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

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Abstract: This study investigates lifetime socioeconomic health disparities through longitudinal biomarkers from the Dutch Lifelines cohort study and biobank. By constructing an allostatic load index from 12 biomarkers, we 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 in life and precede chronic disease onset. Our further analysis investigates the drivers of allostatic load and emphasizes the importance of health behaviors. Our research highlights the need for early interventions targeting SES-related health disparities and provides new insights into the physiological pathways linking SES to long-term health outcomes.

Keywords: Biomarkers; Allostatic load; Health disparity; Life cycle

JEL Classification: D31, I12, I14

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1 Introduction

Despite developments of the economy, health technology, and healthcare systems, health disparities remain large across and within socioeconomic groups. Narrowing health disparities has become a consensus goal for many governments and international organizations. For instance, the EU4 Health Programme 2021-2027 as well as the Dutch Global Strategy 2023-2030, view reducing the health gap as a major way to improve population health. To design effective preventive interventions, we need to know when and how correlations between health and socioeconomic status (SES) arise.

One of the main challenges in examining health evolution and the dynamics of health disparities is the lack of consensus on how to measure health. Much of the prior literature on health disparities across socioeconomic groups has employed measures such as morbidity, mortality, or self-rated health as outcomes (see, e.g., Van Kippersluis et al., 2010; Van Ooijen et al., 2015; Hosseini et al., 2022; Danesh et al., 2024). While these measures have provided valuable insights, self-rated health (SRH) is inherently subjective and nonspecific, and morbidity measures often capture outcomes realized later in life, after most of the cumulative wear and tear has already occurred. In this study, we complement these approaches by focusing on biomarkers, which are objective indicators that can be observable prior to disease onset. Using biomarkers allows us to contribute to the literature by introducing a new dimension to health measurement.

This paper examines the evolution of health and the dynamics of socioeconomic health disparities over the life cycle by using longitudinal 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, longitudinal 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, such as those 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 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 these foundational contributions, this study examines 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 these longitudinal biomarkers with information on chronic diseases, health-related behaviors, and socio-demographic factors, we investigate 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. We test the validity of the ALI by exploring the relationship between allostatic load and aging-related chronic diseases, focusing on how early biological risks predict chronic disease prevalence. Our analysis suggests that biomarker-related risks emerge earlier in adulthood and increase with age. In contrast, aging-related chronic diseases only become prominent in the middle age, which indicates that biomarker-related risks precede these chronic diseases. Then, we conduct age-group-specific regressions to examine the role of the ALI in the development of chronic diseases. The regression results demonstrate that both higher ALI and lagged ALI are significantly associated with an increased risk of chronic diseases.

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 the factors driving allostatic load and the growth allostatic load over the life cycle, highlighting health behaviors as important determinants. We employ the 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. There is also a difference in the results 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 three ways. First, our study aims to contribute to existing literature on socioeconomic health gradients, with a specific emphasis on investigating these gradients before the onset of clinical diagnoses. Typically, individuals with higher SES enjoy longer and healthier lives. The 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 often become statistically significant only in middle and older age, which leaves the question of how the differences in health develop across SES before reaching the clinical endpoints.

Evidence suggests that the socio-economic health gap may begin to widen before clinical endpoints like morbidity or mortality (Danesh et al., 2024). Therefore, we contribute to the measure of health before reaching the onset of chronic disease by utilizing biomarker data from the Lifelines study. Unlike these clinical endpoints health assessments, 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 use of more objective health measurements, the biomarkers, to examine health evolution. This provides empirical evidence on the progression of socioeconomic health disparity over the life cycle. 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 research has examined health evolution 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).

Therefore, recent studies have tried 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. Building on previous work, our research extends the analysis 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) reviewe 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. 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, a large, population-based cohort study that includes over 167,000 participants from the northern Netherlands at baseline (representing approximately 10% of the population). 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 Medical Center Groningen laboratory center, which is certified according to international, European, and Dutch standards.

[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.

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 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

[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?".

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 this 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]

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 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 disorders are represented by responses to 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

[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.

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. Monthly household income data is available for waves 1a and 2b, provided in the form of income range groups. We consider income in our sensitivity analysis.

Covariates: Demographic factors, such as age, sex, 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).

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

[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.

[7] We exclude individuals younger than 18 years old, as most biomarkers in Lifelines are only available for participants aged 18 and older. Additionally, we exclude individuals older than 80 years because they are underrepresented in the Lifelines dataset due to the smaller sample size.

excluded, resulting in the removal of 21,215 observations. Further, we exclude observations with no fasting, missing values for chronic disease, and demographic variables.[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 2023. 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.

3. Allostatic Load and Chronic Disease

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

[8] Many biomarkers are influenced by short-term dietary intake. To ensure reliable results, fasting is often required before blood sample collection or measurement. In line with previous studies, we exclude individuals who did not fast before blood collection from our analysis.

[9] We don't know the percentage of participants among total Lifelines population who withdraw because of enrolling a regular health care programme. We will clarify it more after communicate with Lifelines. However, according to the information provide by Sijtsma et al. (2022), there is only small proportion of participants who withdraw in followups.

established research to construct an ALI 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, 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) (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 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; 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), used 10 biomarkers, while Karimi et al. (2019) included 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. 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 to construct the ALI, focusing on three physiological systems: cardiovascular (n=3), metabolic (n=8), and kidney function (n=1).[10] 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:

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

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.[11] 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 biomarke r-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.

[10] Some prior studies also employ biomarkers from other systems, including the immune system, the HPA 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).
[11] One exception is HDL cholesterol. High risk is defined when its level falls below the threshold, as it is considered "good" cholesterol.

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.

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.

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, 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. 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.[12]

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 the ALI and the 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.[13] The figure reveals that biomarker-related risks emerge significantly 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 Allostatic Load and Disparity in Chronic Disease

As shown above, the clinical endpoints often only become sizeable in the middle or later in life. On the contrary, the biomarker-related risks have already emerged early in adulthood before chronic diseases happen. Previous research has highlighted the significant association between

[12] 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.
[13] 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.

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.

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 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, indicating that higher ALI and the lagged term correspond to increased CDI values. This finding supports the role of ALI as a pre-indicator of aging-related chronic disease prevalence. Additionally, in Table 5-1 and Table 5-2 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 effects intensify in later life.

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 exhibit disparities in biomarkers and related risks among young adults and present the trajectory of educational disparities in allostatic load over the life cycle. 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 Educational Allostatic Load Disparity over the Life Cycle

At the outset, we examine how educational allostatic load disparity evolves over the life cycle, without accounting for other potential confounders. This serves as a preliminary analysis aimed at understanding the onset of health disparity in allostatic load and the pattern over the life cycle.

Figure 4 presents the mean allostatic load for each age group, 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. Furthermore, there are distinct gender differences in both the levels and patterns of allostatic load over the life cycle. 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.1 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 deceleration can be attributed to several factors. First, the prevalence of chronic diseases often leads individuals to begin medication, which can reduce the levels of certain biomarkers, such as HbA1c.[14] 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 can also play a role. For example, individuals with higher allostatic load may drop out of the Lifelines study due to transitioning to regular healthcare programs or, in some cases, due to mortality.

However, static comparisons of health gaps may 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 our study, we are mainly interested in the differences in the health evolution by

[14] In the Lifelines study, we have access to self-reported medication data, which we plan to analyze in greater detail. This will help us better understand how medication interventions contribute to reducing allostatic load and shape the trajectory of the allostatic load gap across educational levels.

education attainment. Education 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 importance 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

Further, we examine the educational disparities in biomarkers and biomarker-related risks between females and males. Figures B.2.1, Figure B.2.2, and Figure B.2.3 in the Appendix present box-and-whisker plots of 12 biomarkers by 10-year age groups, constructed using pooled observations from 3 waves.[15]

[15] 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 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.

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, there is a clear gender difference in the value, but the pattern across age groups is generally similar for both males and females.

We next 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 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[16]. 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.3 in the Appendix.

4.3 Allostatic Load and Socioeconomic Disparity in Chronic Disease

Previous research has suggested that SES-related disparities in chronic diseases are partly explained by health behaviors, demographic and socioeconomic factors, and environmental exposure (Danesh et al., 2024). In the final part of this section, building on prior analysis, we investigate the role of allostatic load in explaining SES differences in aging-related chronic diseases. To do this, we employ a regression model to examine the association between

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

education and chronic disease. We then incorporate the ALI and its lagged term into the model to assess the extent to which allostatic load mediates educational differences in aging-related chronic diseases.

Table 6 presents the results both with and without the inclusion of allostatic load. As shown in column 2 and 3, the coefficient for the high education group decreases significantly after adding ALI and its lagged term to the model. This finding indicates that allostatic load partially accounts for the observed differences in aging-related chronic diseases between individuals with high educational attainment and those with lower educational attainment.

5. Drivers of Allostatic Load over the Lifecycle

5.1 Framework

Our prior graphical analysis demonstrate 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:

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

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.4 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 a biological index to reflect physiological deregulation in response to stress exposure, which also indicates the cumulative risks of chronic conditions. Consistent with previous research, we highlight the significant role of allostatic load as a mediator in SES-related health disparities in aging-related chronic disease.

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 each factor 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 cohort effects 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 simplistic, 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 will 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[17]	>= 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[18] (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.

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

[18] 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 1	Wave 2	Wave 3	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)
Colitis ulcerosa	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 1	Wave 2	Wave 3	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)
Parkinsons	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 on Allostatic Load

	(1) Model 1	(2) Model 2
ALI	0.065***	
	(0.002)	
ALI_{a-t}		0.074***
		(0.002)
Controls	Yes	Yes
Observations	120,083	120,083
R-squared	0.159	0.158

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:Regression Results of Testing the Role Allostatic Load as a Medicator of Educational Differnece in Aging-Related Chronic Disease

	(1) Model 1	(2) Model 2	(3) Model 3
Edu	-0.112***	-0.090***	-0.092***
	(0.006)	(0.006)	(0.006)
ALI		0.062***	
		(0.002)	
ALI_{a-t}			0.071***
			(0.001)
Controls	Yes	Yes	Yes
Observations	120,083	120,083	120,083
R-squared	0.159	0.159	0.160

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

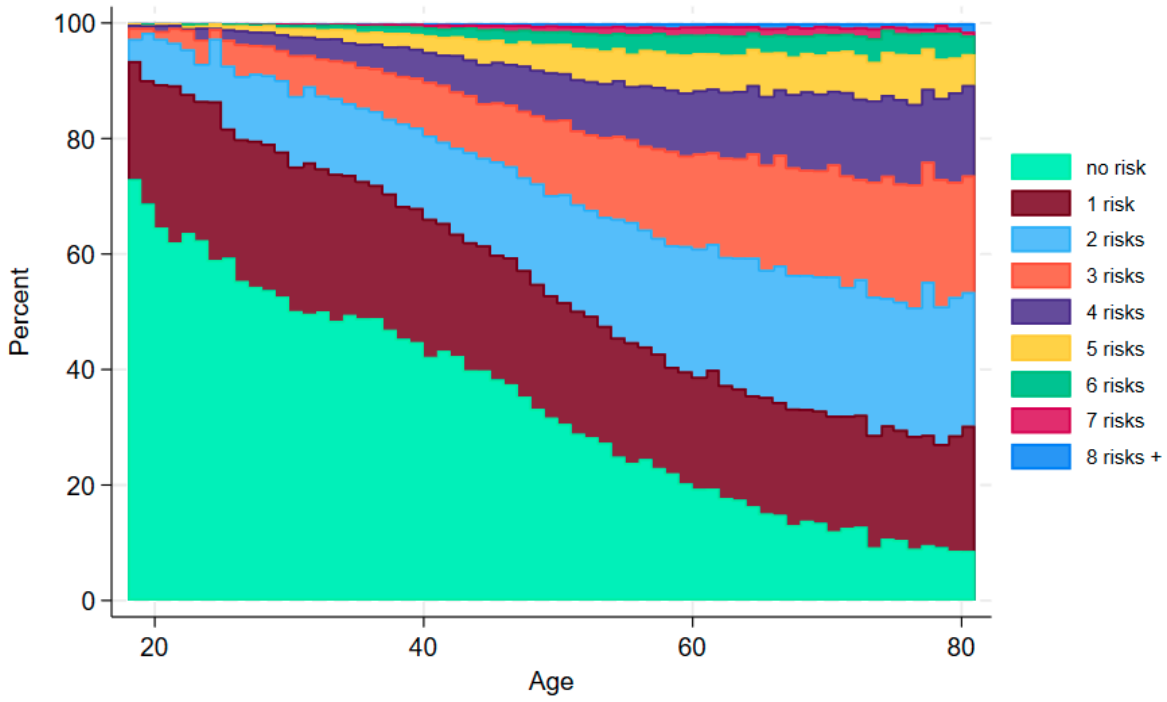

Figure 1: The Evolution of the Number of Biomarker-Related Risks Over the Life Cycle

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.

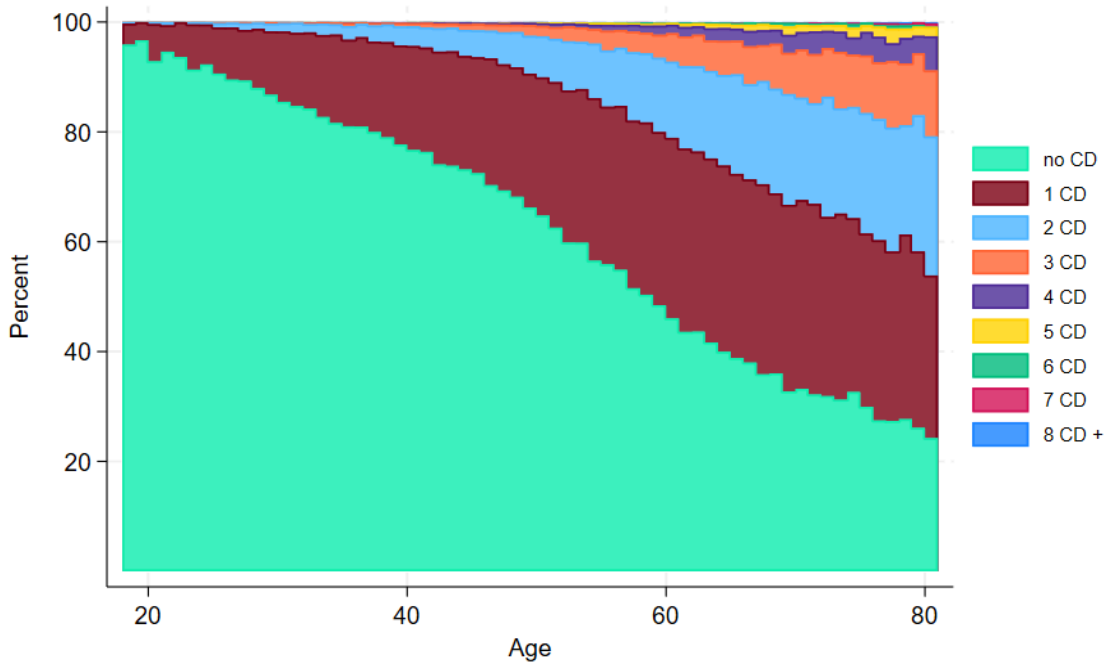

Figure 2: The Evolution of the Number of Aging-Related Chronic Diseases Over the Life Cycle

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.

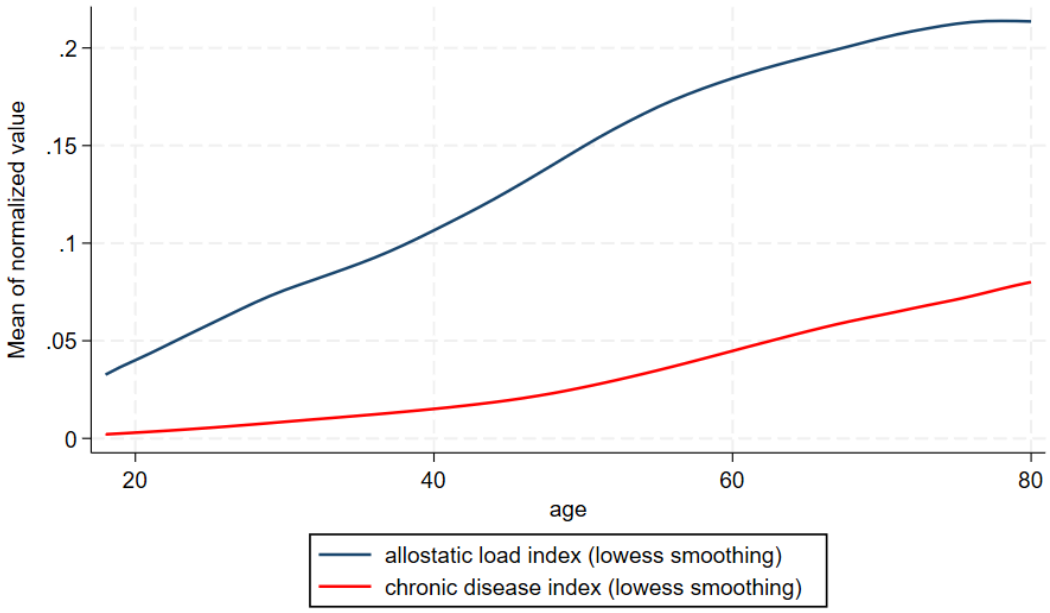

Figure 3: The Life Cycle Profile of Allostatic Load Index and Chronic Disease Index by Age and Gender

Note: To ensure comparability of scale, the indexes are rescaled using the mini-max scaling approach We employ the LOWESS smoothing method to smooth the relationship between age and the age mean values of ALI and CDI. LOWESS, a non-parametric regression technique, facilitates the visualization of trends between two variables. Here, the bandwidth (smoothing parameter) is set to 0.25, indicating that 25% of the data is used for each local regression. This value effectively minimizes the influence of noise while ensuring the curve still represents the true pattern.

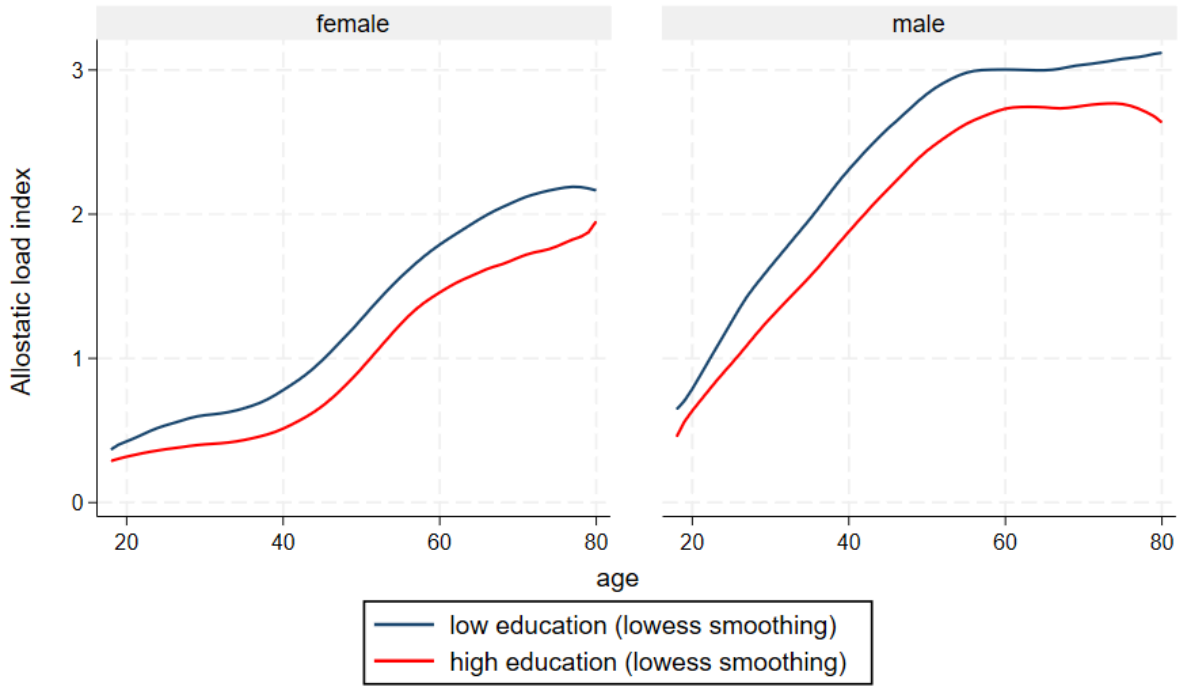

Figure 4: The Educational Allostatic Load Disparities by Age and Gender

Note: The scatter points represent the original mean of allostatic load index, categorized by age, sex, and education. Additionally, we present a LOWESS smoothing curve, which utilizes the LOWESS method to illustrate the smoothed trajectory of allostatic load across the lifecycle, with the bandwidth (smoothing parameter) set to 0.25.

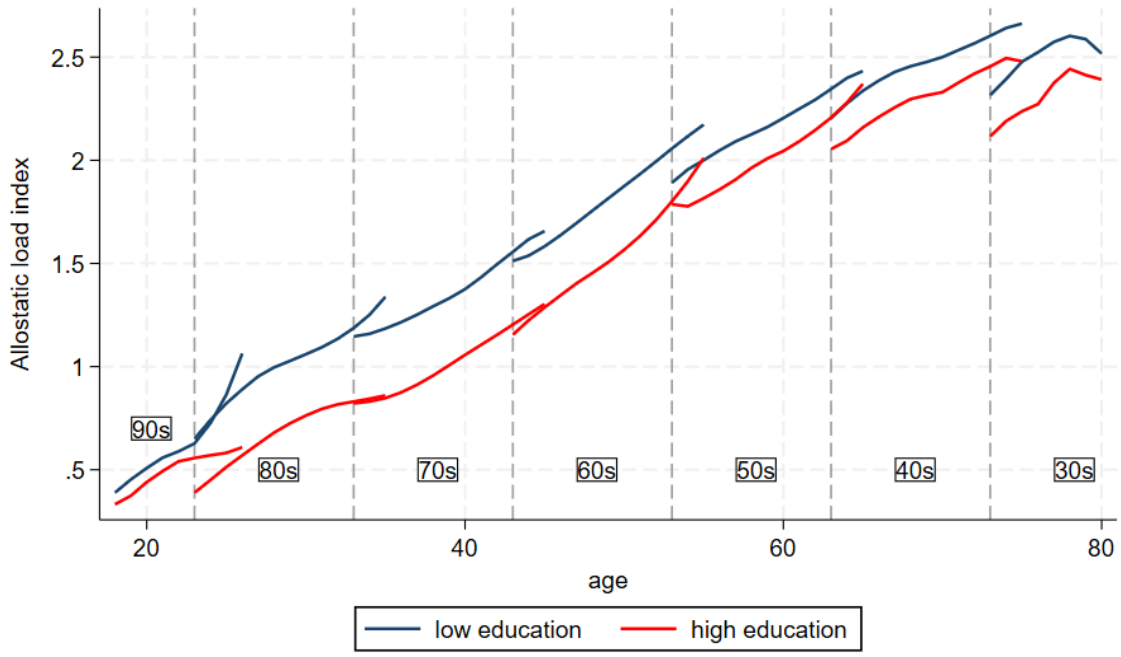

Figure 5: The Educational Allostatic Load Disparities by Age, Cohort, and Gender

Note: The scatter points represent the original mean of allostatic load index, categorized by age, sex, cohort, and education. Additionally, we present a LOWESS smoothing curve, which utilizes the LOWESS method to illustrate the smoothed trajectory of allostatic load across the lifecycle, with the bandwidth (smoothing parameter) set to 0.25.

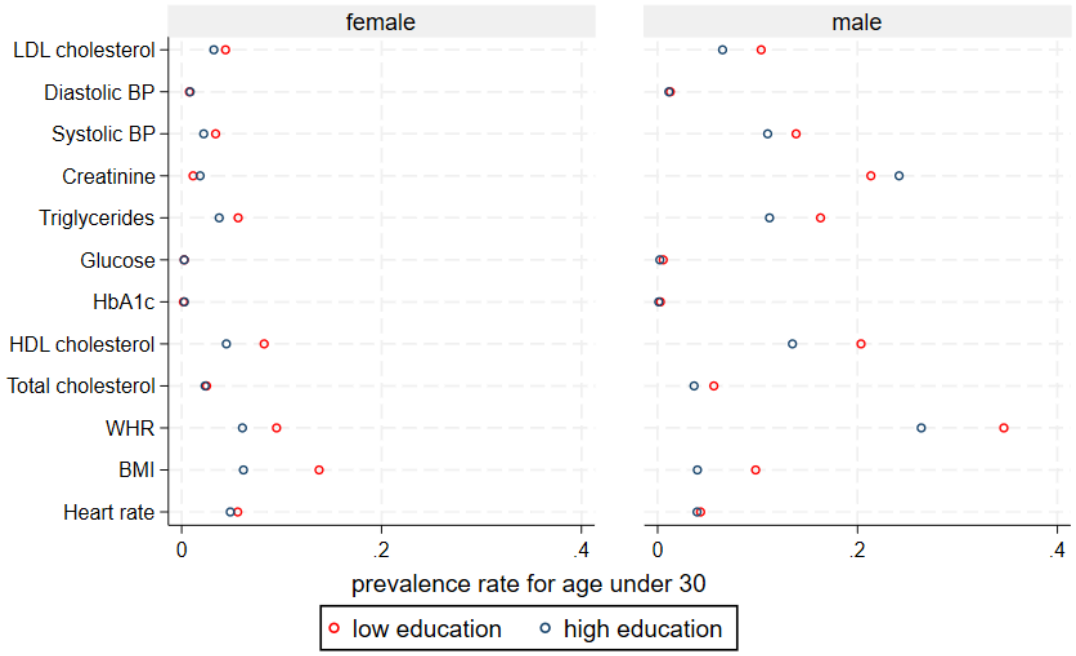

Figure 6: The Prevalence Gap of Having High Risks in Biomarkers for Age Group Under 30

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. 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.

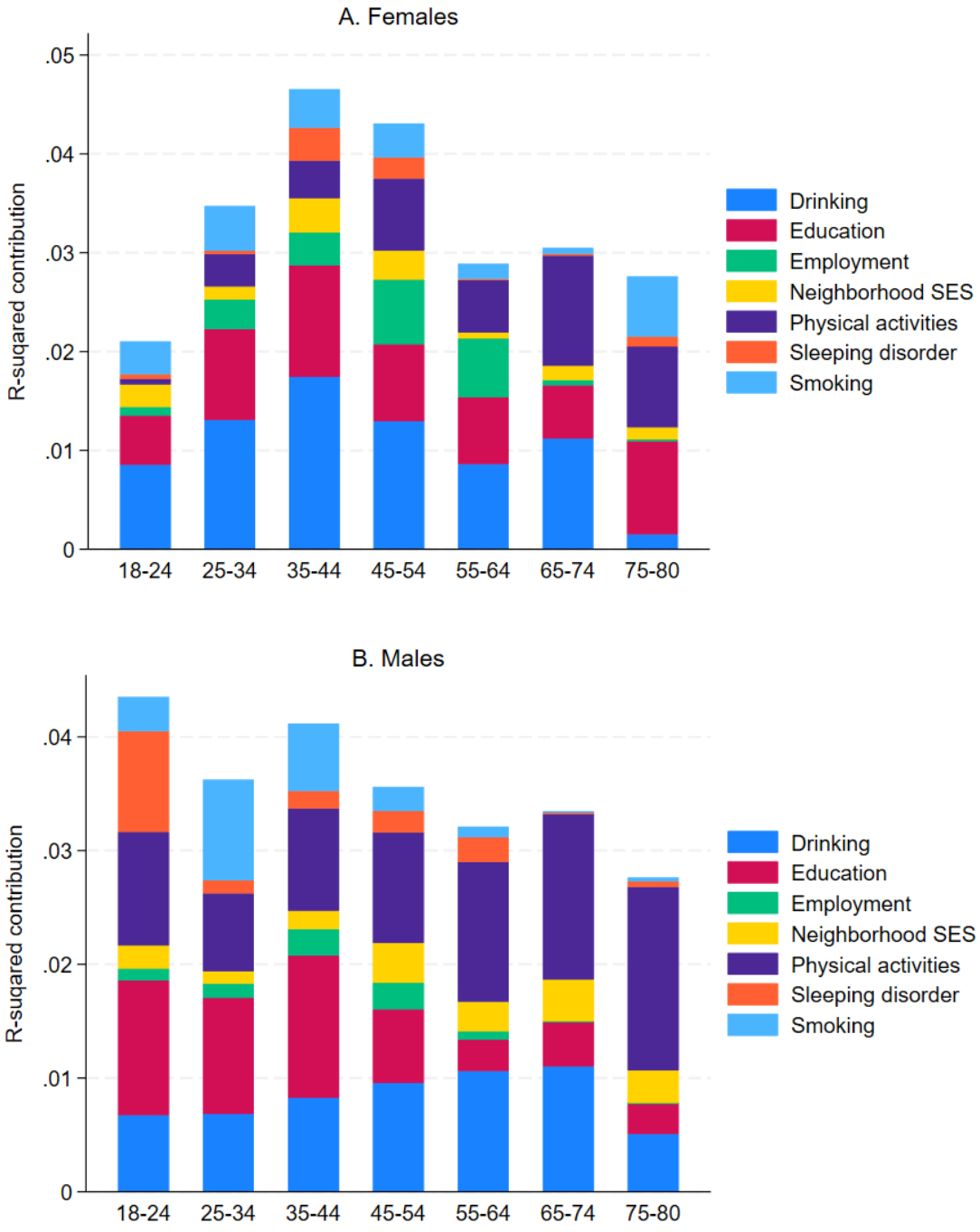

Figure 7: The R-Squared Contribution of Factors to Allostatic Load Index by Gender and Age Groups

Appendix

A Tables

Table A.1: Aging-Related Chronic Disease

Category	Specific Disorder
Cancer	
Cardiovascular diseases	heart attack, heart failure, stroke
Diabetes	
Digestive system diseases	colitis ulcerosa, 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

B Figures

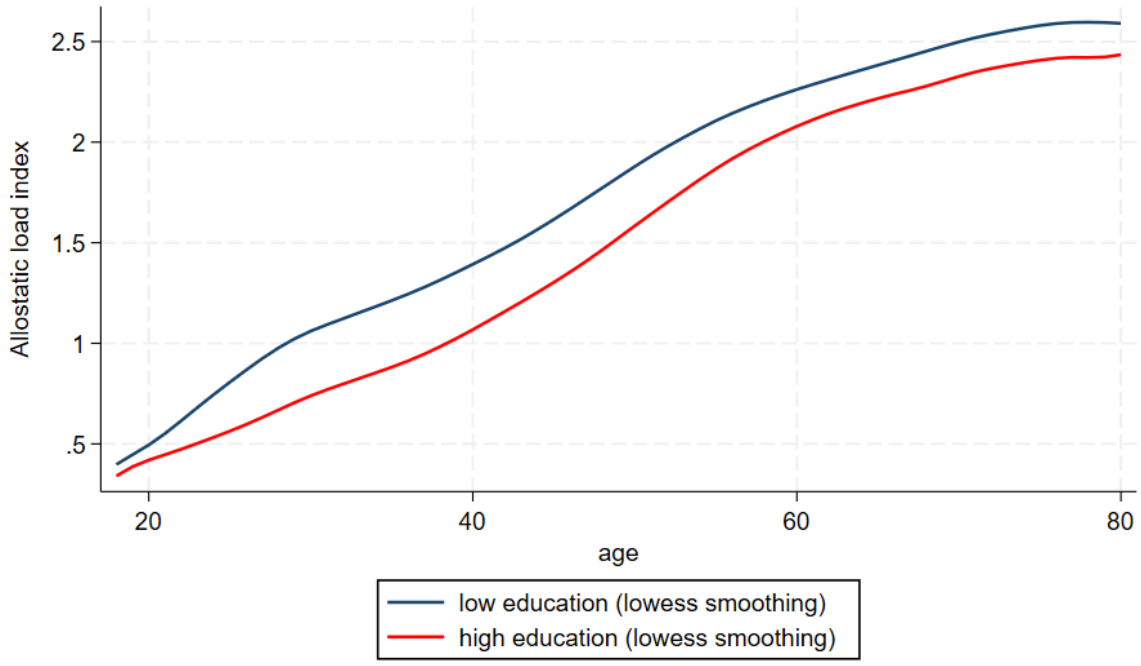

Figure B.1: The Life Cycle Profile of Allostatic Load Index by Age, Gender, and Education for the Whole Sample

Note: we present a LOWESS smoothing curve, which utilizes the LOWESS method to illustrate the smoothed trajectory of allostatic load across the lifecycle, with the bandwidth (smoothing parameter) set to 0.25.

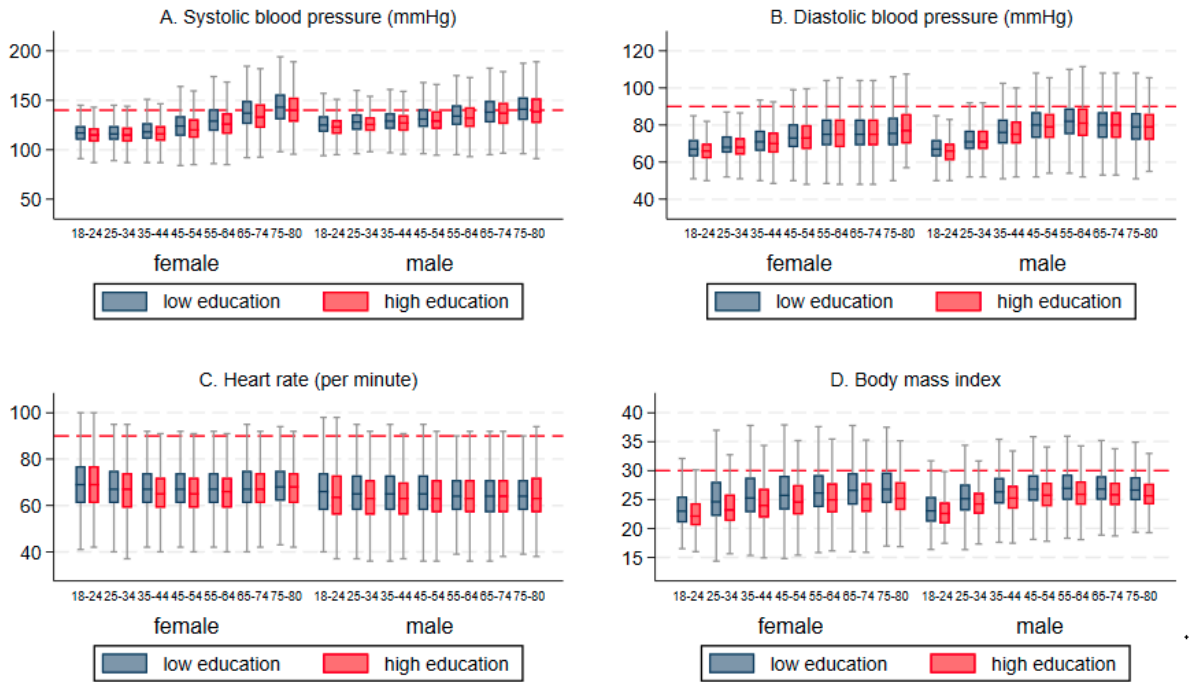

Figure B.2.1: The Distribution of Biomarkers Across Education Levels, Genders, and Age Groups

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.

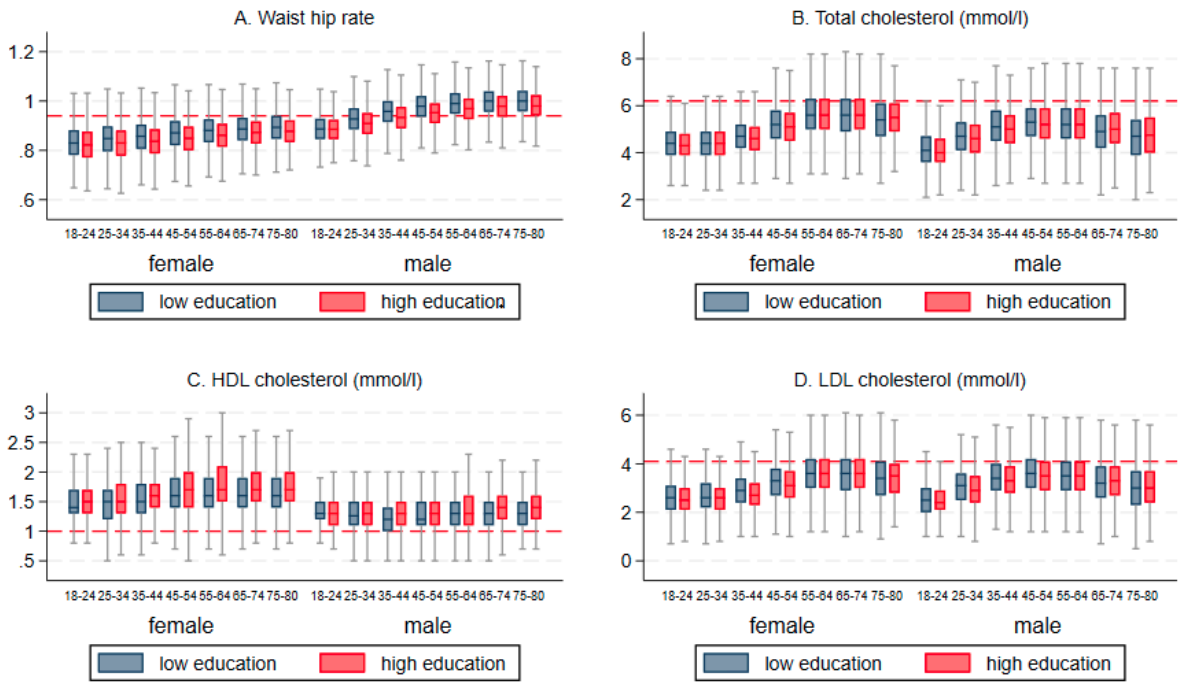

Figure B.2.2: The Distribution of Biomarkers Across Education Levels, Genders, and Age Groups

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.

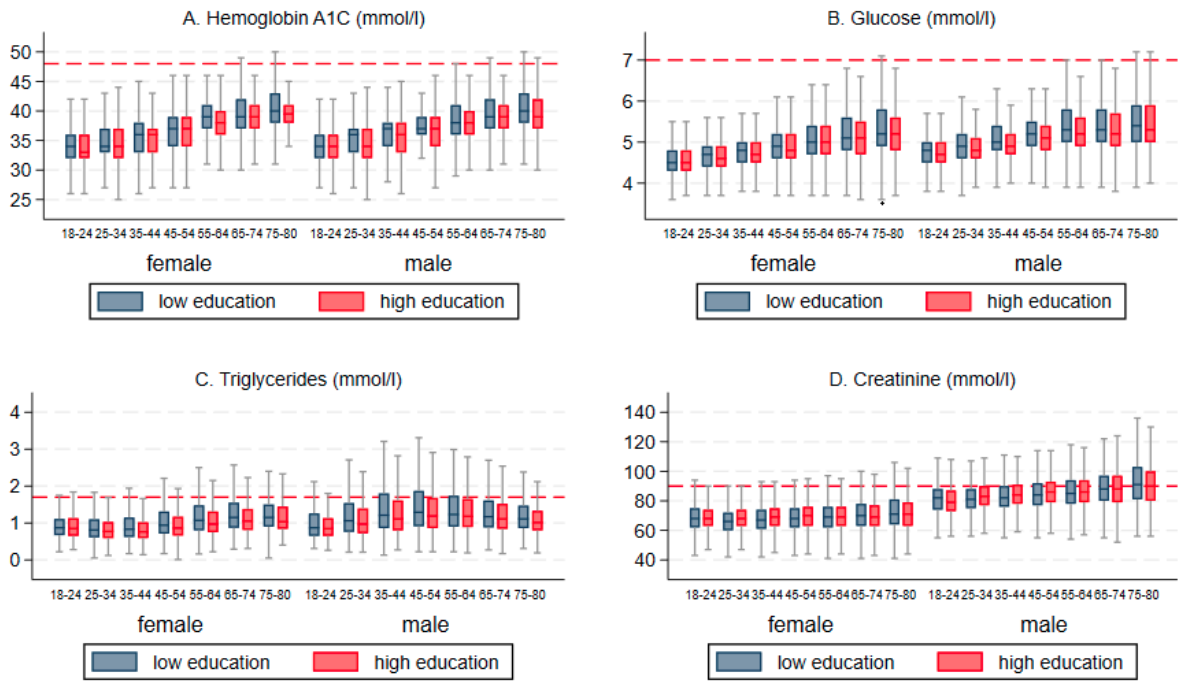

Figure B.2.3: The Distribution of Biomarkers Across Education Levels, Genders, and Age Groups

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.

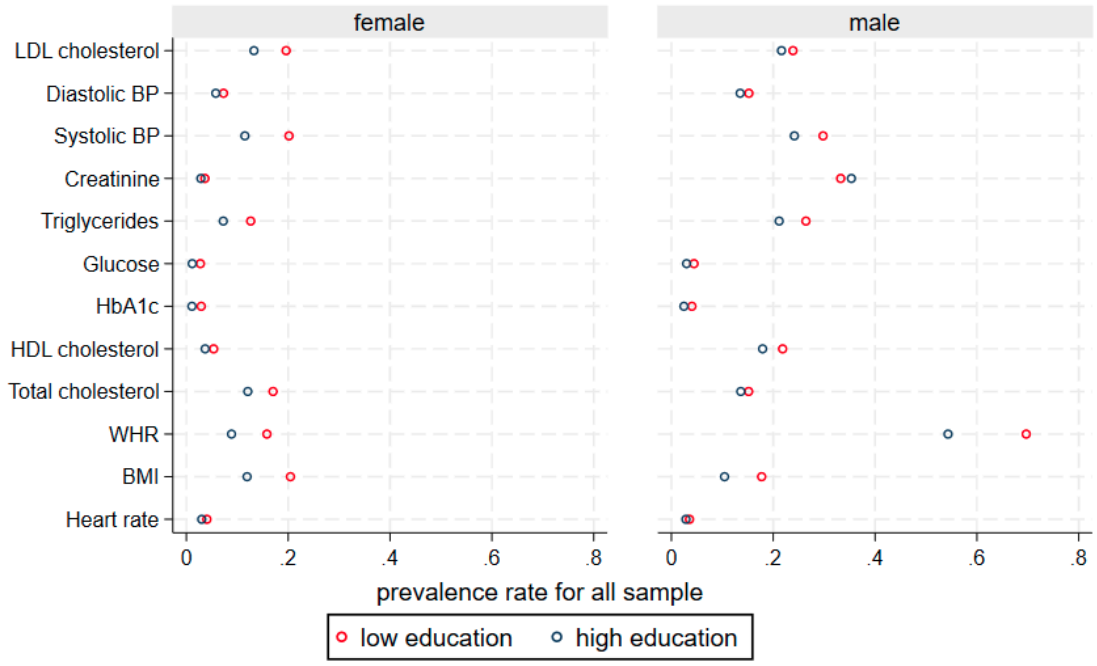

Figure B.3 The prevalence gap of having high risks in biomarkers for whole sample

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.

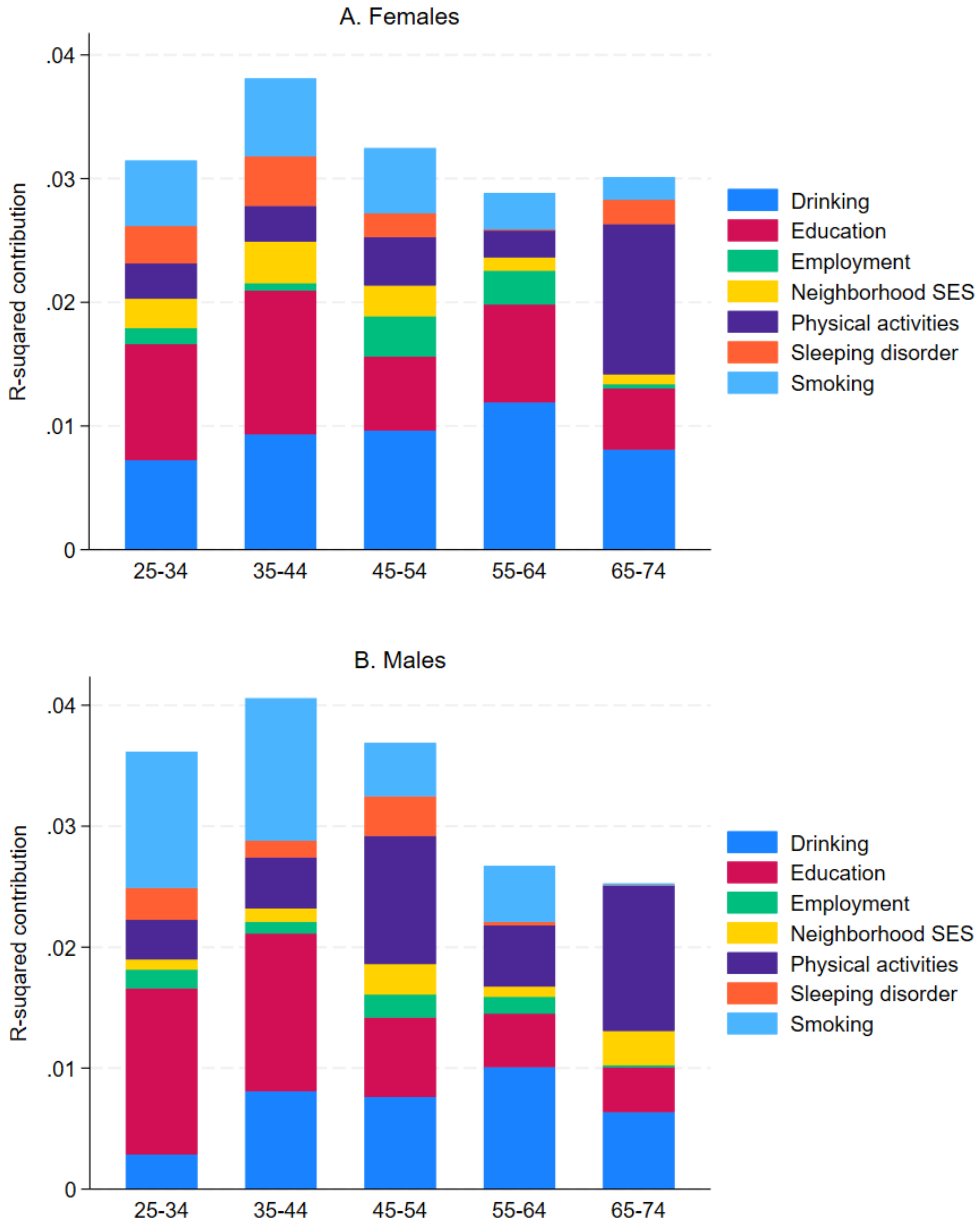

Figure B.4: The R-Squared Contribution of Factors to the Growth of Allostatic Load Index by Gender and Age Groups

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