

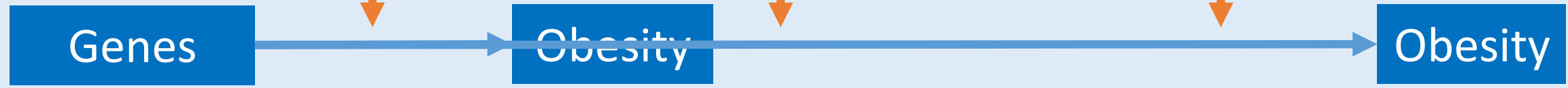
Lifetime Socioeconomic Status, Historical Context, and Genetic Inheritance in Shaping Body Mass in Middle and Late Adulthood

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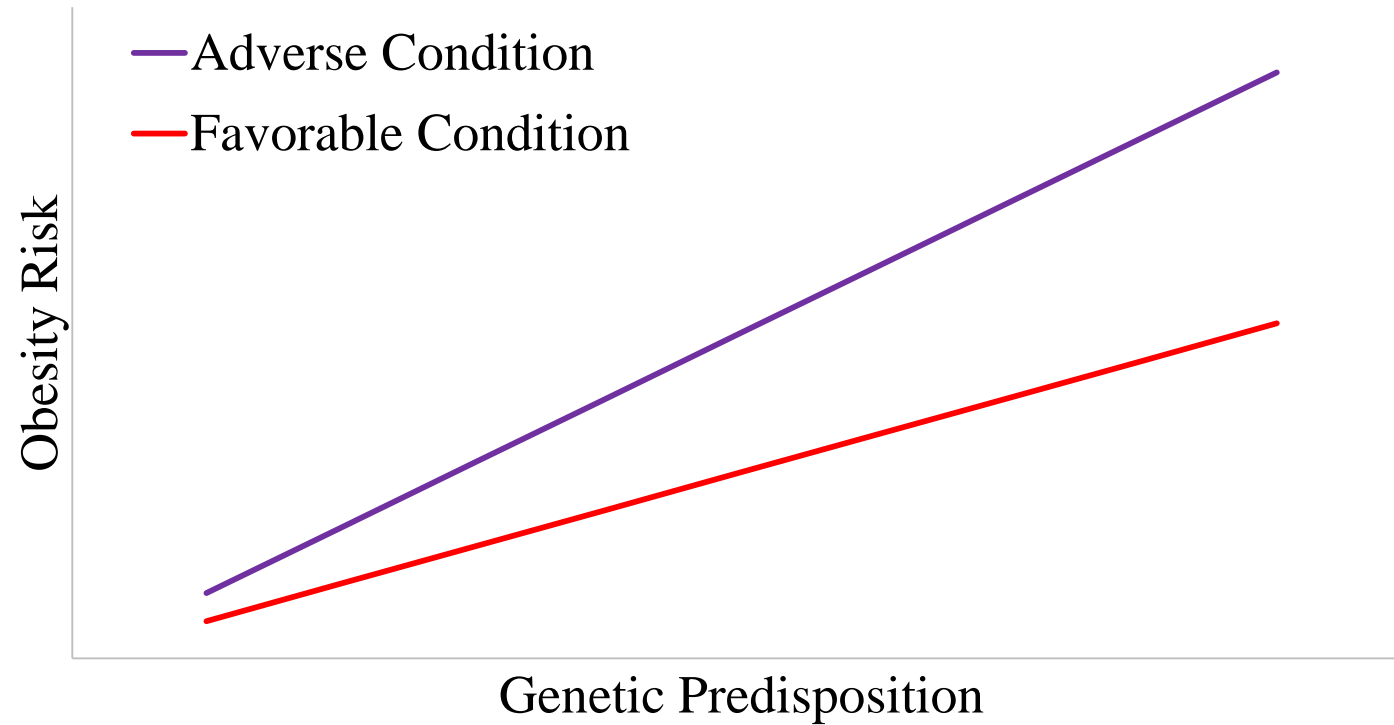
Society



Research Questions

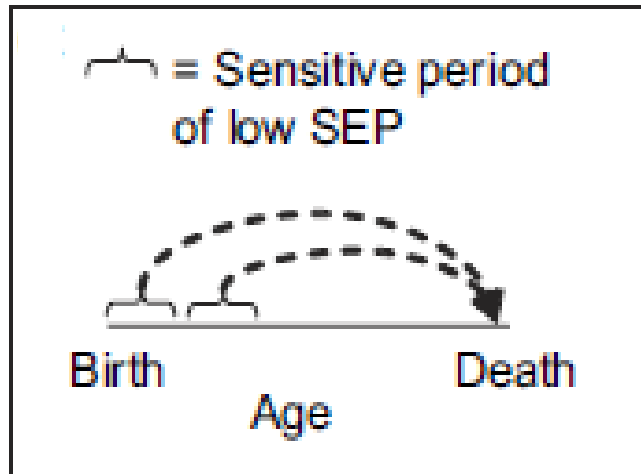
- Whether the genetic influence on body mass index (BMI) in middle or late adulthood depends on socioeconomic status (SES) at different life stages (e.g., childhood, young adulthood, and middle/late adulthood) and, particularly, changes in SES over the life course?
- How the influences of life-course SES , genetic factors, and their interaction on BMI differ across birth cohorts?

How Genes Interact with The Environment Influencing Obesity?

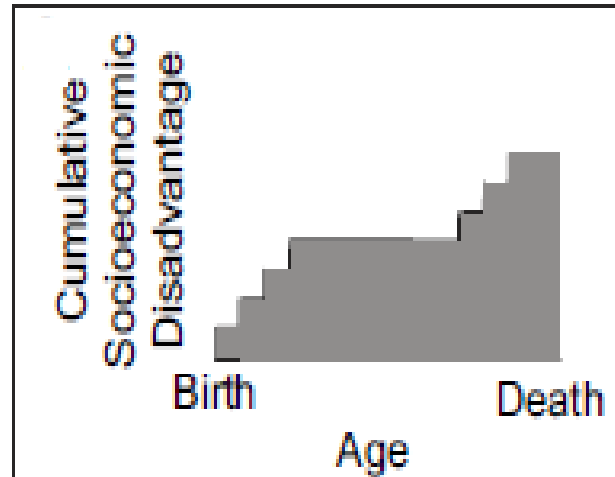


Life-course Perspectives

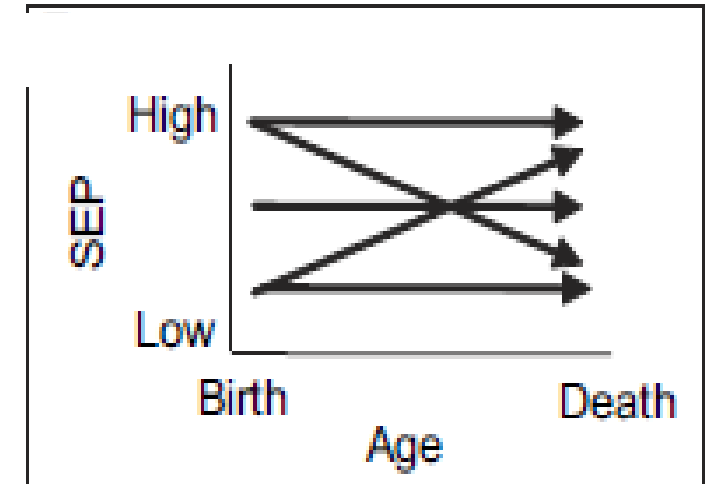
Sensitive Periods
Life Course SEP Framework



Accumulation of Risk
Life Course SEP Framework



Social Mobility
Life Course SEP Framework



Source: Loucks et al. 2010

Data

Health and Retirement Study (HRS):

- Longitudinal study of Americans over age 50 conducted every two years from 1992 to 2012
- Genome-wide genotype data (more than 2 million genetic variants from each of 12,507 individuals)
- Accelerated multi-cohort longitudinal design
 - Assets and Health Dynamics among the Oldest Old (AHEAD) (born before 1924)
 - Children of Depression (CODA) (born 1924 to 1930)
 - HRS (born 1931 to 1941)
 - War Babies (WB) (born 1942 to 1947)
 - Early Baby Boomers (EBB) (born 1948 to 1953)
 - Mid Baby Boomers (MBB) (born 1954 to 1960)

Data

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Key Variables

SES measures in HRS:

- (1) Childhood SES: father's occupation;
- (2) Young adulthood SES: years of education
- (3) Late adulthood SES: wealth

Accumulative advantage score: 0-3

SES mobility trajectories: **stable and low**, **downwardly mobile**,
stable and high, **upwardly mobile**.

Key Variables

- Genetic predisposition score (GPS)
 - Based on 32 single-nucleotide polymorphisms (SNPs) associated with BMI (Speliotes *et al.* 2010);

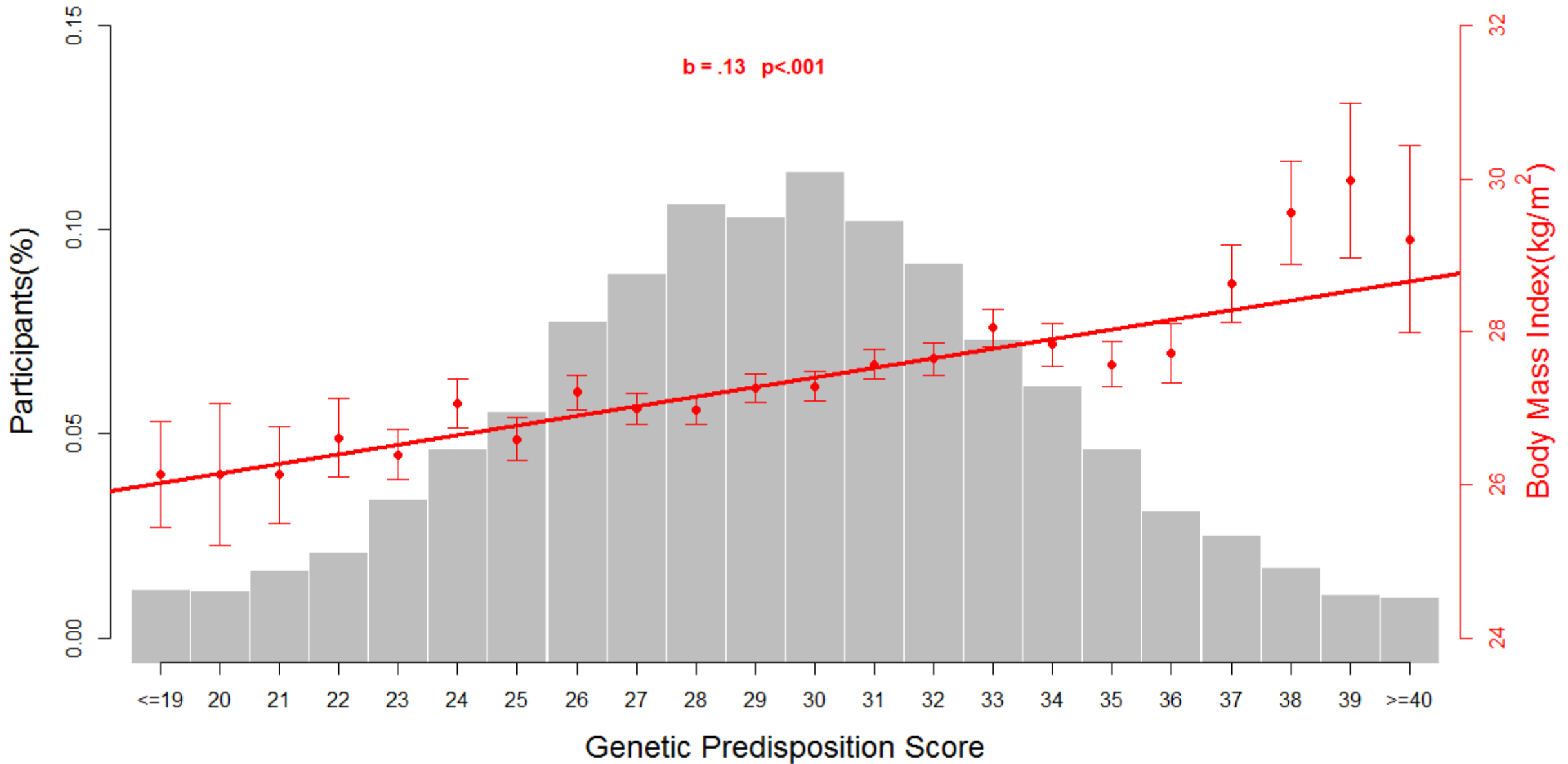
ARTICLES

nature
genetics

Association analyses of 249,796 individuals reveal 18 new loci associated with body mass index

Obesity is globally prevalent and highly heritable, but its underlying genetic factors remain largely elusive. To identify genetic loci for obesity susceptibility, we examined associations between body mass index and ~2.8 million SNPs in up to 123,865 individuals with targeted follow up of 42 SNPs in up to 125,931 additional individuals. We confirmed 14 known obesity susceptibility loci and identified 18 new loci associated with body mass index ($P < 5 \times 10^{-8}$), one of which includes a copy number variant near *GPRC5B*. Some loci (at *MC4R*, *POMC*, *SH2B1* and *BDNF*) map near key hypothalamic regulators of energy balance, and one of these loci is near *GIPR*, an incretin receptor. Furthermore, genes in other newly associated loci may provide new insights into human body weight regulation.

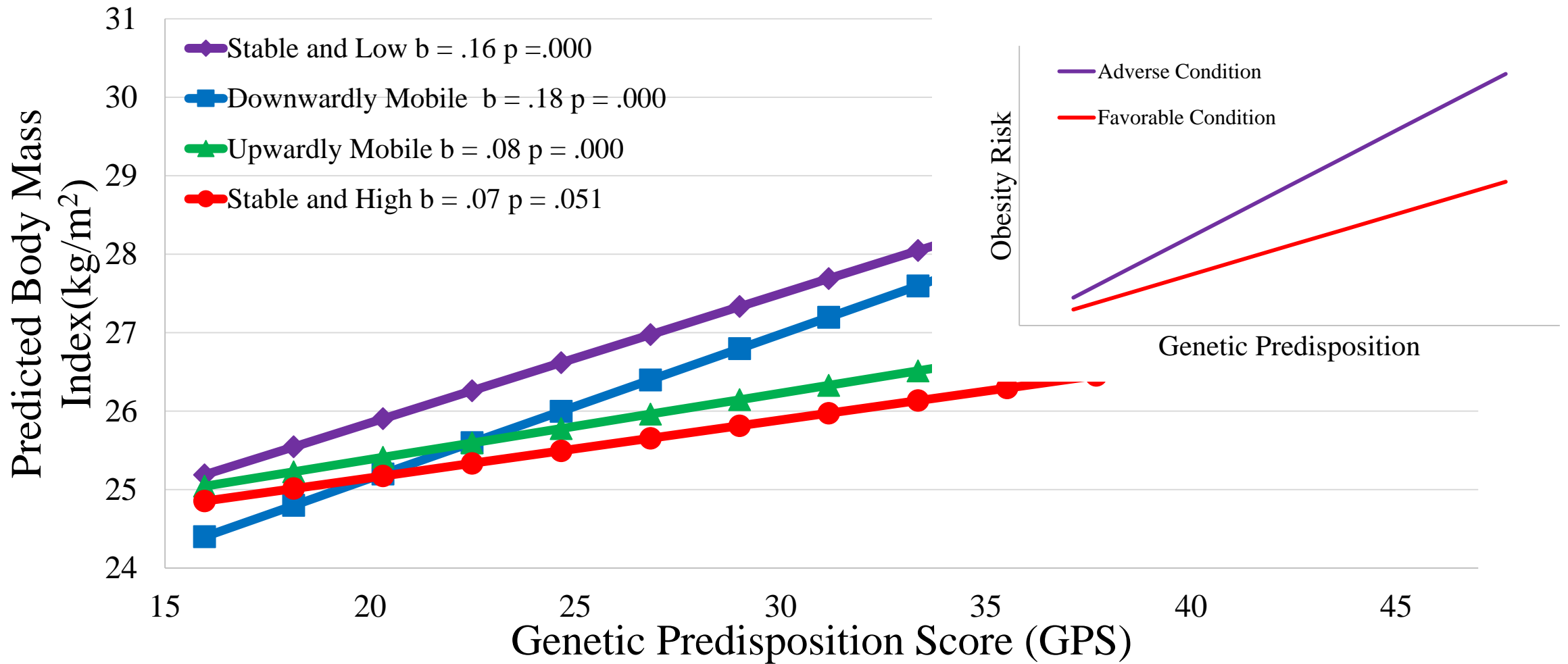
Genetic Predisposition Score and Body Mass Index in the Health and Retirement Study



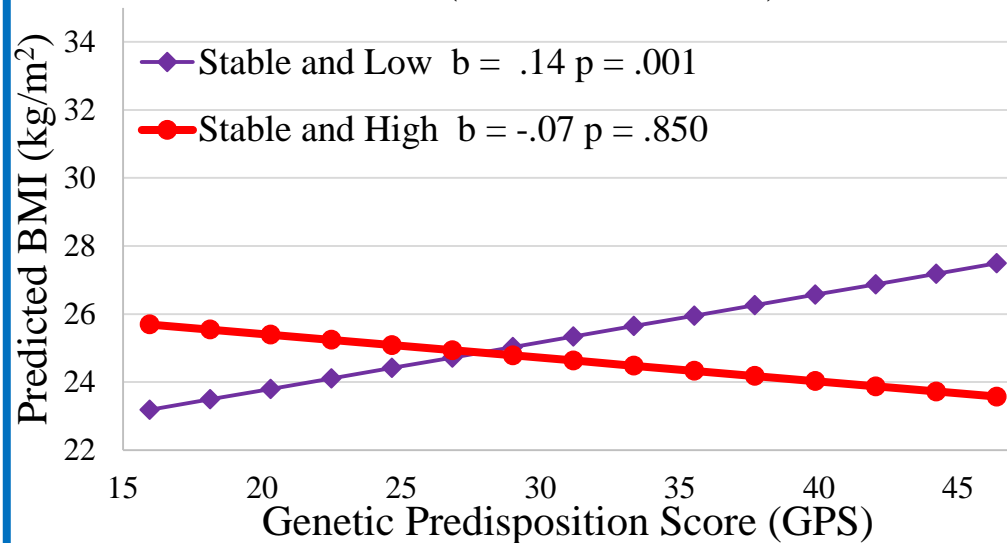
Results

	Moderating Effects of SES on the Genetic Influence
Sensitive Period	$P > .05$
Social Accumulation	$P < .05$
Social Mobility	$P < .05$

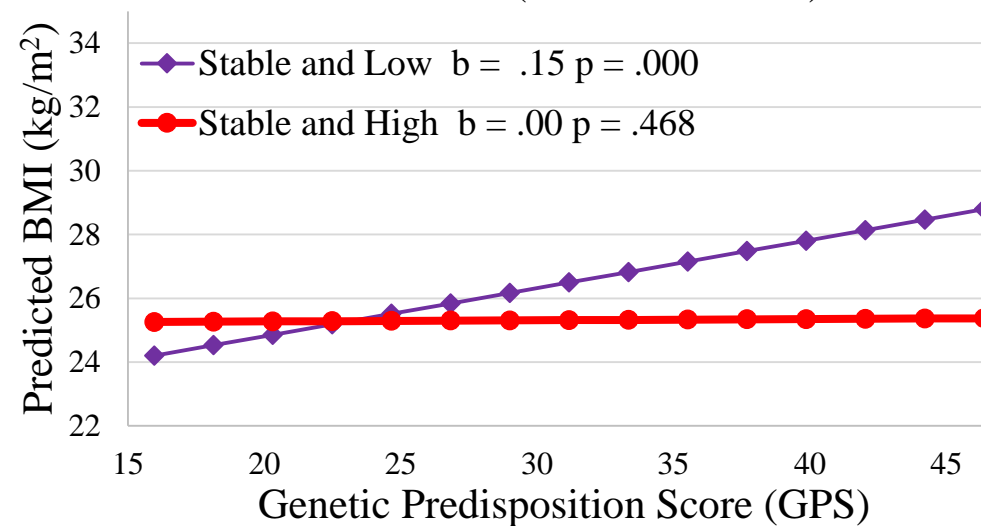
Socioeconomic Differences in The Genetic Association with BMI (Social Mobility)



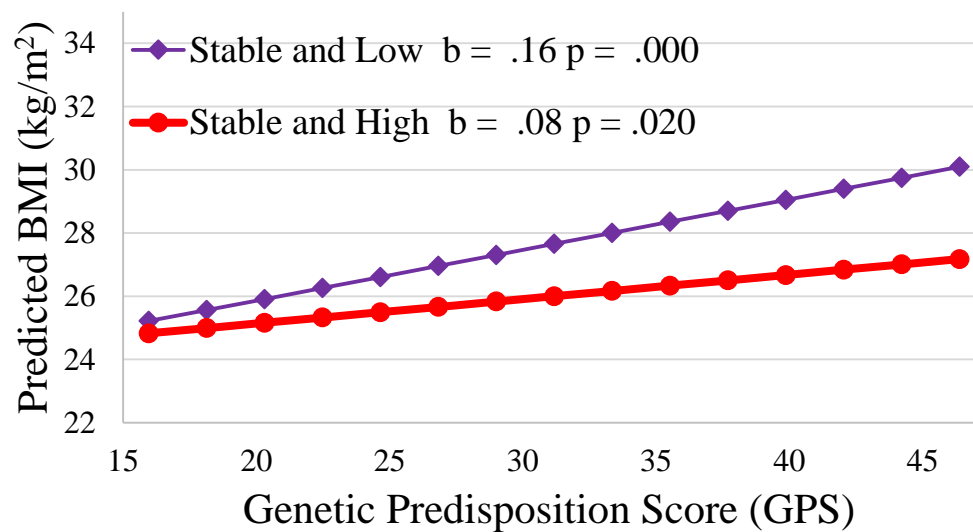
AHEAD (Born Before 1924)



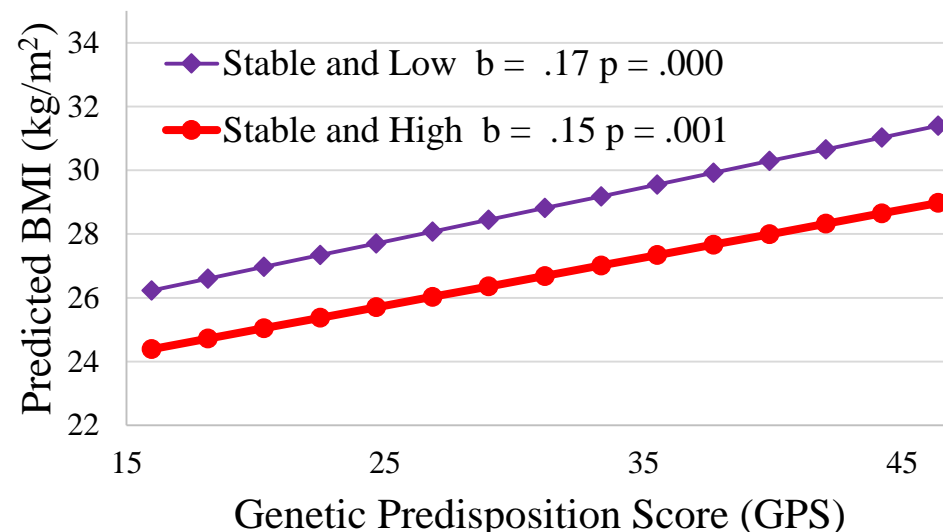
CODA (Born 1924-1930)



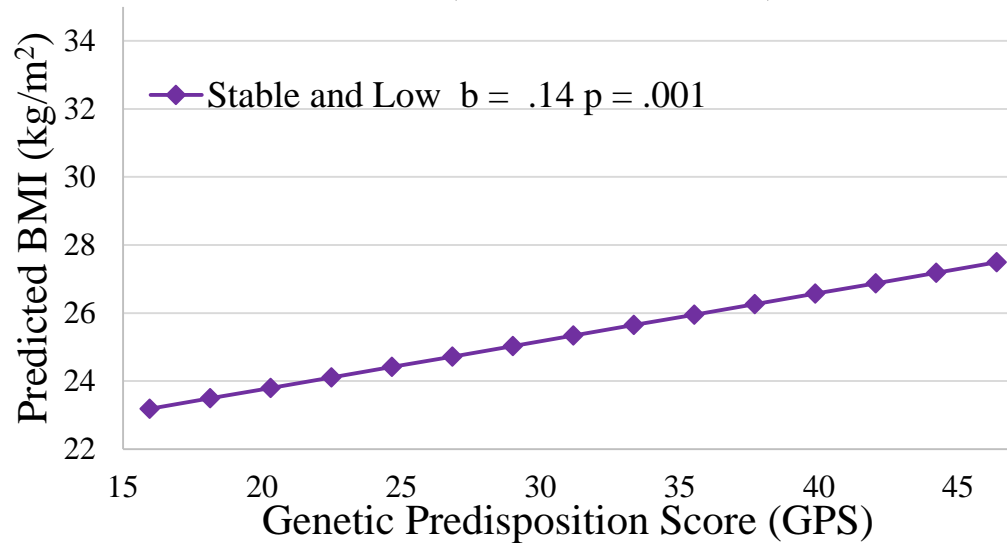
HRS (Born 1931-1941)



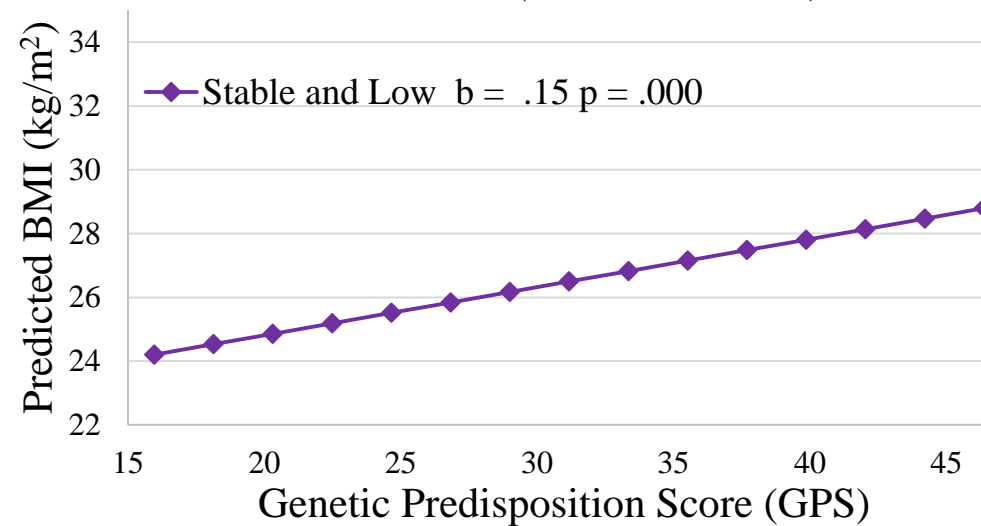
WB (Born 1942-1947)



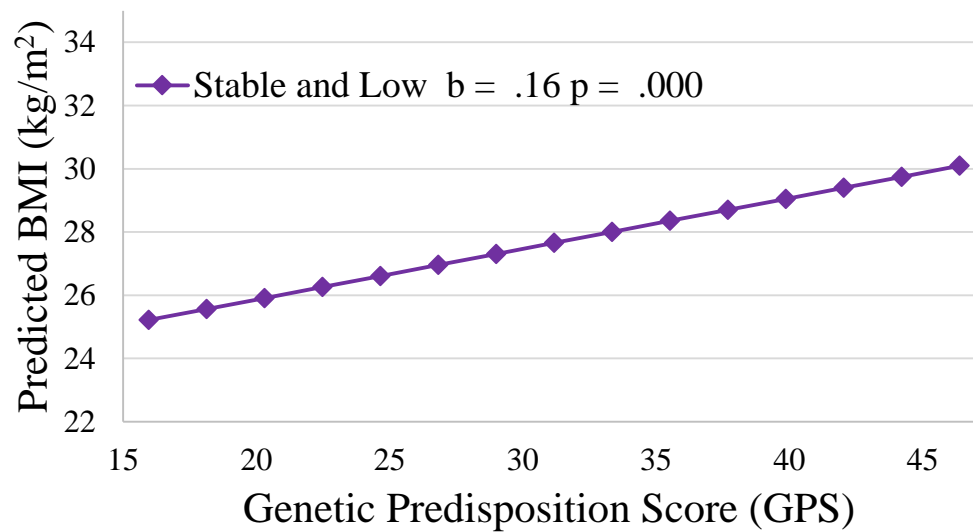
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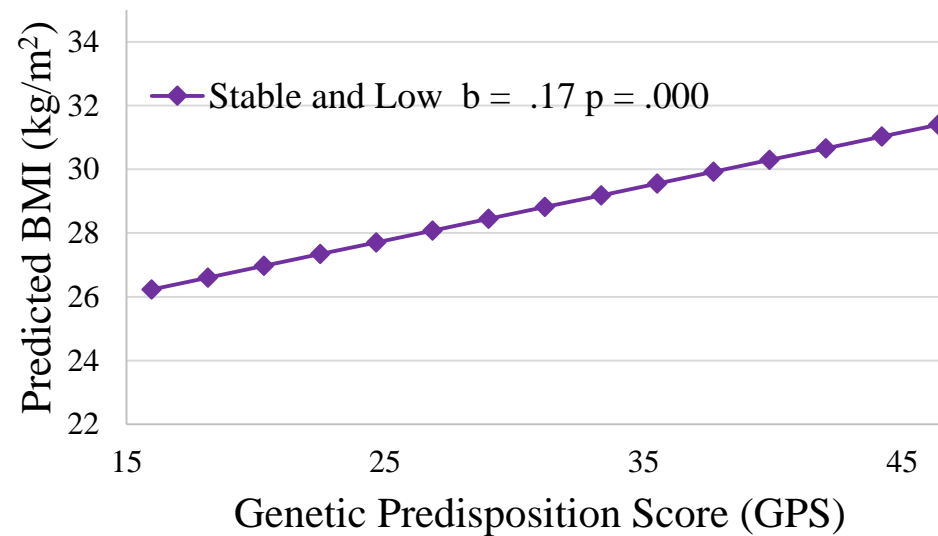
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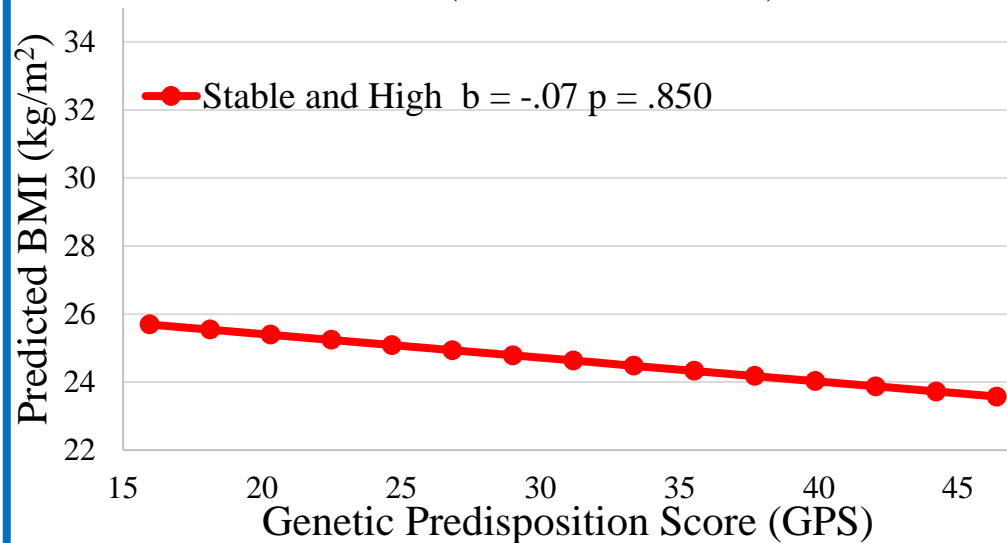
HRS (Born 1931-1941)



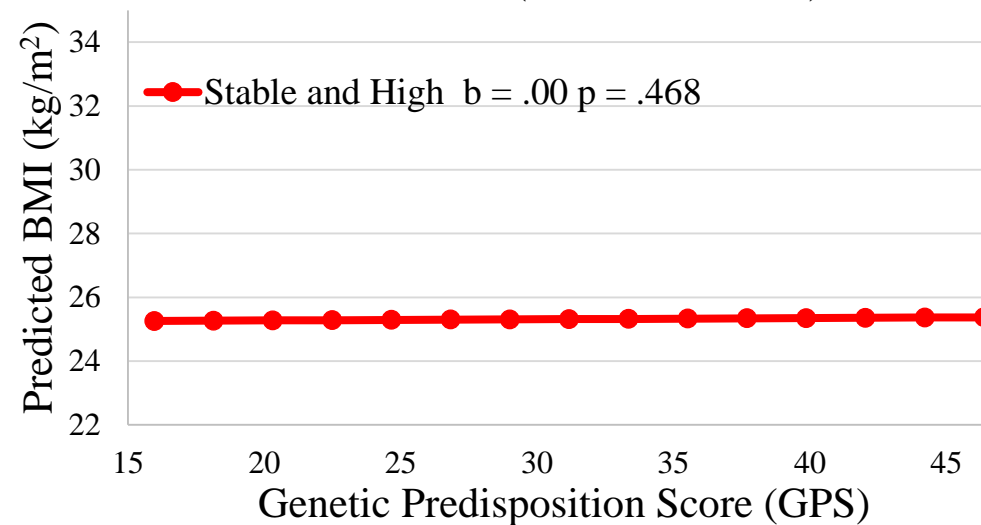
WB (Born 1942-1947)



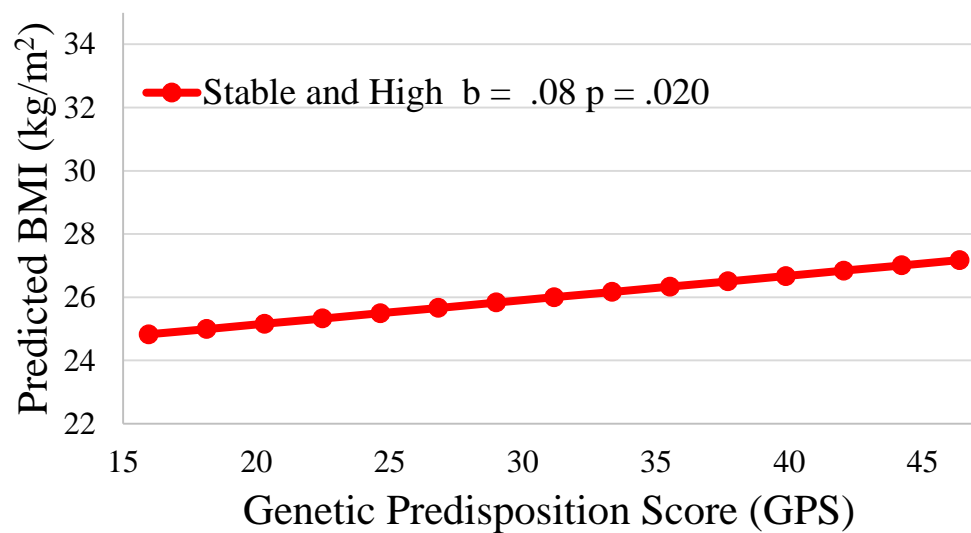
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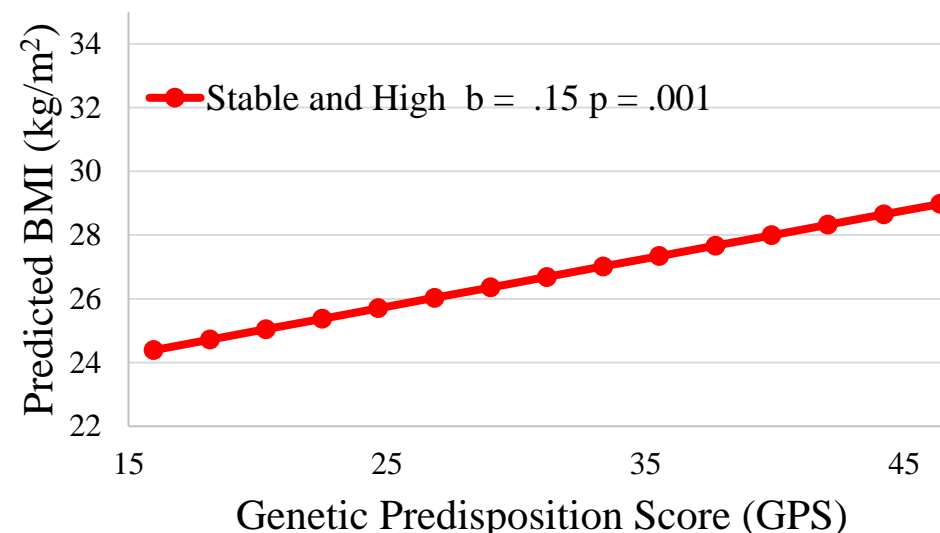
CODA (Born 1924-1930)



HRS (Born 1931-1941)



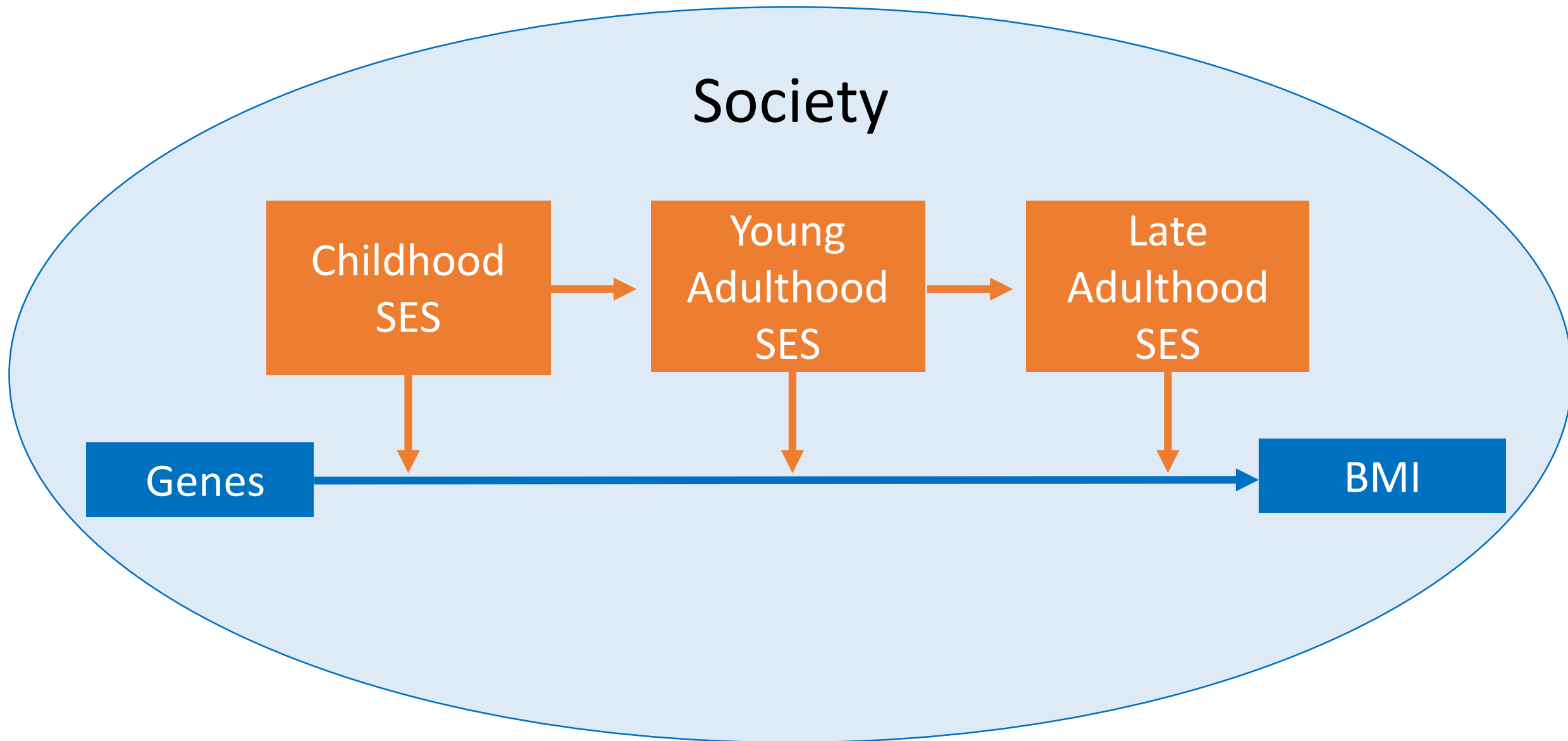
WB (Born 1942-1947)



Main Findings

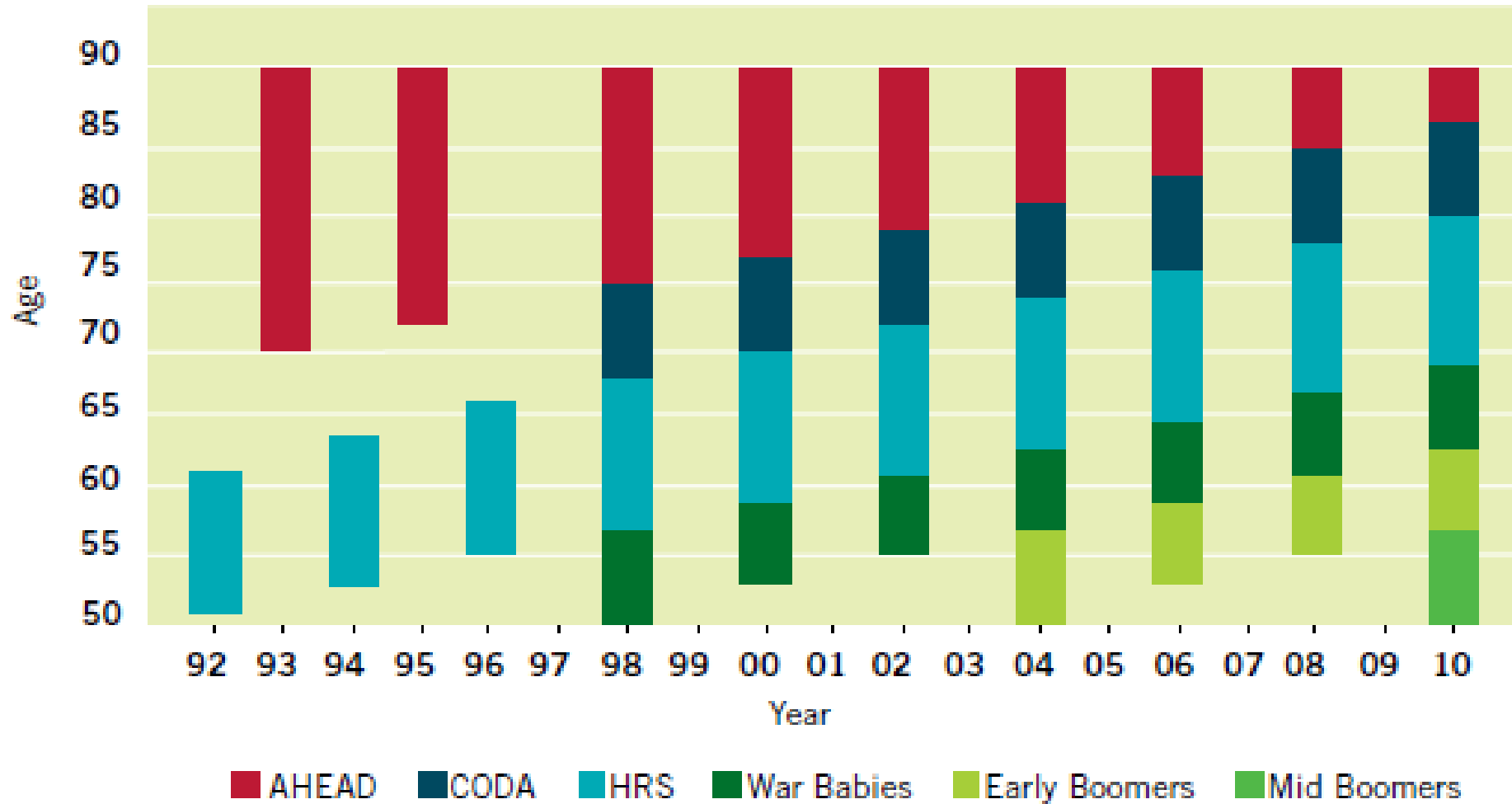
1. The genetic influence on BMI in middle and late adulthood is smaller for socioeconomically advantaged individuals than socioeconomically disadvantaged ones.
2. Compensatory effects of socioeconomic advantages on the genetic influence are less pronounced in more recent birth cohorts than in earlier ones.

Conclusions

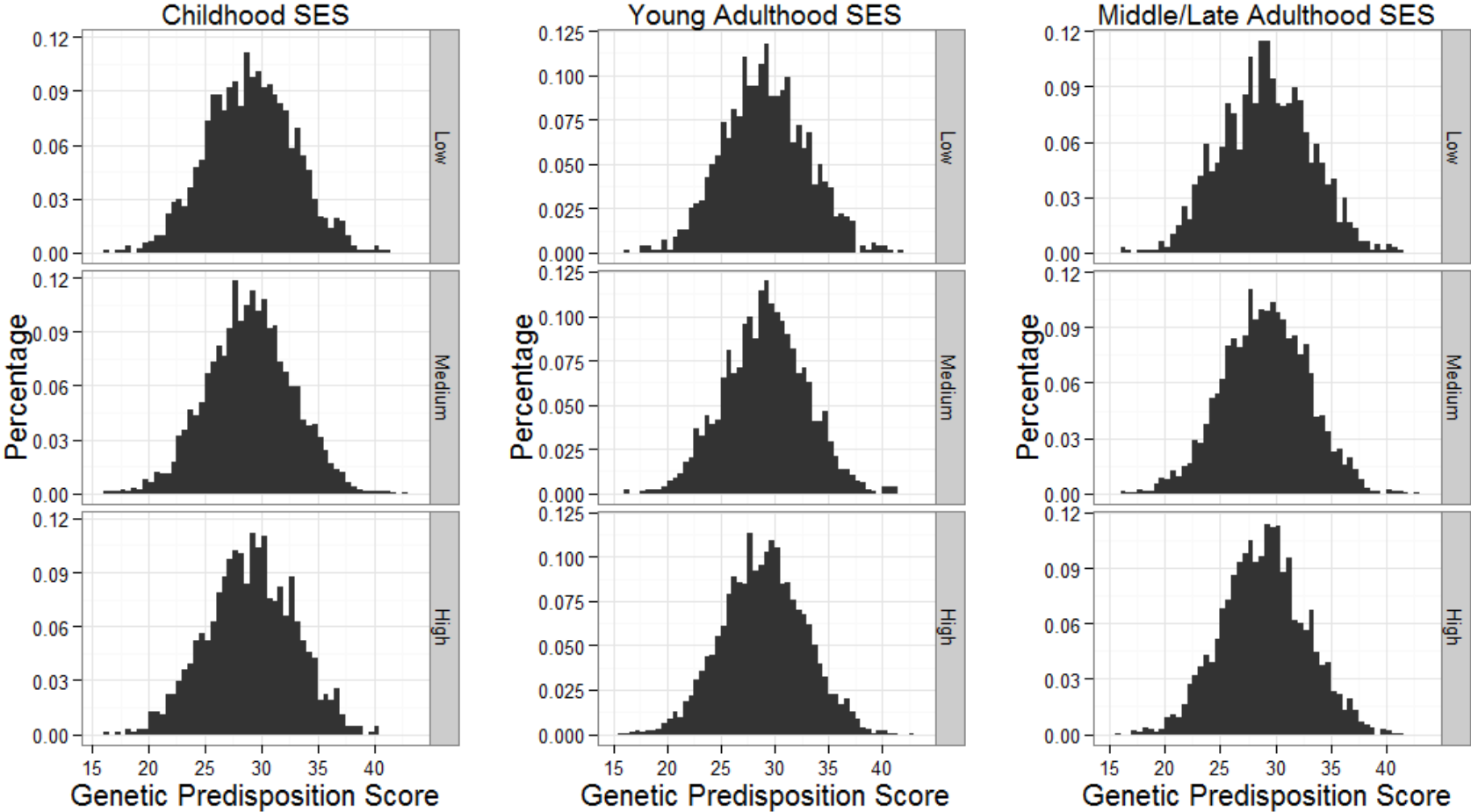


Thank you!

THE HRS LONGITUDINAL SAMPLE DESIGN

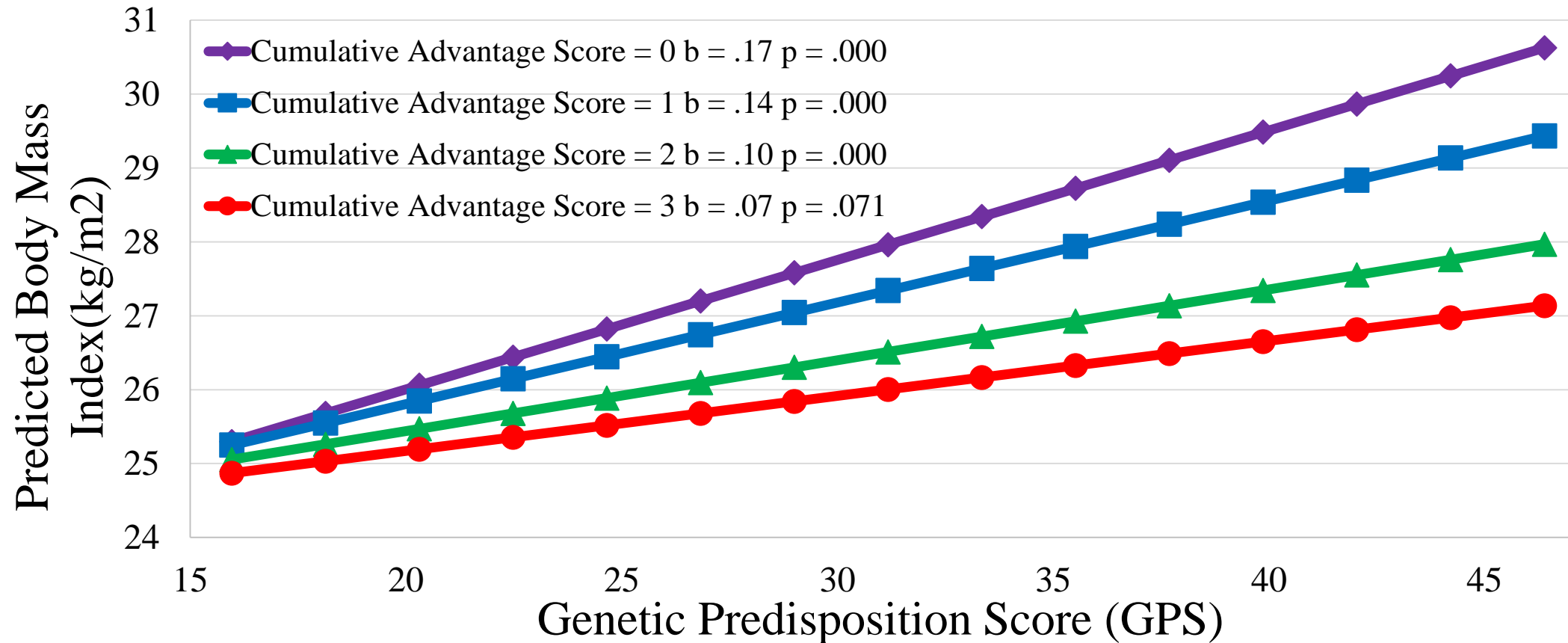


Distribution of the Genetic Predisposition Score by SES

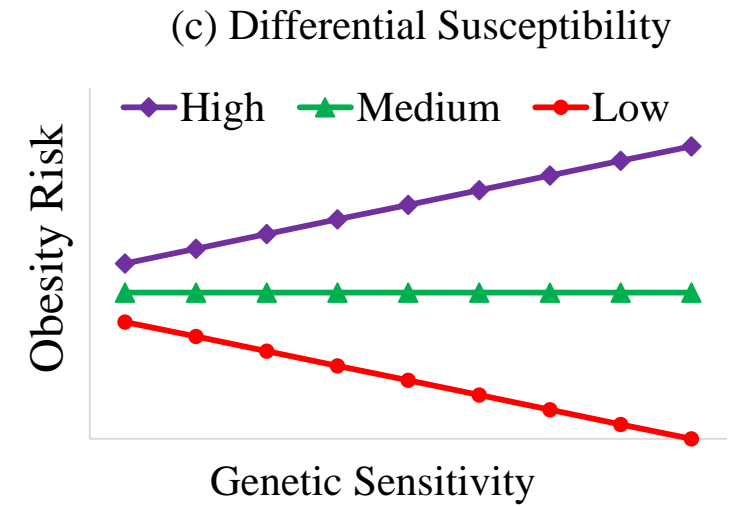
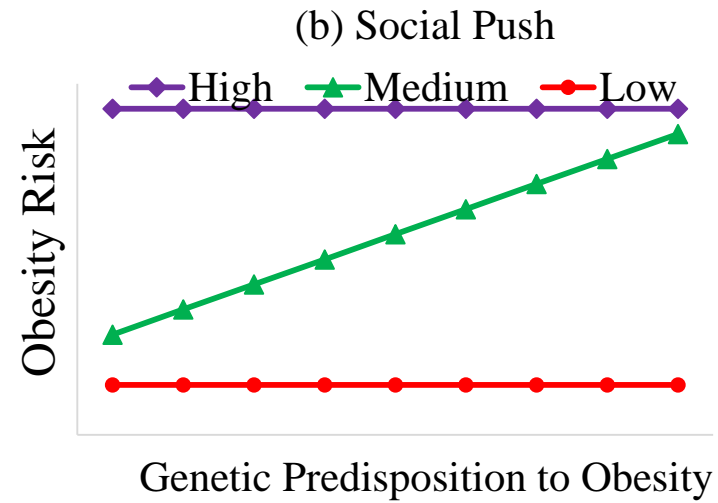
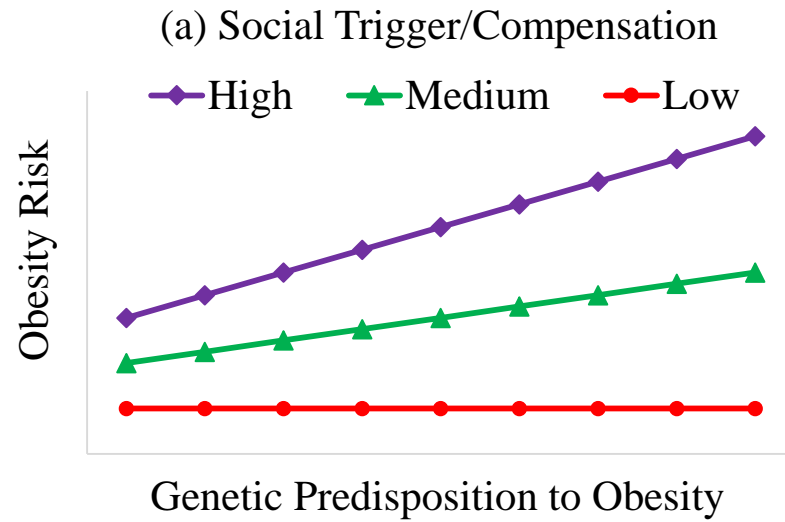


	Sensitive Period		Social Accumulation		Social Mobility	
	Female	Male	Female	Male	Female	Male
Genetic Predisposition Score (GPS)	.13(.05)**	.15(.04)***	.06(.07)	.07(.06)	.06(.07)	.09(.05) [†]
GPS × Childhood SES						
GPS × Low SES	.02(.06)	.01(.06)				
GPS × Medium SES	−.02(.05)	−.01(.05)				
GPS × High SES						
GPS × Cumulative Advantage in SES (CAS)						
GPS × CAS (=0)			.08(.08)	.09(.07)		
GPS × CAS (=1)			.08(.08)	.09(.07)		
GPS × CAS (=2)			.05(.08)	.08(.07)		
GPS × CAS (=3)						
GPS × SES Trajectory						
GPS × Stable and Low					.09(.07)	.08(.06)
GPS × Downwardly Mobile					.13(.09)	.15(.08) [†]
GPS × Upwardly Mobile					.00(.07)	.04(.06)
GPS × Stable and High						
Sample Size	4,325	3,345	4,325	3,345	4,340	3,355

Socioeconomic Differences in The Genetic Association with BMI (Social Accumulation)



Gene-Environment Interaction Models



Statistical Model

- Level 1:

$$\begin{aligned} \text{BMI}_{jit} = & \beta_{0j} + \beta_1 \text{GPS}_{ji} + \beta_2 \text{SES}_{ji} + \beta_3 \text{Cohort}_{ji} \\ & + \beta_4 (\text{GPS}_{ji} \times \text{SES}_{ji}) + \beta_5 (\text{GPS}_{ji} \times \text{Cohort}_{ji}) + \beta_6 (\text{SES}_{ji} \times \text{Cohort}_{ji}) \\ & + \beta_7 (\text{GPS}_{ji} \times \text{SES}_{ji} \times \text{Cohort}_{ji}) + \sum_p \gamma_p C_{pji} + \sum_q \gamma_q C_{qjit} + \varepsilon_{jit}, \end{aligned}$$

- Level 2:

$$\text{cov}(\text{BMI}_{jit_1}, \text{BMI}_{jit_2}) = \sigma^2 \rho^{|t_2 - t_1|},$$

- Level 3:

$$\beta_{0j} = \beta_0 + u_j$$