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Heterogenous trajectories in physical, mental and cognitive health among older Americans: Roles of genetics and life course contextual factors

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ABSTRACT

We investigate the roles of genetic predispositions, childhood SES and adult educational attainment in shaping trajectories for three important components of the overall health of older adults – BMI, depressive symptoms and cognition. We use the Health & Retirement Study (HRS) and group-based trajectory modeling (GBTM) to identify subgroups of people who share the same underlying trajectories ages 51–94 years. After identifying common underlying health trajectories, we use fractional multinomial logit models to estimate associations of (1) polygenic scores for BMI, depression, ever-smoked, education, cognition and subjective wellbeing, (2) childhood SES and (3) educational attainment with the probabilities of trajectory group memberships. While genetic predispositions do play a part in predicting trajectory group memberships, our results highlight the long arm of socioeconomic factors. Educational attainment is the most robust predictor—it predicts increased probabilities of belonging to trajectories with BMI in the normal range, low depressive symptoms and very-high initial cognition. Childhood circumstances are manifested in trajectories to a lesser extent, with childhood SES predicting higher likelihood of being on the low depressive symptoms and very-high initial cognition trajectories. We also find suggestive evidence that associations of educational attainment on the probabilities of being on trajectories with BMI in the normal range, low depressive symptoms and very-high initial cognition vary with genetic predispositions. Our results suggest that policies to increase educational attainment may improve population health by increasing the likelihood of belonging to "good" aging trajectories.

1. Introduction

With an increasing percentage of the world's population "graying", understanding factors affecting health of older adults is of paramount importance. Childhood socioeconomic status (SES) and adult educational attainment are two important factors, as there are striking health disparities at older ages by childhood SES and adult educational attainment. There are several pathways through which these SES-health gradients can arise. Lower childhood SES can directly affect health at older ages through biological imprint processes. For example, lower childhood SES is associated with higher probabilities of being born low birthweight (Finch, 2003; Martinson & Reichman, 2016), which is a marker of inadequate nutrition and in turn is associated with higher risks of hypertension (Falkner, 2002), stroke (Lawlor et al., 2005) and cardiovascular disease (Liang et al., 2021) in adulthood. Children growing up in high SES families are more likely to have better access to health and medical care and live in affluent neighborhoods—with high levels of social capital (e.g., trust in others) and better physical exposures (e.g., green space, clean air)—which are correlated with adult health (Wei et al., 2020; Xue et al., 2020). Low childhood SES could also set in motion adult circumstances that directly affect health. For example, children from high-SES families are likely to attend better schools, where peers may be less likely to engage in risky health behaviors (e.g., smoking) that affect their own health behaviors. In addition to attending higher-quality schools, children from high-SES families are more likely to attain high levels of education, which affects health

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through numerous channels. These include improving one's rank in society, which is associated with better adult health and reduced stress (Rose & Marmot, 1981); increased interactions with other more-educated peers, generating health spillovers (Fletcher, 2010); lower discount rates making individuals more patient and increasing incentives to engage in healthier behaviors (Becker & Mulligan, 1997); increasing productive efficiency to produce more health from given inputs (Grossman, 1972); increasing allocative efficiency through selecting inputs for better health production (Grossman, 1972). Given the multitude of mechanisms through which childhood SES and adult educational attainment can potentially affect health, they are seen by some as fundamental causes of health disparities (Link & Phelan, 1995).

Given the importance of childhood SES and adult educational attainment many studies have sought to understand whether they affect the rate of health decline and thereby affecting the aging process. Theoretically, it is unclear whether childhood SES and adult educational attainment lead to slower declines in health. The cumulative advantage hypothesis (Ross & Wu, 1996) posits that differences in health by SES are established early in life and widen as economic and health disadvantages of low-SES individuals accumulate. The age-as-leveler hypothesis (Beckett, 2000) maintains that SES-health gradients start converging from middle age onward, because health deterioration is an inevitable part of the aging process. The age-as-leveler hypothesis therefore predicts that childhood SES and educational attainment are not associated with health declines, whereas the cumulative disadvantage hypothesis predicts they are associated with an accelerated decline in health.

Empirically, the most common approach is to use growth-curve modeling to estimate health trajectories and determine associations of life course factors with (i) baseline and (ii) rate of change of health. Using this approach, studies have consistently found that lower childhood SES and adult educational attainment are associated with lower baseline levels of health but have reached mixed conclusions regarding health declines. Some studies have found that lower childhood SES and adult educational attainment are associated with accelerated decline in health at older ages (Alley et al., 2007; Hass 2008; Herd, 2006; Lee & Park, 2020; Zaninotto et al., 2018). Some though, have found no associations between childhood SES and adult educational attainment with rates of health decline (Faul et al., 2021; Pavela & Latham, 2016; Torres et al., 2018; Walsemann & Ailshire, 2020; Wu et al., 2020; Zaninotto & Lassale, 2019), while others have found that lower childhood SES and adult educational attainment are associated with a slower decline in health and mortality rates (Aartsen et al., 2019; Zaninotto et al., 2018).[1]

In addition to the mixed results there are two gaps in the literature. First, genetic and SES factors both make substantial contributions to heterogeneity in individuals' health, yet few studies have examined the joint impacts of genetics and SES on the aging process. Two exceptions are Ding et al. (2019) and Kosciuszko et al. (2023). Both studies use growth-curve modeling and measure genetic predisposition with polygenic scores (PGS). Ding et al. (2019) focus on effects of the educational attainment PGS on cognition of older adults in the Health & Retirement Study (HRS) over a 14-year period. Kosciuszko et al. (2023) look at impacts of PGSs for depressive symptoms on mental health of older adults in the English Longitudinal Study of Ageing (ELSA) over a 14-year period. Kosciuszko et al. (2023) found that education and PGSs for depressive symptoms affect the baseline level of mental health but are not associated with the rate of change. Ding et al. (2019) found that a higher education PGS is associated with higher levels of cognitive performance but also faster rates of cognitive decline.[2]

Second, and more importantly growth-curve modeling assumes that all individuals in the population follow a similar trajectory that varies around a single mean trajectory. However, it has long been recognized that there is heterogeneity within aging populations that affects the observed physical health and mortality patterns (Vaupel & Yashin, 1985). Similar arguments pertain to other health dimensions such as cognition and mental health. For instance, Hertzog (2008) remarked that "although there are normative changes across the adult life span at biological, psychological, and social levels, there is also diversity in the expression of age-related changes in structures and mechanisms on cognition." Cognitive aging is therefore likely characterized by qualitatively distinct trajectories of performance across multiple domains of cognition (Casalette et al., 2019). The evidence also suggests that long-term trajectories of depressive symptoms are heterogeneous; for some, depressive symptoms are transient; for others, stable; and for still others, symptoms come and go with varying degrees of frequency (Eaton et al., 2008; Keller et al., 1992; Merikangas et al., 1994; Solomon et al., 1997). Differences in long-term trajectories may be indicative of underlying differences in etiology.

This study addresses these two gaps by using group-based trajectory modeling (GBTM) to understand how genetic dispositions (measured with PGSs), childhood SES, adult educational attainment, and their interactions,—shape trajectory membership for three important components of overall health—physical health (body mass index, BMI), mental health (depressive symptoms) and cognition—for older adults of European and African-Ancestry over ages 51–94 years in the HRS.[3] In contrast to growth-curve modeling, GBTM does not assume that one trajectory fits all. Instead, GBTM assumes that the population is composed of a mixture of distinct groups of individuals defined by their developmental trajectories. It identifies groups of individuals following distinct trajectories over time and estimates trajectory parameters (e.g., shape of trajectory and probability of membership in a group) separately for each group (Nagin & Nagin, 2005). In addition to identifying trajectories, GBTM can be used to identify predictors associated with different trajectories.[4] Since physical, mental and cognitive health are associated with mortality, we use an enhanced version of the basic GBTM model which allows for the joint estimation of trajectories and probabilities of attrition through mortality within each trajectory group (Haviland et al., 2011). After identification of trajectories, we employ fractional multinomial-logit models to estimate associations of PGSs, childhood SES, adult education and their interactions with the *probability* on being on each particular trajectory. We examine interactions of SES with genetics, because the diathesis-stress model (Ellis et al., 2011) holds that unhealthy environments (low SES in our context) trigger risk alleles, while healthy environments (high SES) protect against risk alleles. For example, a college graduate with a high genetic risk of depression is less likely to be on a high-depressive symptoms trajectory compared to a high-school dropout with a high genetic risk of depression. This is because being a college graduate is associated with a higher income, leading a healthier lifestyle, interacting more with other

[1] Zaninotto et al. (2018) use growth curve modeling to examine determinants of cognition trajectories over a 8-year period in the English Longitudinal Study of Ageing. They found conflicting evidence between SES and the rate of cognitive decline. Specifically, low education was related to a faster decline in memory for men, whereas low childhood SES was related to a slower decline in global function for men and women.

[2] Ding et al. (2019) examined four cognition domains—global cognition, episodic memory, attention and concentration; mental status. The education PGS was associated with accelerated declines in global cognition and episodic memory.

[3] We conduct our analysis separately for European-Ancestry and African-Ancestry individuals because the predictive power of PGSs substantially differs for these two groups. We do not look at Hispanic individuals as we do not have genetic data for this group. More details are provided in section 2.

[4] Though GBTM address heterogeneity in aging, we cannot use GBTM to understand how genetics, childhood SES and adult education affect the rate of health decline within groups, since it assumes that there is no variation between individuals within the same trajectory group. GBTM can be informative about how genetics, childhood SES and adult education affect the rate of health decline between groups if trajectories differ in rates of health decline.

healthy peers, having better health knowledge, whereas high-school dropouts are more likely to experience financial stress due to having low incomes or being unemployed, lead unhealthy lifestyles, have limited access to healthcare and interact more frequently with other depressed peers. Some recent studies have found empirical evidence of interactions between genetic background and childhood SES/education.[5]

We are not the first study to employ GBTM to address heterogeneity in aging. GBTM has been used to identify trajectories for BMI (Østbye et al., 2011; Song et al., 2016; Song et al., 2018; Zheng et al., 2013; Zheng et al. 2017), mental health (Andreescu et al., 2008; Liang et al., 2011; Xiang, 2020) and cognition (Elovainio et al., 2018; Howrey et al., 2020; Olaya et al., 2017). However, to our best knowledge this is the first study to employ GBTM and examine how genetics, childhood SES, adult educational attainment and their interactions predict trajectories of health across a 40-year time period in late-middle to old age. We hypothesize that (1) higher genetic predisposition toward higher BMI (higher levels of depression) will be associated with a higher likelihood of belonging to worse BMI (depressive symptom) trajectories; (2) higher genetic predisposition toward higher cognition will be associated with a higher likelihood of belonging to better cognition trajectories; (3) higher childhood SES and adult education attainment will be associated with higher probabilities of belonging to better health trajectories and (4) associations of childhood SES and adult education attainment with trajectory group membership will vary be genetic predisposition.

2. Data

2.1. Study population

The HRS is a nationally representative longitudinal survey of more than 37,000 individuals in 23,000 households over age 50 in the US. The HRS started in 1992 and data are collected every two years. The initial HRS cohort consisted of persons born in 1931–41 (then aged 51–61) and their spouses of any age. A second study, Asset and Health Dynamics Among the Oldest (AHEAD), was fielded the next year to capture an older birth cohort, those born in 1890–1923. In 1998, the two studies were merged, and, in order to make the sample fully representative of the older US population, two new cohorts were enrolled, the Children of the Depression (CODA), born in 1924–1930, and the War Babies, born in 1942–1947. The HRS now employs a steady-state design, replenishing the sample every six years with younger cohorts to continue making it fully representative of the population over age 50 (Fisher & Ryan, 2018). Given the focus on long-term health trajectories, we restrict our analysis to the initial HRS, AHEAD cohorts (followed from 1992 to 2018) and the CODA cohort (followed from 1998 to 2018), in which individuals are observed from age 51–94 years.[6]

2.2. Outcome measures

Outcomes of interest in this analysis are taken from the RAND HRS (version V1) which is a cleaned and streamlined version of the HRS. BMI is calculated as weight kg/height m^2 and is based on self-reported height and weight. Mental health is measured using an eight-item Center for Epidemiologic Studies (CES-D) score based on the following questions with "yes/no" response options: much of the time during the last week: (1) I felt depressed; (2) everything I did was an effort; (3) my sleep was restless; (4) I felt lonely; (5) I felt sad; (6) I felt happy; (7) I enjoyed life, and (8) I could not get going. The total number of "yes" responses (with inverse values for 6 and 7) are summed to calculate the CES-D score. Individuals with a CES-D score of 4 or more are classified as being depressed (Steffick, 2000). The RAND HRS total cognition score sums scores from 10-word immediate and delayed recall tests of memory, a serial 7s subtraction test of working memory, counting backwards to assess attention and processing speed, an object-naming test to assess language, and recall of the date and president and vice-president to assess orientation. The cognition score ranges from 0 to 35.

2.3. SES measures

We use the childhood SES index created by Vable, Gilsanz, Nguyen, Kawachi, and Glymour (2017), which is publicly available for researchers utilizing HRS data. The childhood SES index reflects measures of childhood social, financial and human capital when respondents were younger than 16 years, using retrospective reports. Social capital is measured through the following four questions related to maternal investments and family structure: (1) how much effort did your mother put into watching over you and making sure you had a good upbringing? (2) how much did your mother teach you about life?, (3) how much time and attention did your mother give you when needed?, and (4) number of parent figures. Childhood financial capital is captured by the following eight questions: (1) family moved for financial reasons, (2) received financial help from relatives, (3) family declared bankruptcy, (4) family lost business, (5) self-reported childhood SES, (6) father's occupation, (7) father was unemployed for several months and (8) mother worked outside the home. Relevant human capital for childhood is measured with the mother's and the father's years of education. We operationalize adult SES through the respondents' years of education.

2.4. Genetic measures

We use polygenic scores (PGSs) to measure genetic propensities. PGSs are summary measures of an individual's genetic predisposition for a given trait and are constructed using results from Genome Wide Association Studies (GWAS). In a GWAS, hundreds of thousands to millions of single nucleotide polymorphisms (SNPs) are tested for associations with an outcome. As an example, Lee et al. (2018) conducted a GWAS on a sample of 1.1 million individuals and identified 1271 SNPs as genome-wide significant predictors ($p < 5 \times 10^{-8}$), of educational attainment. The PGS for individual i (equation (1)) is a weighted sum across the number of SNPs (n) of the number of reference alleles A (0, 1 or 2) at that SNP.

$$PGS_i = \sum_{j=1}^{n} \beta_j A_{ij} \quad (1)$$

GWAS used to construct PGSs are largely based on European ancestry (EA) groups, which means that PGSs for other ancestry groups may not have the same predictive power (Martin et al., 2017).[7] Lee et al. (2018) found that the educational attainment PGS explains 10.6% of the variation in education of EA populations, whereas it only explains only 1.6% of the variance in education in the HRS sample of African-Ancestry (AA). We therefore conduct our analysis for EA and AA individuals separately.

HRS collection of genetic data started in 2006. Genotype data on

[5] Using the Wisconsin Longitudinal Study, Moorman et al., (2018) find that higher childhood SES protected against the effect of the APOE4 gene for the memory domain of cognition. Fletcher et al. (2021) find that the effect of education on cognition in midlife is smaller for individuals with a higher PGS for Alzheimer's disease in the UK Biobank. Barcellos et al. (2018) find that education effects on body size in the UK Biobank are larger for those with a higher BMI PGS.

[6] The War Baby (born 1942–47), Early Baby Boomer (born 1948–1953) and Mid Baby Boomer (born 1954–1959) cohorts are excluded from the analysis in order to analyze long-term trajectories of more than 20 years.

[7] We stress that genetic ancestry and race/ethnicity are two different constructs. Genetic ancestry refers to the genetic origin of one's population, whereas race/ethnicity are self or socially ascribed identities on the basis of physical characteristics.

over 19,000 HRS participants were obtained using the llumina HumanOmni2.5 BeadChips. The HRS research team has constructed PGSs for a range of traits, using all SNPs in the relevant GWAS that overlap with the HRS genetic database. Specific details of PGS construction in HRS can be found in Ware et al. (2018). The PGSs (and underlying GWAS studies used in the construction) that we use are: (1) BMI (Locke et al., 2015), (2) depressive symptoms (Okbay et al., 2016; Ripke et al., 2013), (3) subjective wellbeing (Okbay et al., 2016), (4) ever/current smoker (Furberg et al., 2010), (5) educational attainment (Okbay et al., 2016), and (6) cognition (Davies et al., 2015).

2.5. Analytical sample

The HRS provides publicly available constructed PGSs for 12,090 EA individuals and 3100 African genetic-ancestry (AA) individuals. The HRS has not constructed PGSs for Hispanics. We merge the PGS datasets with the RAND HRS dataset. There are 7369 EA and 1192 AA individuals from the HRS, AHEAD and CODA cohorts with genetic data. After dropping individuals with missing data, the final estimation sample consists of 7357 EA and 1189 AA individuals. There are 10 observations on average per individual and a total of 75,776 person-year observations in the EA sample. The AA sample has 13 observations on average per individual and a total of 15,047 person-year observations.

2.6. Attrition

Attrition in the HRS is primarily due to mortality. Appendix figure A1 shows the cumulative dropout rate due to mortality by age in our analytical samples. Our analytic design, which we describe in the next section, explicitly accounts for death among respondents.

3. Analytical strategy

3.1. Group-based trajectory modeling (GBTM)

GBTM is a specialized application of finite mixture-modeling. The aim is to identify groups of individuals with statistically similar developmental patterns or trajectories. We use an extension of the GBTM model that takes into account nonrandom attrition due to mortality (other non-response or attrition is considered as missing-at-random). In the basic GBTM model, let $Y_i = \{y_{i1}, y_{i2}, .., y_{iT}\}$ represent the longitudinal sequence of outcomes and $Age_i = \{age_{i1}, age_{i2}, .., age_{iT}\}$ represent individual i's ages in period $t = \{1,..,T\}$. The distribution of the outcome trajectory is denoted by $P(Y_i|Age_i)$. GBTM assumes that there are J underlying trajectory groups. The likelihood for each individual i conditional on the number of groups J is given by equation (2), where π_j is the probability of membership in group j and $P(Y_i|Age_i, j)$ is the likelihood function conditional on trajectory j.

$$P(Y_i|Age_i) = \sum_{j=1}^{J} \pi_j . P(Y_i|Age_i, j) \tag{2}$$

The model assumes that the random variables y_{it} are independent conditional on membership in group j. The likelihood conditional on trajectory j can thus be written as,

$$P(Y_i|Age_i, j) = \prod_{t=1}^{T} p(y_{it}|\, age_{it}, j) \tag{3}$$

where p(.) is the probability distribution of y_{it} conditional on membership in group j and the age of individual i at time t. We use the normal distribution to estimate trajectories for BMI and cognition whereas for depressive symptoms we use the Poisson distribution to model count data. Trajectories are modeled as a polynomial function of age. In the quadratic case, the link between outcomes and ages is:

$$y_{it} = \beta_0^j + \beta_1^j age_{it} + \beta_2^j age_{it}^2 + u_{it} \tag{4}$$

where $\beta_0^j, \beta_1^j, \beta_2^j$ are parameters that determine the level and shape of trajectory j and u_{it} is an error term with variance σ_j^2 that is allowed to vary by trajectory. In practice, we consider quadratic and cubic functions in age. The basic model provides a predicted shape for each trajectory, an estimated proportion of the sample at baseline that most likely belong to each trajectory, and for each individual the estimated probabilities of belonging to each trajectory (posterior probabilities of group membership).[8]

The basic model assumes that trajectory group membership is independent of attrition. Haviland et al. (2011) have extended the basic model to allow for differential non-random dropout by trajectory group as a function of observed outcomes prior to dropout and of covariates.

Denote by τ_i the period $t > 1$ when individual i drops out and $\Theta_{\tau_i}^j$ the probability of dropout in period τ_i given membership in group j. With probability $(1 - \Theta_t^j)$, the individual has not dropped out in period $t < \tau_i$. Equation (3) must then be adjusted by multiplying the probability of the observed outcome with the probability of not dropping out up to period τ_i. From period τ_i onwards, the individual has dropped out and outcomes are censored. Thus, we must multiply by the probability of dropout at τ_i, $\Theta_{\tau_i}^j$:

$$P(Y_i|Age_i, j) = \left[\prod_{t=1}^{\tau_i - 1} p(y_{it}|w_{it} = 0, age_{it}, j)\left(1 - \Theta_t^j\right)\right] \Theta_{\tau_i}^j \tag{5}$$

Equation (5) is substituted into equation (2) to form the unconditional likelihood for individual i which is to be maximized. The model allows the dropout probability Θ_t^j to vary by trajectory and within trajectory groups across time, as well as specifying Θ_t^j as a function of covariates. We model the dropout probability as a binary logistic function of the outcome prior to dropout and gender.

Inferences about the optimal number and shape of trajectories are made using the combination of criteria laid out in Nagin and Nagin (2005): (i) the Bayesian information criterion (BIC), with lower absolute values indicating a better fit; (ii) the log Bayes factor ($\approx 2\Delta$BIC) > 10 indicating strong evidence in favor of the larger model; (iii) trajectory group size $\geq$5% of the sample; (iv) close correspondence between estimated group membership probability and the proportion of individuals assigned to each trajectory based on the maximum posterior probability rule[9]; (v) average posterior probability (AvePP) > 0.70; (vi) the odds of correct classification (OCC) > 5 for all groups. The GBTM analysis was conducted using the traj command in Stata version 15.

3.2. Trajectory group-membership prediction

Following the GBTM analyses, we compute for each individual i the posterior probabilities of belonging to each of the J trajectories where the probabilities sum to one. Most prior studies assigned individuals to a single trajectory according to the maximum posterior probability rule and conduct multinomial logit regressions of group membership. We depart from this approach because individuals have different propensities of belonging to each of the trajectories, and existing studies ignore the information contained in posterior probabilities for the non-assigned trajectories. Our approach does not ignore this information and

[8] GBTM provides the probability of group membership (π_j) and $P(j|Y_i)$. The posterior probability $P(j|Y_i)$ is calculated using Bayes theorem: $P(j|Y_i) = \frac{P(Y_i|j)\pi_j}{\sum_j^J P(Y_i|j)\pi_j}$.

[9] We first obtain the posterior probability P(j |Y_i) of belonging to trajectory j using the estimates and Bayes' rule. Individual i is then assigned to trajectory j if P(j |Y_i) is the largest among all posterior probabilities.

Table 1
Summary statistics.

	European-Ancestry Sample				African-Ancestry Sample			
	Mean	SD	Min	Max	Mean	SD	Min	Max
Male	0.41	0.49	0.00	1.00	0.35	0.48	0.00	1.00
Year of Birth	1933	8.41	1905	1979	1935	8.66	1906	1969
HRS/AHEAD Overlap	0.00	0.07	0.00	1.00	0.00	0.04	0.00	1.00
AHEAD	0.17	0.37	0.00	1.00	0.12	0.32	0.00	1.00
CODA	0.14	0.35	0.00	1.00	0.08	0.27	0.00	1.00
HRS	0.70	0.46	0.00	1.00	0.80	0.40	0.00	1.00
Years of education	12.87	2.59	0.00	17.00	11.17	3.31	0.00	17.00
High school dropout	0.16	0.37	0.00	1.00	0.41	0.49	0.00	1.00
High school graduate	0.36	0.48	0.00	1.00	0.28	0.45	0.00	1.00
Some college education	0.22	0.41	0.00	1.00	0.16	0.37	0.00	1.00
College graduate	0.21	0.41	0.00	1.00	0.10	0.30	0.00	1.00
Childhood SES	0.17	0.86	−3.32	2.81	−0.26	0.83	−2.84	1.98
BMI Baseline	26.63	4.68	15.30	60.50	29.08	5.96	15.00	102.70
CES-D Baseline	0.99	1.63	0.00	8.00	1.67	2.08	0.00	8.00
Cognition Baseline	24.53	4.07	5.00	35.00	20.69	5.37	3.00	35.00

Notes: SD: Standard Deviation. Health at baseline refers to health at first observation.

models the complete set of GBTM posterior probabilities.[10] A suitable model must reflect the bounded nature of the posterior probabilities and the fact that they sum to one. We therefore use the fractional multinomial logit (FML) model, which is an extension of the multinomial logit to consider cases where the dependent variable is fractions that sum to one (Mullahy, 2015).[11] In the FML model, the specification linking covariates (x_i) to the posterior probability for individual i of belonging to group j (p_{ij}) for $j = 1, \ldots J$ is given by:

$$E[p_{ij}|x_i] = \frac{exp\ (x_i\beta_j)}{\sum_{j=1}^{J} exp\ (x_i\beta_j)} \tag{6}$$

where $p_{ij} \in [0,1]$ and $\sum_{j=1}^{J} p_{ij} = 1$.

As covariates we include a dummy variable for being male, the PGSs, the childhood SES index, years of education, cohort dummies and the first 10 genetic principal components. The principal components are used to control for population stratification—a situation where there are systemic differences in the allele frequencies among subgroups of the population.

Identification of the parameters requires some normalization—usually setting the coefficients of the first equation to zero ($\beta_1 = 0$). The conditional expectations for all equations are:

$$E[p_{ij}|x_i] = \frac{1}{1 + \sum_{j=2}^{J} exp(x_i\beta_j)} \quad for\ j = 1 \tag{7}$$

and

$$E[p_{ij}|x_i] = \frac{exp\ (x_i\beta_j)}{1 + \sum_{j=2}^{J} exp\ (x_i\beta_j)} \quad for\ j = 2, \ldots J$$

By using FML we are able to estimate associations of PGSs and SES with the probability of belonging to each trajectory group. To ease interpretation of the estimates, we report marginal effects evaluated at the means in the empirical analysis. The marginal effects sum to zero across the outcomes.

4. Results

4.1. Summary statistics

Summary statistics are shown in Table 1.[12] The majority of the analytical sample represents the HRS cohort (70% for EA and 80% for AA), while much smaller fractions of the sample are based on the CODA and AHEAD cohorts. The proportion of males is slightly higher in the EA sample (41%) than in the AA sample (35%). Childhood SES and adult educational attainment are lower on average in the AA sample than in the EA sample. Average health at first measurement is also higher in the EA sample compared to the AA sample. For example, the average cognition score at first measurement is 24.53 in the EA sample and 20.69 in the AA sample.

4.2. BMI trajectories

Trajectories for BMI are shown in Fig. 1. We determined the optimal number of trajectories for both the EA and AA samples to be 6 with a quadratic in age. This model had the lowest absolute BIC and met the other criteria with (i) trajectory group size ≥5% of the sample; (ii) close correspondence between estimated group membership probability and the proportion of individuals assigned to each trajectory based on the maximum posterior probability rule; (iii) average posterior probability >0.70 and (iv) the odds of correct classification >5. Model fit statistics are shown in appendix tables A2 and A3.

For both groups a small proportion—8% for the EA sample and 7% for the AA sample— are on the very-high trajectory. In the EA sample this trajectory indicates obese class 2 (35 ≤ BMI≤39.9) over ages 51–70 after which BMI declines. In the AA sample, the very-high trajectory indicates obese class 3 (BMI≥40) over almost the entire age range. The

[10] For instance, consider a hypothetical GBTM estimate that provides a posterior probability for trajectory A of 51%, and for trajectory B of 49%. Prior studies assigned this individual to trajectory A based on the maximum posterior probability. By modeling the complete set of GBTM posterior probabilities (i.e., $p_A = .51$ and $p_B = .49$), our approach utilizes the full information revealed by the GBTM model and thus reflects the fact that the assignment to group A or B is uncertain for this individual based on the GBTM results.

[11] It is possible to estimate trajectories and the predictors of trajectory group membership in one step using the extension described in Roeder et al. (1999). We however take a sequential two-step approach to take account of spouses in the HRS by clustering the standard errors at the household level in FML regressions. To our best knowledge, the Stata Traj package does not allow for the clustering of standard errors when jointly estimating trajectories and predictors of trajectory group membership.

[12] Table 1 does not provide summary statistics for the PGSs because the PGSs are already standardized with mean 0 and standard deviation of 1 by the HRS. After arriving at our analytical samples, we re-standardize the PGSs.

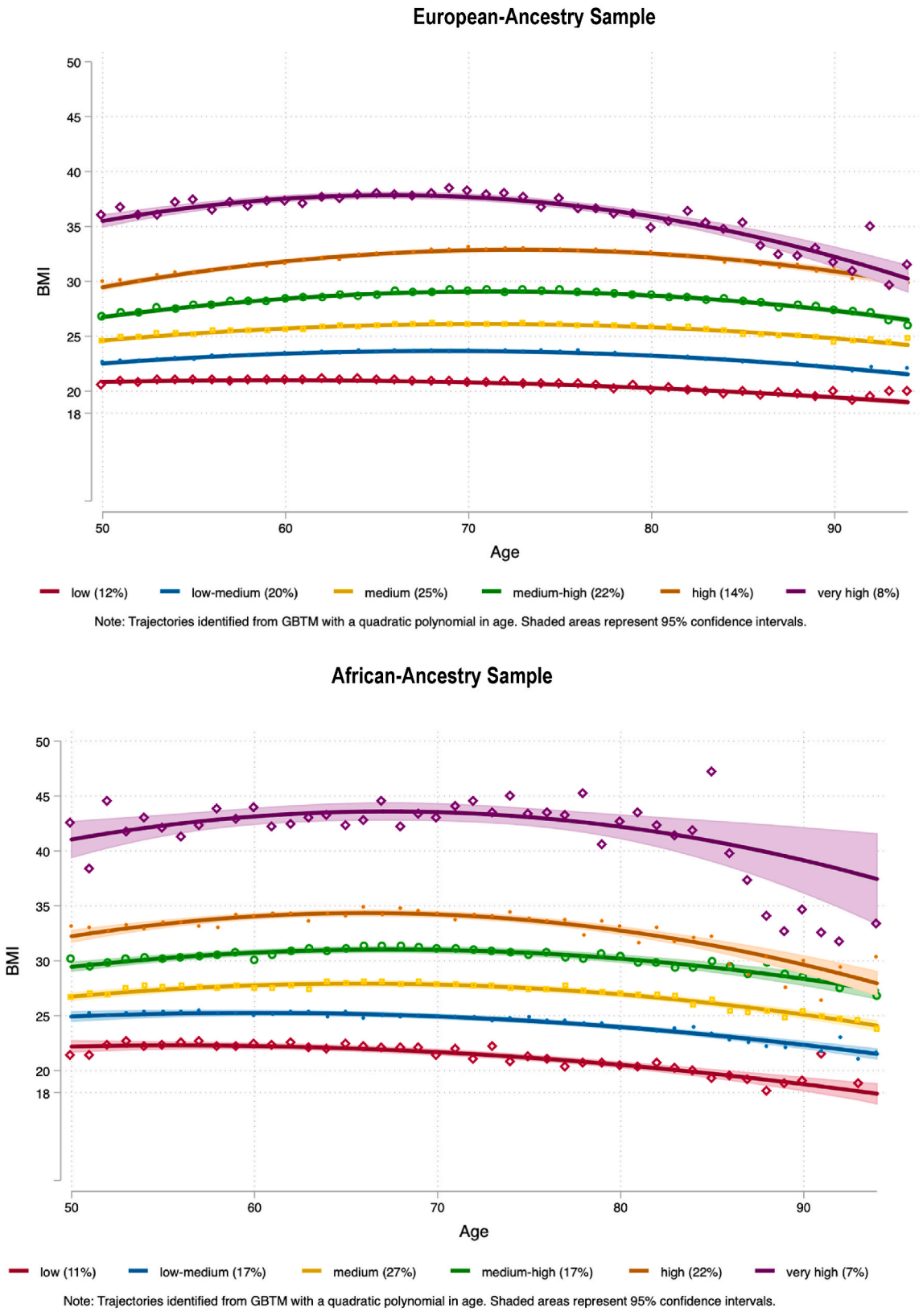


Fig. 1. BMI trajectories.

low, low-medium and medium trajectories all represent BMI in the normal weight range ($18.5 \leq BMI < 25$) over the whole age range in the EA sample. In total, 57% of EA individuals belong to these trajectories. In the AA sample, the low-medium trajectory with 17% of individuals represents BMI in the normal age range over ages 51–94. While the low trajectory starts with BMI in the normal range, it ends with a BMI under 18 after age 91. The medium trajectory in the AA sample has a BMI in the overweight range ($25 \leq BMI \leq 30$) over ages 51–94.

Table 2
Summary statistics of individuals belonging to BMI trajectories.

	European-Ancestry Sample						African-Ancestry Sample					
	Low	Low-Medium	Medium	Medium-High	High	Very-High	Low	Low-Medium	Medium	Medium-High	High	Very-High
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)	(12)
Male	0.18	0.40	0.47	0.47	0.45	0.30	0.41	0.47	0.38	0.36	0.24	0.10
	(0.38)	(0.49)	(0.50)	(0.50)	(0.50)	(0.46)	(0.49)	(0.50)	(0.49)	(0.48)	(0.43)	(0.31)
Education	0.08	0.07	0.01	−0.03	−0.04	−0.17	−0.00	0.06	−0.01	−0.04	0.02	−0.06
PGS	(0.97)	(1.01)	(1.01)	(1.03)	(0.94)	(0.99)	(1.05)	(1.09)	(1.00)	(0.90)	(0.99)	(0.96)
Smoking PGS	−0.05	−0.02	−0.02	0.02	0.05	0.06	−0.10	0.13	−0.09	0.03	−0.02	0.20
	(0.98)	(1.03)	(1.04)	(0.95)	(0.98)	(0.97)	(1.01)	(0.92)	(1.08)	(1.00)	(0.96)	(0.95)
Depression	0.01	0.01	−0.04	0.04	−0.01	−0.02	0.03	0.10	−0.04	−0.05	−0.01	0.02
PGS	(1.03)	(0.99)	(0.99)	(1.03)	(0.98)	(0.98)	(0.99)	(0.99)	(1.01)	(0.96)	(0.99)	(1.14)
BMI PGS	−0.30	−0.25	−0.08	0.12	0.31	0.46	−0.21	−0.10	−0.08	0.14	0.10	0.27
	(0.97)	(0.97)	(1.00)	(0.95)	(0.95)	(0.96)	(1.04)	(0.91)	(1.06)	(0.89)	(1.00)	(1.06)
Wellbeing	0.01	−0.04	0.04	−0.00	0.01	−0.05	−0.09	−0.03	0.14	0.04	−0.11	−0.13
PGS	(0.99)	(1.01)	(0.97)	(1.01)	(1.01)	(1.04)	(0.98)	(1.00)	(1.00)	(0.97)	(1.03)	(0.96)
Cognition PGS	−0.01	0.03	0.02	0.02	−0.05	−0.08	0.00	−0.05	0.06	0.00	−0.02	−0.08
	(1.02)	(1.04)	(0.99)	(1.00)	(0.95)	(0.99)	(0.96)	(1.03)	(1.01)	(1.03)	(0.95)	(1.03)
Childhood	0.04	0.06	−0.01	0.01	−0.06	−0.11	0.12	−0.11	−0.03	0.03	0.05	−0.02
SES	(1.02)	(1.01)	(1.02)	(0.98)	(0.97)	(0.99)	(1.05)	(0.96)	(0.97)	(1.00)	(1.00)	(1.10)
Years of	13.03	13.20	12.90	12.87	12.47	12.45	10.79	11.36	11.35	11.30	11.02	10.77
Education	(2.65)	(2.68)	(2.54)	(2.58)	(2.54)	(2.44)	(3.35)	(3.19)	(3.28)	(3.46)	(3.27)	(3.35)
Cohort	0.23	0.21	0.19	0.14	0.10	0.08	0.12	0.15	0.13	0.11	0.10	0.10
AHEAD	(0.42)	(0.41)	(0.39)	(0.35)	(0.30)	(0.27)	(0.32)	(0.36)	(0.33)	(0.31)	(0.30)	(0.31)
Cohort CODA	0.15	0.16	0.15	0.13	0.11	0.10	0.09	0.06	0.08	0.07	0.08	0.09
	(0.35)	(0.36)	(0.36)	(0.34)	(0.31)	(0.31)	(0.29)	(0.24)	(0.28)	(0.25)	(0.27)	(0.29)
Cohort HRS	0.64	0.63	0.66	0.73	0.79	0.82	0.79	0.79	0.80	0.83	0.82	0.81
	(0.48)	(0.48)	(0.47)	(0.45)	(0.40)	(0.39)	(0.41)	(0.41)	(0.40)	(0.38)	(0.38)	(0.40)
N	873	1439	1949	1623	1008	565	128	205	326	195	258	77

Notes: Standard deviation in parentheses.

Table 2 gives summary statistics of individual characteristics for each of the trajectories, where individuals are assigned to trajectories using the maximum posterior probability rule. Both EA and AA individuals on the high and very-high trajectories have a higher BMI PGS and lower SES characteristics. For example, EA (AA) individuals on the very-high trajectory have an average BMI PGS of 0.46 (0.27) and 12.45 (10.77) years of education. In comparison, EA (AA) individuals on the low-medium trajectory have an average BMI PGS of −0.25 (−0.08) and 13.20 (11.36) years of education on average. Marginal effects evaluated at the mean from FML regressions are presented in Table 3. The results show that being male is associated with higher probabilities of being on the medium, medium-high and high trajectories, and lower probabilities of being on the very-high trajectory in the EA sample. In the AA sample, being male is associated with higher probabilities of being on low-medium trajectory, and lower probabilities of being on the high and very-high trajectories. The BMI PGS is associated with probabilities of being on all trajectories, apart from the medium trajectory in the AA sample. The largest association of the BMI PGS is with the low-medium (low) trajectory in the EA (AA) sample. A one standard-deviation increase in the BMI PGS decreases the probability of being on the low-medium (low) trajectory by 5.6 (4.2) percentage points in the EA (AA) sample. None of the other PGSs are statistically significantly (at the 5% level) associated with trajectory group membership. Higher childhood SES is only associated with a lower probability of being on the very-high trajectory in the EA sample. Specifically, a one-standard deviation increase in the childhood SES index decreases the probability of being on the very-high trajectory by 0.6 percentage points. Educational attainment affects the probabilities of being on the low-medium, high and very-high trajectories in the EA sample. An extra year of education increases (decreases) the probability of being on the low-medium (very-high) trajectory by 0.8 (0.3) percentage points. In the AA sample, an extra year of education increases (decreases) the probabilities of being on the low-medium (very-high) trajectory by 0.7 (0.4) percentage points, though the estimates are only statistically significant at the 10% level.

4.3. Depressive-symptoms trajectories

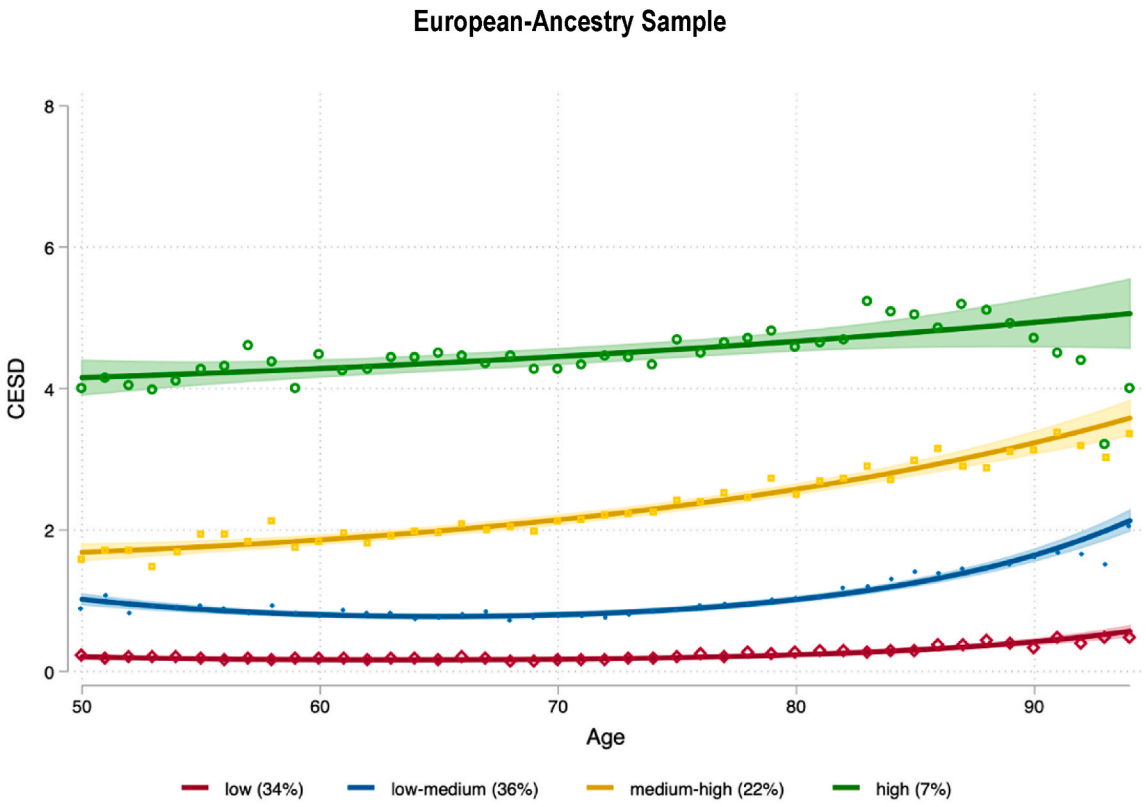
Results are shown in Fig. 2 and Tables 4 and 5. Model fit statistics in appendix tables A2 and A3 showed that the quadratic model with four trajectories in both the EA and AA samples had the lowest BIC and met the group size, average posterior probability, and odds of classification thresholds. A substantially higher proportion of AA individuals (14%) are on the high trajectory compared to EA individuals (7%). The high trajectory for the EA sample corresponds to having a CES-D score of four or more over the whole age range, which represents depression. In the AA sample, individuals on the high trajectory start-off as being depressed at age 51, and this is stable until age 80 after which the CES-D score decline. In the EA sample, the medium-high trajectory (with 22% of individuals) has the steepest increasing slope. A third and one-fifth of individuals in the EA and AA samples respectively belong to the low trajectory, which is flat and stable.

Summary statistics in Table 4 show that individuals on the higher depressive symptoms trajectories have lower SES characteristics and higher depression PGS scores. Marginal effects from FML regressions in Table 5 show that being male is associated with higher (lower) probability of being on the low (high) trajectory in the EA and AA samples. In the EA sample, a one-standard deviation increase in the depression PGS decreases (increases) the probability of being on the low (high) trajectory by 2.7 (1) percentage points. In the AA sample, the estimates of the depression PGS are imprecise but large in magnitude. For example, one-standard deviation increase in the depression PGS decreases (increases) the probability of being on the low (high) trajectory by 1.7 (1.9) percentage points. Childhood SES and educational attainment both affect the likelihood of being on the low and high trajectories in the EA sample. In particular, a one-standard deviation increase in the childhood SES index decreases the probability of being on the high trajectory by 1.8 percentage points, and one extra year of education decreases the probability of being on the high trajectory by 0.9 percentage points. These associations are smaller compared to the associations in the AA sample, where a (1) one-standard deviation increase in the childhood SES index and (2) one extra year of education decrease the probability of being on

Table 3
Association of PGSs, childhood SES and educational attainment with BMI trajectory group membership.

	European-Ancestry Sample						African-Ancestry Sample					
	P(Low)	P(Low-Medium)	P(Medium)	P(Medium-High)	P(High)	P(Very High)	P(Low)	P(Low-Medium)	P(Medium)	P(Medium-High)	P(High)	P(Very- High)
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)	(12)
Male	−0.111*** (0.007)	−0.012 (0.009)	0.074*** (0.010)	0.065*** (0.010)	0.015* (0.008)	−0.030*** (0.005)	0.023 (0.018)	0.102*** (0.024)	0.042 (0.027)	0.012 (0.023)	−0.113*** (0.024)	−0.065*** (0.012)
Education PGS	0.002 (0.004)	−0.005 (0.005)	−0.007 (0.006)	0.004 (0.005)	0.008* (0.004)	−0.001 (0.003)	−0.003 (0.010)	0.007 (0.011)	−0.018 (0.014)	−0.002 (0.011)	0.013 (0.013)	0.004 (0.006)
Smoking PGS	−0.004 (0.004)	−0.003 (0.005)	−0.003 (0.006)	0.007 (0.005)	0.003 (0.004)	0.001 (0.003)	−0.008 (0.009)	0.020* (0.010)	−0.020 (0.013)	0.000 (0.010)	0.000 (0.012)	0.007 (0.005)
Depression PGS	0.005 (0.004)	0.001 (0.005)	−0.007 (0.005)	0.010* (0.005)	−0.005 (0.004)	−0.005 (0.003)	0.002 (0.009)	0.017 (0.011)	0.008 (0.013)	−0.014 (0.011)	−0.011 (0.012)	−0.003 (0.006)
BMI PGS	−0.034*** (0.004)	−0.056*** (0.005)	−0.026*** (0.006)	0.033*** (0.005)	0.047*** (0.004)	0.037*** (0.003)	−0.042*** (0.011)	−0.036** (0.013)	−0.008 (0.018)	0.032* (0.015)	0.033** (0.017)	0.021** (0.008)
Wellbeing PGS	−0.000 (0.004)	−0.002 (0.005)	0.009* (0.005)	−0.000 (0.005)	−0.001 (0.004)	−0.005 (0.003)	−0.007 (0.009)	−0.001 (0.011)	0.038** (0.013)	0.004 (0.011)	−0.026* (0.013)	−0.008 (0.005)
Cognition PGS	−0.001 (0.004)	−0.001 (0.005)	0.002 (0.006)	0.007 (0.005)	−0.005 (0.004)	−0.002 (0.003)	−0.001 (0.010)	−0.013 (0.012)	0.010 (0.014)	0.003 (0.012)	0.002 (0.013)	−0.001 (0.006)
Childhood SES	0.001 (0.004)	0.007 (0.005)	−0.002 (0.005)	0.002 (0.005)	−0.002 (0.004)	−0.006** (0.003)	0.016* (0.010)	−0.018 (0.011)	−0.015 (0.014)	0.002 (0.012)	0.013 (0.012)	0.002 (0.007)
Years of Education	0.004* (0.002)	0.008*** (0.002)	0.001 (0.002)	−0.002 (0.002)	−0.008*** (0.002)	−0.003*** (0.001)	−0.004 (0.003)	0.007* (0.003)	0.007 (0.004)	0.003 (0.004)	−0.010* (0.004)	−0.004* (0.002)
N	7357	7357	7357	7357	7357	7357	1189	1189	1189	1189	1189	1189

Notes: Marginal effects evaluated at the mean from FML regressions where the probability of individual i belonging to group j is regressed on gender, PGSs, childhood SES, years of education, cohort dummies, and the first 10 genetic principal components. The PGSs and childhood SES are standardized to have means of zero and standard deviations of one. Standard errors clustered at the household level. ***significant at 1% **significant at 5% *significant at 10%.



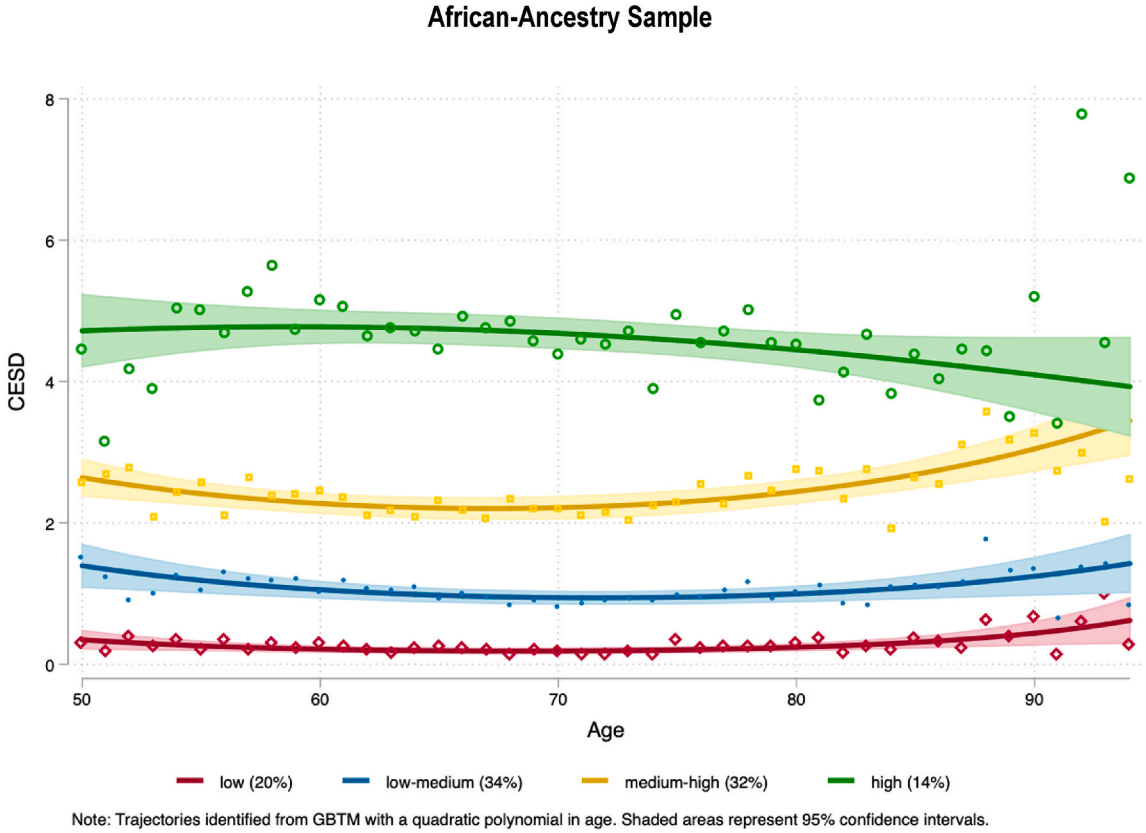


Fig. 2. Depressive symptoms trajectories.

Table 4
Summary statistics of individuals belonging to depressive symptom trajectories.

	European-Ancestry Sample				African-Ancestry Sample			
	Low	Low-Medium	Medium	High	Low	Low-Medium	Medium	High
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
Male	0.49 (0.50)	0.40 (0.49)	0.33 (0.47)	0.25 (0.43)	0.39 (0.49)	0.39 (0.49)	0.32 (0.47)	0.25 (0.43)
Education PGS	0.09 (0.99)	0.01 (0.98)	−0.07 (1.04)	−0.26 (0.98)	0.12 (1.03)	0.10 (0.99)	−0.16 (0.98)	−0.04 (0.98)
Smoking PGS	−0.05 (1.03)	−0.00 (0.99)	0.07 (0.97)	0.08 (0.97)	−0.08 (1.07)	0.02 (1.01)	−0.00 (0.97)	0.09 (0.93)
Depression PGS	−0.11 (1.00)	0.02 (0.98)	0.07 (1.02)	0.23 (1.00)	−0.15 (1.04)	−0.07 (0.98)	0.10 (0.94)	0.14 (1.07)
BMI PGS	−0.06 (0.97)	−0.02 (1.00)	0.06 (1.03)	0.20 (1.06)	−0.15 (1.00)	−0.01 (0.97)	0.11 (1.01)	−0.00 (1.03)
Wellbeing PGS	0.09 (1.01)	−0.02 (1.00)	−0.05 (0.99)	−0.17 (0.96)	0.16 (1.04)	0.02 (0.98)	−0.15 (0.98)	0.04 (0.99)
Cognition PGS	0.03 (1.00)	0.00 (1.00)	−0.03 (1.00)	−0.08 (1.01)	0.09 (1.06)	0.05 (0.96)	−0.07 (1.00)	−0.09 (0.99)
Childhood SES	0.20 (0.95)	−0.01 (0.98)	−0.16 (1.02)	−0.43 (1.02)	0.22 (0.96)	0.08 (0.98)	−0.05 (0.96)	−0.39 (1.07)
Years of Education	13.53 (2.44)	12.89 (2.54)	12.24 (2.57)	11.54 (2.65)	13.04 (2.71)	11.20 (3.20)	10.52 (3.29)	9.80 (3.23)
Cohort AHEAD	0.15 (0.36)	0.20 (0.40)	0.16 (0.37)	0.11 (0.32)	0.10 (0.30)	0.14 (0.34)	0.12 (0.33)	0.11 (0.31)
Cohort CODA	0.14 (0.35)	0.14 (0.34)	0.15 (0.36)	0.10 (0.31)	0.07 (0.25)	0.07 (0.25)	0.08 (0.27)	0.12 (0.33)
Cohort HRS	0.71 (0.45)	0.67 (0.47)	0.70 (0.46)	0.79 (0.41)	0.84 (0.37)	0.80 (0.40)	0.80 (0.40)	0.77 (0.42)
N	2561	2678	1591	527	246	397	385	161

Notes: Standard deviation in parentheses.

Table 5
Association of PGSs, childhood SES and educational attainment with depressive symptom trajectory group membership.

	European-Ancestry Sample				African-Ancestry Sample			
	P(Low)	P(Low-Medium)	P(Medium)	P(High)	P(Low)	P(Low-Medium)	P(Medium)	P(High)
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
Male	0.114*** (0.010)	0.001 (0.010)	−0.072*** (0.008)	−0.043*** (0.004)	0.058** (0.021)	0.072** (0.027)	−0.049* (0.026)	−0.081*** (0.016)
Education PGS	0.005 (0.006)	0.004 (0.005)	−0.004 (0.005)	−0.005** (0.003)	0.003 (0.011)	0.022 (0.013)	−0.026* (0.014)	0.001 (0.009)
Smoking PGS	−0.001 (0.006)	−0.002 (0.006)	0.003 (0.005)	0.001 (0.003)	−0.013 (0.010)	0.008 (0.013)	0.000 (0.012)	0.005 (0.008)
Depression PGS	−0.027*** (0.006)	0.008 (0.006)	0.009* (0.005)	0.010*** (0.003)	−0.017 (0.011)	−0.023* (0.013)	0.021 (0.013)	0.019* (0.010)
BMI PGS	−0.009* (0.006)	−0.005 (0.005)	0.006 (0.005)	0.009** (0.003)	0.011 (0.013)	0.005 (0.017)	0.004 (0.017)	−0.019 (0.013)
Wellbeing PGS	0.027*** (0.006)	−0.014* (0.005)	−0.008 (0.005)	−0.006* (0.002)	0.021* (0.011)	0.000 (0.013)	−0.031* (0.013)	0.010 (0.009)
Cognition PGS	0.005 (0.006)	0.002 (0.006)	−0.005 (0.005)	−0.001 (0.003)	0.001 (0.011)	0.010 (0.014)	−0.002 (0.014)	−0.009 (0.009)
Childhood SES	0.042*** (0.006)	−0.002 (0.005)	−0.022*** (0.005)	−0.018*** (0.002)	0.014 (0.010)	0.026* (0.013)	0.001 (0.014)	−0.040*** (0.009)
Years of Education	0.027*** (0.002)	0.001 (0.002)	−0.019*** (0.002)	−0.009*** (0.001)	0.038*** (0.004)	0.001 (0.004)	−0.022*** (0.004)	−0.016*** (0.003)
N	7357	7357	7357	7357	1189	1189	1189	1189

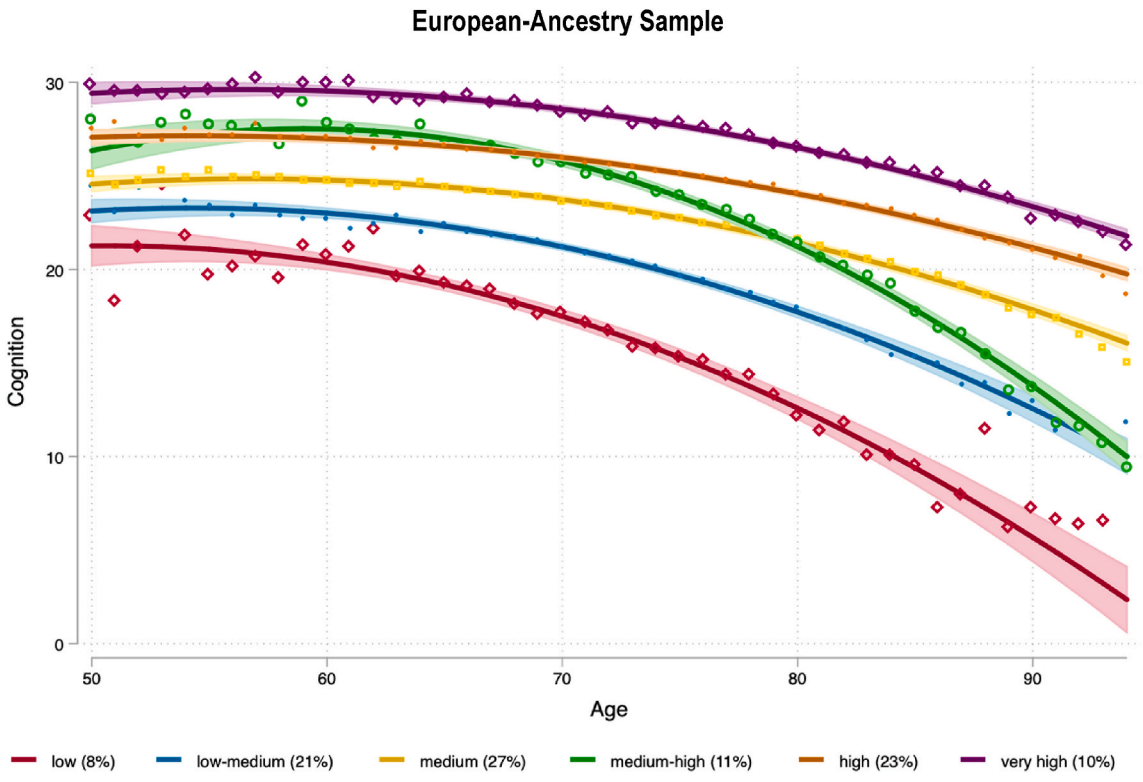
Notes: Marginal effects evaluated at the mean from FML regressions where the probability of individual i belonging to group j is regressed on gender, PGSs, childhood SES, years of education, cohort dummies, and the first 10 genetic principal components. The PGSs and childhood SES are standardized to have means of zero and standard deviations of one. Standard errors clustered at the household level. ***significant at 1% **significant at 5% *significant at 10%.

the high trajectory by 4 and 1.6 percentage points respectively.

4.4. Cognition trajectories

Results are shown in Fig. 3 and Tables 6 and 7. Six distinct trajectories with a quadratic in age were identified in both the EA and AA samples (see appendix tables A2-A3 for model fit statistics), all of which have declining slopes. The low trajectory with 8% of individuals in the EA sample has the steepest decline, whereas the high trajectory with 33% of individuals has the fastest decline in the AA sample.

Summary statistics in Table 6 show that individuals on higher cognition trajectories have higher SES characteristics and higher values on the education and cognition PGSs. Marginal effects from FML regressions in Table 7 show that being male is associated with lower probabilities of being on the very-high trajectories in both samples. The education and cognition PGSs are not predictive of trajectory group membership in the AA sample. In the EA sample, a one-standard deviation increase in the education and cognition PGS increases the



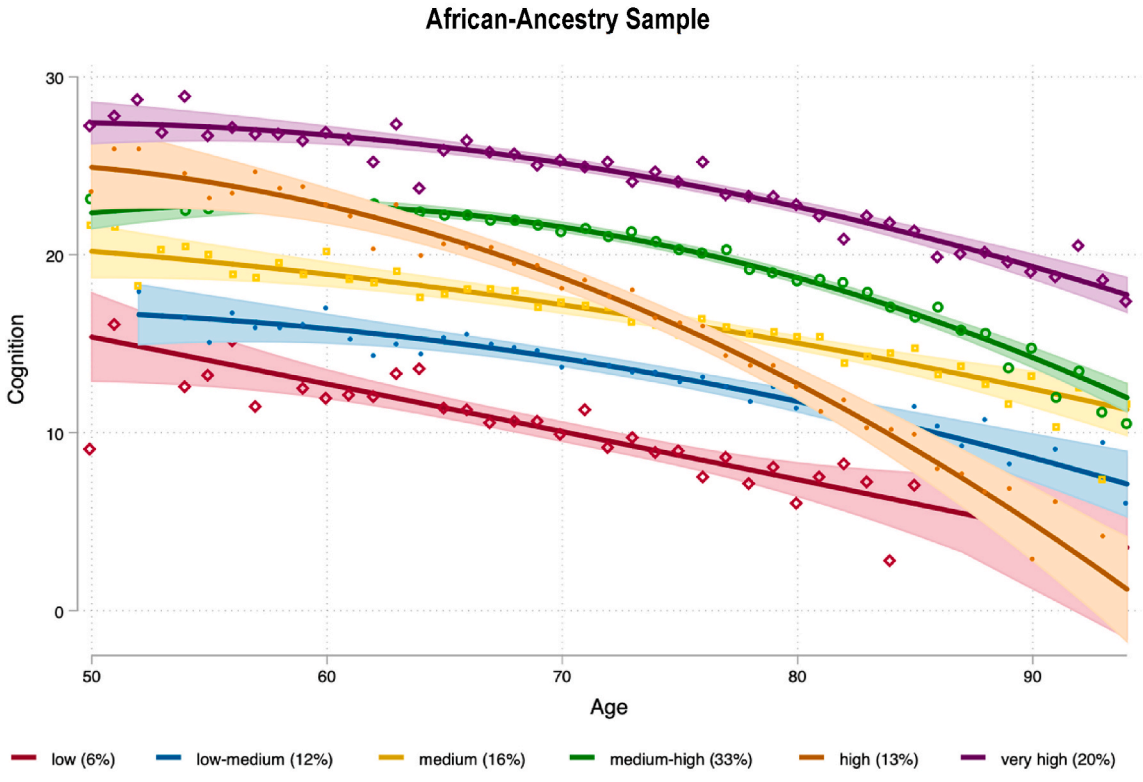


Fig. 3. Cognition trajectories.

Table 6
Summary statistics of individuals belonging to cognition trajectories.

	European-Ancestry Sample						African-Ancestry Sample					
	Low	Low-Medium	Medium	Medium-High	High	Very High	Low	Low-Medium	Medium	Medium-High	High	Very High
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)	(12)
Male	0.48	0.29	0.48	0.43	0.38	0.26	0.33	0.52	0.39	0.43	0.34	0.22
	(0.50)	(0.46)	(0.50)	(0.49)	(0.49)	(0.44)	(0.47)	(0.50)	(0.49)	(0.50)	(0.48)	(0.41)
Education	−0.33	0.06	−0.20	−0.01	0.13	0.33	0.01	−0.30	−0.28	−0.04	0.06	0.18
PGS	(1.01)	(0.99)	(0.99)	(1.00)	(0.96)	(0.95)	(0.99)	(0.90)	(0.97)	(0.95)	(1.03)	(0.99)
Smoking PGS	0.02	−0.05	0.02	−0.00	−0.03	0.07	0.11	−0.12	−0.03	0.07	−0.04	−0.00
	(0.90)	(1.02)	(1.04)	(0.97)	(1.00)	(1.05)	(0.99)	(0.87)	(1.02)	(1.01)	(0.99)	(1.03)
Depression	0.09	−0.02	0.04	−0.00	−0.05	−0.01	0.03	0.10	−0.08	0.09	−0.03	−0.02
PGS	(0.98)	(0.98)	(0.99)	(1.02)	(0.98)	(1.03)	(0.97)	(0.89)	(1.03)	(1.01)	(0.96)	(1.10)
BMI PGS	0.08	−0.06	0.06	−0.00	−0.02	−0.07	−0.14	0.32	0.17	0.16	−0.03	−0.21
	(0.99)	(0.96)	(0.99)	(1.02)	(1.00)	(1.00)	(0.95)	(0.86)	(1.03)	(0.99)	(1.02)	(0.95)
Wellbeing	−0.01	−0.01	−0.02	−0.00	0.03	−0.02	−0.01	−0.21	0.03	−0.04	0.00	0.07
PGS	(1.04)	(1.03)	(1.01)	(0.98)	(1.02)	(0.96)	(1.03)	(0.90)	(0.90)	(0.91)	(1.05)	(1.03)
Cognition PGS	−0.15	−0.01	−0.12	−0.03	0.09	0.23	0.04	−0.15	−0.21	−0.04	0.02	0.15
	(0.93)	(1.01)	(0.97)	(1.01)	(0.99)	(1.05)	(1.02)	(0.88)	(0.89)	(1.00)	(1.00)	(1.07)
Childhood	−0.39	−0.04	−0.19	−0.01	0.16	0.32	0.10	−0.35	−0.31	−0.13	0.07	0.22
SES	(1.01)	(0.98)	(0.99)	(0.98)	(0.98)	(0.96)	(1.02)	(0.86)	(0.95)	(1.02)	(0.99)	(0.99)
Years of	10.59	13.26	11.79	12.80	13.74	14.51	10.77	6.94	8.63	10.26	11.91	13.54
Education	(2.98)	(2.31)	(2.46)	(2.33)	(2.27)	(2.25)	(3.59)	(3.29)	(2.94)	(2.82)	(2.56)	(2.51)
Cohort	0.07	0.30	0.12	0.15	0.17	0.25	0.12	0.05	0.08	0.12	0.12	0.16
AHEAD	(0.25)	(0.46)	(0.33)	(0.36)	(0.37)	(0.44)	(0.33)	(0.21)	(0.27)	(0.33)	(0.32)	(0.37)
Cohort CODA	0.12	0.19	0.14	0.13	0.14	0.14	0.12	0.06	0.10	0.10	0.07	0.05
	(0.32)	(0.39)	(0.35)	(0.34)	(0.34)	(0.34)	(0.32)	(0.24)	(0.30)	(0.30)	(0.25)	(0.23)
Cohort HRS	0.82	0.52	0.74	0.72	0.70	0.62	0.77	0.89	0.82	0.78	0.82	0.79
	(0.39)	(0.50)	(0.44)	(0.45)	(0.46)	(0.49)	(0.42)	(0.31)	(0.38)	(0.41)	(0.39)	(0.41)
N	505	619	1491	2239	1827	676	120	64	142	188	456	219

Notes: Standard deviation in parentheses.

probability of being on the very-high trajectory by 1.2 percentage points. In the EA sample, higher childhood SES is associated with higher probabilities of belonging to the high and very-high cognition trajectories. A one-standard deviation increase in the childhood SES index increases the probability of being on the high (very-high) trajectory by 1.3 (0.8) percentage points. Childhood SES is not predictive of trajectory group membership in the AA sample, with one exception— higher childhood SES is associated with a lower probability (2.2 percentage points) of being on the high trajectory. Educational attainment is associated with all trajectory-group memberships in both samples. An additional year of education increases the probability of being on the very-high trajectory by 2.2 and 4.7 percentage points in the EA and AA samples respectively.

4.5. Gene-environment interplay

In this section, we investigate whether associations of childhood SES and adult educational attainment vary by genetic predisposition. To do so, we interacted years of education and childhood SES with the (1) BMI PGS in FML regressions for BMI, (2) the depression PGS in FML regressions for mental health, and (3) cognition PGS in FML regressions for cognition. The marginal effects of educational attainment and childhood SES evaluated at different values of the PGS are shown in Figs. 4–6 (regression results are in appendix tables A4-A6). Overall, there is some suggestive evidence that the associations of educational attainment with the probabilities of being on "good" trajectories vary by genetic predispositions. Fig. 4 panel A for the AA sample shows that the marginal effects of years of education on the probabilities of being on the low-medium trajectory is higher at lower values of the BMI PGS, though the estimates are imprecise. Panels A and B in Fig. 5 shows that the marginal effects of years of education on the probabilities of being on the low and high depressive symptoms trajectories are higher at lower values of the depression PGS in both the EA and AA samples. In Fig. 6 panel B, the marginal effects of years of education on the probabilities of being on the very-high trajectories varies by the cognition PGS for both EA and AA individuals. For childhood SES, Figs. 4–6 do not provide much evidence that the marginal effects vary by genetic predisposition. The only exception is panel C in Fig. 5 for the EA sample, where the marginal effects of childhood SES on the probability of being on the low depression trajectory is lower at higher values of the depression PGS.

5. Discussion

This study investigates the impact of genetic dispositions, childhood SES and early adult SES in determining long-term trajectories in BMI, depressive symptoms, and cognition using a flexible GBTM approach that allows for heterogenous health trajectories as individuals age. The focus on long-term trajectories is an important distinction from other work that investigates cross-sectional variation and health outcomes, and our GBTM analytic approach is more flexible than other growth-curve models because it allows for the possibility that different groups of individuals may have different developmental trajectories. Using GBTM to identify subgroups of people who share the same underlying trajectory, we identify six trajectories for BMI and cognition and four for depressive symptoms for EA and AA individuals. Importantly, these analyses reveal differences in intercepts but generally did not show clear differences in the slopes of the trajectories.

These findings thus indicate that large differences in physical, mental and cognitive health between subgroups in the early 50s are fairly persistent during the subsequent aging process. The number of identified trajectories and patterns align with findings from other studies employing GBTM. Using the HRS data over a 11-year period, Liang et al. (2011) identified six trajectories of depressive symptoms, with the majority of individuals experiencing very few symptoms. Olaya et al. (2017) identified four trajectories (that differ in levels but not slope) for individuals aged 65–74 at baseline in the English Longitudinal Study of Ageing over a 10-year period. Zheng et al. (2013) identified six trajectories for BMI in the HRS over ages 51–77.

However, none of these prior studies has investigated the associations of these trajectories with PGS scores and how genetic propensities determine trajectories membership as we do in the second part of our analysis. After identifying trajectories across the older age lifecourse, we

Table 7
Association of PGSs, childhood SES and educational attainment with cognition trajectory group membership.

	European-Ancestry Sample						African-Ancestry Sample					
	Low	Low-Medium	Medium	Medium-High	High	Very High	Low	Low-Medium	Medium	Medium-High	High	Very High
	(1)	(2)	(3)	(4)	(5)	(6)	(1)	(2)	(3)	(4)	(5)	(6)
Male	0.016*** (0.004)	−0.074*** (0.008)	0.057*** (0.009)	−0.044*** (0.005)	−0.043*** (0.008)	−0.060*** (0.005)	0.002 (0.006)	−0.013 (0.014)	0.041** (0.021)	0.060* (0.027)	−0.015 (0.017)	−0.075*** (0.017)
Education PGS	−0.008*** (0.002)	−0.021*** (0.004)	0.005 (0.005)	0.003 (0.003)	0.010** (0.005)	0.012*** (0.003)	−0.004 (0.003)	−0.020** (0.008)	0.000 (0.010)	0.019 (0.014)	0.002 (0.009)	0.003 (0.010)
Smoking PGS	−0.002 (0.002)	0.001 (0.005)	0.004 (0.005)	−0.005* (0.003)	−0.006 (0.005)	0.009** (0.003)	−0.003 (0.002)	0.003 (0.007)	0.008 (0.010)	−0.013 (0.013)	0.008 (0.008)	−0.000 (0.008)
Depression PGS	0.001 (0.002)	0.000 (0.004)	−0.002 (0.005)	0.002 (0.003)	−0.004 (0.004)	0.003 (0.003)	0.000 (0.003)	−0.008 (0.008)	0.003 (0.010)	−0.002 (0.013)	0.001 (0.008)	0.005 (0.009)
BMI PGS	0.000 (0.002)	0.001 (0.004)	−0.001 (0.005)	−0.001 (0.003)	0.001 (0.004)	−0.001 (0.003)	0.000 (0.004)	−0.005 (0.011)	0.025* (0.013)	−0.003 (0.017)	−0.018 (0.012)	0.002 (0.011)
Wellbeing PGS	−0.001 (0.002)	−0.002 (0.004)	−0.002 (0.005)	0.001 (0.003)	0.005 (0.005)	−0.001 (0.003)	−0.003 (0.003)	0.001 (0.007)	0.004 (0.009)	−0.005 (0.013)	−0.001 (0.009)	0.004 (0.009)
Cognition PGS	−0.003 (0.002)	−0.017*** (0.005)	−0.008* (0.005)	0.001 (0.003)	0.015*** (0.005)	0.012*** (0.003)	0.001 (0.003)	−0.001 (0.007)	−0.003 (0.010)	−0.001 (0.013)	0.000 (0.010)	0.002 (0.010)
Childhood SES	−0.005** (0.002)	−0.009** (0.004)	−0.006 (0.005)	−0.001 (0.003)	0.013** (0.004)	0.008*** (0.003)	0.001 (0.003)	−0.002 (0.008)	−0.010 (0.011)	−0.008 (0.013)	−0.022** (0.010)	−0.002 (0.009)
Years of Education	−0.019*** (0.001)	−0.038*** (0.002)	−0.006*** (0.002)	0.009** (0.001)	0.032*** (0.002)	0.022*** (0.001)	−0.011** (0.004)	−0.034*** (0.003)	−0.025*** (0.004)	0.035*** (0.005)	−0.012*** (0.004)	0.047*** (0.004)
N	7357	7357	7357	7357	7357	7357	1189	1189	1189	1189	1189	1189

Notes: Marginal effects evaluated at the mean from FML regressions where the probability of individual i belonging to group j is regressed on gender, PGSs, childhood SES, years of education, cohort dummies, and the first 10 genetic principal components. The PGSs and childhood SES are standardized to have means of zero and standard deviations of one. Standard errors clustered at the household level. ***significant at 1% **significant at 5% *significant at 10%.

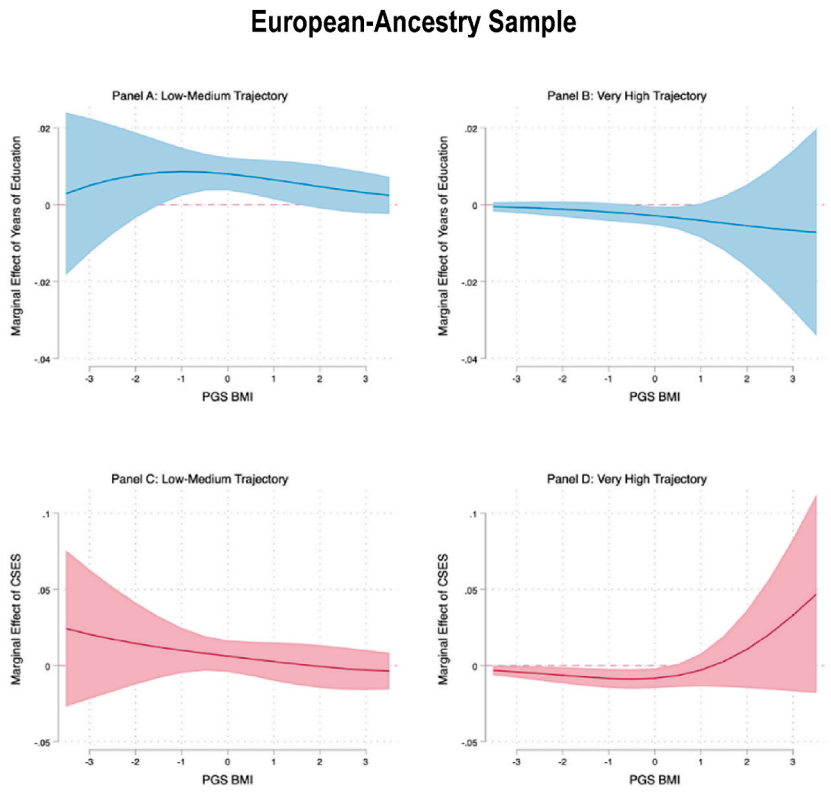


Fig. 4. Marginal effects of years of education and childhood SES with BMI trajectory-group membership by BMI PGS

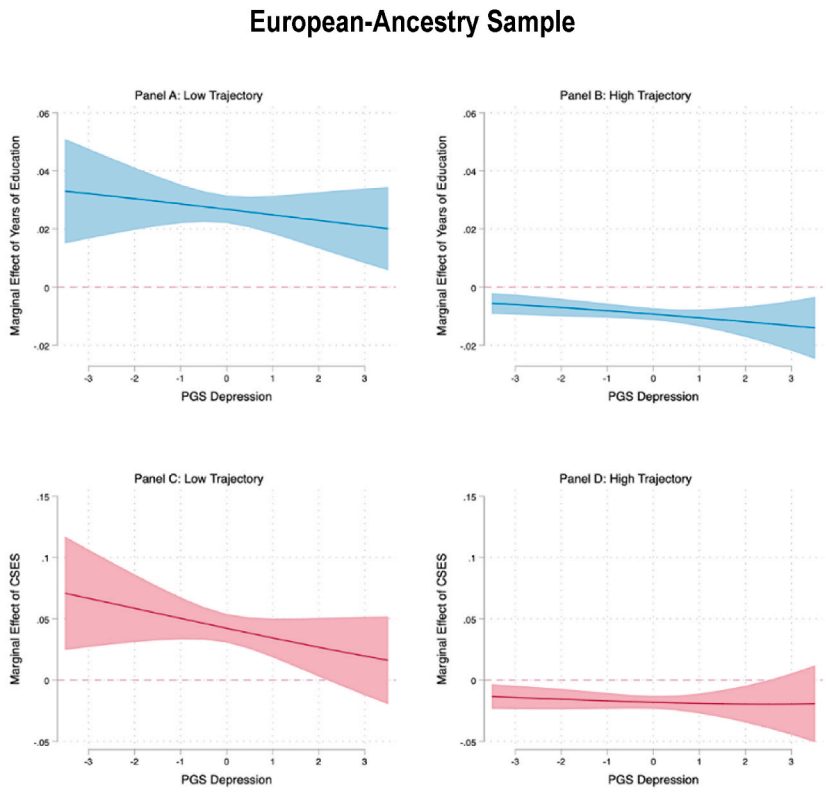


Fig. 5. Marginal effects of years of education and childhood SES with depressive symptom trajectory-group membership by depression PGS

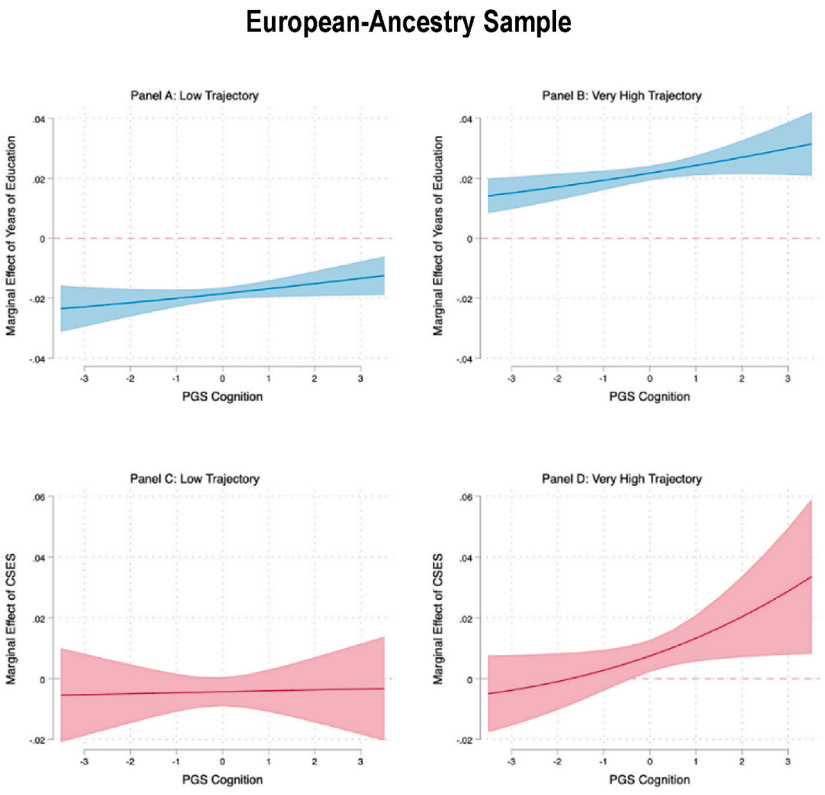


Fig. 6. Marginal effects of years of education and childhood SES with cognition trajectory-group membership by cognition PGS

Table 8
Summary of Association of PGS, Childhood SES and Educational Attainment with Good Health Trajectory Membership.

Sample	European Ancestry	African Ancestry	European Ancestry	African Ancestry	European Ancestry	African Ancestry
Outcome	BMI	BMI	Depressive Symptoms	Depressive Symptoms	Cognition	Cognition
Trajectory Group	Low-Medium	Low-Medium	Low	Low	Vey-High	Very-High
Trajectory Proportion	20%	17%	34%	20%	10%	20%
Trajectory Description	BMI in normal weight range over age 51-94	BMI in normal weight range over age 51-94	Persistently low depressive symptoms over ages 51-94	Persistently low depressive symptoms over ages 51-94	Very-high initial cognition, decreasing over age 51-94	Very-high initial cognition, decreasing over age 51-94
Predictors						
Male	—	↑	↑	↑	↓	↓
Education PGS	—	—	—	—	↑	—
Smoking PGS	—	↑	—	—	↑	—
Depression PGS	—	—	↓	—	—	—
BMI PGS	↓	↓	↓	—	—	—
Wellbeing PGS	—	—	↑	↑	—	—
Cognition PGS	—	—	—	—	↑	—
Childhood SES	—	—	↑	—	↑	—
Years of Education	↑	↑	↑	↑	↑	↑

Notes: Upwards (downwards) blue arrows show the presence of positive (negative) associations. Blue arrows represent associations that are statistically significant at the 1% or 5% level. Red arrows represent associations that are statistically significant at the 10% level.

estimated associations of PGSs, childhood SES and educational attainment with probabilities of trajectory-group memberships. The findings for the likelihood of belonging to BMI in the normal range, low depressive symptoms and high-initial-cognition trajectories are summarized in Table 8. The results show that, as expected, genetic propensities affect trajectory group memberships, but also highlight the long arm of socioeconomic factors. Individuals with a higher BMI (depression) PGS are less likely to be on the normal range BMI (low depressive symptom) trajectory, while individuals with a higher education/cognition PGS are more likely to be on the very-high initial cognition trajectory. Educational attainment is the most robust predictor of health trajectories, increasing the probabilities of belonging to these trajectories. The relative importance of education differs across the health domains. Childhood circumstances are manifested in trajectories to a lesser extent, with childhood SES only predicting the likelihood of being on the low-depressive-symptoms and very-high initial cognition trajectories for EA individuals. We also examined gene-environment interplay and find suggestive evidence that associations of educational attainment on the probabilities of being on trajectories with BMI in the normal range, low depressive symptoms and high initial cognition vary with genetic predispositions.

Finally, we note that only very few individuals are on all good trajectories. For example, appendix table A7 shows that 11% (41%) of EA individuals on the low-medium BMI trajectory are also on the very-high initial cognition (low depressive symptom) trajectory. However, only 6% of EA individuals on the low-medium BMI trajectory are on both the low depressive symptoms and very-high initial cognition trajectory. In the AA sample, 8% of individuals on the low-medium BMI trajectory are on both the low depressive symptoms and very-high initial cognition trajectory. Thus, being on a good trajectory for one outcome does not necessarily mean the individual will be on good trajectories for other outcomes.

There are limitations with our study. First, our data are observational, and we cannot draw causal inferences regarding the roles of SES in predicting trajectory-group memberships. PGSs are also unlikely to reflect pure genetic effects because they are likely confounded by dynastic effects, which occur when parental genetics affect children's outcomes via parental traits. For example, parents with a high educational PGS are likely to be highly educated and may provide a more nurturing environment that affects children's outcomes. PGSs are constructed from meta-analyses of studies that span a wide range of (Western) countries and cohorts. This can make it difficult to detect gene-environment interactions because the PGS captures mean effects that are common across environments rather than genetic influences that are context-specific (Conley, 2017). Second, though we conduct the analysis separately for EA and AA individuals, we cannot make comparisons due to the lack of portability of PGSs in non-European populations. Third, though our GBTM analysis takes accounts for (non-random) attrition due to mortality among individuals for whom PGS data are available in the HRS, we are not able to account for selection (due to mortality or refusals) of individuals for whom PGS data are not available. Specifically, the HRS started collecting genetic data in 2006, and Domingue et al. (2017) have shown that individuals for whom PGS scores are available in the HRS are healthier and better educated than HRS participants for whom no PGS data are available. We are not able to control for this selection (and neither are most other studies that use the HRS genetic data), and our results may thus not be generalizable to all HRS participants.

Despite such limitations we contribute new knowledge about possible multiple aging physical-health, depression and cognitive trajectories for people in the 51–94 age range in the United States, the extent to which genetics and earlier SES predict these trajectories, and similarities and differences between European-ancestry and African-ancestry subpopulations.

Ethics statement

This research analyzed publicly available data from the Health &

Retirement Study, hence no IRB was required.

Author statement

Cung Truong Hoang: Conceptualization; methodology; data curation; formal analysis; writing—original draft; writing—review and editing. Vikesh Amin: Conceptualization; writing—original draft; writing—review and editing; funding acquisition. Jere Behrman: Conceptualization; writing—original draft; writing—review and editing; funding acquisition. Hans Peter-Kohler: Conceptualization; writing—original draft; writing—review and editing; funding acquisition. Illiana V. Kohler: Conceptualization; writing—original draft; writing—review and editing.

Declaration of competing interest

None.

Data availability

Data will be made available on request.

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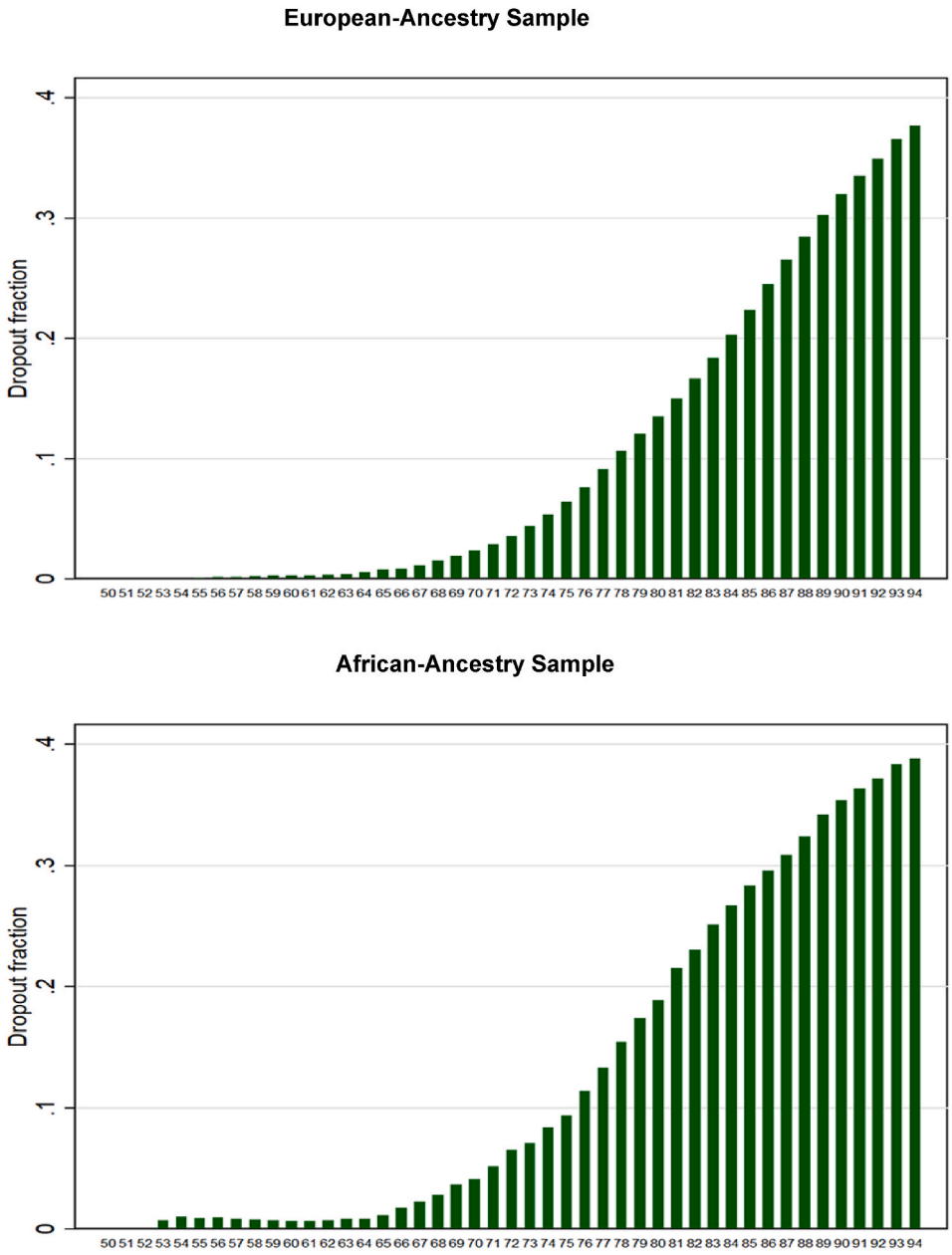
Appendix



Appendix Fig. A1. Cumulative Dropout Fraction by Age, European-Ancestry Sample, African-Ancestry Sample

Appendix Table A2
Model Fit Statistics, European Ancestry Sample

Panel A: Bayesian Information Criterion (BIC) Model Fit Statistics

Outcome	BMI	BMI	BMI	BMI	CES-D	CES-D	CES-D	CES-D	Cognition	Cognition	Cognition	Cognition
Age	Quadratic	Quadratic	Cubic	Cubic	Quadratic	Quadratic	Cubic	Cubic	Quadratic	Quadratic	Cubic	Cubic
Measure	BIC	Log BF	BIC	Log BF	BIC	Log BF	BIC	Log BF	BIC	Log BF	BIC	Log BF
Total Number of Trajectories												
2	−216707		−216714		−108608		−108616		−146085		−146087	
3	−201070	31274	−201079	31270	−104050	9116	−104058	9116	−143257	5656	−143228	5718
4	−192818	16504	−192830	16498	−102801	2498	−102815	2486	−142262	1990	−142233	1990
5	−188290	9056	−188308	9044					−141658	1208	−141648	1170
6	−185639	5302	−185659	5298					−141258	800	−141267	762

Panel B: Group Size Model Fit Statistics; Estimated Group Size (EST) and Actual Group Size (FRAC)

Outcome	BMI	BMI	BMI	BMI	CES-D	CES-D	CES-D	CES-D	Cognition	Cognition	Cognition	Cognition
Age	Quadratic	Quadratic	Cubic	Cubic	Quadratic	Quadratic	Cubic	Cubic	Quadratic	Quadratic	Cubic	Cubic
Measure	EST	FRAC	EST	FRAC	EST	FRAC	EST	FRAC	EST	FRAC	EST	FRAC
Trajectories												
1	25	25.1	11.6	11.6	34.4	34.8	34.4	34.9	7.7	6.9	8.9	8.4
2	13.9	13.7	19.5	19.6	36.4	36.4	36.4	36.3	20.7	20.4	11.4	8.8
3	19.6	19.6	25.1	25.3	21.8	21.6	21.8	21.7	9.6	9	20.8	21.3
4	11.8	11.9	22.1	22.1	7.5	7.2	7.4	7.1	28	31	7.1	5.8
5	22	22.1	7.7	7.7					23.3	24.6	32.6	36.7
6	7.7	7.7	13.9	13.8					10.8	8.1	19.1	19.1

Panel C: Average Posterior Probability (AvePee) and Odds of Classification (OCC) Model Statistics

Outcome	BMI	BMI	BMI	BMI	CES-D	CES-D	CES-D	CES-D	Cognition	Cognition	Cognition	Cognition
Age	Quadratic	Quadratic	Cubic	Cubic	Quadratic	Quadratic	Cubic	Cubic	Quadratic	Quadratic	Cubic	Cubic
Measure	AvePee	OCC	AvePee	OCC	AvePee	OCC	AvePee	OCC	AvePee	OCC	AvePee	OCC
Trajectories												
1	93.8	45.3	96.3	197.5	92	22	92	21.9	89.1	98.4	89.1	83.6
2	95.1	120.7	93.9	63.5	88	12.8	88.1	13	81.8	17.2	78.6	28.6
3	94.1	65.5	93.7	44.4	89.1	29.3	89	29	84.7	52.4	79.2	14.5
4	96	179.4	94.2	57.3	92.9	162.5	93	165.1	74.1	7.4	82.1	60
5	94.1	56.5	96.2	301.9					77.7	11.4	77.8	7.2
6	96.4	319.3	95.1	120.1					78.5	30.2	82.6	20.1

Notes: Each column represents one outcome and polynomial order in age. Panel A shows the BIC and Log Bayes Factor and the rows correspond to the total number of trajectories that are modeled. In Panel B and C we show the model fit statistics by trajectory group setting the total number of trajectories to the optimal number. Panel B shows the estimated group size π_j and the group size according to the maximum posterior probability assignment rule. Panel C shows the average posterior probability and the odds of correct classification. For the outcome CES-D, we consider at most 4 trajectories since we could not obtain standard errors for larger models.

Appendix Table A3
Model Fit Statistics, African-Ancestry Sample

Panel A: Bayesian Information Criterion (BIC) Model Fit Statistics

Outcome	BMI	BMI	BMI	BMI	CES-D	CES-D	CES-D	CES-D	Cognition	Cognition	Cognition	Cognition
Age	Quadratic	Quadratic	Cubic	Cubic	Quadratic	Quadratic	Cubic	Cubic	Quadratic	Quadratic	Cubic	Cubic
Measure	BIC	Log BF	BIC	Log BF	BIC	Log BF	BIC	Log BF	BIC	Log BF	BIC	Log BF
Total Number of Trajectories												
2	−37090		−37094		−20023		−20031		−22945		−22954	
3	−34765	4650	−34772	4644	−19207	1632	−19218	1626	−22500	890	−22513	882
4	−33413	2704	−33422	2700	−19014	386	−19027	382	−22331	338	−22347	332
5	−32745	1336	−32757	1330					−22262	138	−22278	138
6	−32399	692	−32415	684					−22242	40	−22248	60

Panel B: Group Size Model Fit Statistics; Estimated Group Size (EST) and Actual Group Size (FRAC)

Outcome	BMI	BMI	BMI	BMI	CES-D	CES-D	CES-D	CES-D	Cognition	Cognition	Cognition	Cognition
Age	Quadratic	Quadratic	Cubic	Cubic	Quadratic	Quadratic	Cubic	Cubic	Quadratic	Quadratic	Cubic	Cubic
Measure	EST	FRAC	EST	FRAC	EST	FRAC	EST	FRAC	EST	FRAC	EST	FRAC
Trajectories												
1	21.6	21.7	16.7	16.4	20.4	20.7	20.4	20.5	9.7	9.2	9.7	9.1
2	16.9	16.4	26.8	27.1	34.1	33.4	33.9	33.7	16.4	13.3	19.1	19.7
3	17.2	17.2	17.2	17.2	31.6	32.4	31.6	32.2	19.3	20.2	24.3	28.3
4	10.9	10.8	11.2	11.1	13.9	13.5	14.1	13.5	13.5	13.6	16	12.6
5	26.8	27.4	21.5	21.7					31.9	37.3	19.1	19.7
6	6.6	6.5	6.6	6.5					9.3	6.5	11.8	10.7

Panel C: Average Posterior Probability (AvePee) and Odds of Classification (OCC) Model Statistics

Outcome	BMI	BMI	BMI	BMI	CES-D	CES-D	CES-D	CES-D	Cognition	Cognition	Cognition	Cognition
Age	Quadratic	Quadratic	Cubic	Cubic	Quadratic	Quadratic	Cubic	Cubic	Quadratic	Quadratic	Cubic	Cubic
Measure	AvePee	OCC	AvePee	OCC	AvePee	OCC	AvePee	OCC	AvePee	OCC	AvePee	OCC
Trajectories												
1	95.6	79	92.9	65.2	90.9	38.9	91.3	40.9	90.5	88.6	90.7	90.9
2	93.5	70.7	93.6	39.9	88.7	15.2	88.3	14.7	78.6	18.8	81.5	18.6
3	93.5	69.1	93.6	70.4	87.9	15.7	88.3	16.3	79.7	16.4	71.2	7.7
4	97.5	318.3	97.2	276.3	92.3	74.5	93.3	85.1	79.1	24.2	80.3	21.5
5	92.9	35.7	95.5	77.4					76.3	6.9	73.4	11.7
6	97.7	603.7	97.9	661.1					86.1	60.8	84.3	40.2

Notes: Each column represents one outcome and polynomial order in age. Panel A shows the BIC and Log Bayes Factor and the rows correspond to the total number of trajectories that are modeled. In Panel B and C we show the model fit statistics by trajectory group setting the total number of trajectories to the optimal number. Panel B shows the estimated group size π_j and the group size according to the maximum posterior probability assignment rule. Panel C shows the average posterior probability and the odds of correct classification. For the outcome CES-D, we consider at most 4 trajectories since we could not obtain standard errors for larger models.

Appendix Table A4
Association of PGSs, Childhood SES and Educational Attainment with BMI-Trajectory-Group Membership from FML models with Childhood SES and Years of Education Interacted with BMI PGS

	European-Ancestry Sample						African-Ancestry Sample					
	P(Low)	P(Low-Medium)	P(Medium)	P(Medium-High)	P(High)	P(Very High)	P(Low)	P(Low-Medium)	P(Medium)	P(Medium-High)	P(High)	P(Very- High)
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)	(12)
Male	−0.111*** (0.007)	−0.012 (0.009)	0.074*** (0.010)	0.065*** (0.010)	0.015* (0.008)	−0.030*** (0.005)	0.021 (0.018)	0.101*** (0.024)	0.043 (0.027)	0.012 (0.023)	−0.113*** (0.024)	−0.064*** (0.012)
Education PGS	0.002 (0.004)	−0.005 (0.005)	−0.007 (0.006)	0.004 (0.005)	0.008* (0.004)	−0.001 (0.003)	−0.003 (0.010)	0.007 (0.011)	−0.018 (0.014)	−0.002 (0.011)	0.013 (0.013)	0.004 (0.006)
Smoking PGS	−0.004 (0.004)	−0.003 (0.005)	−0.003 (0.006)	0.007 (0.005)	0.003 (0.004)	0.001 (0.003)	−0.007 (0.009)	0.019* (0.010)	−0.020 (0.013)	0.000 (0.010)	0.001 (0.012)	0.007 (0.005)
Depression PGS	0.004 (0.004)	0.001 (0.005)	−0.007 (0.005)	0.010* (0.005)	−0.005 (0.004)	−0.005 (0.003)	0.003 (0.009)	0.017 (0.011)	0.009 (0.013)	−0.014 (0.011)	−0.011 (0.012)	−0.003 (0.006)
BMI PGS	−0.034*** (0.004)	−0.056*** (0.005)	−0.026*** (0.006)	0.033*** (0.005)	0.047*** (0.004)	0.037*** (0.003)	−0.042*** (0.011)	−0.035** (0.013)	−0.008 (0.018)	0.032* (0.015)	0.033* (0.017)	0.021** (0.008)
Wellbeing PGS	−0.000 (0.004)	−0.002 (0.005)	0.009* (0.005)	−0.000 (0.005)	−0.001 (0.004)	−0.005 (0.003)	−0.006 (0.009)	−0.002 (0.011)	0.038** (0.013)	0.004 (0.011)	−0.026* (0.013)	−0.008 (0.005)
Cognition PGS	−0.001 (0.004)	−0.001 (0.005)	0.002 (0.006)	0.007 (0.005)	−0.005 (0.004)	−0.002 (0.003)	−0.001 (0.009)	−0.014 (0.012)	0.011 (0.014)	0.003 (0.012)	0.002 (0.013)	−0.001 (0.006)
Childhood SES	0.003 (0.004)	0.006 (0.005)	−0.001 (0.005)	0.003 (0.005)	−0.002 (0.004)	−0.008*** (0.003)	0.013 (0.009)	−0.017 (0.011)	−0.014 (0.014)	0.003 (0.012)	0.013 (0.013)	0.003 (0.007)
Years of Education	0.003* (0.002)	0.008*** (0.002)	0.002 (0.002)	−0.002 (0.002)	−0.008*** (0.002)	−0.003* (0.001)	−0.004 (0.003)	0.007** (0.003)	0.007* (0.004)	0.003 (0.004)	−0.010** (0.004)	−0.004** (0.002)
N	7357	7357	7357	7357	7357	7357	1189	1189	1189	1189	1189	1189

Notes: Marginal effects evaluated at the mean from FML regressions where the probability of individual i belonging to group j is regressed on gender, PGSs, childhood SES, years of education, cohort dummies, and the first 10 genetic principal components. The PGSs and childhood SES are standardized to have means of zero and standard deviations of one. Standard errors clustered at the household level. ***significant at 1% **significant at 5% *significant at 10%.

Appendix Table A5
Association of PGSs, Childhood SES and Educational Attainment with Depressive-Symptoms-Trajectory-Group Membership from FML models with Childhood SES and Years of Education Interacted with Depression PGS

	European-Ancestry Sample				African-Ancestry Sample			
	P(Low)	P(Low-Medium)	P(Medium)	P(High)	P(Low)	P(Low-Medium)	P(Medium)	P(High)
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
Male	0.114*** (0.010)	0.001 (0.010)	−0.072*** (0.008)	−0.042*** (0.004)	0.058** (0.021)	0.072** (0.027)	−0.049* (0.026)	−0.081*** (0.016)
Education PGS	0.005 (0.006)	0.004 (0.005)	−0.004 (0.005)	−0.005* (0.003)	0.004 (0.011)	0.022 (0.013)	−0.026 (0.014)	0.000 (0.009)
Smoking PGS	−0.001 (0.006)	−0.002 (0.006)	0.003 (0.005)	0.001 (0.003)	−0.012 (0.010)	0.008 (0.013)	−0.001 (0.012)	0.005 (0.008)
Depression PGS	−0.026*** (0.006)	0.007 (0.006)	0.008 (0.005)	0.011*** (0.003)	−0.018 (0.011)	−0.023* (0.013)	0.020 (0.014)	0.020 (0.010)
BMI PGS	−0.010 (0.006)	−0.005 (0.005)	0.006 (0.005)	0.009*** (0.003)	0.011 (0.013)	0.004 (0.017)	0.004 (0.017)	−0.019 (0.012)
Wellbeing PGS	0.027*** (0.006)	−0.014** (0.005)	−0.008 (0.005)	−0.006** (0.002)	0.021** (0.011)	0.000 (0.013)	−0.032** (0.013)	0.011 (0.009)
Cognition PGS	0.005 (0.006)	0.002 (0.006)	−0.005 (0.005)	−0.001 (0.003)	0.001 (0.011)	0.010 (0.014)	−0.002 (0.014)	−0.010 (0.009)
Childhood SES	0.042*** (0.006)	−0.002 (0.005)	−0.022*** (0.005)	−0.018*** (0.002)	0.015 (0.010)	0.025* (0.014)	0.003 (0.014)	−0.042*** (0.009)
Years of Education	0.027*** (0.002)	0.001 (0.002)	−0.019*** (0.002)	−0.009*** (0.001)	0.037*** (0.004)	0.001 (0.004)	−0.023*** (0.004)	−0.016*** (0.003)
N	7357	7357	7357	7537	1189	1189	1189	1189

Notes: Marginal effects evaluated at the mean from FML regressions where the probability of individual i belonging to group j is regressed on gender, PGSs, childhood SES, years of education, cohort dummies, and the first 10 genetic principal components. The PGSs and childhood SES are standardized to have means of zero and standard deviations of one. Standard errors clustered at the household level. ***significant at 1% **significant at 5% *significant at 10%.

Appendix Table A6
Association of PGSs, Childhood SES and Educational Attainment with Cognition-Trajectory-Group Membership from FML models with Childhood SES and Years of Education Interacted with Cognition PGS

	European-Ancestry Sample						African-Ancestry Sample					
	Low	Low-Medium	Medium	Medium-High	High	Very High	Low	Low-Medium	Medium	Medium-High	High	Very High
	(1)	(2)	(3)	(4)	(5)	(6)	(1)	(2)	(3)	(4)	(5)	(6)
Male	0.016*** (0.004)	−0.074*** (0.008)	0.057*** (0.009)	−0.044*** (0.005)	−0.043*** (0.008)	−0.060*** (0.005)	0.003 (0.006)	−0.013 (0.014)	0.039* (0.021)	0.061* (0.027)	−0.015 (0.017)	−0.075*** (0.017)
Education PGS	−0.008*** (0.002)	−0.021*** (0.004)	0.005 (0.005)	0.003 (0.003)	0.010** (0.005)	0.012*** (0.003)	−0.004 (0.003)	−0.021* (0.008)	0.000 (0.010)	0.020 (0.014)	0.002 (0.009)	0.003 (0.010)
Smoking PGS	−0.002 (0.002)	0.001 (0.005)	0.004 (0.005)	−0.005* (0.003)	−0.006 (0.005)	0.009*** (0.003)	−0.003 (0.002)	0.000 (0.007)	0.007 (0.010)	−0.013 (0.013)	0.008 (0.008)	−0.000 (0.008)
Depression PGS	0.001 (0.002)	0.001 (0.004)	−0.002 (0.005)	0.002 (0.003)	−0.004 (0.004)	0.003 (0.003)	0.000 (0.003)	−0.009 (0.008)	0.004 (0.010)	−0.002 (0.013)	0.002 (0.008)	0.006 (0.009)
BMI PGS	0.000 (0.002)	0.001 (0.004)	−0.001 (0.005)	−0.001 (0.003)	0.001 (0.004)	−0.001 (0.003)	0.000 (0.004)	−0.006 (0.011)	0.025* (0.013)	−0.003 (0.017)	−0.018 (0.011)	0.002 (0.011)
Wellbeing PGS	−0.001 (0.002)	−0.002 (0.004)	−0.002 (0.005)	0.001 (0.003)	0.005 (0.005)	−0.001 (0.003)	−0.003 (0.003)	0.001 (0.007)	0.004 (0.009)	−0.006 (0.013)	−0.001 (0.009)	0.005 (0.009)
Cognition PGS	0.000 (0.003)	−0.017*** (0.005)	−0.009* (0.005)	−0.000 (0.003)	0.017*** (0.005)	0.009*** (0.003)	−0.001 (0.003)	−0.003 (0.008)	0.001 (0.010)	0.004 (0.013)	0.002 (0.010)	−0.003 (0.012)
Childhood SES	−0.004* (0.002)	−0.009** (0.004)	−0.006 (0.005)	−0.001 (0.003)	0.013*** (0.005)	0.007*** (0.003)	0.001 (0.003)	−0.001 (0.008)	−0.011 (0.011)	−0.008 (0.014)	0.022** (0.010)	−0.003 (0.009)
Years of Education	−0.019*** (0.001)	−0.038*** (0.002)	−0.006*** (0.002)	0.009*** (0.001)	0.032*** (0.002)	0.022** (0.001)	−0.011*** (0.002)	−0.034*** (0.003)	−0.025*** (0.004)	0.035*** (0.005)	−0.012*** (0.004)	0.047*** (0.004)

Notes: Marginal effects evaluated at the mean from FML regressions where the probability of individual i belonging to group j is regressed on gender, PGSs, childhood SES, years of education, cohort dummies, and the first 10 genetic principal components. The PGSs and childhood SES are standardized to have means of zero and standard deviations of one. Standard errors clustered at the household level. ***significant at 1% **significant at 5% *significant at 10%.

Appendix Table A7
Tabulation of Proportion of Individuals on Good Health Trajectories

	% of individuals from EA Sample classified			
		Cognition: very-high	CESD: low	CESD: low and Cognition: very-high
Conditional on:	**BMI: low-medium**	10.9%	40.8%	5.6%
		BMI: low-medium	**Cognition: very-high**	**BMI: low-medium and Cognition: very high**
	CESD: low	22.9%	12.5%	3.2%
		BMI: low-medium	**CESD: low**	**BMI: low-medium and CESD: low**
	Cognition: Very-High	23.2%	47.3%	12%
	% of individuals from AA Sample classified			
		Cognition: very-high	CESD: low	CESD: low and Cognition: very-high
Conditional on:	**BMI: low-medium**	18.0%	21.5%	7.8%
		BMI: low-medium	**Cognition: very-high**	**BMI: low-medium and Cognition: very high**
	CESD: low	17.9%	37.4%	6.5%
		BMI: low-medium	**CESD: low**	**BMI: low-medium and CESD: low**
	Cognition: Very-High	16.9%	42.0%	7%

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