

The life course construction of social inequalities in health in old age

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DISSERTATION

Presented to the Faculty of Social Sciences
of the University of Geneva

by

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Under the supervision of

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in Candidacy for the Degree of

Doctor in Social Sciences (Demography)

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Dissertation no 136

Geneva, 10 December 2019

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Genève, le 10 Décembre 2019

Le doyen

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Impression d'après le manuscrit de l'auteur

Statement

The present work is a cumulative dissertation based on three articles. It has been prepared as a self-contained work and all chapters were composed specifically for this dissertation. Furthermore, all articles were written by me as first author according to the APA author guidelines with edits from my co-authors. The articles are included in this thesis as they were submitted to the respective journals. All three articles have been published. Terminological and formatting inconsistencies may occur due to the different journal publishing policies.

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Résumé

Le vieillissement de la population, en raison de l'allongement de l'espérance de vie et de la baisse du taux de fécondité, devrait entraîner une augmentation des maladies chroniques et de la multi morbidité. Toutefois, le fait de vivre plus longtemps ne signifie pas forcément vivre en bonne santé. De plus, les facteurs biologiques, les conditions socio-économiques, les comportements liés à la santé et les facteurs environnementaux ont tous un impact sur la santé et ces conditions sont inégalement réparties au sein de la population entraînant des inégalités en matière de santé. Les conditions socio-économiques ont été identifiées comme un facteur clé de ces différences interindividuelles en santé.

Le gradient social en santé décrit la relation entre la condition socio-économique d'une personne et sa santé, ainsi une position élevée dans la hiérarchie sociale, implique une meilleure santé. Plusieurs théories expliquent l'impact persistant des inégalités socio-économiques. L'une des théories, souvent utilisée en épidémiologie et en santé publique, est le parcours de vie. Elle suggère que les inégalités en matière de santé, dans le vieillissement, sont en partie déterminées par les inégalités sociales, psychologiques et biologiques vécues pendant l'enfance. La perspective du parcours de vie est une approche utile dans l'étude du vieillissement, permettant de donner un aperçu des différentes voies ainsi que du rôle joué par les trajectoires et les événements de vie sur la santé à un âge avancé. L'objectif principal de cette thèse était d'étudier les inégalités liées à la santé chez les personnes âgées, dans le contexte de facteurs sociodémographiques. Pour étudier les associations entre les conditions socio-économiques et la santé dans le contexte du vieillissement, nous avons utilisé la perspective du parcours de vie afin de tenir compte des mécanismes et processus causaux sous-jacents au gradient social. Cette thèse est présentée sous la forme d'articles, puisqu'elle contient trois articles, utilisant les données de l'enquête sur la Santé, le Vieillissement et la Retraite en Europe (SHARE).

Le chapitre 2, article 1, décrit l'importance d'adopter la perspective du parcours de vie dans l'étude des inégalités liées à la santé dans la population générale. Le premier objectif était d'étudier les associations entre les conditions socio-économiques pendant l'enfance et l'apparition du cancer lors du vieillissement. Le deuxième objectif était de vérifier si les conditions socio-économiques à l'âge adulte avaient un effet médiateur sur cette association. Les résultats ont montré que les hommes et les femmes issus de milieux socio-économiques très défavorisés à défavorisés, pendant l'enfance, étaient globalement moins susceptibles de développer des cancers au vieillissement. Cependant, les résultats varient selon la localisation du cancer et du sexe. Les femmes ayant vécu, une enfance, dans des conditions socio-économiques favorisées et moyennes étaient deux fois plus susceptibles de développer un cancer de la peau. Tandis que les femmes ayant vécu dans les conditions socio-économiques, les plus favorisées pendant l'enfance étaient plus susceptibles de développer un cancer du sein que les femmes ayant vécu dans les conditions socio-économiques les plus défavorisées à l'enfance. Les hommes ayant vécu

dans des conditions socio-économiques moyennes, pendant l'enfance, étaient deux fois moins susceptibles d'avoir souffert d'un cancer du côlon ou du rectum que les hommes ayant vécu dans les conditions socio-économiques les plus défavorisées. Les conditions socio-économiques à l'âge adulte n'ont pas changé les associations, ne suggérant aucun effet médiateur.

Le chapitre 3, article 2, examine les associations entre les indicateurs du parcours de vie et la fragilité, un syndrome clinique lié aux conditions de vie des personnes âgées. Les objectifs de cette étude étaient de vérifier si les conditions socio-économiques vécues à l'enfance étaient associées à des niveaux de fragilité chez les personnes âgées et si cette association était médiée par les conditions socio-économiques vécues à l'âge adulte. Les résultats ont montré qu'une association entre les conditions socio-économiques vécues à l'enfance et les chances d'être fragile est présente tant chez les femmes que chez les hommes: plus les conditions socio-économiques à l'enfance sont défavorisées, plus les chances d'être fragile sont élevées. Cependant, contrairement à notre précédente étude sur le cancer, les conditions socio-économiques vécues à l'âge adulte sont médiateurs de l'effet des conditions socio-économiques vécues pendant l'enfance sur le risque de fragilité chez les femmes et les hommes.

Le chapitre 4, article 3, explorait différentes voies menant à la fragilité lors du vieillissement. L'article a étudié les associations entre les adversités vécues durant l'enfance (y compris les conditions socio-économiques, les expériences négatives et les problèmes de santé pendant l'enfance), la fragilité pendant le vieillissement, l'effet médiateur des conditions socio-économiques à l'âge adulte et les variations potentielles à travers les régimes de protection sociale. Les résultats ont montré que plus le désavantage socio-économique pendant l'enfance et les confrontations à des expériences négatives durant l'enfance est grand, plus les chances d'être fragile sont élevées. À travers les régimes de protection sociale, on a constaté des associations entre les conditions socio-économiques pendant l'enfance et la fragilité dans les régimes de protection sociale d'Europe de l'Est. Dans les régimes de protection sociale scandinaves et bismarckiens, une association entre les expériences négatives durant l'enfance et la fragilité a été trouvée. Enfin, une association entre les expériences liées à la santé durant l'enfance et la fragilité a été démontrée dans les régimes de protection sociale bismarckiens et d'Europe de l'est. Les conditions socio-économiques à l'âge adulte ont joué un rôle médiateur dans les associations entre les conditions socio-économiques vécues pendant l'enfance et la fragilité, mais pas dans les associations entre les expériences négatives et la fragilité, à la fois dans l'échantillon global et stratifié par le régime de protection sociale.

En conclusion, dans cette thèse, nous avons décrit l'influence de l'aspect socio-économique sur la santé lors du vieillissement, dans une perspective de parcours de vie. Nos résultats montrent une association entre les conditions socio-économiques vécues à l'enfance et la santé à un âge avancé, avec des orientations différentes selon les facteurs de risque, liés aux effets sur la santé, qui ont été étudiés. En ce qui concerne le cancer, nous avons montré que les

personnes ayant vécu dans des conditions socio-économiques très défavorisées et défavorisées, pendant l'enfance, étaient plus susceptibles de ne pas développer de cancers comparativement aux personnes les plus favorisées. En revanche, pour la fragilité, plus le désavantage est grand, plus les chances d'être fragile sont élevées. De plus, d'autres facteurs dans la petite enfance (c.-à-d. les expériences négatives et les problèmes liés à la santé durant l'enfance) et des facteurs macroéconomiques (c.-à-d. le régime de protection sociale) sont associés à la fragilité. De plus, l'effet des conditions socio-économiques au cours de la vie sur ces associations diffère : elles ne sont pas médiatrices des associations entre les conditions socio-économiques pendant l'enfance et le cancer ainsi que des expériences négatives avec la fragilité, mais elles sont médiatrices des associations entre les conditions socio-économiques durant l'enfance et la fragilité. Cela montre l'importance d'améliorer les conditions socio-économiques tout au long de la vie, afin de réduire les inégalités liées à la santé chez les personnes âgées. Nous recommandons la réalisation d'études visant à explorer différentes voies impactant la santé au vieillissement, afin d'appuyer nos résultats et de mieux identifier et comprendre les associations. Pour faciliter la bonne santé lors du vieillissement, il est important d'identifier les promoteurs et les obstacles, tout au long de la vie, qui peuvent être ciblés par la surveillance et les stratégies de santé, réduisant ainsi l'impact des conditions de vie défavorables sur les inégalités de santé.

Abstract

Population ageing as a result of increased life expectancy and declining fertility rates is expected to lead to a rise of chronic conditions and multimorbidity. However, living longer does not automatically mean that those added years in older age are lived in good health. In addition, biological factors, socioeconomic conditions, health behaviours, and environmental factors all have an impact on health and these conditions are unequally distributed among the population, thereby causing health inequalities. Socioeconomic conditions have been identified as a key factor by which health varies.

The social gradient in health describes the relationship between a person's socioeconomic condition and his/her health, where the higher the position in the social hierarchy implies experiencing better health. Several theories exist that explain the persisting impact of socioeconomic inequalities. One of these theories is the life course perspective, often used in epidemiology and public health. It suggests that health inequalities at older ages are partly determined by inequalities in early life social, psychological, and biological conditions. The life course perspective is a useful approach when studying ageing, because it can give insights into different pathways and the role trajectories and life events play in health in later life. Therefore, the main aim of this thesis was to study health inequalities in old age, within the context of socio-demographic factors. To study associations of socioeconomic conditions with health in later life, we used a life course perspective to consider causal mechanisms and processes that lie behind the social gradient. This thesis is in article format and contains three papers using data from the Survey of Health, Ageing, and Retirement in Europe.

Chapter 2, paper 1, described the basis for the importance of adopting a life course research perspective when studying health inequalities in the general population. The first aim was to study associations of childhood socioeconomic conditions with cancer onset in later life. The second aim was to test whether adulthood socioeconomic conditions had a possible mediating effect of on this association. Results showed that both men and women from the most disadvantaged and disadvantaged childhood socioeconomic conditions were most likely to be overall cancer-free over time, but results vary by cancer site and sex. Women with advantaged and middle childhood socioeconomic conditions were more than twice as likely to have had skin cancer and women with the most advantaged childhood socioeconomic conditions were more likely to have had breast cancer compared with women with the most disadvantaged childhood socioeconomic conditions. Men with middle childhood socioeconomic conditions were half as likely to have had colon or rectal cancer compared with the most disadvantaged childhood socioeconomic conditions. Adulthood socioeconomic conditions did not change the associations, suggesting no mediating effect.

Chapter 3, paper 2, examined associations of life course indicators with frailty, a clinical syndrome linked to the daily living conditions of the elderly. The

aims of this study were to test whether childhood socioeconomic conditions were associated with levels of frailty in older adults and whether this association was mediated by adulthood socioeconomic conditions. Results showed an association between childhood socioeconomic conditions and the odds of being frail in both women and men: the more disadvantaged the childhood socioeconomic conditions, the higher the odds of being frail. However, in contrast to our study on cancer, adulthood socioeconomic conditions do mediate the effect of childhood socioeconomic conditions on the odds of being frail in both women and men.

Chapter 4, paper 3, explored different pathways to frailty in later life. The paper studied associations of childhood misfortune (including childhood socioeconomic conditions, adverse childhood experiences, and adverse childhood health experiences) with frailty in later life, the mediating effect of adulthood socioeconomic conditions, and potential variations across welfare regimes. Results showed that the higher the socioeconomic disadvantage at childhood and having had adverse experiences, the higher the odds of being frail. Across welfare regimes, associations of childhood socioeconomic conditions with frailty were found in the Eastern European welfare regime, of adverse childhood experiences with frailty in the Scandinavian and Bismarckian welfare regimes, and of adverse childhood health experiences in the Bismarckian and Eastern European welfare regimes. Adulthood socioeconomic conditions mediated the associations of childhood socioeconomic conditions with frailty, but not the associations of adverse experiences with frailty, in both the overall sample and stratified by welfare regime.

In conclusion, in this thesis we described the influence of socioeconomic on health in later life, using a life course perspective. Our results show an association of childhood socioeconomic conditions on health in later life, with varying directions depending on risk factors related to the health outcomes studied. For overall cancer, the most disadvantaged and disadvantaged childhood socioeconomic conditions were most likely to be cancer-free compared with the most advantaged. In contrast, for frailty, the higher the disadvantage, the higher the odds of being frail. In addition, other factors in early life (i.e. adverse childhood experiences and adverse childhood health experiences) and macro level factors (i.e. welfare regime) are associated with frailty. Moreover, the effect of life course socioeconomic conditions on these associations differs: they do not mediate associations of childhood socioeconomic conditions with cancer and adverse experiences with frailty, but they do mediate associations of childhood socioeconomic conditions with frailty. This indicates the importance of improving socioeconomic conditions over the whole life course in order to reduce health inequalities in old age. We recommend future studies to explore different pathways to health outcomes in later life to support our results and to better identify and understand associations. In order to facilitate healthy ageing, it is important to identify promoters and barriers across the life course that can be targeted by health surveillance and strategies, thereby reducing the impact of unfavourable life conditions on health inequalities.

Acknowledgements

The last three years, from starting my PhD to handing in my thesis, have flown by. Since some friends were saying I was doing a PhD in tourism, I guess it has literally flown by. It has been a very special and important time in my life course and I am grateful for all the help, advice, and support I have received. I would like to say a special word of thank you to a selection of people whose support has been vital in getting me to where I am today.

First, I have been lucky with my supervisors Matthias Kliegel and Michel Oris and I have to thank them for giving me the opportunity of doing my PhD at the Centre for the Interdisciplinary Study of Gerontology and Vulnerabilities. It has been a pleasure working with both of you and being part of your teams. With the different backgrounds we have, discussing my projects and ideas with you gave new perspectives and helped me to make my research truly interdisciplinary. Thank you for your time and involvement and supporting me in developing my ideas.

Next, I would like to thank the other members of my dissertation committee for agreeing to be part of my thesis jury: Prof. Thomas Abel, Prof. Claudine Burton-Jeangros, Dr. Stéphane Cullati, and Dr. Rainer Gabriel. I appreciate your expertise on the topics and the assessment of my thesis.

Of course, I have to thank all my colleagues at the CIGEV and of the Cognitive Aging Lab, for integrating me into their teams, in particular my 'academic family' for the relaxing times at and outside of work. Nicola and Alexandra, thank you for getting me started in Geneva, for always being there to help me out, for nice chats, and of course for the crazy workouts together. Stéphanie, for the short but good time we spend together in the office and Sascha, for putting up with me for a bit longer. I am happy we shared the fit office together with time for serious, but also entertaining talks. Oana, for supporting me throughout my PhD, being down-to-earth, and helping me to survive my first days in a French-speaking environment. Sarah, when joining Oana's project you integrated easily into the teams with your positive attitude. Rainer, for always making time to help me figure out how to

proceed with my research. Maximilian, for the humorous times and for all your baking. Andreas, for being available pretty much 24/7 to help out with statistical questions. I was happy to no longer be the 'peewee' of the team when the CAL expanded: Morgane, Gianvito, Greta, and Doriana. Thank you all for your help and collaboration, but probably even more for the fun times at and outside of work.

Further, I would like to thank the researchers that I have had the chance to collaborate with on projects and who shared their expertise with me. The inspiring lecturers of my Master's program and the EnCoRe team, in particular Christel, Martijn, Matty, and Eline. My internships with you have definitely motivated me to continue doing research and have prepared me for my PhD. The Lifetrail team, especially Boris, St  phane, Dan, and Stefan, for their expertise and support in carrying out this successful project. Adrien, for your expertise in statistics and your enthusiasm to collaborate on projects.

This PhD thesis has been part of the LONGPOP project, supported by the European Union's Horizon 2020 research and innovation programme under the Marie Sklodowska-Curie Grant agreement No. 676060. I would like to express my gratitude to the driving forces behind the LONGPOP project: Diego,   ngela, and all partners in the project, without whose commitment and competence this project would not have been possible. Special thanks to my colleague early-stage researchers for the good times at the workshops, conferences, and secondments and for sharing our experiences.

Finally, from my academic family to my actual family and to my friends. You all contribute and support me in your unique ways, so thank you for filling my life with joy and smiles, keeping me sane, and being crazy together. I may not be always near, but I am thankful you are always there for me. Special thanks to my parents, Mark and Bernadet, and my brother, Tom, for giving me a strong foundation, believing in me, traveling around to spend time together, but also for always keeping my feet on the ground and giving me a warm home.

Chapter 1. General Introduction

1.1 Population ageing

In 2017, the global population aged 60 years or over counted 962 million, which was more than twice the size as in 1980 (United Nations, 2017). Projections indicate that by 2050, the number of people aged 60 years or over is expected to double again reaching the 2.1 billion. Moreover, in 2018, the number of people aged 65 or over was larger than the number of children under the age of five and by 2050 people aged 60 years and over are even expected to outnumber people aged 15 years and under (United Nations, 2019). Population ageing, an increasing proportion of older persons in the population, is being experienced in all regions of the world and is affected by several factors.

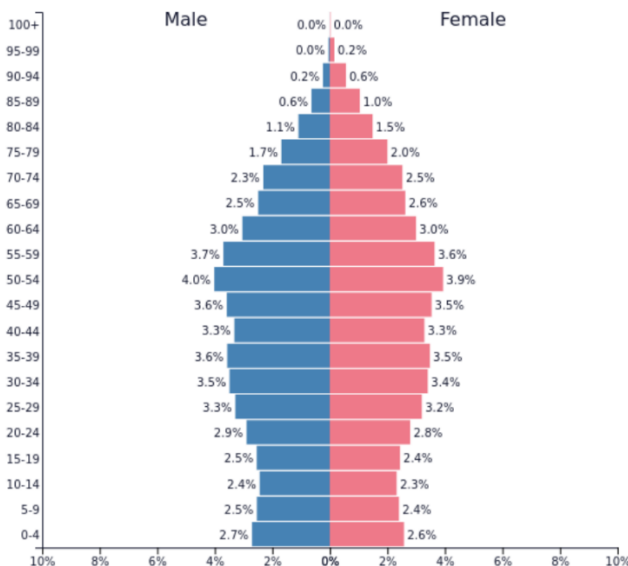


Figure 1 Population pyramid of Switzerland, 2019 (Source: PopulationPyramid.net)

First, an important impact of the demographic transition is declining fertility rates, which leads to a smaller proportion of the population in the younger age group (Land & Lamb, 2017). Second, in the older age groups, we see an increasing proportion, which can be explained by the epidemiologic transition: life expectancy increased as a result of lower mortality from infectious and chronic diseases

(World Health Organization, 2015). This changing disease pattern is mainly the effect of improved public health measures and rising standards of living, resulting in improvements of nutrition, hygiene, sanitation, and healthcare interventions (Huber et al., 2011). A third, however less influential, factor is patterns of migration, where it is often seen that immigrants tend to be younger, causing countries experiencing more out-migration to have an older population (Land & Lamb, 2017). These factors can be made visible by looking at the population pyramid, or age-sex-pyramid of countries, that shows the overall age distribution of a population by sex and reflects the evolution of the fertility rate and life expectancy. For example, the population pyramid of Switzerland, shown in Figure 1, is narrowed at the bottom, indicating a lower birth rate, and illustrates the long life expectancy and low death rate.

Due to the growing proportion of the population being of pension age relative to those of working age, societies are facing social, economic, and political challenges. For example, increasing expenditures in terms of pension benefits and social and health care place a strain on public finances. Even though several countries are encouraging longer periods of employment by delaying retirement, leading to a rise in employment rates at older ages, a large proportion of adults will still retire before the retirement age, either voluntary or because they are no longer welcome on the labour market. After World War II, when most of the welfare states have been established, the first research in gerontology saw retirement as a withdrawal from society for exhausted individuals who deserved to have a final peaceful period in life (Banks, 2006; Nazroo, 2017). This theory of 'disengagement' is nowadays outdated, since a second generation of researchers, observing the rise of life expectancy and of health above the age of 65, invented the term 'third age'. This third age referred to the period after retirement that is lived in good health and free from the constraints of work and the charge of children, a time for personal achievement and fulfilment (Laslett, 1987). More recently, models of 'active ageing' and 'healthy ageing' have been dominant (Baltes & Baltes, 1990; Rowe & Kahn, 1997).

1.1.1 Definitions of health and healthy ageing

Health has been defined as “a state of complete physical, mental and social wellbeing and not merely the absence of disease or infirmity” (World Health Organization, 1946). However, with the ageing of the population and changing disease patterns, studying health as per the definition of health as described by the World Health Organization (WHO) has received criticism (Baltes & Baltes, 1990; Jadad & O'Grady, 2008; Larson, 1999; "What is health? The ability to adapt," 2009). First, the emphasis on 'complete wellbeing' would mean that most of the population would be unhealthy: diseases are being redefined by medical technology and drug industries through new screening technologies that are able to detect illnesses at lower levels and through lowering thresholds for interventions. This lowering of levels and thresholds could often lead to the identification of conditions that would not cause disease and do not need intervention (Huber et al., 2011). Second, as a result of the demographic and epidemiologic transitions, as described earlier, more people worldwide are living with chronic diseases for a longer time and those people would not be considered as healthy, thereby putting pressure on social, economic, and political systems (Huber et al., 2011). Third, the WHO has developed the Family of International Classifications, such as the International Classification of Functioning, Disability and Health, to classify diseases and human functioning in a universally systematic and standardized way (World Health Organization, 2001). However, the 'complete' state of wellbeing is neither operational nor measurable (Jadad & O'Grady, 2008). A starting point for a proposition of health as a dynamic and measurable concept is the formulation of health as 'the ability to adapt and to self manage' (Baltes & Baltes, 1990; Huber et al., 2011).

Living longer does not automatically mean that those added years in older age are lived in good health. Even though it is important for society and the individual, evidence that people live a longer healthier life is unclear (World Health Organization, 2015). With the current time trends, an important question that needs to be studied is whether the increased life expectancy also means an increased healthy life expectancy. People in good health are better able to stay

part of society than those suffering from declines in their physical and mental health. In addition, engaging in socially productive and meaningful activities is associated with better social and mental wellbeing and is important for healthy ageing (Bound & Waidmann, 2007; Coyle, 2003; Drentea, 2002; Hao, 2008).

Biologically, ageing can be regarded as the accumulation of molecular and cellular damage, which over time leads to increased risk of disease and a decline in the capacity of an individual (World Health Organization, 2015). Healthy ageing is a concept that is often used to distinguish between disease-free, healthy versus unhealthy individuals. Given that many people at older age have health conditions that may have only little influence on their functioning, the World Health Organization defines healthy ageing as 'the process of developing and maintaining the functional ability that enables well-being in older age' (World Health Organization, 2015). Functional ability includes an individual's physical and mental capacities, contextual factors such as built and social environment, and interactions between the individual and their environment. However, biological factors, such as genetics, lead to a different ageing process for every individual. In addition, socioeconomic conditions, health behaviours such as exercising or smoking, and environmental factors such as living in polluted areas, have an impact on health and these conditions are unequally distributed among the population, thereby causing health inequalities (M. Marmot, Friel, Bell, Houweling, & Taylor, 2008; World Health Organization Commission on social determinants of health, 2008).

1.2 Social inequalities in health

One of the key factors by which health varies is socioeconomic position, which can be measured by education, occupation, or income (Galobardes, Shaw, Lawlor, Lynch, & Davey Smith, 2006). This social gradient in health is one of the

most documented patterns: the relationship between a person's socioeconomic condition and his/her health, where the higher the position in the social hierarchy implies experiencing better health. Health inequalities between people from a high versus a low socioeconomic position have been shown to be between 5 and 10 years difference in average life expectancy at birth, and between 10 and 20 years in disability-free life expectancy (Commission of Social Determinants of Health, 2008; Mackenbach et al., 2008; Sihvonen, Kunst, Lahelma, Valkonen, & Mackenbach, 1998). Several European countries have successfully reduced inequalities in income, living conditions, and access to services by developing welfare policies (Gøsta Esping-Andersen, 1990; Ferrera, 1996). However, socioeconomic inequalities in health are still present and are even widening (Fawcett, Blakely, & Kunst, 2005; Mackenbach et al., 2003; Strand et al., 2010; Valkonen et al., 2000; Wilkinson, 1989).

1.2.1 Theories of health inequalities

A series of theories have been brought forward to explain the persisting impact of socioeconomic inequalities (Bambra, 2011; Mackenbach, 2012). In sociology, the major frame refers to the systems of social stratification that consist of three components that can further be used to see mechanisms that underlie health inequalities (Mackenbach, 2012). First, social reproduction and social mobility sorts individuals into different strata, with corresponding personal characteristics. Second, distribution of and access to material and immaterial resources differs between the strata. Third, some resources are seen as more valuable in one stratum than in another, which may be related to health promotion. Mackenbach identified nine theories¹ that may help explain socioeconomic inequalities in health; three general theories and six that are closely related to one of the three components mentioned above (Mackenbach, 2012). One of the three general theories is the life course perspective that suggests that health inequality at older

¹ In this thesis, we will only describe the theories directly related to the included papers. For more information on the nine theories, we would like to refer to the article written by Mackenbach.

ages is partly determined by inequalities in early life social, psychological, and biological conditions (Bambra, Netuveli, & Eikemo, 2010; Wadsworth, 1997). This theory forms the basis of the research presented in this thesis and will be discussed in section 1.3 below.

1.2.2 Health inequalities in cancer and frailty

Health, whatever its definition, is an incredibly large concept including many diseases and conditions. In this thesis on health and ageing, we study a subpopulation of individuals aged 50 years and over (more details on the data in section 1.4.2), the so-called 'second half of life' (Wanner, Sauvain-Dugerdil, Guilley, & Hussy, 2005). We focus on health issues that are associated with social challenges and test if they can be explained by individual life courses, including the first half of life. Article 1 is devoted to a well-known multifactorial pathology, cancer, while in articles 2 and 3 we consider a condition, frailty.

Cancer is one of the leading causes of death worldwide, accounting for an estimate of 9.6 million deaths in 2018 and an expected 13 million deaths in 2030 (World Health Organization, 2019). In addition, due to the increased life expectancy and exposure to risk factors, the incidence of cancer is rising: between 2008 and 2030, an increase of 40% is expected in high-income countries and of even more than 80% in low-income countries (World Health Organization, 2019). The highest incidence rates are found in the 85-89 age group for both sexes and almost 90% of all cancer deaths are older than 50 years (Roser & Ritchie, 2019). In addition, age-specific incidence rates rise steeply from age 55-59 on. Socioeconomic differences in cancer incidence, prevalence, and survival are seen across populations. Studies have found associations of lower socioeconomic status with higher incidence of respiratory, oesophagus, stomach, and cervical cancer and of higher socioeconomic status and colon, breast, and ovary cancer, and skin melanoma (Bryere et al., 2016; Faggiano, Partanen, Kogevinas, & Boffetta, 1997; Weiderpass & Pukkala, 2006). Overall, patients from higher socioeconomic status were found to have higher survival rates (Bouchardy,

Verkooijen, & Fioretta, 2006). Key risk factors associated to cancer are tobacco and alcohol use, unhealthy diet, and physical inactivity, but part of the variation is still unexplained. However, it is suggested that stressful conditions and adverse events in early life, such as trauma, abuse, and maltreatment increase the risk of developing cancer in adulthood (Kelly-Irving, Lepage, et al., 2013; Kelly-Irving, Mabile, Grosclaude, Lang, & Delpierre, 2013). Given the complex aetiology of cancer and often long latency period, adopting a life course perspective may aid in a better understanding of the different pathways that affect cancer onset in later life, thereby explaining more of the variation (Potischman, Troisi, & Vatten, 2004).

Another major social challenge related to the increase in life expectancy is the rise of chronic conditions, multi-morbidity, and frailty in older age (Lalive d'Epinay & Spini, 2007). Frailty, a clinical syndrome of increased vulnerability to stressors caused by cumulative decline across biological systems, is thus a relevant public health issue for societies worldwide (Clegg, Young, Iliffe, Rikkert, & Rockwood, 2013). With an ageing population, the number of frail people will rise rapidly: the prevalence of frailty increases with each five-year older age group, with prevalence rates of 17% among community-dwelling older adults aged 65 years and older and 25-40% among adults aged 80 years and over (Bandein-Roche et al., 2015; Fried et al., 2001; Santos-Eggimann, Cuenoud, Spagnoli, & Junod, 2009). In addition, studies have found that frailty is more prevalent in persons with lower education and lower income, thus making socioeconomic conditions an interesting point of research when studying frailty (Buckinx et al., 2015; Etman, Burdorf, Van der Cammen, Mackenbach, & Van Lenthe, 2012). Moreover, a life course perspective could unravel associations of socioeconomic conditions with frailty, as it has been suggested that its key risk is rooted in childhood socioeconomic conditions (Alvarado, Zunzunegui, Beland, & Bamvita, 2008; Gale, Booth, Starr, & Deary, 2016).

Since cancer and frailty are both health outcomes with (1) rising incidence rates related to increased life expectancy and (2) socioeconomic inequalities, these outcomes are particularly interesting to study in the context of this thesis.

Moreover, the results could help in unravelling pathways and explaining variation, thus making it is possible to intervene at an early stage, thereby preventing onset or deteriorating conditions. Early intervention could thus aid in decreased incidence, higher survival rates or increased life expectancy, which would in turn be beneficial both at the individual and societal level. Furthermore, this could potentially decrease socioeconomic inequalities.

Health is by nature dynamic and a result of individual exposures to risks as well as physiological and social resources to cope with these risks. Therefore, when studying health, it is important to consider how individual trajectories change over time. In addition to individual exposures, also an individual's sociohistorical context and its evolvement across time influences health in old age. In order to study health in old age while considering individual and contextual changes across time, the life course perspective offers a helpful framework.

1.3 Life course perspective

The use of longitudinal data in studying associations between socioeconomic conditions and health is suitable to address that determinants of health inequalities, such as material and social conditions, have a time dependent relationship with health (Benzeval & Judge, 2001; Sacker, Wiggins, Bartley, & McDonough, 2007). Understanding these associations calls for a dynamic perspective of conditions, i.e. taking variations over time into account (Benzeval & Judge, 2001). In addition, using longitudinal data allows for studying causal relationships and helps to better understand how socioeconomic conditions affect health over time (Bartley, Blane, & Montgomery, 1997; Graham, 2002). These advantages have led to an interest in adopting a life course approach for studying health inequalities. Life course research aims at analysing human life over the life course while simultaneously studying biological, sociological, and psychological

processes, with the ultimate goal to understand human development (G. H. Elder, Jr., 1998; Featherman & Lerner, 1985).

1.3.1 The life course approach

The life course perspective is a popular approach often used in epidemiology and public health (D. Kuh & Ben-Shlomo, 2004). This approach is useful when studying the interaction between individual lives and social changes, i.e. lives within the contexts of families, society and (historical) time (Kok, 2007). Elder defined the life course as ‘the social trajectories of education, work, and family that are followed by individuals and groups through society’ (G. H. Elder, Jr., 1998).

The life course approach has five principles (Glen H. Elder, Johnson, & Crosnoe, 2003). The first principle is life-span development and is characterized by the idea that human development starts in the early stages of life and thus to understand biological, social, and psychological situations in adulthood, the whole life course should be taken into account. Agency is the second principle and assumes that individuals make decisions and thereby determine their own life course. The third principle, time and place, acknowledges that humans are influenced by their sociohistorical context and location. Timing, the fourth principle, emphasizes that the effect of events depends on the timing in the life course in terms of an individual's age or the order of events. Finally, the fifth principle, linked lives, stresses that lives are interdependent and thereby social relationships shape an individual's life course.

Trajectories are one of the central concepts in life course research and can be measured by successive states that represent social roles or positions such as education, employment, marital status, and parenthood, or describes a long-term continuous development of a person's health history (Colerick Clipp, Pavalko, & Elder, 1992). Trajectories can be stable, i.e. remaining in poor or good health, decline, e.g. loss of functional and cognitive capacities in elderly, resilient, e.g.

recovering from a disease, or fluctuate in an unclear trend, i.e. episodes of good and poor health (Burton-Jeangros, Cullati, Sacker, & Blane, 2015). These trajectories have a distinctive form and meaning in that states influence life changes and they do not occur at random (G.H. Elder & Social Science Research Council, 1985). However, the idea that life courses follow a specific order of states or events, thereby forming a 'standardized' life pattern, for example a retirement process where everyone retires at age 65, has been under debate (Brückner & Mayer, 2005). It has been suggested that there is more a de-standardization of the life course where states, events, and their order are more dispersed in terms of timing, duration, and population (Brückner & Mayer, 2005; Widmer & Ritschard, 2009).

A second central concept in life course research are life course transitions or events. These transitions are defined as the changes between (health) states within a trajectory: they are initiated by short-term events that can occur at the physiological level or in social circumstances (Burton-Jeangros et al., 2015; D. Kuh, Ben-Shlomo, Lynch, Hallqvist, & Power, 2003). Transitions represent the turning points 'when roles are transformed, redefined, or left behind for new roles' (Wheaton & Gotlib, 1997).

1.3.2 Models on health inequalities from the life course perspective

Those concepts of trajectories and transitions are central in the three models that life course researchers have designed to explain relations between socioeconomic circumstances and health inequalities in later life: the sensitive or critical period model, the accumulation model, and the pathway model (D. Blane, Netuveli, & Stone, 2007).

First, the sensitive or critical period model hypothesizes that health inequalities can be explained by exposures that occur in critical or sensitive periods of development. These sensitive or critical periods take place mainly in early life, as this is the time in which most developmental processes occur. During

developmental processes, biological systems are more sensitive to external influences (Bruer, 2001). When exposures in these critical periods occur, they might cause durable biological damage and disease and have the potential to create stable behavioural tendencies (Ben-Shlomo & Kuh, 2002; Wadsworth, 1997). For example, the influential works of Dr. Barker have shown that fetuses adapt to poor nutrition, which permanently changes their structure and metabolism, which leads to an increased risk of coronary heart disease, stroke, diabetes, and hypertension later in life, also known as the biological programming hypothesis (Barker, 1998). Recent research focused on cancer suggested that stressful conditions and adverse events in early life, such as trauma, abuse, or maltreatment, increase the risk of developing cancer in adulthood (Kelly-Irving, Lepage, et al., 2013; Kelly-Irving, Mabile, et al., 2013; Uauy & Solomons, 2005). Other biological and social critical periods in life that have been identified include entry into and exit from the labour market, leaving the parental home, transition to parenthood, and job insecurity (Bartley et al., 1997).

Second, the accumulation model assumes that adverse conditions accumulate over time. Within this model, two theories are identified. First, the accumulative risk model, which looks at the sums of adverse events throughout the life course and how this leads to a subsequent increasing negative effect on health (Burton-Jeangros et al., 2015). Second, the cumulative dis/advantage theory assumes that dis/advantage in early life leads to an accumulation of subsequent dis/advantages (Dannefer, 2003). Early life disadvantages initiate a chain of life course insults: earlier disadvantages lead to later disadvantages and a decreased capacity to overcome new disadvantages (Hayward & Gorman, 2004; A. M. O'Rand & Hamil-Luker, 2005). In contrast, early life advantages are followed by an environment that facilitates positive development, such as structural factors, life course transitions, and behaviours that promote health (A. M. O'Rand, 1996; A. M. O'Rand & Hamil-Luker, 2005). This implies that health inequalities between people born into advantageous in contrast to disadvantageous backgrounds are diverging over time. Research supporting this theory found that children who grew up in deprived circumstances had subsequently a higher level of labour market

disadvantage and lower quality of life in older ages (Wahrendorf & Blane, 2015). Schroder-Butterfill and Marianti (2006) demonstrated how low resources lead to an additional exposure to risk which in turn leads to stress. This is very likely to be a downward spiral leading to psychological disorders and social exclusion (M. Oris, 2017). In addition, the association between conditions and events in terms of onset, magnitude, and duration of exposure and dimensionality of adversity has been studied (K. F. Ferraro & Schafer, 2017; Schafer, Shippee, & Ferraro, 2009).

Third, the pathway model links early life factors indirectly to adult disease by taking into account social and biological risks occurring during life (Graham, 2002). This view describes that convergence between advantageous and disadvantageous background is possible through mediating factors such as lifestyle, education, and social class at different life stages (Power & Hertzman, 1997). This is related to social mobility, suggesting that risk associated to childhood disadvantage could be decreased or partially compensated for individuals moving from low childhood socioeconomic status to a higher status in adulthood (Y. Luo & L.J. Waite, 2005). In addition, social, psychological, and human capital may help people in avoiding or adapting to distressful outcomes, also known as resilience (G.H. Elder & Shanahan, 2006).

1.3.3 The life course perspective and health inequalities in old age

In addition to the three models on health inequalities, a new theory for the scientific study of ageing that integrates the cumulative dis/advantage theory and the life course has been developed: the cumulative inequality theory (Kenneth F. Ferraro & Shippee, 2009). This theory emphasizes that using a life course perspective helps in studying ageing as a life-long process where disadvantage accumulates over time (Wilmoth & Ferraro, 2013). Moreover, the theory recognizes that 'social systems generate inequality, which is manifested over the life course via demographic and developmental processes, and that personal trajectories are shaped by the accumulation of risk, available resources, perceived trajectories, and human agency' (Kenneth F. Ferraro & Shippee, 2009). It attempts to study

the accumulation of inequality considering both micro (from the life course perspective) and macro (from the cumulative dis/advantage theory) level processes in the life course that influence ageing.

As an addition to the life course perspective that has been relatively ignored in the American life course theory, but highly important in the European perspective, Dannefer suggested to also pay attention to the institutional and political dimensions that also evolve across time (Dannefer, 2003, 2018). The process of institutionalization structured life trajectories of the earlier birth cohorts in Europe (Brückner & Mayer, 2005; Kohli, 2007). One way of studying health outcomes while considering institutional and political dimensions is by looking at variation between welfare regimes. Gøsta Esping-Andersen (1990) classified welfare states into regimes based on four principles that reflect the roles of the state, family, and market provision of welfare. The first principle, decommodification, considers the extent to which the welfare of an individual relies upon the market. Second, welfare states play a role in maintaining or breaking down social stratification. The third principle is the private-public mix that describes the roles of the state, family, and market in welfare provision. Finally, defamilisation is the degree to which an individual can have a socially acceptable standard of living through paid work or social security provisions, independently of family relationships (G. Esping-Andersen, 1999). In addition to these principles that reflect roles, Ferrera (1996) added a focus on different dimensions of how social benefits are organised.

Together, these principles can be used to classify four types of welfare regimes: Anglo-Saxon (liberal), Bismarckian (conservative), Scandinavian (social democratic), and Southern countries. The Anglo-Saxon regime is characterized by basic and minimal levels of provision (Eikemo, Bambra, Judge, & Ringdal, 2008). The Bismarckian regime is characterized by a 'status differentiating' welfare program where benefits are related to earnings and administered by employers (Eikemo et al., 2008). The Scandinavian regime aims at promoting social equality through a redistributive social security system (Eikemo et al.,

2008). The Southern regime is more fragmented in terms of welfare provision and relies strongly on the family (Ferrera, 1996).

In this thesis in Article 3, this classification of welfare regimes is used to consider the contextual factors that influence health in old age. For reasons of data availability the Anglo-Saxon regime is not included, but the classification is augmented by the Eastern European welfare regime. This regime is less easy to capture from a life course perspective, since it can currently be characterised by limited health service provision and poor population health, but when studying the earlier birth cohorts, care and school systems were inspired by a communist egalitarian ethos (Eikemo et al., 2008).

Building on those foundations, this thesis adopts the relatively holistic approach of the life course perspective when studying ageing, with the objective of providing insights into different pathways and the role trajectories and life events play in health in later life. The five principles make clear that the life course approach allows for studying both development of biological and social processes at the same time, such as how social factors influence health, while taking a person's context into account (D. Blane et al., 2007). It is important to take context into account since individuals should be considered within their specific place, historical time, and society (Kok, 2007). The life course perspective can take social changes and variations between birth cohorts into account by considering spatial and sociohistorical context. The effect of changes at specific time points can be tested, such as lifestyle, e.g. smoking patterns, or vaccination programmes that changed over generations (Wadsworth, 1997).

Regarding the cumulative disadvantage, health inequalities, and the life course perspective, childhood socioeconomic conditions could have a long lasting effect on health in later life, on top of socioeconomic conditions in adulthood. This would suggest that health inequalities are related to both childhood and adulthood socioeconomic conditions. In addition, it allows for testing whether childhood

socioeconomic conditions channel individuals into life course trajectories leading to social destinations or pathways, thus suggesting that childhood socioeconomic conditions are the actual determinants of health at older age, over adulthood socioeconomic conditions. Much empirical evidence has already been established. For example, poor socioeconomic circumstances during childhood have been shown to be associated with negative health outcomes during adulthood, such as higher risk of cardiovascular disease, lower quality of life, poorer physical capability, and higher mortality rates (D. Blane et al., 1996; Juarez, Goodman, & Koupil, 2016; D. J. Kuh & Ben-Shlomo, 1997; D. J. Kuh & Hardy, 2002; Wadsworth & Kuh, 1997; Wahrendorf & Blane, 2015).

In order to facilitate healthy ageing, it is important to identify promoters and barriers across the life course that can be targeted by health surveillance and strategies, thereby reducing the impact of unfavourable life conditions on health inequalities. Understanding the development of health trajectories by including individual level socio-demographic may help to do so.

1.4 Research context and data

1.4.1 Context of this thesis

My interest in health and problems with maintaining public health already developed throughout my Bachelor of Health Sciences. With a multidisciplinary first year, I covered the foundations of the field of health and healthcare. Since good health is a result of interactions between many factors, such as lifestyle, social and physical environment, biology, and healthcare, I became interested in finding out how we can promote healthy behaviours so people can stay healthy. My interest in these questions made me choose the specialization 'Prevention and Health'. After this, I studied a Research Master in Health Sciences and specialized in Clinical Epidemiology to learn more about these topics and to improve my practical research skills. During my research internships at the Department of

Epidemiology, I was involved in the ongoing prospective observational Energy for life after ColoRectal cancer (EnCoRe) study for which I conducted statistical analyses to unravel associations of lifestyle with quality of life in colorectal cancer survivors. This background has shaped the basis of this thesis: a combination of health challenges (i.e. ageing) and finding factors that hinder or promote health trajectories in the population.

I was highly motivated to conduct my PhD at the University of Geneva as part of the Marie Skłodowska-Curie Innovative Training Network Project LONGPOP (Methodologies and Data mining techniques for the analysis of Big Data based on Longitudinal Population and Epidemiological Registers), a large collaborative network including some of the most advanced centres in Europe on quantitative analysis, within the Horizon 2020 Programme of the European Commission. In addition, being affiliated to the Centre for the Interdisciplinary Study of Gerontology and Vulnerabilities and the Swiss National Centre of Competence in Research LIVES, were the most advantageous environment for this interdisciplinary research. In addition, being part of the research project LIFETRAIL: Life course influences on health trajectories at older age: longitudinal analyses using retrospective data, perfectly fitted this thesis.

1.4.2 Survey of Health, Ageing, and Retirement in Europe

For all research in this thesis, data from the Survey of Health, Ageing, and Retirement in Europe (SHARE) were used. SHARE was designed to investigate population ageing processes and is a longitudinal survey on individuals aged 50 years and over (Borsch-Supan et al., 2013). The birth cohorts included are 1919 to 1928 [post First World War], 1929 to 1938 [Great Depression], 1939 to 1945 [Second World War], and post-1945. SHARE was approved by the relevant research ethics committees in the participating countries and all participants provided written informed consent. At the start of this thesis, SHARE included six waves of data that were collected every two years between 2004 and 2016 by means of standardized computer-assisted face-to-face interviews. Data collected

included information on aspects ranging from economic variables and demographics to health variables (Alcer et al., 2005). In addition, wave three included a module on retrospective life course data, including socioeconomic conditions. Participants were selected from 14 European countries — all those cited below plus Ireland — based on probability sampling adapted to each country. Specifically for Article 3, the classification of welfare regimes is as follows: Scandinavian (Denmark and Sweden), Bismarckian (Austria, Belgium, France, Germany, the Netherlands, Switzerland), Southern European (Greece, Italy, Spain), and Eastern European (Czech Republic and Poland). With all these characteristics, SHARE appears to be a good database to study health inequalities in old age using a life course perspective, in Europe. We are however aware of several limitations, such as attrition, selection bias, and self-reporting bias. These limitations are discussed in Chapter 5 of this thesis.

1.5 Aims and outline of this thesis

The main aim of the research presented in this thesis was to study health inequalities in old age, within the context of socio-demographic factors. To study associations of socioeconomic conditions with health in later life, we used a life course perspective and focused on the cumulative dis/advantage theory to study causal mechanisms and processes that lie behind social inequalities. This thesis is in article format and contains three papers.

1.5.1 Chapters

In **Chapter 2**, paper 1 describes the importance of doing life course research in the general population by looking at the effect of childhood socioeconomic conditions on cancer in later life. Subsequently, we added adulthood socioeconomic conditions to determine possible mediating pathways, and thereby examined the usefulness of the life course perspective in studying health

inequalities. We hypothesized that disadvantaged early life socioeconomic circumstances directly influence health in later life, which can be either positively or negatively, depending on risk factors for site-specific cancers. In addition, we hypothesized that adulthood socioeconomic conditions would mediate the effect of early-life socioeconomic conditions on cancer in later life.

Chapter 3, paper 2, describes associations of life course indicators with health. In particular, we studied frailty which, as we have seen earlier, is an important clinical syndrome used in geriatric medicine. Moreover, it is directly linked to the daily living conditions of the elderly. Our hypothesis was that disadvantaged early life socioeconomic conditions directly and negatively influence frailty in later life, and that adulthood socioeconomic conditions mediate this association.

After having established that there is an effect of life course socioeconomic conditions on health in later life, it is important to know the different pathways that may explain this. In **Chapter 4**, paper 3, different possible pathways in the life course that influence health in later life, including adverse life events, are described with a focus on the cumulative dis/advantage theory and its potential variation across welfare regimes. We hypothesized that childhood misfortune, including disadvantaged socioeconomic conditions, adverse experiences, and poor health, are associated with higher risk of frailty in later life. Subsequently, adult-life socioeconomic conditions were hypothesized to mediate this relationship. Further we hypothesized that welfare regimes, as macro level factors, would influence these associations through their pension systems and social benefits.

Finally, **Chapter 5** provides a summary of the main findings and a discussion of methodological considerations concerning the research described in this thesis, potential mechanisms that could explain the results, implications for practice, and our recommendations for further research in this area.

Chapter 2. Effect of childhood socioeconomic conditions on cancer onset in later life: an ambidirectional cohort study (Article 1)

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Abstract

Objectives Living in low socioeconomic conditions during childhood is associated with poor health outcomes in later life. Whether this link also applies to cancer is unclear. We examined whether childhood socioeconomic conditions (CSCs) are associated with cancer risk in later life and whether this effect remained after adjusting for adulthood socioeconomic conditions (ASCs).

Methods Data for 26,431 individuals ≥ 50 years old included in SHARE were analyzed. CSCs were constructed by using indicators of living conditions at age 10. ASC indicators were education, main occupation and household income. Gender-stratified associations of CSCs with cancer onset (overall and by site) were assessed by Cox regression.

Results 2,852 individuals were diagnosed with cancer. For both men and women, risk of overall cancer was increased for advantaged CSCs and remained so after adjusting for ASCs (hazard ratio=1.36, 95% CI 1.10, 1.63 and 1.70, 95% CI 1.41, 2.07).

Conclusions Advantaged CSCs are associated with increased risk of overall cancer at older age, but results vary by cancer sites and sex. Participation in cancer screening or exposure to risk factors may differ by social conditions.

Introduction

Socioeconomic differences in health exist and can also be seen in cancer incidence, prevalence, and survival across populations. Studies found an association between lower socioeconomic status and higher incidence of respiratory, oesophagus, stomach, and cervical cancers, and higher socioeconomic status and colon, breast, and ovary cancers, and skin melanoma, with overall better survival in patients from higher socioeconomic status (Bouchardy et al., 2006; Faggiano et al., 1997; Weiderpass & Pukkala, 2006). These differences are thought to be largely attributed to aetiological factors, such as diet, physical activity, and smoking, but part of the variation remains unexplained (Weiderpass & Pukkala, 2006). Given the complex aetiology of cancer and often long latency period, adopting a life course perspective helps to better understand the different pathways that may affect cancer onset in later life and thus explain more of the variation (Potischman et al., 2004).

From a life course perspective, three theories on the relation between socioeconomic conditions and cancer onset in later life can be considered. First of all, during developmental processes, biological systems are more sensitive to external influences (Bruer, 2001). These sensitive periods take place mainly in early life, as this is the time in which most developmental processes occur. Recent research focused on cancer suggested that stressful conditions and adverse events in early life such as trauma, abuse, or maltreatment increase the risk of developing cancer in adulthood (Kelly-Irving, Lepage, et al., 2013; Kelly-Irving, Mabile, et al., 2013). A second theory refers to cumulative (dis)advantage, considering that (dis)advantage in early life leads to an accumulation of subsequent (dis)advantages (Dannefer, 2003). The third theory is related to social mobility, suggesting that risk associated to childhood disadvantage could be decreased or partially compensated for individuals moving from low childhood socioeconomic status to a higher status in adulthood (Y. Luo & L.J. Waite, 2005).

Taking into account both childhood and adulthood socioeconomic conditions (ASCs) could give suggestions on whether childhood socioeconomic conditions (CSCs) have a long lasting effect on cancer in later life, beyond ASCs, i.e. health inequalities would be related to both CSCs and ASCs. Alternatively, it

allows testing whether CSCs channel individuals into life course trajectories leading to social destinations or pathways, thus suggesting that CSCs are the actual determinant of health at older age, over ASCs [i.e. there is no longer an association between CSCs and cancer in later life once adjusting for ASCs] (Hertzman & Power, 2003). Additionally, it is known that some risk factors for site-specific cancers are more closely related to adulthood. For example, one study showed that mortality from stomach cancer was dependent on CSCs, whereas mortality from lung cancer was mainly dependent on adulthood factors (Smith, Hart, Blane, & Hole, 1998). This suggests that low socioeconomic conditions in different life stages may be related to risk of different site-specific cancers.

A recent review on CSCs and adult cancer identified only two studies that investigated both the independent and joint effect of CSCs and ASCs on cancer incidence (Vohra, Marmot, Bauld, & Hiatt, 2016). The first study, looking at breast cancer incidence and survival, found increased breast cancer incidence for a higher level of mothers' education and family income in early life (Pudrovska & Anikputa, 2012). The effect of mothers' education was mediated by women's socioeconomic status in adulthood and reproductive behaviour. Education of the father was negatively related to breast cancer survival and this effect was further mediated by women's education. The second study found an association between low CSCs and higher risk of colorectal cancer and reduced risk of basal cell carcinoma, which remained significant after adjusting for ASCs. Conversely, no associations between CSCs and total cancer, lung, breast, and prostate cancer was found (de Kok et al., 2008).

To sum up, the review on the relationship of poor CSCs and cancer later in life, finds overall weak and inconsistent evidence in term of the direction of the effect (Vohra et al., 2016). Additionally, evidence on both direct and indirect effects via possible ASCs mediating pathways is scarce. Since there are only a few studies with heterogeneous results, the first aim of this study was to examine whether CSCs are associated with cancer onset in later life by using longitudinal data for older adults from 14 countries across Europe. The second aim was to test whether this effect remained after adjusting for ASCs, both for cancer overall and by site.

Methods

Study design and population

Data for 26,431 individuals were retrieved from the Survey of Health, Ageing, and Retirement in Europe (SHARE) database. SHARE is a longitudinal, cross-national, and ambidirectional survey designed to investigate population ageing processes and includes data for individuals ≥ 50 years old (Borsch-Supan et al., 2013). SHARE includes six waves of data, collected every 2 years between 2004 and 2016. Participants were eligible for the current analyses if they participated in the third wave and at least one other wave. Participation in the third wave was a prerequisite since retrospective life course information related to socioeconomic conditions was collected in this wave (SHARELIFE). Any other wave was used to collect information on cancer cases. The duration of follow-up was 12 years at maximum, but it was not equal for all participants as some did not participate the whole time. Participants were from 14 European countries — Austria, Belgium, Czech Republic, Denmark, France, Germany, Greece, Ireland, Italy, The Netherlands, Poland, Spain, Sweden, and Switzerland — based on probability sampling adapted to each country. SHARE was approved by the relevant research ethics committees in the participating countries and all participants provided written informed consent.

Cancer

Cancer was operationalized by using the SHARE question “Has a doctor ever told you that you had/Do you currently have any of the conditions on this card?” (de Souto Barreto, Cesari, Andrieu, Vellas, & Rolland, 2017). It was specified that a doctor had told the participants that they currently have this condition or that they were treated for or were affected by this condition. If participants selected the option “Cancer: ever diagnosed/currently having”, they were included in the analyses as having cancer. Additionally, the question on the individual’s age at diagnosis was used to determine when the cancer was diagnosed, which can be before follow-up in the study. The follow-up question on specific cancer sites was

used for analyses by site. These questions were asked at every wave except wave three. Only the first diagnosis was taken into consideration since the event is first cancer diagnosis.

Childhood socioeconomic conditions

The variable CSCs was determined by using the measure of childhood circumstances by Wahrendorf and Blane (Wahrendorf & Blane, 2015). It was constructed by combining four binary indicators of socioeconomic conditions at age 10 that are relevant when assessing the long-term effects of early life socioeconomic conditions on health; the occupational position of the main breadwinner in the household, the number of books at home, overcrowding in the household, and housing quality (Dedman, Gunnell, Davey Smith, & Frankel, 2001; M. D. R. Evans, J. Kelley, J. Sikora, & D. J. Treiman, 2010) (see Online Resource 1 for details). These variables were measured as part of the retrospective SHARELIFE module in wave 3.

Covariates, confounders, and mediators

All analyses were adjusted for attrition (no dropout, dropped out, deceased) and for potential confounders, including birth cohort (no crisis or war period, first or second world war, and the Great Depression), living with biological parents at the age of ten (both parents, mother or father, or without parents). Birth cohort was measured at every wave during follow-up, living with biological parents was measured as part of the SHARELIFE module in wave 3. As indicators of lifestyle, the following health behavior and condition variables were included in the analyses; body mass index (BMI; ≤ 24.9 , 25.0-29.9, ≥ 30.0 kg/m²), smoking, number of chronic conditions, and physical activity (see Online Resource 2 for details).

As potential mediators, the following indicators of ASCs were included: participant's level of education (low or high), participant's main occupation (high or low skill), and satisfaction with household income (derived from the question "Is household able to make ends meet?", ranging from 1, with great difficulty, to 4,

easily). Education was based on the highest educational attainment, along the ISCED classification. Participants having reached tertiary education level were classified as “high” and others as “low and middle”. Main occupation — high- or low-skilled — was based on the International Standard Classification of Occupations (International Labour Office, 2012) of the main job during the working life, derived from the questions “Which of the jobs you have told me about was the final job of your main career or occupation? By this we mean the last job in the career or the occupation that took up most of your working life, even though you might have had other jobs afterwards”. We considered occupation as a proxy of skills that individuals can develop over their life course. Participants who reported never having performed paid work were classified as low skill.

Statistical analyses

Prevalence of cancer was based on proportions of respondents reporting the first occurrence of cancer. Differences in cancer types by CSCs was assessed with chi-square tests (all cancer types, breast and prostate) and Fisher exact tests (all other types of cancer: colon or rectum, etc.). Duration started with date of birth and ended with age of first cancer, or with end of follow-up or death, whichever came first. For ease of visualization, Kaplan-Meier curves for the cumulative proportion of cancer-free participants were plotted between 50 and 105 years.

The association of CSCs with first self-reported diagnosis of cancer (overall and by site) was assessed separately by sex by using Cox proportional-hazards regression, adjusting for the confounders age, birth cohort, living with biological parents, and reason for attrition (Model 0). Hazard ratios and 95% confidence intervals were estimated. Because the prevalence was low, such analyses by cancer site were limited to the following sites; colon or rectum, skin, breast and cervix (women only), and prostate.

The following models were used to examine if CSCs remained associated when adjusting for ASCs and health situation: Models 1 to 3 adjusted for ASCs (M1: education; M2: main occupation; M3: income; M4: adjusted for all three ASCs). A fifth model further included health status and health behaviors (BMI, smoking status, chronic health conditions, and physical activity). We verified the

assumptions for Cox models using both visual inspection of residuals and statistical tests, and confirmed the validity of the Cox models used in this study. We used strata for country in the Cox regression analysis to allow for varying baseline hazards. To assess the impact of including a retrospective assessment of cancer (for participants who reported a cancer before inclusion in SHARE), we ran two sensitivity analyses; one excluding participants with cancer before age 50, and one excluding all participants reporting cancer before inclusion in SHARE to examine the impact of potential reverse causality. Statistical analyses involved use of the R language version 3.4.1.

Results

Participant characteristics

A total of 14,836 (56%) women and 11,595 (44%) men were included in the analyses (mean [SD] age 62.2 [10.3] and 63.0 [9.2] years) (Table 1). For both men and women, participants with middle CSCs were the largest group, followed by disadvantaged, while the most advantaged group was the smallest (Table 2). Participant characteristics by CSCs are presented in Online Resource 3. Among the included participants, 1,517 (10.2%) women and 1,335 (11.5%) men reported having or having had a first diagnosis of cancer (Table 2). By cancer site, the numbers for colon or rectal cancer were 142 women and 151 men; skin cancer, 119 women and 113 men; breast cancer, 618 women; cervical cancer, 123 women, and prostate cancer, 368 men. Among women, the distribution of overall cancer, breast, colon or rectum, skin, and cervix cancer were different by CSCs strata (Table 2). Among men, no difference was observed.

Association of life course socioeconomic conditions on overall cancer

Figure 1 shows the Kaplan-Meier curve for the cumulative proportion of cancer-free participants between 50 and 105 years by sex and CSCs. Both men and women with the most disadvantaged CSCs were most likely to be cancer-free. Differences in CSCs seemed to slightly disappear over time; however, for people

≥ 80 years old, women with advantaged CSCs seemed most likely to have had cancer. For people < 75 years old, men with advantaged CSCs seemed most likely to have had cancer. For men ≥ 75 years old, those from middle and most advantaged CSCs were most likely to have had a cancer. In women, like in men, differences in CSCs slightly disappear in very old age, except that men with advantaged CSCs who were ≥ 90 years old were most likely to still be cancer-free.

The results of multivariable analyses are in Table 3. When adjusting for confounders and attrition, as compared with women with the most disadvantaged CSCs, those with more advantaged CSCs were more likely to have had cancer, especially those with advantaged CSCs (HR = 1.50, 1.72, and 1.18, for most advantaged, advantaged, and middle CSCs, respectively, Table 3, Model 0). When adjusting for ASCs, sociodemographic characteristics, health-status, and health behaviours, the effects remained significant (HR = 1.49, 1.70, and 1.19, for the most advantaged, advantaged, and middle CSCs, respectively, Table 3, Model 5). For men, results were similar. Men with more advantaged CSCs were more likely to have had a cancer as compared with men with the most disadvantaged CSCs. Those with advantaged CSCs were most likely to have had a cancer (HR = 1.48, Table 3, Model 0, and 1.36, Table 3, Model 5). ASCs did not change the effect of CSCs on cancer onset later in life.

Association of life course socioeconomic conditions on cancer by site

Table 3 reports results from multivariable Cox proportional-hazard regression analyses for non-sex-specific cancers and Table 4 reports these results for sex-specific cancers. Women with advantaged and middle CSCs were more likely to have had skin cancer (HR = 3.10 and 2.56, respectively, Table 3, Model 0). This association remained significant when controlling for ASCs (HR = 2.55 and 2.13, respectively, Table 3, Model 4). Risk of breast cancer was 1.53 times more likely for women with the most advantaged than most disadvantaged CSCs (Table 4, Model 0). This remained significant after adjusting for ASCs (HR = 1.49, Table 4, Model 4). Additionally, we found no significant associations for colon and rectal or cervical cancer.

For men, results for colon and rectal cancer were opposite from those for cancer overall. Men with middle CSCs were less likely to have had colon or rectal cancer than those with the most advantaged CSCs, and ASCs did not change this effect (HR = 0.57, Table 3, Model 4). We found no significant associations for skin and prostate cancer.

Sensitivity analysis

None of the tests for violation of the proportional-hazards assumption gave significant results. Results from the Cox models including strata for country showed a similar pattern of results, with HRs increasing with CSCs up to advantaged and a slight decrease for the most advantaged. However, the HRs were closer to the null and that for the advantaged group was often the only one significantly different from 1. The two sensitivity analyses showed similar results with the same gradient, though closer to the null.

Discussion

In this study, we examined whether CSCs were associated with cancer onset in later life by using longitudinal data for older adults, ≥ 50 years old, from 14 countries across Europe. The second aim was to test whether this effect remained after adjusting for adult life conditions, ASCs, for cancer overall and by site. Overall, both men and women with the most disadvantaged CSCs were most likely to be cancer-free over time, but results vary by cancer sites and by sex. Women with advantaged and middle CSCs were more than twice as likely to have had skin cancer than those with the most disadvantaged CSCs. As compared with men or women with the most disadvantaged CSCs, men with middle CSCs were half as likely to have had colon or rectal cancer and women with the most advantaged CSCs were more likely to have had breast cancer. Our findings suggested no mediating effects of ASCs.

Studies on socioeconomic inequalities in overall cancer mortality and survival show inconsistent results, as site-specific cancers have different aetiologies and mortality and survival are related to incidence and factors that

influence survival such as health care (Vohra et al., 2016). However, findings of two other studies also found lower risk of overall cancer in people from more advantaged conditions (Lawlor, Sterne, Tynelius, Davey Smith, & Rasmussen, 2006; Strand & Kunst, 2007). For site-specific cancers, most evidence from previous studies are inconsistent and imprecise (Vohra et al., 2016). Three studies on risk of bowel and rectal cancer support our findings that poorer CSCs are associated with higher risk (de Kok et al., 2008; Naess, Claussen, & Davey Smith, 2004; Naess, Strand, & Smith, 2007). For skin and breast cancer, previous studies on cancer incidence are in line with our findings that can partly be explained by socioeconomic related risk factors, such as higher exposure to ultraviolet radiation for skin, and older age at first birth for breast cancer (Bryere et al., 2016; de Kok et al., 2008; Pudrovska & Anikputa, 2012). Bryere and colleagues also found an association between low social class and higher risk of cervical and lower risk of prostate cancer (Bryere et al., 2016). Our findings do not show this, which may be due to low number of cases by cancer subtype and CSCs. Like de Kok and colleagues, we found no mediation by ASCs (de Kok et al., 2008). The results support studying cancer from a life course perspective to find possible pathways by different cancer-specific risk factors and exposure by social class over the life course.

A possible explanation for the findings might be socioeconomic differences in health behaviours, such as cancer screening, and cancer risk factors. Some studies found that individuals from low socioeconomic status may have barriers that impact participation in screening and thus detection (Deding, Henig, Salling, Torp-Pedersen, & Boggild, 2017; Wang et al., 2017). This situation may lead to higher cancer rates for individuals from high than low socioeconomic status that are actually caused by increased detection and not true differences. Regarding risk factors, women from higher socioeconomic class show increased alcohol intake and age at first offspring birth and reduced parity, which are related to increased risk of breast cancer (Lundqvist, Andersson, Ahlberg, Nilbert, & Gerdtham, 2016). Similarly, the incidence of skin cancer with high socioeconomic class may be explained by holidays abroad and exposure to UV irradiation (Shack, Jordan, Thomson, Mak, & Moller, 2008).

A strength of this study was the use of a European longitudinal database with rich information on life course socioeconomic conditions and a potential observation period of 12 years. The sample size of this database may be sufficient to draw convincing conclusions for overall cancer. To limit the risk of misclassification bias, we used pre-defined and previously used methods for defining and analysing socioeconomic conditions. Additionally, we tried to minimise health selection bias by including respondents who participated in only one wave and completed the retrospective life-course module. Finally, our sample includes participants from 14 European countries. This has the advantages to capture a more representative sample of the general population and to increase statistical power, and at the same time the disadvantage to increase variability due to the heterogeneity in terms of cancer country profile within Europe (Ferlay et al., 2013).

This study has three main limitations. First, the self-reported cancer diagnosis instead of cancer registry data, which may imply reporting bias. Previous studies found an overall rate of false-negative self-reporting of 39.2%, with a wide variation by cancer site (Desai, Bruce, Desai, & Druss, 2001). Older age may also be associated with more frequent false-positive reporting (Loh et al., 2014). However, studies showed that respondents can accurately report a past cancer diagnosis, especially for breast, prostate and colon cancer, with an overall sensitivity of self-reported cancer of up to 89% (Bergmann et al., 1998; Loh et al., 2014). Second, by its design (inclusion of respondents aged 50 years old and older at baseline), SHARE is impeded by a cancer survivor bias. The importance of this bias may affect our finding, especially among the oldest old. Nevertheless, this bias is also limited as (1) the probability of dying from cancer before age 50 year is low, and (2) the overall cancer death rate in Europe and United States is decreasing (Malvezzi et al., 2015; Siegel, Miller, & Jemal, 2018). Third, the life course span of the three ASCs raises the question of causality of exposure, mediators and the outcome (e.g. onset of cancer before educational achievement) and of potential reverse causality. Twenty-three participants reported cancer before the age of 30 and 44 before the age of 50, so it is reasonable to assume that reverse causality on education and main occupation will not bias the results.

Concerning satisfaction with income (a time-varying mediator measured at each wave, i.e. at age 50 and later), it is reasonable to think that a part of the income and cancer onset association is influenced by reverse association (i.e. cancer causes income to decrease). We preferred keeping this important measure of ASCs in the analyses. This temporality issue should reinforce the effect size of income because the reverse causation association is probably stronger than the direct causation (i.e. income causes cancer). If the association of income and cancer is overestimated, then the mediating effect of income on the association of CSCs and cancer should also be overestimated. Thus, still finding an association between CSCs and cancer after adjusting for income is a strong sign of the independent impact of CSCs on later health.

Additionally, we did not have information on all cancer risk factors and confounders, such as genes, perinatal, and environmental factors, such as air pollution, pesticides and herbicides (IARC Publications, 2013). Another limitation is the retrospective and self-reported information on CSCs and ASCs, which may be subject to recall bias. Still, previous studies found evidence for the accuracy of recall of simple measures of socioeconomic conditions in a survey of older adults (Lacey, Belcher, & Croft, 2012). Also, sample sizes for site-specific cancers stratified by CSCs differ by cancer type and might have insufficient power to detect an association. Finally, given the longitudinal data, participants dropped out or died during follow-up, which may influence the results. For example, Bouchardy et al. reported an increased risk of dying from breast cancer for patients with low versus high social class (Bouchardy et al., 2006). To limit this bias, we adjusted for attrition in the analyses. By including attrition in all models, we adjusted for mediator-outcome confounding, although this statistical adjustment did not solve the issue of missing data due to attrition.

Conclusion

The present study is the first longitudinal European study to analyse the direct association of CSCs with cancer later in life as well as via pathways exploring the role of ASCs as a mediator. Our results suggest an association of advantaged CSCs with increased overall cancer onset in older age, but results vary by cancer

sites and by sex. Additionally, pathways to cancer may start in early life and ASCs does not completely mediate this relation.

The findings give evidence of the long-term impact of CSCs as well as the influence of ASCs on adult health. The findings may in turn help in developing interventions and targeting groups at increased risk of not participating in cancer screening programmes and/or developing cancer. Future studies are warranted to examine the relation of CSCs with cancers by site in a larger sample to increase power and with detailed information on health behaviours and risk exposure to explore more pathways by including a formal test of mediation. More evidence on the association between CSCs and the risk of specific cancers could help better identify and understand the relation, which in turn could lead to the improvement and tailoring of prevention programmes.

Compliance with Ethical Standards

Conflict of interest

The authors declare no conflict of interest.

Ethical approval

The study was part of the Survey of Health, Ageing and Retirement in Europe (SHARE) study, which is a multidisciplinary and cross-national panel database of micro data on health, socio-economic status and social and family networks of more than 120,000 individuals aged 50 or older and covers 27 European countries and Israel (see www.share-project.org). During Waves 1 to 4, SHARE was reviewed and approved by the Ethics Committee of the University of Mannheim. From wave 4 onwards, SHARE was reviewed and approved by the Ethics Council of the Max Planck Society for the Advancement of Science (MPG).

Informed consent

Written informed consent was obtained from all individuals included in the study.

References

- Bergmann MM, Calle EE, Mervis CA, et al (1998) Validity of self-reported cancers in a prospective cohort study in comparison with data from state cancer registries *American journal of epidemiology* 147:556-562
- Borsch-Supan A, Brandt M, Hunkler C, et al. (2013) Data Resource Profile: the Survey of Health, Ageing and Retirement in Europe (SHARE) *International journal of epidemiology* 42:992-1001 doi:10.1093/ije/dyt088
- Bouchardy C, Verkooijen HM, Fioretta G (2006) Social class is an important and independent prognostic factor of breast cancer mortality *International journal of cancer* 119:1145-1151 doi:10.1002/ijc.21889
- Bruer JT (2001) A critical and sensitive period primer. In: Bailey JDB, Bruer J.T., Symons, F.J. (ed) *Critical thinking about critical periods*. Paul H. Brookes, Baltimore,
- Bryere J, Dejardin O, Launay L, et al (2016) Socioeconomic status and site-specific cancer incidence, a Bayesian approach in a French Cancer Registries Network study *European journal of cancer prevention : the official journal of the European Cancer Prevention Organisation (ECP)* doi:10.1097/cej.0000000000000326
- Dannefer D (2003) Cumulative advantage/disadvantage and the life course: cross-fertilizing age and social science theory *J Gerontol B Psychol Sci Soc Sci* 58:S327-337
- de Kok IM, van Lenthe FJ, Avendano M, et al (2008) Childhood social class and cancer incidence: results of the globe study *Social science & medicine* (1982) 66:1131-1139 doi:10.1016/j.socscimed.2007.11.035
- de Souto Barreto P, Cesari M, Andrieu S, et al (2017) Physical Activity and Incident Chronic Diseases: A Longitudinal Observational Study in 16 European Countries *American journal of preventive medicine* 52:373-378 doi:10.1016/j.amepre.2016.08.028
- Deding U, Henig AS, Salling A, et al (2017) Sociodemographic predictors of participation in colorectal cancer screening *International journal of colorectal disease* doi:10.1007/s00384-017-2832-6
- Dedman DJ, Gunnell D, Davey Smith G, Frankel S (2001) Childhood housing conditions and later mortality in the Boyd Orr cohort *Journal of epidemiology and community health* 55:10-15
- Desai MM, Bruce ML, Desai RA, Druss BG (2001) Validity of self-reported cancer history: a comparison of health interview data and cancer registry records *American journal of epidemiology* 153:299-306
- Evans MDR, Kelley J, Sikora J, Treiman DJ (2010) Family scholarly culture and educational success: Books and schooling in 27 nations *Research in Social Stratification and Mobility* 28:171-197 doi:<http://dx.doi.org/10.1016/j.rssm.2010.01.002>
- Faggiano F, Partanen T, Kogevinas M, Boffetta P (1997) Socioeconomic differences in cancer incidence and mortality *IARC scientific publications*:65-176
- Ferlay J, Steliarova-Foucher, Lortet-Tieulent J, et al. (2013) Cancer incidence and mortality patterns in Europe: Estimates for 40 countries in 2012 *European*

- Journal of Cancer 49:1374-1403
doi:<https://doi.org/10.1016/j.ejca.2012.12.027>
- Hertzman C, Power C (2003) Health and human development: understandings from life-course research *Developmental neuropsychology* 24:719-744
doi:10.1080/87565641.2003.9651917
- IARC Publications (2013) Air Pollution and Cancer.
- International Labour Office (2012) International Standard Classification of Occupations: ISCO-08 vol 1. International Labour Organization,, Geneva: ILO
- Kelly-Irving M, Lepage B, Dedieu D, et al (2013a) Childhood adversity as a risk for cancer: findings from the 1958 British birth cohort study *BMC public health* 13:767 doi:10.1186/1471-2458-13-767
- Kelly-Irving M, Mabile L, Grosclaude P, et al (2013b) The embodiment of adverse childhood experiences and cancer development: potential biological mechanisms and pathways across the life course *International journal of public health* 58:3-11 doi:10.1007/s00038-012-0370-0
- Lacey RJ, Belcher J, Croft PR (2012) Validity of two simple measures for estimating life-course socio-economic position in cross-sectional postal survey data in an older population: results from the North Staffordshire Osteoarthritis Project (NorStOP) *BMC medical research methodology* 12:88 doi:10.1186/1471-2288-12-88
- Lawlor DA, Sterne JA, Tynelius P, et al (2006) Association of childhood socioeconomic position with cause-specific mortality in a prospective record linkage study of 1,839,384 individuals *American journal of epidemiology* 164:907-915 doi:10.1093/aje/kwj319
- Loh V, Harding J, Koshkina V, et al (2014) The validity of self-reported cancer in an Australian population study *Australian and New Zealand journal of public health* 38:35-38 doi:10.1111/1753-6405.12164
- Lundqvist A, Andersson E, Ahlberg I, et al (2016) Socioeconomic inequalities in breast cancer incidence and mortality in Europe-a systematic review and meta-analysis *European journal of public health* 26:804-813 doi:10.1093/eurpub/ckw070
- Luo Y, Waite LJ (2005) The Impact of Childhood and Adult SES on Physical, Mental, and Cognitive Well-Being in Later Life *The journals of gerontology Series B, Psychological sciences and social sciences* 60:S93-S101
- Malvezzi M, Bertuccio P, Rosso T, et al (2015) European cancer mortality predictions for the year 2015: does lung cancer have the highest death rate in EU women? *Annals of Oncology* 26:779-786 doi:10.1093/annonc/mdv001
- Marsh A, Gordon, D., Pantazis, C., Heslop, P. (1999) Home Sweet Home? The impact of poor housing on health. The Policy Press, University of Bristol, Bristol
- Naess O, Claussen B, Davey Smith G (2004) Relative impact of childhood and adulthood socioeconomic conditions on cause specific mortality in men *Journal of epidemiology and community health* 58:597-598 doi:10.1136/jech.2003.012229
- Naess O, Strand BH, Smith GD (2007) Childhood and adulthood socioeconomic position across 20 causes of death: a prospective cohort study of 800,000

- Norwegian men and women *Journal of epidemiology and community health* 61:1004-1009 doi:10.1136/jech.2006.052811
- Potischman N, Troisi R, Vatten L (2004) A life course approach to cancer epidemiology. In: Kuh D, & Ben-Shlomo, Y. (ed) *A life course approach to chronic disease epidemiology*. Oxford University Press, Oxford, pp 260-280
- Pudrovska T, Anikputa B (2012) The role of early-life socioeconomic status in breast cancer incidence and mortality: unraveling life course mechanisms *Journal of aging and health* 24:323-344 doi:10.1177/0898264311422744
- Shack L, Jordan C, Thomson CS, et al (2008) Variation in incidence of breast, lung and cervical cancer and malignant melanoma of skin by socioeconomic group in England *BMC cancer* 8:271 doi:10.1186/1471-2407-8-271
- Siegel RL, Miller KD, Jemal A (2018) *Cancer statistics, 2018* CA: A Cancer Journal for Clinicians 68:7-30 doi:10.3322/caac.21442
- Smith GD, Hart C, Blane D, Hole D (1998) Adverse socioeconomic conditions in childhood and cause specific adult mortality: prospective observational study *BMJ (Clinical research ed)* 316:1631-1635
- Strand BH, Kunst A (2007) Childhood socioeconomic position and cause-specific mortality in early adulthood *American journal of epidemiology* 165:85-93 doi:10.1093/aje/kwj352
- Vohra J, Marmot MG, Bauld L, Hiatt RA (2016) Socioeconomic position in childhood and cancer in adulthood: a rapid-review *Journal of epidemiology and community health* 70:629-634 doi:10.1136/jech-2015-206274
- Wahrendorf M, Blane D (2015) Does labour market disadvantage help to explain why childhood circumstances are related to quality of life at older ages? Results from SHARE *Aging & mental health* 19:584-594 doi:10.1080/13607863.2014.938604
- Wahrendorf M, Blane D, Bartley M, et al (2013) Working conditions in mid-life and mental health in older ages *Advances in life course research* 18:16-25 doi:10.1016/j.alcr.2012.10.004
- Wang H et al. (2017) Barriers and Facilitators of Colorectal Cancer Screening for Patients of Rural Accountable Care Organization Clinics: A Multilevel Analysis *The Journal of rural health : official journal of the American Rural Health Association and the National Rural Health Care Association* doi:10.1111/jrh.12248
- Weiderpass E, Pukkala E (2006) Time trends in socioeconomic differences in incidence rates of cancers of gastro-intestinal tract in Finland *BMC gastroenterology* 6:41 doi:10.1186/1471-230x-6-41

Table 1 Participant characteristics, stratified by gender, from the Survey of Health, Ageing and Retirement in Europe (Collected in Austria, Belgium, Czech Republic, Denmark, France, Germany, Greece, Ireland, Italy, the Netherlands, Poland, Spain, Sweden, and Switzerland, 2016)

	Women (n=14,836)	Men (n=11,595)
<i>Confounders</i>		
Age at baseline, years (SD)	62.2 (10.3)	63.0 (9.2)
<i>Birth cohort</i>		
No war and no great depression	7018 (51.6)	5499 (49.0)
War	3335 (24.5)	2852 (25.4)
Great depression	3236 (23.8)	2861 (25.5)
<i>Living with biological parents</i>		
Both parents	13413 (90.4)	10504 (90.6)
One biological parent	1127 (7.6)	881 (7.6)
Without biological parent	296 (2.0)	209 (1.8)
<i>Attrition</i>		
No drop out	10391 (70.0)	7788 (67.2)
Drop out	3226 (21.7)	2487 (21.4)
Death	1219 (8.2)	1320 (11.4)
<i>Covariates</i>		
<i>BMI, kg/m²</i>		
<24.9	6129 (41.9)	3492 (30.5)
25.0–29.9	5701 (39.0)	5937 (51.8)
≥30.0	2794 (19.1)	2024 (17.7)
<i>Smoking status at baseline</i>		
Never smoker	5892 (66.7)	2434 (35.7)
Ex-smoker	1521 (17.2)	2800 (41.0)
Current smoker	1420 (16.1)	1587 (23.3)
<i>No. of chronic conditions</i>		
< 2	8196 (55.3)	7165 (61.8)
≥2	6629 (44.7)	4422 (38.2)
<i>Physical activity</i>		
Low	9989 (67.4)	8404 (72.5)
High	4825 (32.6)	3181 (27.5)
<i>Adult socioeconomic status</i>		
<i>Level of education</i>		
Low	11849 (83.0)	8532 (76.8)
High	2428 (17.0)	2571 (23.2)
<i>Main occupation</i>		
Low skill	12291 (83.7)	7883 (69.1)
High skill	2395 (16.3)	3523 (30.9)
<i>Household income (able to make ends meet)</i>		
Easily	5175 (34.9)	4503 (38.9)
Fairly easily	4529 (30.6)	3603 (31.1)
With some difficulty	3369 (22.8)	2396 (20.7)
With great difficulty	1734 (11.7)	1082 (9.3)

Data are n (%) unless indicated.

BMI body mass index, SD standard deviation

Table 2 Cancer incidence overall and by site, stratified by gender and childhood socioeconomic conditions (The Survey of Health, Ageing and Retirement in Europe, collected in Austria, Belgium, Czech Republic, Denmark, France, Germany, Greece, Ireland, Italy, the Netherlands, Poland, Spain, Sweden, and Switzerland, 2016)

Women (n=14836)													
All	Most advantaged (n=821)	Advantaged (n=2674)	Middle (n=4798)	Disad- vantaged (n=3771)	Most Disadvan- tagged (n=2772)	All	Most advantaged (n=654)	Advantaged (n=2123)	Middle (n=3610)	Disadvantaged (n=2918)	Most disadvantaged (n=2290)	p	
All cancer types	1517 (10.2)	92 (11.2)	338 (12.6)	454 (9.5)	363 (9.6)	270 (9.7)	<0.001	1335 (11.5)	77 (11.7)	254 (12.0)	327 (11.2)	287 (12.5)	0.30
Breast	618 (4.2)	49 (6.0)	142 (5.3)	183 (3.8)	150 (4.0)	94 (3.4)	<0.001	16 (0.1)	2 (0.3)	4 (0.2)	2 (0.1)	1 (0.0)	0.28
Prostate	-	-	-	-	-	-	368 (3.2)	23 (3.5)	84 (4.0)	117 (3.2)	85 (2.9)	59 (2.6)	0.10
Colon or rectum	142 (1.0)	6 (0.7)	39 (1.5)	42 (0.9)	27 (0.7)	28 (1.0)	0.04	151 (1.3)	9 (1.4)	36 (1.7)	31 (1.1)	37 (1.6)	0.11
Skin	119 (0.8)	7 (0.9)	37 (1.4)	40 (0.8)	26 (0.7)	9 (0.3)	<0.001	113 (1.0)	10 (1.5)	27 (1.3)	24 (0.8)	15 (0.7)	0.11
Lung	35 (0.2)	1 (0.1)	8 (0.3)	9 (0.2)	9 (0.2)	8 (0.3)	0.82	82 (0.7)	5 (0.8)	12 (0.6)	23 (0.8)	17 (0.7)	0.90
Cervix	123 (0.8)	6 (0.7)	38 (1.4)	26 (0.5)	32 (0.8)	21 (0.8)	0.004	-	-	-	-	-	-
Kidney	31 (0.2)	2 (0.2)	6 (0.2)	8 (0.2)	13 (0.3)	2 (0.1)	0.15	48 (0.4)	4 (0.6)	9 (0.4)	9 (0.3)	10 (0.4)	0.76
Stomach	30 (0.2)	0 (0.0)	8 (0.3)	7 (0.1)	10 (0.3)	5 (0.2)	0.38	43 (0.4)	3 (0.5)	7 (0.3)	8 (0.3)	11 (0.5)	0.74
Ovary	102 (0.7)	5 (0.6)	22 (0.8)	26 (0.5)	30 (0.8)	19 (0.7)	0.56	-	-	-	-	-	-
Leukaemia	23 (0.2)	0 (0.0)	4 (0.1)	5 (0.1)	8 (0.2)	6 (0.2)	0.52	41 (0.4)	2 (0.3)	11 (0.5)	16 (0.5)	4 (0.2)	0.06
Endometrium	77 (0.5)	3 (0.4)	18 (0.7)	23 (0.5)	19 (0.5)	14 (0.5)	0.81	-	-	-	-	-	-
Bladder	25 (0.2)	1 (0.1)	6 (0.2)	6 (0.1)	10 (0.3)	2 (0.1)	0.31	67 (0.6)	6 (0.9)	13 (0.6)	15 (0.5)	12 (0.5)	0.76
Thyroid	44 (0.3)	1 (0.1)	8 (0.3)	14 (0.3)	13 (0.3)	8 (0.3)	0.94	6 (0.1)	0 (0.0)	1 (0.0)	2 (0.1)	1 (0.0)	1.00
Liver	23 (0.2)	1 (0.1)	6 (0.2)	5 (0.1)	9 (0.2)	2 (0.1)	0.32	31 (0.3)	2 (0.3)	6 (0.3)	5 (0.2)	6 (0.3)	0.77

Data are n (%); p-values comes from chi-square tests for all cancer types, breast and prostate cancers, and from Fisher exact tests for other cancer types (Colon or rectum, etc.).

Data are n (%); p-values comes from chi-square tests for all cancer types, breast and prostate cancers, and from Fisher exact tests for other cancer types (Colon or rectum, etc.).

Table 3 Associations between childhood socioeconomic conditions (CSCs) and cancer overall and by site at older age, stratified by gender (The Survey of Health, Ageing and Retirement in Europe, collected in Austria, Belgium, Czech Republic, Denmark, France, Germany, Greece, Ireland, Italy, the Netherlands, Poland, Spain, Sweden, and Switzerland, 2016)

Model/CSCs	Women			Men		
	All cancer types (n=1517)	Colon or rectum (n=142)	Skin (n=119)	All cancer types (n=1335)	Colon or rectum (n=151)	Skin (n=113)
Model 0						
Most advantaged	1.50 (1.18-1.91)	0.61 (0.25-1.48)	2.28 (0.84-6.17)	1.34 (1.04-1.73)	0.61 (0.29-1.27)	1.99 (0.89-4.45)
Advantaged	1.72 (1.46-2.04)	1.14 (0.69-1.87)	3.10 (1.48-6.48)	1.48 (1.24-1.76)	0.80 (0.50-1.27)	1.73 (0.91-3.29)
Middle	1.18 (1.01-1.38)	0.91 (0.56-1.49)	2.56 (1.23-5.33)	1.25 (1.07-1.46)	0.60 (0.38-0.96)	1.70 (0.92-3.12)
Disadvantaged	1.09 (0.93-1.28)	0.66 (0.39-1.14)	1.99 (0.93-4.27)	1.11 (0.95-1.31)	0.62 (0.38-1.00)	1.30 (0.68-2.50)
Most disadvantaged	1	1	1	1	1	1
Model 1						
Most advantaged	1.44 (1.12-1.87)	0.59 (0.24-1.46)	2.30 (0.84-6.35)	1.26 (0.97-1.65)	0.52 (0.24-1.13)	1.52 (0.64-3.62)
Advantaged	1.70 (1.42-2.02)	1.07 (0.63-1.80)	3.13 (1.48-6.59)	1.43 (1.19-1.71)	0.71 (0.42-1.17)	1.56 (0.80-3.03)
Middle	1.19 (1.01-1.39)	0.89 (0.54-1.47)	2.55 (1.22-5.33)	1.20 (1.02-1.42)	0.59 (0.37-0.95)	1.67 (0.91-3.09)
Disadvantaged	1.11 (0.94-1.31)	0.67 (0.39-1.15)	1.95 (0.91-4.18)	1.11 (0.94-1.30)	0.63 (0.39-1.03)	1.33 (0.69-2.55)
Most disadvantaged	1	1	1	1	1	1
Model 2						
Most advantaged	1.44 (1.12-1.85)	0.58 (0.23-1.45)	1.91 (0.69-5.30)	1.20 (0.92-1.56)	0.53 (0.25-1.14)	2.06 (0.88-4.82)
Advantaged	1.67 (1.41-1.99)	1.12 (0.67-1.88)	2.82 (1.33-5.96)	1.36 (1.13-1.63)	0.70 (0.42-1.16)	1.81 (0.92-3.56)
Middle	1.16 (0.99-1.37)	0.91 (0.55-1.50)	2.40 (1.15-5.03)	1.18 (1.00-1.39)	0.57 (0.35-0.91)	1.77 (0.94-3.31)
Disadvantaged	1.10 (0.93-1.29)	0.66 (0.38-1.14)	1.90 (0.89-4.07)	1.09 (0.92-1.28)	0.60 (0.37-0.98)	1.37 (0.70-2.65)
Most disadvantaged	1	1	1	1	1	1
Model 3						
Most advantaged	1.43 (1.11-1.83)	0.58 (0.24-1.44)	1.88 (0.68-5.16)	1.28 (0.99-1.66)	0.58 (0.27-1.25)	1.90 (0.83-4.37)
Advantaged	1.63 (1.39-1.97)	1.10 (0.66-1.86)	2.66 (1.26-5.64)	1.42 (1.19-1.70)	0.76 (0.46-1.25)	1.64 (0.84-3.20)
Middle	1.14 (0.97-1.34)	0.89 (0.53-1.48)	2.24 (1.06-4.72)	1.21 (1.03-1.42)	0.59 (0.36-0.95)	1.64 (0.88-3.06)
Disadvantaged	1.07 (0.91-1.26)	0.66 (0.38-1.15)	1.83 (0.86-3.99)	1.10 (0.93-1.29)	0.61 (0.37-0.99)	1.23 (0.63-2.38)
Most disadvantaged	1	1	1	1	1	1
Model 4						
Most advantaged	1.38 (1.06-1.80)	0.58 (0.23-1.48)	1.71 (0.61-4.80)	1.15 (0.87-1.52)	0.48 (0.22-1.08)	1.62 (0.66-4.00)
Advantaged	1.63 (1.36-1.96)	1.07 (0.62-1.86)	2.55 (1.19-5.46)	1.31 (1.08-1.59)	0.65 (0.38-1.12)	1.64 (0.81-3.31)
Middle	1.15 (0.97-1.36)	0.90 (0.53-1.52)	2.13 (1.01-4.50)	1.13 (0.95-1.34)	0.57 (0.35-0.93)	1.74 (0.92-3.31)
Disadvantaged	1.10 (0.93-1.30)	0.68 (0.39-1.19)	1.73 (0.80-3.72)	1.07 (0.91-1.27)	0.63 (0.38-1.03)	1.33 (0.68-2.62)
Most disadvantaged	1	1	1	1	1	1
Model 5						
Most advantaged	1.25 (0.91-1.72)	0.54 (0.18-1.65)	2.60 (0.78-8.72)	1.13 (0.80-1.59)	0.41 (0.15-1.11)	1.50 (0.51-4.36)
Advantaged	1.50 (1.19-1.88)	0.83 (0.41-1.72)	3.35 (1.41-8.93)	1.37 (1.08-1.74)	0.61 (0.31-1.18)	1.41 (0.60-3.32)
Middle	0.94 (0.76-1.16)	0.86 (0.44-1.69)	2.55 (0.99-6.58)	1.18 (0.95-1.46)	0.49 (0.27-0.91)	1.32 (0.59-2.93)
Disadvantaged	1.14 (0.93-1.39)	0.69 (0.35-1.37)	1.74 (0.68-4.46)	1.09 (0.88-1.35)	0.51 (0.27-0.95)	1.49 (0.66-3.37)
Most disadvantaged	1	1	1	1	1	1

Data are hazard ratios (HRs) and 95% confidence intervals (CIs), 1 reference category

Model 0 adjusted for confounders and attrition: age, birth cohort, living with biological parents, reason for dropout if drop out, *Model 1* M0 + adjusted for education, *Model 2* M1 + adjusted for main occupation, *Model 3* M2 + adjusted for household income, *Model 4* M3 + adjusted for all life course socioeconomic conditions, *Model 5* M4 + adjusted for sociodemographics, health status, health behaviours

Table 4 Associations between CSCs and gender-specific cancer at older age (The Survey of Health, Ageing and Retirement in Europe, collected in Austria, Belgium, Czech Republic, Denmark, France, Germany, Greece, Ireland, Italy, the Netherlands, Poland, Spain, Sweden, and Switzerland, 2016)

Model/CSCs	Breast ¹ (n=618)	Cervix ¹ (n=123)	Prostate ¹ (n=368)
Model 0			
Most advantaged	1.53 (1.07-2.19)	0.77 (0.30-1.96)	1.18 (0.72-1.91)
Advantaged	0.99 (0.75-1.30)	1.33 (0.74-2.41)	1.29 (0.92-1.81)
Middle	1.01 (0.78-1.31)	0.75 (0.40-1.40)	1.31 (0.95-1.80)
Disadvantaged	1.05 (0.81-1.37)	1.14 (0.63-2.08)	1.12 (0.80-1.56)
Most disadvantaged	1	1	1
Model 1			
Most advantaged	1.48 (1.01-2.15)	0.67 (0.26-1.76)	1.13 (0.68-1.88)
Advantaged	0.98 (0.74-1.30)	1.22 (0.66-2.25)	1.22 (0.86-1.74)
Middle	1.00 (0.77-1.30)	0.71 (0.38-1.33)	1.21 (0.88-1.68)
Disadvantaged	1.06 (0.81-1.39)	1.10 (0.61-2.01)	1.11 (0.79-1.55)
Most disadvantaged	1	1	1
Model 2			
Most advantaged	1.61 (1.11-2.32)	0.85 (0.32-2.26)	1.11 (0.67-1.84)
Advantaged	1.00 (0.76-1.32)	1.49 (0.79-2.79)	1.22 (0.86-1.74)
Middle	0.99 (0.76-1.28)	0.84 (0.44-1.62)	1.28 (0.93-1.77)
Disadvantaged	1.02 (0.78-1.33)	1.27 (0.68-2.36)	1.10 (0.79-1.55)
Most disadvantaged	1	1	1
Model 3			
Most advantaged	1.48 (1.02-2.14)	0.86 (0.33-2.26)	1.14 (0.69-1.89)
Advantaged	0.97 (0.73-1.28)	1.47 (0.79-2.69)	1.26 (0.89-1.80)
Middle	0.99 (0.76-1.30)	0.82 (0.43-1.55)	1.29 (0.93-1.79)
Disadvantaged	1.04 (0.79-1.36)	1.18 (0.65-2.17)	1.11 (0.79-1.56)
Most disadvantaged	1	1	1
Model 4			
Most advantaged	1.49 (1.01-2.19)	0.83 (0.30-2.28)	1.09 (0.64-1.84)
Advantaged	0.97 (0.72-1.30)	1.48 (0.77-2.85)	1.16 (0.80-1.68)
Middle	0.96 (0.73-1.26)	0.86 (0.44-1.68)	1.19 (0.85-1.66)
Disadvantaged	1.02 (0.78-1.33)	1.27 (0.68-2.38)	1.10 (0.78-1.55)
Most disadvantaged	1	1	1
Model 5			
Most advantaged	1.28 (0.79-2.08)	0.76 (0.23-2.69)	1.37 (0.74-2.56)
Advantaged	0.95 (0.67-1.35)	1.45 (0.65-3.26)	1.16 (0.73-1.83)
Middle	0.87 (0.62-1.23)	0.70 (0.29-1.72)	1.40 (0.92-2.13)
Disadvantaged	0.96 (0.69-1.32)	1.19 (0.55-2.60)	1.27 (0.83-1.93)
Most disadvantaged	1	1	1

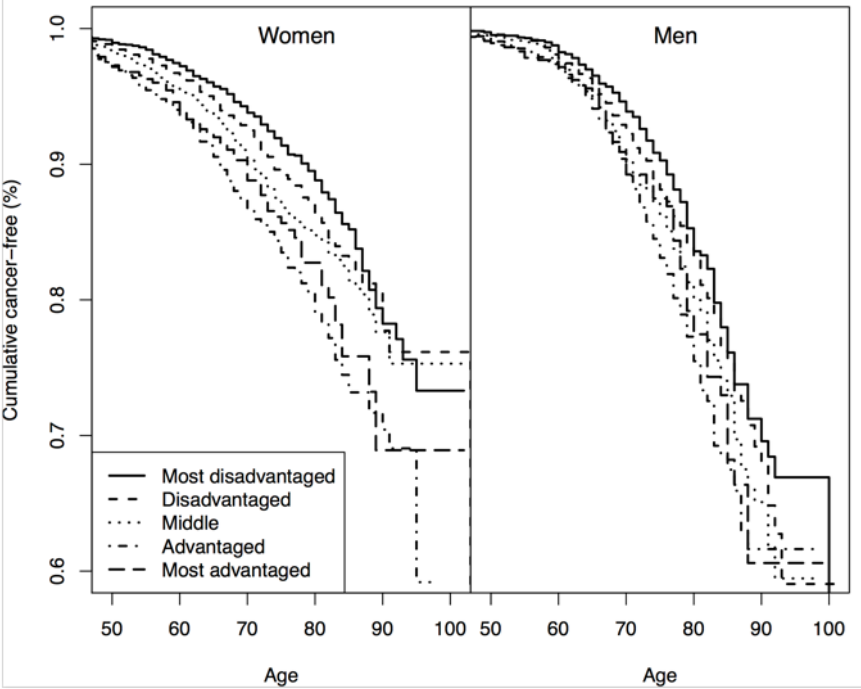
Data are hazard ratios (HRs) and 95% confidence intervals (CIs), 1 reference category

¹Only in women

²Only in men

Model 0 adjusted for confounders and attrition: age, birth cohort, living with biological parents, reason for dropout if drop out, *Model 1* M0 + adjusted for education, *Model 2* M1 + adjusted for main occupation, *Model 3* M2 + adjusted for household income, *Model 4* M3 + adjusted for all life course socioeconomic conditions, *Model 5* M4 + adjusted for sociodemographics, health status, health behaviours

Fig. 1 Kaplan-Meier curve for the cumulative proportion of cancer-free participants over time by gender and childhood socioeconomic conditions (The Survey of Health, Ageing and Retirement in Europe, collected in Austria, Belgium, Czech Republic, Denmark, France, Germany, Greece, Ireland, Italy, the Netherlands, Poland, Spain, Sweden, and Switzerland, 2016)



Note: In the analyses, age started at birth, but is presented from age 50 onwards in the figure

Online Resource 1 Operationalization of childhood socioeconomic conditions

The occupational position of the main breadwinner was constructed based on a reclassification of the 10 main occupational groups of the International Standard Classification of Occupations (ISCO-08) according to their skill levels (International Labour Office, 2012; Wahrendorf, Blane, Bartley, Dragano, & Siegrist, 2013). The first and second skill levels were classified as “low” and the third and fourth skill levels as “high” occupational position. For the number of books at home, a binary item was constructed with the category 0–10 books used as indicator of social disadvantage (M. D. R. Evans et al., 2010). To construct a measure of overcrowding, we combined information on the number of people living in the household and the number of rooms in the house (excluding the kitchen, bathrooms, and hallways), with more than one person per room considered overcrowding (Marsh, 1999). Housing quality was assessed by a fixed bath, cold and hot running water supply, indoor toilet, and central heating. If none of these were present, the household was considered disadvantaged (Dedman et al., 2001). By combining the four indicators, a categorical variable for CSCs was computed, with the categories most advantaged (no disadvantaged socioeconomic conditions at age 10), advantaged (1 of the indicators), middle (2 indicators), disadvantaged (3 indicators), and most disadvantaged (all 4 indicators of disadvantaged socioeconomic conditions).

Online Resource 2 Operationalization covariates and confounders

Birth cohort was categorized into; no crisis or war period [i.e., born before 1914, between 1919 and 1928, or after 1945], first or second world war [i.e. born between 1914 and 1918 or between 1939 and 1945], and the Great Depression [i.e., born between 1929 and 1938]. As indicators of lifestyle, the following health behavior and condition variables were included in the analyses; body mass index (BMI; ≤ 24.9 , $25.0-29.9$, ≥ 30.0 kg/m²), measured in every wave except in wave 3. The average over all waves was calculated in order to obtain a time unvarying variable and to not lose observations. Further, smoking, number of chronic conditions, and physical activity (low, high) were added. Smoking status at baseline assessed if respondents were never, ex- or current smoker. For the average number of chronic conditions, a score was computed based on the following conditions across all waves: stroke, heart attack, hypertension, diabetes, Parkinson disease, and asthma. Physical activity was based on two items assessing the level of daily life physical activity in every wave except wave 3. Vigorous physical activity was assessed with the question “How often do you engage in vigorous physical activity, such as sports, heavy housework, or a job that involves physical labour?” Moderate physical activity was assessed with the question “How often do you engage in activities that require a low or moderate level of energy, such as gardening, cleaning the car, or walking?”. Answers were based on a 4-point scale (1, more than once a week; 2, once a week; 3, one to three times a month; 4, hardly ever, or never). Participants were classified as having low physical activity if they did not engage in any activity more than once a week. Average scores over the participant’s follow-up period were obtained to measure their physical activity.

Online Resource 3 Participant characteristics by gender and childhood socioeconomic conditions (The Survey of Health, Ageing and Retirement in Europe, collected in Austria, Belgium, Czech Republic, Denmark, France, Germany, Greece, Ireland, Italy, the Netherlands, Poland, Spain, Sweden, and Switzerland, 2016)

	Women (n=14825)					Men (n=11587)						
	All	Most advantaged (n=820)	Advantaged (n=2672)	Middle (n=4794)	Disadvantaged (n=3768)	Most disadvantaged (n=2771)	All	Most advantaged (n=654)	Advantaged (n=2121)	Middle (n=3609)	Disadvantaged (n=2914)	Most disadvantaged (n=2289)
<i>Confounders</i>												
Age, years (SD)	62.2 (10.3)	59.9 (10.1)	59.9 (9.7)	60.6 (9.8)	63.4 (10.3)	66.4 (10.2)	63.0 (9.2)	61.9 (9.1)	60.8 (8.7)	61.5 (8.8)	63.7 (9.2)	66.8 (9.1)
Birth cohort												
No war and no great depression	7016 (51.7)	412 (57.8)	1365 (57.3)	2404 (55.6)	1697 (48.2)	1138 (43.0)	5497 (49.1)	336 (53.3)	1143 (56.5)	1825 (52.8)	1318 (46.5)	875 (38.7)
War	3330 (24.5)	175 (24.5)	598 (23.1)	1059 (24.5)	882 (25.1)	616 (23.3)	2850 (25.4)	171 (27.1)	512 (25.3)	877 (25.4)	738 (26.1)	552 (24.4)
Great depression	3234 (23.8)	126 (17.7)	418 (17.6)	838 (19.9)	939 (26.7)	893 (33.7)	2857 (25.5)	123 (19.5)	368 (18.2)	755 (21.8)	776 (27.4)	835 (36.9)
Living with biological parents												
Both parents	13403 (90.4)	752 (91.7)	2408 (90.1)	4370 (91.2)	3362 (89.2)	2511 (90.6)	10498 (90.6)	592 (90.5)	1917 (90.4)	3266 (90.5)	2646 (90.8)	2077 (90.7)
One biological parent	1126 (7.6)	48 (5.9)	202 (7.6)	334 (7.0)	321 (8.5)	221 (8.0)	880 (7.6)	49 (7.5)	139 (7.5)	275 (7.6)	220 (7.5)	177 (7.7)
Without biological parent	296 (2.0)	20 (2.4)	62 (2.3)	90 (1.9)	85 (2.2)	39 (1.4)	208 (1.8)	13 (2.0)	45 (2.1)	67 (1.9)	48 (1.6)	35 (2.1)
<i>Attrition</i>												
No drop out	10391 (70.1)	597 (72.8)	1958 (73.3)	3388 (70.7)	2583 (68.6)	1865 (67.3)	7788 (67.2)	440 (67.3)	1479 (69.7)	2475 (68.6)	1934 (66.4)	1460 (63.8)
Drove out	3226 (21.8)	169 (20.6)	596 (22.3)	1103 (23.0)	841 (22.5)	517 (18.7)	2487 (21.5)	155 (23.7)	472 (22.5)	820 (22.7)	634 (21.8)	406 (17.7)
Death	1208 (8.1)	54 (6.6)	118 (4.4)	505 (6.3)	344 (9.3)	389 (14.0)	1312 (11.5)	59 (9.0)	170 (8.0)	314 (8.7)	346 (11.9)	425 (18.5)
<i>Covariates</i>												
BMI, kg m ⁻²												
<21.9	6129 (41.9)	476 (58.7)	1341 (50.8)	2055 (43.3)	1408 (37.9)	849 (31.3)	3482 (30.5)	280 (43.3)	751 (35.6)	1041 (29.1)	792 (27.5)	628 (27.9)
25.0-29.9	5701 (39.0)	254 (31.3)	910 (34.5)	1814 (38.2)	1335 (41.3)	1188 (43.8)	5937 (51.8)	282 (43.6)	1030 (48.9)	1909 (53.4)	1551 (53.9)	1165 (51.7)
≥30.0	2794 (19.1)	81 (10.0)	390 (14.8)	874 (18.4)	773 (20.8)	676 (24.9)	2024 (17.7)	85 (13.1)	326 (15.5)	622 (17.4)	532 (18.3)	459 (20.4)
Smoking status												
Never smoker	5892 (66.7)	261 (50.6)	908 (56.1)	1726 (62.5)	1676 (72.3)	1321 (81.7)	2434 (53.7)	162 (39.0)	459 (35.2)	724 (35.0)	620 (35.1)	449 (37.0)
Ex-smoker	1521 (17.2)	154 (29.8)	410 (25.3)	525 (19.0)	302 (13.0)	130 (8.0)	2800 (41.0)	164 (39.5)	533 (42.3)	848 (41.1)	690 (39.1)	545 (43.0)
Current smoker	1420 (16.1)	101 (19.6)	300 (18.5)	512 (18.5)	341 (14.7)	166 (10.3)	1587 (23.3)	89 (21.5)	294 (22.5)	494 (23.9)	457 (25.9)	253 (20.0)
<i>No. of chronic conditions</i>												
<2	8196 (55.3)	557 (67.9)	1705 (63.8)	2842 (59.3)	1944 (51.6)	1148 (41.4)	7165 (61.8)	448 (68.5)	1406 (66.3)	2366 (65.6)	1727 (59.3)	1218 (53.2)
≥2	6629 (44.7)	263 (32.1)	967 (36.2)	1952 (40.7)	1824 (48.4)	1623 (58.6)	4422 (38.2)	206 (31.5)	715 (33.7)	1243 (34.4)	1187 (40.7)	1071 (46.8)
<i>Physical activity</i>												
Low	9989 (67.4)	632 (79.6)	2029 (76.0)	3419 (71.4)	2391 (63.5)	1498 (54.1)	8404 (72.5)	517 (79.1)	1658 (78.2)	2742 (76.0)	2027 (69.6)	1460 (63.8)
High	4825 (32.6)	167 (20.4)	642 (24.0)	1370 (28.6)	1376 (36.5)	1270 (45.9)	3181 (27.5)	317 (20.9)	462 (21.8)	867 (24.0)	887 (30.4)	828 (36.2)
<i>Adult socioeconomic status</i>												
Level of education												
Low	11849 (85.0)	361 (45.5)	1736 (67.8)	3767 (81.7)	3385 (93.0)	2600 (97.3)	8531 (76.8)	240 (38.3)	1214 (59.3)	2594 (75.0)	2440 (87.8)	2043 (93.2)
High	2428 (17.0)	432 (54.5)	824 (32.2)	846 (18.3)	255 (7.0)	71 (2.7)	2571 (23.2)	386 (61.7)	832 (40.7)	865 (25.0)	340 (12.2)	148 (6.8)
<i>Main occupation class</i>												
Low skill	12282 (83.7)	408 (50.2)	1865 (70.2)	3932 (82.8)	3440 (92.3)	2617 (96.7)	7878 (69.1)	197 (30.2)	1047 (49.6)	2337 (65.2)	2323 (81.2)	1974 (90.1)
High skill	2393 (16.3)	405 (49.8)	795 (29.8)	819 (17.2)	286 (7.7)	90 (3.3)	3520 (30.9)	455 (69.8)	1065 (50.4)	1245 (34.8)	537 (18.8)	218 (9.9)
<i>(able to make ends meet)</i>												
Easy	5170 (34.9)	485 (59.3)	1333 (49.9)	1908 (39.9)	998 (26.5)	446 (16.1)	4999 (38.9)	421 (64.4)	1159 (54.6)	1597 (44.3)	887 (30.5)	435 (19.0)
Fairly easy	4235 (30.6)	226 (27.6)	802 (30.0)	1493 (31.2)	1201 (31.9)	803 (29.0)	3402 (31.1)	161 (24.6)	638 (30.1)	1169 (32.4)	926 (31.8)	708 (31.0)
With some difficulty	3368 (24.5)	87 (10.6)	391 (14.6)	977 (20.4)	1008 (26.8)	905 (32.7)	2396 (20.7)	61 (9.3)	232 (11.9)	625 (17.3)	377 (12.3)	740 (32.4)
With great difficulty	1733 (12.5)	20 (2.4)	144 (5.4)	402 (8.4)	556 (14.8)	611 (22.1)	1081 (9.3)	11 (1.7)	72 (3.4)	218 (6.0)	718 (13.0)	403 (17.6)

BMI body mass index, *SD* standard deviation

Data are n (%) unless indicated

Chapter 3. Life course socioeconomic conditions and frailty at older ages (Article 2)

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Abstract

Objectives. This paper aimed to assess associations of childhood socioeconomic conditions (CSC) with the risk of frailty in old age and whether adulthood socioeconomic conditions (ASC) influence this association.

Methods Data from 21 185 individuals aged 50 years and older included in the longitudinal Survey of Health, Ageing, and Retirement in Europe were used. Frailty was operationalized as a sum of presenting weakness, shrinking, exhaustion, slowness, or low activity. Confounder-adjusted multilevel logistic regression models were used to analyze associations of CSC and ASC with frailty.

Results While disadvantaged CSC was associated with higher odds of (pre-)frailty in women and men (OR=1.73, 95%CI 1.34, 2.24; OR=1.84, 95%CI 1.27, 2.66, respectively), this association was mediated by ASC. Personal factors and demographics, such as birth cohort, chronic conditions and difficulties with activities of daily living, increased the odds of being (pre-)frail.

Discussion Findings suggest that CSC are associated with frailty at old age. However, when taking into account ASC, this association no longer persists. The results show the importance of improving socioeconomic conditions over the whole life course in order to reduce health inequalities in old age.

Keywords

Health Outcomes; Socioeconomic Status; Successful Aging

Introduction

Frailty is a clinical syndrome used in geriatric medicine characterized by cumulative declines across multiple biological systems and, as a result, an increased vulnerability to stressors (Clegg et al., 2013). Frail people are at an increased risk of disability, falls, dementia, institutionalization, healthcare utilization, and death (Romero-Ortuno, 2013). Although there is an important heterogeneity in measures and definitions of frailty, one operationalization that has been validated, widely used, and accepted is the phenotype of frailty, previously described by Fried et al. (2001) (Etman et al., 2012; Romero-Ortuno, 2013; Santos-Eggimann et al., 2009). It is defined as the presence of at least three of five specific attributes; shrinking, weakness, exhaustion, slowness, and low activity (Fried et al., 2001; Macklai, Spagnoli, Junod, & Santos-Eggimann, 2013). The presence of one or two of the attributes can be considered as pre-frailty, a precursor of frailty. As frailty is a dynamic process, transitions between the states take place and each of the states are predictive of outcomes such as hospitalization or worsening disability. Thus, it is important to take the different states into consideration when studying frailty (Gill, Gahbauer, Allore, & Han, 2006).

Previous research has shown that the prevalence of frailty increases with each five-year older age group: studies found prevalence rates of 17% among community-dwelling older adults aged 65 years and older and 25% to 40% among adults aged 80 years and over (Bandein-Roche et al., 2015; Fried et al., 2001; Santos-Eggimann et al., 2009). Moreover, it was found that 52% of community-dwelling older adults over the age of 65 years were in a pre-frail state (Santos-Eggimann et al., 2009). Additionally, frailty was found to be more prevalent in women than in men, persons with lower education and lower income, poorer health, higher rates of comorbid chronic disease and disabilities, and in residents of nursing homes (Buckinx et al., 2015; Etman et al., 2012). With an ageing population, the number of (pre-)frail people will increase rapidly, thus identifying people at risk and preventing the process of becoming frail is important.

Poor socioeconomic circumstances during childhood have already been shown to be associated with negative health outcomes during adulthood, such as higher risk of cardiovascular disease, lower quality of life, poorer physical

capability, and higher mortality rates (Ben-Shlomo, 2013; D. Kuh, & Ben-Shlomo, Y., 2004; Wahrendorf & Blane, 2015). Multiple life course and life stage models exist in which childhood is regarded as the period in which people are most vulnerable to external influences (D. Blane, Kelly-Irving, M. d'Errico, A., Bartley, M., Montgomery, S., 2013; Bruer, 2001; Strachan, 2004; Stringhini et al., 2015). Childhood is thought to influence health in later life through different possible pathways including biological and developmental processes, cumulative (dis)advantage of structural stress exposure, and social mobility (Bruer, 2001; Dannefer, 2003; Y. Luo & L. J. Waite, 2005).

Besides individual level behaviors of children growing up in lower childhood socioeconomic circumstances, structural factors can also influence health and may have been prominent in the studied cohort during this period in Europe (Sharpe et al., 2018). For example, growing up in poor socioeconomic circumstances may also mean growing up in a lower-income neighborhood and home with poor environmental conditions, less access to quality education, quality health care and high quality social networks, which in turn may impact health at older age (Doku, Acacio-Claro, Koivusilta, & Rimpela, 2018; Lazar & Davenport, 2018; Sharpe et al., 2018). Previous studies also suggest that socioeconomic factors contribute to differences in frailty and pre-frailty and that health inequalities as a result of education, occupational class, and wealth persist throughout old age (Santos-Eggimann et al., 2009; Stolz, Mayerl, Waxenegger, Rasky, & Freidl, 2017). Across birth cohorts, wealthier earlier birth cohorts show similar levels of frailty as recent cohorts, but the poorest cohort shows higher levels of frailty compared to earlier cohorts (Marshall, Nazroo, Tampubolon, & Vanhoutte, 2015). Additionally, recent studies found an increased risk in the worsening of frailty over time in lower educated persons aged 55 years and older compared to higher educated persons (Etman, Kamphuis, van der Cammen, Burdorf, & van Lenthe, 2015; Franse et al., 2017; Gill et al., 2006). This persisting inequality in old age can be partly explained by lifestyle and health, such as lower alcohol consumption, higher sedentariness, higher obesity, higher chronic disease rates, and being depressed (Cheval et al., 2018; Etman et al., 2015; Franse et al., 2017; Hoogendijk et al., 2014; Soler-Vila et al., 2016).

So far, available studies have mainly looked at the influence of socioeconomic factors in mid- and late adulthood. However, not many studies exist on the effect of socioeconomic conditions in the sensitive build-up stage in the life course (i.e., childhood) on frailty, using longitudinal data and a comprehensive operationalization of frailty (Strachan, 2004; Vineis, Kelly-Irving, Rappaport, & Stringhini, 2016). In addition, how childhood socioeconomic conditions (CSC) may influence the development of frailty along with the effects of ageing and of life-course socioeconomic conditions is not well studied. Using longitudinal and multinational data enabled us to study whether (1) CSC are associated with levels of frailty in older adults as well as its rate of change and (2) whether this association is mediated by adulthood socioeconomic conditions (ASC). As a final, exploratory, aim, we examined this association while including other potentially related variables to frailty, such as chronic conditions and difficulties with activities of daily living (ADL).

Methods

Study design and population

Data from individuals aged 50 years and over included in the longitudinal Survey of Health, Ageing, and Retirement in Europe (SHARE) were used. SHARE includes six waves of data that were collected every two years between 2004 and 2016 (Borsch-Supan et al., 2013). By means of standardized computer-assisted face-to-face interviews, information on aspects ranging from economic variables and demographics to health variables was collected (Alcer et al., 2005). Additionally, measurements of grip strength were performed for all participants. Retrospective life course data on CSC were only collected in wave three.

For the current analyses we used all 6 currently available waves. SHARE participants were eligible for the analyses if they were aged between 50 and 95 years old, participated in the third wave, and had at least one complete measure of frailty in wave 1, 2, 4, 5 and 6. Participants were drawn from 14 European countries based on probability samples adapted to each country (Klevmarken, 2005). SHARE was approved by the relevant research ethics committees in the participating countries and all participants provided written informed consent.

Frailty

The operationalization of frailty required adaptation of the SHARE data to the original attributes from the phenotype of frailty by Fried and colleagues (Fried et al., 2001). In order to construct the dependent variable with the provided information in SHARE, we adhered to Santos-Eggimann et al.'s (2009) proposition of the operationalization of frailty, which was measured similarly at each wave. This operationalization was constructed by selecting the most suitable metric and has been tested and validated in the SHARE population (Macklai et al., 2013; Romero-Ortuno, 2013). The shrinking attribute was operationalized using the question, "What has your appetite been like" and was fulfilled when participants reported the answer "diminution in desire for food" or, in the case of an unclear response to this question, the answer "less" to the follow-up item "So have you been eating more or less than usual?". Weakness was derived from the grip strength measures, where the highest out of four consecutive dynamometer measures (two from each hand) was analysed using cut-offs calculated for each wave separately, stratified by gender and body mass index quartiles as proposed by Fried et al. (Fried et al., 2001). The weakness criterion was fulfilled by the weakest 20% in each category. Exhaustion was operationalized by a positive answer to the question, "In the last month, have you had too little energy to do things you wanted to do?". The slowness attribute was defined through mobility questions, as SHARE measured walking speed only for individuals aged 75 or older. According to Santos-Eggimann et al. (2009), previous analyses showed that low speed and positive answers to either of the following two items were strongly associated: "Because of a health problem, do you have any difficulty [expected to last three or more months] walking 100 meters" or "...climbing one flight of stairs without resting". For the low activity attribute, the question "How often do you engage in activities that require a low or moderate level of energy such as gardening, cleaning the car, or going for a walk?" was considered. The criterion was fulfilled for individuals answering either "one to three times a month" or "hardly ever or never".

Based on the operationalization of the five attributes, we created a score ranging from zero to five. Individuals with zero points were classified as non-frail, with one or two points as pre-frail, and with three or more points as frail (Fried et

al., 2001). In the main analyses, frailty was dichotomised as either non-frail or (pre-)frail, in which those in pre-frail and frail states were combined.

Childhood and Adulthood Socioeconomic Conditions

CSC was computed according to Wahrendorf and Blane's (2015) measure of childhood circumstances. This measure was constructed by combining four binary indicators of socio-economic conditions at age 10; the occupational position of the main breadwinner, number of books at home, overcrowding, and housing quality. Previous studies showed that those four indicators are relevant when assessing the long-term effects of CSC on health (Chittleborough, Baum, Taylor, & Hiller, 2006; Dedman et al., 2001; M. D. Evans, J. Kelley, J. Sikora, & D. J. Treiman, 2010; Marsh, 1999). This information was collected in the third wave of SHARE as part of the SHARELIFE module, which is a retrospective survey focused on people's life histories (Schröder, 2011).

The occupational position of the main breadwinner was constructed by reclassifying the 10 main occupational groups of the International Standard Classification of Occupations (ISCO) according to their skill levels (Wahrendorf et al., 2013). The first and second skill levels were categorised as 'low' and the third and fourth skill levels were regrouped as 'high' occupational position. A binary item was constructed using the number of books at home, with the category '0 – 10 books' being an indicator of social disadvantage (M. D. Evans et al., 2010). The measure of overcrowding was constructed using survey answers regarding the number of people living in the household and the number of rooms (excluding kitchen, bathrooms, and hallways). Having more than one person per room in the household was considered as overcrowding (Marsh, 1999). Finally, housing quality was assessed by the presence of the following items; fixed bath, cold running water supply, hot running water supply, indoor toilet, and central heating. Where none of these were present, the household was coded as disadvantaged (Dedman et al., 2001). A categorical variable for CSC ranging from zero (most advantaged) to four (most disadvantaged) was computed by combining the information of the four indicators.

The following variables were used as indicators of ASC; highest educational attainment (number of years), occupational class (high skill and low

skill), and satisfaction with household income (from the question “Is household able to make ends meet?”, from one ‘with great difficulty’ to four ‘easily’). Occupational class – high- or low-skilled – was based on the International Standard Classification of Occupations (ISCO) of the main job using the question ‘Which of the jobs you have told me about was the final job of your main career or occupation? By this we mean the last job in the career or the occupation that took up most of your working life, even though you might have had other jobs afterwards’. Participants who never performed paid work were classified as low skill.

Potential confounders and predictors

All analyses were adjusted for age and attrition (no dropout, dropped, deceased) and potential confounders, including birth cohort (no crisis or war period [i.e., born before 1914, between 1919 and 1928, or after 1945], first and second world war [i.e., born between 1914 and 1918 or between 1939 and 1945], and Great Depression [i.e., born between 1929 and 1938]), and growing up with biological parents (both parents, either mother or father, without parents). Final models (model 3) were adjusted for other possible predictors of frailty; partnership status (living with partner: yes, no), cognitive functioning (delayed recall memory and verbal fluency), smoking (ever, not), number of chronic conditions (total number), difficulties with ADL (score range zero to five), and difficulties with instrumental activities of daily living (IADL, score range zero to five). For the number of chronic conditions, a score was computed based on the following conditions: stroke, heart attack, hypertension, diabetes, cancer, Parkinson’s disease, and asthma. ADL was based on bathing, dressing, eating, getting in and out of bed, and walking across a room. IADL was based on using the telephone, managing money, managing medications, shopping for groceries, and preparing meals.

Statistical analyses

To describe the associations of CSC with frailty, logistic mixed effects models were estimated. These models have been developed to take the nested structure of the data into account (e.g., multiple observations within a single participant), thereby providing accurate parameter estimates with acceptable type 1 error rates

(Boisgontier & Cheval, 2016). Additionally, using this modelling approach, we did not have to exclude participants that had missing observations in certain waves, as they do not require an equal number of observations from all participants (See Supplementary Figure 1 for a flow chart for more information on participants' selection criteria). We also checked if missing observations were country-specific, which was not the case. Models' Bayesian Information Criterion (BIC) as well as likelihood ratio tests revealed that the best random structure was random intercepts for participants and random linear slopes of age. Random slopes estimate the linear growth trajectory of the individual participant. In order to see the estimates per country, countries were included as fixed effect (Supplementary materials Tables 3-6).

Analyses were stratified by gender based on expected differences between men and women in the prevalence of frailty (Buckinx et al., 2015). All analyses were adjusted for age, country, and living with biological parents during childhood. All models were additionally adjusted for birth cohort, as people from earlier cohorts were more likely to come from more disadvantaged socioeconomic conditions. Age was centred at 73 years, which was the sample's midpoint, and then divided by ten so the coefficients yield the effect of the overall frailty evolution over a 10-year interval. Age squared was included to account for possible accelerated changes in frailty over ageing. Interaction terms between CSC and age were included to test whether CSC moderated the effects of ageing on (pre-)frailty. A significant interaction means that the rate of change in frailty differs across CSC. As potential mediators, we ran a second model that included indicators of ASC. A third model additionally included health- and lifestyle variables.

Four sensitivity analyses were performed; two analyses with frailty as a dichotomous outcome comparing (1) non-frail to pre-frail individuals, and (2) non-frail and pre-frail versus frail individuals (to check for the associations in different frailty states, as the number of participants who were frail within each CSC were low), one where participants older than 90 were excluded (as descriptive statistics showed that observations in this age category within each CSC were very low, which may lead to problems with estimation), and one where clinically depressed participants were excluded (as the definition of frailty overlaps to some extent with

depression, particularly exhaustion and low activity). Additionally, we ran ordinal multilevel regression models, where frailty was divided into three categories; frail, pre-frail, and non-frail. Statistical analyses were performed using the R language and the lme4 and lmerTest packages (Bates, Mächler, Bolker, & Walker, 2015; Kuznetsova, 2016; R Core Team, 2017).

Results

Participant characteristics

Participant characteristics are reported in Table 1. The final sample consisted of 21 185 people (55% female) (See Supplementary Figure 1 for a flow chart). Mean age was 63.4 years (9.5 standard deviation (SD)) for women and 63.4 (9.0) for men. A CSC gradient was observed in women and men: the percentage of (pre-)frail people increased from most advantaged to most disadvantaged CSC (See Supplementary Tables 1 and 2). Participants had on average 3 complete (information on all attributes was available) measures of frailty over the five waves and the number of participants with only one measurement wave was 13%.

Effects of childhood socioeconomic conditions on risk of frailty over ageing

The results of the confounder-adjusted logistic mixed-effects models for the association of CSC with the odds of being (pre-)frail are shown in models 1 in Table 2 (women) and Table 3 (men). Women who grew up in disadvantaged and most disadvantaged CSC had higher odds of being (pre-)frail compared to those in the most advantaged CSC. This result was similar among men, where additionally a higher odds was found among those from middle CSC. Among women and men, a positive age indicated that as people age, the odds of being (pre-)frail increased. The significant quadratic effect of age coefficient indicated that there was an accelerated change of frailty over ageing. Interactions of CSC with age and age squared showed no significant effects, indicating that CSC did not moderate the level nor the rate of change in (pre-)frailty over ageing (Supplementary Tables 3 and 4).

Figure 1 shows the predicted probability of being (pre-)frail in women and men for each CSC (model 1). The figure suggests a difference between the CSC that is relatively stable, but diminishes from age 85 onwards.

Effects of adulthood socioeconomic conditions on risk of frailty over ageing

When educational attainment, main occupational class, and satisfaction with household income were added as potential mediators in the model including CSC, results indicated that these indicators of ASC mediate the association of CSC with odds of being (pre-)frail in both women and men (see model 2 in Tables 2 and 3).

In both women and men, lower education, having a low skilled job, and higher satisfaction with income were associated with higher odds of (pre-)frailty. Regarding the health- and lifestyle variables, living without a partner increased the odds of being (pre-)frail in both women and men. Having smoked and more difficulties with IADL were associated with higher odds of being (pre-)frail in women (see model 3 in Tables 2 and 3).

The results of the sensitivity analyses for frailty as dichotomous outcome comparing non-frail to pre-frail can be found in the Supplementary Tables 5 and 6. For the other sensitivity analyses as well as results from ordinal multilevel regression models, tables are not shown. Overall, the results of the sensitivity analyses were consistent with these findings in the main analyses.

Discussion

In this study, the association of CSC, ASC, and other life course factors with (pre-)frailty at older age was analysed using large scale, multinational, longitudinal data. With respect to our first research question, results showed a relation between CSC and the odds of being (pre-)frail in both women and men: the more disadvantaged the CSC, the higher the odds of being (pre-)frail. However, these results no longer hold when looking at our second research question, the effects of ASC (i.e., level of education, main occupation class, and level of household income) on the relation between CSC and frailty, as findings showed that ASC mediated the effect of CSC on the odds of being (pre-)frail in both women and men.

Our findings corroborate cross-sectional studies showing a relationship between disadvantaged socioeconomic conditions over the life course, measured by, amongst others, education, standard of living, and household income, and a higher risk of frailty in old age in France, Italy, and Latin America (Alvarado et al.,

2008; Herr, Robine, Aegerter, Arvieu, & Ankri, 2015; Poli et al., 2016). Our study went further by showing that socioeconomic differences persisted over age, and even increased among women. Two studies from Latin America and the United Kingdom support our findings of a relationship between poor CSC and higher odds of frailty in both men and women (Alvarado et al., 2008; Gale et al., 2016). Our study added to these findings by using a more comprehensive indicator of CSC. Other research supports the idea that not only CSC, but also socioeconomic circumstances across the life course are determinants of frailty in later life. Alvarado et al. found that adulthood and current social conditions, measured as low education, non-white collar occupation, and insufficient income, were cross-sectionally associated with higher odds of frailty in both men and women (Alvarado et al., 2008). Gardiner et al. studied frailty trajectories in older women and found that late-life socioeconomic status has a strong impact on frailty, but did not look at the effects of CSC (Gardiner, Mishra, & Dobson, 2016). Similar to the findings in the present study, they found that women who had difficulties in managing their income were more likely to be frail. Dury and colleagues also found that older people who had a lower household income were more at risk for frailty (Dury et al., 2016). Similarly, Herr et al. found that the most important risk factor of frailty was a poor level of financial security in old age (Herr et al., 2015). These findings all support the idea that socioeconomic circumstances across the life course are strong determinants of frailty in older age.

Importantly, the present study is the first longitudinal and cross-national European study to reveal that pathways to (pre-)frailty already start in childhood and are associated with CSC. However, what this study adds to the existing knowledge is that these findings on the association with CSC no longer qualify when taking a life-course perspective: taking ASC (i.e. education, occupation, and income) into account mediates the association.

Apart from the findings on socioeconomic conditions, in several exploratory analyses, we also revealed that key demographic variables, such as age and individual differences in life history, such as not having a partner, may be associated with frailty. These results corroborate previous cross-sectional reports on increasing age being associated with increasing prevalence of frailty, or multimorbidity (Woo, Zheng, Leung, & Chan, 2015). Increased age was also found to

be a risk factor for frailty by Dury et al (Dury et al., 2016). Further, they found that having no partner was a risk characteristic, which was also a finding in this study, but only in men. More in-depth research in the findings regarding demographics and personal factors over the life course may help in explaining its pathways with frailty.

Strengths and limitations

A major strength of this study is the use of a multinational and longitudinal database with a large sample size with a potential observation period of 10 years. Additionally, pre-defined and previously used methods for defining and analysing socioeconomic conditions and frailty were used, thereby limiting chances of misclassification bias. Also, using the same methods of operationalizing frailty as other SHARE studies makes it easy to compare the results of this study with other SHARE studies. We minimised the health selection bias by including respondents participating in only one wave.

The present study has some limitations. First, information on CSC and ASC was measured retrospectively and was self-reported. The data may therefore be subject to recall bias. However, previous research found evidence for the accuracy of recall of simple measures of socioeconomic conditions in a survey of older adults (Lacey et al., 2012). Second, as we used longitudinal data, we had participants who dropped out or died during follow-up. However, to deal with this, we adjusted for attrition in the analyses, which is a statistical adjustment for mediator-outcome confounding, although this does not solve the issue of missing data due to attrition. Third, different definitions and methods of operationalizing frailty exist which may lead to different estimates of frailty, depending on the definition used and the population being studied. Even though several SHARE studies used the same operationalization, it may be more difficult to compare to studies using a different operationalization. Yet, this strategy seems most optimal to allow better comparison with other studies using SHARE data. Additionally, in our analyses we combined the pre-frail and frail groups, whereas some other studies only look at frailty (3 or more attributes) or a sum score. Even though this may make direct comparison more difficult, in our sensitivity analyses we did not

find changes to the main analyses and are thus confident about the associations we found.

Conclusion

The present study is the first longitudinal cross-national European study to analyse the associations of CSC with frailty and explore the role of ASC as mediators in this association. In conclusion, our findings suggest that pathways to (pre-)frailty start in early life. Importantly, they also demonstrate that these effects are mediated by socioeconomic factors later in life. These findings give clear evidence of the long-term impact of socioeconomic conditions over the life course on frailty at older age. This may help in developing public health policies improving frailty trajectories by targeting individuals at risk of becoming frail. Early interventions for (pre-)frail individuals are expected to improve their quality of life and reduce costs of care (Buckinx et al., 2015). Policies aiming to improve socioeconomic conditions in adulthood, can have beneficial effects across the life course and may help in reducing the impact of unfavourable early life conditions on health inequalities.

References

- Alcer, K., Benson, G., Blom, A. G., Börsch-Supan, A., Brugiavini, A., Christelis, D., . . . Weerman, B. (2005). *The Survey of Health, Aging, and Retirement in Europe - Methodology*. Mannheim: Mannheim Research Institute for the Economic of Aging.
- Alvarado, B. E., Zunzunegui, M. V., Beland, F., & Bamvita, J. M. (2008). Life course social and health conditions linked to frailty in Latin American older men and women. *J Gerontol A Biol Sci Med Sci*, 63(12), 1399-1406. doi:10.1093/gerona/63.12.1399
- Bandeem-Roche, K., Seplaki, C. L., Huang, J., Buta, B., Kalyani, R. R., Varadhan, R., . . . Kasper, J. D. (2015). Frailty in Older Adults: A Nationally Representative Profile in the United States. *The Journals of Gerontology: Series A*, 70(11), 1427-1434. doi:10.1093/gerona/glv133
- Bates, D., Mächler, M., Bolker, B., & Walker, S. (2015). Fitting Linear Mixed-Effects Models Using lme4. 2015, 67(1), 48. doi:10.18637/jss.v067.i01
- Ben-Shlomo, Y. (2013). *A Life Course Approach to Healthy Ageing*: Oxford University Press.
- Blane, D., Kelly-Irving, M., d'Errico, A., Bartley, M., Montgomery, S. (2013). Social-biological Transitions: how does the social become biological? *Longitudinal Life Course Studies*, 4(2), 136-146. doi:10.14301/llcs.v4i2.236
- Boisgontier, M. P., & Cheval, B. (2016). The anova to mixed model transition. *Neurosci Biobehav Rev*, 68, 1004-1005. doi:10.1016/j.neubiorev.2016.05.034
- Borsch-Supan, A., Brandt, M., Hunkler, C., Kneip, T., Korbmacher, J., Malter, F., . . . Zuber, S. (2013). Data Resource Profile: the Survey of Health, Ageing and Retirement in Europe (SHARE). *Int J Epidemiol*, 42(4), 992-1001. doi:10.1093/ije/dyt088
- Bruer, J. T. (2001). A critical and sensitive period primer. In J. D. B. Bailey, Bruer J.T., Symons, F.J. (Ed.), *Critical thinking about critical periods*. Baltimore: Paul H. Brookes.
- Buckinx, F., Rolland, Y., Reginster, J. Y., Ricour, C., Petermans, J., & Bruyere, O. (2015). Burden of frailty in the elderly population: perspectives for a public health challenge. *Arch Public Health*, 73(1), 19. doi:10.1186/s13690-015-0068-x
- Cheval, B., Boisgontier, M. P., Orsholits, D., Sieber, S., Guessous, I., Gabriel, R., . . . Cullati, S. (2018). Association of early- and adult-life socioeconomic circumstances with muscle strength in older age. *Age Ageing*, 47(3), 398-407. doi:10.1093/ageing/afy003
- Chittleborough, C. R., Baum, F. E., Taylor, A. W., & Hiller, J. E. (2006). A life-course approach to measuring socioeconomic position in population health

- surveillance systems. *J Epidemiol Community Health*, 60(11), 981-992. doi:10.1136/jech.2006.048694
- Clegg, A., Young, J., Iliffe, S., Rikkert, M. O., & Rockwood, K. (2013). Frailty in elderly people. *Lancet*, 381(9868), 752-762. doi:10.1016/s0140-6736(12)62167-9
- Dannefer, D. (2003). Cumulative advantage/disadvantage and the life course: cross-fertilizing age and social science theory. *J Gerontol B Psychol Sci Soc Sci*, 58(6), S327-337.
- Dedman, D. J., Gunnell, D., Davey Smith, G., & Frankel, S. (2001). Childhood housing conditions and later mortality in the Boyd Orr cohort. *J Epidemiol Community Health*, 55(1), 10-15. doi:10.1136/jech.55.1.10
- Doku, D. T., Acacio-Claro, P. J., Koivusilta, L., & Rimpela, A. (2018). Health and socioeconomic circumstances over three generations as predictors of youth unemployment trajectories. *Eur J Public Health*. doi:10.1093/eurpub/cky242
- Dury, S., De Roeck, E., Duppen, D., Fret, B., Hoeyberghs, L., Lambotte, D., . . . Dierckx, E. (2016). Identifying frailty risk profiles of home-dwelling older people: focus on sociodemographic and socioeconomic characteristics. *Aging Ment Health*, 1-9. doi:10.1080/13607863.2016.1193120
- Etman, A., Burdorf, A., Van der Cammen, T. J., Mackenbach, J. P., & Van Lenthe, F. J. (2012). Socio-demographic determinants of worsening in frailty among community-dwelling older people in 11 European countries. *J Epidemiol Community Health*, 66(12), 1116-1121. doi:10.1136/jech-2011-200027
- Etman, A., Kamphuis, C. B., van der Cammen, T. J., Burdorf, A., & van Lenthe, F. J. (2015). Do lifestyle, health and social participation mediate educational inequalities in frailty worsening? *Eur J Public Health*, 25(2), 345-350. doi:10.1093/eurpub/cku093
- Evans, M. D., Kelley, J., Sikora, J., & Treiman, D. J. (2010). Family scholarly culture and educational success: Books and schooling in 27 nations. *Research in social stratification and mobility*, 28(2), 171-197. doi:10.1016/j.rssm.2010.01.002
- Franse, C. B., van Grieken, A., Qin, L., Melis, R. J. F., Rietjens, J. A. C., & Raat, H. (2017). Socioeconomic inequalities in frailty and frailty components among community-dwelling older citizens. *PLoS One*, 12(11), e0187946. doi:10.1371/journal.pone.0187946
- Fried, L. P., Tangen, C. M., Walston, J., Newman, A. B., Hirsch, C., Gottdiener, J., . . . McBurnie, M. A. (2001). Frailty in older adults: evidence for a phenotype. *J Gerontol A Biol Sci Med Sci*, 56(3), M146-156.
- Gale, C. R., Booth, T., Starr, J. M., & Deary, I. J. (2016). Intelligence and socioeconomic position in childhood in relation to frailty and cumulative

- allostatic load in later life: the Lothian Birth Cohort 1936. *J Epidemiol Community Health*, 70(6), 576-582. doi:10.1136/jech-2015-205789
- Gardiner, P. A., Mishra, G. D., & Dobson, A. J. (2016). The Effect of Socioeconomic Status Across Adulthood on Trajectories of Frailty in Older Women. *J Am Med Dir Assoc*, 17(4), 372.e371-373. doi:10.1016/j.jamda.2015.12.090
- Gill, T. M., Gahbauer, E. A., Allore, H. G., & Han, L. (2006). Transitions between frailty states among community-living older persons. *Arch Intern Med*, 166(4), 418-423. doi:10.1001/archinte.166.4.418
- Herr, M., Robine, J. M., Aegerter, P., Arvieu, J. J., & Ankri, J. (2015). Contribution of socioeconomic position over life to frailty differences in old age: comparison of life-course models in a French sample of 2350 old people. *Ann Epidemiol*, 25(9), 674-680.e671. doi:10.1016/j.annepidem.2015.05.006
- Hoogendijk, E. O., van Hout, H. P., Heymans, M. W., van der Horst, H. E., Frijters, D. H., Broese van Groenou, M. I., . . . Huisman, M. (2014). Explaining the association between educational level and frailty in older adults: results from a 13-year longitudinal study in the Netherlands. *Ann Epidemiol*, 24(7), 538-544.e532. doi:10.1016/j.annepidem.2014.05.002
- Klevmarken, A., Swensson, B., Hesselius, P. (2005). The SHARE sampling procedures and calibrated design weights. In A. Börsch-Supan, Jürges, H. (Ed.), *The Survey of Health, Aging and Retirement in Europe: Methodology* (pp. 28-69). Mannheim, Germany: Mannheim Research Institute for the Economics of Aging.
- Kuh, D., & Ben-Shlomo, Y. (2004). *A life course approach to chronic disease epidemiology*. Oxford: Oxford University Press.
- Kuznetsova, A., Brockhoff, P.B., Christensen, R.H.B. (2016). lmerTest: Tests in Linear Mixed Effects Models. R package version 2.0-33. Retrieved from <https://CRAN.R-project.org/package=lmerTest>
- Lacey, R. J., Belcher, J., & Croft, P. R. (2012). Validity of two simple measures for estimating life-course socio-economic position in cross-sectional postal survey data in an older population: results from the North Staffordshire Osteoarthritis Project (NorStOP). *BMC Med Res Methodol*, 12, 88. doi:10.1186/1471-2288-12-88
- Lazar, M., & Davenport, L. (2018). Barriers to Health Care Access for Low Income Families: A Review of Literature. *J Community Health Nurs*, 35(1), 28-37. doi:10.1080/07370016.2018.1404832
- Luo, Y., & Waite, L. J. (2005). The impact of childhood and adult SES on physical, mental, and cognitive well-being in later life. *J Gerontol B Psychol Sci Soc Sci*, 60(2), S93-s101.
- Macklai, N. S., Spagnoli, J., Junod, J., & Santos-Eggimann, B. (2013). Prospective association of the SHARE-operationalized frailty phenotype with adverse

- health outcomes: evidence from 60+ community-dwelling Europeans living in 11 countries. *BMC Geriatr*, 13, 3. doi:10.1186/1471-2318-13-3
- Marsh, A., Gordon, D., Pantazis, C., Heslop, P. (1999). *Home Sweet Home? The impact of poor housing on health*. Bristol: The Policy Press, University of Bristol.
- Marshall, A., Nazroo, J., Tampubolon, G., & Vanhoutte, B. (2015). Cohort differences in the levels and trajectories of frailty among older people in England. *J Epidemiol Community Health*. doi:10.1136/jech-2014-204655
- Poli, S., Cella, A., Puntoni, M., Musacchio, C., Pomata, M., Torriglia, D., . . . Pilotto, A. (2016). Frailty is associated with socioeconomic and lifestyle factors in community-dwelling older subjects. *Aging Clin Exp Res*. doi:10.1007/s40520-016-0623-5
- R Core Team. (2017). R: A language and environment for statistical computing. Retrieved from <https://www.R-project.org/>
- Romero-Ortuno, R. (2013). The SHARE operationalized frailty phenotype: a comparison of two approaches. *Eur Geriatr Med*, 4(4). doi:10.1016/j.eurger.2013.04.003
- Santos-Eggimann, B., Cuenoud, P., Spagnoli, J., & Junod, J. (2009). Prevalence of frailty in middle-aged and older community-dwelling Europeans living in 10 countries. *J Gerontol A Biol Sci Med Sci*, 64(6), 675-681. doi:10.1093/gerona/glp012
- Schröder, M. (2011). *Retrospective Data Collection in the Survey of Health, Ageing and Retirement in Europe. SHARELIFE Methodology*. Mannheim: Mannheim Research Institute for the Economics of Ageing.
- Sharpe, R. A., Taylor, T., Fleming, L. E., Morrissey, K., Morris, G., & Wigglesworth, R. (2018). Making the Case for "Whole System" Approaches: Integrating Public Health and Housing. *Int J Environ Res Public Health*, 15(11). doi:10.3390/ijerph15112345
- Soler-Vila, H., Garcia-Esquinas, E., Leon-Munoz, L. M., Lopez-Garcia, E., Banegas, J. R., & Rodriguez-Artalejo, F. (2016). Contribution of health behaviours and clinical factors to socioeconomic differences in frailty among older adults. *J Epidemiol Community Health*, 70(4), 354-360. doi:10.1136/jech-2015-206406
- Stolz, E., Mayerl, H., Waxenegger, A., Rasky, E., & Freidl, W. (2017). Impact of socioeconomic position on frailty trajectories in 10 European countries: evidence from the Survey of Health, Ageing and Retirement in Europe (2004-2013). *J Epidemiol Community Health*, 71(1), 73-80. doi:10.1136/jech-2016-207712
- Strachan, D. P., Sheikh, A. (2004). A life course approach to respiratory and allergic diseases. In D. Kuh, Ben Shlomo, Y. (Ed.), *A life course approach to chronic disease epidemiology* (pp. 240-259). Oxford: Oxford University Press.

- Stringhini, S., Polidoro, S., Sacerdote, C., Kelly, R. S., van Veldhoven, K., Agnoli, C., . . . Vineis, P. (2015). Life-course socioeconomic status and DNA methylation of genes regulating inflammation. *Int J Epidemiol*, 44(4), 1320-1330. doi:10.1093/ije/dyv060
- Vineis, P., Kelly-Irving, M., Rappaport, S., & Stringhini, S. (2016). The biological embedding of social differences in ageing trajectories. *J Epidemiol Community Health*, 70(2), 111-113. doi:10.1136/jech-2015-206089
- Wahrendorf, M., & Blane, D. (2015). Does labour market disadvantage help to explain why childhood circumstances are related to quality of life at older ages? Results from SHARE. *Aging Ment Health*, 19(7), 584-594. doi:10.1080/13607863.2014.938604
- Wahrendorf, M., Blane, D., Bartley, M., Dragano, N., & Siegrist, J. (2013). Working conditions in mid-life and mental health in older ages. *Adv Life Course Res*, 18(1), 16-25. doi:10.1016/j.alcr.2012.10.004
- Woo, J., Zheng, Z., Leung, J., & Chan, P. (2015). Prevalence of frailty and contributory factors in three Chinese populations with different socioeconomic and healthcare characteristics. *BMC Geriatr*, 15, 163. doi:10.1186/s12877-015-0160-7

Table 1. Participant characteristics

	Women n(%)	Men n(%)
Non-frail	5168 (45%)	5289 (55%)
Pre-frail	5169 (45%)	3723 (39%)
Frail	1267 (11%)	569 (6%)
Age, years (SD)	63.4 (9.5)	63.4 (9.0)
Birth cohort		
No war, no economic crisis	5996 (52%)	4680 (49%)
War	2886 (25%)	2461 (26%)
Economic crisis	2722 (23%)	2440 (25%)
Living with biological parents		
Both parents	10459 (90%)	8681 (91%)
One biological parent	902 (8%)	729 (8%)
Without biological parent	243 (2%)	171 (2%)
Attrition		
No drop out	8402 (72%)	6609 (69%)
Drop out	2299 (20%)	1926 (20%)
Death	903 (9%)	1046 (11%)
Level of education, in years (SD)	10.3 (4.1)	11.2 (4.4)
Main occupation low skill (vs high)	9681 (83%)	6566 (69%)
Satisfaction with income (SD)	2.8 (0.9)	2.9 (0.9)
Delayed recall memory (SD)	0.4 (1.8)	0.4 (1.9)
Verbal fluency (SD)	2.1 (6.6)	2.1 (6.8)
Ever smoked (SD)	0.3 (0.5)	0.6 (0.5)
Number chronic conditions (SD)	1.7 (1.3)	1.5 (1.2)
Partnership status, living with partner (vs without)	7760 (67%)	8001 (84%)
Difficulties ADL (SD)	-0.0 (0.6)	-0.0 (0.5)
Difficulties IADL (SD)	-0.0 (0.8)	-0.1 (0.7)

Note. ADL, activities of daily living; IADL, instrumental activities of daily living; SD, standard deviation; vs, versus. N women = 11604, N men = 9581. Satisfaction with income ranges between 1 (great difficulty) and 4 (easily).

Table 2. Associations between childhood socioeconomic conditions and (pre-)frailty^a at older age, women

	Model 1 OR (95% CI)	Model 2 OR (95% CI)	Model 3 OR (95% CI)
Age	3.52 (2.72, 4.55)***	3.49 (2.35, 5.19)***	3.69 (2.07, 6.60)***
Age squared	1.45 (1.25, 1.68)***	1.34 (1.05, 1.69)*	1.57 (1.10, 2.23)*
Birth cohort, war ^b	0.97 (0.87, 1.08)	0.95 (0.85, 1.05)	0.99 (0.87, 1.10)
Birth cohort, economic crisis ^b	1.02 (0.91, 1.17)	0.99 (0.87, 1.11)	0.93 (0.79, 1.10)
Living with one parent ^c	1.09 (0.87, 1.08)	1.01 (0.88, 1.18)	1.02 (0.85, 1.23)
Living without parents ^c	1.23 (0.94, 1.63)	1.18 (0.90, 1.56)	1.17 (0.84, 1.63)
CSC advantaged ^d	1.04 (0.81, 1.34)	0.92 (0.74, 1.18)	0.98 (0.72, 1.34)
CSC middle ^d	1.17 (0.93, 1.63)	0.94 (0.74, 1.20)	1.09 (0.80, 1.48)
CSC disadvantaged ^d	1.33 (1.04, 1.70)*	0.96 (0.74, 1.23)	0.92 (0.67, 1.26)
CSC most disadvantaged ^d	1.73 (1.34, 2.24)***	1.12 (0.85, 1.47)	1.06 (0.75, 1.50)
Age x CSC advantaged ^d	0.90 (0.67, 1.21)	0.91 (0.68, 1.22)	1.02 (0.66, 1.58)
Age x CSC middle ^d	1.04 (0.78, 1.38)	1.08 (0.81, 1.44)	1.05 (0.68, 1.60)
Age x CSC disadvantaged ^d	1.02 (0.77, 1.35)	1.02 (0.76, 1.38)	0.98 (0.63, 1.51)
Age x CSC most disadvantaged ^d	0.87 (0.65, 1.16)	0.89 (0.65, 1.21)	1.01 (0.64, 1.60)
Level of education in years		0.96 (0.95, 0.98)***	0.97 (0.95, 0.99)*
Age x education		1.00 (0.98, 1.02)	1.00 (0.97, 1.03)
Main occupation, low ^e		1.20 (1.02, 1.40)*	1.13 (0.92, 1.39)
Age x low occupation ^e		0.98 (0.81, 1.18)	0.75 (0.56, 1.00)
Satisfaction with income		1.37 (1.30, 1.44)***	1.30 (1.22, 1.39)***
Age x satisfaction with income		1.05 (0.99, 1.12)	1.01 (0.92, 1.10)
Partnership, without partner ^f			1.12 (1.00, 1.25)*
Delayed recall			0.99 (0.96, 1.02)
Fluency			1.00 (0.99, 1.01)
Ever smoked ^g			1.14 (1.03, 1.26)*
Number of chronic conditions			1.01 (0.98, 1.05)
Difficulties ADL			0.90 (0.82, 1.00)
Difficulties IADL			1.09 (1.01, 1.18)*

Note. ADL, activities of daily living; CI, confidence interval; CSC, childhood socioeconomic conditions; IADL, instrumental activities of daily living; OR, odds ratio; Ref, reference category. Models are adjusted for attrition, country, aged squared x education, age squared x occupation, age squared x satisfaction with income. N = 11604. Satisfaction with income ranges between 1 (great difficulty) and 4 (easily).

^aFrailty, reference category non-frail

^bBirth cohort, reference category no war and no economic crisis

^cLiving with biological parents, reference category both parents

^dChildhood socioeconomic conditions, reference category most advantaged

^eMain occupation, reference category high occupation

^fPartnership status, reference category with partner

^gSmoking, reference category never

* $p < .05$, ** $p < .01$, *** $p < .001$

Table 3. Associations between childhood socioeconomic conditions and (pre-)frailty^a at older age, men

	Model 1 OR (95% CI)	Model 2 OR (95% CI)	Model 3 OR (95% CI)
Age	3.44 (2.36, 5.00)***	2.75 (1.56, 4.84)***	2.70 (1.53, 4.75)***
Age squared	1.41 (1.10, 1.81)**	1.18 (0.81, 1.72)	1.16 (0.80, 1.70)
Birth cohort, war ^b	0.95 (0.81, 1.11)	0.94 (0.80, 1.10)	0.95 (0.81, 1.11)
Birth cohort, economic crisis ^b	0.90 (0.75, 1.08)	0.87 (0.73, 1.05)	0.88 (0.74, 1.06)
Living with one parent ^c	0.88 (0.71, 1.10)	0.90 (0.72, 1.12)	0.89 (0.71, 1.11)
Living without parents ^c	1.25 (0.81, 1.94)	1.25 (0.81, 1.93)	1.21 (0.78, 1.87)
CSC advantaged ^d	1.27 (0.88, 1.84)	1.10 (0.76, 1.60)	1.09 (0.75, 1.57)
CSC middle ^d	1.44 (1.02, 2.04)*	1.11 (0.78, 1.59)	1.12 (0.78, 1.59)
CSC disadvantaged ^d	1.61 (1.13, 2.31)**	1.11 (0.76, 1.61)	1.11 (0.77, 1.62)
CSC most disadvantaged ^d	1.84 (1.27, 2.66)**	1.16 (0.78, 1.71)	1.18 (0.80, 1.75)
Age x CSC advantaged ^d	0.85 (0.55, 1.32)	0.82 (0.52, 1.28)	0.83 (0.53, 1.29)
Age x CSC middle ^d	0.95 (0.63, 1.44)	0.93 (0.61, 1.43)	0.95 (0.63, 1.45)
Age x CSC disadvantaged ^d	0.90 (0.60, 1.37)	0.87 (0.56, 1.35)	0.88 (0.57, 1.38)
Age x CSC most disadvantaged ^d	0.97 (0.64, 1.48)	0.93 (0.58, 1.49)	0.94 (0.59, 1.50)
Level of education in years		0.98 (0.96, 1.00)*	0.98 (0.96, 1.00)*
Age x education		1.02 (0.99, 1.04)	1.02 (0.99, 1.04)
Main occupation, low ^e		1.32 (1.10, 1.59)**	1.29 (1.07, 1.55)**
Age x low occupation ^e		1.17 (0.93, 1.48)	1.17 (0.93, 1.48)
Satisfaction with income		1.37 (1.27, 1.48)***	1.36 (1.26, 1.47)***
Age x satisfaction with income		1.02 (0.93, 1.12)	1.02 (0.93, 1.13)
Partnership, without partner ^f			1.36 (1.19, 1.63)***
Delayed recall			0.99 (0.96, 1.03)
Fluency			1.00 (0.99, 1.01)
Ever smoked ^g			1.12 (1.00, 1.27)
Number of chronic conditions			0.98 (0.94, 1.02)
Difficulties ADL			1.04 (0.92, 1.17)
Difficulties IADL			1.02 (0.93, 1.12)

Note. ADL, activities of daily living; CI, confidence interval; CSC; childhood socioeconomic conditions; IADL, instrumental activities of daily living; OR, odds ratio; Ref, reference category. Models are adjusted for attrition, country, aged squared x education, age squared x occupation, age squared x satisfaction with income. N = 9581. Satisfaction with income ranges between 1 (great difficulty) and 4 (easily).

^aFrailty, reference category non-frail

^bBirth cohort, reference category no war and no economic crisis

^cLiving with biological parents, reference category both parents

^dChildhood socioeconomic conditions, reference category most advantaged

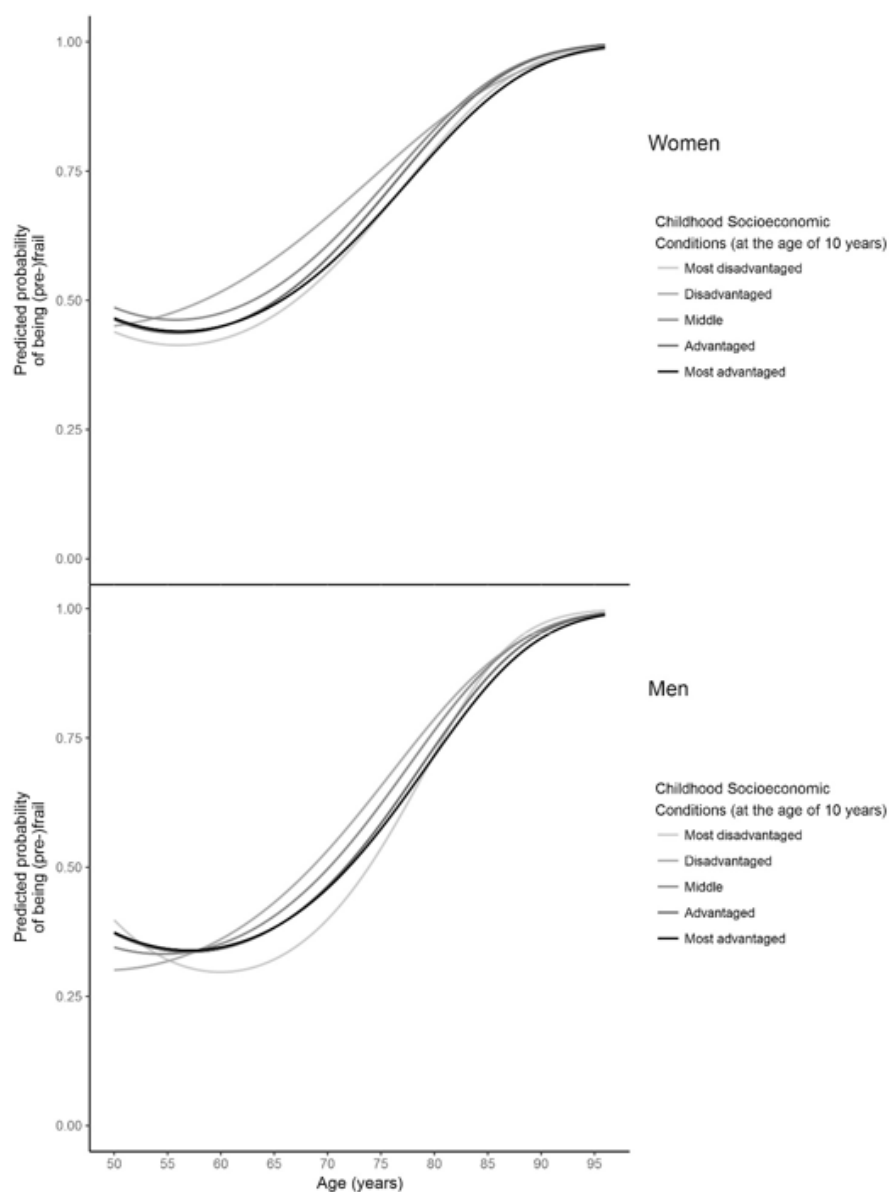
^eMain occupation, reference category high occupation

^fPartnership status, reference category with partner

^gSmoking, reference category never

* $p < .05$, ** $p < .01$, *** $p < .001$

Figure 1 Predicted probability of being (pre-)frail for each childhood socioeconomic condition, adjusted^a



^aAdjusted for age, age squared, attrition, birth cohort, living with biological parents, age*CSC, age squared*CSC (see Table 2 and Table 3, Model 1)

Supplementary Material

Supplementary Figure 1: Flow chart of respondent inclusion

Supplementary Table 1. Participant characteristics, women, stratified by childhood socioeconomic circumstances

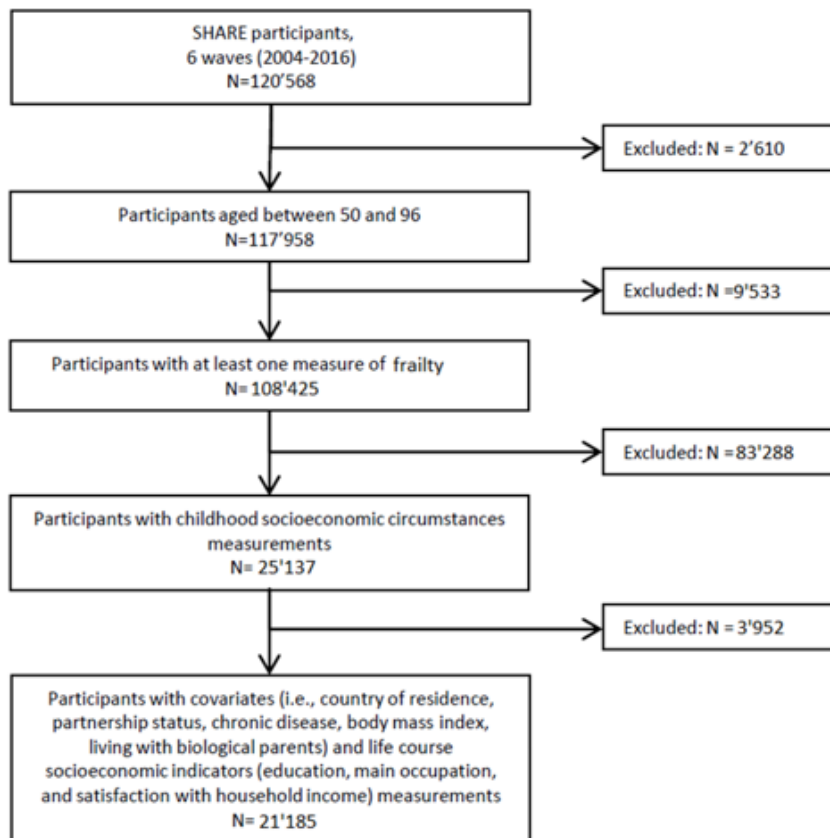
Supplementary Table 2. Participant characteristics, men, stratified by childhood socioeconomic circumstances

Supplementary Table 3. Associations between childhood socioeconomic conditions and (pre-)frailty at older age, women

Supplementary Table 4. Associations between childhood socioeconomic conditions and (pre-)frailty at older age, men

Supplementary Table 5. Sensitivity analysis, non-frail versus pre-frail, women

Supplementary Table 6. Sensitivity analysis, non-frail versus pre-frail, men

Supplementary Figure 1: Flow chart of respondent inclusion

Supplementary Table 1. Participant characteristics, women, stratified by childhood socioeconomic circumstances

	All	Most advantaged	Advantaged	Middle	Disadvantaged	Most disadvantaged
	n(%)	625 (5%)	2092 (18%)	3764 (32%)	2962 (26%)	2161 (19%)
Non-frail	5168 (45%)	338 (54%)	1095 (52%)	1820 (48%)	1228 (41%)	687 (32%)
Pre-frail	5169 (45%)	259 (41%)	883 (42%)	1632 (43%)	1356 (46%)	1039 (48%)
Frail	1267 (11%)	28 (4%)	114 (5%)	312 (8%)	378 (13%)	435 (20%)
Age, years (SD)	63.4 (9.5)	61.9 (9.2)	61.5 (9.0)	62.0 (8.9)	64.3 (9.4)	67.0 (9.2)
Birth cohort						
No war, no economic crisis	5996 (52%)	355 (57%)	1208 (58%)	2081 (55%)	1432 (48%)	920 (43%)
War	2886 (25%)	158 (25%)	513 (25%)	944 (25%)	762 (26%)	509 (24%)
Economic crisis	2722 (23%)	112 (18%)	371 (18%)	739 (20%)	768 (26%)	732 (34%)
Living with biological parents						
Both parents	10459 (90%)	566 (91%)	1889 (90%)	3420 (91%)	2640 (89%)	1944 (90%)
One biological parent	902 (8%)	41 (7%)	157 (8%)	270 (7%)	253 (9%)	181 (8%)
Without biological parent	243 (2%)	18 (3%)	46 (2%)	74 (2%)	69 (2%)	36 (2%)
Attrition						
No drop out	8402 (72%)	470 (75%)	1586 (76%)	2714 (72%)	2097 (71%)	1535 (71%)
Drop out	2299 (20%)	112 (18%)	412 (20%)	809 (20%)	606 (20%)	360 (16%)
Death	903 (8%)	43 (7%)	94 (4%)	241 (6%)	259 (9%)	266 (12%)
Level of education, in years (SD)	10.3 (4.1)	14.3 (3.4)	12.4 (3.6)	11.1 (3.6)	8.9 (3.6)	7.1 (3.5)
Main occupation						
Low skill	9681 (83%)	311 (50%)	1458 (70%)	3094 (82%)	2731 (92%)	2087 (97%)
High skill	1923 (17%)	314 (50%)	634 (30%)	670 (18%)	231 (8%)	74 (3%)
Satisfaction with income (SD)	2.8 (0.9)	3.3 (0.7)	3.1 (0.8)	2.9 (0.8)	2.6 (0.9)	2.3 (0.8)
Delayed recall memory (SD)	0.4 (1.8)	0.4 (1.9)	0.3 (1.9)	0.3 (1.9)	0.5 (1.9)	0.5 (1.8)
Verbal fluency (SD)	2.1 (6.6)	1.8 (6.9)	2.1 (7.0)	1.8 (6.9)	2.3 (7.2)	2.5 (6.7)
Ever smoked (SD)	0.3 (0.5)	0.5 (0.5)	0.4 (0.5)	0.4 (0.5)	0.3 (0.5)	0.2 (0.4)
Number chronic conditions (SD)	1.7 (1.3)	1.4 (1.2)	1.5 (1.3)	1.6 (1.3)	1.8 (1.4)	2.2 (1.5)

	All	Most advantaged	Advantaged	Middle	Disadvantaged	Most disadvantaged
	n(%)	625 (5%)	2092 (18%)	3764 (32%)	2962 (26%)	2161 (19%)
Partnership status						
Living with partner	7760 (67%)	415 (66%)	1430 (68%)	2552 (68%)	1970 (67%)	1393 (64%)
Without partner	3844 (33%)	210 (34%)	662 (32%)	1212 (32%)	992 (33%)	768 (36%)
Difficulties ADL (SD)	-0.0 (0.6)	0.0 (0.8)	-0.1 (0.5)	-0.0 (0.7)	-0.0 (0.7)	-0.0 (0.7)
Difficulties IADL (SD)	-0.0 (0.8)	-0.0 (1.0)	-0.0 (0.9)	-0.0 (0.8)	-0.1 (0.9)	-0.1 (0.8)
Countries						
Austria	358 (3%)	10 (2%)	60 (3%)	120 (3%)	107 (4%)	61 (3%)
Belgium	1220 (11%)	106 (17%)	298 (14%)	333 (9%)	300 (10%)	183 (8%)
Czech Republic	861 (7%)	15 (2%)	151 (7%)	475 (13%)	172 (6%)	48 (2%)
Denmark	916 (8%)	92 (15%)	285 (14%)	330 (9%)	157 (5%)	52 (2%)
France	996 (9%)	86 (14%)	178 (9%)	334 (9%)	261 (9%)	137 (6%)
Germany	804 (7%)	39 (6%)	178 (9%)	344 (9%)	172 (6%)	71 (3%)
Greece	1194 (10%)	12 (2%)	86 (4%)	310 (8%)	440 (15%)	346 (16%)
Italy	1100 (9%)	18 (3%)	82 (4%)	215 (6%)	374 (13%)	411 (19%)
The Netherlands	871 (8%)	73 (12%)	235 (11%)	361 (10%)	181 (6%)	21 (1%)
Poland	835 (7%)	2 (0%)	35 (2%)	123 (3%)	232 (8%)	443 (21%)
Spain	774 (7%)	14 (2%)	75 (4%)	170 (5%)	245 (8%)	270 (12%)
Sweden	819 (7%)	77 (12%)	223 (11%)	337 (9%)	128 (4%)	54 (3%)
Switzerland	604 (5%)	62 (10%)	163 (8%)	235 (6%)	114 (4%)	30 (1%)

Note. ADL, activities of daily living; IADL, instrumental activities of daily living; SD, standard deviation. N = 11604. Satisfaction with income ranges between 1 (great difficulty) and 4 (easily).

Supplementary Table 2. Participant characteristics, men, stratified by childhood socioeconomic circumstances

	All	Most advantaged	Advantaged	Middle	Disadvantaged	Most disadvantaged
Non-frail	5289 (55%)	339 (61%)	1796 (19%)	3003 (31%)	2367 (25%)	1857 (19%)
Pre-frail	3723 (39%)	201 (36%)	1090 (61%)	1787 (60%)	1278 (54%)	795 (43%)
Frail	569 (6%)	18 (3%)	655 (36%)	1081 (36%)	930 (39%)	856 (46%)
Age, years (SD)	63.4 (9.0)	62.5 (9.0)	61.4 (8.4)	62.1 (8.6)	64.0 (8.8)	66.9 (8.9)
Birth cohort						
No war, no economic crisis	4680 (49%)	291 (52%)	1015 (57%)	1582 (53%)	1087 (46%)	705 (38%)
War	2461 (26%)	154 (28%)	452 (25%)	755 (25%)	630 (27%)	470 (25%)
Economic crisis	2440 (25%)	113 (20%)	329 (18%)	666 (22%)	650 (27%)	682 (37%)
Living with biological parents						
Both parents	8681 (91%)	504 (90%)	1616 (90%)	2712 (90%)	2156 (91%)	1693 (91%)
One biological parent	729 (8%)	41 (7%)	141 (8%)	237 (8%)	171 (7%)	139 (7%)
Without biological parent	171 (2%)	13 (2%)	39 (2%)	54 (2%)	40 (2%)	25 (1%)
Attrition						
No drop out	6609 (69%)	384 (69%)	1278 (71%)	2108 (73%)	1603 (68%)	1236 (67%)
Drop out	1926 (20%)	119 (21%)	373 (21%)	640 (21%)	487 (21%)	307 (17%)
Death	1046 (11%)	55 (10%)	145 (8%)	255 (8%)	277 (12%)	314 (17%)
Level of education, in years (SD)	11.2 (4.4)	15.3 (3.6)	13.4 (3.9)	12.0 (4.0)	9.9 (3.9)	8.1 (3.8)
Main occupation						
Low skill	6566 (69%)	168 (30%)	881 (49%)	1947 (65%)	1905 (80%)	1665 (90%)
High skill	3111 (31%)	390 (70%)	915 (51%)	1056 (35%)	462 (20%)	192 (10%)
Satisfaction with income (SD)	2.9 (0.9)	3.4 (0.7)	3.2 (0.7)	3.0 (0.8)	2.7 (0.9)	2.4 (0.9)
Delayed recall memory (SD)	0.4 (1.9)	0.2 (1.9)	0.4 (1.9)	0.4 (1.9)	0.4 (1.9)	0.5 (1.9)
Verbal fluency (SD)	2.1 (6.8)	2.1 (7.2)	2.1 (6.9)	1.9 (6.8)	2.3 (7.0)	2.3 (6.7)
Ever smoked (SD)	0.6 (0.5)	0.6 (0.5)	0.6 (0.5)	0.6 (0.5)	0.6 (0.5)	0.6 (0.5)
Number chronic conditions (SD)	1.5 (1.2)	1.4 (1.2)	1.3 (1.1)	1.4 (1.2)	1.6 (1.2)	1.7 (1.3)

	All	Most advantaged	Advantaged	Middle	Disadvantaged	Most disadvantaged
Partnership status		558 (6%)	1796 (19%)	3003 (31%)	2367 (25%)	1857 (19%)
Living with partner	8001 (84%)	464 (83%)	1493 (83%)	2504 (83%)	1968 (83%)	1572 (85%)
Without partner	1580 (16%)	94 (17%)	303 (17%)	499 (17%)	399 (17%)	285 (15%)
Difficulties ADL (SD)	-0.0 (0.5)	0.0 (0.7)	-0.0 (0.7)	-0.0 (0.7)	-0.1 (0.6)	-0.1 (0.6)
Difficulties IADL (SD)	-0.1 (0.7)	-0.0 (0.9)	-0.0 (0.9)	-0.1 (0.9)	-0.1 (0.9)	-0.1 (0.8)
Countries						
Austria	275 (3%)	10 (2%)	46 (3%)	90 (3%)	70 (3%)	59 (3%)
Belgium	1036 (11%)	84 (15%)	246 (14%)	314 (10%)	243 (10%)	149 (8%)
Czech Republic	640 (7%)	16 (3%)	106 (6%)	343 (11%)	125 (5%)	50 (3%)
Denmark	806 (8%)	82 (15%)	246 (14%)	315 (10%)	118 (5%)	45 (2%)
France	785 (8%)	70 (13%)	171 (10%)	227 (8%)	210 (9%)	107 (6%)
Germany	705 (7%)	50 (9%)	185 (10%)	269 (9%)	150 (6%)	51 (3%)
Greece	1029 (11%)	11 (2%)	75 (4%)	255 (8%)	350 (15%)	338 (18%)
Italy	961 (10%)	16 (3%)	69 (4%)	167 (6%)	339 (14%)	370 (20%)
The Netherlands	740 (8%)	64 (11%)	200 (11%)	285 (9%)	168 (7%)	23 (1%)
Poland	651 (7%)	4 (1%)	31 (2%)	87 (3%)	165 (7%)	364 (20%)
Spain	615 (6%)	14 (3%)	58 (3%)	151 (5%)	200 (8%)	192 (10%)
Sweden	663 (7%)	75 (13%)	185 (10%)	257 (9%)	95 (4%)	51 (3%)
Switzerland	471 (5%)	47 (8%)	140 (8%)	185 (6%)	86 (4%)	13 (1%)

Note. ADL, activities of daily living; IADL, instrumental activities of daily living; SD, standard deviation. N = 9581.

Satisfaction with income ranges between 1 (great difficulty) and 4 (easily).

Supplementary Table 3. Associations between childhood socioeconomic conditions and (pre-)frailty^a at older age in women

	Model 1 OR (95% CI)	Model 2 OR (95% CI)	Model 3 OR (95% CI)
Age	3.52 (2.72, 4.55)***	3.49 (2.35, 5.19)***	3.69 (2.07, 6.60)***
Age squared	1.45 (1.25, 1.68)***	1.34 (1.05, 1.69)*	1.57 (1.10, 2.23)*
Birth cohort, war ^b	0.97 (0.87, 1.08)	0.95 (0.85, 1.05)	0.99 (0.87, 1.10)
Birth cohort, economic crisis ^b	1.02 (0.91, 1.17)	0.99 (0.87, 1.11)	0.93 (0.79, 1.10)
Living with one parent ^c	1.09 (0.87, 1.08)	1.01 (0.88, 1.18)	1.02 (0.85, 1.23)
Living without parents ^c	1.23 (0.94, 1.63)	1.18 (0.90, 1.56)	1.17 (0.84, 1.63)
CSC advantaged ^d	1.04 (0.81, 1.34)	0.92 (0.74, 1.18)	0.98 (0.72, 1.34)
CSC middle ^d	1.17 (0.93, 1.63)	0.94 (0.74, 1.20)	1.09 (0.80, 1.48)
CSC disadvantaged ^d	1.33 (1.04, 1.70)*	0.96 (0.74, 1.23)	0.92 (0.67, 1.26)
CSC most disadvantaged ^d	1.73 (1.34, 2.24)***	1.12 (0.85, 1.47)	1.06 (0.75, 1.50)
Age x CSC advantaged ^d	0.90 (0.67, 1.21)	0.91 (0.68, 1.22)	1.02 (0.66, 1.58)
Age x CSC middle ^d	1.04 (0.78, 1.38)	1.08 (0.81, 1.44)	1.05 (0.68, 1.60)
Age x CSC disadvantaged ^d	1.02 (0.77, 1.35)	1.02 (0.76, 1.38)	0.98 (0.63, 1.51)
Age x CSC most disadvantaged ^d	0.87 (0.65, 1.16)	0.89 (0.65, 1.21)	1.01 (0.64, 1.60)
Age squared x CSC advantaged ^d	0.97 (0.82, 1.15)	0.99 (0.83, 1.17)	0.95 (0.74, 1.23)
Age squared x CSC middle ^d	1.01 (0.86, 1.19)	1.05 (0.89, 1.24)	0.94 (0.73, 1.20)
Age squared x CSC disadvantaged ^d	1.00 (0.85, 1.18)	1.03 (0.86, 1.23)	0.93 (0.72, 1.21)
Age squared x CSC most disadvantaged ^d	0.86 (0.72, 1.02)	0.91 (0.75, 1.10)	0.89 (0.67, 1.19)
Level of education in years		0.96 (0.95, 0.98)***	0.97 (0.95, 0.99)*
Age x education		1.00 (0.98, 1.02)	1.00 (0.97, 1.03)
Main occupation, low ^e		1.20 (1.02, 1.40)*	1.13 (0.92, 1.39)
Age x low occupation ^e		0.98 (0.81, 1.18)	0.75 (0.56, 1.00)
Satisfaction with income		1.37 (1.30, 1.44)***	1.30 (1.22, 1.39)***
Age x satisfaction with income		1.05 (0.99, 1.12)	1.01 (0.92, 1.10)
Partnership, without partner ^f			1.12 (1.00, 1.25)*
Delayed recall			0.99 (0.96, 1.02)
Fluency			1.00 (0.99, 1.01)
Ever smoked ^g			1.14 (1.03, 1.26)*
Number of chronic conditions			1.01 (0.98, 1.05)

	Model 1 OR (95% CI)	Model 2 OR (95% CI)	Model 3 OR (95% CI)
Difficulties ADL			0.90 (0.82, 1.00)
Difficulties IADL			1.09 (1.01, 1.18)*
Austria ^b	0.50 (0.39, 0.64)***	0.48 (0.68, 0.61)***	0.50 (0.37, 0.66)***
Czech Republic ^b	0.86 (0.71, 1.04)	0.69 (0.57, 0.83)***	0.64 (0.51, 0.79)***
Denmark ^b	0.59 (0.49, 0.70)***	0.70 (0.58, 0.83)***	0.70 (0.57, 0.86)**
France ^b	1.38 (1.16, 1.65)***	1.30 (1.10, 1.55)**	1.29 (1.05, 1.58)**
Germany ^b	0.55 (0.46, 0.67)***	0.58 (0.48, 0.70)***	0.60 (0.48, 0.76)***
Greece ^b	0.95 (0.80, 1.14)	0.66 (0.55, 0.79)***	0.80 (0.64, 1.01)
Italy ^b	1.88 (1.58, 2.24)***	1.39 (1.17, 1.67)***	1.45 (1.18, 1.78)***
The Netherlands ^b	0.64 (0.53, 0.77)***	0.66 (0.55, 0.79)***	0.63 (0.50, 0.80)***
Poland ^b	2.28 (1.85, 2.81)***	1.72 (1.39, 2.12)***	1.68 (1.29, 2.19)***
Spain ^b	2.69 (2.20, 3.29)***	2.06 (1.68, 2.52)***	2.14 (1.69, 2.72)***
Sweden ^b	0.66 (0.55, 0.79)***	0.74 (0.62, 0.89)**	0.83 (0.67, 1.03)
Switzerland ^b	0.65 (0.53, 0.79)***	0.67 (0.55, 0.82)***	0.68 (0.54, 0.84)**

Note. ADL, activities of daily living; CI, confidence interval; CSC; childhood socioeconomic conditions; IADL, instrumental activities of daily living; OR, odds ratio; Ref, reference category. Models are adjusted for attrition, aged squared x education, age squared x occupation, age squared x satisfaction with income. N = 11604. Satisfaction with income ranges between 1 (great difficulty) and 4 (easily).

^aFrailty, reference category non-frail

^bBirth cohort, reference category no war and no economic crisis

^cLiving with biological parents, reference category both parents

^dChildhood socioeconomic conditions, reference category most advantaged

^eMain occupation, reference category high occupation

^fPartnership status, reference category with partner

^gSmoking, reference category never

^hCountries, reference: Belgium

*p<0.05, **p<0.01, ***p<.001

Supplementary Table 4. Associations between childhood socioeconomic conditions and (pre-)frailty^a at older age in men

	Model 1 OR (95% CI)	Model 2 OR (95% CI)	Model 3 OR (95% CI)
Age	3.44 (2.36, 5.00)***	2.75 (1.56, 4.84)***	2.70 (1.53, 4.75)**
Age squared	1.41 (1.10, 1.81)**	1.18 (0.81, 1.72)	1.16 (0.80, 1.70)
Birth cohort, war ^b	0.95 (0.81, 1.11)	0.94 (0.80, 1.10)	0.95 (0.81, 1.11)
Birth cohort, economic crisis ^b	0.90 (0.75, 1.08)	0.87 (0.73, 1.05)	0.88 (0.74, 1.06)
Living with one parent ^c	0.88 (0.71, 1.10)	0.90 (0.72, 1.12)	0.89 (0.71, 1.11)
Living without parents ^c	1.25 (0.81, 1.94)	1.25 (0.81, 1.93)	1.21 (0.78, 1.87)
CSC advantaged ^d	1.27 (0.88, 1.84)	1.10 (0.76, 1.60)	1.09 (0.75, 1.57)
CSC middle ^d	1.44 (1.02, 2.04)*	1.11 (0.78, 1.59)	1.12 (0.78, 1.59)
CSC disadvantaged ^d	1.61 (1.13, 2.31)**	1.11 (0.76, 1.61)	1.11 (0.77, 1.62)
CSC most disadvantaged ^d	1.84 (1.27, 2.66)**	1.16 (0.78, 1.71)	1.18 (0.80, 1.75)
Age x CSC advantaged ^d	0.85 (0.55, 1.32)	0.82 (0.52, 1.28)	0.83 (0.53, 1.29)
Age x CSC middle ^d	0.95 (0.63, 1.44)	0.93 (0.61, 1.43)	0.95 (0.63, 1.45)
Age x CSC disadvantaged ^d	0.90 (0.60, 1.37)	0.87 (0.56, 1.35)	0.88 (0.57, 1.38)
Age x CSC most disadvantaged ^d	0.97 (0.64, 1.48)	0.93 (0.58, 1.49)	0.94 (0.59, 1.50)
Age squared x CSC advantaged ^d	0.96 (0.72, 1.28)	0.98 (0.73, 1.31)	0.98 (0.74, 1.31)
Age squared x CSC middle ^d	0.99 (0.76, 1.30)	1.05 (0.79, 1.39)	1.06 (0.80, 1.40)
Age squared x CSC disadvantaged ^d	0.93 (0.70, 1.22)	0.98 (0.73, 1.32)	0.99 (0.73, 1.33)
Age squared x CSC most disadvantaged ^d	0.87 (0.65, 1.16)	0.93 (0.68, 1.29)	0.93 (0.67, 1.28)
Level of education in years		0.98 (0.96, 1.00)*	0.98 (0.96, 1.00)*
Age x education		1.02 (0.99, 1.04)	1.02 (0.99, 1.04)
Main occupation, low ^e		1.32 (1.10, 1.59)**	1.29 (1.07, 1.55)**
Age x low occupation ^e		1.17 (0.93, 1.48)	1.17 (0.93, 1.48)
Satisfaction with income		1.37 (1.27, 1.48)***	1.36 (1.26, 1.47)***
Age x satisfaction with income		1.02 (0.93, 1.12)	1.02 (0.93, 1.13)
Partnership, without partner ^f			1.36 (1.19, 1.63)***
Delayed recall			0.99 (0.96, 1.03)
Fluency			1.00 (0.99, 1.01)
Ever smoked ^g			1.12 (1.00, 1.27)
Number of chronic conditions			0.98 (0.94, 1.02)

	Model 1 OR (95% CI)	Model 2 OR (95% CI)	Model 3 OR (95% CI)
Difficulties ADL			1.04 (0.92, 1.17)
Difficulties IADL			1.02 (0.93, 1.12)
Austria ^a	0.69 (0.48, 0.98)*	0.63 (0.44, 0.91)*	0.64 (0.45, 0.92)*
Czech Republic ^b	0.95 (0.73, 1.24)	0.74 (0.56, 0.97)*	0.76 (0.58, 0.99)*
Denmark ^b	0.90 (0.71, 1.13)	0.97 (0.77, 1.23)	0.97 (0.77, 1.22)
France ^b	1.29 (1.01, 1.64)*	1.20 (0.94, 1.53)	1.20 (0.94, 1.53)
Germany ^b	0.85 (0.65, 1.11)	0.83 (0.63, 1.08)	0.85 (0.65, 1.11)
Greece ^b	1.53 (1.18, 1.97)**	1.02 (0.78, 1.33)	1.03 (0.79, 1.35)
Italy ^b	1.50 (1.02, 1.88)***	1.06 (0.84, 1.34)	1.10 (0.87, 1.39)
Netherlands ^b	0.67 (0.50, 0.89)**	0.67 (0.50, 0.89)**	0.66 (0.49, 0.87)**
Poland ^b	2.21 (1.63, 3.01)***	1.54 (1.13, 2.10)**	1.56 (1.14, 2.13)**
Spain ^b	2.67 (2.06, 3.46)***	1.96 (1.50, 2.55)***	1.99 (1.52, 2.59)***
Sweden ^b	0.52 (0.40, 0.68)***	0.54 (0.41, 0.71)***	0.56 (0.43, 0.73)***
Switzerland ^b	0.76 (0.58, 0.99)*	0.78 (0.60, 1.03)	0.79 (0.61, 1.04)

Note. ADL, activities of daily living; CI, confidence interval; CSC; childhood socioeconomic conditions; IADL, instrumental activities of daily living; OR, odds ratio; Ref, reference category. Models are adjusted for attrition, aged squared x education, age squared x occupation, age squared x satisfaction with income. N = 9581. Satisfaction with income ranges between 1 (great difficulty) and 4 (easily).

^aFrailty, reference category non-frail

^bBirth cohort, reference category no war and no economic crisis

^cLiving with biological parents, reference category both parents

^dChildhood socioeconomic conditions, reference category most advantaged

^eMain occupation, reference category high occupation

^fPartnership status, reference category with partner

^gSmoking, reference category never

^hCountries, reference: Belgium

*p < 0.05, **p < 0.01, ***p < 0.001

Supplementary Table 5. Sensitivity analysis, non-frail versus pre-frail, women

	Model 1 OR (95% CI)	Model 2 OR (95% CI)	Model 3 OR (95% CI)
Age	3.52 (2.72, 4.55)***	3.49 (2.35, 5.19)***	3.41 (2.29, 5.06)***
Age squared	1.45 (1.25, 1.68)***	1.34 (1.05, 1.69)*	1.33 (1.05, 1.69)*
Birth cohort, war ^a	0.97 (0.87, 1.08)	0.95 (0.85, 1.05)	0.96 (0.87, 1.06)
Birth cohort, economic crisis ^a	1.02 (0.91, 1.15)	0.99 (0.87, 1.11)	0.98 (0.87, 1.10)
Living with one parent ^b	1.09 (0.94, 1.26)	1.01 (0.88, 1.18)	1.01 (0.87, 1.17)
Living without parents ^b	1.23 (0.93, 1.63)	1.18 (0.90, 1.56)	1.17 (0.89, 1.54)
CSC Advantaged ^c	1.04 (0.81, 1.34)	0.92 (0.72, 1.18)	0.93 (0.72, 1.19)
CSC Middle ^c	1.17 (0.93, 1.49)	0.94 (0.74, 1.20)	0.95 (0.75, 1.21)
CSC Disadvantaged ^c	1.33 (1.04, 1.70)*	0.96 (0.74, 1.23)	0.97 (0.75, 1.25)
CSC Most disadvantaged ^c	1.73 (1.34, 2.24)***	1.12 (0.85, 1.47)	1.15 (0.87, 1.51)
Age x CSC advantaged ^c	0.90 (0.67, 1.21)	0.91 (0.68, 1.22)	0.92 (0.68, 1.23)
Age x CSC middle ^c	1.04 (0.78, 1.38)	1.08 (0.81, 1.44)	1.09 (0.82, 1.45)
Age x CSC disadvantaged ^c	1.02 (0.77, 1.35)	1.02 (0.76, 1.38)	1.02 (0.76, 1.38)
Age x CSC most disadvantaged ^c	0.87 (0.65, 1.16)	0.89 (0.65, 1.21)	0.89 (0.65, 1.22)
Age squared x CSC advantaged ^c	0.97 (0.82, 1.15)	0.99 (0.83, 1.17)	0.99 (0.83, 1.18)
Age squared x CSC middle ^c	1.01 (0.86, 1.19)	1.05 (0.89, 1.24)	1.06 (0.89, 1.25)
Age squared x CSC disadvantaged ^c	1.00 (0.85, 1.18)	1.03 (0.86, 1.23)	1.04 (0.87, 1.24)
Age x squared CSC most disadvantaged ^c	0.86 (0.72, 1.02)	0.91 (0.75, 1.10)	0.92 (0.76, 1.11)
Level of education in years		0.96 (0.95, 0.98)***	0.96 (0.95, 0.98)***
Age x education		1.00 (0.98, 1.02)	1.00 (0.98, 1.02)
Main occupation, low ^d		1.20 (1.02, 1.40)*	1.22 (1.04, 1.43)*
Age x low occupation ^d		0.98 (0.81, 1.18)	0.98 (0.81, 1.19)
Satisfaction with income		1.37 (1.30, 1.44)***	1.35 (1.28, 1.42)***
Age x satisfaction with income		1.05 (0.99, 1.12)	1.05 (0.99, 1.12)
Partnership, without partner ^e			1.22 (1.11, 1.33)***
Delayed recall			0.99 (0.97, 1.01)
Fluency			1.00 (0.99, 1.00)
Ever smoked ^f			1.19 (1.09, 1.29)***
Number of chronic conditions			1.02 (1.00, 1.04)

	Model 1 OR (95% CI)	Model 2 OR (95% CI)	Model 3 OR (95% CI)
Difficulties ADL			0.96 (0.90, 1.02)
Difficulties IADL			1.03 (0.98, 1.08)
<i>Note.</i> ADL, activities of daily living; CI, confidence interval; CSC; childhood socioeconomic conditions; IADL, instrumental activities of daily living; OR, odds ratio; Ref, reference category. Models are adjusted for attrition, countries, aged squared x education, age squared x occupation, age squared x satisfaction with income. N = 11604. Satisfaction with income ranges between 1 (great difficulty) and 4 (easily).			
^a Birth cohort, reference category no war and no economic crisis			
^b Living with biological parents, reference category both parents			
^c Childhood socioeconomic conditions, reference category most advantaged			
^d Main occupation, reference category high occupation			
^e Partnership status, reference category with partner			
^f Smoking, reference category never			
*p<.05, **p<.01, ***p<.001			

Supplementary Table 6. Sensitivity analysis, non-frail versus pre-frail, men

	Model 1 OR (95% CI)	Model 2 OR (95% CI)	Model 3 OR (95% CI)
Age	4.35 (3.34, 5.66)***	3.98 (2.69, 5.88)***	4.03 (2.73, 5.96)***
Age squared	1.76 (1.49, 2.07)***	1.74 (1.36, 2.24)***	1.75 (1.36, 2.25)***
Birth cohort, war ^a	0.99 (0.88, 1.11)	1.00 (0.89, 1.12)	1.01 (0.90, 1.13)
Birth cohort, economic crisis ^a	0.93 (0.82, 1.06)	0.93 (0.82, 1.05)	0.94 (0.83, 1.07)
Living with one parent ^b	1.15 (0.98, 1.35)	1.13 (0.96, 1.33)	1.12 (0.95, 1.31)
Living without parents ^b	1.00 (0.72, 1.39)	1.00 (0.72, 1.38)	0.97 (0.70, 1.34)
CSC Advantaged ^c	1.29 (0.99, 1.68)	1.17 (0.90, 1.52)	1.16 (0.90, 1.51)
CSC Middle ^c	1.34 (1.04, 1.72)*	1.10 (0.85, 1.42)	1.10 (0.85, 1.42)
CSC Disadvantaged ^c	1.62 (1.25, 2.09)***	1.17 (0.90, 1.53)	1.17 (0.90, 1.53)
CSC Most disadvantaged ^c	1.96 (1.50, 2.57)***	1.31 (0.99, 1.74)	1.33 (1.00, 1.76)
Age x CSC advantaged ^c	0.77 (0.57, 1.05)	0.75 (0.55, 1.02)	0.76 (0.56, 1.03)
Age x CSC middle ^c	0.83 (0.62, 1.11)	0.82 (0.61, 1.11)	0.83 (0.62, 1.11)
Age x CSC disadvantaged ^c	0.88 (0.65, 1.18)	0.86 (0.63, 1.18)	0.88 (0.64, 1.19)
Age x CSC most disadvantaged ^c	0.88 (0.65, 1.18)	0.88 (0.63, 1.22)	0.88 (0.64, 1.22)
Age squared x CSC advantaged ^c	0.83 (0.69, 1.00)	0.83 (0.68, 1.00)*	0.83 (0.69, 1.00)
Age squared x CSC middle ^c	0.85 (0.71, 1.02)	0.87 (0.72, 1.04)	0.87 (0.73, 1.05)
Age squared x CSC disadvantaged ^c	0.82 (0.68, 0.98)*	0.84 (0.70, 1.03)	0.85 (0.70, 1.04)
Age x squared CSC most disadvantaged ^c	0.75 (0.62, 0.91)**	0.79 (0.64, 0.97)*	0.79 (0.64, 0.97)*
Level of education in years		0.98 (0.97, 1.00)*	0.98 (0.97, 1.00)*
Age x education		1.01 (0.99, 1.02)	1.01 (0.99, 1.02)
Main occupation, low ^d		1.31 (1.15, 1.50)***	1.29 (1.13, 1.48)***
Age x low occupation ^d		1.05 (0.90, 1.23)	1.03 (0.88, 1.20)
Satisfaction with income		1.41 (1.34, 1.49)***	1.41 (1.33, 1.49)***
Age x satisfaction with income		0.99 (0.93, 1.06)	0.99 (0.93, 1.06)
Partnership, without partner ^e		1.29 (1.15, 1.45)***	1.29 (1.15, 1.45)***
Delayed recall			1.00 (0.98, 1.02)
Fluency			1.00 (0.99, 1.00)
Ever smoked ^f			1.17 (1.07, 1.27)**
Number of chronic conditions			0.98 (0.96, 1.01)

	Model 1 OR (95% CI)	Model 2 OR (95% CI)	Model 3 OR (95% CI)
Difficulties ADL			1.03 (0.96, 1.11)
Difficulties IADL			1.00 (0.95, 1.05)
<p><i>Note.</i> ADL, activities of daily living; CI, confidence interval; CSC; childhood socioeconomic conditions; IADL, instrumental activities of daily living; OR, odds ratio; Ref, reference category. Models are adjusted for attrition, countries, aged squared x education, age squared x occupation, age squared x satisfaction with income. N = 9581. Satisfaction with income ranges between 1 (great difficulty) and 4 (easily).</p> <p>^aBirth cohort, reference category no war and no economic crisis</p> <p>^bLiving with biological parents, reference category both parents</p> <p>^cChildhood socioeconomic conditions, reference category most advantaged</p> <p>^dMain occupation, reference category high occupation</p> <p>^ePartnership status, reference category with partner</p> <p>^fSmoking, reference category never</p> <p>*$p < .05$, **$p < .01$, ***$p < .001$</p>			

Chapter 4. Life-course circumstances and frailty in old age within different European welfare regimes: a longitudinal study with SHARE (Article 3)

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Abstract

Objectives This study aimed to assess whether cumulative disadvantage in childhood misfortune and adult-life socioeconomic conditions influence the risk of frailty in old age and whether welfare regimes influence these associations.

Methods Data from 23358 participants aged 50 years and older included in the longitudinal SHARE survey were used. Frailty was operationalized according to Fried's phenotype as presenting either weakness, shrinking, exhaustion, slowness, or low activity. Confounder-adjusted mixed-effects logistic regression models were used to analyse associations of childhood misfortune and life-course socioeconomic conditions with frailty.

Results Childhood misfortune and poor adult-life socioeconomic conditions increased the odds of (pre-)frailty at older age. With aging, differences narrowed between categories of adverse childhood experiences (driven by Scandinavian welfare regime) and adverse childhood health experiences (driven by Eastern European welfare regime), but increased between categories of occupational position (driven by Bismarckian welfare regime).

Discussion These findings suggest that childhood misfortune is linked to frailty in old age. Such a disadvantaged start in life does not seem to be compensated by a person's life-course socioeconomic trajectory, though certain types of welfare regimes affected this relationship. Apart from main occupational position, our findings do not support the cumulative dis/advantage theory, but rather show narrowing differences.

Keywords

Health Outcomes; Successful Aging; Childhood Disadvantage; Socioeconomic Status

Introduction

One of the major social challenges related to the increase in life expectancy is the rise of chronic conditions and multi-morbidity in older age. Frailty, a syndrome of increased vulnerability to stressors caused by cumulative decline across biological systems, is thus a relevant public health issue for societies worldwide (Clegg et al., 2013; Fried et al., 2001). An issue is the often perceived social patterning of frailty across time and societies (Mackenbach, 2012; M. G. Marmot, 2003), indicating unequal risk of becoming frail. Moreover, these inequalities tend to widen in older age (Etman et al., 2015; Franse et al., 2017; van der Linden et al., 2019). The reason for this widening is not known, but from a life-course perspective, the relationship between childhood conditions and later life health may be explained by the cumulative dis/advantage (CDA) theory, defined as the 'systemic tendency for interindividual divergence in a given characteristic (e.g. money, health, or status) with the passage of time' (Dannefer, 2003). This theory posits a widening social gradient of frailty in old age.

Based on the CDA hypothesis, three aspects of the theory can be tested in the context of frailty. First, is there a social gradient of frailty in old age and are there growing differences in frailty trajectories with aging? Second, we will investigate the principle of life-course reflexivity (Dannefer, 2018) by focusing not only on childhood effects, but also targeting interactive dynamics that occur between an individual and his or her social system across the life-course by including socioeconomic conditions in adulthood, thereby examining changes in mid- and later life. Third, as welfare policies regulate the level to which individual life-courses are affected by macro-level changes (Dannefer, 2018; Leisering, 2003; Sieber et al., 2019), we test the CDA mechanism at the micro (childhood misfortune and adult-life socioeconomic conditions (SEC)) as well as the macro (welfare regimes) level.

Childhood has been shown to influence later life health through biological and psychosocial pathways and represents a period in which people are most vulnerable to external influences (Ben-Shlomo et al., 2016; Blane, 2013; Stringhini et al., 2015). Regarding frailty, several studies suggested that its key risk is rooted in childhood socioeconomic conditions (Alvarado et al., 2008; Gale et al., 2016;

Hughes et al., 2017; van der Linden et al., 2019). Other childhood circumstances often linked to negative health outcomes later in life are traumatic events referred to as adverse childhood experiences (ACE) (Nurius, Fleming, & Brindle, 2019; Wade et al., 2016). However, studies examining the effect of ACE on the risk of frailty in older age are lacking. Moreover, later life health is not only influenced by childhood health, but also by poor socioeconomic and adverse psychosocial conditions during early life, as already reported for outcomes related to frailty such as successful aging and functional health (Brandt, Deindl, & Hank, 2012; Haas, 2008; Huang, Soldo, & Elo, 2011). Based on this, we expect that childhood exposure to adverse conditions increases the risk of frailty.

In addition, growing up in adverse circumstances can influence later life health through a linkage with structural factors in several domains that are important in the studied cohort. During the period the studied cohort was growing up, disadvantaged socioeconomic conditions often went hand in hand with living in poor environmental and low-income conditions, restricted access to high quality education, health care and social network (Doku et al., 2018; Sharpe et al., 2018). Several socioeconomic factors in adulthood such as education, occupational class and wealth were found to contribute to persisting health and frailty inequalities in old age (Santos-Eggimann et al., 2009; Stolz et al., 2017; van der Linden et al., 2019). Therefore, we expect to find that lower education, occupation, and income will be associated with a greater risk of frailty in later life.

When taking a life-course perspective, not only individual factors, but also macro level influences, such as welfare regimes should be considered, as nation states' policies may influence accumulation of dis/advantage through pension systems and social benefits (Michel Oris, Gabriel, Ritschard, & Kliegel, 2017). More supportive welfare regimes are more likely to favour redistribution and absorb the impact of material shortfalls through the provision of higher benefits (Bartley et al., 1997; Raphael & Bryant, 2015). By contrast, less generous welfare regimes may increase the impact of accumulated disadvantages. Ferrera's typology, augmented by the Eastern European welfare regime, can be used as a basis for grouping countries into welfare regimes based on how social benefits are granted and organised, with different roles of the state, family, and market in

the provision of welfare (Eikemo et al., 2008; Ferrera, 1996; Sieber et al., 2019). The Bismarckian welfare regime is known for its 'status differentiating' welfare programs where benefits are related to earnings and administered by employers. This regime is minimally redistributive (Eikemo et al., 2008). Conversely, the Scandinavian welfare regime aims at promoting social equality through a redistributive social security system (Eikemo et al., 2008). The Southern European welfare regime is more fragmented in terms of welfare provision and strongly relies on the family (Eikemo et al., 2008; Ferrera, 1996). The Eastern European welfare regime is less easy to capture in a life-course perspective since it can currently be characterised by limited health service provision and poor population health, but when the elderly we study were children, they grew up in a care and school system inspired by an egalitarian ethos (Eikemo et al., 2008). Considering these characteristics, we hypothesize that the Bismarckian welfare regime will be the least able to compensate accumulation of dis/advantage, whereas the Scandinavian welfare regime will be more efficient. For Southern and East European regimes, we expect less clear results.

In line with the three aspects of the CDA theory, this study has three objectives. First, to examine the associations of different forms of childhood misfortune (poor socioeconomic conditions, adverse experiences, and poor health) with levels and trajectories of frailty over aging. Second, to examine the role of adult-life SEC (education, main occupation, and satisfaction with household income) in the association of childhood adversities with levels and trajectories of frailty at older age. Third, to assess the role of welfare regimes in these associations.

Methods

Study design and population

Data from the longitudinal Survey of Health, Ageing, and Retirement in Europe (SHARE) were used. SHARE was designed to investigate population ageing processes (Borsch-Supan et al., 2013). We included six waves of data that were

collected every two years between 2004 and 2016. Participants were eligible for the analyses if they participated in the third wave and had at least one complete measure of frailty in wave 1, 2, 4, 5 or 6. Participation in the third wave was necessary since retrospective life-course data on socioeconomic conditions was only collected in wave 3 (SHARELIFE).

Frailty

To construct the frailty variable, the attributes from the phenotype of frailty were used; shrinking, weakness, exhaustion, slowness, and low activity (Fried et al., 2001). The operationalization was adapted to the provided information in SHARE, for which we adhered to Santos-Eggimann et al.'s (2009) proposition of the operationalization of frailty. It was constructed by selecting the most suitable metric and has been tested and validated in SHARE (Macklai et al., 2013; Romero-Ortuno, 2013; van der Linden et al., 2019). For shrinking, the question, "What has your appetite been like" was used and the criterion was fulfilled when participants reported a "diminution in desire for food" or, in the case of an unclear response to this question, the answer "less" to the follow-up item "So have you been eating more or less than usual?". Weakness was operationalized using grip strength measures and the highest out of four dynamometer measures was analysed. Cut-offs were calculated for each wave separately, stratified by gender and body mass index quartiles (Fried et al., 2001) and the criterion was fulfilled by the weakest 20% in each category. The question, "In the last month, have you had too little energy to do things you wanted to do?" was used to define exhaustion. The slowness attribute was operationalized using mobility questions, as SHARE measured walking speed only for individuals aged 75 or older. Previous analyses showed that low speed and positive answers to either of the following two items were strongly associated: "Because of a health problem, do you have any difficulty [expected to last three or more months] walking 100 meters" or "...climbing one flight of stairs without resting" (Santos-Eggimann et al., 2009). The question "How often do you engage in activities that require a low or moderate level of energy such as gardening, cleaning the car, or going for a

walk?” was used for the low activity attribute which was fulfilled for individuals answering either “one to three times a month” or “hardly ever or never”.

A score ranging from zero to five was created, based on fulfilment of the attributes. Individuals with zero points were classified as non-frail, one or two points as pre-frail, and three or more points as frail (Fried et al., 2001). To create a binary outcome, pre-frail and frail states were combined to (pre-)frail as opposed to non-frail (van der Linden et al., 2019).

Childhood misfortune

Adverse Childhood Experiences (ACE)

ACE were defined as a set of traumatic events (emotional, physical, or linked to household dysfunction) that occurred during childhood (from 0 to 15 years) and that were outside a child’s control (Felitti et al., 1998). The following indicators for specific ACE matching this definition were selected; child in care (living in a children’s home or with a foster family), parental death (father, mother or both), parental mental illness, parental drinking abuse, period of hunger, and property taken away. An ACE score ranging from 0 to 7 was created by combining the six indicators: one point for presence of each indicator and two points when a participant lost both parents in childhood. To examine the overall chronic stress response induced by having experienced any ACE, we dichotomised the score into participants who experienced no ACE (i.e., participants who only answered “no”) versus participants who experienced at least one ACE (i.e., participants who answered “yes” at least once) (Barboza Solís et al., 2015; Cheval et al., 2019). When information was missing, the score was computed using the non-missing data of all available items.

Adverse Childhood Health Experiences (ACHE)

The following indicators of childhood health problems up until the age of 15 were included; long hospitalization (hospitalization for at least one month), multiple hospitalizations (more than three times within a 12-month period), childhood illness (including polio, asthma, or meningitis/encephalitis), serious health

conditions (including severe headaches, psychiatric problem, fractures, heart trouble, cancers), and physical injury that has led to permanent handicap, disability or limitation in daily life (Cheval et al., 2019). The ACHE variable was created by computing a binary variable of participants who experienced no ACHE versus participants who experienced at least one AHCE. For missing information, the score was computed using the non-missing data of the available items.

Childhood Socioeconomic Conditions (CSC)

Four binary indicators of socioeconomic conditions at age 10, according to Wahrendorf and Blane's (2015) measure of childhood circumstances were used; occupational position of the main breadwinner, number of books at home, overcrowding, and housing quality. The 5-level categorical CSC variable was constructed by combining these indicators creating a score from "most disadvantaged" to "most advantaged". The same score was used in a previous article which provides more detailed information about the coding of this variable (Cheval et al., 2018).

Adult-life Socioeconomic Conditions

As indicators of adult-life socioeconomic conditions, variables were included that represent young adult life, middle age, and old age, respectively; highest educational attainment (primary, secondary, or tertiary) during follow-up, main occupational position based on the skill classification of the main job over the life-course (high skill versus low skill), and satisfaction with current household income, using the question "Is the household able to make ends meet?" (ranging from 1 "with great difficulty" to 4 "easily"). To keep as many observations as possible, the mode over follow-up for each individual was computed.

Welfare regimes

Countries were classified into 4 welfare regimes based on the classification proposed by Eikemo and colleagues (2008); Scandinavian (Denmark and Sweden), Bismarckian (Austria, Belgium, France, Germany, the Netherlands,

Switzerland), Southern European (Greece, Italy, Spain), and Eastern European (Czech Republic and Poland). Welfare regime was measured at follow-up as a proxy of individuals' life-course regime.

Potential confounders and predictors

All analyses were adjusted for age, sex, attrition (no dropout, dropout, deceased), and birth cohort (1919 to 1928, 1929 to 1938 [Great Depression], 1939 to 1945 [Second World War], and post-1945) as these variables have been shown to be related to later life health (Cheval et al., 2019; Sieber et al., 2019; van der Linden et al., 2019). Final models were additionally adjusted for other possible health- and lifestyle related predictors of frailty as final adjustment; living with partner (yes, no), delayed recall memory and verbal fluency as indicators of cognitive functioning, smoking (ever, not), number of chronic conditions (including stroke, heart attack, hypertension, diabetes, cancer, Parkinson's disease, and asthma), difficulties with ADL (score range zero to five), and difficulties with instrumental activities of daily living (IADL, score range zero to five) (Gale et al., 2016; Hughes et al., 2017; van der Linden et al., 2019).

Statistical analyses

We used logistic mixed-effects models to analyse the data (Boisgontier & Cheval, 2016). The models' Bayesian Information Criterion as well as likelihood tests revealed that the best random structure was random intercepts. Age was centred at the beginning of the trajectory (i.e., 50 years) and divided by ten so that the coefficient yielded effects of increase in the odds of being frail over a 10-year period. For the time varying covariates, we used the mode in order to reduce the loss of observations. Model 1a tested the association between childhood misfortune (CSC, ACE, ACHE) and the odds of being frail. In addition, model 1a included interaction terms between age and childhood misfortune to test whether the differences between childhood categories were growing or narrowing as people age. In model 2a we added the adult-life SEC (education, main occupational position, satisfaction with household income) and their respective

interactions. Coherently with the latest formulation of the CDA theory that posits the capacity of the welfare regime to moderate associations of early- and adult-life experiences with old age outcomes (Dannefer, 2018), we tested triple interactions between age, predictors and welfare regime to assess whether this was also the case for frailty. Since the interactions were significant, we stratified the models by welfare regime, i.e. models 1b and 2b which correspond to the unstratified models 1a and 2a (Tables S2 for Scandinavian and Bismarckian welfare regimes and S3 for Southern and Eastern European welfare regimes, see Supplementary Material). Models 1a, 1b, 2a, and 2b were adjusted for sex, birth cohort, and sample-attrition. Models 3a and 3b additionally includes health- and lifestyle variables (without interactions) to fully adjust the models (Table S4, see Supplementary Material).

Finally, we performed a series of sensitivity analyses by excluding participants older than 90 years (1), who died during the survey (2), and those who dropped out (3), and finally testing the effect of each ACE on the risk of frailty in later life (4). We also ran stratified analyses by sex, since the prevalence of frailty is expected to differ between men and women. Statistical analyses were performed using R with the lme4 and lmerTest packages (Bates et al., 2015; Kuznetsova, 2016; R Core Team, 2017)

Results

Participant characteristics

The final sample consisted of 23 358 participants (56% female) with a mean age of 60.6 years in the non-frail and 64.6 in the (pre-)frail group (See Table 1 for the total sample and Table S1 in Supplementary Material for the sample stratified by welfare regime). Most participants did not experience any ACE (79%) and ACHE (75%). A gradient in CSC and ACE was observed: the percentage of (pre-)frail people was 41.4% in the most advantaged category compared to 62.8% in the most disadvantaged and 48.5% in the no ACE category compared to 54.5% in the category with at least one ACE. A similar gradient was found for the adult-life indicators: the lower the educational attainment, occupational position, and satisfaction with household income, the higher the proportion of (pre-)frail.

Descriptive trajectories of frailty for each childhood misfortune and adult-life SEC show an overall parallel evolution until 70 years (See Figure 1). After the age of 70, differences between the categories narrow, mainly for the childhood misfortune variables.

Effects of childhood misfortune on risk of frailty over ageing

The results for the association of childhood misfortune with the odds of being (pre-)frail are shown for model 1a in Table 2. At the beginning of the trajectory (i.e. age 50), participants growing up in more disadvantaged CSC, having at least one ACE, or having at least one ACHE had higher odds of being (pre-)frail compared to those in more advantaged CSC and having no ACE or ACHE. The linear trajectories of higher odds of frailty over aging differed by ACHE and CSC categories. Those reporting at least one ACHE as well as respondents growing up in middle or advantaged CSC had a less steep linear increase in the odds of being (pre-)frail than those who had no ACHE and those who grew up in most disadvantaged CSC. For ACE, no differing trajectories were found.

Accumulation of disadvantage over the life-course

When adult-life SEC were added to the model, CSC were no longer associated with frailty, suggesting that they mediate the associations of CSC with odds of being (pre-)frail (Table 2, model 2a). Lower educational attainment and having difficulty making ends meet were associated with higher odds of being (pre-)frail. Occupational position did not have an effect on the odds of being (pre-)frail. Over aging, the trajectories for the categories of educational attainment and satisfaction with household income did not differ. After adjusting for health- and lifestyle variables, the results did not change (Table S4, model 3a).

Effect of welfare regimes on the association of childhood misfortune with frailty

When stratifying by welfare regime, differences in the associations of childhood misfortune with frailty were found (Tables S2 and S3, model 1b). With the exception of those growing up in middle or advantaged CSC in Eastern Europe

having a lower odds of being (pre-)frail compared to those in most disadvantaged CSC, associations of CSC with frailty in the other welfare regimes were no longer observed. The association between having at least one ACE and higher odds of being (pre-)frail was still significant in the Scandinavian and Bismarckian welfare regime, but not in the Southern and Eastern European welfare regimes. In the Bismarckian and Eastern European welfare regime the association of ACHE with frailty was still present, but not in the Scandinavian and Southern European welfare regimes.

The associations of the childhood misfortune indicators with linear trajectories of frailty over aging differed between welfare regimes. The trajectories in the odds of being (pre-)frail over aging by ACE changed across welfare regimes, where only respondents in the Scandinavian welfare regime having at least one ACE had a less steep increase of odds of being (pre-)frail compared to those who did not experience ACE. The association of ACHE with linear trajectories of frailty over aging (less steep decline) observed in the overall sample (model 1a) disappeared in the Scandinavian and Southern European welfare regime, but remained in the Eastern European and Bismarckian regimes. Finally, also for CSC, trajectories of frailty over aging differed by welfare regimes. In the Eastern European welfare regime respondents growing up in middle or advantaged CSC still had a less steep linear increase of odds of being (pre-)frail than those growing up in most disadvantaged CSC. This was also present in the Bismarckian welfare regime for those in the advantaged CSC, but not in the middle CSC, but was not found in the other welfare regimes.

Effect of welfare regimes on the accumulation of disadvantage in adult-life

Associations of those growing up in middle or advantaged CSC in Eastern Europe having a lower odds of being (pre-)frail compared to those in most disadvantaged CSC, disappeared when adult-life SEC were taken into account. By contrast, they appeared in the Bismarckian welfare regime where the advantaged CSC showed higher odds of being (pre-)frail compared to the most disadvantaged. Lower educational attainment was associated with higher odds of being (pre-)frail in the Bismarckian welfare regime. In the other welfare regimes, no associations were

found. The association of occupational position with frailty differed by welfare regime: with the exception of those being low skilled in the Scandinavian having higher odds of being (pre-)frail compared to the high skilled, no association was found. Having difficulty making ends meet with household income differed by welfare regime and was associated with higher odds of being (pre-)frail, with the exception of those in the fairly easily category in Southern and Eastern European welfare regimes.

Over aging, the trajectories of frailty in relation to educational attainment and satisfaction with household income did not differ by welfare regime. However, those having great difficulty making ends meet with household income in the Bismarckian welfare regime had a less steep increase of being (pre-)frail over aging compared to those who could easily make ends meet. For main occupational position the previously observed growing difference between high skilled and those who never worked was no longer present across the welfare regimes. However, in the Bismarckian welfare regime a growing difference between those who were low skilled and those who were high skilled was found. After adjusting for health- and lifestyle variables, the results did not markedly change (Table S4, model 3b).

Sensitivity analyses

The results of the sensitivity analyses were consistent with the findings in the main analyses. The stratified analyses revealed some sex differences as well as differences with the main analyses. For men overall, having at least one ACE was not associated with odds of being (pre-)frail, whereas for women it was. For the full sample, educational attainment was not associated with odds of being (pre-)frail in women, but men having tertiary education compared to primary education had lower odds of being (pre-)frail. However, for women in the Bismarckian welfare regime, those having primary education had higher odds of being (pre-)frail compared to tertiary education. Results for the analysis testing the effect of each of the ACE measures on the risk of frailty in later life showed an effect of child in care, parental mental illness, and parental drinking abuse with higher risk of frailty in later life.

Discussion

The aims of this study were (1) to examine the associations of different forms of childhood misfortune with frailty over aging, (2) to examine the role of adult-life SEC in the association of childhood adversities with frailty at older age, and (3) to assess the role of welfare regimes on these associations. Several novel and conceptually relevant findings were revealed.

For the first aim, we observed associations between childhood misfortune and frailty at older age: the higher the disadvantage and having had adverse experiences, the higher the odds of being (pre-)frail at the age of 50. However, differences in frailty became smaller over time for the various ACE and CSC categories, suggesting a diminishing validity of the CDA theory with increasing age. This convergence of frailty trajectories in later life can be explained by mortality selection in old age – also referred to as the ‘age-as-leveller’ effect - or by reversible life-course processes where disadvantaged origins can be overcome by for example unexpected shifts in life conditions (A.M. O’Rand, 2009). When looking at ACE in relation to concepts close to frailty, previous research support our findings that people who experienced at least one ACE had higher functional limitations in adulthood and old age (Amemiya, Fujiwara, Murayama, Tani, & Kondo, 2018; Laditka & Laditka, 2018). Other research supports the idea that childhood health is associated with levels of functional limitations in adulthood (Haas, 2008; Huang et al., 2011). Our study examined these findings for the concept of frailty and extended it by looking at old age.

For the second research question on the role of adult-life SEC, results showed that lower educational attainment and having difficulty making ends meet with household income was associated with higher odds of being (pre-)frail at the age of 50. Additionally, when taking adult-life SEC into account, the association between CSC and frailty no longer persists. This suggests that adult-life SEC captures the cumulative effect produced by CSC in relation to frailty. With respect to changes in frailty with aging, no differences were found for education and satisfaction with household income. Our findings corroborate previous cross-sectional studies on SEC and frailty showing that poorer CSC and adult-life SEC

are associated with higher risk of frailty in older age (Alvarado et al., 2008; Dury et al., 2016; Gale et al., 2016; Landos et al., 2019). Our study went further by taking three childhood misfortune indicators (CSC, ACE, and ACHE) into account when studying frailty at older age.

With respect to differences in the associations with the odds of being (pre-)frail across the different welfare regimes, it seemed that the Bismarckian welfare regime is the least able to deal with cumulative disadvantage. Originally, this is a regime where social reproduction is high in terms of inequality in educational attainment (Allmendinger & Leibfried, 2003). Moreover, our results showed that childhood misfortune and educational attainment are all consistently associated with higher odds of (pre-)frailty in old age. The frailty trajectories were similarly impacted: initial inequalities have not been absorbed and they affect health in later life. Also Eastern Europe exhibited a large persistence of social inequalities along the life-course. Part of the explanation might be the disruption of social institutions and structures after the collapse of the Soviet regime, which resulted in an increase of mortality and a privatisation of many sectors, including health. Therefore, participants in SHARE are survivors and it seems that their social distribution of health in old age depends on current conditions that are unable to overcome inequalities in early life (Cornia, 2016; Meslé, 2004). The most egalitarian welfare regimes in relation to frailty appear to be the Scandinavian, social equality being the objective of this regime since its onset (Eikemo et al., 2008) and the Southern European, despite the frequent criticisms against this regime. Another study on self-rated health also looked at these associations and their differences in these associations across welfare regimes (Sieber et al., submitted). Results are similar to our findings on frailty: the more disadvantaged respondents in terms of childhood misfortune and adult-life SEC also experienced poorer self-rated health. In addition, the study further supported our finding of similar patterns across welfare regimes for associations of satisfaction with household income with health at older age and differing patterns for CSC, education, and occupation.

Strengths and limitations

A major strength of this study is the use of a longitudinal survey with 12-year follow-up with a large sample size. Additionally, the comprehensive multinational data on both childhood and adult-life indicators allowed us to study trajectories of frailty across different welfare regimes. This enabled us to do a comparative analysis testing three aspects of the CDA framework; growing differences in frailty trajectories over aging, interactive dynamics across the life-course, and the interactions of the micro and macro level from age 50 onwards (Dannefer, 2018).

This study has some limitations. First, data used for the childhood misfortune and adult-life SEC indicators was self-reported and measured retrospectively. This may be subject to recall bias and social desirability. However, studies on recall measures of adverse experiences and SEC in older adults have showed adequate validity (Barboza Solís et al., 2015; Lacey et al., 2012). Second, selection bias may have occurred as longitudinal data was used and participants have dropped out or died during follow-up. We adjusted our models for attrition to deal with this and we conducted a sensitivity analysis excluding participants who dropped out or died. Third, our measure of ACE is an overall score of adversity. Even though combining different indicators has been done in previous studies (Cheval et al., 2019), this does not enable us to disentangle the specific effect of each indicator, nor to explore a possible threshold of adversity. Fourth, other variables could be important in these analyses, such as the late-life adverse events, genetic predispositions, and other psychosocial factors. Unfortunately, data on this was not available. Finally, the definition and operationalization of frailty and CDA differs between studies, which may make comparisons between studies more difficult. The operationalization of frailty used in this study is similar to previous studies using SHARE data and seems to be the optimal choice.

Conclusion

The present study is the first to analyse associations of childhood misfortune and adult-life SEC with frailty at older age. In addition, it is the first time that the influence of welfare regimes on these associations is studied. In conclusion, our findings suggest that childhood misfortune and adult-life SEC influence (pre-

)frailty at older age. It also demonstrates that the effect of CSC, but not ACE and ACHE, is mediated by adult-life SEC, suggesting that adult-life SEC capture the cumulative disadvantage produced by CSC. Narrowing differences over aging were found for the different categories of adverse childhood experiences, which were driven by the Scandinavian welfare regime, and of adverse childhood health experiences, driven by the Eastern European welfare regime. For main occupational position an increased difference was found, which was driven by the Bismarckian welfare regime. In terms of conceptual conclusions for the CDA theory, apart from occupational position, after the age of 50 differences in frailty trajectories by the various childhood misfortune and adult-life SEC variables were narrowing, which does not support the CDA theory. These results show the importance of childhood as well as adult-life SEC on health in later life. Moreover, we demonstrate that policies of welfare regimes do not necessarily compensate for this.

References

- Allmendinger, J., & Leibfried, S. (2003). Education and the welfare state: the four worlds of competence production. *Journal of European Social Policy*, 13(1), 63-81. doi:10.1177/0958928703013001047
- Alvarado, B. E., Zunzunegui, M. V., Beland, F., & Bamvita, J. M. (2008). Life course social and health conditions linked to frailty in Latin American older men and women. *J Gerontol A Biol Sci Med Sci*, 63(12), 1399-1406. doi:10.1093/gerona/63.12.1399
- Amemiya, A., Fujiwara, T., Murayama, H., Tani, Y., & Kondo, K. (2018). Adverse Childhood Experiences and Higher-Level Functional Limitations Among Older Japanese People: Results From the JAGES Study. *J Gerontol A Biol Sci Med Sci*, 73(2), 261-266. doi:10.1093/gerona/glx097
- Barboza Solís, C., Kelly-Irving, M., Fantin, R., Darnaudéry, M., Torrisani, J., Lang, T., & Delpierre, C. (2015). Adverse childhood experiences and physiological wear-and-tear in midlife: Findings from the 1958 British birth cohort. *Proceedings of the National Academy of Sciences*, 112(7), E738-E746. doi:10.1073/pnas.1417325112
- Bartley, M., Blane, D., & Montgomery, S. (1997). Health and the life course: why safety nets matter. *Bmj*, 314(7088), 1194-1196.
- Bates, D., Mächler, M., Bolker, B., & Walker, S. (2015). Fitting Linear Mixed-Effects Models Using lme4. 2015, 67(1), 48. doi:10.18637/jss.v067.i01
- Boisgontier, M. P., & Cheval, B. (2016). The anova to mixed model transition. *Neurosci Biobehav Rev*, 68, 1004-1005. doi:10.1016/j.neubiorev.2016.05.034
- Borsch-Supan, A., Brandt, M., Hunkler, C., Kneip, T., Korbmacher, J., Malter, F., . . . Zuber, S. (2013). Data Resource Profile: the Survey of Health, Ageing and Retirement in Europe (SHARE). *Int J Epidemiol*, 42(4), 992-1001. doi:10.1093/ije/dyt088
- Brandt, M., Deindl, C., & Hank, K. (2012). Tracing the origins of successful aging: the role of childhood conditions and social inequality in explaining later life health. *Soc Sci Med*, 74(9), 1418-1425. doi:10.1016/j.socscimed.2012.01.004
- Cheval, B., Boisgontier, M. P., Orsholits, D., Sieber, S., Guessous, I., Gabriel, R., . .

- . Cullati, S. (2018). Association of early- and adult-life socioeconomic circumstances with muscle strength in older age. *Age Ageing*, 47(3), 398-407. doi:10.1093/ageing/afy003
- Cheval, B., Chabert, C., Sieber, S., Orsholits, D., Cooper, R., Guessous, I., . . . Cullati, S. (2019). Association between Adverse Childhood Experiences and Muscle Strength in Older Age. *Gerontology*. doi:10.1159/000494972
- Clegg, A., Young, J., Iliffe, S., Rikkert, M. O., & Rockwood, K. (2013). Frailty in elderly people. *Lancet*, 381(9868), 752-762. doi:10.1016/s0140-6736(12)62167-9
- Cornia, G. (2016). The mortality crisis in transition economies. *IZA World of Labor*(298). doi:doi: 10.15185/izawol.298
- Dannefer, D. (2003). Cumulative advantage/disadvantage and the life course: cross-fertilizing age and social science theory. *J Gerontol B Psychol Sci Soc Sci*, 58(6), S327-337.
- Dannefer, D. (2018). Systemic and Reflexive: Foundations of Cumulative Dis/Advantage and Life-Course Processes. *J Gerontol B Psychol Sci Soc Sci*. doi:10.1093/geronb/gby118
- Doku, D. T., Acacio-Claro, P. J., Koivusilta, L., & Rimpela, A. (2018). Health and socioeconomic circumstances over three generations as predictors of youth unemployment trajectories. *Eur J Public Health*. doi:10.1093/eurpub/cky242
- Dury, S., De Roeck, E., Duppen, D., Fret, B., Hoeyberghs, L., Lambotte, D., . . . Dierckx, E. (2016). Identifying frailty risk profiles of home-dwelling older people: focus on sociodemographic and socioeconomic characteristics. *Aging Ment Health*, 1-9. doi:10.1080/13607863.2016.1193120
- Eikemo, T. A., Bambra, C., Judge, K., & Ringdal, K. (2008). Welfare state regimes and differences in self-perceived health in Europe: a multilevel analysis. *Soc Sci Med*, 66(11), 2281-2295. doi:10.1016/j.socscimed.2008.01.022
- Etman, A., Kamphuis, C. B., van der Cammen, T. J., Burdorf, A., & van Lenthe, F. J. (2015). Do lifestyle, health and social participation mediate educational inequalities in frailty worsening? *Eur J Public Health*, 25(2), 345-350. doi:10.1093/eurpub/cku093
- Felitti, V. J., Anda, R. F., Nordenberg, D., Williamson, D. F., Spitz, A. M., Edwards, V., . . . Marks, J. S. (1998). Relationship of childhood abuse and household dysfunction to many of the leading causes of death in adults. *The*

- Adverse Childhood Experiences (ACE) Study. *Am J Prev Med*, 14(4), 245-258.
- Ferrera, M. (1996). The 'Southern Model' of Welfare in Social Europe. *Journal of European Social Policy*, 6(1), 17-37. doi:10.1177/095892879600600102
- Franse, C. B., van Grieken, A., Qin, L., Melis, R. J. F., Rietjens, J. A. C., & Raat, H. (2017). Socioeconomic inequalities in frailty and frailty components among community-dwelling older citizens. *PLoS One*, 12(11), e0187946. doi:10.1371/journal.pone.0187946
- Fried, L. P., Tangen, C. M., Walston, J., Newman, A. B., Hirsch, C., Gottdiener, J., . . . McBurnie, M. A. (2001). Frailty in older adults: evidence for a phenotype. *J Gerontol A Biol Sci Med Sci*, 56(3), M146-156.
- Gale, C. R., Booth, T., Starr, J. M., & Deary, I. J. (2016). Intelligence and socioeconomic position in childhood in relation to frailty and cumulative allostatic load in later life: the Lothian Birth Cohort 1936. *J Epidemiol Community Health*, 70(6), 576-582. doi:10.1136/jech-2015-205789
- Haas, S. (2008). Trajectories of functional health: the 'long arm' of childhood health and socioeconomic factors. *Soc Sci Med*, 66(4), 849-861. doi:10.1016/j.socscimed.2007.11.004
- Huang, C., Soldo, B. J., & Elo, I. T. (2011). Do early-life conditions predict functional health status in adulthood? The case of Mexico. *Soc Sci Med*, 72(1), 100-107. doi:10.1016/j.socscimed.2010.09.040
- Hughes, K., Bellis, M. A., Hardcastle, K. A., Sethi, D., Butchart, A., Mikton, C., . . . Dunne, M. P. (2017). The effect of multiple adverse childhood experiences on health: a systematic review and meta-analysis. *Lancet Public Health*, 2(8), e356-e366. doi:10.1016/s2468-2667(17)30118-4
- Kuznetsova, A., Brockhoff, P. B., Christensen, R. H. B. (2016). lmerTest: Tests in Linear Mixed Effects Models. R package version 2.0-33. Retrieved from <https://CRAN.R-project.org/package=lmerTest>
- Lacey, R. J., Belcher, J., & Croft, P. R. (2012). Validity of two simple measures for estimating life-course socio-economic position in cross-sectional postal survey data in an older population: results from the North Staffordshire Osteoarthritis Project (NorStOP). *BMC Med Res Methodol*, 12, 88. doi:10.1186/1471-2288-12-88
- Laditka, J. N., & Laditka, S. B. (2018). Adverse Childhood Circumstances and Functional Status Throughout Adult Life. *J Aging Health*, 30(9), 1347-1368. doi:10.1177/0898264317715976

- Landos, A., von Arx, M., Cheval, B., Sieber, S., Kliegel, M., Gabriel, R., . . . Cullati, S. (2019). Childhood socioeconomic circumstances and disability trajectories in older men and women: a European cohort study. *Eur J Public Health*, 29(1), 50-58. doi:10.1093/eurpub/cky166
- Leisering, L. (2003). Government and the Life Course. In J. T. Mortimer & M. J. Shanahan (Eds.), *Handbook of the Life Course* (pp. 205-225). Boston, MA: Springer US.
- Mackenbach, J. P. (2012). The persistence of health inequalities in modern welfare states: the explanation of a paradox. *Soc Sci Med*, 75(4), 761-769. doi:10.1016/j.socscimed.2012.02.031
- Macklai, N. S., Spagnoli, J., Junod, J., & Santos-Eggimann, B. (2013). Prospective association of the SHARE-operationalized frailty phenotype with adverse health outcomes: evidence from 60+ community-dwelling Europeans living in 11 countries. *BMC Geriatr*, 13, 3. doi:10.1186/1471-2318-13-3
- Marmot, M. G. (2003). Understanding social inequalities in health. *Perspect Biol Med*, 46(3 Suppl), S9-23.
- Meslé, F. (2004). Mortality in Central and Eastern Europe: long-term trends and recent upturns. *Demographic Research*, Special Collection 2, 45-70. doi:10.4054/DemRes.2004.S2.3
- Nurius, P. S., Fleming, C. M., & Brindle, E. (2019). Life Course Pathways From Adverse Childhood Experiences to Adult Physical Health: A Structural Equation Model. *J Aging Health*, 31(2), 211-230. doi:10.1177/0898264317726448
- O'Rand, A. M. (2009). Cumulative Processes in the Life Course. In G. H. Elder & J. Z. Giele (Eds.), *The Craft of Life Course Research*. New York: Guilford Press.
- Oris, M., Gabriel, R., Ritschard, G., & Kliegel, M. (2017). Long Lives and Old Age Poverty: Social Stratification and Life-Course Institutionalization in Switzerland. *Research in Human Development*, 14(1), 68-87. doi:10.1080/15427609.2016.1268890
- R Core Team. (2017). R: A language and environment for statistical computing. Retrieved from <https://www.R-project.org/>
- Raphael, D., & Bryant, T. (2015). Power, intersectionality and the life-course:

- Identifying the political and economic structures of welfare states that support or threaten health. *Social Theory & Health*, 13(3), 245-266. doi:10.1057/sth.2015.18
- Romero-Ortuno, R. (2013). The SHARE operationalized frailty phenotype: a comparison of two approaches. *Eur Geriatr Med*, 4(4). doi:10.1016/j.eurger.2013.04.003
- Santos-Eggimann, B., Cuenoud, P., Spagnoli, J., & Junod, J. (2009). Prevalence of frailty in middle-aged and older community-dwelling Europeans living in 10 countries. *J Gerontol A Biol Sci Med Sci*, 64(6), 675-681. doi:10.1093/gerona/glp012
- Sharpe, R. A., Taylor, T., Fleming, L. E., Morrissey, K., Morris, G., & Wigglesworth, R. (2018). Making the Case for "Whole System" Approaches: Integrating Public Health and Housing. *Int J Environ Res Public Health*, 15(11). doi:10.3390/ijerph15112345
- Sieber, S., Cheval, B., Orsholits, D., Van der Linden, B. W., Guessous, I., Gabriel, R., . . . Cullati, S. (2019). Welfare regimes modify the association of disadvantaged adult-life socioeconomic circumstances with self-rated health in old age. *Int J Epidemiol*. doi:10.1093/ije/dyy283
- Sieber, S., Cheval, B., Orsholits, D., van der Linden, B. W. A., Guessous, I., Gabriel, R., . . . Cullati, S. (submitted). Do welfare regimes moderate cumulative dis/advantages over the life course? Cross-national evidence from longitudinal SHARE data.
- Stolz, E., Mayerl, H., Waxenegger, A., Rasky, E., & Freidl, W. (2017). Impact of socioeconomic position on frailty trajectories in 10 European countries: evidence from the Survey of Health, Ageing and Retirement in Europe (2004-2013). *J Epidemiol Community Health*, 71(1), 73-80. doi:10.1136/jech-2016-207712
- van der Linden, B. W. A., Cheval, B., Sieber, S., Orsholits, D., Guessous, I., Stringhini, S., . . . Cullati, S. (2019). Life Course Socioeconomic Conditions and Frailty at Older Ages. *J Gerontol B Psychol Sci Soc Sci*. doi:10.1093/geronb/gbz018
- Wade, R., Jr., Cronholm, P. F., Fein, J. A., Forke, C. M., Davis, M. B., Harkins-Schwarz, M., . . . Bair-Merritt, M. H. (2016). Household and community-level Adverse Childhood Experiences and adult health outcomes in a diverse urban population. *Child Abuse Negl*, 52, 135-145. doi:10.1016/j.chiabu.2015.11.021

Wahrendorf, M., & Blane, D. (2015). Does labour market disadvantage help to explain why childhood circumstances are related to quality of life at older ages? Results from SHARE. *Aging Ment Health*, 19(7), 584-594. doi:10.1080/13607863.2014.938604

Table 1. Participant characteristics

	Non-frail N (%)	(pre-)Frail N (%)
Age, mean (SD)	60.6 (7.8)	64.6 (9.8)
Sex		
Female	5954 (45.8)	7038 (54.2)
Male	5777 (55.7)	4589 (44.3)
Welfare regime		
Scandinavian	2019 (56.2)	1571 (43.8)
Bismarckian	5559 (55.3)	4495 (44.7)
Southern European	2782 (42.3)	3795 (57.7)
Eastern European	1371 (43.7)	1766 (56.3)
Adverse childhood experiences		
None	9465 (51.5)	8914 (48.5)
At least one	2266 (45.5)	2713 (54.5)
Adverse childhood health experiences		
None	8723 (50.1)	8698 (49.9)
At least one	3008 (50.7)	2929 (49.3)
Childhood socioeconomic conditions		
Most disadvantaged	1598 (37.2)	2697 (62.8)
Disadvantaged	2810 (48.0)	3041 (52.0)
Middle	4097 (54.3)	3454 (45.7)
Advantaged	2448 (56.5)	1886 (43.5)
Most advantaged	778 (58.6)	549 (41.4)
Education		
Primary	2560 (36.9)	4380 (63.1)
Secondary	6396 (53.9)	5462 (46.1)
Tertiary	2775 (60.9)	1785 (39.1)
Main occupational position		
High skill	3207 (60.0)	2138 (40.0)
Low skill	7876 (48.9)	8242 (51.1)
Never worked	648 (34.2)	1247 (65.8)
Satisfaction with household income		
Easily	5223 (59.4)	3567 (40.6)
Fairly easily	3650 (51.1)	3492 (48.9)
With some difficulty	2093 (41.7)	2924 (58.3)
With great difficulty	765 (31.8)	1644 (68.2)

Note. SD, standard deviation. N non-frail = 11731, N (pre-)frail = 11627.

Table 2. Associations of childhood misfortune and adult-life socioeconomic circumstances with level and trajectories of frailty at old age

	M1a	M2a
	OR (95% CI)	OR (95% CI)
Age (10-y period)	2.47 (2.27-2.69)***	2.32 (2.05-2.63)***
At least one ACE ^a	1.31 (1.14-1.49)***	1.30 (1.14-1.48)***
At least one ACHE ^b	1.37 (1.22-1.54)***	1.40 (1.24-1.57)***
CSC ^c (ref. Most disadvantaged)		
Disadvantaged	0.80 (0.66-0.96)*	1.00 (0.83-1.20)
Middle	0.63 (0.53-0.75)***	1.00 (0.84-1.20)
Advantaged	0.63 (0.52-0.76)***	1.17 (0.96-1.44)
Most advantaged	0.43 (0.33-0.55)***	0.92 (0.70-1.21)
Education ^d		
Secondary		1.15 (1.00-1.33)
Primary		1.35 (1.11-1.63)**
Main Occupational Position ^e		
Low skill		1.11 (0.96-1.27)
Never worked		1.04 (0.80-1.33)
Satisfaction with household income ^f		
Fairly easily		1.36 (1.20-1.55)***
With some difficulty		2.21 (1.91-2.56)***
With great difficulty		4.34 (3.55-5.31)***
Interactions		
Age x at least one ACE ^a	0.97 (0.91-1.05)	0.97 (0.90-1.04)
Age x at least one ACHE ^b	0.92 (0.86-0.98)*	0.92 (0.86-0.98)*
Age x CSC ^c		
Age x Disadvantaged	0.92 (0.84-1.00)	0.92 (0.84-1.01)
Age x Middle	0.87 (0.80-0.95)**	0.88 (0.80-0.96)**
Age x Advantaged	0.82 (0.74-0.90)***	0.83 (0.74-0.92)***
Age x Most advantaged	0.92 (0.81-1.06)	0.93 (0.81-1.08)
Age x Education ^d		
Age x Secondary		0.99 (0.91-1.08)
Age x Primary		1.04 (0.94-1.16)
Age x Main occupational position ^e		
Age x Low skill		1.03 (0.95-1.11)
Age x Never worked		1.20 (1.05-1.36)**
Age x Satisfaction with household income ^f		
Age x Fairly easily		1.06 (0.99-1.13)
Age x With some difficulty		1.05 (0.97-1.14)
Age x With great difficulty		0.97 (0.86-1.09)

Note. ACE, adverse childhood experiences; ACHE, adverse childhood health experiences; CI, confidence interval; CSC, childhood socioeconomic conditions; OR, odds ratio. All models are adjusted for sex, birth cohort and attrition. Age was centered at 50 y and divided by 10 so that the coefficients yielded the effects for a 10-year period.

^aAdverse childhood experiences, reference category none

^bAdverse childhood health experiences, reference category none

^cChildhood socioeconomic conditions, reference category most disadvantaged

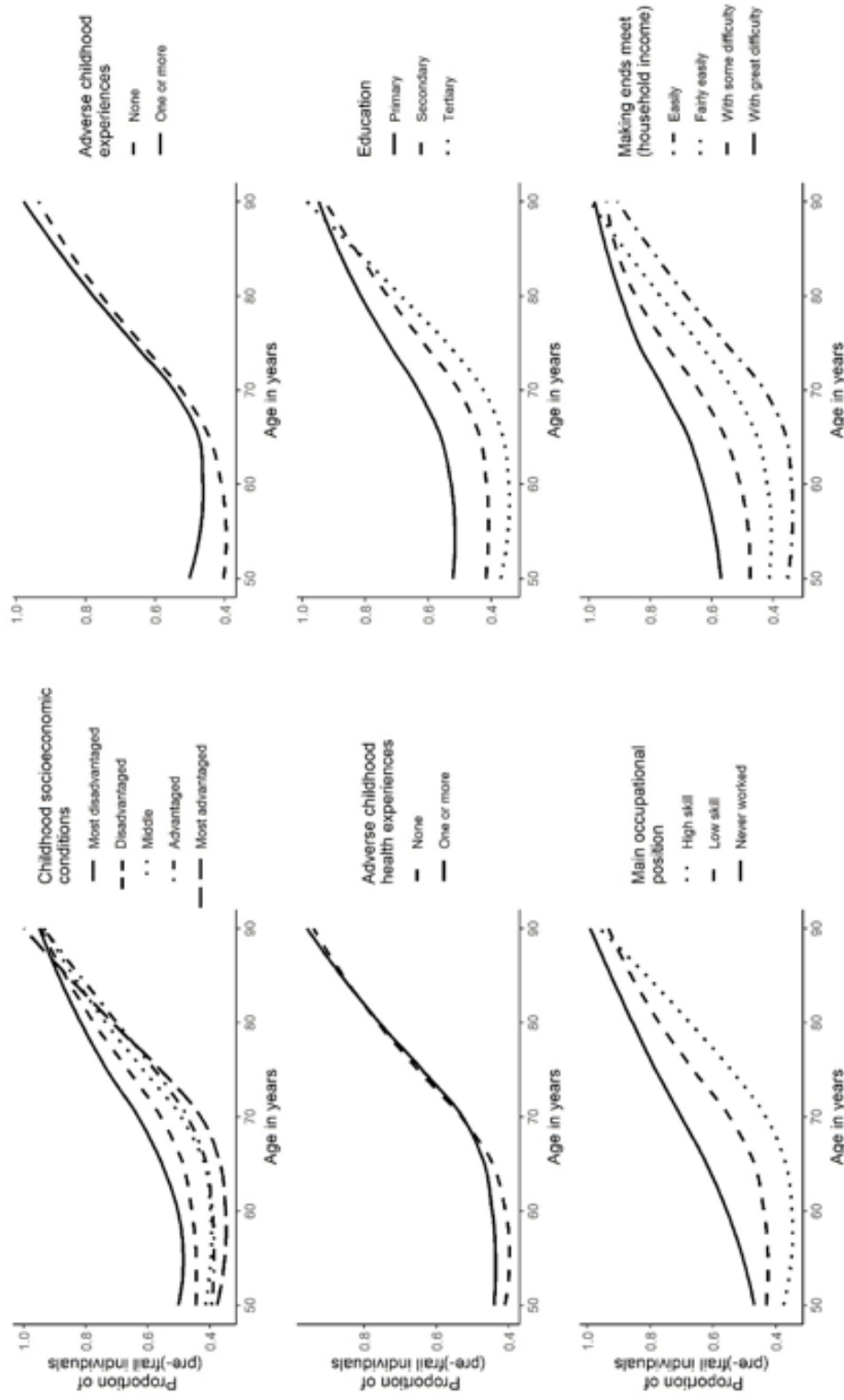
^dEducation, reference category tertiary

^eMain occupational position, reference category high skill

^fSatisfaction with household income, reference category easily

*** $p < .001$, ** $p < .01$, * $p < .05$

Figure 1. Descriptive plot of observed evolution over aging of (pre-)frailty proportions by childhood misfortune and adult-life socioeconomic conditions



Supplementary Material

Content

- **Table S1.** Participant characteristics for total and stratified sample by welfare regime
- **Table S2.** Associations of childhood misfortune and adult-life socioeconomic circumstances with level and trajectories of frailty at old age stratified by Scandinavian and Bismarckian welfare regime
- **Table S3.** Associations of childhood misfortune and adult-life socioeconomic circumstances with level and trajectories of frailty at old age stratified by Southern and Eastern European welfare regime
- **Table S4.** Fully adjusted associations (health- and lifestyle variables) of childhood misfortune and adult-life socioeconomic circumstances with level and trajectories of frailty at old age for total and stratified sample by welfare regime

Table S1. Participant characteristics for total and stratified sample by welfare regime

	Total		Scandinavian		Bismarckian		Southern European		Eastern European	
	Non-frail N (%)	(pre-)frail N (%)	Non-frail N (%)	(pre-)frail N (%)	Non-frail N (%)	(pre-)frail N (%)	Non-frail N (%)	(pre-)frail N (%)	Non-frail N (%)	(pre-)frail N (%)
Total	11731 (50.2)	11627 (49.8)	2019 (56.2)	1571 (43.8)	5559 (55.3)	4495 (44.7)	2782 (57.7)	3795 (42.3)	1371 (43.7)	1766 (56.3)
Age, mean (SD)	60.6 (7.8)	64.6 (9.8)	61.2 (8.2)	64.0 (9.9)	60.9 (8.0)	64.6 (10.0)	59.8 (7.5)	64.8 (9.5)	60.0 (7.2)	65.0 (9.7)
Sex										
Female	5954 (45.8)	7038 (54.2)	1030 (52.2)	942 (47.8)	2825 (50.8)	2740 (49.2)	1397 (38.2)	2260 (61.8)	702 (39.0)	1096 (61.0)
Male	5777 (55.7)	4589 (44.3)	989 (61.1)	629 (38.9)	2734 (60.9)	1755 (39.1)	1385 (47.4)	1535 (52.6)	669 (50.0)	670 (50.0)
Birth cohort										
After 1945	5941 (57.8)	4330 (42.2)	927 (60.7)	601 (39.9)	2672 (61.5)	1672 (38.5)	1506 (53.0)	1338 (47.0)	836 (53.8)	719 (46.2)
Between 1939 and 1945	2983 (54.6)	2479 (45.4)	542 (60.0)	361 (40.0)	1430 (60.8)	922 (39.2)	679 (45.4)	815 (54.6)	332 (46.6)	381 (53.4)
Between 1929 and 1938	2312 (42.4)	3142 (57.6)	421 (53.5)	366 (46.5)	1185 (50.4)	1168 (49.6)	527 (31.6)	1141 (68.4)	179 (27.7)	467 (72.3)
Between 1919 and 1928	495 (22.8)	1676 (77.2)	129 (34.7)	243 (65.3)	272 (27.1)	733 (72.9)	70 (12.3)	501 (87.7)	24 (10.8)	199 (89.2)
Attrition										
No dropout	8846 (52.3)	8074 (47.7)	1638 (58.4)	1168 (41.6)	4042 (57.6)	2979 (42.4)	2167 (43.8)	2778 (56.2)	999 (46.5)	1149 (53.5)
Dropped	2318 (52.2)	2125 (47.8)	263 (59.5)	179 (40.5)	1312 (53.8)	1126 (46.2)	479 (48.4)	510 (51.6)	264 (46.0)	310 (54.0)
Deceased	567 (28.4)	1428 (71.6)	118 (34.5)	224 (65.5)	205 (34.5)	390 (65.5)	136 (21.2)	507 (78.8)	108 (26.0)	307 (74.0)
ACE										
None	9465 (51.5)	8914 (48.5)	1631 (57.7)	1195 (42.3)	4409 (56.6)	3385 (43.4)	2327 (44.2)	2933 (55.8)	1098 (43.9)	1401 (56.1)
At least one	2266 (45.5)	2713 (54.5)	388 (50.8)	376 (49.2)	1150 (50.9)	1110 (49.1)	455 (34.5)	862 (65.5)	273 (42.8)	365 (57.2)
ACHE										
None	8723 (50.1)	8698 (49.9)	1405 (56.4)	1086 (43.6)	3967 (55.8)	3146 (44.2)	2329 (42.8)	3113 (57.2)	1022 (43.0)	1353 (57.0)
At least one	3008 (50.7)	2929 (62.8)	614 (55.9)	485 (44.1)	1592 (54.1)	1349 (45.9)	453 (39.9)	682 (60.1)	349 (45.8)	413 (54.2)
CSC										
Most disadvantaged	1598 (37.2)	2697 (62.8)	87 (41)	125 (59)	480 (47.0)	542 (53.0)	742 (34.8)	1388 (65.2)	289 (31.0)	642 (69.0)
Disadvantaged	2810 (48.0)	3041 (52.0)	268 (49.8)	270 (50.2)	1225 (52.8)	1094 (47.2)	1006 (44.5)	1256 (55.5)	311 (42.5)	421 (57.5)
Middle	4097 (54.3)	3454 (45.7)	774 (56.0)	609 (44.0)	2041 (57.9)	1486 (42.1)	732 (47.2)	820 (52.8)	550 (50.5)	539 (49.5)
Advantaged	2448 (56.5)	1886 (43.5)	648 (60.3)	426 (39.7)	1350 (56.8)	1027 (43.2)	254 (47.3)	283 (52.7)	196 (56.6)	150 (43.3)
Most advantaged	778 (58.6)	549 (41.4)	242 (63.2)	141 (36.8)	463 (57.2)	346 (42.8)	48 (50.0)	48 (50.0)	25 (64.1)	14 (35.9)

Table S2. Associations of childhood misfortune and adult-life socioeconomic circumstances with level and trajectories of frailty at old age stratified by Scandinavian and Bismarckian welfare regime

	Scandinavian		Bismarckian	
	M1b	M2b	M1b	M2b
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Age (10-y period)	2.14 (1.53-2.99)***	2.08 (1.42-3.05)***	2.72 (2.34-3.18)***	2.64 (2.17-3.20)***
At least one ACE ^a	2.14 (1.56-2.92)***	2.07 (1.51-2.82)***	1.55 (1.27-1.88)***	1.39 (1.15-1.69)***
At least one ACHE ^b	1.12 (0.84-1.48)	1.13 (0.85-1.49)	1.53 (1.29-1.81)***	1.49 (1.26-1.76)***
CSC ^c				
Disadvantaged	1.09 (0.45-2.65)	1.05 (0.43-2.57)	1.05 (0.75-1.49)	1.16 (0.82-1.63)
Middle	1.11 (0.48-2.53)	1.11 (0.48-2.59)	0.92 (0.66-1.28)	1.19 (0.85-1.67)
Advantaged	0.93 (0.41-2.14)	1.01 (0.43-2.37)	1.17 (0.83-1.64)	1.63 (1.15-2.30)**
Most advantaged	0.52 (0.21-1.26)	0.58 (0.23-1.45)	0.97 (0.65-1.44)	1.41 (0.93-2.14)
Education ^d				
Secondary		1.10 (0.81-1.51)		1.16 (0.95-1.42)
Primary		0.65 (0.39-1.09)		1.81 (1.34-2.44)***
Main Occupational Position ^e				
Low skill		1.65 (1.21-2.23)**		0.94 (0.78-1.15)
Never worked		1.00 (0.14-6.85)		1.53 (0.90-2.61)
Satisfaction with household income ^f				
Fairly easily		1.39 (1.01-1.91)*		1.57 (1.32-1.88)***
With some difficulty		2.56 (1.44-4.55)**		2.94 (2.31-3.75)***
With great difficulty		3.82 (1.23-11.86)*		7.35 (5.05-10.71)***
Interactions				
Age x at least one ACE ^a	0.75 (0.64-0.88)**	0.75 (0.64-0.89)**	0.92 (0.83-1.02)	0.96 (0.87-1.06)
Age x at least one ACHE ^b	1.04 (0.89-1.20)	1.03 (0.89-1.19)	0.91 (0.82-1.00)*	0.91 (0.83-0.99)*
Age x CSC ^c				
Age x Disadvantaged	0.94 (0.66-1.35)	0.97 (0.67-1.39)	0.95 (0.81-1.11)	0.96 (0.82-1.13)
Age x Middle	0.81 (0.58-1.13)	0.85 (0.60-1.21)	0.92 (0.79-1.08)	0.93 (0.80-1.09)
Age x Advantaged	0.83 (0.59-1.17)	0.87 (0.61-1.25)	0.81 (0.69-0.95)*	0.83 (0.70-0.98)*

Age x Most advantaged				
Age x Education ^d	1.01 (0.69-1.49)	1.10 (0.73-1.65)	0.87 (0.72-1.06)	0.91 (0.74-1.12)
Age x Secondary		1.03 (0.87-1.22)		0.95 (0.84-1.06)
Age x Primary		1.26 (0.99-1.60)		0.92 (0.79-1.07)
Age x Main occupational position ^e				
Age x Low skill		0.88 (0.75-1.02)		1.12 (1.00-1.25)*
Age x Never worked		1.24 (0.56-2.76)		1.05 (0.83-1.33)
Age x Satisfaction with household income ^f				
Age x Fairly easily		1.05 (0.90-1.24)		1.00 (0.91-1.10)
Age x With some difficulty		0.93 (0.71-1.23)		0.91 (0.79-1.04)
Age x With great difficulty		1.08 (0.58-2.00)		0.72 (0.58-0.91)**

Note. ACE, adverse childhood experiences; ACHE, adverse childhood health experiences; CI, confidence interval; CSC, childhood socioeconomic conditions; OR, odds ratio. All models are adjusted for sex, birth cohort and attrition. Age was centered at 50 y and divided by 10 so that the coefficients yielded the effects for a 10-year period. N Scandinavian = 3590, N Bismarckian = 10054.

^aAdverse childhood experiences, reference category none

^bAdverse childhood health experiences, reference category none

^cChildhood socioeconomic conditions, reference category most disadvantaged

^dEducation, reference category tertiary

^eMain occupational position, reference category high skill

^fSatisfaction with household income, reference category easily

***p<0.01, **p<0.05

Table S3. Associations of childhood misfortune and adult-life socioeconomic circumstances with level and trajectories of frailty at old age stratified by Southern and Eastern European welfare regime

	Southern European		Eastern European	
	M1b	M2b	M1b	M2b
Age (10-y period)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
At least one ACE ^a	2.42 (2.11-2.78)***	2.11 (1.58-2.82)***	2.20 (1.78-2.73)***	2.35 (1.60-3.44)**
At least one ACHE ^b	1.02 (0.75-1.37)	0.94 (0.70-1.26)	1.02 (0.71-1.46)	1.00 (0.70-1.42)
CSC ^c	1.21 (0.93-1.37)	1.24 (0.95-1.62)	1.89 (1.39-2.59)***	1.71 (1.26-2.33)**
Disadvantaged	0.95 (0.72-1.26)	1.03 (0.78-1.37)	0.80 (0.53-1.21)	0.90 (0.60-1.36)
Middle	0.86 (0.64-1.15)	1.05 (0.78-1.43)	0.58 (0.40-0.84)**	0.73 (0.50-1.07)
Advantaged	0.76 (0.51-1.14)	1.00 (0.65-1.52)	0.57 (0.35-0.92)*	0.84 (0.51-1.38)
Most advantaged	0.44 (0.19-1.07)	0.71 (0.29-1.72)	0.40 (0.13-1.26)	0.72 (0.23-2.27)
Education ^d				
Secondary		1.35 (0.95-1.92)		1.12 (0.67-1.87)
Primary		1.39 (0.94-2.05)		1.07 (0.58-1.97)
Main Occupational Position ^e				
Low skill		0.91 (0.64-1.28)		1.32 (0.90-1.93)
Never worked		0.71 (0.47-1.08)		1.26 (0.43-3.71)
Satisfaction with household income ^f				
Fairly easily		1.12 (0.81-1.54)		0.98 (0.64-1.50)
With some difficulty		1.48 (1.08-2.03)*		1.81 (1.18-2.78)**
With great difficulty		2.59 (1.81-3.72)***		3.71 (2.19-6.30)***
Interactions				
Age x at least one ACE ^a	1.14 (0.98-1.32)	1.15 (0.99-1.34)	1.00 (0.82-1.23)	1.00 (0.82-1.23)
Age x at least one ACHE ^b	1.02 (0.87-1.19)	1.00 (0.86-1.17)	0.77 (0.63-0.93)**	0.80 (0.66-0.97)*
Age x CSC ^c				
Age x Disadvantaged	0.90 (0.78-1.05)	0.90 (0.78-1.05)	0.82 (0.65-1.03)	0.84 (0.67-1.07)
Age x Middle	0.89 (0.76-1.05)	0.92 (0.78-1.09)	0.80 (0.65-0.99)*	0.84 (0.67-1.05)
Age x Advantaged	1.02 (0.80-1.29)	1.12 (0.87-1.44)	0.75 (0.56-1.00)*	0.75 (0.56-1.01)

Age x Most advantaged	1.07 (0.67-1.70)	1.19 (0.73-1.93)	0.88 (0.45-1.71)	0.84 (0.43-1.64)
Age x Education ^d				
Age x Secondary		1.00 (0.79-1.25)		1.01 (0.75-1.37)
Age x Primary		1.15 (0.90-1.46)		1.16 (0.81-1.65)
Age x Main occupational position ^e				
Age x Low skill		1.05 (0.86-1.29)		0.94 (0.74-1.17)
Age x Never worked		1.20 (0.95-1.52)		1.46 (0.76-2.80)
Age x Satisfaction with household income ^f				
Age x Fairly easily		0.95 (0.80-1.14)		1.00 (0.79-1.28)
Age x With some difficulty		1.05 (0.88-1.26)		0.85 (0.61-1.18)
Age x With great difficulty		0.99 (0.81-1.21)		0.87 (0.68-1.11)

Note. ACE, adverse childhood experiences; ACHE, adverse childhood health experiences; CI, confidence interval; CSC, childhood socioeconomic conditions; OR, odds ratio. All models are adjusted for sex, birth cohort and attrition. Age was centered at 50 y and divided by 10 so that the coefficients yielded the effects for a 10-year period. N Southern European = 6577, N Eastern European = 3137.

^aAdverse childhood experiences, reference category none

^bAdverse childhood health experiences, reference category none

^cChildhood socioeconomic conditions, reference category most disadvantaged

^dEducation, reference category tertiary

^eMain occupational position, reference category high skill

^fSatisfaction with household income, reference category easily

*** $p < .001$, ** $p < .01$, * $p < .05$

Table S4. Fully adjusted associations (health- and lifestyle variables) of childhood misfortune and adult-life socioeconomic circumstances with level and trajectories of frailty at old age for total and stratified sample by welfare regime

	Total Sample		Scandinavian		Bismarckian		Southern European		Eastern European	
	M3b	OR (95% CI)	M3b	OR (95% CI)	M3b	OR (95% CI)	M3b	OR (95% CI)	M3b	OR (95% CI)
Age (10-y period)										
At least one ACE ^a	1.90 (1.68-2.14)***		1.75 (1.21-2.54)**		2.12 (1.76-2.57)***		1.59 (1.20-2.11)**		2.02 (1.40-2.93)***	
At least one ACHE ^b	1.19 (1.05-1.35)**		1.84 (1.36-2.47)***		1.33 (1.11-1.60)**		0.86 (0.64-1.14)		0.94 (0.67-1.33)	
At least one ACHE ^b	1.26 (1.13-1.41)***		1.06 (0.81-1.38)		1.35 (1.15-1.58)***		1.11 (0.86-1.44)		1.49 (1.11-2.01)**	
CSC ^c										
Disadvantaged	0.99 (0.83-1.18)		0.94 (0.40-2.22)		1.15 (0.83-1.61)		1.04 (0.80-1.37)		0.87 (0.59-1.30)	
Middle	1.01 (0.85-1.21)		1.05 (0.47-2.37)		1.17 (0.85-1.62)		1.08 (0.80-1.45)		0.78 (0.54-1.13)	
Advantaged	1.17 (0.96-1.42)		1.02 (0.45-2.32)		1.61 (1.15-2.25)**		0.98 (0.65-1.48)		0.93 (0.58-1.50)	
Most advantaged	0.89 (0.69-1.16)		0.55 (0.23-1.34)		1.40 (0.94-2.09)		0.65 (0.28-1.55)		1.00 (0.33-3.00)	
Education ^d										
Secondary	1.11 (0.97-1.27)		1.07 (0.79-1.44)		1.12 (0.93-1.36)		1.18 (0.84-1.66)		1.24 (0.76-2.03)	
Primary	1.21 (1.01-1.46)*		0.60 (0.36-0.98)*		1.60 (1.19-2.13)*		1.10 (0.76-1.61)		1.17 (0.65-2.12)	
Main Occupational Position ^e										
Low skill	1.08 (0.95-1.23)		1.43 (1.07-1.91)*		0.98 (0.81-1.18)		0.88 (0.63-1.23)		1.31 (0.91-1.89)	
Never worked	1.14 (0.89-1.45)		1.06 (0.17-6.63)		1.50 (0.90-2.52)		0.75 (0.50-1.13)		1.57 (0.55-4.45)	
Satisfaction with household income ^f										
Fairly easily	1.35 (1.19-1.53)***		1.40 (1.03-1.89)*		1.49 (1.26-1.77)***		1.14 (0.84-1.56)		0.98 (0.65-1.49)	
With some difficulty	2.01 (1.74-2.32)***		2.09 (1.20-3.63)**		2.44 (1.93-3.09)***		1.48 (1.09-2.00)*		1.60 (1.06-2.42)*	
With great difficulty	3.45 (2.84-4.19)***		2.58 (0.87-7.67)		4.99 (3.46-7.18)***		2.48 (1.75-3.51)***		2.57 (1.54-4.30)***	
Interactions										
Age x at least one ACE ^a	0.97 (0.91-1.04)		0.76 (0.65-0.89)**		0.93 (0.85-1.03)		1.17 (1.01-1.36)*		1.02 (0.84-1.25)	
Age x at least one ACHE ^b	0.93 (0.88-0.99)*		1.02 (0.89-1.18)		0.92 (0.84-1.01)		1.03 (0.88-1.20)		0.83 (0.69-1.00)*	
Age x CSC ^c										
Age x Disadvantaged	0.92 (0.85-1.01)		1.01 (0.71-1.43)		0.95 (0.81-1.11)		0.91 (0.79-1.05)		0.87 (0.69-1.09)	
Age x Middle	0.89 (0.81-0.97)**		0.89 (0.64-1.25)		0.94 (0.81-1.09)		0.93 (0.79-1.09)		0.84 (0.68-1.04)	
Age x Advantaged	0.84 (0.75-0.92)**		0.89 (0.63-1.25)		0.81 (0.69-0.96)*		1.14 (0.89-1.46)		0.74 (0.56-0.99)*	

Age x Most advantaged						
Age x Education ^d	0.97 (0.84-1.12)	1.15 (0.78-1.71)	0.91 (0.75-1.12)	1.28 (0.80-2.06)	0.87 (0.46-1.66)	
Age x Secondary	1.00 (0.92-1.08)	0.81 (0.67-0.99)*	0.98 (0.87-1.09)	1.04 (0.83-1.30)	0.97 (0.73-1.29)	
Age x Primary	1.08 (0.98-1.19)	0.81 (0.64-1.02)	0.97 (0.83-1.12)	1.20 (0.95-1.52)	1.11 (0.79-1.57)	
Age x Main occupational position ^e						
Age x Low skill	1.03 (0.96-1.11)	0.90 (0.77-1.06)	1.08 (0.97-1.20)	1.08 (0.89-1.32)	0.93 (0.74-1.16)	
Age x Never worked	1.14 (1.01-1.30)*	1.22 (0.57-2.63)	1.02 (0.81-1.28)	1.20 (0.95-1.51)	1.28 (0.68-2.41)	
Age x Satisfaction with household income ^f						
Age x Fairly easily	1.03 (0.96-1.10)	1.03 (0.88-1.20)	0.99 (0.90-1.08)	0.96 (0.80-1.14)	0.97 (0.77-1.22)	
Age x With some difficulty	0.96 (0.86-1.07)	0.93 (0.71-1.21)	0.88 (0.78-1.01)	1.02 (0.86-1.21)	0.86 (0.68-1.09)	
Age x With great difficulty	1.00 (0.93-1.08)	1.08 (0.60-1.95)	0.74 (0.60-0.92)**	0.96 (0.79-1.17)	0.90 (0.67-1.28)	

Note. ACE, adverse childhood experiences; ACHE, adverse childhood health experiences; CI, confidence interval; CSC, childhood socioeconomic conditions; OR, odds ratio. All models are adjusted for sex, birth cohort, attrition, living with a partner, delayed recall memory, verbal fluency, smoking, number of chronic conditions, difficulties with activities of daily living, and difficulties with instrumental activities of daily living. Age was centered at 50 y and divided by 10 so that the coefficients yielded the effects for a 10-year period. N total sample = 23358, N Scandinavian = 3590, N Bismarkian = 10054, N Southern European = 6577, N Eastern European = 3137.

^aAdverse childhood experiences, reference category none

^bAdverse childhood health experiences, reference category none

^cChildhood socioeconomic conditions, reference category most disadvantaged

^dEducation, reference category tertiary

^eMain occupational position, reference category high skill

^fSatisfaction with household income, reference category easily

***p<0.01, **p<.01, *p<.05

Chapter 5. General Discussion

As the numbers and proportions of people who are over the age of 60 is increasing worldwide, also a rise of chronic conditions and multimorbidity is also expected (United Nations, 2019; World Health Organization, 2015). However, biological and environmental factors, socioeconomic conditions, and health behaviours lead to a different ageing process for every individual, thereby causing health inequalities that are unequally distributed among the population (M. Marmot et al., 2008; World Health Organization Commission on social determinants of health, 2008). The main aim of this thesis was to study associations of socioeconomic conditions with health outcomes in later life using a life course perspective to take into account different causal mechanisms and processes that underlie these inequalities. To investigate these life course trajectories, data from the longitudinal Survey of Health, Ageing, and Retirement in Europe (SHARE) were used. To our knowledge, our studies on the associations of childhood socioeconomic conditions (CSC) with cancer and frailty in later life were the first longitudinal European study to analyse this association directly as well as via pathways exploring the role of adulthood socioeconomic conditions (ASC) as a mediator. In addition, we were the first to study associations of childhood misfortune and ASC with frailty at older age. Furthermore, this was the first time that the influence of welfare regimes on these associations was studied.

Within this chapter, I provide an overview of our main results and discuss several methodological considerations. After that, I will speculate on the potential policy implications of this research and provide recommendations for future studies in this area.

5.1 Main findings

Within this section, we will first summarize the main findings of Chapters 2-4. After this, we will discuss how our findings support the life course perspective and the cumulative dis/advantage theory.

5.1.1 Summary of main findings

Table 1 provides a qualitative summary of the main findings of Chapters 2-4. In **Chapter 2** of this thesis, we examined associations of CSC with cancer in later life and the possible mediating effect of ASC on this association. For overall cancer, both men and women of the lowest CSC categories (the most disadvantaged and disadvantaged) were most likely to be cancer-free over time. Compared with women with the most disadvantaged CSC, women with advantaged and middle CSC were more likely to have had skin cancer and women with the most advantaged CSC were more likely to have had breast cancer. Compared with men from the most disadvantaged CSC, men with middle CSC were less likely to have had colon or rectal cancer. No mediating effects of ASC were found.

In **Chapter 3**, we studied associations of CSC and ASC with frailty as outcome. Results showed a gradient between CSC and the odds of being frail in both men and women. Compared to women with the most advantaged CSC, women with the most disadvantaged and disadvantaged CSC were more likely to be frail. Apart from men in the advantaged CSC, all other categories were more likely to be frail compared with men from the most advantaged CSC. In addition, ASC mediated the effects of CSC on the odds of being frail.

Finally, in **Chapter 4** we investigated associations of childhood misfortune (CSC, adverse childhood experiences, and adverse childhood health experiences) with frailty at older age and whether ASC mediate this effect. In addition, we looked at differences in these associations between welfare regimes. Overall, results showed that compared with people from the most disadvantaged CSC, individuals

from all other CSC categories were less likely to become frail. In addition, people who experienced at least one adverse childhood experience or at least one adverse childhood health experience were more likely to be frail compared with people who had experienced none. ASC were mediating all associations of CSC with frailty, but not of the adverse experiences with frailty. Moreover, results varied between the welfare regimes. Significant associations between CSC and frailty were only found in the Eastern European welfare regime where, compared with the most disadvantaged CSC, people from the disadvantaged and middle CSC were less likely to become frail. The significant association of adverse childhood experiences with frailty found in the overall sample was still present in the Scandinavian and Bismarckian welfare regimes and the association of adverse childhood health experiences with frailty was present in the Bismarckian and Eastern European welfare regimes. ASC were mediating the associations of CSC with frailty in the Eastern European welfare regime where the association disappeared. However, an association appeared in the Bismarckian welfare regime where the advantaged CSC showed higher odds of being frail compared to the most disadvantaged. Again, ASC were not mediating the associations of adverse experiences with frailty.

5.1.2 How do the findings support the theories

Altogether, for the life course perspective, the results of the research described in Chapters 2-4 were in line with our prior hypotheses that early life socioeconomic conditions influence health in later life, either positively or negatively depending on risk factors for the specific health outcomes. These findings confirm the life course perspective suggesting that health at adult ages is partly determined by early life conditions. For frailty, we expected to find an association between higher disadvantage and an increased risk of becoming frail, which was found in Chapters 3 and 4. In addition, Chapter 4 supported our hypothesis that apart from CSC, also other factors in early life, i.e. experiencing adverse childhood experiences and adverse childhood health experiences, have a negative influence on becoming frail in later life.

Results contribute to the theoretical model by showing that not only early life status influence health, but also early life experiences. Moreover, concerning the life course principle of time and place, the regional and social context have been shown to lead to variation in health outcomes. One important aspect is the welfare regime where an individual is growing up as this is expected to influence health outcomes through roles of the state, family, and market in welfare provision (Eikemo et al., 2008; Gøsta Esping-Andersen, 1990). Chapter 4 proved that this macro level factor, i.e. the welfare regime, has an influence on associations of childhood circumstances and frailty in later life, as the results showed that the associations differed between the welfare regimes. As supported by other studies, the Scandinavian welfare regime is the most beneficial for population health as it is characterized by a generous and universal welfare provision through income redistribution and low unemployment (Dahl, Ivar Elstad, Hofoss, & Martin-Mollard, 2006; Ferrie, Shipley, Stansfeld, & Marmot, 2002). This leads to higher protection against the association between lower socioeconomic conditions and worse health outcomes (Eikemo et al., 2008). In contrast, the Bismarckian regime is known for transferring initial inequalities into adulthood and old age. Our results showed that this regime was least able to deal with cumulative disadvantage, where even growing differences between low and high skilled workers in the odds of being (pre-)frailt were found.

Since the Bismarckian and Scandinavian welfare regimes have been relatively well-documented and stable across time, it might be fairly easy to interpret these regimes and their effects on health across the life course. However, the Southern and Eastern European regimes are historically speaking more difficult to understand. The Southern nations have evolved from dictatorship (in Portugal, Spain, and Greece) to democratic regimes, and since being included in the European Union, those countries have seen great development. The Southern welfare regime is usually negatively perceived and associated with familism but also nepotism (Andreotti et al., 2001; Petmesidou, 1996). Despite this bad reputation, results show that this regime does relatively well in terms of health outcomes compared to for example the Bismarckian regime. Results for Eastern

Europe are a bit less clear, which is not necessarily a surprise. Indeed, the Eastern European regime used to be egalitarian in terms of education and health, but was disrupted after the fall of the Soviet regime and then reconstructed to a more neoliberal one (Dale & Fabry, 2018). It goes beyond the objectives of this thesis to study in-depth the history of these welfare regimes and how their historical trajectories affect individual health in old age, but this is for sure an interesting starting point for future research.

Considering more specifically the cumulative dis/advantage (CDA) theory, in contrast to our hypotheses that adult socioeconomic conditions (ASC) mediate the associations of early life conditions with health in later life, we overall did not find this effect for cancer outcomes in Chapter 2 nor for the adverse childhood experiences and adverse childhood health experiences in Chapter 4. Nevertheless, results from Chapters 3 and 4 on associations of CSC with frailty show an effect, indicating that ASC do mediate this association, i.e. ASC capture the cumulative disadvantage produced by CSC. Conceptually for the CDA theory, after the age of 50, differences in frailty trajectories by childhood misfortune and ASC, apart from occupational position, were narrowing, which does not support the CDA theory.

5.2 Methodological considerations

Within this section, we discuss methodological considerations associated with the research described in this thesis. First, we discuss issues concerning attrition and how we tried to limit the potential impact (Chapters 2-4). Second, we describe how selection bias might have affected our results (Chapters 2-4). Third, we consider that the design of SHARE has potentially influenced our ability to draw conclusions about the causal nature of relationships of socioeconomic conditions with cancer (Chapter 2). Fourth, we discuss several issues concerning the measurement of cancer (Chapter 2), socioeconomic conditions (Chapters 2-4), childhood misfortune (Chapter 4), our measurement and operationalisation of frailty (Chapters 3 and 4) and adverse childhood experiences (Chapter 4), and the lack

of data on important potential confounders (Chapters 2-4). Fifth, we provide our perspective on the sample size of our study and its associated power to detect associations (Chapters 2 and 4). Sixth, we discuss how confounding and effect modification might have influenced our results (Chapters 2-4).

5.2.1 Attrition

A frequent issue in longitudinal studies is attrition. Attrition occurs when participants leave during a study due to drop out, death, or loss to follow-up (Z. Hill, 2004). This leads to missing data that may influence the results, for example due to systematic differences between respondents who drop out compared to those who continue. The risk is that the remaining sample is no longer a good representation of the population (Z. Hill, 2004). Several studies already showed that socio-demographic variables such as age, employment status, and partnership are correlated to survey participatory behaviour (Groves & Couper, 1996; Nicoletti & Peracchi, 2005; Stoop, 2005). In addition, healthy participants are more likely to continue their participation (Gray, Campanelli, Deepchand, & Prescott-Clarke, 1996; Lipps, 2007).

To limit the effect of attrition bias on our results, we only included respondents who participated in the third wave (SHARELIFE for retrospective life course information) and at least one other wave; in the Chapters on frailty, we included participants with at least three complete measures of frailty. In addition, we included attrition in all models thus adjusting for mediator-outcome confounding. However, this statistical adjustment does not solve the issue of missing data due to attrition. Yet, several studies showed that the effect of attrition bias on associations of health with socioeconomic conditions is negligible (Carter, Imlach-Gunasekara, McKenzie, & Blakely, 2012; Contoyannis, Jones, & Rice, 2004; Powers & Loxton, 2010; Reinhardt, Hussey, & Anderson, 2002). Moreover, techniques to correct for attrition, such as multiple imputation for missing outcome data or using longitudinal weights, have been shown to make little difference

(Jones, Koolman, & Rice, 2006; Lewin, Brondeel, Benmarhnia, Thomas, & Chaix, 2018).

5.2.2 Selection bias

Selection bias occurs when the relation between exposure and outcome is different for the participants included in the study compared to all the individuals theoretically eligible for the study, including those who did not participate or those who dropped out (Rothman, Greenland, & Lash, 2008e). This type of bias is a result of the procedure used to select participants and of factors that influence study participation. It occurs when the chances to be included in the study population and to continue participation in the study are associated with the exposure and/or outcome under investigation (Bouter, van Dongen, & Zielhuis, 2005; Rothman et al., 2008e). However, we think this has not biased the findings described in Chapters 2-4. For selecting the sample of the first wave of SHARE, sampling procedures and calibrated design weights were determined to accomplish probability samples to infer objectively from the sample to the finite population of Europeans aged 50 years and older or to subgroups thereof (Klevmarken, 2005).

One type of selection bias is survivor bias, which occurs when there is selective survival of participants that is related to the exposure and factors that are also related to the outcome (Rothman, Greenland, & Lash, 2008f). The design of SHARE is impeded by this survivor bias by including respondent aged 50 years old and older at baseline. It is possible that people with an unhealthier lifestyle and comorbidities had already died before inclusion and could therefore not participate. This survivor bias will be especially relevant in Chapter 2 on cancer, as selective survival of cancer survivors is likely to influence longitudinal associations, especially among the oldest old. However, this bias is limited because the probability of dying from cancer before age 50 is low and the overall cancer death rate in Europe is decreasing (Malvezzi et al., 2015; Siegel et al., 2018).

5.2.3 Causality

An observed association between two variables can only be considered as a causation when the temporality of the association is substantiated. In 1965, the English epidemiologist Sir Austin Bradford Hill proposed his famous and widely-used viewpoints or perspectives for causation (A. B. Hill, 1965). The nine criteria to provide epidemiologic evidence for causality are strength, consistency, specificity, temporality, biological gradient, plausibility, coherence, experiment, and analogy. Even though these criteria are widely accepted, they have also been criticized (Glass, Goodman, Hernan, & Samet, 2013). However, the criteria are useful to test causality and aid in explaining the data using scientific deduction.

The temporality criterion, that proposes that the effect needs to occur after the cause, for a causal relation to be present (Bocquier, 1996), is definitely a prerequisite for a causal relationship. Prospective data can give insight in the temporality of associations. Because both the exposure and outcome are repeatedly measured, it is possible to determine whether a baseline level of a certain exposure is associated with the outcome at a later point in time. By using the longitudinal data from SHARE we were able to speak of causality in the studied associations, since childhood conditions, as exposure, occurred before the health outcomes. Also in the case of frailty, the three ASC occurred before the onset of frailty. However, the life course span of ASC may raise questions of causality, as cancer onset may have occurred before either one of the ASC. We verified for each of the ASC whether temporality may have been an issue that influenced our results. Twenty-three participants reported cancer before the age of 30 and 44 before the age of 50, so it is reasonable to assume that reverse causality on education and main occupation will not bias the results. Concerning satisfaction with income (a time-varying mediator measured at each wave, i.e. at age 50 and later), it is reasonable to think that a part of the income and cancer onset association is influenced by reverse association (i.e. cancer causes income to decrease). We preferred keeping this important measure of ASCs in the analyses. This temporality issue should reinforce the effect size of income because the reverse causation association is probably stronger than the direct

causation (i.e. income causes cancer). If the association of income and cancer is overestimated, then the mediating effect of income on the association of CSCs and cancer should also be overestimated. Thus, still finding an association between CSCs and cancer after adjusting for income is a strong sign of the independent impact of CSCs on later health.

For the other eight criteria, coherence and experiment are not applicable, as our results cannot be reproduced in laboratory experiments. Regarding strength, some of the associations were rather large, thus strengthening the likelihood of causality. For consistency, several studies by different research groups on different samples found similar results, which makes the effect more likely to be true. Concerning specificity, as many factors could influence the associations of socioeconomic conditions on health in later life and we were not able to consider all of them, nor to select a specific population, we cannot guarantee the probability of a causal relationship. Regarding the biological gradient, or dose-response relationship, we could consider the five CSC as dose. In this case, our results show that, depending on the health outcome, the higher the (dis)advantage, the higher the likelihood of getting cancer or becoming (pre-)frail. For plausibility, literature suggested models that could explain an association of socioeconomic conditions with health outcomes in later life. However, we cannot demonstrate biological plausibility as the interplay between many different factors is too complex. Finally, when considering analogy, we can compare our results to similar studies on socioeconomic conditions and health in later life, that for example looked at different health outcomes or indicators of socioeconomic conditions. As we discussed our results in light of other studies that found similar results, mainly using different health outcomes, we can be more confident in the associations presented in our studies.

In conclusion, our results should be interpreted with caution, but in combination with evidence from the literature, they suggest that early-life conditions influence health in later life and that ASC may mediate this association.

5.2.4 Quality of measurements and information bias

Within the research described in Chapter 2-4 of this thesis, many variables were measured and analysed. Almost no measurement is perfect, i.e. free from measurement error. As a result, potential errors in our study measurements could have resulted in biased estimates of the associations. If these errors were different in subgroups of our study population, with regard to the exposures and/or outcome under study, this would be considered as information bias or misclassification (Althubaiti, 2016; Rothman, Greenland, & Lash, 2008c). Within this sub-section, we describe some considerations regarding the measurement of cancer, socioeconomic conditions, childhood misfortune, and our measurement and operationalisation of frailty and adverse childhood experiences in our study, and how the properties of the applied methods could have influenced our results.

Self-reporting bias

All measures were self-reported. However, self-reported data are often considered as not completely reliable and may be limited by measurement error and bias due to potentially underreporting or misreporting (Althubaiti, 2016). For frailty, the attributes shrinking, exhaustion, slowness and low activity were based on questions available in SHARE, because no actual tests were performed. For weakness, actual grip strength measures were performed. Still, the questions used were adapted and validated to SHARE (Macklai et al., 2013; Romero-Ortuno, 2013). For cancer diagnosis, data from cancer registries would have been more reliable than self-reported. Nevertheless, previous studies found an overall rate of false-negative self-reporting of 39.2%, with a wide variation by cancer site (Desai et al., 2001). Older age may also be associated with more frequent false-positive reporting (Loh et al., 2014). Yet, studies showed that respondents can accurately report a past cancer diagnosis, especially for breast, prostate and colon cancer, with an overall sensitivity of self-reported cancer of up to 89% (Bergmann et al., 1998; Loh et al., 2014).

Recall bias

Information on CSC, ASC, and childhood misfortune was measured retrospectively. The data may therefore be subject to recall bias: respondents incorrectly provide answers based on their ability to recall a past event (Althubaiti, 2016). However, this type of bias is more common in dietary surveys. Even though the length of the recall period is long, previous research found evidence for the accuracy of recall of simple measures of socioeconomic conditions in a survey of older adults (Lacey et al., 2012). Also research on adverse experiences showed that recall measures were adequately valid in older adults (Barboza Solís et al., 2015). In addition, questions on socioeconomic conditions and adversity are private and sensitive topics and may be affected by trauma or social desirability bias: an external bias caused by social desirability or approval (Althubaiti, 2016). However, data collection and its subsequent analysis was anonymous, thereby limiting this type of bias.

Operationalisation

In the social science and medical literature, frailty has been defined and operationalised differently, which may lead to different estimates of frailty. In Chapters 3 and 4, we used the same operationalisation, which has also been used in several other SHARE studies, making it easier to compare these results. Additionally, we have combined the pre-frail and the frail categories instead of comparing all three groups or using a sum score. Sensitivity analyses did not find changes to the main results, thus we are confident about the results we found.

Like frailty, adverse childhood experiences have been measured and operationalised differently across studies. In our research, we wanted to look at the overall effect of adverse childhood experiences and not at the specific effects of each indicator. In addition, combining these different indicators into an overall score has been done in previous studies with consistent results (Cheval et al., 2019).

5.2.5 Sample size and power

The power of a study can be defined as ‘the ability to detect a certain effect size’ (Field, 2009). This is the inverse of a type 2 error, which occurs when in reality there is an effect, but the researchers conclude there is no effect (Field, 2009; Petrie & Sabin, 2005). Next to other factors, such as the variability of the variables within the study population and the significance level, the power of a study is determined by its sample size (Petrie & Sabin, 2005). The larger the sample size, the higher the power of a study to detect a certain effect.

Our sample sizes were sufficient to draw convincing conclusions for overall cancer and frailty. However, when our sample was stratified, such as by CSC for site-specific cancers and by welfare regimes, we may have had insufficient power to detect significant associations of socioeconomic conditions with health in later life. In these cases, when no associations were observed which were expected, it can be questioned whether this could be due to a lower power caused by a limited sample size.

5.2.6 Confounding and effect modification

Associations of socioeconomic conditions with health in later life can be influenced by several socio-demographic and clinical factors. In our analyses of Chapters 2-4, we tried to include possible confounding and effect modifying factors identified in previous literature. However, in SHARE, not all information on cancer and frailty risk factors and confounders, such as late-life adverse events or genetics, was available.

Confounding

One of the main threats for the validity of observational studies, in this case investigating associations of socioeconomic conditions (exposure) with cancer or frailty (outcome), is confounding. A definition of confounding is ‘the distortion of an apparent effect of an exposure on an outcome, because the effect of

extraneous factors is mistaken for, or mixed with, the actual exposure effect' (Rothman, Greenland, & Lash, 2008a). Confounding can be explained as the presence of factors that influence the outcome being studied (e.g. cancer or frailty), which are not equally divided among the exposure groups compared (e.g. different categories of CSC). Therefore, one cannot simply compare the exposure groups in terms of the outcome, as this will lead to biased results: apart from the exposure being studied, there are other factors that cause differences in the outcome between the groups. A solution to this problem is that these potential confounding factors need to be adjusted for during data analyses (McNamee, 2005). In order to perform these adjustments, it needs to be determined, based on theoretical knowledge about potential confounders, which factors are potential confounders for the relation being studied before performing the analyses (Lee, 2014; McNamee, 2005). There are some general conditions for a variable to be a confounder: it needs to be (1) associated with both the exposure and the outcome (the outcome being independent from the exposure), but (2) influenced by neither the exposure nor the outcome (Rothman et al., 2008a). This second condition suggests that a factor is not considered as a confounder when it is an intermediate between the exposure and the outcome, i.e. when the factor is on the causal pathway from exposure to outcome. Causal diagrams can be used to explore whether a certain factor could be a potential confounder, based on hypothesized associations with the exposure and outcome, and the direction of these associations.

Based on our hypotheses regarding potential confounding factors for the research questions studied based on previous literature, we identified a set of potential confounders in Chapters 2-4 and included these as covariates in our models. However, in SHARE, not all information on cancer and frailty risk factors and confounders was available, such as late-life adverse events or genetics. As a result, we might have missed potentially relevant confounders, which could have resulted in residual confounding, i.e. confounding still present after multivariable adjustment (Rothman, Greenland, & Lash, 2008d).

Effect modification

In addition to confounding, we also explored if and how effect modification could have influenced the associations studied. Effect modification occurs when there is variation in the effect of an exposure on an outcome across levels of another variable (Knol & VanderWeele, 2012; Rothman, Greenland, & Lash, 2008b). In other words, the direction and/or strength of an association of a certain exposure (e.g. CSC) with an outcome (e.g. cancer or frailty) is different in separate groups of the total study population (e.g. in men and women). For each of the investigated exposures in Chapters 2-4 we identified potential effect modifiers, including sex (Chapters 2 and 3) and welfare regime (Chapter 4).

To explore effect modification within our analyses by potential effect modifying factors, we performed stratified analyses within Chapters 2-4. We saw some interesting differences in associations of CSC with health in later life. For example in Chapter 2, we observed different patterns between men and women in site-specific cancer occurrence and within Chapter 3, the gradient of frailty differed. Additionally, in Chapter 4, when stratifying by welfare regime, some clear differences were detected. Unfortunately, since stratification leads to reduced sample sizes in the strata, we were not able to perform certain stratified analyses (e.g. when stratifying for certain site-specific cancers) or might have been unable to detect associations.

5.3 Theoretical and policy implications

In Chapter 1, one of the general theories of health inequalities was brought forward: the life course perspective. The results of this thesis can be related to these theories. The research in this thesis was focused on the life course and our results support the idea that early life conditions influence health in later life. Our results did not confirm a cumulative dis/advantage, but rather showed that socioeconomic conditions during life have the potential to change an unfavourable

pathway. This is an interesting finding, because for wealth we know that safety-net benefits buffer inequalities in old age, but for health, it is new that in this social gradient we do not see a decline. Our results thus offer new insights in the theories and could help in improving these theories on health inequalities. We showed that the life course is important for health in old age, but that early life experiences are likely more influential. In addition, as our results offer new insights and contribute to the literature, they are starting points for future research on health inequalities and ageing. Some ideas will be further discussed in section 5.4.

The findings of the research described in this thesis provide some new clues for promising targets for interventions to reduce health inequalities which need further investigation. Our results give evidence of an influence of ASC on health in later life, but show an even stronger effect of the long-term impact of childhood disadvantage. This indicates that in order to improve health later in life as well as to improve health trajectories from an early age, it is important to invest in early life conditions. Especially when looking at the results of Article 3 on welfare regimes, it seems that certain regimes have a stronger beneficial effect. For example, the Scandinavian welfare regime seems to cancel the negative effect of early-life on later life health. Investing in life conditions may on the long term therefore be very efficient. When developing policies, it may be beneficial to look at the promising effects of strategies that work in other regimes. This may help in decreasing health inequalities and improving socioeconomic conditions in adulthood, which has beneficial effects across the life course and across welfare regimes and may help in reducing the impact of disadvantaged early life conditions on health inequalities. In addition, early interventions are expected to aid in improving quality of life and reducing costs of care in (pre-)frail individuals (Buckinx et al., 2015).

We need to keep in mind that the cohort studied grew up under certain conditions that in the meantime likely have already changed. Still, identifying subpopulations and determinants that influenced health are likely nowadays at a higher risk and thus need to be watched. In addition, the results can have an impact on current

policy making. For example, our study on the impact of different welfare regimes on frailty showed clear differences. This indicates that certain welfare regimes have the potential to improve their policy and welfare provision in order to improve health and to reduce health inequalities. In theory, all welfare regimes have various strategies to address (health) inequalities in different extents (Gøsta Esping-Andersen, 1990). Different aspects of the welfare regimes may influence public health and thereby explain the variation in health inequalities between the different regimes. Characteristics such as the extent to which an individual's welfare relies upon the market and the accessibility and availability of welfare services are important factors that could help in understanding the differences (Bambra, 2005; Eikemo et al., 2008).

5.4 Recommendations for future research

To eventually be able to reduce health inequalities and implement effective and tailored interventions and health policies, we recommend some points for future research, based on the results of the research described in this thesis. First, we suggest that these studies use different, and if possible objective, measurements to accurately measure important variables. Second, we recommend that studies are needed to investigate potential high-risk groups. Third, it would be useful that future studies will investigate several important life course influences with health in later life to identify other possible pathways. Fourth, the research in this thesis focuses on European countries, but ageing trajectories in low-income countries are poorly documented and understood. Future studies in a low-income context could identify ageing patterns and its challenges.

5.4.1 Data quality

As discussed earlier, SHARE has some limitations. For some variables, having objective methods to accurately measure them could improve the quality of data. For example, for frailty, actual tests could be performed to measure the attributes

shrinking, exhaustion, slowness and low activity instead of using questions. For information on health or demographic variables, registry data is often available, which is more reliable than self-reported data. In addition, in contrast to SHARE which is already remarkable since it is a retrospective longitudinal study, birth cohort studies, such as the Lothian Birth Cohorts, have the advantage of being prospective on the long-term and thus overcome the disadvantage of having retrospective information on childhood and other life course information from before baseline.

5.4.2 Detect risk groups

In order to target groups in the population that are at high-risk of developing health problems, it is important to identify them. Future studies are warranted to for example examine the relation of CSC with cancers by site and of CSC with frailty by welfare regime in a larger sample to increase power. In Chapter 4, differences across welfare regime were found, showing that the Scandinavian welfare regime seems to be most equal. However, when looking at life expectancy, Spain, as one of the Southern European welfare states, has a higher life expectancy. Future studies could explore this paradox in more detail by looking into different pathways and risk factors. As discussed earlier, the Bismarckian and Scandinavian welfare regimes have been relatively stable across time and are well known. The Eastern and Southern regimes are more difficult to explore and it was beyond this thesis to study the history of these regimes. For future research it would be interesting to further disentangle the effects of the different regimes, especially for the Southern and Eastern European welfare regimes.

Risk stratification is often used in health care for categorizing patients to optimize care management. Assigning risk levels based on people's objective and subjective individual characteristics, makes it easier to make better use of limited resources, anticipate needs, and proactively manage and involve a population or specific groups of the population (Dom Dera, 2019). We are however aware that

this kind of analyses require large sample sizes so that vulnerable sub-populations are large enough to establish robust results.

5.4.3 Life course influences and pathways

More information on health behaviours and risk exposures is needed to explore potential pathways. First, we have studied the influences of early life conditions and experiences, but for future research it might also be interesting to study the interaction between CSC and ACE. Second, as mentioned earlier, SHARE does not provide all information on cancer and frailty risk factors and confounders. As a result, we were not able to (1) fully control all models, which may have led to residual confounding, and (2) explore different underlying pathways of early life conditions to health in later life. In addition to studying the effects of socioeconomic conditions on health, future studies could study biological mechanisms. For example, experiencing poor health in later life could be associated with the presence of specific biomarkers, which could in turn be accelerated by specific life course influences, such as socioeconomic conditions. Identifying risk factors could prevent the process of deteriorating health. For example for frailty, some research has already found associations with decreased sex hormone levels (Carcaillon et al., 2012). These hormones are important for body mass, muscle strength and bone mineral density, and have a suppressive effect on inflammatory cytokines (Malkin et al., 2004; Mekli, Marshall, Nazroo, Vanhoutte, & Pendleton, 2015). One cross-sectional study already found that the higher the frailty status, the higher the levels of tumour necrosis factor (Hubbard, O'Mahony, Savva, Calver, & Woodhouse, 2009). Studying this further can provide more insight in the mechanisms that could be involved in the associations of early life and health in later life. For example, taking into account biological variation when studying associations of childhood conditions with health in later life might shed light on possible biological pathways, following the sensitive or critical period model, where early stress influences biological functioning, or on how socioeconomic conditions may moderate genetic risk (Moorman, Carr, & Greenfield, 2018; South, Schafer, & Ferraro, 2015).

5.4.4 Expand research to low-income ageing population

In sub-Saharan Africa, the growth rate of the population aged 60 years and over is expected to increase from 2% per year to over 4% during the next 45 years. This equals 4-times the growth rate in the developed countries, implying many challenges for societies that are among the poorest of the world. The 'quality' of the added years of life is one of those challenges. Research on ageing and its consequences in low-income countries is lacking. In the South, global ageing is leading to a rising chronic disease burden, which in turn impacts poor health, disability and poverty, thereby limiting development in low- and middle-income countries ("Global, regional, and national disability-adjusted life-years (DALYs) for 359 diseases and injuries and healthy life expectancy (HALE) for 195 countries and territories, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017," 2018).

Much of the existing ageing research is focused on health in developed countries while life course studies on developing countries are rare. However, as mentioned, ageing is often more rapid in low-income countries, and societies and health systems are poorly prepared to address health and care needs of older persons. In addition, social, economic, and health trajectories are expected to be different compared to high-income countries, because of higher exposure to life-course adversities, distinct family, transfers and/or migration patterns, and interactions of aging patterns with infectious diseases such as HIV/AIDS (Hontelez et al., 2011). Evidence from developed countries is generally not sufficient for addressing the distinctive knowledge gaps about aging in low-income countries as epidemiological, market, policy, and resource context differ so much that useful guidance cannot simply be transferred from high-income country research studies.

To properly target the health programs and reach cost-effectiveness in poor counties, it is important to study the mortality gradient in health, i.e. the most advantaged in terms of healthy years added, and inversely the most vulnerable.

In fact, the most crucial is to identify the roots of those inequalities to know where priority actions are needed.

5.5 Concluding remarks

Within this thesis, we described the results of studies on health inequalities in old age, within the context of socio-demographic factors, using a life course perspective. With a background in epidemiology, doing a PhD in demography, working at the Centre for the Interdisciplinary Study of Gerontology and Vulnerabilities, we were able to bridge gaps between disciplines, thereby making this research truly interdisciplinary. The results of this research show that early life socioeconomic conditions influence health in later life, either positively or negatively depending on risk factors for the specific health outcomes. For frailty, we found an association between higher disadvantage and an increased risk of becoming frail. In addition, apart from CSC, also other factors in early life, i.e. experiencing adverse childhood experiences and adverse childhood health experiences, have a negative influence on becoming frail in later life. Moreover, also macro level factors such as the welfare regime have an influence on associations of childhood circumstances and frailty in later life. Although we overall did not find a mediating effect of ASC for cancer outcomes nor for the adverse childhood experiences and adverse childhood health experiences on frailty, ASC do mediate associations of CSC with frailty.

Overall, more evidence on the associations of CSC with health in later life could help support our results and thus better identify and understand relations, which in turn could lead to the improvement and tailoring of prevention programmes, thereby reducing health inequalities in old age.

References

- Althubaiti, A. (2016). Information bias in health research: definition, pitfalls, and adjustment methods. *Journal of multidisciplinary healthcare*, 9, 211-217. doi:10.2147/JMDH.S104807
- Barboza Solís, C., Kelly-Irving, M., Fantin, R., Darnaudéry, M., Torrisani, J., Lang, T., & Delpierre, C. (2015). Adverse childhood experiences and physiological wear-and-tear in midlife: Findings from the 1958 British birth cohort. *Proceedings of the National Academy of Sciences*, 112(7), E738-E746. doi:10.1073/pnas.1417325112
- Bergmann, M. M., Calle, E. E., Mervis, C. A., Miracle-McMahill, H. L., Thun, M. J., & Heath, C. W. (1998). Validity of self-reported cancers in a prospective cohort study in comparison with data from state cancer registries. *Am J Epidemiol*, 147(6), 556-562.
- Bouter, L. M., van Dongen, M. C. J. M., & Zielhuis, G. A. (2005). Selectiebias. In L. M. Bouter, M. C. J. M. van Dongen, & G. A. Zielhuis (Eds.), *Epidemiologisch onderzoek: Opzet en interpretatie* (5 ed., pp. 132). Houten: Bohn Stafleu van Loghum.
- Buckinx, F., Rolland, Y., Reginster, J. Y., Ricour, C., Petermans, J., & Bruyere, O. (2015). Burden of frailty in the elderly population: perspectives for a public health challenge. *Arch Public Health*, 73(1), 19. doi:10.1186/s13690-015-0068-x
- Carcaillon, L., Blanco, C., Alonso-Bouzon, C., Alfaro-Acha, A., Garcia-Garcia, F. J., & Rodriguez-Manas, L. (2012). Sex differences in the association between serum levels of testosterone and frailty in an elderly population: the Toledo Study for Healthy Aging. *PLoS One*, 7(3), e32401. doi:10.1371/journal.pone.0032401
- Carter, K. N., Imlach-Gunasekara, F., McKenzie, S. K., & Blakely, T. (2012). Differential loss of participants does not necessarily cause selection bias. *Aust N Z J Public Health*, 36(3), 218-222. doi:10.1111/j.1753-6405.2012.00867.x
- Cheval, B., Chabert, C., Sieber, S., Orsholits, D., Cooper, R., Guessous, I., . . . Cullati, S. (2019). Association between Adverse Childhood Experiences and Muscle Strength in Older Age. *Gerontology*. doi:10.1159/000494972
- Contoyannis, P., Jones, A. M., & Rice, N. (2004). The dynamics of health in the British Household Panel Survey. 19(4), 473-503. doi:10.1002/jae.755
- Desai, M. M., Bruce, M. L., Desai, R. A., & Druss, B. G. (2001). Validity of self-reported cancer history: a comparison of health interview data and cancer registry records. *Am J Epidemiol*, 153(3), 299-306.
- Dom Dera, J. (2019). Risk Stratification: A Two-Step Process for Identifying Your Sickest Patients. *Fam Pract Manag*, 26(3), 21-26.

- Field, A. (2009). Statistical power. In A. Field (Ed.), *Discovering Statistics Using SPSS* (pp. 58). London: SAGE Publications Ltd.
- Gray, R., Campanelli, P., Deepchand, K., & Prescott-Clarke, P. (1996). Exploring Survey Non-Response: The Effect of Attrition on a Follow-Up of the 1984-85 Health and Life Style Survey. *Journal of the Royal Statistical Society. Series D (The Statistician)*, 45(2), 163-183. doi:10.2307/2988406
- Groves, R., & Couper, M. (1996). Contact-Level Influences on Cooperation in Face-to-Face Surveys. *Journal of Official Statistics*, 12, 63-83.
- Hill, A. B. (1965). The environment and disease: association or causation? . *Proc R Soc Med*, 58, 295-300.
- Hill, Z. (2004). Reducing attrition in panel studies in developing countries. *Int J Epidemiol*, 33(3), 493-498. doi:10.1093/ije/dyh060 %J International Journal of Epidemiology
- Hubbard, R. E., O'Mahony, M. S., Savva, G. M., Calver, B. L., & Woodhouse, K. W. (2009). Inflammation and frailty measures in older people. *J Cell Mol Med*, 13(9b), 3103-3109. doi:10.1111/j.1582-4934.2009.00733.x
- Jones, A., Koolman, X., & Rice, N. (2006). Health-related non-response in the British Household Panel Survey and European Community Household Panel: using inverse-probability-weighted estimators in non-linear models. *Journal of the Royal Statistical Society Series A*, 169(3), 543-569.
- Klevmarken, A., Swensson, B., Hesselius, P. (2005). The SHARE sampling procedures and calibrated design weights. In A. Börsch-Supan, Jürges, H. (Ed.), *The Survey of Health, Aging and Retirement in Europe: Methodology* (pp. 28-69). Mannheim, Germany: Mannheim Research Institute for the Economics of Aging.
- Knol, M. J., & VanderWeele, T. J. (2012). Recommendations for presenting analyses of effect modification and interaction. *Int J Epidemiol*, 41(2), 514-520. doi:10.1093/ije/dyr218
- Lacey, R. J., Belcher, J., & Croft, P. R. (2012). Validity of two simple measures for estimating life-course socio-economic position in cross-sectional postal survey data in an older population: results from the North Staffordshire Osteoarthritis Project (NorStOP). *BMC Med Res Methodol*, 12, 88. doi:10.1186/1471-2288-12-88
- Lee, P. H. (2014). Should we adjust for a confounder if empirical and theoretical criteria yield contradictory results? A simulation study. *Sci Rep*, 4, 6085. doi:10.1038/srep06085
- Lewin, A., Brondeel, R., Benmarhnia, T., Thomas, F., & Chaix, B. (2018). Attrition Bias Related to Missing Outcome Data: A Longitudinal Simulation Study. *Epidemiology*, 29(1), 87-95. doi:10.1097/ede.0000000000000755
- Lipps, O. (2007). Attrition in the Swiss Household Panel. *Methoden, Daten, Analysen (mda)*, 1(1), 45-68.

- Loh, V., Harding, J., Koshkina, V., Barr, E., Shaw, J., & Magliano, D. (2014). The validity of self-reported cancer in an Australian population study. *Aust N Z J Public Health*, 38(1), 35-38. doi:10.1111/1753-6405.12164
- Macklai, N. S., Spagnoli, J., Junod, J., & Santos-Eggimann, B. (2013). Prospective association of the SHARE-operationalized frailty phenotype with adverse health outcomes: evidence from 60+ community-dwelling Europeans living in 11 countries. *BMC Geriatr*, 13, 3. doi:10.1186/1471-2318-13-3
- Malkin, C. J., Pugh, P. J., Jones, R. D., Kapoor, D., Channer, K. S., & Jones, T. H. (2004). The effect of testosterone replacement on endogenous inflammatory cytokines and lipid profiles in hypogonadal men. *J Clin Endocrinol Metab*, 89(7), 3313-3318. doi:10.1210/jc.2003-031069
- Malvezzi, M., Bertuccio, P., Rosso, T., Rota, M., Levi, F., La Vecchia, C., & Negri, E. (2015). European cancer mortality predictions for the year 2015: does lung cancer have the highest death rate in EU women? *Annals of Oncology*, 26(4), 779-786. doi:10.1093/annonc/mdv001
- Marmot, M., Friel, S., Bell, R., Houweling, T. A. J., & Taylor, S. (2008). Closing the gap in a generation: health equity through action on the social determinants of health. *The Lancet*, 372(9650), 1661-1669. doi:[https://doi.org/10.1016/S0140-6736\(08\)61690-6](https://doi.org/10.1016/S0140-6736(08)61690-6)
- McNamee, R. (2005). Regression modelling and other methods to control confounding. *Occup Environ Med*, 62(7), 500-506, 472. doi:10.1136/oem.2002.001115
- Mekli, K., Marshall, A., Nazroo, J., Vanhoutte, B., & Pendleton, N. (2015). Genetic variant of Interleukin-18 gene is associated with the Frailty Index in the English Longitudinal Study of Ageing. *Age and Ageing*, 44(6), 938-942. doi:10.1093/ageing/afv122
- Moorman, S. M., Carr, K., & Greenfield, E. A. (2018). Childhood socioeconomic status and genetic risk for poorer cognition in later life. *Soc Sci Med*, 212, 219-226. doi:10.1016/j.socscimed.2018.07.025
- Nicoletti, C., & Peracchi, F. (2005). Survey response and survey characteristics: microlevel evidence from the European Community Household Panel. *Journal of the Royal Statistical Society Series A*, 168(4), 763-781.
- Petrie, A., & Sabin, C. (2005). Errors in hypothesis testing. In A. Petrie & C. Sabin (Eds.), *Medical statistics at a glance* (2 ed., pp. 44). Oxford: Blackwell Publishing Ltd.
- Powers, J., & Loxton, D. (2010). The impact of attrition in an 11-year prospective longitudinal study of younger women. *Ann Epidemiol*, 20(4), 318-321. doi:10.1016/j.annepidem.2010.01.002
- Reinhardt, U. E., Hussey, P. S., & Anderson, G. F. (2002). Cross-national comparisons of health systems using OECD data, 1999. *Health Aff (Millwood)*, 21(3), 169-181.

- Romero-Ortuno, R. (2013). The SHARE operationalized frailty phenotype: a comparison of two approaches. *Eur Geriatr Med*, 4(4). doi:10.1016/j.eurger.2013.04.003
- Rothman, K. J., Greenland, S., & Lash, T. L. (2008a). Confounding. In K. J. Rothman, S. Greenland, & T. L. Lash (Eds.), *Modern epidemiology* (3 ed., pp. 129-134). Philadelphia: Lippincott Williams & Wilkins.
- Rothman, K. J., Greenland, S., & Lash, T. L. (2008b). Heterogeneity versus confounding. In K. J. Rothman, S. Greenland, & T. L. Lash (Eds.), *Modern epidemiology* (3 ed., pp. 259). Philadelphia: Lippincott Williams & Wilkins.
- Rothman, K. J., Greenland, S., & Lash, T. L. (2008c). Information bias. In K. J. Rothman, S. Greenland, & T. L. Lash (Eds.), *Modern epidemiology* (3 ed., pp. 137-146). Philadelphia: Lippincott Williams & Wilkins.
- Rothman, K. J., Greenland, S., & Lash, T. L. (2008d). Residual confounding. In K. J. Rothman, S. Greenland, & T. L. Lash (Eds.), *Modern epidemiology* (3 ed., pp. 198-199). Philadelphia: Lippincott Williams & Wilkins.
- Rothman, K. J., Greenland, S., & Lash, T. L. (2008e). Selection bias. In K. J. Rothman, S. Greenland, & T. L. Lash (Eds.), *Modern epidemiology* (3 ed., pp. 134). Philadelphia: Lippincott Williams & Wilkins.
- Rothman, K. J., Greenland, S., & Lash, T. L. (2008f). Survivor bias. In K. J. Rothman, S. Greenland, & T. L. Lash (Eds.), *Modern epidemiology* (3 ed., pp. 198). Philadelphia: Lippincott Williams & Wilkins.
- Siegel, R. L., Miller, K. D., & Jemal, A. (2018). Cancer statistics, 2018. *CA: A Cancer Journal for Clinicians*, 68(1), 7-30. doi:10.3322/caac.21442
- South, S. C., Schafer, M. H., & Ferraro, K. F. (2015). Genetic and Environmental Overlap Between Childhood Maltreatment and Adult Physical Health. *Twin research and human genetics : the official journal of the International Society for Twin Studies*, 18(5), 533-544. doi:10.1017/thg.2015.62
- Stoop, I. (2005). *The Hunt for the Last Respondent: Nonresponse in Sample Surveys*. (PhD Thesis), Utrecht University,
- United Nations. (2019). *World Population Prospects 2019: Highlights*. Retrieved from New York: United Nations:
- World Health Organization. (2015). *World report on ageing and health*. Retrieved from Geneva:
- World Health Organization Commission on social determinants of health. (2008). *Final report: closing the gap in a generation: health equity through action on the social determinants of health*. Retrieved from Geneva:

Bibliography

- Alcer, K., Benson, G., Blom, A. G., Börsch-Supan, A., Brugiavini, A., Christelis, D., . . . Weerman, B. (2005). *The Survey of Health, Aging, and Retirement in Europe - Methodology*. Mannheim: Mannheim Research Institute for the Economic of Aging.
- Allmendinger, J., & Leibfried, S. (2003). Education and the welfare state: the four worlds of competence production. *Journal of European Social Policy*, 13(1), 63-81. doi:10.1177/0958928703013001047
- Althubaiti, A. (2016). Information bias in health research: definition, pitfalls, and adjustment methods. *Journal of multidisciplinary healthcare*, 9, 211-217. doi:10.2147/JMDH.S104807
- Alvarado, B. E., Zunzunegui, M. V., Beland, F., & Bamvita, J. M. (2008). Life course social and health conditions linked to frailty in Latin American older men and women. *J Gerontol A Biol Sci Med Sci*, 63(12), 1399-1406. doi:10.1093/gerona/63.12.1399
- Amemiya, A., Fujiwara, T., Murayama, H., Tani, Y., & Kondo, K. (2018). Adverse Childhood Experiences and Higher-Level Functional Limitations Among Older Japanese People: Results From the JAGES Study. *J Gerontol A Biol Sci Med Sci*, 73(2), 261-266. doi:10.1093/gerona/glx097
- Andreotti, A., Garcia, S. M., Gomez, A., Hespanha, P., Kazepo, Y., & Mingione, E. (2001). Does a Southern European Model Exist? *Journal of European Area Studies*, 9(1), 43-62. doi:10.1080/14608460120061948
- Baltes, P. B., & Baltes, M. M. (1990). Psychological perspectives on successful aging: The model of selective optimization with compensation. In *Successful aging: Perspectives from the behavioral sciences*. (pp. 1-34). New York, NY, US: Cambridge University Press.
- Bambra, C. (2005). Cash versus services : 'worlds of welfare' and the decommodification of cash benefits and health care services. 34(2), 195-213.
- Bambra, C. (2011). Health inequalities and welfare state regimes: theoretical insights on a public health 'puzzle'. 65(9), 740-745. doi:10.1136/jech.2011.136333 %J Journal of Epidemiology and Community Health
- Bambra, C., Netuveli, G., & Eikemo, T. A. (2010). Welfare state regime life courses: the development of western European welfare state regimes and age-related patterns of educational inequalities in self-reported health. *Int J Health Serv*, 40(3), 399-420. doi:10.2190/HS.40.3.b
- Bandeem-Roche, K., Seplaki, C. L., Huang, J., Buta, B., Kalyani, R. R., Varadhan, R., . . . Kasper, J. D. (2015). Frailty in Older Adults: A Nationally Representative Profile in the United States. *The Journals of Gerontology: Series A*, 70(11), 1427-1434. doi:10.1093/gerona/glv133
- Banks, J. (2006). Employment and labour market transitions at older ages in England, 2002–2003 to 2014–2015. In J. Banks, D. Batty, J. Nazroo, & A. Steptoe (Eds.), *The Dynamics of Ageing: Evidence from the English Longitudinal Study of Ageing 2002-2015*. London, UK: The Institute for Fiscal Studies.
- Barboza Solís, C., Kelly-Irving, M., Fantin, R., Darnaudéry, M., Torrisani, J., Lang, T., & Delpierre, C. (2015). Adverse childhood experiences and physiological wear-and-tear in midlife: Findings from the 1958 British birth

- cohort. *Proceedings of the National Academy of Sciences*, 112(7), E738-E746. doi:10.1073/pnas.1417325112
- Barker, D. J. (1998). In utero programming of chronic disease. *Clin Sci (Lond)*, 95(2), 115-128.
- Bartley, M., Blane, D., & Montgomery, S. (1997). Health and the life course: why safety nets matter. *Bmj*, 314(7088), 1194-1196.
- Bates, D., Mächler, M., Bolker, B., & Walker, S. (2015). Fitting Linear Mixed-Effects Models Using lme4. 2015, 67(1), 48. doi:10.18637/jss.v067.i01
- Ben-Shlomo, Y. (2013). *A Life Course Approach to Healthy Ageing*: Oxford University Press.
- Ben-Shlomo, Y., & Kuh, D. (2002). A life course approach to chronic disease epidemiology: conceptual models, empirical challenges and interdisciplinary perspectives. *Int J Epidemiol*, 31(2), 285-293.
- Benzeval, M., & Judge, K. (2001). Income and health: the time dimension. *Soc Sci Med*, 52(9), 1371-1390. doi:10.1016/s0277-9536(00)00244-6
- Bergmann, M. M., Calle, E. E., Mervis, C. A., Miracle-McMahill, H. L., Thun, M. J., & Heath, C. W. (1998). Validity of self-reported cancers in a prospective cohort study in comparison with data from state cancer registries. *Am J Epidemiol*, 147(6), 556-562.
- Blane, D., Hart, C. L., Smith, G. D., Gillis, C. R., Hole, D. J., & Hawthorne, V. M. (1996). Association of cardiovascular disease risk factors with socioeconomic position during childhood and during adulthood. *Bmj*, 313(7070), 1434-1438.
- Blane, D., Kelly-Irving, M., d'Errico, A., Bartley, M., Montgomery, S. (2013). Social-biological Transitions: how does the social become biological? *Longitudinal Life Course Studies*, 4(2), 136-146. doi:10.14301/llds.v4i2.236
- Blane, D., Netuveli, G., & Stone, J. (2007). The development of life course epidemiology. *Rev Epidemiol Sante Publique*, 55(1), 31-38. doi:10.1016/j.respe.2006.12.004
- Bocquier, P. (1996). *L'analyse des enquêtes biographiques à l'aide du logiciel STATA*: Institut national d'études démographiques.
- Boisgontier, M. P., & Cheval, B. (2016). The anova to mixed model transition. *Neurosci Biobehav Rev*, 68, 1004-1005. doi:10.1016/j.neubiorev.2016.05.034
- Borsch-Supan, A., Brandt, M., Hunkler, C., Kneip, T., Korbmacher, J., Malter, F., ... Zuber, S. (2013). Data Resource Profile: the Survey of Health, Ageing and Retirement in Europe (SHARE). *Int J Epidemiol*, 42(4), 992-1001. doi:10.1093/ije/dyt088
- Bouchardy, C., Verkooyen, H. M., & Fioretta, G. (2006). Social class is an important and independent prognostic factor of breast cancer mortality. *Int J Cancer*, 119(5), 1145-1151. doi:10.1002/ijc.21889
- Bound, J., & Waidmann, T. (2007). Estimating the health effects of retirement. *Michigan Retirement Research Center Research Paper No. UM WP*, 168.
- Bouter, L. M., van Dongen, M. C. J. M., & Zielhuis, G. A. (2005). Selectiebias. In L. M. Bouter, M. C. J. M. van Dongen, & G. A. Zielhuis (Eds.), *Epidemiologisch onderzoek: Opzet en interpretatie* (5 ed., pp. 132). Houten: Bohn Stafleu van Loghum.

- Brandt, M., Deindl, C., & Hank, K. (2012). Tracing the origins of successful aging: the role of childhood conditions and social inequality in explaining later life health. *Soc Sci Med*, 74(9), 1418-1425. doi:10.1016/j.socscimed.2012.01.004
- Brückner, H., & Mayer, K. U. (2005). De-Standardization of the Life Course: What it Might Mean? And if it Means Anything, Whether it Actually Took Place? *Advances in Life Course Research*, 9, 27-53. doi:[https://doi.org/10.1016/S1040-2608\(04\)09002-1](https://doi.org/10.1016/S1040-2608(04)09002-1)
- Bruer, J. T. (2001). A critical and sensitive period primer. In J. D. B. Bailey, Bruer J.T., Symons, F.J. (Ed.), *Critical thinking about critical periods*. Baltimore: Paul H. Brookes.
- Bryere, J., Dejardin, O., Launay, L., Colonna, M., Grosclaude, P., & Launoy, G. (2016). Socioeconomic status and site-specific cancer incidence, a Bayesian approach in a French Cancer Registries Network study. *Eur J Cancer Prev*. doi:10.1097/cej.0000000000000326
- Buckinx, F., Rolland, Y., Reginster, J. Y., Ricour, C., Petermans, J., & Bruyere, O. (2015). Burden of frailty in the elderly population: perspectives for a public health challenge. *Arch Public Health*, 73(1), 19. doi:10.1186/s13690-015-0068-x
- Burton-Jeangros, C., Cullati, S., Sacker, A., & Blane, D. (2015). Introduction. In C. S. Burton-Jeangros C, Sacker A, et al., (Ed.), *A Life Course Perspective on Health Trajectories and Transitions*. Cham: Springer.
- Carcaillon, L., Blanco, C., Alonso-Bouzon, C., Alfaro-Acha, A., Garcia-Garcia, F. J., & Rodriguez-Manas, L. (2012). Sex differences in the association between serum levels of testosterone and frailty in an elderly population: the Toledo Study for Healthy Aging. *PLoS One*, 7(3), e32401. doi:10.1371/journal.pone.0032401
- Carter, K. N., Imlach-Gunasekara, F., McKenzie, S. K., & Blakely, T. (2012). Differential loss of participants does not necessarily cause selection bias. *Aust N Z J Public Health*, 36(3), 218-222. doi:10.1111/j.1753-6405.2012.00867.x
- Cheval, B., Boisgontier, M. P., Orsholits, D., Sieber, S., Guessous, I., Gabriel, R., . . . Cullati, S. (2018). Association of early- and adult-life socioeconomic circumstances with muscle strength in older age. *Age Ageing*, 47(3), 398-407. doi:10.1093/ageing/afy003
- Cheval, B., Chabert, C., Sieber, S., Orsholits, D., Cooper, R., Guessous, I., . . . Cullati, S. (2019). Association between Adverse Childhood Experiences and Muscle Strength in Older Age. *Gerontology*. doi:10.1159/000494972
- Chittleborough, C. R., Baum, F. E., Taylor, A. W., & Hiller, J. E. (2006). A life-course approach to measuring socioeconomic position in population health surveillance systems. *J Epidemiol Community Health*, 60(11), 981-992. doi:10.1136/jech.2006.048694
- Clegg, A., Young, J., Iliffe, S., Rikkert, M. O., & Rockwood, K. (2013). Frailty in elderly people. *Lancet*, 381(9868), 752-762. doi:10.1016/s0140-6736(12)62167-9
- Colerick Clipp, E., Pavalko, E. K., & Elder, G. H. (1992). Trajectories of health: In concept and empirical pattern. *Behavior, Health, & Aging*, 2(3), 159-179.

- Commission of Social Determinants of Health. (2008). *Closing the gap in generation: Health equity through action on the social determinants of health*. Retrieved from Geneva:
- Contoyannis, P., Jones, A. M., & Rice, N. (2004). The dynamics of health in the British Household Panel Survey. *19*(4), 473-503. doi:10.1002/jae.755
- Cornia, G. (2016). The mortality crisis in transition economies. *IZA World of Labor*(298). doi:doi: 10.15185/izawol.298
- Coyle, J. T. (2003). Use it or lose it--do effortful mental activities protect against dementia? *N Engl J Med*, *348*(25), 2489-2490. doi:10.1056/NEJMp030051
- Dahl, E., Ivar Elstad, J., Hofoss, D., & Martin-Mollard, M. (2006). For whom is income inequality most harmful? A multi-level analysis of income inequality and mortality in Norway. *Soc Sci Med*, *63*(10), 2562-2574. doi:10.1016/j.socscimed.2006.06.002
- Dale, G., & Fabry, A. (2018). Neoliberalism in Eastern Europe and the former Soviet Union. In D. Cahill, M. Cooper, & M. Konings (Eds.), *The SAGE Handbook of Neoliberalism*. 55 City Road
- 55 City Road, London: SAGE Publications Ltd. Retrieved from <http://sk.sagepub.com/reference/the-sage-handbook-of-neoliberalism>. doi:10.4135/9781526416001
- Dannefer, D. (2003). Cumulative advantage/disadvantage and the life course: cross-fertilizing age and social science theory. *J Gerontol B Psychol Sci Soc Sci*, *58*(6), S327-337.
- Dannefer, D. (2018). Systemic and Reflexive: Foundations of Cumulative Dis/Advantage and Life-Course Processes. *J Gerontol B Psychol Sci Soc Sci*. doi:10.1093/geronb/gby118
- de Kok, I. M., van Lenthe, F. J., Avendano, M., Louwman, M., Coebergh, J. W., & Mackenbach, J. P. (2008). Childhood social class and cancer incidence: results of the globe study. *Soc Sci Med*, *66*(5), 1131-1139. doi:10.1016/j.socscimed.2007.11.035
- de Souto Barreto, P., Cesari, M., Andrieu, S., Vellas, B., & Rolland, Y. (2017). Physical Activity and Incident Chronic Diseases: A Longitudinal Observational Study in 16 European Countries. *Am J Prev Med*, *52*(3), 373-378. doi:10.1016/j.amepre.2016.08.028
- Deding, U., Henig, A. S., Salling, A., Torp-Pedersen, C., & Boggild, H. (2017). Sociodemographic predictors of participation in colorectal cancer screening. *Int J Colorectal Dis*. doi:10.1007/s00384-017-2832-6
- Dedman, D. J., Gunnell, D., Davey Smith, G., & Frankel, S. (2001). Childhood housing conditions and later mortality in the Boyd Orr cohort. *J Epidemiol Community Health*, *55*(1), 10-15. doi:10.1136/jech.55.1.10
- Desai, M. M., Bruce, M. L., Desai, R. A., & Druss, B. G. (2001). Validity of self-reported cancer history: a comparison of health interview data and cancer registry records. *Am J Epidemiol*, *153*(3), 299-306.
- Doku, D. T., Acacio-Claro, P. J., Koivusilta, L., & Rimpela, A. (2018). Health and socioeconomic circumstances over three generations as predictors of youth unemployment trajectories. *Eur J Public Health*. doi:10.1093/eurpub/cky242

- Dom Dera, J. (2019). Risk Stratification: A Two-Step Process for Identifying Your Sickest Patients. *Fam Pract Manag*, 26(3), 21-26.
- Drentea, P. (2002). Retirement and mental health. *J Aging Health*, 14(2), 167-194. doi:10.1177/089826430201400201
- Dury, S., De Roeck, E., Duppen, D., Fret, B., Hoeyberghs, L., Lambotte, D., . . . Dierckx, E. (2016). Identifying frailty risk profiles of home-dwelling older people: focus on sociodemographic and socioeconomic characteristics. *Aging Ment Health*, 1-9. doi:10.1080/13607863.2016.1193120
- Eikemo, T. A., Bambra, C., Judge, K., & Ringdal, K. (2008). Welfare state regimes and differences in self-perceived health in Europe: a multilevel analysis. *Soc Sci Med*, 66(11), 2281-2295. doi:10.1016/j.socscimed.2008.01.022
- Elder, G. H., Johnson, M. K., & Crosnoe, R. (2003). The Emergence and Development of Life Course Theory. In J. T. Mortimer & M. J. Shanahan (Eds.), *Handbook of the Life Course* (pp. 3-19). Boston, MA: Springer US.
- Elder, G. H., Jr. (1998). The life course as developmental theory. *Child Dev*, 69(1), 1-12.
- Elder, G. H., & Shanahan, M. J. (2006). The life course and human development. In R. M. Lerner (Ed.), *Handbook of child psychology: Vol. 1. Theoretical models of human development* (pp. 665-715). Hoboken, NJ: Wiley.
- Elder, G. H., & Social Science Research Council. (1985). *Life course dynamics: trajectories and transitions, 1968-1980*. Cornell University Press.
- Esping-Andersen, G. (1990). *The three worlds of welfare capitalism*. Princeton, N.J.: Princeton University Press.
- Esping-Andersen, G. (1999). *Social Foundations of Postindustrial Economies*. Oxford: Oxford University Press.
- Etman, A., Burdorf, A., Van der Cammen, T. J., Mackenbach, J. P., & Van Lenthe, F. J. (2012). Socio-demographic determinants of worsening in frailty among community-dwelling older people in 11 European countries. *J Epidemiol Community Health*, 66(12), 1116-1121. doi:10.1136/jech-2011-200027
- Etman, A., Kamphuis, C. B., van der Cammen, T. J., Burdorf, A., & van Lenthe, F. J. (2015). Do lifestyle, health and social participation mediate educational inequalities in frailty worsening? *Eur J Public Health*, 25(2), 345-350. doi:10.1093/eurpub/cku093
- Evans, M. D., Kelley, J., Sikora, J., & Treiman, D. J. (2010). Family scholarly culture and educational success: Books and schooling in 27 nations. *Research in social stratification and mobility*, 28(2), 171-197. doi:10.1016/j.rssm.2010.01.002
- Evans, M. D. R., Kelley, J., Sikora, J., & Treiman, D. J. (2010). Family scholarly culture and educational success: Books and schooling in 27 nations. *Research in Social Stratification and Mobility*, 28(2), 171-197. doi:http://dx.doi.org/10.1016/j.rssm.2010.01.002
- Faggiano, F., Partanen, T., Kogevinas, M., & Boffetta, P. (1997). Socioeconomic differences in cancer incidence and mortality. *IARC Sci Publ*(138), 65-176.
- Fawcett, J., Blakely, T., & Kunst, A. (2005). Are mortality differences and trends by education any better or worse in New Zealand? A comparison study with Norway, Denmark and Finland, 1980-1990s. *Eur J Epidemiol*, 20(8), 683-691. doi:10.1007/s10654-005-7923-y

- Featherman, D. L., & Lerner, R. M. (1985). Ontogenesis and sociogenesis: Problematics for theory and research about development and socialization across the lifespan. *American Sociological Review*, 50(5), 659-676. doi:10.2307/2095380
- Felitti, V. J., Anda, R. F., Nordenberg, D., Williamson, D. F., Spitz, A. M., Edwards, V., . . . Marks, J. S. (1998). Relationship of childhood abuse and household dysfunction to many of the leading causes of death in adults. The Adverse Childhood Experiences (ACE) Study. *Am J Prev Med*, 14(4), 245-258.
- Ferlay, J., Steliarova-Foucher, E., Lortet-Tieulent, J., Rosso, S., Coebergh, J. W. W., Comber, H., . . . Bray, F. (2013). Cancer incidence and mortality patterns in Europe: Estimates for 40 countries in 2012. *European Journal of Cancer*, 49(6), 1374-1403. doi:<https://doi.org/10.1016/j.ejca.2012.12.027>
- Ferraro, K. F., & Schafer, M. H. (2017). Visions of the Life Course: Risks, Resources, and Vulnerability. *Res Hum Dev*, 14(1), 88-93. doi:10.1080/15427609.2016.1268895
- Ferraro, K. F., & Shippee, T. P. (2009). Aging and Cumulative Inequality: How Does Inequality Get Under the Skin? *The Gerontologist*, 49(3), 333-343. doi:10.1093/geront/gnp034 %J The Gerontologist
- Ferrera, M. (1996). The 'Southern Model' of Welfare in Social Europe. *Journal of European Social Policy*, 6(1), 17-37. doi:10.1177/095892879600600102
- Ferrie, J. E., Shipley, M. J., Stansfeld, S. A., & Marmot, M. G. (2002). Effects of chronic job insecurity and change in job security on self reported health, minor psychiatric morbidity, physiological measures, and health related behaviours in British civil servants: the Whitehall II study. *J Epidemiol Community Health*, 56(6), 450-454. doi:10.1136/jech.56.6.450
- Field, A. (2009). Statistical power. In A. Field (Ed.), *Discovering Statistics Using SPSS* (pp. 58). London: SAGE Publications Ltd.
- Franse, C. B., van Grieken, A., Qin, L., Melis, R. J. F., Rietjens, J. A. C., & Raat, H. (2017). Socioeconomic inequalities in frailty and frailty components among community-dwelling older citizens. *PLoS One*, 12(11), e0187946. doi:10.1371/journal.pone.0187946
- Fried, L. P., Tangen, C. M., Walston, J., Newman, A. B., Hirsch, C., Gottdiener, J., . . . McBurnie, M. A. (2001). Frailty in older adults: evidence for a phenotype. *J Gerontol A Biol Sci Med Sci*, 56(3), M146-156.
- Gale, C. R., Booth, T., Starr, J. M., & Deary, I. J. (2016). Intelligence and socioeconomic position in childhood in relation to frailty and cumulative allostatic load in later life: the Lothian Birth Cohort 1936. *J Epidemiol Community Health*, 70(6), 576-582. doi:10.1136/jech-2015-205789
- Galobardes, B., Shaw, M., Lawlor, D. A., Lynch, J. W., & Davey Smith, G. (2006). Indicators of socioeconomic position (part 1). *J Epidemiol Community Health*, 60(1), 7-12. doi:10.1136/jech.2004.023531
- Gardiner, P. A., Mishra, G. D., & Dobson, A. J. (2016). The Effect of Socioeconomic Status Across Adulthood on Trajectories of Frailty in Older Women. *J Am Med Dir Assoc*, 17(4), 372.e371-373. doi:10.1016/j.jamda.2015.12.090

- Gill, T. M., Gahbauer, E. A., Allore, H. G., & Han, L. (2006). Transitions between frailty states among community-living older persons. *Arch Intern Med*, 166(4), 418-423. doi:10.1001/archinte.166.4.418
- Glass, T. A., Goodman, S. N., Hernan, M. A., & Samet, J. M. (2013). Causal inference in public health. *Annu Rev Public Health*, 34, 61-75. doi:10.1146/annurev-publhealth-031811-124606
- Global, regional, and national disability-adjusted life-years (DALYs) for 359 diseases and injuries and healthy life expectancy (HALE) for 195 countries and territories, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. (2018). *Lancet*, 392(10159), 1859-1922. doi:10.1016/s0140-6736(18)32335-3
- Graham, H. (2002). Building an inter-disciplinary science of health inequalities: the example of lifecourse research. *Soc Sci Med*, 55(11), 2005-2016. doi:10.1016/s0277-9536(01)00343-4
- Gray, R., Campanelli, P., Deepchand, K., & Prescott-Clarke, P. (1996). Exploring Survey Non-Response: The Effect of Attrition on a Follow-Up of the 1984-85 Health and Life Style Survey. *Journal of the Royal Statistical Society. Series D (The Statistician)*, 45(2), 163-183. doi:10.2307/2988406
- Groves, R., & Couper, M. (1996). Contact-Level Influences on Cooperation in Face-to-Face Surveys. *Journal of Official Statistics*, 12, 63-83.
- Haas, S. (2008). Trajectories of functional health: the 'long arm' of childhood health and socioeconomic factors. *Soc Sci Med*, 66(4), 849-861. doi:10.1016/j.socscimed.2007.11.004
- Hao, Y. (2008). Productive activities and psychological well-being among older adults. *J Gerontol B Psychol Sci Soc Sci*, 63(2), S64-72. doi:10.1093/geronb/63.2.s64
- Hayward, M. D., & Gorman, B. K. (2004). The long arm of childhood: the influence of early-life social conditions on men's mortality. *Demography*, 41(1), 87-107. doi:10.1353/dem.2004.0005
- Herr, M., Robine, J. M., Aegerter, P., Arvieu, J. J., & Ankri, J. (2015). Contribution of socioeconomic position over life to frailty differences in old age: comparison of life-course models in a French sample of 2350 old people. *Ann Epidemiol*, 25(9), 674-680. doi:10.1016/j.annepidem.2015.05.006
- Hertzman, C., & Power, C. (2003). Health and human development: understandings from life-course research. *Dev Neuropsychol*, 24(2-3), 719-744. doi:10.1080/87565641.2003.9651917
- Hill, A. B. (1965). The environment and disease: association or causation? . *Proc R Soc Med*, 58, 295-300.
- Hill, Z. (2004). Reducing attrition in panel studies in developing countries. *Int J Epidemiol*, 33(3), 493-498. doi:10.1093/ije/dyh060 %J International Journal of Epidemiology
- Hontelez, J. A., Lurie, M. N., Newell, M. L., Bakker, R., Tanser, F., Barnighausen, T., . . . de Vlas, S. J. (2011). Ageing with HIV in South Africa. *Aids*, 25(13), 1665-1667. doi:10.1097/QAD.0b013e32834982ea
- Hoogendijk, E. O., van Hout, H. P., Heymans, M. W., van der Horst, H. E., Frijters, D. H., Broese van Groenou, M. I., . . . Huisman, M. (2014). Explaining the association between educational level and frailty in older adults: results

- from a 13-year longitudinal study in the Netherlands. *Ann Epidemiol*, 24(7), 538-544.e532. doi:10.1016/j.annepidem.2014.05.002
- Huang, C., Soldo, B. J., & Elo, I. T. (2011). Do early-life conditions predict functional health status in adulthood? The case of Mexico. *Soc Sci Med*, 72(1), 100-107. doi:10.1016/j.socscimed.2010.09.040
- Hubbard, R. E., O'Mahony, M. S., Savva, G. M., Calver, B. L., & Woodhouse, K. W. (2009). Inflammation and frailty measures in older people. *J Cell Mol Med*, 13(9b), 3103-3109. doi:10.1111/j.1582-4934.2009.00733.x
- Huber, M., Knottnerus, J. A., Green, L., Horst, H. v. d., Jadad, A. R., Kromhout, D., . . . Smid, H. (2011). How should we define health? , 343, d4163. doi:10.1136/bmj.d4163 %J BMJ
- Hughes, K., Bellis, M. A., Hardcastle, K. A., Sethi, D., Butchart, A., Mikton, C., . . . Dunne, M. P. (2017). The effect of multiple adverse childhood experiences on health: a systematic review and meta-analysis. *Lancet Public Health*, 2(8), e356-e366. doi:10.1016/s2468-2667(17)30118-4
- IARC Publications. (2013). *Air Pollution and Cancer*. Retrieved from International Labour Office. (2012). *International Standard Classification of Occupations: ISCO-08*. Retrieved from Geneva: ILO:
- Jadad, A. R., & O'Grady, L. (2008). How should health be defined? *Bmj*, 337, a2900. doi:10.1136/bmj.a2900
- Jones, A., Koolman, X., & Rice, N. (2006). Health-related non-response in the British Household Panel Survey and European Community Household Panel: using inverse-probability-weighted estimators in non-linear models. *Journal of the Royal Statistical Society Series A*, 169(3), 543-569.
- Juarez, S. P., Goodman, A., & Koupil, I. (2016). From cradle to grave: tracking socioeconomic inequalities in mortality in a cohort of 11 868 men and women born in Uppsala, Sweden, 1915-1929. *J Epidemiol Community Health*, 70(6), 569-575. doi:10.1136/jech-2015-206547
- Kelly-Irving, M., Lepage, B., Dedieu, D., Lacey, R., Cable, N., Bartley, M., . . . Delpierre, C. (2013). Childhood adversity as a risk for cancer: findings from the 1958 British birth cohort study. *BMC Public Health*, 13, 767. doi:10.1186/1471-2458-13-767
- Kelly-Irving, M., Mabile, L., Grosclaude, P., Lang, T., & Delpierre, C. (2013). The embodiment of adverse childhood experiences and cancer development: potential biological mechanisms and pathways across the life course. *Int J Public Health*, 58(1), 3-11. doi:10.1007/s00038-012-0370-0
- Klevmarken, A., Swensson, B., Hesselius, P. (2005). The SHARE sampling procedures and calibrated design weights. In A. Börsch-Supan, Jürges, H. (Ed.), *The Survey of Health, Aging and Retirement in Europe: Methodology* (pp. 28-69). Mannheim, Germany: Mannheim Research Institute for the Economics of Aging.
- Knol, M. J., & VanderWeele, T. J. (2012). Recommendations for presenting analyses of effect modification and interaction. *Int J Epidemiol*, 41(2), 514-520. doi:10.1093/ije/dyr218
- Kohli, M. (2007). The Institutionalization of the Life Course: Looking Back to Look Ahead. *Research in Human Development*, 4(3-4), 253-271. doi:10.1080/15427600701663122

- Kok, J. (2007). Principles and Prospects of the Life Course Paradigm. [Principles and Prospects of the Life Course Paradigm]. 113(1), 203-230. doi:10.3917/adh.113.0203
- Kuh, D., & Ben-Shlomo, Y. (2004). *A life course approach to chronic disease epidemiology*. Oxford: Oxford University Press.
- Kuh, D., & Ben-Shlomo, Y. (2004). *A life course approach to chronic disease epidemiology*. Oxford: Oxford University Press.
- Kuh, D., Ben-Shlomo, Y., Lynch, J., Hallqvist, J., & Power, C. (2003). Life course epidemiology. *J Epidemiol Community Health*, 57(10), 778-783. doi:10.1136/jech.57.10.778
- Kuh, D. J., & Ben-Shlomo, Y. (1997). *A life course approach to chronic disease epidemiology*. Oxford: Oxford University Press.
- Kuh, D. J., & Hardy, R. (2002). *Lifecourse approach to women's health*. Oxford: Oxford University press.
- Kuznetsova, A., Brockhoff, P.B., Christensen, R.H.B. (2016). lmerTest: Tests in Linear Mixed Effects Models. R package version 2.0-33. Retrieved from <https://CRAN.R-project.org/package=lmerTest>
- Lacey, R. J., Belcher, J., & Croft, P. R. (2012). Validity of two simple measures for estimating life-course socio-economic position in cross-sectional postal survey data in an older population: results from the North Staffordshire Osteoarthritis Project (NorStOP). *BMC Med Res Methodol*, 12, 88. doi:10.1186/1471-2288-12-88
- Laditka, J. N., & Laditka, S. B. (2018). Adverse Childhood Circumstances and Functional Status Throughout Adult Life. *J Aging Health*, 30(9), 1347-1368. doi:10.1177/0898264317715976
- Lalivé d'Epinay, C., & Spini, D. (Eds.). (2007). *Les années fragiles: La vie au-delà de quatre-vingts ans*. Québec: Les Presses de l'Université de Laval.
- Land, K. C., & Lamb, V. L. (2017). Demography of Aging. In S. R. Quah (Ed.), *International Encyclopedia of Public Health (Second Edition)* (pp. 226-232). Oxford: Academic Press.
- Landos, A., von Arx, M., Cheval, B., Sieber, S., Kliegel, M., Gabriel, R., . . . Cullati, S. (2019). Childhood socioeconomic circumstances and disability trajectories in older men and women: a European cohort study. *Eur J Public Health*, 29(1), 50-58. doi:10.1093/eurpub/cky166
- Larson, J. S. (1999). The conceptualization of health. *Med Care Res Rev*, 56(2), 123-136. doi:10.1177/107755879905600201
- Laslett, P. (1987). The Emergence of the Third Age. *Ageing and Society*, 7(2), 133-160. doi:10.1017/S0144686X00012538
- Lawlor, D. A., Sterne, J. A., Tynelius, P., Davey Smith, G., & Rasmussen, F. (2006). Association of childhood socioeconomic position with cause-specific mortality in a prospective record linkage study of 1,839,384 individuals. *Am J Epidemiol*, 164(9), 907-915. doi:10.1093/aje/kwj319
- Lazar, M., & Davenport, L. (2018). Barriers to Health Care Access for Low Income Families: A Review of Literature. *J Community Health Nurs*, 35(1), 28-37. doi:10.1080/07370016.2018.1404832
- Lee, P. H. (2014). Should we adjust for a confounder if empirical and theoretical criteria yield contradictory results? A simulation study. *Sci Rep*, 4, 6085. doi:10.1038/srep06085

- Leisering, L. (2003). Government and the Life Course. In J. T. Mortimer & M. J. Shanahan (Eds.), *Handbook of the Life Course* (pp. 205-225). Boston, MA: Springer US.
- Lewin, A., Brondeel, R., Benmarhnia, T., Thomas, F., & Chaix, B. (2018). Attrition Bias Related to Missing Outcome Data: A Longitudinal Simulation Study. *Epidemiology*, 29(1), 87-95. doi:10.1097/ede.0000000000000755
- Lipps, O. (2007). Attrition in the Swiss Household Panel. *Methoden, Daten, Analysen (mda)*, 1(1), 45-68.
- Loh, V., Harding, J., Koshkina, V., Barr, E., Shaw, J., & Magliano, D. (2014). The validity of self-reported cancer in an Australian population study. *Aust N Z J Public Health*, 38(1), 35-38. doi:10.1111/1753-6405.12164
- Lundqvist, A., Andersson, E., Ahlberg, I., Nilbert, M., & Gerdtham, U. (2016). Socioeconomic inequalities in breast cancer incidence and mortality in Europe-a systematic review and meta-analysis. *Eur J Public Health*, 26(5), 804-813. doi:10.1093/eurpub/ckw070
- Luo, Y., & Waite, L. J. (2005). The impact of childhood and adult SES on physical, mental, and cognitive well-being in later life. *J Gerontol B Psychol Sci Soc Sci*, 60(2), S93-S101.
- Luo, Y., & Waite, L. J. (2005). The Impact of Childhood and Adult SES on Physical, Mental, and Cognitive Well-Being in Later Life. *The journals of gerontology. Series B, Psychological sciences and social sciences*, 60(2), S93-S101.
- Mackenbach, J. P. (2012). The persistence of health inequalities in modern welfare states: the explanation of a paradox. *Soc Sci Med*, 75(4), 761-769. doi:10.1016/j.socscimed.2012.02.031
- Mackenbach, J. P., Bos, V., Andersen, O., Cardano, M., Costa, G., Harding, S., . . . Kunst, A. E. (2003). Widening socioeconomic inequalities in mortality in six Western European countries. *Int J Epidemiol*, 32(5), 830-837. doi:10.1093/ije/dyg209
- Mackenbach, J. P., Stirbu, I., Roskam, A. J., Schaap, M. M., Menvielle, G., Leinsalu, M., & Kunst, A. E. (2008). Socioeconomic inequalities in health in 22 European countries. *N Engl J Med*, 358(23), 2468-2481. doi:10.1056/NEJMsa0707519
- Macklai, N. S., Spagnoli, J., Junod, J., & Santos-Eggimann, B. (2013). Prospective association of the SHARE-operationalized frailty phenotype with adverse health outcomes: evidence from 60+ community-dwelling Europeans living in 11 countries. *BMC Geriatr*, 13, 3. doi:10.1186/1471-2318-13-3
- Malkin, C. J., Pugh, P. J., Jones, R. D., Kapoor, D., Channer, K. S., & Jones, T. H. (2004). The effect of testosterone replacement on endogenous inflammatory cytokines and lipid profiles in hypogonadal men. *J Clin Endocrinol Metab*, 89(7), 3313-3318. doi:10.1210/jc.2003-031069
- Malvezzi, M., Bertuccio, P., Rosso, T., Rota, M., Levi, F., La Vecchia, C., & Negri, E. (2015). European cancer mortality predictions for the year 2015: does lung cancer have the highest death rate in EU women? *Annals of Oncology*, 26(4), 779-786. doi:10.1093/annonc/mdv001
- Marmot, M., Friel, S., Bell, R., Houweling, T. A., & Taylor, S. (2008). Closing the gap in a generation: health equity through action on the social determinants of health. *The Lancet*, 372(9650), 1661-1669. doi:[https://doi.org/10.1016/S0140-6736\(08\)61690-6](https://doi.org/10.1016/S0140-6736(08)61690-6)

- Marmot, M. G. (2003). Understanding social inequalities in health. *Perspect Biol Med*, 46(3 Suppl), S9-23.
- Marsh, A., Gordon, D., Pantazis, C., Heslop, P. (1999). *Home Sweet Home? The impact of poor housing on health*. Bristol: The Policy Press, University of Bristol.
- Marshall, A., Nazroo, J., Tampubolon, G., & Vanhoutte, B. (2015). Cohort differences in the levels and trajectories of frailty among older people in England. *J Epidemiol Community Health*. doi:10.1136/jech-2014-204655
- McNamee, R. (2005). Regression modelling and other methods to control confounding. *Occup Environ Med*, 62(7), 500-506, 472. doi:10.1136/oem.2002.001115
- Mekli, K., Marshall, A., Nazroo, J., Vanhoutte, B., & Pendleton, N. (2015). Genetic variant of Interleukin-18 gene is associated with the Frailty Index in the English Longitudinal Study of Ageing. *Age and Ageing*, 44(6), 938-942. doi:10.1093/ageing/afv122
- Meslé, F. (2004). Mortality in Central and Eastern Europe: long-term trends and recent upturns. *Demographic Research, Special Collection 2*, 45-70. doi:10.4054/DemRes.2004.S2.3
- Moorman, S. M., Carr, K., & Greenfield, E. A. (2018). Childhood socioeconomic status and genetic risk for poorer cognition in later life. *Soc Sci Med*, 212, 219-226. doi:10.1016/j.socscimed.2018.07.025
- Naess, O., Claussen, B., & Davey Smith, G. (2004). Relative impact of childhood and adulthood socioeconomic conditions on cause specific mortality in men. *J Epidemiol Community Health*, 58(7), 597-598. doi:10.1136/jech.2003.012229
- Naess, O., Strand, B. H., & Smith, G. D. (2007). Childhood and adulthood socioeconomic position across 20 causes of death: a prospective cohort study of 800,000 Norwegian men and women. *J Epidemiol Community Health*, 61(11), 1004-1009. doi:10.1136/jech.2006.052811
- Nazroo, J. (2017). Class and Health Inequality in Later Life: Patterns, Mechanisms and Implications for Policy. *International journal of environmental research and public health*, 14(12), 1533. doi:10.3390/ijerph14121533
- Nicoletti, C., & Peracchi, F. (2005). Survey response and survey characteristics: microlevel evidence from the European Community Household Panel. *Journal of the Royal Statistical Society Series A*, 168(4), 763-781.
- Nurius, P. S., Fleming, C. M., & Brindle, E. (2019). Life Course Pathways From Adverse Childhood Experiences to Adult Physical Health: A Structural Equation Model. *J Aging Health*, 31(2), 211-230. doi:10.1177/0898264317726448
- O'Rand, A. M. (1996). The precious and the precocious: understanding cumulative disadvantage and cumulative advantage over the life course. *Gerontologist*, 36(2), 230-238. doi:10.1093/geront/36.2.230
- O'Rand, A. M. (2009). Cumulative Processes in the Life Course. In G. H. Elder & J. Z. Giele (Eds.), *The Craft of Life Course Research*. New York: Guilford Press.
- O'Rand, A. M., & Hamil-Luker, J. (2005). Processes of cumulative adversity: childhood disadvantage and increased risk of heart attack across the life course. *J Gerontol B Psychol Sci Soc Sci*, 60 Spec No 2, 117-124. doi:10.1093/geronb/60.special_issue_2.s117

- Oris, M. (2017). Vulnerability. A life course perspective. *Revue de droit comparé du travail et de la sécurité sociale* %J *Revue de droit comparé du travail et de la sécurité sociale*(4), 6-17.
- Oris, M., Gabriel, R., Ritschard, G., & Kliegel, M. (2017). Long Lives and Old Age Poverty: Social Stratification and Life-Course Institutionalization in Switzerland. *Research in Human Development*, 14(1), 68-87. doi:10.1080/15427609.2016.1268890
- Petmesidou, M. (1996). Social protection in southern Europe: Trends and prospects. . *Journal of Area Studies*, 4(9), 95-125.
- Petrie, A., & Sabin, C. (2005). Errors in hypothesis testing. In A. Petrie & C. Sabin (Eds.), *Medical statistics at a glance* (2 ed., pp. 44). Oxford: Blackwell Publishing Ltd.
- Poli, S., Cella, A., Puntoni, M., Musacchio, C., Pomata, M., Torriglia, D., . . . Pilotto, A. (2016). Frailty is associated with socioeconomic and lifestyle factors in community-dwelling older subjects. *Aging Clin Exp Res*. doi:10.1007/s40520-016-0623-5
- Potischman, N., Troisi, R., & Vatten, L. (2004). A life course approach to cancer epidemiology. In D. Kuh, & Ben-Shlomo, Y. (Ed.), *A life course approach to chronic disease epidemiology* (pp. 260-280). Oxford: Oxford University Press.
- Power, C., & Hertzman, C. (1997). Social and biological pathways linking early life and adult disease. *British Medical Bulletin*, 53(1), 210-221. doi:10.1093/oxfordjournals.bmb.a011601 %J *British Medical Bulletin*
- Powers, J., & Loxton, D. (2010). The impact of attrition in an 11-year prospective longitudinal study of younger women. *Ann Epidemiol*, 20(4), 318-321. doi:10.1016/j.annepidem.2010.01.002
- Pudrovskaya, T., & Anikputa, B. (2012). The role of early-life socioeconomic status in breast cancer incidence and mortality: unraveling life course mechanisms. *J Aging Health*, 24(2), 323-344. doi:10.1177/0898264311422744
- R Core Team. (2017). R: A language and environment for statistical computing. Retrieved from <https://www.R-project.org/>
- Raphael, D., & Bryant, T. (2015). Power, intersectionality and the life-course: Identifying the political and economic structures of welfare states that support or threaten health. *Social Theory & Health*, 13(3), 245-266. doi:10.1057/sth.2015.18
- Reinhardt, U. E., Hussey, P. S., & Anderson, G. F. (2002). Cross-national comparisons of health systems using OECD data, 1999. *Health Aff (Millwood)*, 21(3), 169-181.
- Romero-Ortuno, R. (2013). The SHARE operationalized frailty phenotype: a comparison of two approaches. *Eur Geriatr Med*, 4(4). doi:10.1016/j.eurger.2013.04.003
- Roser, M., & Ritchie, H. (2019). Cancer. Retrieved from <https://ourworldindata.org/cancer>
- Rothman, K. J., Greenland, S., & Lash, T. L. (2008a). Confounding. In K. J. Rothman, S. Greenland, & T. L. Lash (Eds.), *Modern epidemiology* (3 ed., pp. 129-134). Philadelphia: Lippincott Williams & Wilkins.

- Rothman, K. J., Greenland, S., & Lash, T. L. (2008b). Heterogeneity versus confounding. In K. J. Rothman, S. Greenland, & T. L. Lash (Eds.), *Modern epidemiology* (3 ed., pp. 259). Philadelphia: Lippincott Williams & Wilkins.
- Rothman, K. J., Greenland, S., & Lash, T. L. (2008c). Information bias. In K. J. Rothman, S. Greenland, & T. L. Lash (Eds.), *Modern epidemiology* (3 ed., pp. 137-146). Philadelphia: Lippincott Williams & Wilkins.
- Rothman, K. J., Greenland, S., & Lash, T. L. (2008d). Residual confounding. In K. J. Rothman, S. Greenland, & T. L. Lash (Eds.), *Modern epidemiology* (3 ed., pp. 198-199). Philadelphia: Lippincott Williams & Wilkins.
- Rothman, K. J., Greenland, S., & Lash, T. L. (2008e). Selection bias. In K. J. Rothman, S. Greenland, & T. L. Lash (Eds.), *Modern epidemiology* (3 ed., pp. 134). Philadelphia: Lippincott Williams & Wilkins.
- Rothman, K. J., Greenland, S., & Lash, T. L. (2008f). Survivor bias. In K. J. Rothman, S. Greenland, & T. L. Lash (Eds.), *Modern epidemiology* (3 ed., pp. 198). Philadelphia: Lippincott Williams & Wilkins.
- Rowe, J. W., & Kahn, R. L. (1997). Successful Aging1. *Gerontologist*, 37(4), 433-440. doi:10.1093/geront/37.4.433 %J The Gerontologist
- Sacker, A., Wiggins, R. D., Bartley, M., & McDonough, P. (2007). Self-rated health trajectories in the United States and the United Kingdom: a comparative study. *Am J Public Health*, 97(5), 812-818. doi:10.2105/ajph.2006.092320
- Santos-Eggimann, B., Cuenoud, P., Spagnoli, J., & Junod, J. (2009). Prevalence of frailty in middle-aged and older community-dwelling Europeans living in 10 countries. *J Gerontol A Biol Sci Med Sci*, 64(6), 675-681. doi:10.1093/gerona/glp012
- Schafer, M. H., Shippee, T. P., & Ferraro, K. F. (2009). When Does Disadvantage Not Accumulate? Toward a Sociological Conceptualization of Resilience. *Schweiz Z Soziol*, 35(2), 231-251.
- Schroder-Butterfill, E., & Mariani, R. (2006). A framework for understanding old-age vulnerabilities. *Ageing Soc*, 26(1), 9-35. doi:10.1017/s0144686x05004423
- Schröder, M. (2011). *Retrospective Data Collection in the Survey of Health, Ageing and Retirement in Europe. SHARELIFE Methodology*. Mannheim: Mannheim Research Institute for the Economics of Ageing.
- Shack, L., Jordan, C., Thomson, C. S., Mak, V., & Moller, H. (2008). Variation in incidence of breast, lung and cervical cancer and malignant melanoma of skin by socioeconomic group in England. *BMC Cancer*, 8, 271. doi:10.1186/1471-2407-8-271
- Sharpe, R. A., Taylor, T., Fleming, L. E., Morrissey, K., Morris, G., & Wigglesworth, R. (2018). Making the Case for "Whole System" Approaches: Integrating Public Health and Housing. *Int J Environ Res Public Health*, 15(11). doi:10.3390/ijerph15112345
- Sieber, S., Cheval, B., Orsholits, D., Van der Linden, B. W., Guessous, I., Gabriel, R., . . . Cullati, S. (2019). Welfare regimes modify the association of disadvantaged adult-life socioeconomic circumstances with self-rated health in old age. *Int J Epidemiol*. doi:10.1093/ije/dyy283
- Sieber, S., Cheval, B., Orsholits, D., van der Linden, B. W. A., Guessous, I., Gabriel, R., . . . Cullati, S. (submitted). Do welfare regimes moderate cumulative dis/advantages over the life course? Cross-national evidence from longitudinal SHARE data.

- Siegel, R. L., Miller, K. D., & Jemal, A. (2018). Cancer statistics, 2018. *CA: A Cancer Journal for Clinicians*, 68(1), 7-30. doi:10.3322/caac.21442
- Sihvonen, A. P., Kunst, A. E., Lahelma, E., Valkonen, T., & Mackenbach, J. P. (1998). Socioeconomic inequalities in health expectancy in Finland and Norway in the late 1980s. *Soc Sci Med*, 47(3), 303-315. doi:10.1016/s0277-9536(98)00020-3
- Smith, G. D., Hart, C., Blane, D., & Hole, D. (1998). Adverse socioeconomic conditions in childhood and cause specific adult mortality: prospective observational study. *Bmj*, 316(7145), 1631-1635.
- Soler-Vila, H., Garcia-Esquinas, E., Leon-Munoz, L. M., Lopez-Garcia, E., Banegas, J. R., & Rodriguez-Artalejo, F. (2016). Contribution of health behaviours and clinical factors to socioeconomic differences in frailty among older adults. *J Epidemiol Community Health*, 70(4), 354-360. doi:10.1136/jech-2015-206406
- South, S. C., Schafer, M. H., & Ferraro, K. F. (2015). Genetic and Environmental Overlap Between Childhood Maltreatment and Adult Physical Health. *Twin research and human genetics : the official journal of the International Society for Twin Studies*, 18(5), 533-544. doi:10.1017/thg.2015.62
- Stolz, E., Mayerl, H., Waxenegger, A., Rasky, E., & Freidl, W. (2017). Impact of socioeconomic position on frailty trajectories in 10 European countries: evidence from the Survey of Health, Ageing and Retirement in Europe (2004-2013). *J Epidemiol Community Health*, 71(1), 73-80. doi:10.1136/jech-2016-207712
- Stoop, I. (2005). *The Hunt for the Last Respondent: Nonresponse in Sample Surveys*. (PhD Thesis), Utrecht University,
- Strachan, D. P., Sheikh, A. (2004). A life course approach to respiratory and allergic diseases. In D. Kuh, Ben Shlomo, Y. (Ed.), *A life course approach to chronic disease epidemiology* (pp. 240-259). Oxford: Oxford University Press.
- Strand, B. H., Groholt, E. K., Steingrimsdottir, O. A., Blakely, T., Graff-Iversen, S., & Naess, O. (2010). Educational inequalities in mortality over four decades in Norway: prospective study of middle aged men and women followed for cause specific mortality, 1960-2000. *Bmj*, 340, c654. doi:10.1136/bmj.c654
- Strand, B. H., & Kunst, A. (2007). Childhood socioeconomic position and cause-specific mortality in early adulthood. *Am J Epidemiol*, 165(1), 85-93. doi:10.1093/aje/kwj352
- Stringhini, S., Polidoro, S., Sacerdote, C., Kelly, R. S., van Veldhoven, K., Agnoli, C., . . . Vineis, P. (2015). Life-course socioeconomic status and DNA methylation of genes regulating inflammation. *Int J Epidemiol*, 44(4), 1320-1330. doi:10.1093/ije/dyv060
- Uauy, R., & Solomons, N. (2005). Diet, nutrition, and the life-course approach to cancer prevention. *J Nutr*, 135(12 Suppl), 2934s-2945s.
- United Nations. (2017). *World Population Prospects: The 2017 Revision*. Retrieved from New York: United Nations: https://www.un.org/en/development/desa/population/publications/pdf/ag_eing/WPA2017_Report.pdf
- United Nations. (2019). *World Population Prospects 2019: Highlights*. Retrieved from New York: United Nations:

- Valkonen, T., Martikainen, P., Jalovaara, M., Koskinen, S., Martelin, T., & Mäkelä, P. (2000). Changes in socioeconomic inequalities in mortality during an economic boom and recession among middle-aged men and women in Finland. *European Journal of Public Health*, 10(4), 274-280. doi:10.1093/eurpub/10.4.274 %J European Journal of Public Health
- van der Linden, B. W. A., Cheval, B., Sieber, S., Orsholits, D., Guessous, I., Stringhini, S., . . . Cullati, S. (2019). Life Course Socioeconomic Conditions and Frailty at Older Ages. *J Gerontol B Psychol Sci Soc Sci*. doi:10.1093/geronb/gbz018
- Vineis, P., Kelly-Irving, M., Rappaport, S., & Stringhini, S. (2016). The biological embedding of social differences in ageing trajectories. *J Epidemiol Community Health*, 70(2), 111-113. doi:10.1136/jech-2015-206089
- Vohra, J., Marmot, M. G., Bauld, L., & Hiatt, R. A. (2016). Socioeconomic position in childhood and cancer in adulthood: a rapid-review. *J Epidemiol Community Health*, 70(6), 629-634. doi:10.1136/jech-2015-206274
- Wade, R., Jr., Cronholm, P. F., Fein, J. A., Forke, C. M., Davis, M. B., Harkins-Schwarz, M., . . . Bair-Merritt, M. H. (2016). Household and community-level Adverse Childhood Experiences and adult health outcomes in a diverse urban population. *Child Abuse Negl*, 52, 135-145. doi:10.1016/j.chiabu.2015.11.021
- Wadsworth, M. E. (1997). Health inequalities in the life course perspective. *Soc Sci Med*, 44(6), 859-869. doi:10.1016/s0277-9536(96)00187-6
- Wadsworth, M. E., & Kuh, D. J. (1997). Childhood influences on adult health: a review of recent work from the British 1946 national birth cohort study, the MRC National Survey of Health and Development. *Paediatr Perinat Epidemiol*, 11(1), 2-20.
- Wahrendorf, M., & Blane, D. (2015). Does labour market disadvantage help to explain why childhood circumstances are related to quality of life at older ages? Results from SHARE. *Aging Ment Health*, 19(7), 584-594. doi:10.1080/13607863.2014.938604
- Wahrendorf, M., Blane, D., Bartley, M., Dragano, N., & Siegrist, J. (2013). Working conditions in mid-life and mental health in older ages. *Adv Life Course Res*, 18(1), 16-25. doi:10.1016/j.alcr.2012.10.004
- Wang, H., Qiu, F., Gregg, A., Chen, B., Kim, J., Young, L., . . . Chen, L. W. (2017). Barriers and Facilitators of Colorectal Cancer Screening for Patients of Rural Accountable Care Organization Clinics: A Multilevel Analysis. *J Rural Health*. doi:10.1111/jrh.12248
- Wanner, P., Sauvain-Dugerdil, C., Guilley, E., & Hussy, C. (2005). *Âges et générations : la vie après 50 ans en Suisse*. Neuchâtel: Office fédéral de la statistique.
- Weiderpass, E., & Pukkala, E. (2006). Time trends in socioeconomic differences in incidence rates of cancers of gastro-intestinal tract in Finland. *BMC Gastroenterol*, 6, 41. doi:10.1186/1471-230x-6-41
- What is health? The ability to adapt. (2009). *Lancet*, 373(9666), 781. doi:10.1016/s0140-6736(09)60456-6
- Wheaton, B., & Gotlib, I. H. (1997). Trajectories and turning points over the life course: concepts and themes. In B. Wheaton & I. H. Gotlib (Eds.), *Stress and Adversity over the Life Course: Trajectories and Turning Points* (pp. 1-26). Cambridge: Cambridge University Press.

- Widmer, E. D., & Ritschard, G. (2009). The de-standardization of the life course: Are men and women equal? *Advances in Life Course Research*, 14(1), 28-39. doi:<https://doi.org/10.1016/j.alcr.2009.04.001>
- Wilkinson, R. G. (1989). Class mortality differentials, income distribution and trends in poverty 1921-1981. *J Soc Policy*, 18(3), 307-335.
- Wilmoth, J., & Ferraro, K. (2013). *Gerontology: Perspectives and issues*: Springer Publishing Company.
- Woo, J., Zheng, Z., Leung, J., & Chan, P. (2015). Prevalence of frailty and contributory factors in three Chinese populations with different socioeconomic and healthcare characteristics. *BMC Geriatr*, 15, 163. doi:10.1186/s12877-015-0160-7
- World Health Organization. (1946). *Preamble to the Constitution of the World Health Organization as adopted by the international health conference*. Retrieved from New York: <https://www.who.int/about/who-we-are/constitution>
- World Health Organization. (2001). *International Classification of Functioning, Disability and Health: ICF*. Retrieved from Geneva:
- World Health Organization. (2015). *World report on ageing and health*. Retrieved from Geneva:
- World Health Organization. (2019). Cancer. Retrieved from <https://www.who.int/health-topics/cancer#tab=overview>
- World Health Organization Commission on social determinants of health. (2008). *Final report: closing the gap in a generation: health equity through action on the social determinants of health*. Retrieved from Geneva:

The life course construction of social inequalities in health in old age

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Thèse 136 – December 2019

Population ageing is expected to lead to a rise of chronic conditions and multimorbidity. The life-course perspective is a useful approach when studying aging, because it can give insights into different pathways and the role trajectories and life events play in health in later life. Moreover, socioeconomic conditions have been identified as a key factor by which health varies. Therefore, the main aim of this thesis was to study the life course construction of health inequalities in old age. More precisely, the cumulative dis/advantage theory was tested and enriched, so that causal mechanisms and processes that lie behind social inequalities in health among the elderly could be identified. This thesis is in article format and contains three papers using data from the Survey of Health, Ageing, and Retirement in Europe. Article 1 describes the importance of doing life course research in the general population by looking at the effect of childhood socioeconomic conditions on cancer in later life. Article 2 studies associations of life course socioeconomic conditions with frailty, an important clinical syndrome used in geriatric medicine. Article 3 further explores different possible pathways in the life course that influence health in later life, including adverse life events, with a focus on potential variation across welfare regimes.

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This project has received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie grant agreement No 676060