.1-1.9	15.2	14.3	16.1	15.5
2.0-7.9	22.2	31.2	21.3	35.3
8+	8.7	16.4	8.7	20.9

[a] Based on hospitalizations during 10 years before hip fracture or matching date. Excluding hospitalization for index hip fracture.

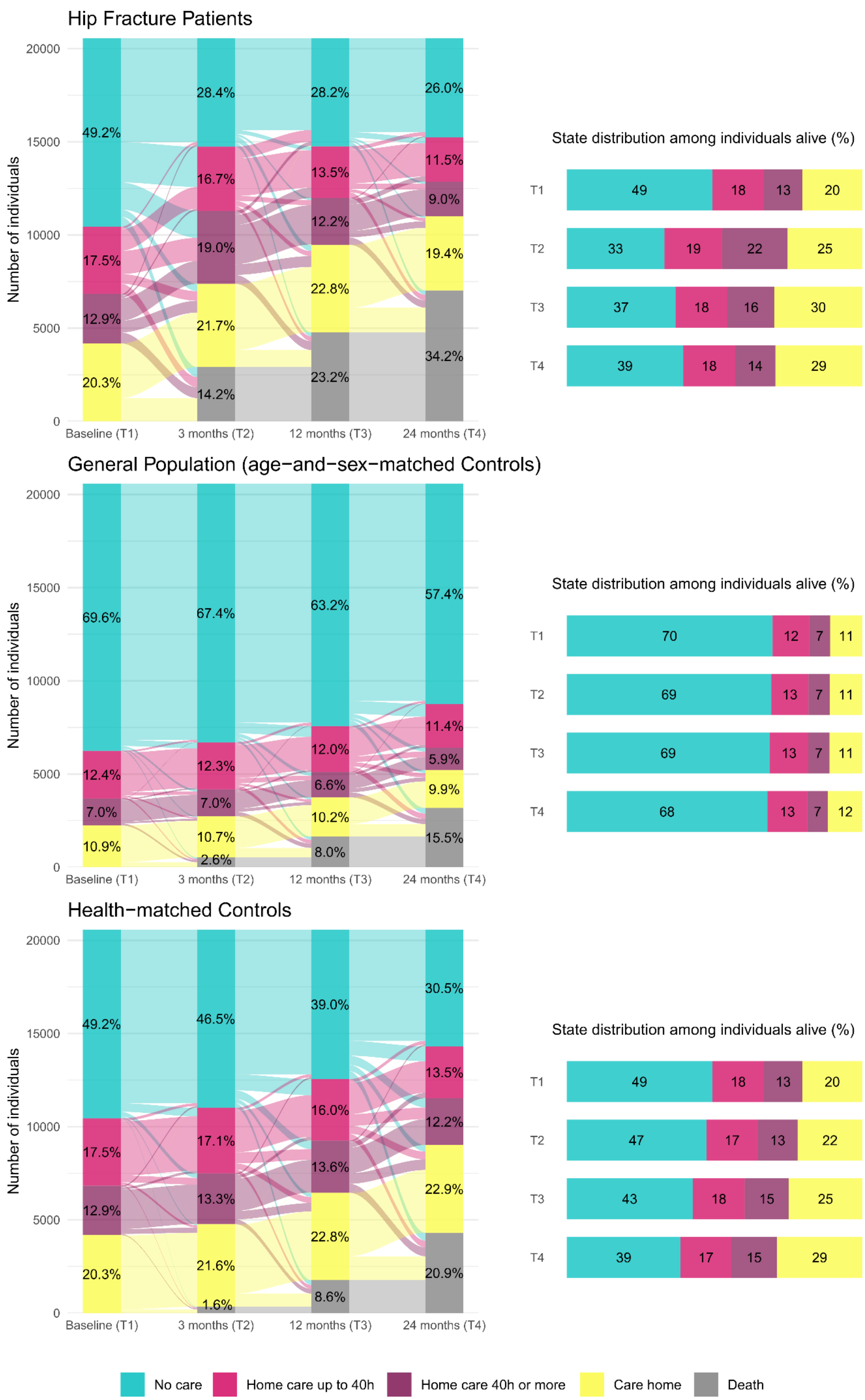

Figure 14: Transitions between care states among hip fracture patients, the general population control group and propensity-score-matched control group (N=61,719)

Several risk factors for transitions between care states were identified using multistate modelling (Figure 15). Men had higher mortality than women but were less likely to transition to receiving home care. Cohabiting individuals had a lower risk of transitioning from living without care to home care and from home care to care home admission. Higher education was associated with a lower risk of death but only among those living without care. Higher frailty scores were associated with increased rates of care home admission and death both among individuals with home care and individuals without care. By contrast, higher frailty scores were not associated with transition to home care among individuals without care and only weakly correlated with higher mortality among care home residents. Having a dementia diagnosis was, aside from age, the strongest predictor for transitioning into care homes.

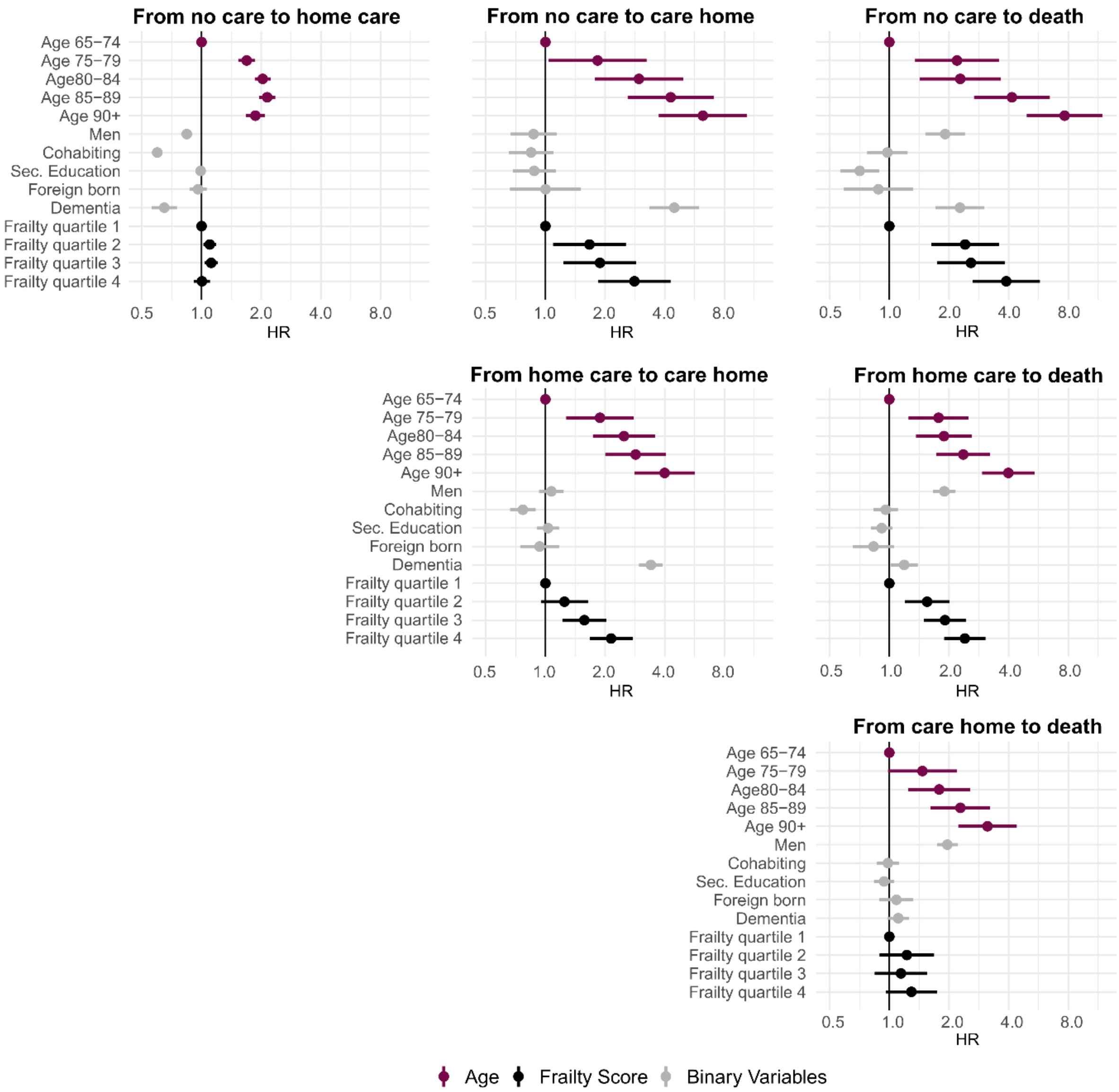

Figure 15: Hazard ratios and 95%-confidence intervals for care status transitions during 3 months after hip fracture (N=20,573; Note: individuals with hip fracture only)
HR: Hazard ratio.

6 DISCUSSION

6.1 SUMMARY OF MAIN FINDINGS

In Study I we found that remaining life expectancy in old age has increased faster in subpopulations with a history of many diseases than it has in the general population although it still remains lower. If the prolonged life expectancy with disease is not counterbalanced by declining disease incidence, it results in increasing prevalence, that is, a growing proportion of men and women with disease history in the population. Indeed, Study II shows that the prevalence of all diseases under study increased during the past decades. Study II also demonstrates that these two processes – increasing disease prevalence and longer survival – have counteracting influences on the development of life expectancy in the total population. Especially declining mortality among men and women with myocardial infarction and stroke has contributed substantially to the rise of Swedish life expectancy since the 1990s. At the same time, the growing proportion of people with a history of these conditions in the population has curbed the rise of life expectancy albeit to a smaller extent.

Studies I and II further show that trends were not uniform across different diseases. For example, life expectancy hardly increased among men and women who experienced a hip fracture. This finding motivated Studies III to V which examine trends in hip fracture incidence and the consequences of sustaining a hip fracture among the old. Study III explored whether and how the SHR and NPR can be used to study the epidemiology of hip fracture Sweden. Although we identified some limitations, our findings indicate that both registers are valuable data sources, and that the NPR specifically is suitable for monitoring hip fracture occurrence in the Swedish population. Study IV presents hip fracture incidence, recurrence, and mortality in population strata defined by gender, education, comorbidity level, and birth country. In all of these strata, hip fracture incidence has declined during the past 20 years – and even more so for recurrent than for first hip fractures. In line with our findings in Study I, however, comorbidity levels among hip fracture patients have been rising and as a result, survival chances among older adults with hip fracture remained essentially unchanged.

Exploring the consequences of sustaining a hip fracture in greater detail, Study V demonstrates that hip fractures have an immediate negative impact on both mortality and care use of older patients. However, already before their fracture, hip fracture patients are frailer and more likely to receive geriatric care than the general older population. Our comparison to a health-matched control group suggests that the increase in care use among hip fracture patients might have also occurred in absence of the fracture, even if somewhat later.

6.2 CONTRIBUTION TO EXISTING KNOWLEDGE

6.2.1 Main results in context

The findings presented in Studies I and II are consistent with previous research on trends in disease survival. Several studies found substantial improvements in survival with CVD and common types of cancer during the past decades, albeit less pronounced for lung cancer [84,90-92,96].

Our work adds to the existing body of evidence by taking on a period perspective, allowing us to capture recent trends in survival chances and to compare the pace of life expectancy improvements between diseases and to the total population. We show that rising life expectancy is at least in part a result of higher life expectancy in subpopulations with disease history. This indicates that life expectancy increases can be attributed not only to primary or secondary prevention efforts, i.e., preventing diseases from occurring or delaying the onset of diseases to higher ages, but also to tertiary prevention that enables more patients to survive in the long term. Remaining life expectancy among women with breast cancer in particular closely approaches that of all women in Sweden – an uplifting finding for breast cancer patients.

The tremendous improvements in remaining life expectancy among individuals with a history of CVD are also noteworthy. One could hypothesize that the considerable decreases in CVD incidence amounting to almost 50% compared to peak levels as shown in previous research [93,96,97,123,131-135] has been a result of preventing "milder" cases with better prognosis. Our findings, however, show that incidence rates and survival chances have improved simultaneously. Taken together, this results in a substantially reduced burden of CVD in the ageing Swedish population.

The underlying explanations for the observed mortality trends and for the differences between diseases are probably multifactorial. The advances in life expectancy among subpopulations with a history of CVD partly reflect the increased survival of patients in the acute phases, for instance through advancing surgical techniques, more frequent treatment in specialized hospital units, or a faster arrival at the hospital. Still, sensitivity analyses in Study I, in which deaths during the first 28 days of disease onset were excluded, show that improvements in the acute setting are not the only explanation. Medication, monitoring of risk factors, or behavioral interventions have likely become more effective in preventing adverse events such as disease recurrence. Study IV indeed found that the incidence of recurrent hip fractures in Sweden has declined considerably since the 1990s and others have observed similar trends for CVD recurrence in Sweden and elsewhere [131,132,160,289].

Yet, survival after hip fracture did not improve. In accordance with our findings, earlier studies reported stable or only slowly declining mortality rates among hip fracture patients [104,105,290] which can at least partly be attributed to rising comorbidity levels [102-105]. However, previous research also found increasing comorbidity levels among individuals with myocardial infarction and stroke [93,95,98], among whom life expectancy increased at a fast pace and even without adjustment for rising comorbidity levels. It is possible that comorbidity levels have risen faster in the hip fracture population than among individuals with CVD, but variations in the prevalence of specific comorbid diseases and disease combinations might also account for part of the observed differences. The CCI and similar indices are convenient summary measures that enable comparisons between studies, but they cannot completely capture complex and evolving comorbidity patterns.

In accordance with Study II, previous research found increasing prevalence for many diseases in Sweden including several cancer types and diabetes [89,117-119,121-125]. The prevalence of acute diseases such as myocardial infarction, stroke, or hip fracture, is seldomly reported because most epidemiological studies choose to report incidence rates. However, since acute disease events are usually the result of chronic underlying risk factors and associated with a sustained excess risk of poor health outcomes, the prevalence of such conditions, or the prevalence of having a history of such conditions, is an important aspect of public health, especially if patients' survival length increases. While we found increasing stroke prevalence, one previous study has shown a declining prevalence of stroke in Sweden during a similar time period [132]. This is likely explained by the 7-year lookback period applied in previous work while our lookback period was not restricted. Study II found an increasing prevalence of *distant cases*, men and women who had experienced a stroke several years ago, but a declining prevalence of *recent cases*. In addition, we found a growing proportion of *distant cases* for all other diseases under study; increasing numbers of older individuals in Sweden are thus long-term survivors of severe diseases.

Study IV adds to a growing body of research showing declining hip fracture incidence in the Nordic and in other countries during the past 30 years [109,136,137,139,143,168,291]. Our work is, to the best of my knowledge, the second study to explore trends in hip fracture incidence and recurrence for population groups with different CCI scores. Pedersen et al. presented trends in hip fracture incidence stratified by comorbidity levels in Denmark [109] but did not assign correct denominators, i.e., the correct person-time at risk, in their analyses [252,253]. In the revised version of their paper, Pedersen et al. found trends distinctly different from their original publication but similar to our work in Study IV [253]. This highlights the importance of assigning appropriate denominators when estimating incidence rates.

Recurrent hip fractures are debilitating conditions but secular trends in their occurrence have rarely been presented. Since recurrent fractures are rare, studies on hip fracture recurrence require large-scale data but their identification in routinely collected inpatient registers has some caveats. Study III allowed us to develop methods to operationalize recurrent fractures in the Swedish NPR. One previous study examined trends in hip fracture recurrence in the Nordic countries, finding stable incidence rates of recurrent fractures between 1999 and 2008 in Norway [162], while we found declining incidence rates within the same time frame. Unlike our work, the Norwegian study followed patients for one year only and it is possible that improvements in recurrent fracture rates were less pronounced within the first year after sustaining a hip fracture.

Several explanations for the declining hip fracture incidence have been proposed. An increased uptake of walking aids may have prevented some fractures [167,292,293] and the earlier detection and more aggressive treatment of osteoporosis may have also contributed to reduced fracture risk [139,291]. Improved osteoporosis treatment might have particularly affected the incidence of recurrent fractures [163] since osteoporosis often remains undetected until a fracture occurs [294]. Lower fracture incidence in later-born cohorts could also be attributable to lifestyle factors including nutrition and vitamin-D-supplementation, smoking, exercise, or working conditions throughout the life-course [137,139,162]. The rising prevalence of overweight is another proposed mechanism, since a higher body mass index is associated with increased bone mineral density [139,295]. Such lifestyle factors have probably also affected the incidence of CVD and many types of cancer. However, while obesity is associated with a lower hip fracture incidence, it is among the most prominent risk factors of CVD for which dramatic declines in incidence were observed in numerous studies [93,96,97,123,131-135,296-298]. In addition, many behavioral factors theorized to reduce fracture incidence have also been linked to lower risks of some cancer types [299-306] but cancer incidence increased rather than declined [121-124]. Altogether, these differences highlight the complexity of the relationship between behavioral factors and disease occurrence on the population level.

Even beyond the operationalization of recurrent hip fractures described above, Study III allowed us to draw several conclusions about register-based research. Like other quality registers, the SHR is not complete; both patients and hospitals can opt out of being registered. This does not always result in selection bias but knowledge about the mechanisms behind missing registration is necessary in order to evaluate the risk of bias and to evaluate the generalizability of studies using these data. In Study III, we showed that the SHR today includes 80% of hip fracture patients in Sweden and that at least half of the non-coverage can be attributed to hospitals that do not cooperate with the SHR. Non-coverage attributable to administrative decisions on the hospital level is arguably less likely to induce bias in many epidemiological studies than a selection of individual patients, for instance related to cognitive status, physical health, or socioeconomic factors. Yet, we also found some selection on the individual patient level. Most notably, patients with very short survival were less likely to be not included in the SHR. It is possible that clinicians cannot retrieve consent for participation from these patients or do not have the time or motivation to register them in the SHR. Since only few hip fracture patients die within days of their fracture, this may not be a large issue in many studies. However, research on short-term survival chances should carefully discuss potential selection in the SHR. These considerations exemplify some of the strengths and limitations of administrative and of quality registers when exploring disease patterns in the entire population.

Previous research showed that, in accordance with Study V, notable proportions of individuals are admitted to permanent care homes after experiencing a hip fracture [286,307,308]. To the best of my knowledge, however, there are no previous population-based studies examining the uptake of home care although it is common among hip fracture patients and of growing importance for geriatric care in Sweden and in many other countries [202,309]. The impact of hip fractures on older individuals' home care use and on their risk of moving to care homes found in Study V is reasonable. Almost all hip fracture patients are surgically treated and especially among the oldest old, a temporary immobilization can trigger a deterioration of muscle mass and strength that may be difficult to regain. In addition, hip fracture patients are at high risk of complications such as hospital-acquired infections, readmissions, or cardiovascular events [310-317]. Such complications may not only increase short-term mortality but also long-term physical impairment owing to prolonged immobilization and interrupted rehabilitation.

Yet, our results in Study V also show that the impact of diseases on health outcomes may be overestimated if one does not properly account for selection. Older adults who experience a hip fracture are a selected group of people and not representative for the total population. We aimed to isolate the effect of the fracture itself on care trajectories by comparing hip fracture patients to two control groups: a group randomly drawn from the general population and a health-matched control group. Our results in Study V indeed suggest that those who develop a hip fracture probably had experienced poorer health outcomes and consumed a higher amount of care than the average person even in a counterfactual scenario in which they did not sustain a fracture. Hip fractures have an immediate impact on care status but in the long run, care use may not be attributable to the fracture itself, but to underlying health and risk profiles. Receiving geriatric care and sustaining a hip fracture may thus share common risk factors and as a result, some previous studies, especially those with a long follow-up spanning over several years, may have exaggerated the negative impact of hip fractures on care trajectories.

Nevertheless, one needs to consider a further layer of selection when interpreting these findings: After two years, hip fracture patients had similar care statuses as the control group *conditioning on survival.* However, they were less likely to survive and had especially high mortality rates during the first months after their fracture. The elevated short-term mortality is likely a direct result of complications, such as infections acquired in hospital or cardiovascular complications related to immobilization [310,312,314-318]. Once this acute phase is overcome, hip fracture patients face essentially the same mortality risk as men and women in the health-matched control group.

Our findings in Study V, together with previous research [205,319], indicate that patients' care status is an important factor to consider in hip fracture research. For example, previous studies suggested that shorter hospital length of stay might lead to poorer survival after hip fracture [205]. However, we did not find support for a negative impact of shorter hospitalizations on hip fracture survival in another study [319]. Instead, the correlation between short hospitalizations and mortality was confounded through care home residence; hip fracture patients living in care homes have higher mortality rates but are also discharged earlier than those living in the community [319]. This is of utmost importance for public health because such findings inform policy makers and clinicians when allocating healthcare resources, prioritizing patients, and structuring clinical processes.

6.2.2 Sociodemographic differences

The female advantage in life expectancy is found in almost all populations globally [54,65]. This stands in contrast to Study I which found small, or even non-existent, gender differences in remaining life expectancy among populations with disease history. Women without disease survive longer than men but women who are affected have a life expectancy closer to their male counterparts. These findings are supported by studies showing that women have lower incidence rates of both stroke and myocardial infarction than men, but that the risks of recurrent events and survival chances barely differ between genders [131,132]. The higher life expectancy among women than among men may hence be more closely linked to disease risk than to prognosis once a disease has occurred.

However, these findings could be limited to some diseases, including CVD. In line with a number of previous studies [104,140,143,313,320], we observed a different pattern for hip fractures. Men are less likely to experience a hip fracture but, once affected, have considerably poorer survival than women. There is, furthermore, strong evidence for a higher prevalence of multimorbidity as well as disability among older women than among older men [30,53,101,122,149,157,159,174-180]. The longer life expectancy but poorer health among women is referred to as the male-female health-survival-paradox. Several studies have explored underlying mechanisms and maintain that this paradox can only partly be explained by lifestyle factors, biological differences, and selection into old age [176-180] and it hence remains to be studied further.

In accordance with previous research [66,67], we found that life expectancy increased faster among men than among women during the past decades. Yet, Study IV has also shown that declines in hip fracture incidence were less pronounced among men than women, which is, again, supported by earlier studies [104,109,136,137,139,168]. Taken together, our findings together with previous research show that gender differences among the Swedish old and their development over time vary depending on the specific diseases and health outcomes under study.

The importance of socioeconomic resources for health in old age has received much scientific attention. Previous research indicated that socioeconomic disparities in health have increased in recent years even in the Nordic countries where social inequality is – at least comparatively – low [16,72,78,79,182,321]. In Study I, we found somewhat longer life expectancy among the highly educated but no support for widening educational disparities. We also found only minor differences in hip fracture incidence and survival between two educational levels in Study IV. By contrast, other studies found more pronounced socioeconomic differences in hip fracture incidence [184,185,242-251] as well as post-fracture mortality [322-326].

The small socioeconomic disparities found in our work are probably due to the choice of a dichotomous variable for education. We chose to specifically examine education rather than other socioeconomic indicators due to its stability over the life course, its association with health-related behaviours, and high completeness of data in population registers. In numerous other studies, higher education has been linked to lower mortality and a lower risk of various other health outcomes [69,70,72,182,321,327]. The link between education and health builds upon a strong theoretical foundation [328] and there is at least some evidence for a causal effect of education on health in old age [329]. However, a dichotomous indicator of attained educational level is only a crude proxy for socioeconomic position, especially among the old. The majority of older individuals in the AHC merely attained a compulsory educational level [330] but they have probably experienced diverse occupational trajectories and attained varying socioeconomic positions throughout their lifetime. Larger socioeconomic disparities could come to light when using a more fine-grained categorization of education or other indicators of socioeconomic position, such as income or former occupation.

Marital status, cohabitation, and the availability of close kin are important further sociodemographic factors affecting health patterns in an ageing society. In Study V, and in previous work [331,332], we have shown that living alone and childlessness are linked to the reception of home care, the amount of granted home care, and care home residence among the Swedish old. Furthermore, older individuals' number of children is associated both with the risk of some diseases including hip fracture, with disease prognosis including survival after stroke and hip fracture, and with longevity in general [333-337]. Since cohort fertility and marriage patterns are changing, this has probably influenced trends in disease incidence, care use, and longevity, but to which extent is, to my knowledge, not known.

6.3 IMPLICATIONS FOR AGEING RESEARCH

6.3.1 Selection and the changing population composition

While many studies on population ageing examined heterogeneity with regards to sociodemographic factors, this thesis also aimed to explore heterogeneity with regards to health – operationalized through disease history and comorbidity level. Previous research put forth hypotheses that health improvements have occurred primarily among the healthy, leaving the ill and frail behind [80-82], but also hypotheses that especially the ill and frail have benefitted from health improvements, ultimately leading to a compression of morbidity [10-12,191]. Our findings do not support the idea that health improvements were limited to the "upper end of the health distribution". If anything, life expectancy increased *faster* among older people who experienced a number of severe disease than in the total population.

In order to interpret secular trends in population health and draw correct conclusions, it is important to consider how population groups are changing. This may be especially challenging in ageing research since old age health is shaped throughout the entire life course and disentangling period and cohort effects is not always possible. A specific educational level in contemporary Sweden is, for instance, not comparable to the same educational level 50 years ago when access to higher education was more limited and curricula were unlike today. Since low education has become increasingly rare in some settings, it has been argued that trends towards poorer health outcomes among the low educated are to be expected and do not necessarily represent growing inequalities [338]. Likewise, a certain comorbidity profile today may not be comparable to the same profile several decades ago. Diagnostic manuals and procedures are constantly evolving which may lead to increasing numbers of diseases being recognized by the medical profession or being detected. As a result, trend studies – including our work – likely produce conservative estimates of improvements in population health when disregarding advances in disease detection and management.

Disregarding heterogeneity within the population, too, can result in disputable conclusions about population-wide trends. Even if all subgroups of the population experience improvements, the total population may not– a phenomenon known as Simpson's paradox [339]. Since the group of individuals who experience a hip fracture is increasingly frail and multimorbid, this selection effect naturally leads to a poorer prognosis even if advances in treatments have reached all patient groups. From a different perspective, one could also conceptualize such selection processes as *confounding* and argue in Study IV, for example, that rising comorbidity levels have confounded survival trends in the hip fracture population. One should note, however, that this selection does not necessarily entail a *bias*. Instead, it can be considered an explanation for the observed patterns.

6.3.2 Consequences of improved survival

Prolonged survival after acute disease events, such as hip fracture or myocardial infarction, could hypothetically lead to increasing recurrence rates. However, Study IV does not support this hypothesis for the example of hip fracture and previous research found similar patterns for CVD [131,132,160,289]. The declining recurrence rates for these conditions together with the life expectancy increases found for most diseases in Study I point towards improvements in tertiary prevention, that is, a reduction of the negative disease impact.

Prolonged survival with many diseases increases the risk of attaining more than one condition. As a result, multimorbidity has become more common in several Western countries, including Sweden, since the 1990s [150-159]. Multimorbidity has a considerable impact on survival and functioning of older adults [340] and polypharmacy, often required to manage several diseases, is associated with an increased risk of drug-drug interactions and other negative health outcomes [341]. We found comorbidities to be among the most important predictors of both mortality and care trajectories in Studies I, IV, and V. However, the higher mortality of individuals with comorbidities in Studies I and IV is perhaps not surprising given that comorbidity level was measured through the CCI, an indicator developed specifically to capture mortality risk. Various other comorbidity and multimorbidity indices have been developed and even though a number of studies have identified common clusters of comorbid diseases, patterns are complex and many findings have not been replicated in different settings and populations [147,154,342-346]. Improving the understanding of multimorbidity patterns and addressing their consequences should therefore be a public health priority in ageing societies.

6.3.3 Indicators of population health and their relationships

Monitoring a single indicator of health is not sufficient to capture the dynamics of changing morbidity and mortality patters in a population. We have shown in Study II how prolonged survival with disease, a fundamentally positive development, has both positive and negative effects on (period) life expectancy. Disease survivors continue to carry with them a higher mortality than their same-aged peers even many years after disease onset. In theory, improved disease survival could – all else equal – even lead to declining life expectancy. This paradoxical relationship is due to the life table method which draws on a cross-sectional snapshot of the population rather than a cohort of individuals followed over time.

It should also be noted that in growing and ageing societies, decreasing incidence rates do not necessarily result in declining numbers of disease events or declining prevalence in the population. If survival improves, so does person-time at risk which lowers incidence rates but not necessarily prevalence or lifetime risk [143].

Finally, regardless of how population groups are delineated, there often remain within-group differences. Even if life expectancy increases among groups with high and among groups with low educational levels, disparities could, for instance, increase within the subgroup with low education. Further stratification into more and more population groups quickly leads to very complex pictures and to difficulties synthesizing a large number of results. One strategy may be the use of health indicators that capture variability, such as lifespan disparity which can be used as a complement to life expectancy. Although life expectancy continues to increase in many countries, several studies provide evidence for growing lifespan disparities, even in the Nordic countries and even within specific socioeconomic strata [16,79].

6.4 PUBLIC HEALTH RELEVANCE

This thesis points to a number of public health issues in the ageing Swedish population. Firstly, increasing numbers of older individuals are long-term survivors of severe diseases and often have comorbidities.

Secondly, older adults with hip fracture are a particularly vulnerable population group with high mortality risk, especially among men. In Sweden, one in five women and one in nine men are expected to sustain a hip fracture during their life [143]. Despite this, previous research indicated that osteoporosis is still undertreated, often not detected until an osteoporotic fracture occurs, and men face an even higher risk to receive insufficient treatment than women [294,347]. Enhanced detection and treatment of osteoporosis together with improved fall prevention focusing on both genders may be strategies to reduce the burden of hip fractures in the older population.

The prognosis after a hip fracture is still poor. In Study V, almost half of patients without care at the time of their hip fracture transitioned to receiving care within three months and more than a third of hip fracture patients died within two years. There may thus be room for improving care and rehabilitation for some older individuals with hip fracture.

The vast majority of older adults who initiate home care after a hip fracture do not manage to return to independent living even when surviving for several years. It is possible that many individuals, once home care is granted, continue to utilize it out of convenience. If this were true, care resources may be allocated ineffectively. On the other hand, many hip fracture patients may indeed suffer from lasting disabilities which could be ameliorated through improved rehabilitation programs. Either way, our study has also shown that a minority of hip fracture patients *do* return to living without care. Identifying factors that promote such recoveries and promote resilience to debilitating diseases and other life events is an important prospect for future research.

Finally, little is known so far about the determinants and consequences of receiving home care and care home residence in Sweden. The reorganization of health and elder care systems as well as staff shortages [210,211] could result in care deficits, particularly among older individuals without close family ties [192,193,196,200]. Epidemiological research should continue to investigate whether such deficits exist, how they affect older people, and how they can be addressed in order to meet older individuals' needs and mitigate disparities.

6.5 METHODOLOGICAL CONSIDERATIONS

6.5.1 Data availability

Administrative population registers have several advantages for research on population ageing. Unlike clinical trials or survey data they cover everyone, even the oldest old, frailest, and socioeconomically disadvantaged. In addition, they include institutionalized older adults who are often excluded from other epidemiological studies thereby limiting their generalizability [30]. Drawing on nationwide data moreover maximizes study size and statistical power needed to examine health at very high ages, to study rare events such as disease recurrence, and to stratify the population into several groups.

Nevertheless, administrative registers also have limitations. As described in section 4.1.2.1, over-coverage may constitute a problem because not all emigrations are reported to the Swedish authorities [255]. In the entire population, this over-coverage may introduce a comparatively small bias, estimated to lie below 0.5% [255]. Among the oldest old and particularly older migrants, however, a bias may be more substantial. For the studies in this thesis, including Study IV which stratified analyses by birth country, we assured that individuals in the study population were continuously registered in each year. Individuals were censored once a data gap occurred, even despite a missing date of death or emigration. One should also note that the Swedish Cause of Death Register even records deaths of Swedish residents that occurred outside the country once they are reported to authorities. Still, it cannot be ruled out that a few older individuals continue to appear in the registers without residing in Sweden.

The time periods during which Swedish registers are available vary which entails limitations for research on time trends. Many registers, including the NPR and Cancer Register, have been virtually complete for several decades, enabling us to trace back disease history over long periods of time. Other registers have been introduced more recently, including the Dwelling Register and Prescribed Drug Register which have only been established in the 21st century. The structure of some registers has also been altered over time. The Social Service Register was introduced in 2007 but structural changes render data collected from 2013 onwards incomparable to earlier data. Therefore, our data did not allow us to study secular trends in geriatric care. Educational levels were not recorded for individuals born before 1911 in any Swedish register, not even in the earliest available censuses. In Study IV, we included all individuals in the main analyses but excluded those born before 1911 from the analyses stratified by education. For the multistate models in Study V, individuals with missing education were categorized as having the lower education level (1.6%). It is possible that educational differences were more (or less) pronounced in the excluded birth cohorts, but they constituted only a small part of our study populations.

6.5.2 Measuring health in population registers – Potential biases and other considerations

In order to perform trend studies, data must be comparable over time. However, disease classifications, diagnostic techniques, and administrative procedures change over time. While medical professionals could historically report only six (and later eight) diagnoses for each hospitalization to the Swedish NPR, this restriction has been abandoned in 2010 [256], potentially affecting the number of comorbidities identified through the register. Our data show that only very few hospitalizations have more than six diagnoses and we detected no sudden increase in comorbidities after 2010, but whether this administrative change may have promoted the detection of some specific diseases or comorbidities is, to my knowledge, not known.

Changing diagnostic techniques and accuracy may also have a large impact on observed disease frequency in the population. During the past decades, the proportion of strokes with undefined subtype in the NPR has declined. Today, a larger proportion of strokes is classified as either ischemic or hemorrhagic than in the past. Register-based estimates of both ischemic and hemorrhagic stroke incidence were thus more notably underestimated in the past than they may be today. Since Study II relied on an accurate estimation of changes in disease prevalence, we were hence only able to examine stroke as a single disease.

A trend towards earlier cancer diagnoses may be one mechanism behind the rising life expectancy of cancer populations in Study I and the increased cancer prevalence and survival found in Study II. Diagnostic sensitivity, precision, and cancer awareness have likely increased over time. Therefore, we cannot rule out that our findings are influenced by lead time bias, that is, a trend towards earlier detection of cancer, towards cancer being less advanced at diagnosis, and thus towards longer survival [348]. Lead time bias is of particular concern if screening programs are introduced. In Sweden, breast cancer screening had already been established in 1986 [349] and no additional screening programs were introduced during our study period and for the cancer types we examined. Still, attendance rates in the existing screening program for breast cancer may have changed over time thereby influencing the timing of breast cancer diagnosis.

Misclassification of comorbidity levels may have occurred because of limited sensitivity of disease detection through the NPR. Therefore, part of our study populations certainly had higher comorbidity levels than their CCI scores suggest, leading to a dilution of the differences between comorbidity levels. In addition, in groups without comorbidities, this may have led to an underestimation of life expectancy (Study I) or to an underestimation of survival chances after hip fracture (Study IV), respectively. It remains also possible that the increasing capacity to record secondary diagnoses in the NPR discussed above has artificially increased CCI scores over time.

Dementia is a condition that is particularly difficult to detect in inpatient records, because dementia itself seldomly requires hospitalization. One should note that in Study V, all hip fracture patients were hospitalized and dementia, if present, should be registered as co-diagnosis. Still, the sensitivity of this assessment method is not perfect and it is possible that dementia is not always registered, especially in mild cases. As a result of this misclassification, the association between dementia presence and care trajectories may be underestimated in Study V.

Our comparison in Study III shows that both the NPR and the SHR have some limitations for epidemiological research. While the sensitivity of detecting recurrent fractures in the NPR is likely high, the PPV is lower. Study III concludes that, while the NPR can be used to identify recurrent fractures, their incidence may be overestimated, presumably by 10 to 15%. Therefore, the recurrence rates presented in Study IV are probably overestimated to a similar extent. It is evident, however, that an overestimation of such magnitude is unlikely to have caused the pronounced declines in recurrence rates of up to 50%.

6.5.3 Strengths and limitations

Apart from some exceptions discussed in the previous sections, the register data used in this thesis have high levels of completeness and validity [256,257,272]. Although the diseases we examined cannot completely account for the complex morbidity patterns in the ageing society, they represent frequent and severe medical conditions that occur at older ages in Sweden and elsewhere.

Our studies add to prior evidence by exploring heterogeneity in population health with regards to health using a composite measure, the CCI score, to operationalize comorbidity. Although the CCI is today arguably one of the most commonly used comorbidity indices in epidemiological studies, it remains contested and several modified versions as well as alternative comorbidity and multimorbidity measures have been developed – all of which are accompanied by their own strengths and limitations [112,147,279,281,350]. Moving beyond a composite measure and exploring how specific comorbid conditions are associated with life expectancy or hip fracture epidemiology will eventually increase the understanding of trends in population health.

One limitation of Study III is the absence of a gold standard, such as independent expert reviews of patient records. While our method of comparing two registers allowed us to draw a number of conclusions about their data quality and completeness, it is possible that some information is incorrect in both registers and, in case of conflicting data, we were not able to determine which – if any – of the two registers contained the correct data. However, conflicting data was rare and previous research validating hip fracture diagnoses in inpatient registers against gold standards suggested that data quality is indeed excellent [256,264,268,269].

Lastly, Study V did not take into account informal care provided by close kin or private care paid entirely out of pocket. The municipal care examined in Study V constitutes more than 90% of formal care for older people in Sweden while care paid entirely out of pocket is still rare but increasing [192-194]. Informal care provided by close kin, most often spouses and adult children, is becoming more common, too [192,199]. However, our multistate model in Study V showed that the association between cohabitation, likely a proxy for the availability of informal support provided by a spouse, and care trajectories was relatively modest. This could indicate that informal support provided by cohabiting partners does not play a major role for older hip fracture patients' care trajectories.

6.5.4 Generalizability

The external validity of our findings varies. The disease panorama in Sweden is known to be overall similar to that in many other Western countries, at least with regards to cancer and CVD incidence and the distribution of causes of death [88,89]. Advances in medical treatments, too, have probably occurred simultaneously in Sweden and in other high-income countries that are able to afford innovative technology and treatments. Disease prevalence and life expectancy in these countries may have therefore developed in a way similar to Sweden. As such, the general findings of Studies I and II may be transferable to many other high-income countries.

Although the disease panorama is similar in most Western countries, there are naturally some differences in disease frequency and survival chances due to the genetic makeup of the population, sociocultural factors, or the welfare system. For reasons not yet completely understood, incidence rates of hip fractures in the Nordic countries are among the highest worldwide [351] and thus, incidence and recurrence rates found in Study IV may be comparable to Norway or Finland, but probably not many other countries. Furthermore, the health selection of hip fracture patients discussed in Study V may not be comparable to other settings with much lower incidence rates.

The estimated coverage of national quality registers in Sweden varies [260]. Still, some of our conclusions in Study III are likely transferable to other quality registers covering acute diseases that are almost always treated in a hospital setting. Specifically, part of the non-coverage of other quality registers may result from opting out on the hospital level and, moreover, patients with poor survival chances may be less likely to appear in quality registers.

Subgroup-specific findings from Sweden are probably only transferable to other high-income countries with similar patterns of sociodemographic inequality. In the Nordic countries, access to education is free. Virtually all older adults alive today have completed secondary education [330] and social inequality is, at least comparatively, low. Every Swedish resident has access to treatments, specialist care, and rehabilitation, even those at the lower end of the income distribution. In addition, the ethnic composition of the older population is rather homogenous. Although international migration among younger adults has picked up pace in the past few decades, most older residents were born either in Sweden or in other countries located in Northern and Western Europe. Socioeconomic and ethnic disparities in Sweden may thus not be comparable to more diverse countries or settings with more pronounced social inequalities. In addition, gender differences in the Nordic countries may not be transferable to many other settings. In Sweden and the other Nordic countries, gender equality has long been emphasized by policy makers and many older women today have been employed in the labour market during much of their life instead of working as homemakers.

Sweden is also a setting with publicly funded care accessible to all residents and a heavy emphasis on “ageing in place” policies. Care trajectories presented in Study V may thus not be generalizable to other countries in which care systems build more heavily upon family support or care homes (as is the case is most countries outside Scandinavia) or to settings where home care services come with substantial costs for the individual.

7 CONCLUSIONS

In this thesis, I present trends in population health in Sweden since the 1990s while highlighting heterogeneity within the population. Based on the results of five studies I draw the following conclusions:

- Increases in life expectancy were not limited to the healthy part of the population. Longer survival with myocardial infarction specifically explained almost half of the total rise in life expectancy.
- Rising life expectancy can not only be attributed to primary and secondary prevention, but also to tertiary prevention, enabling patients to survival longer.
- Increasing proportions of older adults have a history of severe diseases. The growing prevalence of disease history and the longer disease survival have counteracting influences on life expectancy trends. For CVD, the positive impact of improved survival far outweighs the negative impact caused by increasing disease prevalence.
- Hip fracture incidence has declined in all population groups under study – and even more so for recurrent than for first hip fractures.
- Survival chances among hip fracture patients remained stable, but improved when taking into account their rising comorbidity levels. Hip fracture patients remain a vulnerable group with increasing comorbidity levels and high mortality, especially among men.
- Already before their fracture, hip fracture patients receive geriatric care more often than their same-aged peers. Hip fractures have an immediate impact on care trajectories but long-term care needs are largely attributable to poorer health profiles already present before the fracture occurs. Studies that do not account for such selection overestimate the negative impact of hip fractures and possibly other diseases.
- Swedish population registers are valuable resources for studies on hip fractures, but both the SHR and the NPR have some limitations. Studies using the NPR may overestimate number of recurrent fractures and while the SHR covers 80% of hip fractures in Sweden, it is not complete.
- Half of missing fractures in the SHR were a result of opting out on the hospital level. Such non-coverage attributable to administrative decisions is arguably less likely to induce bias than non-coverage on the patient level. However, there is also some selection on the patient level; patients dying shortly after their fracture are less likely to be included in the SHR.
- Increasing numbers of older adults are long-term survivors of severe diseases and have comorbidities. Improving the understanding of multimorbidity patterns and addressing their consequences should therefore be a public health priority in ageing populations.

8 FUTURE DIRECTIONS

The continuous mortality improvements during the past decades prompt questions about their sustainability in the future. How long can life expectancy continue to increase? Or, perhaps more importantly, how old can we become? Is there a limit to human lifespan and can we reach the highest ages in good health? So far, not much is known about disease incidence and mortality rates among centenarians and super-centenarians, but population registers provide an increasingly rich data source in times in which more and more men and women reach their 100th birthday.

Lying at the core of public health sciences, socioeconomic, gender, ethnic, and other disparities remain an important area for research. Epidemiologists should continue to explore whether such disparities exist even at extreme ages and how they develop as societies age. Future epidemiological studies may also turn towards heterogeneity in the population with regards to characteristics that are as of yet less explored and examine how, for example, latent characteristics such as individuals' genetic or biological profiles or more complex measurements of gender identity, childlessness, and living arrangements affect population health.

Health and care systems are changing both in Sweden and in many other countries. The consequences of such changes for older people's health and wellbeing need to be monitored. Do financial cutbacks, staff shortages, or ageing-in-place policies imply increasing care deficits for at least some groups of older people? Epidemiological research should continue to investigate whether such deficits exist, how they affect older individuals, and how they could be ameliorated. Moreover, the rising prevalence of multimorbidity is likely associated with changing demands and challenges for health and care systems, but patterns of multimorbidity in the population are complex and, so far, poorly understood. Structuring and operationalizing complex and evolving patterns of disease co-occurrence, and understanding their consequences, is an important objective of ageing research.

Finally, this thesis showed that hip fractures are debilitating conditions occurring among the oldest old, but also that some patients *do* manage to recover their independence. How can we promote such recoveries from – and resilience to – severe diseases, extreme weather, injuries, or other negative life events? Perhaps we can shift the focus of ageing epidemiology also towards developing strategies that allow older adults to better face diseases and other challenges.

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