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ABSTRACT

Lifetime Trajectories and Drivers of Socioeconomic Health Disparities: Evidence from Longitudinal Biomarkers in the Netherlands*

This study investigates lifetime socioeconomic health disparities through longitudinal biomarkers from the Dutch Lifelines cohort study and biobank. We construct an allostatic load index from 12 biomarkers and analyze the dynamics of health and its association with socioeconomic status (SES) over the life cycle. Our findings reveal that health risks linked to lower SES emerge early and precede chronic disease onset. Further analysis investigates the drivers of allostatic load and emphasizes health behaviors. The results highlight the need for early interventions targeting SES-related health disparities and provide new insights into the physiological pathways linking SES to long-term health outcomes.

JEL Classification: D31, I12, I14

Keywords: biomarkers, allostatic load, chronic diseases, life cycle, lifestyle

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1 Introduction

Narrowing health disparities has become a consensus goal for many governments and international organizations; see for instance the EU4 Health Programme 2021-2027 and the Netherlands Global Strategy 2023-2030. These programs argue that reducing the health gap is a major way to improve population health. To design effective preventive interventions, we need to know when and how associations between health and socioeconomic status (SES) arise.

One of the main challenges in this endeavor concerns the lack of consensus on how to measure health. Much of the prior literature on health disparities across socioeconomic groups has employed morbidity, mortality or self-rated health as outcome measures (see, e.g., Van Kippersluis et al., 2010; Van Ooijen et al., 2015; Hosseini et al., 2022; Danesh et al., 2024). This has provided valuable insights, but self-rated health (SRH) is inherently subjective and nonspecific, while morbidity measures often capture outcomes realized later in life, after much of the cumulative wear and tear has already occurred. In this study, we contribute to the existing evidence by focusing on biomarkers which are objective indicators that can be observed prior to disease onset.

Specifically, we study the evolution of health and the dynamics of socioeconomic health disparities over the life cycle by using longitudinal data on biomarkers derived from blood, urine, electrocardiograms (ECG), anthropometric measurements, and blood pressure within a large-scale, population-based, prospective cohort and biobank. Biomarkers are normally defined as objective, quantifiable indicators of biological processes (Strimbu & Tavel, 2010). The dynamics of biomarkers are often linked to the aging process, the onset of diseases, and mortality (Arbeev et al., 2016). Consequently, biomarkers not only reflect an individual's current health

status but also serve as predictive indicators of morbidity or mortality. Complementing clinical health assessments, the longitudinally observed biomarkers from prospective cohort studies offer an opportunity to investigate socioeconomic health gradients before the emergence of diseases. Moreover, by tracking the accumulation of physiological health deficits, these biomarkers provide deeper insights into the interplay between SES, biological processes, and clinical outcomes, over the life cycle (Arbeev et al., 2016).

An emerging literature in economics and epidemiology has started to employ biomarkers to investigate health disparities. Prior studies have identified significant SES-related disparities in biomarkers associated with diabetes and cardiovascular disease (Kavanagh et al., 2010;), as well as body mass index (Baum & Ruhm, 2009). Furthermore, systematic combinations of biomarkers that indicate cumulative health risks reveal considerable disparities in biological health across SES groups (e.g., Seeman et al., 2004; Carrieri et al., 2020; Davillas & Jones, 2020).

Building on this, we examine the dynamics of health disparities using dynamic biomarkers from the Dutch Lifelines cohort study and biobank, which includes data from over 167,000 individuals at baseline. By linking the longitudinally observed biomarkers with information on chronic diseases, health-related behaviors, and socio-demographic factors, we are in the unique position to study the evolution of socioeconomic health disparities across the life cycle and the role of biomarkers in the relationship between SES and health outcomes.

Following the approach of Seeman et al. (1997, 2004), we adopt the concept of allostatic load and construct an allostatic load index (ALI) based on 12 biomarkers from cardiovascular, metabolic, and kidney systems, representing cumulative physiological dysregulation due to stress

and aging. To assess the validity of the ALI in predicting health outcomes, we examine its relationship with aging-related chronic disease, with a particular focus on how early biological risks predict chronic disease prevalence. To engage with the literature focusing on mortality outcomes, we also conduct analyses that investigate whether biomarker-related risks can predict mortality.

Our analysis suggests that biomarker-related risks emerge earlier in adulthood and increase with age. In contrast, aging-related chronic diseases become prominent only in middle age, which indicates that biomarker-related risks precede the onset of these diseases. Then, we conduct age-group specific regressions to examine the role of the ALI in chronic disease development and 3-year mortality. The results demonstrate that both higher ALI and lagged ALI are significantly associated with an increased risk of chronic diseases and 3-year mortality.

Second, we examine how educational disparities in biomarkers and allostatic load evolve across the life cycle through graphical analysis. Our findings show that allostatic load disparities emerge in early adulthood, widen with age, and peak in late middle age, stabilizing thereafter. Gender differences are significant, with males consistently exhibiting higher ALI levels than females throughout the life course. Additionally, we analyze the prevalence gap for individual biomarkers and biomarker-related risks. The results reveal that disparities in biomarker-related risks emerge early, often before age 30, and exhibit pronounced educational and gender differences, with males generally showing higher risk levels for most biomarkers. While these patterns may be influenced by factors such as cohort effects, health-based attrition, and medication use, the findings highlight the early onset and cumulative nature of socioeconomic health disparities.

Finally, we investigate factors driving allostatic load levels and the growth of allostatic load over the life cycle, highlighting health behaviors as possible determinants. We employ age-group specific regression by gender and decompose the total R-squared using Shapley and Owen decomposition method. The decomposition reveals that alcohol consumption and physical activity are important contributors to the ALI across genders and age groups. In addition, educational attainment and employment also play notable roles, with education having a consistent impact and employment being more influential during working years. The results differ by gender. For females, alcohol consumption and education have stronger effects, while for males, physical activity and smoking are more important contributors, particularly before age 55. When examining the growth of the ALI, health behaviors remain key drivers, but their importance shifts, where smoking plays a more substantial role for males. While these findings provide valuable insights into the relative importance of these factors, they reflect correlations rather than causation and are driven by the biomarkers included in the study.

We contribute to the literature in a number of ways. First, we contribute to the existing literature on socioeconomic health gradients by investigating these gradients before the onset of clinical diagnoses. Typically, individuals with higher SES enjoy longer and healthier lives. SES-related health differences have been found in mortality (e.g., see, Deaton, 2003; Cutler & Lleras-Muney, 2006; Van Kippersluis et al., 2010; Chetty et al., 2016) and in most diseases and conditions (Kivimäki et al., 2020; Pallesen et al., 2024; Danesh et al., 2024). However, morbidity and mortality differences are often only prominent at middle and higher ages, which leaves the question of how the differences in health develop across SES before reaching the clinical endpoints. Evidence suggests that the socioeconomic health gap may begin to widen before

clinical endpoints like morbidity or mortality (Danesh et al., 2024). Biomarkers allow us to objectively assess health risks and understand how socioeconomic health gradients develop before adverse health outcomes manifest themselves (Arbeev et al., 2016).

Second, our study contributes to the literature on health evolutions. While socioeconomic health gradients have been widely explored in prior studies, data limitations make it challenging to achieve a consensus on how to define and measure these gradients over the life cycle (Hosseini et al., 2022; Danesh et al., 2024). Previous work examined health evolutions across the life cycle using indicators such as SRH, morbidity, and mortality. Among these, SRH is often employed as a health measure in studies on socioeconomic health disparities and is generally regarded as a reliable predictor of other health outcomes. For instance, Van Kippersluis et al. (2010) use SRH to analyze the life cycle profile of adverse health by income in the Netherlands. Similarly, Van Ooijen et al. (2015) develop a health model that combines SRH with administrative health data to capture the evolution of health as individuals age. However, SRH has inherent limitations: it is subjective, lacks specificity, and does not provide a cardinal metric (Hosseini et al., 2022). Recent studies have attempted to overcome these issues by using more objective health indicators. For example, Danesh et al. (2024) introduced a chronic disease index based on pharmaceutical dispensation data to track health evolution before death. Hosseini et al. (2022) developed a frailty index incorporating factors such as medical diagnoses, mental health conditions, and cognitive impairments to predict health dynamics over the life cycle. We expand on this by relying on biomarkers to examine the progression of socioeconomic health disparities over the life cycle.

Third, our study offers insight into the drivers of health disparities in biomarkers. Economic and epidemiological research underscores the important role of health-risk behaviors — such as smoking, alcohol consumption, physical inactivity, and poor dietary habits — particularly among adults. These behaviors serve as critical pathways linking SES to health outcomes (Adler & Stewart, 2010). Previous studies have estimated that health behaviors account for approximately 40% of premature mortality (McGinnis et al., 2002) and significantly influence the prevalence and incidence of chronic diseases (Danesh et al., 2024). Among these behaviors, smoking has been identified as having a particularly detrimental impact on both physical and mental health. Furthermore, health-risk behaviors are closely associated with allostatic load. For instance, Suvarna et al. (2020) review 26 studies examining the relationship between health behaviors and allostatic load and find robust evidence of significant associations. Specifically, 65% of studies on obesity and substance abuse, 75% of studies on sleep, and 62.5% of studies on combined lifestyle factors report significant correlations with allostatic load. In this research, we contribute to understanding how these factors contribute to the allostatic load and the growth of allostatic load and how they differ across age and gender.

The remainder of the paper is organized as follows: Section 2 describes the data. Section 3 outlines the methodology for constructing the ALI and explores its role of allostatic load to the aging-related chronic disease and mortality. Section 4 provides graphical evidence of the evolution of socioeconomic allostatic load disparities over the life cycle. Section 5 presents the decomposition results and discusses their interpretation. Section 6 concludes.

2. Data

2.1 Lifelines

We utilize data from the Dutch Lifelines cohort study and biobank. Lifelines is a multi-disciplinary prospective population-based cohort study examining in a unique three-generation design the health and health-related behaviours of 167,729 persons living in the North of the Netherlands. It employs a broad range of investigative procedures in assessing the biomedical, socio-demographic, behavioural, physical and psychological factors which contribute to the health and disease of the general population, with a special focus on multi-morbidity and complex genetics. This prospective cohort study is designed to explore the complex relationships among various factors in the development of chronic diseases and healthy aging (Scholtens et al., 2015). The Lifelines study began in 2006, and by 2023, three main waves (including the baseline) and three follow-up questionnaires have been completed.[1]

Every five years, participants are invited to Lifelines facilities for physical examinations, during which biomaterials are collected (Scholtens et al., 2015). These samples are promptly processed for analysis and preserved for long-term biobanking. Additionally, every 1.5 years, participants complete questionnaires that gather information on demographics, health status, lifestyle, environmental exposures, and psychosocial factors. All examinations are conducted by trained nurses following medical standards, and all assessments take place at the University

[1] Specifically, two follow-up (wave 1b and wave 1c) questionnaires were conducted after the wave 1a, and one follow-up (wave 2b) took place after the wave 2a. Since 2024, the fourth wave of assessment is underway, with plans to include new participants, particularly from younger generations, in the Lifelines cohort. We do not include the data from wave 4a because it is still in the process. For more information about Lifelines, please visit https://www.lifelines-biobank.com.

Medical Center Groningen laboratory center, which is certified according to international, European, and Dutch standards.

2.2 Variables

Biomarkers Biomarker data were obtained during physical examinations and biomaterial collection as part of the Lifelines cohort study. As of the end of 2023, three waves of biomarker data have been made available, encompassing a wide range of measurements, including anthropometric data, blood and urine analyses, blood pressure, and ECG, among others. Specifically, the first wave was collected between 2006 and 2013, the second wave between 2014 and 2018, and the third wave between 2019 and 2023. This longitudinal data enables us to follow individuals' health over a relatively long period.

For our analysis, we selected twelve biomarkers and they are related to cardiovascular, metabolic, and kidney functions. Table 1 summarizes the selected biomarkers, along with brief descriptions and clinically defined high-risk thresholds. To capture the cumulative dysregulation of physiological systems, we employ the concept of allostatic load and construct an index to be the indicator of biological health status. A detailed description of the allostatic load and the construction of the index is provided in Section 3.

Chronic Disease In the Lifelines self-reported questionnaires, administered every 1.5 years, participants were asked whether they had been diagnosed with specific diseases.[2] These diseases are categorized into groups such as cancer, cardiovascular diseases, diabetes, kidney and bladder diseases, mental illnesses, and neurological disorders. Within each category, specific conditions

[2] In wave 1a, participants were asked, "Have you ever had a certain disease?" For all subsequent waves, participants were asked, "Did any of the health problems listed below begin since the last time you completed the Lifelines questionnaire?".

are further detailed. For example, cardiovascular diseases include stroke, heart failure, and heart attacks. To evaluate the overall burden of aging-related chronic diseases among Lifelines participants, we use a composite score as a proxy measure. The selection of chronic diseases is guided by the design of the Lifelines questionnaires, their definitions, and the availability of corresponding data.[3] We include most of the chronic conditions from Lifelines list, while considering the timing of disease onset and the data availability in Lifelines.[4] The complete list of 19 aging-related chronic diseases is provided in Table A.1 (in Appendix).[5]

Mortality Lifelines continuously receives death updates for participants from the Personal Records Database (BRP), which contains personal data of individuals residing in the Netherlands as recorded by municipalities. Participants' mortality information is updated even if they withdraw from Lifelines, and the cutoff date for death records in our current dataset is September 2024.

Health Behavior Health behavior data is collected from the Lifelines questionnaire. Participants were queried about various health-related behaviors, including alcohol consumption, tobacco use, smoking habits, sleeping disorder, and overall physical activity levels. To measure drinking behavior, we use self-reported data on both the frequency of alcohol consumption over a month and the number of glasses consumed over a day. These variables capture both the frequency and intensity of drinking. Smoking behavior is represented by a dummy variable based

[3] For participants aged 18 years and older, the questionnaires assess whether they have experienced any of the specified chronic diseases since their last participation in the Lifelines survey and associated assessments. Our identification of chronic diseases primarily relies on the list provided in the questionnaires.

[4] Since our focus is on lifetime trajectories, we limit our analysis to "aging-related" chronic conditions. Specifically, we include only diseases with prevalence that increase with age, excluding chronic conditions primarily observed in childhood and predominantly caused by genetic factors. Additionally, we do not consider chronic diseases that are only available in limited waves of Lifelines.

[5] While self-reported data on chronic diseases offer valuable health insights, they are subject to limitations, including non-classical measurement errors and underdiagnosis. These issues are particularly prevalent among lower-income or less-educated groups, potentially introducing bias into health assessments.

on responses to the question, "Do you smoke now, or have you smoked in the past month?". Finally, physical activity is proxied by the average number of days per week participants engaged in activities such as cycling, doing odd jobs, gardening, sports, or other strenuous tasks for at least 30 minutes. We calculate the average for these physical activities across winter and summer seasons. Finally, sleep disorder is captured by the question: "Do you have trouble sleeping nearly every night?"

Socioeconomic Status Lifelines provides socioeconomic data on education, income, and occupation. For this study, we use the highest educational attainment as the primary measure of SES. Educational attainment is categorized into two groups based on the Dutch school system: low (no education, primary education, lower or preparatory secondary vocational education, junior general secondary education, secondary vocational education or work-based learning pathway, senior general secondary education, pre-university secondary education), and high (higher vocational education and university education).[6] For participants under the age of 25, we use their parent's highest educational attainment as a proxy, given that individuals typically complete their education in their mid-twenties.

Covariates Demographic factors, such as age, gender, cohort, and province are available for all participants in Lifelines. In addition, we obtain the degree of urbanization information at Postal Code-4 level from Statistics Netherlands (Centraal Bureau voor de Statistiek).

[6] In the Netherlands, higher vocational education and university education correspond to levels 6, 7, and 8 of the International Standard Classification of Education (ISCED). Consequently, the low-education group in our dataset includes individuals with ISCED levels ranging from 0 to 5. The mandatory nature of most types of secondary education is the primary reason for dividing it into two categories.

2.3 Sample Selection and Summary Statistics

We build an unbalanced panel based on the data from waves 1a, 2a, and 3a of the Lifelines study, covering the period from 2006 to 2023. Table 2 presents our sample selection process. The baseline sample includes 150,605 observations of participants aged from 18 to 80.[7] Among these, 99,608 participants from the baseline sample participated in wave 2a, and 60,794 participated in wave 3a. Observations with missing values for any of the 12 biomarkers of interest are also excluded, resulting in the removal of 21,215 observations. Further, we exclude observations with missing values for chronic diseases or demographic characteristics or who did not fast before blood sampling.[8]

Our final sample consists of 137,110 individuals. Of these, 46,796 participated in only one wave, 50,906 participated in two waves, and 39,408 participated in all three waves. As shown in the Table 2, there is an attrition across the three waves. Approximately 3.1% of participants passed away during the study period, which extended until 2024. Other reasons for withdrawal include time-intensive participation requirements, loss of interest, relocation from the research area, or enrollment in a regular health care program (Sijtsma et al., 2022). [9]

Table 3 presents selected summary statistics on demographic and socioeconomic information, biomarkers, and chronic diseases across three waves in Lifelines.

[7] We exclude individuals aged below 18, as most biomarkers in Lifelines are only available for participants aged 18 and above. Additionally, we exclude individuals older than 80 years because they are underrepresented in Lifelines.
[8] Many biomarkers are influenced by short-term dietary intake. To ensure reliable results, fasting is required before blood sample collection or measurement. It is therefore imperative to exclude individuals who did not fast before blood collection from our sample.
[9] We currently do not observe data drop-out due to enrollment into a regular health care facility. However, Sijtsma et al. (2022) show that only a small proportion of participants withdraws in follow-ups.

3. Allostatic Load, Chronic Disease and Mortality

3.1 Allostatic Load Index

Aging is a complex process involving numerous biological changes and interactions that gradually result in physiological dysregulation, disease, and ultimately death (Arbeev et al., 2016). Although individual biomarker changes may seem small, the cumulative effect of multiple dysregulated biomarkers can significantly deteriorate health, impacting various body systems over time. To measure this cumulative biological dysregulation, we aim to build an index that captures the overall burden of dysregulated biomarkers. To do so, we follow established research to construct an index by summing biomarkers for which individual values deviate from clinical thresholds (Seeman et al., 2004; Howard & Sparks, 2016; Davillas & Jones, 2020).

Allostatic load, often referred to as wear and tear, represents the cumulative dysregulation of physiological systems over time due to stress,[10] including factors such as social, environmental, and life event exposures (Seeman et al., 2004; Beckie, 2012). The allostatic load has been widely used in health research, especially in studies on health measurements and inequalities, as it potentially provides insight into biological mechanisms underlying health disparities. The ALI is essential for understanding how sociodemographic factors and environmental stressors influence both physical and mental health, shaping individual aging trajectories (Beckie, 2012).

Depending on the data availability, the number of biomarkers varies between studies. Most include at least one biomarker related to the metabolic and cardiovascular systems (Johnson et

[10] The concept of allostatic load was introduced by McEwen & Stellar (1993) and does not directly measure stress itself.

al., 2017). The initial study calculating the ALI used 10 biomarkers associated with the cardiovascular and metabolic systems and the hypothalamic-pituitary-adrenal (HPA) axis (Seeman et al., 1997). Subsequent studies expanded this scope as additional biomarker data became available, for example, follow-up research employed 16 biomarkers to assess allostatic load (Seeman et al., 2004). More recent studies, such as those by Howard and Sparks (2016), use 10 biomarkers, while Karimi et al. (2019) include 16 biomarkers spanning four body systems and two organs. While this flexibility allows researchers to adapt the ALI to different datasets, it also complicates cross-study comparisons.[11] Nonetheless, the ALI remains a valuable tool for understanding the biological pathways connecting SES to morbidity and mortality.

In our study, we use 12 biomarkers (see Table 1) to construct the ALI,[12] focusing on three physiological systems: cardiovascular (n=3), metabolic (n=8), and kidney function (n=1).[13] The ALI is calculated by applying clinically established threshold cut points to each biomarker and we calculate the ALI by counting the number of biomarker-related risks that individual i have at age a:

$$ALI_{i,a} = \sum_{k=1}^{12} I_{i,a}^{k}. \quad (1)$$

[11] A systematic review by Johnson et al. (2017) summarizes the most commonly used biomarkers for measuring allostatic load in previous research.

[12] The use of BMI for assessing clinical obesity has been a topic of ongoing discussion in the literature. Research suggests that BMI might misclassify or overestimate adiposity, potentially leading to inappropriate conclusions. In particular, as suggested by Rubino et al. (2025), BMI should be treated as a surrogate measure of health risk at the population level rather than a direct measure of individual health outcomes. Therefore, rather than treating BMI as a marker of chronic conditions, we use it as an indicator of health risks, aligning with previous research on the construction of allostatic load. To assess the role of BMI, we also constructe an alternative ALI excluding BMI. Additionally, in a regression of allostatic load on education, we include BMI as a control variable. The results show that the coefficient for education remains statistically significant, although its magnitude is reduced by approximately half when BMI is controlled for.

[13] Some prior studies also employ biomarkers from other systems, including the immune system, the hypothalamic-pituitary-adrenal axis, the respiratory system, and the parasympathetic nervous system. However, biomarkers from the cardiovascular and metabolic systems are the most commonly used to construct the ALI (Johnson et al., 2017).

Where k denotes the biomarkers and $I_{i,a}^{k}$ is a binary variable indicating whether the level of biomarker k in individual i at age a is above the threshold.[14] The $I_{i,a}^{k}$ is equal to 1 if individuals are identified as "at-risk" based on a certain biomarker's cut-point. The value of the ALI for individual i at age a represents the current number of biomarker-related risks based on 12 selected biomarkers.

To gain a preliminary understanding of the ALI without considering any other factors, we visualize the dynamics of these biomarker-related risks across age. We pool the observations from three waves and group them by the number of risks. Figure 1 illustrates the proportion of individuals at different ages with differing numbers of biomarker-related risks, depicting the evolution of risk number throughout the life cycle. As shown, first, the number of biomarker-related risks increases with age, with a different speed by the categories in the number of risks. Notably, there is a significant rise in the development of risks after the age of 40. Additionally, biomarker-related risks are relatively prevalent even among young adults and over 25 percent of participants under the age of 25 have at least one risk.

Despite the insights gained from constructing ALI using clinical cutpoints, this approach may overlook health risks below the threshold. Therefore, following previous studies (e.g., see Seplaki et al. 2005 and Hawkley et al. 2011), we also adopt an alternative allostatic load scoring algorithm based on z-scores, which provides an index derived from continuous biological variables rather than categorical ones. Compared to ALI constructed using clinical cutpoints,

[14] One exception is HDL cholesterol, often called "good" cholesterol. A low HDL cholesterol level is considered high risk because HDL cholesterol helps remove excess cholesterol from the blood.

z-ALI accounts for risks both below and above the clinical threshold and reduces the influence of extreme values and outliers.

To compute the z-ALI, we standardize each biomarker to have a mean of 0 and a standard deviation of 1 (e.g., a score of 1 indicates a value that is one standard deviation above the mean), then sum the standardized values. HDL cholesterol, often referred to as "good" cholesterol, is reversed so that higher values reflect a greater health risk. Additionally, we identify extreme values, those exceeding five standard deviations above or below the mean, for each biomarker. To mitigate the impact of outliers, we replace these values with 5 or -5, thereby reducing noise in the data. Figure B.1 (in Appendix) illustrates the trajectory of z-ALI across the life cycle, demonstrating a consistent pattern compared to ALI constructed using clinical cutpoints.

3.2 Chronic Disease

Chronic diseases are widely recognized as a substantial burden on healthcare systems, with many conditions becoming prominent in middle adulthood. These diseases significantly contribute to socioeconomic disparities in healthcare expenditures and mortality rates, further exacerbating health inequalities later in life (Danesh et al., 2024). To assess whether allostatic load precedes chronic disease development, we develop a chronic disease index (CDI) using self-reported disease data from the Lifelines study.[15]

Our objective is to construct a CDI that aggregates self-reported information across a broad spectrum of aging-related chronic diseases, including cardiovascular conditions, diabetes,

[15] There is a clear distinction between the biomarkers we included and the aging-related chronic diseases we considered. While chronic disease indicates a diseased state in the body, biomarkers are biological measures that frequently but not perfectly correlate with an illness. For example, total cholesterol and triglyceride levels exceeding clinical thresholds do not immediately indicate a diagnosis of cardiovascular disease. However, high levels of these biomarkers increase the risk of stroke and heart attack, which offer insights into potential health risks.

neurological disorders, etc. One approach is to adapt the methodology used to create a frailty index (Hosseini et al., 2022). This method accounts for the cumulative number of adverse health events an individual has experienced. The resulting index can be treated as a continuous variable or normalized to a scale ranging from 0 to 1. For example, Hosseini et al. (2022) develop a frailty index using variables such as activities of daily living, medical diagnoses, and mental and cognitive functioning.

We use a total of 19 aging-related chronic diseases in Lifelines to construct the CDI (see Table A.1 in Appendix). Each chronic disease is represented by a binary variable, taking a value of either 0 or 1 for each individual, indicating whether the individual currently has or has previously had the disease. The CDI is calculated as the total number of chronic diseases an individual has experienced by a given age.[16]

Similar to the analysis of ALI, we employ a stacked area graph to examine the progression of chronic disease prevalence across age groups by pooling all observations. As illustrated in Figure 2, the onset of aging-related chronic diseases typically occurs after early adulthood. Among young adults, the majority do not have any of the selected chronic diseases, while only a small proportion have one chronic condition. Furthermore, the prevalence of these chronic diseases becomes substantial after age 35, with a marked increase observed only after around age 45.

Next, we compare the trajectories of ALI and CDI across the life cycle. Figure 3 illustrates these trajectories by age. To ensure comparability of scale, the indexes are rescaled using the mini-max scaling approach.[17] The figure reveals that biomarker-related risks emerge significantly

[16] Notably, we do not assign different weights to the chronic diseases in this calculation, which may be considered arbitrary. In addition, the CDI is subject to potential non-classical measurement errors and underdiagnosis due to the limitations of the available data.

[17] The mini-max scaling approach is a data normalization technique used to scale the values of a dataset to a specific range, often from 0 to 1.

earlier than chronic diseases. This raises a critical question: to what extent can ALI predict the CDI? From an intervention perspective, understanding whether early intervention before the onset of diseases is necessary is essential. Additionally, it is important to acknowledge that these trajectories may be confounded by cohort effects, health-based attrition, and medication intervention.

3.3 Mortality

Mortality, as the final stage of the life cycle, typically becomes significant only later in life, occurring well after the onset of chronic diseases. To connect with previous research on mortality, we also aim to examine whether ALI can predict mortality. We determine 3-year mortality based on the survey date and the recorded date of death from Lifelines and BPR. However, due to data limitations, we are unable to identify the 3-year mortality of participants who took the survey after September 2021 and remained alive until the cutoff date for death records. As a result, our sample size for mortality analysis is smaller than that for biomarkers and chronic diseases.[18]

Figure 3 also illustrates the trajectory of 3-year mortality among Lifelines participants. Compared to previous research, the absolute 3-year mortality rate is relatively low. This can be attributed to the fact that the Lifelines cohort consists of a relatively young, non-institutionalized population, with older individuals not being the primary focus. Additionally, mortality rates derived from survey data tend to be lower than those observed in the general population (Keyes et al., 2018). As we can see, the 3-year mortality remains relatively low before age 50 but rises sharply after age 60. In contrast, CDI increases steeply before age 50, while biomarker-related

[18] Specifically, the 3-year mortality for 35,240 observations in wave 3a are missing because these participants took part in the third wave of Lifelines after September 2021.

risks become significant and escalate already before age 30. This progression demonstrates a transition from biomarker-related risks to the onset of chronic diseases and, ultimately, to mortality.

3.4 Allostatic Load and Disparity in Chronic Disease and Mortality

As shown above, the number of aging-related chronic diseases increases later in life while biomarker-related risks have already emerged early in adulthood before chronic diseases happen. Previous research has highlighted the significant association between the ALI and mortality risk and shown it explains a significant portion of the SES-related mortality gap, with findings suggesting that the ALI accounts for a substantial portion of the differences in mortality risks across SES groups (e.g., Seeman et al., 2004; Howard & Sparks, 2016). Here, we build on prior work by investigating whether a cumulative index of biological risk, namely ALI, can predict the prevalence of chronic disease and 3-year mortality.

We start with a linear regression of $CDI_{i,a}$ on a set of controls $X_{i,a}$, including age, age squared, age group, gender, cohort, urban, province, and survey year. Then, we add the $ALI_{i,a}$ and the lagged term of ALI into the regression. To do that, we restrict our sample to individuals who participated in at least two consecutive surveys and pool all the observations. Afterward, we do the regression by age groups with 10-year intervals.

$$CDI_{i,a} = \alpha + \beta ALI_{i,a} + X_{i,a}\gamma + \epsilon_i \qquad (2)$$

Table 4 examines the extent to which the ALI and its lagged term predict the CDI and 3-year mortality when sequentially added into the model. Two key points can be drawn from the regression analysis. First, both the ALI and its lagged term demonstrate a significant positive association with the CDI and 3-year mortality, indicating that higher ALI and the lagged term

correspond to increased CDI and mortality values. This finding supports the role of ALI as a pre-indicator of aging-related chronic disease prevalence and mortality. Additionally, in Table 5-1, Table 5-2, Table 6-1, and Table 6-2, we present the regression results by 10-year age bins. The coefficients for both ALI and its lagged term increase with age group, indicating that their association intensifies in later life.

As a sensitivity analysis, we use z-ALI and its lagged term to predict CDI and 3-year mortality. The results, reported in Table A.2 (in Appendix), are consistent with those obtained using ALI. This finding aligns with previous studies (e.g., see McLoughlin et al. 2020) suggesting that the choice of allostatic load scoring algorithm has a relatively small impact on predicting general health outcomes.

4. The Socioeconomic Health Disparities over the Life Cycle

In this section, we start by considering educational disparities in health by graphical analysis. Specifically, we aim to present the trajectory of educational disparities in allostatic load over the life cycle and exhibit disparities in each biomarker and related risks among young adults. This analysis provides insights into the timing through which socioeconomic health disparities emerge and evolve.

The health gap between educational groups is defined as $\triangle Health_a = Health_{a,\,high} - Health_{a,\,low}$, representing the difference in health outcomes between individuals with high and low levels of education at a given age. Simply tracking how this gap changes with age offers insight into when and how the educational disparities in

biomarkers and allostatic load open. This simple comparison is valuable because it provides information on the timing of education-related health disparities before endpoints.

4.1 The Trajectory of the Allostatic Load Disparity over the Life Cycle

At the outset, we examine how allostatic load disparity across education groups evolves over the life cycle, without considering other potential confounders. This analysis aims at understanding the onset of health disparities in allostatic load and the pattern over the life cycle.

Figure 4 presents the trajectory of educational allostatic load disparity by age, pooling observations from three waves of data, separately for males and females. The figure highlights that educational disparity in allostatic load becomes evident in early adulthood and consistently increases with age, peaking in late middle age. To interpret the magnitude of these differences, consider the ALI for the low education group at age 30, which is comparable to that of the high education group at around age 44 for females and age 37 for males. This indicates a substantial biological health gap across socioeconomic groups. Additionally, the absolute gap in allostatic load reflects the cumulative burden of biological risks. For instance, at age 40, females in the low education group have, on average, 0.24 more biological risks than their high education counterparts. Given that the ALI for the high education group at this age is 0.52, this represents a relatively large disparity.

Gender differences are also evident in both the levels and trajectories of allostatic load over the life course. For females, the ALI is consistently lower than that for males throughout the life cycle. The rate of increase in the ALI for females begins to accelerate slightly before age 40 and rises more sharply till age 60. The educational disparity in ALI for females continues to widen until around age 50, after which it stabilizes. For males, the average ALI is higher than that for

females across the entire lifespan. The increase in ALI and the corresponding educational disparity occur more rapidly for males compared to females and tend to stabilize around age 55. We also present the trajectory of educational ALI disparity for all samples in Figure B.2 in the Appendix.

For both females and males, the increase in allostatic load tends to slow down around the ages of 50 to 60. This pattern aligns with the findings of Lleras-Muney & Moreau (2022), who demonstrate that SES gradients in mortality widen with age but eventually decline after a certain point. Our study complements their work by providing evidence of the evolution of SES-related gradients in biomarker-based health measures. Several factors may explain this decline. First, the prevalence of chronic diseases at late middle age often leads individuals to begin medication, which can reduce the levels of certain biomarkers, such as HbA1c.[19] Second, as individuals experience health issues, they tend to place greater value on maintaining their health. This shift in priorities often leads to increased investment in healthier behaviors and lifestyles, such as engaging in more physical activity or adopting healthier lifestyle habits. Third, health-based attrition may contribute to this trend, as individuals with higher allostatic load may exit the Lifelines study due to transitioning to regular healthcare programs or, in some cases, mortality.

The static comparisons of health gaps could be confounded by factors such as cohort effects, health-based sorting, and health-based attrition. These factors will shape our graphic analysis. For example, SES measures may be endogenous to individual health, as poor health may lead to lower SES, potentially shaping the pattern of SES-related health disparities over the life cycle. In

[19] In the Lifelines study, we have access to limited self-reported medication data. Unfortunately, the quality of this data is insufficient to test this assumption due to the categorization of medication information and the available sample size.

our study, we are mainly interested in the differences in the health evolution by educational attainment. Educational attainment often becomes stable after early adulthood, which reduces the issue of health-based sorting.

Another concern is the cohort effects. While the longitudinal nature of the Lifelines study supports cohort analysis, the currently available biomarker data include only three waves, allowing us to track individuals for an average of 11.2 years and a maximum of 17 years. Ideally, we would construct a cohort specific to each birth year, but this results in too few observations for each cohort in each wave. Instead, to test for the significance of cohort effects, we create eight cohorts using 10-year birth intervals and then compare the average health outcomes of different cohorts at the same age across waves. Due to limited observations in the oldest cohort, we exclude individuals born before 1930 from the analysis. Although we do not aim to capture the cohort effect, this setting allows us to observe the extent of cohort effects by comparing the average ALI at the same age but in different cohorts. We present the graphical analysis in Figure 5 by showing the extent of cohort effect.

4.2 The Distribution of Biomarkers and the Prevalence of Biomarker-Related Risk

In this section, we examine educational disparities in biomarkers and biomarker-related risks separately for females and males. Figure B.3.1, Figure B.3.2, and Figure B.3.3 in the Appendix present box-and-whisker plots of 12 biomarkers by 10-year age groups, constructed using pooled observations from 3 waves.[20]

[20] The bottom and top edges of each box represent the 25th and 75th percentiles, respectively, while the middle line within the box denotes the median. The lower whisker extends from the first quartile to 1.5 times the interquartile range below the first quartile, and the upper whisker extends from the third quartile to the largest data point within 1.5 times the interquartile range above the third quartile. A red line indicating the clinical threshold for each

Several stylized facts emerge from these figures. First, for most biomarkers, such as systolic and diastolic blood pressure, BMI, and total cholesterol, values tend to increase with age and decrease with educational attainment. The rate of increase slows down with age, and some biomarker values begin to decline after middle age, likely due to factors such as medical treatment, changes in health behaviors, and mortality. Second, for biomarkers like systolic and diastolic blood pressure, glucose, and creatinine, the cross-sectional dispersion increases with age and is greater in the low-education group. Third, the percentage of individuals whose biomarker values exceed the clinical threshold for certain biomarkers begins to emerge before age 35, or even 25, with a noticeable gap in prevalence between different education groups. Finally, for some biomarkers (e.g., HDL cholesterol and creatinine), there is a clear gender difference in the value, but the pattern across age groups is generally similar for both males and females.

Next we examine the prevalence gap in biomarker-related risks across education groups. Specifically, an individual i at age a is considered to have a risk for a specific biomarker if their biomarker value exceeds the threshold. The prevalence gap is defined as $Bio_{high,\,a} - Bio_{low,\,a}$, where $Bio_{high,\,a}$ represents the average value of individuals with high educational attainment at age a and $Bio_{low,\,a}$ represents those with low educational attainment.

Figure 6 illustrates the difference in the percentage of samples with high-risk biomarker values between individuals with low and high educational attainment for ages under 30. Several key observations can be drawn from this. First, the figure reveals a noticeable biomarker-related

biomarker is also included. Outliers, defined as values below the first quartile or above the third quartile by more than 1.5 times the interquartile range, are not shown in these figures.

risk for young adults, which contrasts with the more substantial morbidity and mortality typically observed in middle-aged and older individuals. For instance, the prevalence of BMI and WHR risks for males is 9.8% and 34.6%, respectively, indicating that 9.8% of males under age 30 have BMI values above 30 and 34.6% have WHR values above 0.94. Both BMI and WHR are commonly associated with diseases such as diabetes and metabolic syndrome, which generally manifest later in life.

Second, we observe a significant educational gradient in the prevalence of biomarker-related risks before age 30. For example, the prevalence gap for HDL cholesterol is 4.4% for females and 13.4% for males.[21] HDL cholesterol helps to prevent the buildup of plaque in arteries. Additionally, gaps are also observed for LDL cholesterol, systolic blood pressure, creatinine, triglycerides, total cholesterol (for males), WHR, and BMI. One exception is creatinine, where the lower education group exhibits lower values than the higher education group for females.

Third, we find a pronounced gender difference in the prevalence of biomarker-related risks. The risk tends to be higher in males for LDL cholesterol, systolic blood pressure, creatinine, triglycerides, total cholesterol, HDL cholesterol, and WHR. In contrast, females exhibit slightly higher prevalence rates for BMI and heart rate. Furthermore, the prevalence gap is generally larger for males across most biomarkers compared to females. Additionally, we also present the results for the whole sample, see Figure B.4 in the Appendix.

[21] HDL cholesterol is considered "good" cholesterol, so here we report the percentage of individuals with HDL cholesterol below the clinical threshold.

5. Drivers of Allostatic Load over the Lifecycle

5.1 Framework

Our prior graphical analysis demonstrates the educational disparities in biomarkers and allostatic load that begin to manifest in early adulthood and progressively widen until late middle age. In this section, we focus on the factors contributing to allostatic load and its growth, as well as how the contribution of these factors differs across gender and age groups. Although our analysis is primarily descriptive, it offers valuable insights into the relative importance of various determinants and highlights how targeted health interventions can mitigate biomarker-related risks. Specifically, our analysis emphasizes the role of health-related behaviors in driving the growth of allostatic load.

To estimate the role of these factors in determining allostatic load, we use a linear regression approach across 10-year age bins to analyze the associations between the ALI and its potential drivers:

$$ALI_{i,a} = \sum_{j=1}^{J} X_{i,a}^{j} \gamma_{j,a} + \varepsilon_{i,a} \qquad (3)$$

In these equations, $ALI_{i,a}$ the ALI for individual i in age group. $X_{i,a}^{j}$ is a vector of explanatory variables that includes health behaviors (e.g., smoking, drinking, physical activity, and sleep disorders), educational attainment, employment status, and neighborhood SES. To assess the relative contribution of these variables, we decompose the total R-squared of these regressions using Shapley and Owen decomposition methods (Huettner & Sunder, 2012). This

approach enables us to evaluate the average contribution of each predictor to the explained variance across all possible sequences of regressors.

5.2 Decomposition Results

Figure 7 illustrates the relative importance of various drivers contributing to allostatic load, as derived from gender- and age-specific regression decompositions. The columns represent the total R-squared values from each regression. Health behaviors emerge as significant contributors to the current allostatic load across both gender and age groups. For females, alcohol consumption accounts for a relatively large contribution to the allostatic load. The contribution of physical activity shows a gradual increase after the age of 25. Educational attainment provides a relatively stable contribution to allostatic load, while employment plays a notable role primarily during the working years, particularly in middle age. Smoking exhibits a moderate contribution across age groups, whereas the impact of sleep disorders is more pronounced during middle age. For males, physical activity consistently contributes significantly to allostatic load across all age groups, with its influence becoming particularly pronounced after age 55. The contribution of alcohol consumption increases steadily with age, while smoking demonstrates a substantial impact only up to age 55. The role of education in allostatic load shows a declining trend as age progresses.

Figure B.5 in Appendix illustrates the decomposition results, highlighting the relative importance of various factors driving the growth of allostatic load. Similar to Figure 7, health behaviors emerge as significant contributors to the growth of allostatic load for both females and males. Specifically, among females, drinking and education make relatively large contributions to this growth. For males, however, smoking shows a more substantial contribution compared to

drinking, marking a departure from the patterns observed in Figure 7. While both figures underscore the role of health behaviors, their implications differ slightly.

It is important to emphasize that the decomposition results presented here reflect correlations rather than causal relationships. Furthermore, these results are influenced by the selection of biomarkers used in the study and should not be interpreted as evidence that, for example, smoking is less important than drinking in affecting the whole biological health. For instance, biomarkers related to lung function, the nervous system, the immune system, and the skeletal system are excluded due to data constraints. Consequently, the ALI constructed in this study may be more closely associated with some of the health behaviors under investigation than others. Nevertheless, the decomposition results provide valuable insights into the relative importance of these behaviors in influencing key physiological systems, including the cardiovascular system, metabolic system, and kidney function.

6. Conclusion

Using representative data from Dutch Lifelines, we investigate the life-cycle profile of biomarker-related health and its underlying determinants using objective biomarkers obtained from longitudinal biomaterial collection and measurements. We develop an allostatic load index to reflect physiological dysregulation in response to stress exposure, which also indicates the cumulative risks of chronic conditions. Complementing previous research, our study underscores the significant role of allostatic load as a predictor of chronic disease development and mortality.

In our life-cycle analysis, we observe that the biomarker-related health disparity in SES emerges early in adulthood for both males and females. For instance, the biomarkers exhibit notable gradients at the onset of adulthood. Educational differences in allostatic load continue to widen during adulthood for both males and females, while also showing a large difference in the pattern by gender. Furthermore, we decompose the total R-squared of regression to assess the average contribution of various factors to the allostatic load. We find health behaviors play an important role in allostatic load and the growth of allostatic load, with different behaviors demonstrating distinct relative importance across age groups and genders. Educational attainment emerges as a significant determinant for both males and females throughout the life cycle.

The current analysis has several limitations that need to be acknowledged. Firstly, the construction of the ALI lacks a uniform approach across the literature, making comparisons with other studies challenging, and the results might be driven by the number and type of biomarkers we selected. Second, potential confounders, such as medication use and health-based attribution, have not been accounted for in the graphical analysis, which could affect the observed patterns of health disparity across the life cycle. Third, the decomposition method employed is relatively straightforward, and the findings are partially shaped by the selected biomarkers and health-related behaviors. The analysis does not account for the impact of, such as environmental exposure, early life conditions and parents' SES, both of which are considered to have a significant influence on chronic health outcomes. Moving forward, addressing these limitations is essential. Future analyses may put effort into accounting for confounders of graphical analysis and capture the biological aging speed based on our dynamic biomarkers.

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Tables and Figures

A Tables

Table 1: Clinical Cut-Off Points of Biomarkers

System	Biomarker	Description	Threshold
Cardiovascular system	Systolic blood pressure (mmHg)	The maximum pressure in arteries during the active phase of the heartbeat	>= 140
	Diastolic blood pressure (mmHg)	The heart refills with blood and the pressure in the arteries is at its lowest	>= 90
	Heart rate (per minute)	The number of times the heart beats in one minute (electrocardiogram)	>= 90
Metabolic system	Body mass index (BMI)	A simple calculation used to assess whether a person has a healthy body weight for their height[22]	>= 30
	Waist-to-hip ratio (WHR)	A measurement used to assess body fat distribution	>= 0.94
	Total cholesterol (mmol/l)	The sum of different types of cholesterol in the blood	>= 6.2
	High-density lipoprotein (HDL) cholesterol (mmol/l)	"Good" cholesterol that helps clear other forms of cholesterol	<= 1
	Low-density lipoprotein (LDL) cholesterol (mmol/l)	"Bad" cholesterol that high levels can lead to the buildup of cholesterol in the arteries	>= 4.1
	Glycosylated hemoglobin (hba1c)(mmol/mol)	A blood test that measures the average level of blood sugar (glucose) over the past 2-3 months	> 48
	Glucose (mmol/mol)	A simple sugar and a primary energy source for the body's cells	>= 7
	Triglycerides[23] (mmol/l)	A type of fat (lipid) found in blood	>= 1.7
Kidney function	Creatinine (mmol/l)	Creatinine is a waste product that forms when muscles break down creatine, a substance found in the muscles and consumed through meat and fish	>= 90

Note: For HbA1c, the variable measured in mmol/L contains 23,000 missing values in wave 1a, whereas the variable measured in percentages has only 764 missing values. To address this issue, we use the alternative variable for HbA1c and convert its unit accordingly. Consequently, there is a small transformation error in this variable due to rounding.

[22] BMI is calculated by BMI = Weight (kg) / Height (m)^2.

[23] Compared to other cohort studies, the triglycerides seem to be lower in Lifelines in all percentiles. This is mainly because current criteria are largely based on the studies that were carried out in the 1970s (Balder et al., 2017).

Table 2: Sample Selection

	Selected in	Selected out: missing value in 12 biomarkers	Selected out: fasting	Selected out: missing value in 19 chronic diseases	Selected out: missing in demographics (including education)	Selected sample
Wave 1a	150,605	8,676	2,226	3,148	8,885	127,047
Wave 2a	99,608	7,535	2,121	0	3,108	86,513
Wave 3a	60,794	5,004	1,617	0	901	53,272
Number of observations	311,007	21,215	6,918	3,148	12,894	266,832

Table 3-1: Summary Statistics

	Wave			
	Wave 1a	Wave 2a	Wave 3a	Total
Number of observations	127,047 (47.6%)	86,513 (32.4%)	53,272 (20.0%)	266,832 (100.0%)
A. Demographics				
Age	45.303 (11.839)	50.147 (12.013)	55.887 (11.158)	48.987 (12.441)
Gender	0.421 (0.494)	0.416 (0.493)	0.415 (0.493)	0.418 (0.493)
B. Education				
Low	87,296 (68.7%)	57,493 (66.5%)	32,108 (60.3%)	176,897 (66.3%)
High	39,751 (31.3%)	29,020 (33.5%)	21,164 (39.7%)	89,935 (33.7%)
C. Biomarkers				
Systolic blood pressure	125.565 (15.213)	128.724 (16.324)	131.968 (15.983)	127.867 (15.928)
Diastolic blood pressure	73.999 (9.333)	74.209 (9.472)	82.435 (10.995)	75.751 (10.288)
Heart rate (ECG)	67.311 (11.199)	66.887 (11.192)	65.001 (10.525)	66.712 (11.100)
Body mass index (BMI)	26.135 (4.285)	26.137 (4.273)	26.841 (4.473)	26.276 (4.329)
Waist-hip ratio (WHR)	0.907 (0.084)	0.903 (0.089)	0.931 (4.602)	0.911 (2.058)
Total cholesterol	5.098 (0.999)	5.097 (0.984)	5.194 (1.008)	5.117 (0.997)
High-density lipoprotein cholesterol	1.491 (0.397)	1.518 (0.423)	1.515 (0.421)	1.504 (0.411)
Low-density lipoprotein cholesterol	3.248 (0.913)	3.328 (0.912)	3.334 (0.906)	3.291 (0.912)
Glucose	5.016 (0.822)	5.074 (0.885)	5.366 (0.972)	5.105 (0.884)
Hemoglobin A1C	37.243 (4.860)	36.726 (5.236)	38.085 (5.645)	37.243 (5.169)
Triglycerides	1.184 (0.812)	1.213 (0.814)	1.285 (0.787)	1.213 (0.809)
Creatinine	73.572 (13.397)	78.635 (14.647)	77.800 (14.853)	76.057 (14.309)
D. Chronic disease				
Cancer	0.046 (0.209)	0.061 (0.238)	0.088 (0.284)	0.059 (0.236)
Stroke	0.007 (0.084)	0.011 (0.102)	0.012 (0.109)	0.009 (0.096)
Heart attack	0.010 (0.099)	0.014 (0.118)	0.017 (0.131)	0.013 (0.112)
Heart failure	0.007 (0.083)	0.019 (0.136)	0.024 (0.154)	0.014 (0.119)
Diabetes	0.024 (0.153)	0.036 (0.186)	0.042 (0.201)	0.031 (0.175)
Ulcerative colitis	0.006 (0.076)	0.008 (0.091)	0.010 (0.098)	0.007 (0.086)
Gallstones	0.037 (0.188)	0.046 (0.208)	0.046 (0.209)	0.041 (0.199)
Hepatitis	0.010 (0.100)	0.011 (0.105)	0.012 (0.107)	0.011 (0.103)

Table 3-2: Summary Statistics

	Wave			
	Wave 1a	Wave 2a	Wave 3a	Total
Chronic fatigue	0.013 (0.114)	0.016 (0.127)	0.015 (0.123)	0.015 (0.120)
Kidney Stones	0.031 (0.173)	0.038 (0.191)	0.040 (0.195)	0.035 (0.184)
Renal Failure	0.000 (0.000)	0.002 (0.040)	0.002 (0.046)	0.001 (0.030)
Arthritis	0.021 (0.145)	0.033 (0.178)	0.037 (0.188)	0.028 (0.165)
Fibromyalgia	0.033 (0.178)	0.042 (0.201)	0.046 (0.208)	0.038 (0.192)
Osteoarthritis	0.077 (0.267)	0.159 (0.365)	0.198 (0.399)	0.128 (0.334)
Osteoporosis	0.015 (0.122)	0.029 (0.168)	0.034 (0.180)	0.023 (0.151)
Repetitive strain injury	0.022 (0.148)	0.035 (0.183)	0.044 (0.205)	0.031 (0.173)
Chronic obstructive pulmonary disease	0.053 (0.224)	0.068 (0.252)	0.067 (0.249)	0.061 (0.239)
Dementia	0.000 (0.011)	0.001 (0.030)	0.001 (0.032)	0.001 (0.024)
Parkinson's	0.001 (0.023)	0.001 (0.037)	0.002 (0.042)	0.001 (0.033)

Note: for biomarkers, we report the mean of the original values. For chronic diseases, we show the prevalence of specific conditions.

Table 4: Regression Results of Chronic Disease and 3-Year Mortality on Allostatic Load

	Panel A. Chronic disease		Panel B. 3-Year mortality	
	(1)	(2)	(1)	(2)
ALI	0.065***		0.0005***	
	(0.002)		(0.0001)	
ALI_{a-t}		0.074***		0.0005***
		(0.002)		(0.0001)
Controls	Yes	Yes	Yes	Yes
Observations	120,083	120,083	93,503	93,503
R-squared	0.159	0.158	0.009	0.009

Note: Standard errors in parentheses, *** p<0.01, ** p<0.05, * p<0.1. Controls are age, age squared, age group, gender, cohort, urban, province, and survey year.

Table 5-1:Regression Results of Chronic Disease on Allostatic Load by Age Group

	25-34		35-44		45-54	
	(1)	(2)	(1)	(2)	(1)	(2)
ALI	0.024***		0.048***		0.056***	
	(0.004)		(0.003)		(0.002)	
ALI_{a-t}		0.033***		0.051***		0.070***
		(0.005)		(0.003)		(0.003)
Controls	Yes	Yes	Yes	Yes	Yes	Yes
Observations	8,287	8,287	20,789	20,789	40,046	40,046
R-squared	0.019	0.025	0.027	0.037	0.027	0.041

Table 5-2: Regression Results of Chronic Disease on Allostatic Load by Age Group

	55-64		65-74	
	(1)	(2)	(1)	(2)
ALI	0.068***		0.075***	
	(0.004)		(0.005)	
ALI_{a-t}		0.086***		0.072***
		(0.004)		(0.006)
Controls	Yes	Yes	Yes	Yes
Observations	30,120	30,120	16,898	16,898
R-squared	0.041	0.057	0.031	0.039

Note: Standard errors in parentheses, *** p<0.01, ** p<0.05, * p<0.1. Controls are age, age squared, gender, cohort, urban, province, and survey year.

Table 6-1: Regression Results of 3-Year Mortality on Allostatic Load by Age Group

	25-34		35-44		45-54	
	(1)	(2)	(1)	(2)	(1)	(2)
ALI	0.0003*		0.0003**		0.0005***	
	(0.0002)		(0.0002)		(0.0002)	
ALI_{a-t}		0.0001		0.0011***		0.0007***
		(0.0002)		(0.0002)		(0.0002)
Controls	Yes	Yes	Yes	Yes	Yes	Yes
Observations	7,451	7,451	17,680	17,680	33,164	33,164
R-squared	0.001	0.001	0.001	0.002	0.001	0.001

Table 6-2: Regression Results of 3-Year Mortality on Allostatic Load by Age Group

	55-64		65-74	
	(1)	(2)	(1)	(2)
ALI	0.0005		0.0006	
	(0.0003)		(0.0007)	
ALI_{a-t}		0.0003		0.0000
		(0.0004)		(0.0006)
Controls	Yes	Yes	Yes	Yes
Observations	20,634	20,634	11,962	11,962
R-squared	0.001	0.001	0.003	0.003

Note: Standard errors in parentheses, *** p<0.01, ** p<0.05, * p<0.1. Controls are age, age squared, gender, cohort, urban, province, and survey year.

B Figures

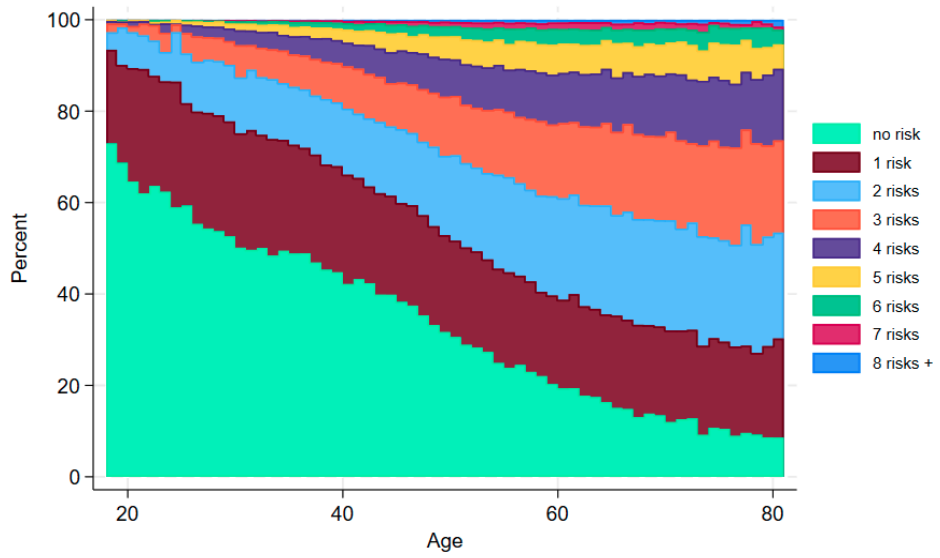

Figure 1: The Evolution of the Number of Biomarker-Related Risks Over the Life Cycle

Note: The number of risks refers to the count of biomarkers exceeding the threshold for an individual at a given age. The figure illustrates the percentage of participants with varying numbers of risks across different ages.

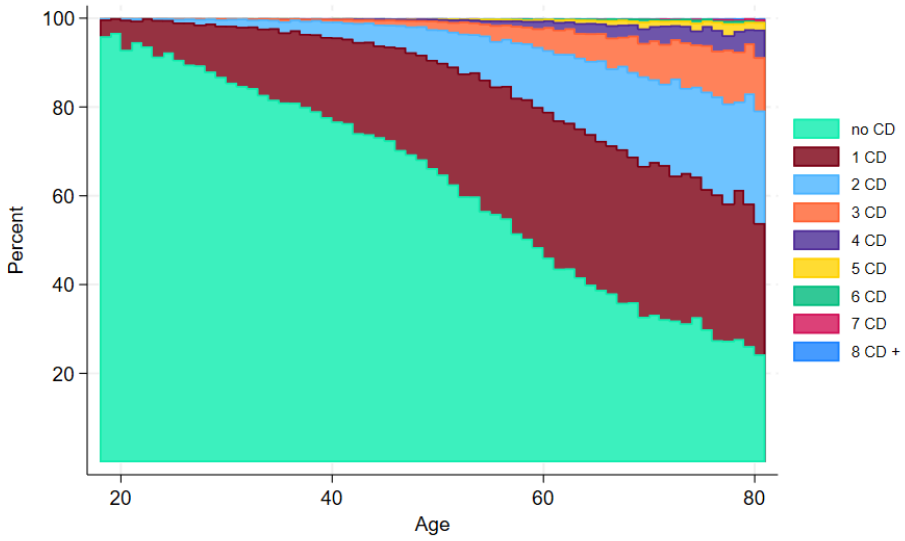

Figure 2: The Evolution of the Number of Aging-Related Chronic Diseases Over the Life Cycle

Note: The number of chronic diseases refers to the count of chronic dieases for an individual has or has previously had at a given age. The figure illustrates the percentage of participants with varying numbers of chronic diseases across different ages.

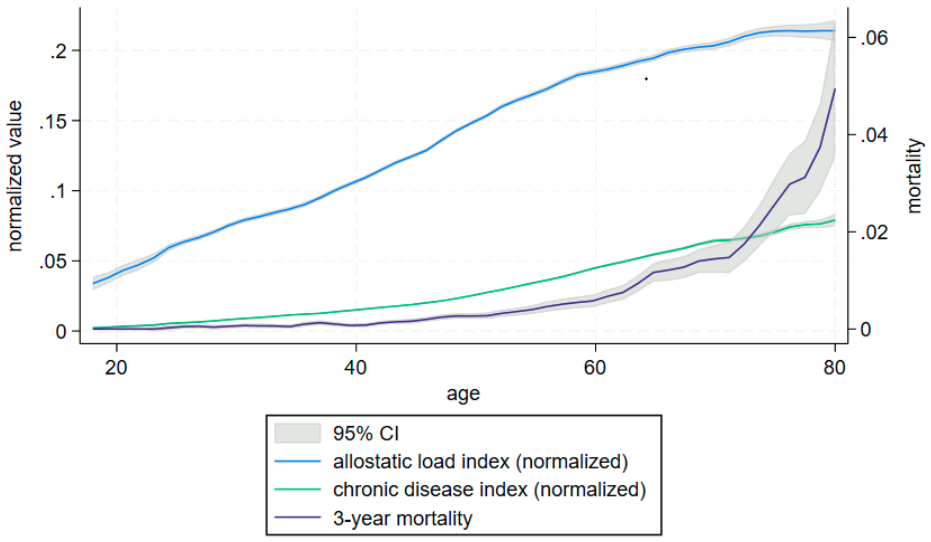

Figure 3: The Life Cycle Profile of Allostatic Load Index, Chronic Disease Index and 3-Year Mortality

Note: To ensure comparability of scale, the indexes are rescaled using the min-max scaling approach. We apply the lpoly smoothing method to capture the relationship between age and the ALI, CDI, and 3-year mortality. The lpoly is a kernel-weighted local polynomial regression of yvar on xvar. Here, we use the Epanechnikov kernel function with a zero-degree polynomial, effectively minimizing noise while preserving the true pattern of the data. Due to limitations in death record availability, the number of observations for 3-year mortality is smaller than that for ALI and CDI, with 35,240 observations missing in wave 3a.

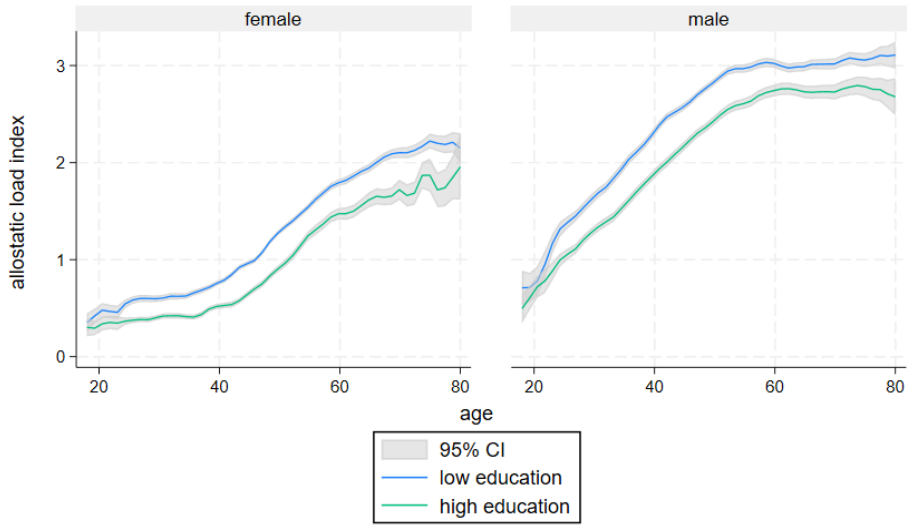

Figure 4: The Educational Allostatic Load Disparities by Age and Gender

Note: We apply the lpoly smoothing method to capture the relationship between age and th ALI. The lpoly is a kernel-weighted local polynomial regression of yvar on xvar. Here, we use the Epanechnikov kernel function with a zero-degree polynomial.

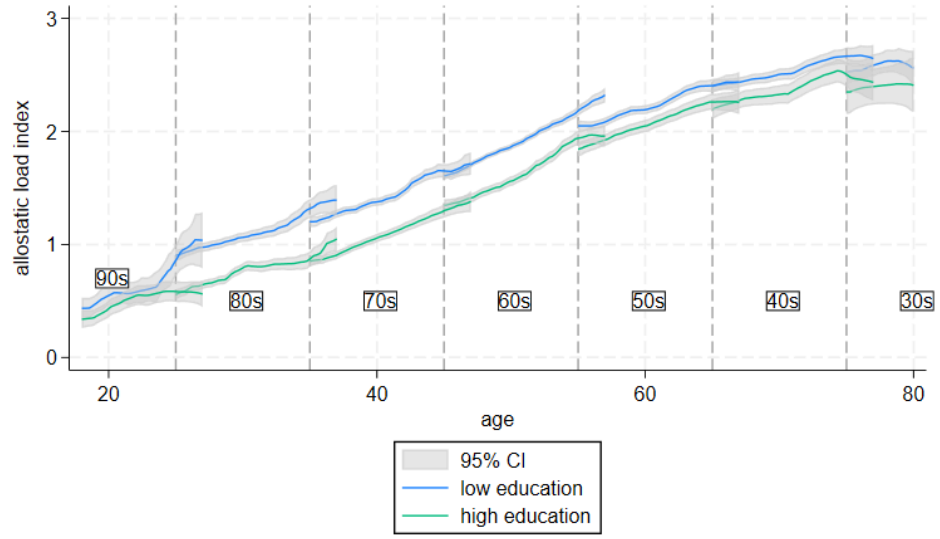

Figure 5: The Educational Allostatic Load Disparities by Age, Cohort, and Gender

Note: We apply the lpoly smoothing method to capture the relationship between age and the ALI. The lpoly is a kernel-weighted local polynomial regression of yvar on xvar. Here, we use the Epanechnikov kernel function with a zero-degree polynomial.

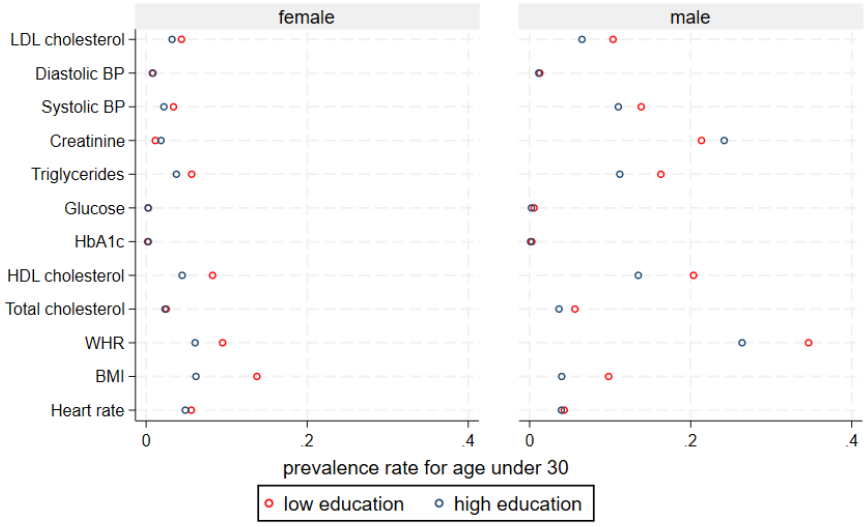

Figure 6: The Prevalence Gap of Having High Risks in Biomarkers for Age Group Under 30

Note: This figure illustrates the prevalence of high-risk biomarkers across education groups, segmented by gender. Observations from all three waves are pooled for this analysis. For example, a value of 0.027 for females' heart rate indicates that 2.7% of females have a heart rate above 90 beats per minute, exceeding the clinical threshold. For females, the differences in total cholesterol, HbA1c, glucose, and diagnostic blood pressure between low and high education groups are statistically insignificant at the 10% level. For males, the differences in heart rate and diastolic blood pressure between education groups are statistically insignificant at the 10% level.

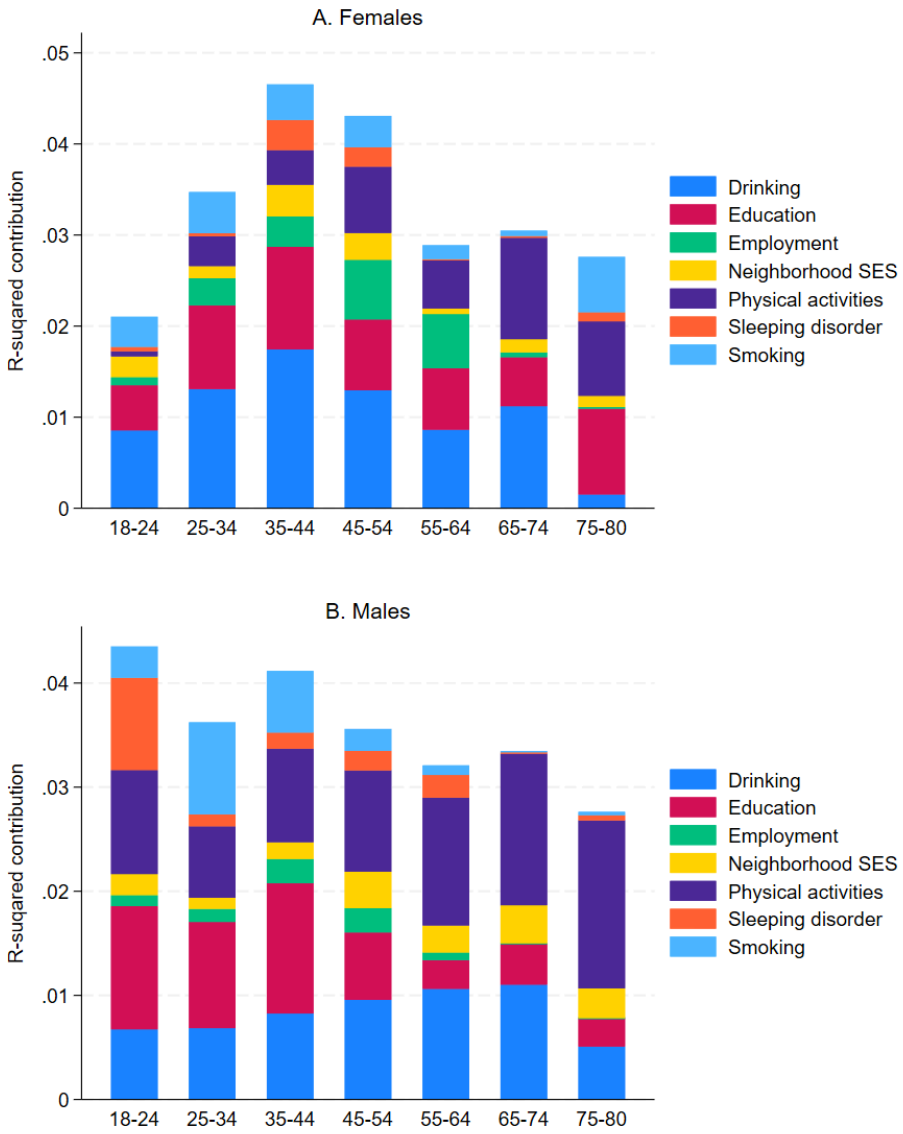

Figure 7: The R-Squared Contribution of Modifiable Factors to Allostatic Load Index by Gender and Age Groups

Online Appendix (Supplementary Materials)

A Tables

Table A.1: Aging-Related Chronic Disease

Category	Specific Disorder
Cancer	
Cardiovascular diseases	heart attack, heart failure, stroke
Diabetes	
Digestive system diseases	ulcerative colitis, gallstones, hepatitis
Chronic fatigue syndrome	
Kidney and bladder diseases	kidney stones, renal failure
Musculoskeletal conditions	arthritis, fibromyalgia, osteoarthritis, osteoporosis, repetitive strain injury
Neurological disorders	dementia, parkinson's disease
Respiratory diseases	emphysema, chronic bronchitis

Table A.2: Regression Results of Chronic Disease and 3-Year Mortality on Allostatic Load (Z-Scores)

	Panel A. Chronic disease		Panel B. 3-Year mortality	
	(1)	(2)	(1)	(2)
z-ALI	0.0233***		0.0001***	
	(0.0005)		(0.0000)	
z-ALI_{a-t}		0.0251***		0.0001**
		(0.0005)		(0.0001)
Controls	Yes	Yes	Yes	Yes
Observations	120,083	120,083	93,503	93,503
R-squared	0.158	0.160	0.009	0.009

Note: Standard errors in parentheses, *** p<0.01, ** p<0.05, * p<0.1. Controls are age, age squared, age group, gender, cohort, urban, province, and survey year.

B Figures

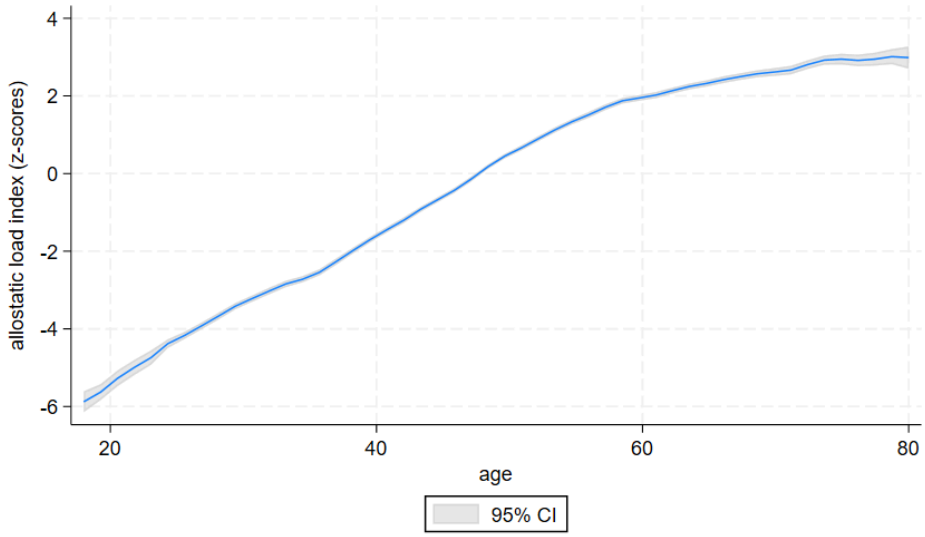

Figure B.1: The Life Cycle Profile of Allostatic Load Index Using Z-Scores

Note: We apply the lpoly smoothing method to capture the relationship between age and the z-ALI. The lpoly is a kernel-weighted local polynomial regression of yvar on xvar. Here, we use the Epanechnikov kernel function with a zero-degree polynomial.

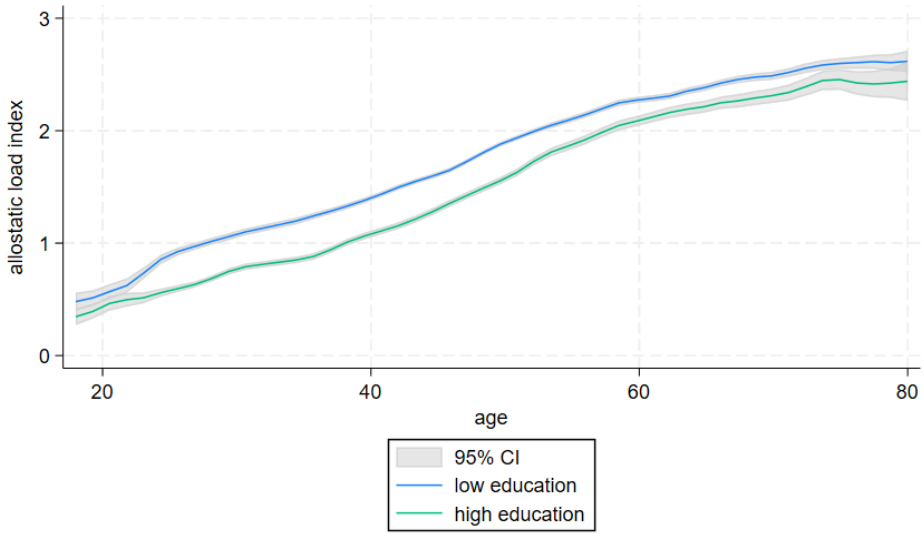

Figure B.2: The Life Cycle Profile of Allostatic Load Index by Age, and Education for the Whole Sample

Note: We apply the lpoly smoothing method to capture the relationship between age and the values of ALI. The lpoly is a kernel-weighted local polynomial regression of yvar on xvar. Here, we use the Epanechnikov kernel function with a zero-degree polynomial, effectively minimizing noise while preserving the true pattern of the data.

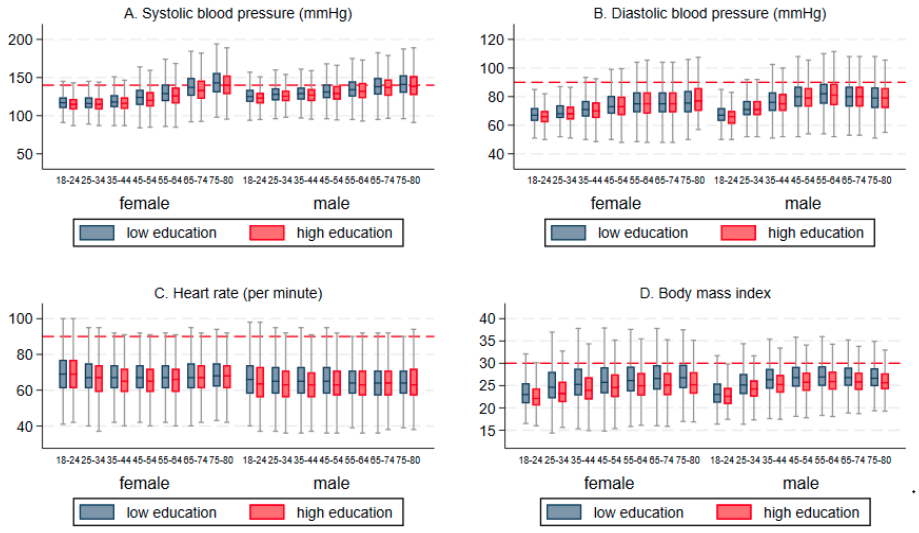

Figure B.3.1: The Distribution of Biomarkers Across Education Levels, Gender, and Age Groups

Note: The figure is based on a selected sample with no missing data for all 12 biomarkers of interest, pooling observations across three waves. The red line indicates the clinical thresholds: systolic blood pressure at 140, diastolic blood pressure at 90, heart rate at 90, and body mass index at 30. Outliers have been excluded.

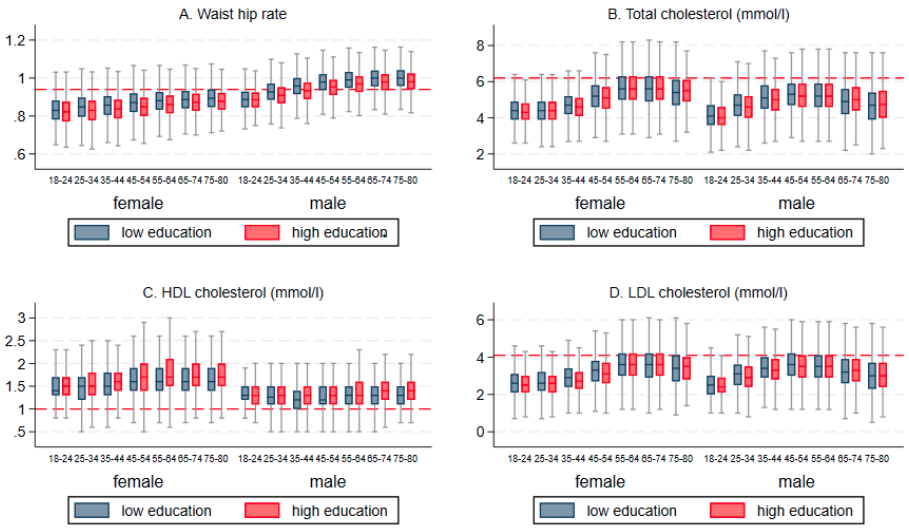

Figure B.3.2: The Distribution of Biomarkers Across Education Levels, Gender, and Age Groups

Note: The figure is based on a selected sample with no missing data for all 12 biomarkers of interest, pooling observations across three waves. The red line indicates the clinical thresholds: waist hip rate at 0.94, total cholesterol at 6.2, HDL cholesterol at 1, and LDL cholesterol at 4.1. Outliers have been excluded.

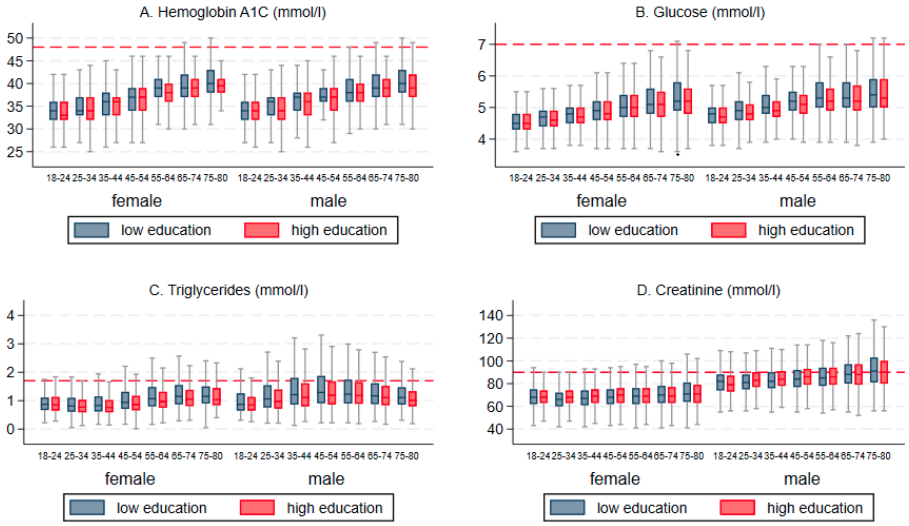

Figure B.3.3: The Distribution of Biomarkers Across Education Levels, Gender, and Age Groups

Note: The figure is based on a selected sample with no missing data for all 12 biomarkers of interest, pooling observations across three waves. The red line indicates the clinical thresholds: hemoglobin A1C at 48, glucose at 7, triglycerides at 1.7, and creatinine at 90. Outliers have been excluded.

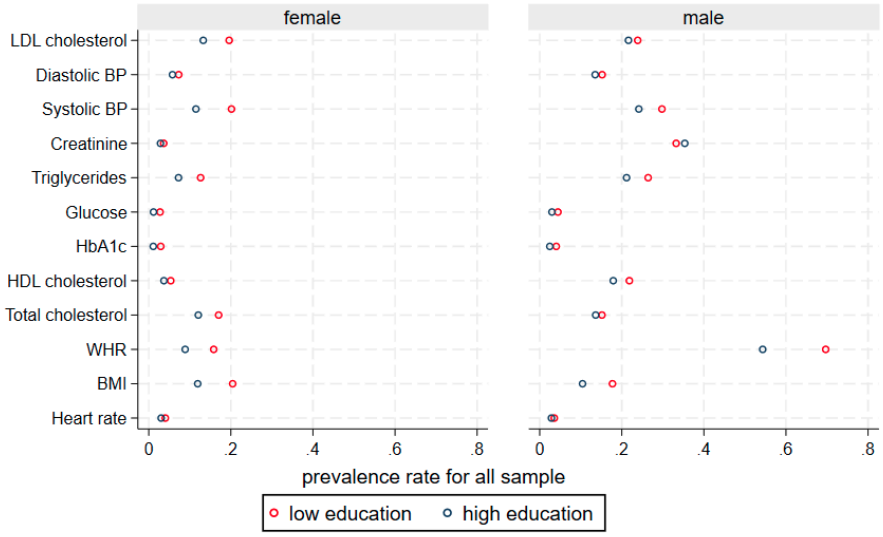

Figure B.4 The prevalence gap of having high risks in biomarkers for whole sample

Note: This figure illustrates the prevalence of high-risk biomarkers across education levels, segmented by gender. Observations from all three waves were pooled for this analysis. For example, a value of 0.027 for females' heart rate indicates that 2.7% of females have a heart rate above 90 beats per minute, which is above the clinical threshold. The difference between low and high education groups is statistically significant at the 1% level.

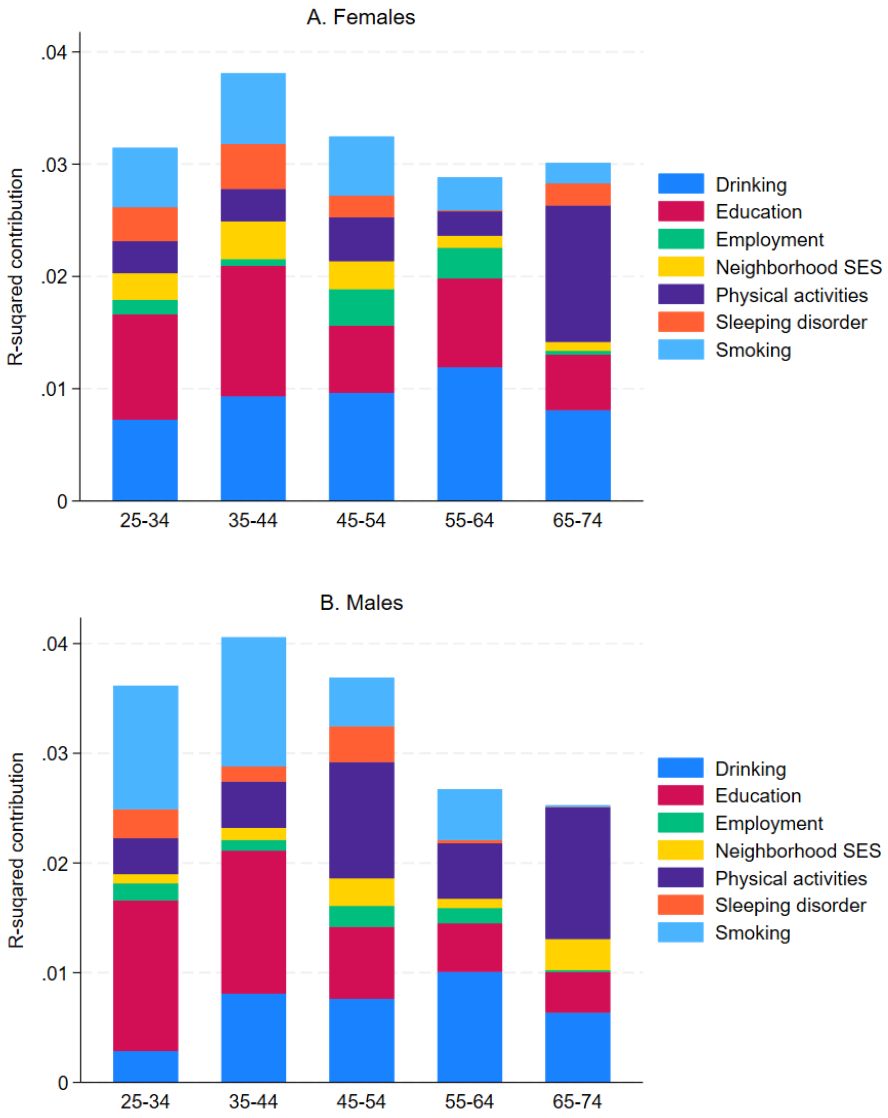

Figure B.5: The R-Squared Contribution of Modifiable Factors to the Growth of Allostatic Load Index by Gender and Age Groups

Note: We do not include the age groups of 18-24 and 75-80 due to the very small number of observations we have.