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

Ailun Shui[1] Gerard J.van den Berg[1,2]
Jochen Mierau[1,2,3] Laura Viluma[1]

[1]University of Groningen

[2]University Medical Center Groningen

[3]Lifelines

Jan 9, 2025

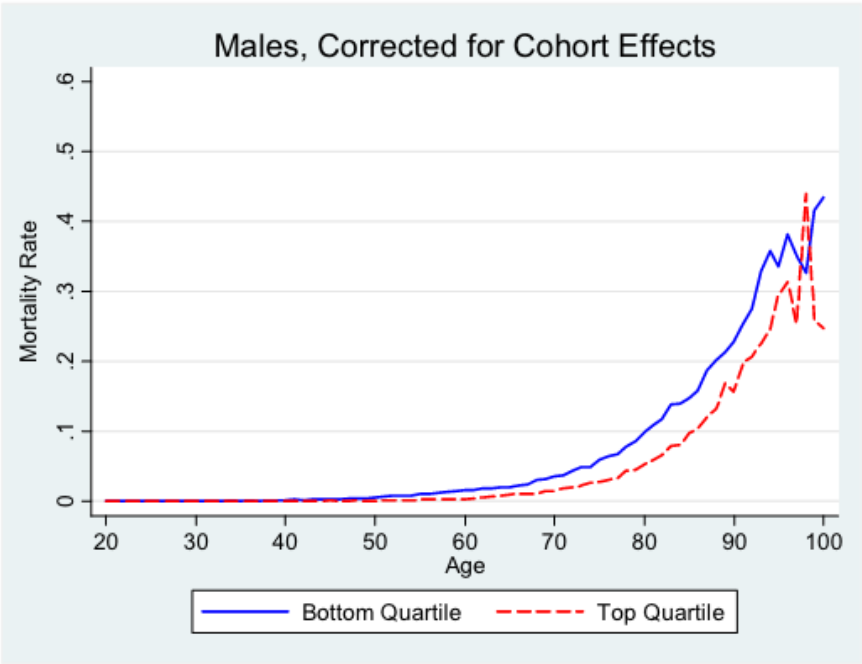
Outline

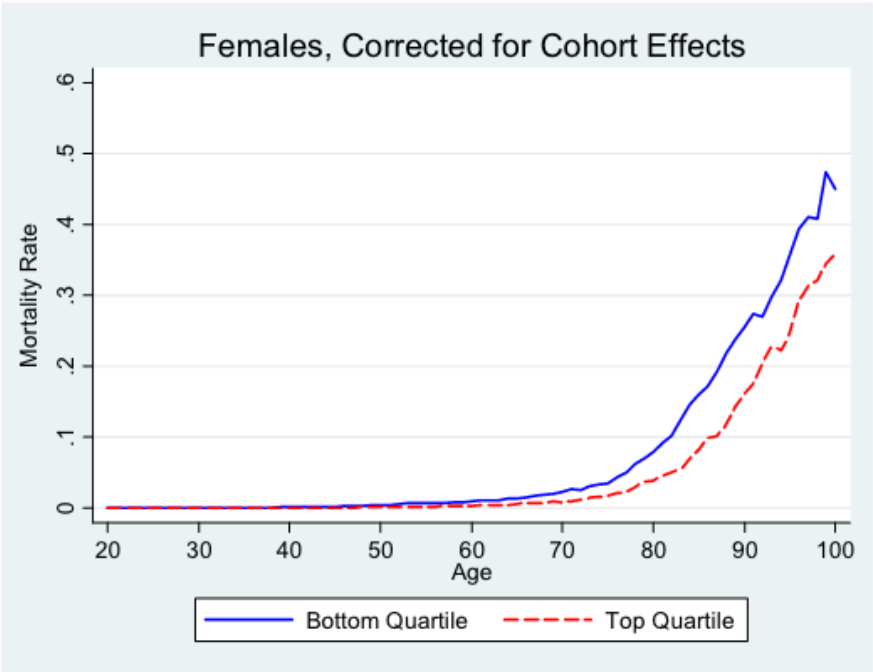
Motivation

- Substantial health disparities exist over the lifespan and across the individuals:
  - Reducing the health gap is a common goal.
- Many existing studies measuring health disparities use metrics such as mortality or self-rated health:
  - Mortality often becomes apparent only later in life,
  - Self-rated health is inherently subjective and non-specific.
- **Limited knowledge exists regarding health disparities before they are clinically diagnosed.**

Mortality rate by age and current income in the NL

Absolute mortality rate





Source: Van Kippersluis et al., 2010

The role of biomarkers

- Biomarkers are objective, quantifiable indicators of biological processes.
- The dynamic of biomarkers is often linked to the aging process, onset of diseases, and mortality.
- Biomarkers provide objective measures and can indicate medical conditions before a clinical diagnosis is reached.
- Offer policy insights for early interventions before diseases fully develop.

Sketch of Literature

- Socioeconomic health disparities:
  - Morbidity (Cutler & Lleras-Muney, 2006; Kivimäki et al., 2020; Pallesen et al., 2024; Danesh et al., 2024)
  - Mortality/life expectancy (Deaton, 2003; Van Kippersluis et al., 2010; Chetty et al., 2016)
  - Self-rated health (Van Kippersluis et al, 2010; Van Ooijen et al., 2015)
- Biomarkers and allostatic load
  - Health disparities in biomarkers (Kavanagh et al., 2010; Davillas & Jones, 2020)
  - Allostatic load (Seeman et al., 2004; Carrieri et al., 2020)
- The determinants of health disparities
  - Health-related behaviors and lifestyles (Adler & Stewart, 2010; Suvarna et al., 2020; Danesh et al., 2024)
  - Early-life conditions (Van den Berg et al. 2010; Alessie et al., 2019)
  - Environmental exposure (Danesh et al., 2024)

Research questions and contribution

- Research questions:
  - Do patterns in biomarkers predict the onset of chronic disease burden?
  - Is the socioeconomic health gap already visible in biomarkers at lower ages?
  - To what extent are those biomarkers driven by modifiable (lifestyle) factors?
- Additional contributions:
  - Leverages large-scale biomarker data to examine the biological health prior to reaching the diagnosis.
  - Employs objective measurements to analyze socioeconomic health disparities across the life cycle.

Overview of the Dutch Lifelines cohort study and biobank

- A large-scale longitudinal cohort study conducted in the northern Netherlands:
  - More than 167,000 participants at baseline in 2006, representing approximately 10% of the population,
  - Currently includes 3 waves of biomarker measurements,
  - Participants range in age from 18 to over 80 years,
  - Includes family connections.
- Repeated measures of various biomarkers, including:
  - Anthropometry (e.g., body measurements)
  - Blood pressure
  - Electrocardiogram (ECG)
  - Biomaterial collection (fasting blood and urine)
  - Lung function
- Comprehensive survey data:
  - Demographic and socioeconomic status.
  - Health-related behaviors.
  - Information on diseases, medication use, and mortality.

Allostatic load index

- Concept: Allostatic load measures the cumulative dysregulation of physiological systems in response to social and environmental stress (Seeman et al., 1997, 2004).
- We create an index based on 12 biomarkers:
  - Cardiovascular system (n=3): systolic blood pressure, diastolic blood pressure, ECG heart rate.
  - Metabolic system (n=8): body mass index, waist-to-hip ratio, total cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, glycosylated hemoglobin, glucose, triglycerides.
  - Kidney function (n=1): creatinine.

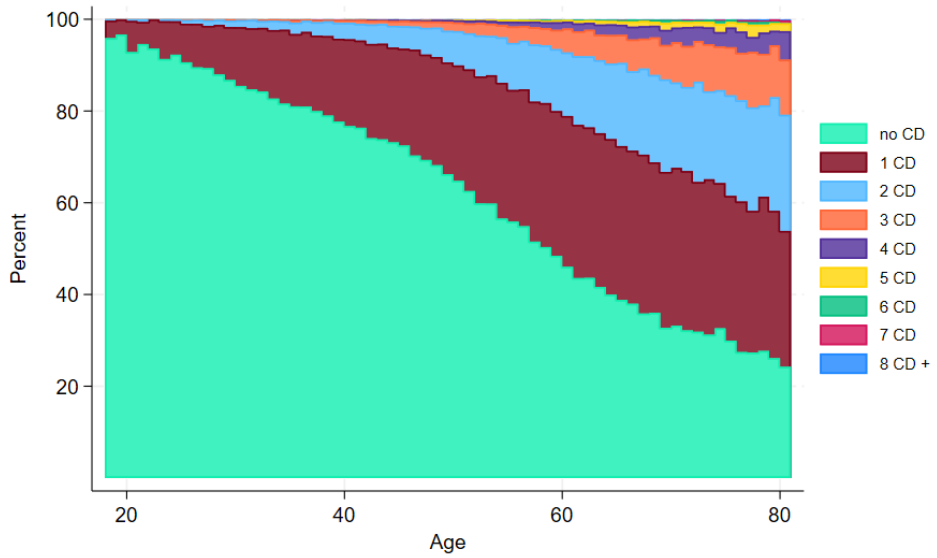
Allostatic load index

- Clinically established threshold cut points are applied for each biomarker.

$$ALI_{i,a} = \sum_{k=1}^{12} I_{i,a}^{k} \tag{1}$$

- Where:
  - $I_{i,a}^{k}$ is a binary variable indicating whether the level of biomarker k in individual i at age a is above the threshold.
  - $ALI_{i,t}$ is the allostatic load index.
- Higher ALI scores indicate greater physiological stress.

Allostatic load index and aging-related chronic disease index



Regression analysis

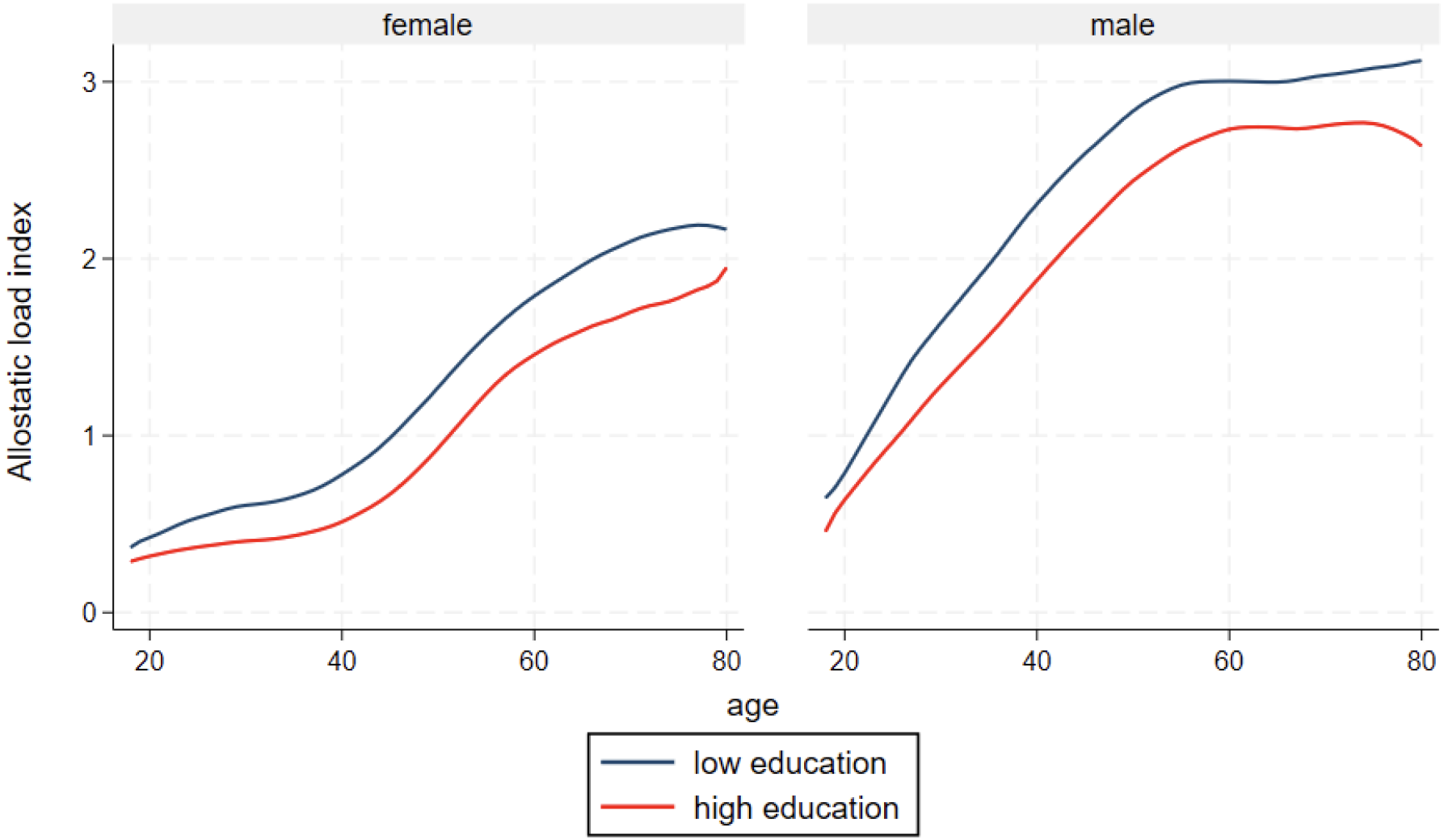
Regression Results of Chronic Disease on Allostatic Load

	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

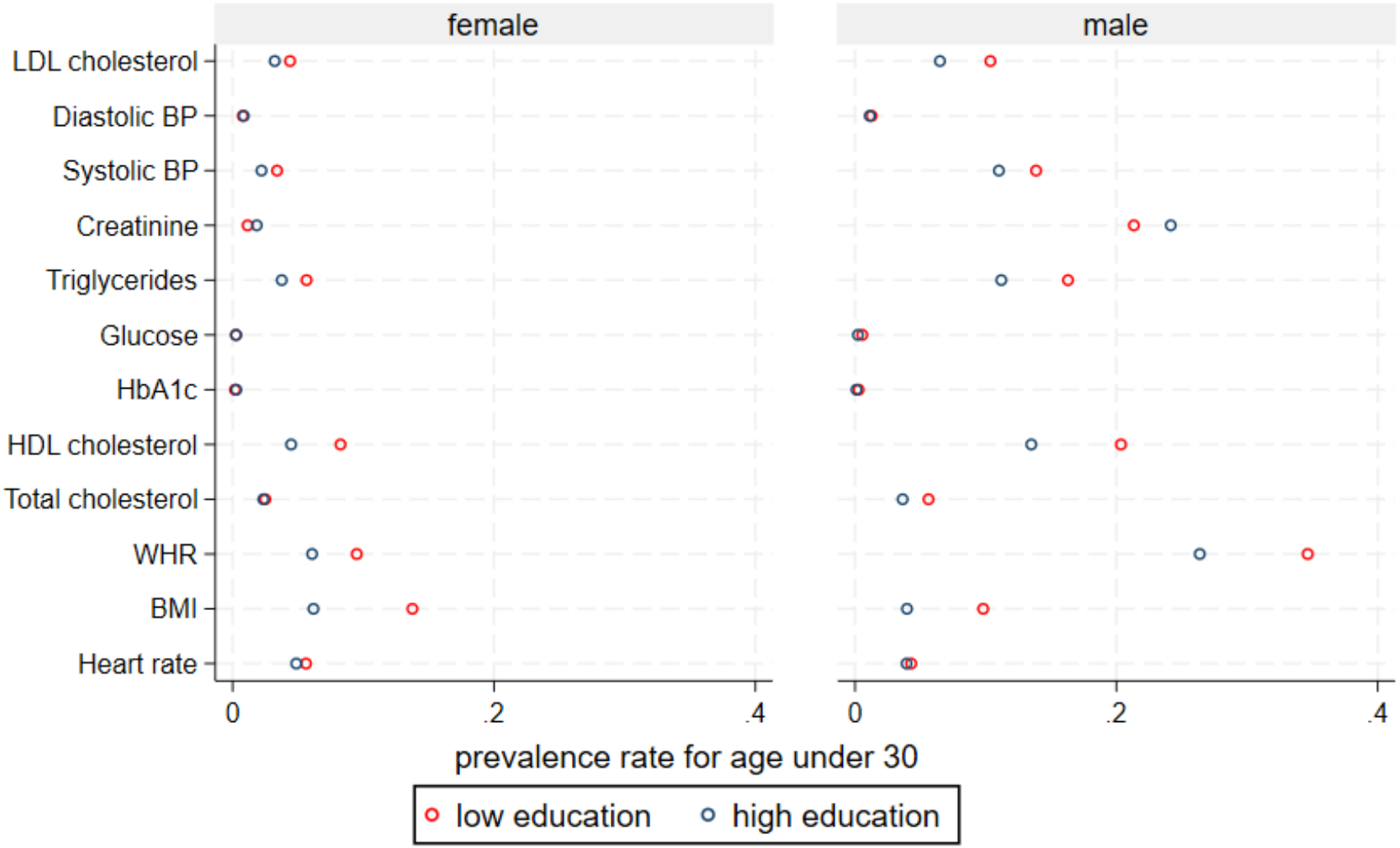
	55-64		65-74	
	(1)	(2)	(1)	(2)
ALI	0.068***		0.075***	
	(0.004)		(0.005)	
ALI_{a-t}		0.086***		0.072***
		(0.004)		(0.006)
Controls	Yes	Yes	Yes	Yes
Observations	30,120	30,120	16,898	16,898
R-squared	0.041	0.057	0.031	0.039

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.

Educational allostatic load disparities by age and gender



The gender gap in biomarkers at ages below 30



Regression analysis

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.

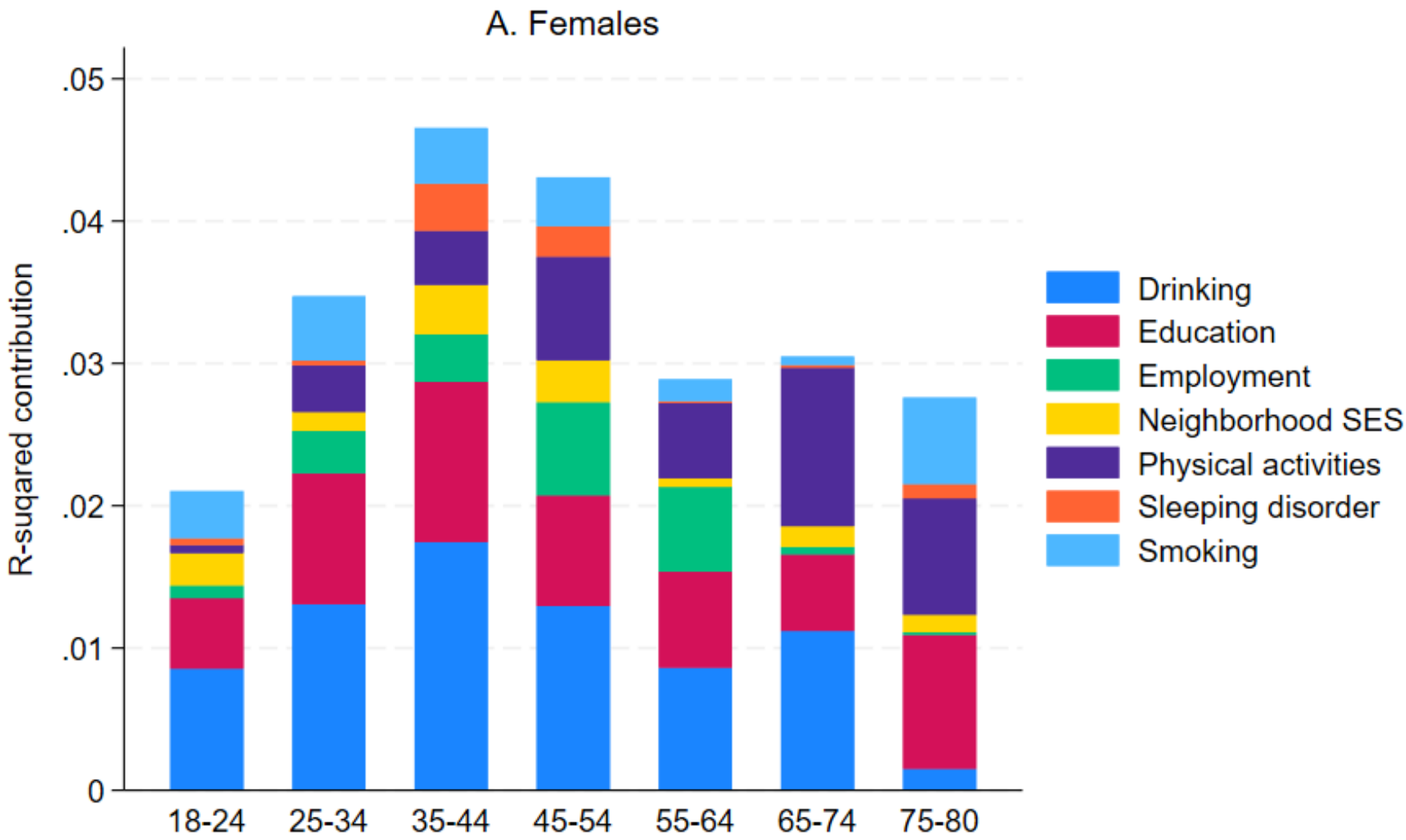
A framework

- We employ a linear regression for different 10-year age bins:

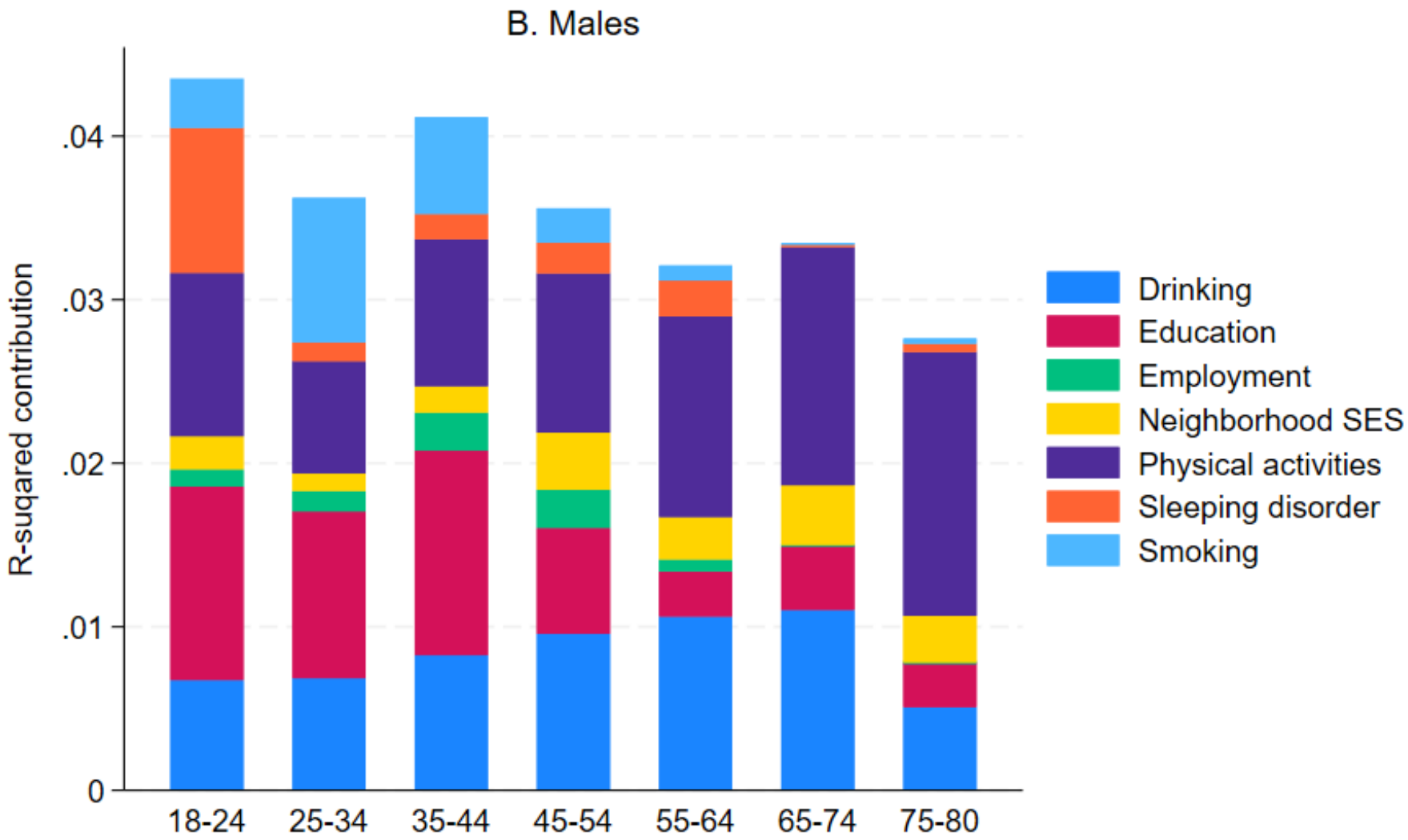
$$ALI_{i,a} = \sum_{j=1}^{J} X_{i,a}^{j} \gamma_{j,a} + \epsilon_{i,a} \tag{2}$$

- Where:
  - $ALI_{i,a}$ is the level of the current allostatic load index,
  - $X_{i,a}^{j}$ is a vector of factors, including health behaviors, educational attainment, employment status, and neighborhood SES.
- Then, we decompose the total R-squared of this regression based on Shapley-Owen values (Huettner & Sunder, 2012):-
  - This method calculates the average contribution of each regressor to R-squared among all possible regression sequences.

The decomposition results



The decomposition results



Take away for current analysis

- Biomarker-related health risks emerge early in adulthood, preceding aging-related chronic disease.
- Biomarker-related socioeconomic health disparities emerges early in adulthood, widens with age, and peaks in late middle age.
- Health behaviors play an important role in allostatic load.
- There are clear gender differences in the life cycle pattern and drivers of biomarker-related risks.
- Robustness analysis shows that using parental education gives rise to qualitatively similar findings.

Limitations and Next Steps

- Limitations:
  - The results may be influenced by the number and types of biomarkers we selected.
  - The current analysis does not account for time-varying confounders.
  - The analysis does not consider the impact of factors such as environmental exposure and early life conditions in the decomposition analysis.
- Next Steps:
  - Future analyses will focus on accounting for confounders in the analysis:
  - We aim to capture biological aging speed based on our dynamic biomarkers.

Thanks!