Effect of life course socioeconomic trajectories on multimorbidity and mortality

Study protocol for a PhD thesis

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Overarching Goal

To assess the effect of socioeconomic trajectories on multimorbidity and mortality.

Background

The global rise in populations suffering from multiple health conditions, that is, multimorbidity, is a major public health concern [1]. Multimorbidity, the co-occurrence of two or more chronic health conditions, does not only decrease quality of life, but has also been associated with increased risks for disability and mortality [2-4]. Research suggests that compared to frailty and disability, multimorbidity has the strongest association with mortality, making it a central target for population health interventions [5]. Further, according to WHO data, deaths due to chronic diseases make up around 70% of all global deaths and that number is expected to rise if no interventions are implemented [6, 7].

While multimorbidity is a wide-spread problem in aged populations, it has been shown to disproportionally affect individuals exposed to socioeconomic deprivation, raising the question of how socioeconomic conditions (SEC), e.g. education, income, or wealth, are linked with the development of chronic health conditions. Previous research has already investigated this association and proposes SEC as both a cause and a predictor for morbidity and mortality [8, 9]. However, the focus has primarily been on either current SEC, like current income or current employment, or SEC during one life period, either during childhood or adulthood [10, 11]. This is a limited perspective since it has been shown that SEC trajectories across the life course are a stronger predictor for disease outcome in later life than SEC at any singular life point [12]. Therefore, what is currently missing from the literature is a life course perspective.

This research aims to fill this gap by using data from population-based longitudinal cohorts in high-income countries. Data from seven different cohort studies across more than 30 countries will be used to perform a multi-cohort analysis to elucidate the association between SEC trajectories across the life course and multimorbidity and mortality in later life. This work will be descriptive and predictive in its statistical operationalization and intends to identify individuals with increased risk of multimorbidity and mortality in order to inform future public health policies aiming to decrease the burden of disease in the ageing population [13].

Common Methods

Cohorts

The included cohorts feature harmonized data sets with variables that are as identical as possible to allow for cross-country comparisons. All cohorts are nationally representative with the exception of JSTAR, which recruits samples from five pre-chosen municipalities [14].

Name	Country	Age eligibility	Number of waves	Sample size at latest released wave (year)
HRS	United States	51+	14 waves	n = 20,912 (2019)
SHARE	20+ European countries and Israel	50+	7 waves	n = 77,263 (2017)
TILDA	Ireland	50+	4 waves	n = 6,400 (2017)
ELSA	England	50+	8 waves	n = 10,078 (2017)
KLoSA	South Korea	45+	6 waves	n = 6,940 (2017)

Name	Country	Age eligibility	Number of waves	Sample size at latest released wave (year)
CHARLS	China*****	45+	3 waves	n = 19,816 (2015)
JSTAR	Japan	50-75	4 waves	n = 4,021 (2013)

Gateway to Global Ageing Data [15]

***** This project considers longitudinal cohort studies from high-income countries. China is currently considered an upper middle-income country, but is projected to become a high-income country by 2025 and may therefore be considered for this research [16].

Exposures

Childhood SES will be measured using parental education and the occupation of the main breadwinner during childhood. Potential additional variables are the number of rooms in the childhood household and the number of people living in the household, which are indicators of overcrowding, as well as the number of books in the household, which is a frequently used proxy for social and economic background [17].

Adulthood SES will be measured via variables across four main domains, that is, educational attainment, economic power, employment, and social class. Educational attainment will be measured either as a continuous (years of completed schooling) or a categorical variable following the *International Standard Classification of Education* (ISCED) [18]. Economic power encompasses both income and wealth which are measured separately in all cohorts. Lastly, employment and social class are closely linked measures of SEC. In practice, the *British Registrar General's occupational classification* is often applied, which divides the working population into six categories according to their occupation, ranging from "professional" positions (e.g. lawyers, doctors) to "unskilled" manual labor (e.g. construction workers) [18]. Across cohorts, the *International Standard Classification of Occupation* (ISCO) will be used. Employment further considers employment status, i.e. full-time, part-time, or unemployment, as well as changes in occupation across the life course.

Since childhood measurements are not included in all cohorts, sub-groups of cohorts will be created to cover the entire life course. ELSA and SHARE feature harmonized life history data and will therefore be used to describe the trajectory from childhood to young adulthood, while the other cohorts describe the trajectory from young adulthood to adulthood.

Health Outcomes

Multimorbidity is defined as the co-occurrence of two or more chronic diseases, though other definitions exist, "ranging from simple counts of the number of diseases or clusters of diseases, and the number of medications, up to severity measures like the Charlton index which differentially weight diseases" [19]. For this research, I use the definition of min. two chronic conditions occurring at the same time. Multimorbidity is self-reported in all cohorts but hinging on previous diagnoses, i.e. via the question "Has a physician ever diagnosed you with…".

All-cause and cause-specific **mortality** will be considered. The included cohorts collect this information during exit interviews, where relatives of the deceased provide details on date and cause of the respondent's death.

For multimorbidity and cause-specific mortality, diseases will further be grouped into clusters, i.e., cardiovascular diseases (CVDs), neuro-degenerative disorders, cancer, chronic respiratory diseases, etc. [20]. Research suggests that in the case of upward social mobility there can be a trade-off between different health indicators, leading, for example, to better psychological well-being but worse cardiometabolic health [21]. Therefore, it cannot be assumed that higher SEC across the life course has a favorable effect on all health outcomes. To test this hypothesis, I want to explore whether associations between SEC trajectories and multimorbidity and mortality change depending on the morbidity in question.

Specific Aims

Aim 1: Mapping review on the effect of life course socioeconomic trajectories on multimorbidity and mortality

Goals: (1) To synthesize the evidence on the association between SEC trajectories throughout the life course and multimorbidity and mortality; (2) to describe the life course frameworks supported by the studies included in the mapping review.
Main data science task: Description.
Statistical analysis: A qualitative synthesis of the included studies will be performed. I will draw an "evidence map" of the associations between SEC across different periods during the life course and health outcomes, and synthesize the degree of evidence supporting each life course framework.

Aim 2 & 3: Assessment of the life course socioeconomic determinants of mortality and multimorbidity in later life

Goals: To identify individuals at higher risk of mortality and multimorbidity based on their SEC trajectory across the life course.
Main data science task: Prediction.
Hypothesis: Individuals exposed to favorable SEC throughout the life course have a lower risk for mortality (aim 2) and multimorbidity (aim 3) compared to individuals exposed to favorable SEC only in one life period or never. Additionally, this association differs depending on the morbidity in question [22].
Statistical analysis: Aim 2 and 3 will use survival models to estimate mortality rates on both the absolute and relative scale (hazard differences and ratios) for groups with various socioeconomic trajectories across two life periods, e.g. low-low, low-high, high-low, high-high. For aim 2, we will consider all-cause and cause-specific mortality and may consider premature mortality (deaths before the age of 70). The cohort data will be analyzed via a two-step approach of first performing intra-cohort analyses and then pooling the data across cohorts using meta-analysis.

Limitations

- **Retrospective and self-reported data:** Much of the data stems from self-reported questionnaires. Similarly, childhood data is collected retrospectively, which might introduce bias. A study analyzing the accuracy of recalled events as part of SHARELIFE concludes that overall, respondents seemed to remember fairly well their health status and living conditions during childhood, but it is unclear whether this

applies to other life periods and/or other cohorts as well [23]. To overcome this limitation, I will conduct sensitivity analyses.

- **Bias:** Misclassification might exist, both for exposures, as a result of uncertainty regarding SEC during different life periods, and for outcomes (more so for multimorbidity than for mortality). Residual confounding is also a possibility. To overcome this limitation, I will conduct quantitative bias analysis [24].

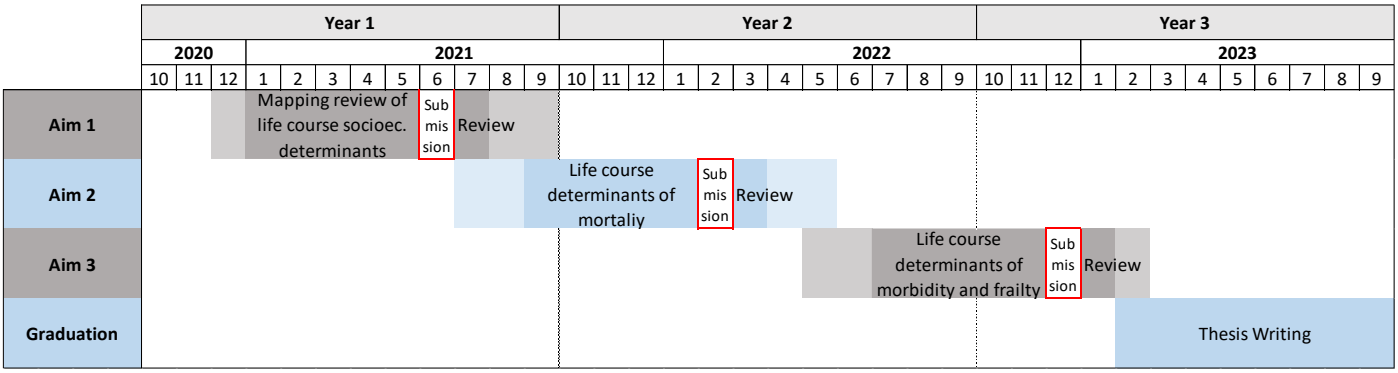
Strengths

- **Multi-cohort analysis:** The use of multiple cohorts creates a large sample size and the harmonization of the data sets allows for comparability between cohorts. Further, the amount of collected data makes it possible to describe SEC across multiple variables in different dimensions and to test its association with different health outcomes.
- **Multiple life periods:** To implement a life course perspective, this project considers multiple periods during the life course which has not been extensively studies in past research. Studying SEC trajectories gives insight into the importance of social mobility and highlights the potential compensatory effects of later life periods.

Expected Outcomes and Public Health Context

The expected outcome of this project are three peer-reviewed papers, of which one is a mapping review and two are original research papers based on multi-cohort data. These papers will make up the bulk of the PhD thesis. One major contribution of this research to the existing literature is its life course approach that does not consider only one period during the life course, e.g. childhood or adulthood, but a minimum of two periods. Further, contributing empirical evidence from several cohorts across different countries strengthens the potential external validity of my research. Highlighting the people, exposures, and life periods that are associated with an increased risk of adverse health outcomes in later life is an important first step to mitigates health inequalities. Only once these risks have been identified can social and economic policy making adapt toward the strengthening of the health of the ageing population.

Timeframe



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