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Heterogenous Trajectories in Physical, Mental and Cognitive Health among Older Americans: Roles of Genetics and Earlier SES

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Abstract

We investigate the roles of genetic predispositions, childhood SES and adult schooling attainment in shaping trajectories for three important components of the overall health and wellbeing of older adults -- BMI, depressive symptoms and cognition. We use the Health & Retirement Study (HRS) and group-based trajectory modelling (GBTM) to identify subgroups of people who share the same underlying trajectories over ages 50-94 years. After identifying common underlying 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) schooling attainment on the probabilities of trajectory group membership. While genetic predispositions do play a part in predicting trajectory group membership, our results highlight the long arm of socioeconomic factors. Schooling attainment is the most robust predictor—it predicts increased probabilities of belonging to trajectories with BMI in the normal rage, low depressive symptoms and high initial cognition. Childhood circumstances are manifested in trajectories to a lesser extent, with childhood SES only predicting the likelihood of being on the low depressive symptoms trajectory. We also find suggestive evidence that associations of schooling attainment on the probabilities of being on trajectories with BMI in the normal rage, low depressive symptoms and high initial cognition vary with genetic predispositions.

Key Words: aging trajectories; polygenic scores; childhood socioeconomic status; schooling; HRS; GBTM

1. Introduction

With an increasing percentage of the world's population "graying", understanding factors affecting the overall health and wellbeing of older adults is of paramount importance. SES is recognized as among the most pervasive factors affecting health because it embodies an array of resources, such as money, knowledge, prestige, power, and beneficial social connections that are perceived to protect health (Addler et al. 1994; Link & Phlean 1995). Physical, mental and cognitive health—three important components of overall health—tend to decline with age on average and are related to leading causes of death and mortality in older adults (Batty et al 2016; Schulz et al. 2000; Stokes et al. 2016). Studies using growth curve modelling have found that lower SES is associated with accelerated decline in health at older ages (Hass 2008; Faul et al. 2021; Marden et al. 2017; Ramsay et al. 2011), suggesting that less affluent members of society age more rapidly than more privileged groups. Some, though, have found no associations between SES and rates of health decline (Walsemann & Ailshire 2020; Zaninotto & Lassale 2019; Wu et al. 2020), while others have found that lower SES is associated with a slower decline in health and mortality rates (Aartsen et al. 2019; Zaninotto et al. 2018).

Growth curve modelling, which is by far the most common approach for studying trajectories of health during the aging process, assumes that all individuals in the population follow a similar trajectory that varies around a single mean. However, it has long been recognized that there is heterogeneity within aging populations that affects the observed physical health and mortality patterns (Vaupel et al. 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 ageing 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 (Merikangas et al. 1994; Eaton et al. 2008; Keller et al. 1992; Solomon et al. 1997). Differences in long-term trajectories may be indicative of underlying differences in etiology. In light of these findings, growth curve modelling is an unsatisfactory modeling approach as it fails to reflect the diverse trajectories that different dimensions of health can take during the aging process.

In recognition of heterogeneity in health and resulting diversity in trajectory patterns, recent studies are increasingly using group-based trajectory modelling (GBTM), which 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., probability of membership in a group for each individual) separately for each group (Nagin 2005). 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. 2020), 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). In addition to identifying trajectories, GBTM can be used to identify predictor and outcome variables associated with different trajectories. For example, Song et al. (2016) identified five trajectories for body shape from age 5 to 50 in the Nurse's Health Study and Health Professionals Follow-up Study. They then examined associations between trajectory group membership and mortality and found that individuals in the "good" trajectory had the lowest mortality. Song et al. (2018) identified four trajectories of body fatness from age 5 to 65 and examined associations between a genetic risk score for BMI (that was based on 97 genetic variants associated with BMI in adulthood) with trajectory group membership. They found that individuals with a higher genetic risk score were more likely to belong to the bad trajectory. Using

the Whitehall II cohort Elovainio et al. (2018) identified three distinct cognition trajectories over ages 35-55 that differed in baseline cognition levels but not in shape. They focused on variables pertaining to social relations as predictors and found that more frequent social contacts and having spouses were associated with belonging to more favorable cognition trajectories.

Building on this prior research, the purpose of this study is to understand how early-life determinants—genetic dispositions (measured via polygenic scores), childhood SES and adult schooling attainment—shape trajectory membership for physical (body mass index, BMI) and mental (depressive symptoms) health and cognition for older adults over ages 50-94 years in the Health & Retirement Study (HRS). 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 polygenic scores, childhood SES and adult schooling with the *probability* on being on a particular trajectory.

Several novel and key findings emerge from this approach: First, we document persistent and often parallel trajectories for physical, mental and cognitive health, a finding that indicates that major differences in health across substantial age ranges are relatively stable in the HRS population. Second, our analyses reveal how early-life determinants affect these health trajectories at older ages. Specifically, while polygenic scores in our analys predict trajectory group membership across all outcomes studied here, schooling attainment is the most robust predictor across the health domains. Childhood circumstances are related to later-life health trajectories to a lesser extent, with childhood SES predicting trajectory group membership for mental health only. Third, in line with studies on differential susceptibility (or stress diathesis) showing that the same environmental shocks can have heterogeneous impacts on health (Amin et al. 2019; Barcellos et al. 2018; Cook & Fletcher 2014; Fletcher et al. 2021; Noorman & Greenfield 2018;), we also find suggestive evidence that associations of schooling attainment on the probabilities of being on trajectories with BMI in the normal rage, low depressive symptoms and high initial cognition vary with genetic predispositions vary with genetic predispositions. To our best knowledge, this study is the first to employ GBTM to examine how genetics, childhood SES, adult schooling attainment and their interactions predict trajectories of health across a 40-year time period in late-middle to old age.

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 on income and wealth, health, cognition, use of healthcare services; work and retirement, and family connections. 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 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 1992-2018) and the CODA cohort (followed from 1998-2018), where individuals are observed from age 50 to 94 years.

2.2 Outcome Measures

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. The CES-D score ranges from 0 to 8, with higher values corresponding to poorer mental health. Individuals with a CES-D score of 4 or more are classified as being depressed (Steffick 2000). The HRS includes several tests to assess cognitive function. The tests included are 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. A summary measure of cognitive function is created by summing the scores to these tests. The cognition score ranges from 0 to 35.

2.3 SES Measures

We use the childhood SES index created by Vable et al. (2007), 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 completed grades of schooling. We operationalize adult SES through the respondents' grades of schooling attainment.

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 1,271 SNPs as genome-wide significant predictors ($p<5x10^{-8}$), of educational attainment. The PGS for individual *i* (equation 1) is a weighted average across the number of SNPs (n) of the number of reference alleles A (0, 1 or 2) at that SNP.

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

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). Lee et al. (2018) find that the educational attainment PGS explains about 11-13% of the variation in education and 7-10% of the variance in cognitive performance in EA populations.

HRS collection of genetic data started in 2006. Genotype data on over 19,000 HRS participants were obtained using the Illumina HumanOmni2.5 BeadChips. The HRS research team has constructed PGSs for a range of traits, using of all SNPs identified in the relevant GWAS, as this increases predictive power. Specific details of PGS construction 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. 2018), (3) subjective wellbeing (Okbay et al. 2016), (4) ever/current smoker (Furberg et al. 2010), (5) educational attainment (Lee et al. 2018), and (6) cognition (Lee et al. 2018).

2.5 Analytical Sample

The HRS provides publicly available constructed PGSs for 12,090 EA individuals and 3,100 African Americans (AA) ancestry individuals. The HRS has not constructed PGSs for Hispanics. We merge the PGS datasets with the RAND HRS dataset (version V1), which is a cleaned and streamlined version of the HRS. There are 7,369 EA and 1,192 AA individuals from the HRS, AHEAD and CODA cohorts with genetic data. After dropping individuals with missing data, the final estimation sample consists of 7,357 EA and 1,189 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. Figure 1 shows the cumulative dropout rate due to mortality by age in our analytical samples. Our analytic design explicitly accounts for death among respondents, which we explain in the next section.

3. Analytical Strategy

3.1 Group-Based Trajectory Modelling (GBTM)

GBTM is a specialized application of finite mixture modelling. 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 represent individual $i's$ age when each of those outcomes is recorded (i.e., age_{it}). The distribution of the outcome is denoted $P(Y_i|Age_i)$. GBTM assumes that there are J underlying trajectory groups. The likelihood for each individual i condition on the number of groups J is given by equation (2), where π_j is the probability of membership in group j.

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

Trajectories are modelled with polynomial functions of age. The model assumes that the random variables y_{it} are independent conditional on membership in group j. The likelihood can thus be written as,

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

where p(.) is the distribution of y_{it} conditional on membership in group j and the age of individual i at time t. We use the censored normal distribution to estimate trajectories for BMI, depressive symptoms and cognition, and a quadratic in age to model the link between age and the outcomes:

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

where $\beta_0, \beta_1, \beta_2$, are parameters that determine the shape of trajectory j and $u_{it}$is an error term. Each trajectory is estimated using a unique set of parameters. The basic model provides a predicted shape for each trajectory, an estimated proportion of the sample at baseline that most likely belong to each group, and for each individual the estimated probabilities of belonging to each group (posterior probabilities of group membership).

The basic model assumes that trajectory group membership is independent of attrition. Haviland et al. (2011) have extended the basic model to allow the dropout probability to vary as a function of observed outcomes prior to dropout and covariates. The elements of Y_i, y_{it}, are redefined to incorporate dropout information. As before y_{it} equals its realized value prior to dropout. At the time of dropout and thereafter y_{it} is designated as missing. The revised likelihood specifies the joint probability of realized values prior to dropout and their missingness thereafter.

Suppose that individuals are measured over a total of T measurement occasions. Let $w_{it} = 1$ if individual i dropped out by $t \leq T$ and 0 otherwise; t_i = the period $t > 1$ that individual i drops out and $T + 1$ if individual i does not drop out; and Θ_t = the probability of dropout in period $2 \leq t \leq T$ given membership in group J. The probabilities of dropout are dependent over time since $w_{it} = 0$ in a given period implies $w_{it} = 0$ in prior periods. Similarly, $w_{it} = 1$ in a given period implies $w_{it} = 1$ in subsequent periods. To account for dropout at $t_i < T + 1$ and for the attendant data censoring equation (3) must be altered. For each period up to t_i for which there are data, the probability of the observed outcome given membership in group j is $p(y_{it}|w_{it} = 0, age_{it}, j)\left(1 - \Theta_t^j\right)$. Multiplying across $t_i - 1$ periods prior to dropout for which there are data the probabilities become $\prod_{t=1}^{t_i-1} p(y_{it}|w_{it} = 0, age_{it}, j)(1 - \Theta_t^j)$. Finally, to account for censoring due to dropout from period t_i onward, this probability must be multiplied by the probability of dropout at $t_i, \Theta_j^{t_i}$. Equation (3) in its more general form is:

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

Equation (5) is substituted into equation (2) to form the unconditional likelihood for individual i which is maximized. The model allows 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 function of the outcome prior to dropout, gender, childhood SES, grades of schooling, and the PGSs using the logit distribution.

Inferences about the optimal number of trajectories are made using the combination of criteria laid out in Nagin (2005): (i) the Akaike information criterion (AIC), with lower absolute values indicating a better fit; (ii) the Bayesian information criterion (BIC), with lower absolute values indicating a better fit; (iii) the log Bayes factor (2ΔBIC) > 10; (iv) trajectory group size ≥5% of the sample; (v) average posterior probability (AvePP) > 0.70; (vi) the odds of correct classification (OCC) > 5 for all groups; and (vii) model interpretability. 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 models the complete set of GBTM posterior probabilities.[1] 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). In the FML model the specification linking covariates (x_i) to the posterior probability for individual i of belonging to group j $\left(y_{ij}\right)$ for $j = 1, \ldots . M$is given by:

$$(6) E\left[y_{ij}\middle|x_i\right] = \frac{exp(x_i\beta_j)}{\sum_{h=1}^{M} exp(x_i\beta_h)}$$

As covariates we include a dummy variable for being male, the PGSs, the childhood SES index, grades of schooling attainment, indicator variables for year of birth, cohort 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. If these populations also systematically have different schooling outcomes, then this could lead to a spurious correlation between the PGSs and the outcome. A common approach to alleviate concerns about population stratification is to limit analyses to ethnically homogenous groups and include the top 10 genetic principal components as controls (Price et al. 2006). To allow for comparisons between the associations of genetics and SES, the PGSs, childhood SES index and grades of schooling are all standardized to have a mean of zero and standard deviation of one.

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

$$(7) E\left[y_{ij}\middle|x_i\right] = \frac{1}{1 + \sum_{h=2}^{M} exp(x_i\beta_h)} for j = 1$$

and

$$E\left[y_{ij}\middle|x_i\right] = \frac{exp\left(x_i\beta_j\right)}{1 + \sum_{h=2}^{M} exp(x_i\beta_h)} for j = 2, \ldots M$$

By using FML we are able to estimate associations of PGSs and SES with the probability of belonging to each trajectory group. Due to the normalization, the interpretation of the signs and magnitudes of the coefficients from FML regressions is difficult. For this reason, we report marginal effects evaluated at the mean in the empirical analysis which are readily interpretable. The marginal effects sum to zero across the outcomes. We used the fmlogit command in Stata 15 to estimate the FML regressions.

[1] 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 (ie., 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.

4. Results

4.1 Summary Statistics

Summary statistics of the HRS EA and AA samples used in the present analysis are provided in Table 1.[2] 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 schooling 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

Results for BMI are shown in Figure 2 and Table 2. Figure 2 shows four distinct trajectories for the EA sample and three for the AA sample. For both groups a small proportion (5% for the EA sample and 7% for the AA sample) are on the high trajectory, which indicates obese class 2 ($35 \leq BMI \leq 39.9$) in the EA sample over most of the age range, and obese class 3 ($BMI \geq 40$) in the AA sample over the whole age range. In the AA sample the BMI of individuals on the high trajectory increases till about age 80 and slightly decreases afterwards. EA individuals on the high trajectory on average have increasing BMI till about age 70 and decreasing BMI thereafter. The majority of the EA individuals are on the low-medium trajectory (43%) representing BMI in the overweight range ($25 \leq BMI < 30$) over the whole age range. Half of AA individuals are on the low trajectory, which has BMI in the overweight range to about age 70, and then BMI in the normal weight range ($18.5 \leq BMI < 25$) from age 70 to 90.

Marginal effects evaluated at the mean from the FML regressions are presented in Table 2. The results show that being male is associated with higher probabilities of being on the middle (low and low-medium) trajectories in the EA sample, and with a higher probability of being on the low trajectory in the AA sample. The BMI PGS is associated with the probabilities of being on all trajectories, apart from the low-medium trajectory in the EA sample. The largest association of the BMI PGS for both groups is with the low trajectory. A one standard deviation increase in the BMI PGS decreases the probability of being on the low trajectory by 7.1 percentage points in the EA sample and 9.2 percentage points in the AA sample. None of the other PGSs are statistically significantly associated with trajectory group membership in the EA sample. In the AA sample the depression PGS has a considerable association with membership of the low trajectory. A one standard deviation increase in the depression PGS increases the probability of being on the low trajectory by 3.7 percentage points, which is large relative to the association of the BMI PGS. Childhood SES does not affect the probabilities of being on any of the trajectories. The marginal effects are small in magnitude and statistically insignificant. Schooling attainment affects the probabilities of being on the low, medium-high trajectories in the EA sample. Similar to the BMI PGS, the strongest influence of schooling attainment is on the likelihood of being on the low trajectory—a one standard deviation in grades of schooling increases the probability of being on the low trajectory by 2.3 percentage points. The marginal effects for schooling attainment in the AA sample are not statistically significant, but they are fairly large. For example, a one standard deviation increase in grades of schooling increases the probability of being on the low trajectory by 2.9 percentage points, similar to the EA sample.

[2] 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.

4.3 Depressive Symptoms Trajectories

Results for depressive symptoms are shown in Figure 3 and Table 3. Four trajectories were again identified for the EA sample and three for the AA sample. A substantially higher proportion of individuals are on the high trajectory in the AA sample (23%) compared to the EA sample (7%). The high trajectory for the EA sample corresponding 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 50 but have a declining CES-D score over the whole age range. The medium trajectory which has 22% of individuals on it has the steepest slope in the EA sample. A third of the individuals are on the low trajectories in both groups, which are flat and stable.

Marginal effects from the FML regressions in Table 3 show that being male is associated with higher (lower) probability of being on the low (high) trajectory in the EA and AA samples. The depression PGS has similar associations with low trajectory group membership in both samples. A one standard deviation increase in the depression PGS decreases the probability of being on the low trajectory by 2.8 percentage points in the EA sample and 2.1 percentage points in the AA sample, though the latter is not statistically significant. Childhood SES and schooling attainment both affect the likelihood of being on the low and high trajectories for both groups, with larger associations for schooling attainment. The associations for grades of schooling in the AA sample are double the size of the associations in the EA sample. For example, a one standard deviation increase in grades of schooling increases the probability of being on the low trajectory by 7 percentage points in the EA sample and 15.2 percentage points in the AA sample.

4.4 Cognition Trajectories

Results for cognition are shown in Figure 4 and Table 4. The four cognition trajectories for EA individuals in Figure 4 all show declining slopes above age 60, with the low trajectory (including 5% of individuals) having the fastest decline. Five cognition trajectories were identified for the AA sample, which have decreasing slopes but are much flatter compared to the trajectories for the EA sample.

Marginal effects in Table 4 show that being male is associated with lower probabilities of being on the high trajectories in both the EA and AA samples. In the EA sample the educational attainment PGS predicts membership of all trajectory groups apart from the medium trajectory. The largest associations are for the low-medium and high trajectories. A one standard deviation increase in the educational attainment PGS increases (decreases) the probability of being on the high (low-medium) trajectory by about 2 percentage points. The cognition PGS also has a similar association with membership of these trajectory groups. In the AA sample, the educational attainment PGS only predicts membership of the low-medium trajectory. There are no associations between childhood SES and trajectory group membership in the AA sample. There are some small associations in the EA sample. A one standard deviation increase in the childhood SES index increases the probability of being on the high trajectory by 1.8 percentage points. Schooling attainment is associated with all trajectory group membership in both samples. The largest associations are with the high trajectory. A one standard deviation increase in grades of schooling increases the probability of being on the high trajectory by 11.8 percentage points in the EA sample and 12.1 percentage points in the AA sample.

5. Discussion

This study attempts to understand 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 analyses are more flexible

than other growth curve models because they allow 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 for each health outcomes and subpopulation (EA and AA individuals) three to five distinct trajectories. 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 are fairly persistent during the aging process. The number of trajectories identified, 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 different 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.

After identifying trajectories, we then estimated associations of PGSs, childhood SES and schooling attainment with probabilities of trajectory group membership. The findings for the likelihood of belonging to BMI in the normal rage, low depressive symptoms and high initial cognition trajectories are summarized in Table 5. The results show that, as expected, genetic propensities affect trajectory group membership, 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 high initial cognition trajectory. Schooling attainment is the most robust predictor of health trajectories, increasing the probabilities of belonging to these trajectories. The relative importance of schooling differs across the health domains. Genetic factors are the strongest predictors for BMI trajectories. In the EA sample, the association of the BMI PGS with probabilities of belonging to the normal range (low) BMI trajectory was three times as large as the association of grades of schooling. In contrast for mental and cognitive health, schooling attainment had the largest associations with trajectory group membership in both the EA and AA samples. This lends support to the cumulative disadvantage hypothesis whereby those disadvantaged by less schooling in early life are potentially exposed to greater social inequality thereafter. Childhood circumstances are manifested in trajectories to a lesser extent, with childhood SES only predicting the likelihood of being on the low depressive symptoms trajectory.

While schooling attainment and childhood SES to a lesser extent predict trajectory group membership, the associations may vary by genetic background. The diathesis-stress model (Ellis et al. 2011) holds that unhealthy environments (low schooling in our context) trigger risk alleles, while healthy environments (high schooling) 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, and interacting more with other healthy peers, whereas high school dropouts are more likely to experience financial stress due to having a low income or being unemployed, lead an unhealthy lifestyle and interact with other depressed peers. Some recent studies have found empirical evidence of interactions between genetic background and childhood SES/schooling. Using the Wisconsin Longitudinal Study Amin et al. (2019) find some evidence that the effect of a depressive symptoms PGS on mental health is smaller for college graduates than non-college graduates. Also using the Wisconsin Longitudinal Study, Moorman & Greenfield (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 schooling 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 schooling effects on body size in the UK Biobank are larger for those with a higher BMI PGS.

Given previous evidence on genetic-SES interplay, we interacted grades of schooling 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 to examined whether associations of SES on trajectory group membership vary by genetic propensities. The marginal effects of schooling attainment and childhood SES evaluated at different values of the PGSs are shown in Figures 5-7 (regression results are in Appendix A). Overall, there is some suggestive evidence that the associations of schooling attainment on the probabilities of being on "good" trajectories vary by genetic predispositions. Figure 5 shows that the marginal effects of grades of schooling on the probabilities of being on the low trajectories are higher at lower values of the BMI PGS for both EA and AA individuals, though the estimates are more imprecise for the latter. Figure 6 shows that the marginal effects of grades of schooling on the probabilities of being on the low and high trajectories are higher at lower values of the depression PGS in both the EA and AA samples. In Figure 7 the marginal effects of grades of schooling on the probabilities of being on the high trajectories varies by the cognition PGS for both EA and AA individuals.

There are limitations with our study. First, our study is 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 education PGS are likely to be highly educated and may provide a more nurturing environment that affects child outcomes. Second, though we conduct the analysis for 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 is available in the HRS, we are not able to account for selection (due to mortality or refusals) of individuals for whom PGS data is 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 is 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.

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Figure 1: Cumulative Dropout Fraction by Age

European Ancestry Sample

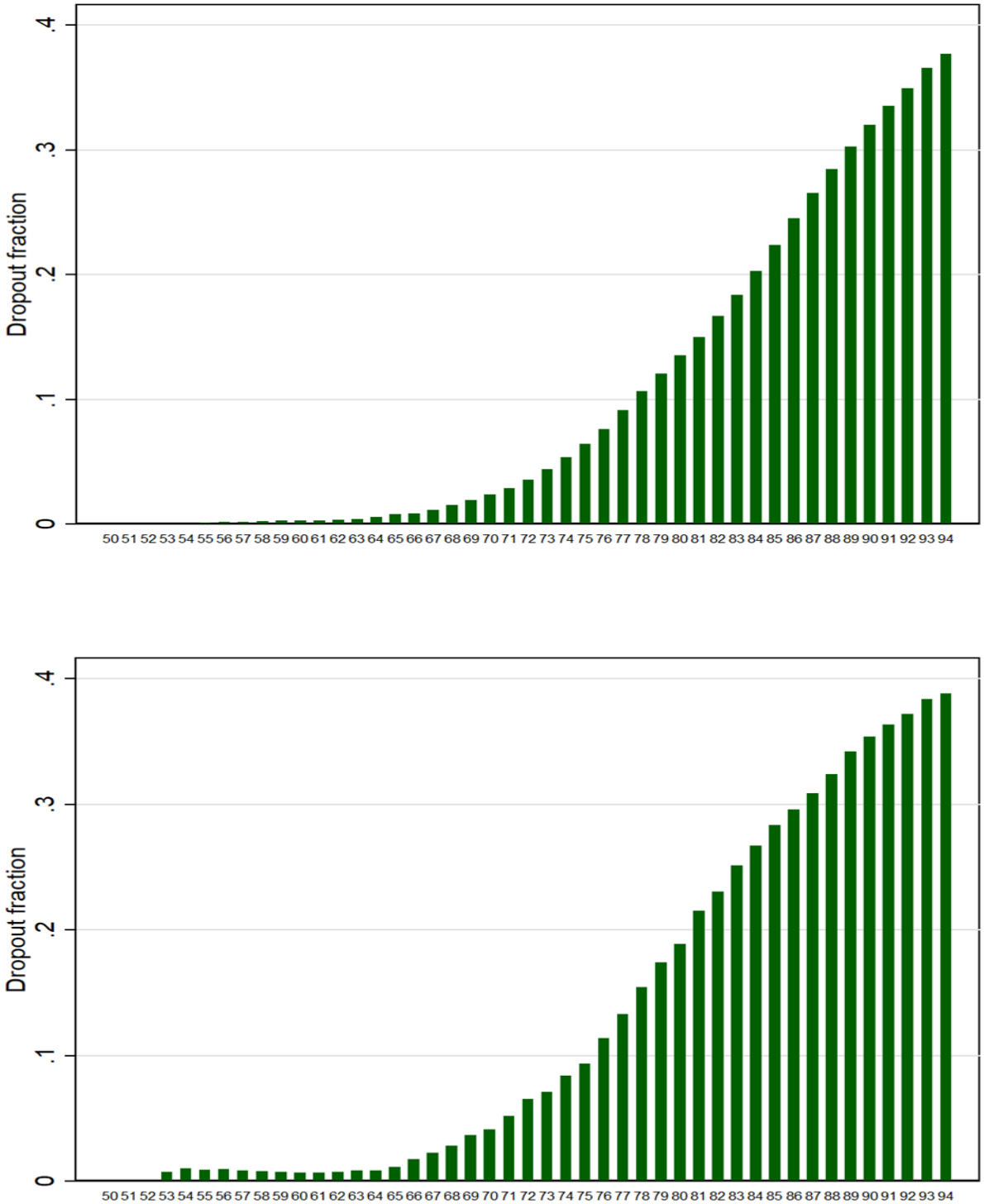


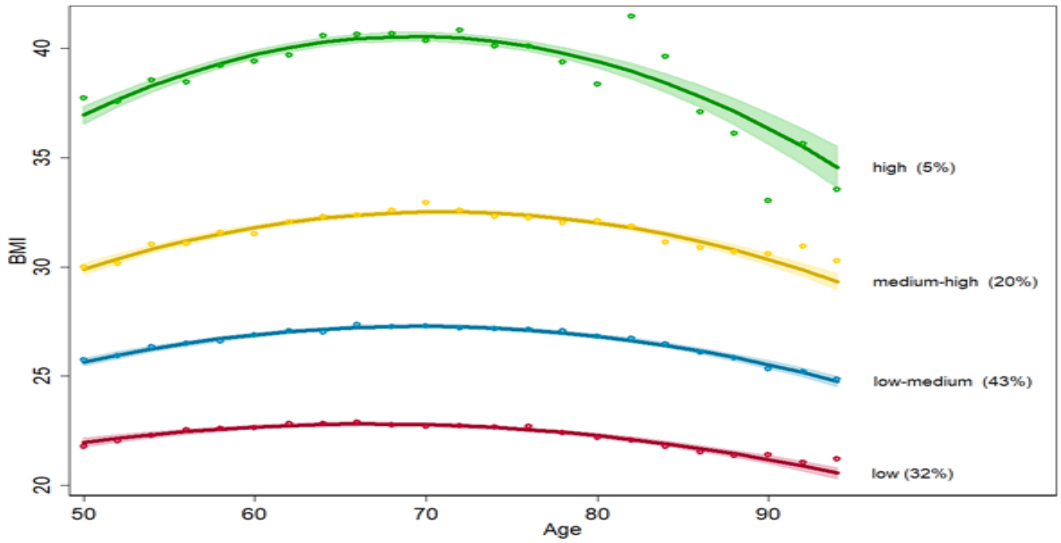
Table 1: Summary Statistics

	European Ancestry Sample				African American 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	1933.42	8.41	1905.00	1979.00	1935.44	8.66	1906.00	1969.00
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
Grades of Schooling	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

Figure 2: BMI Trajectories

European Ancestry Sample



African American Ancestry Sample

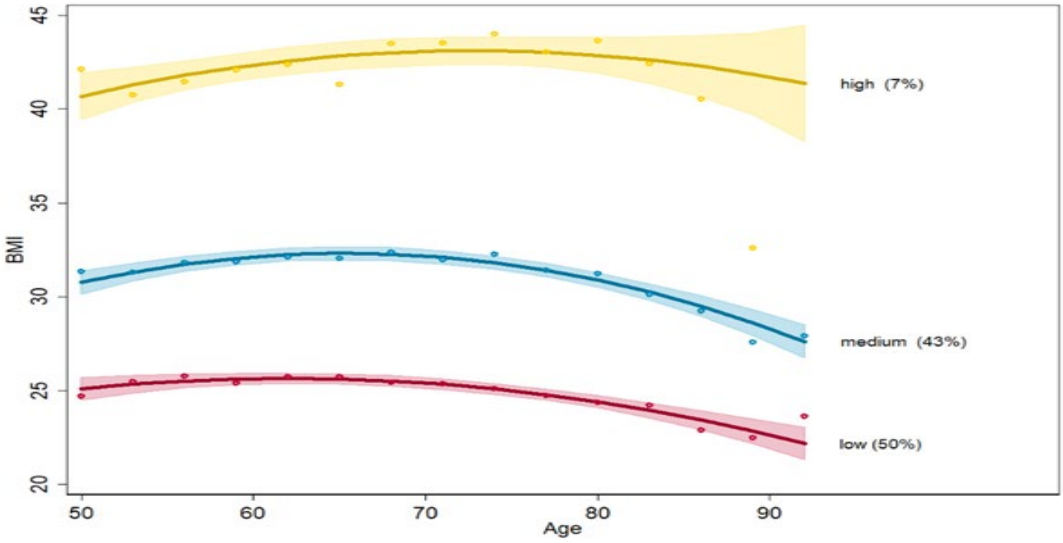


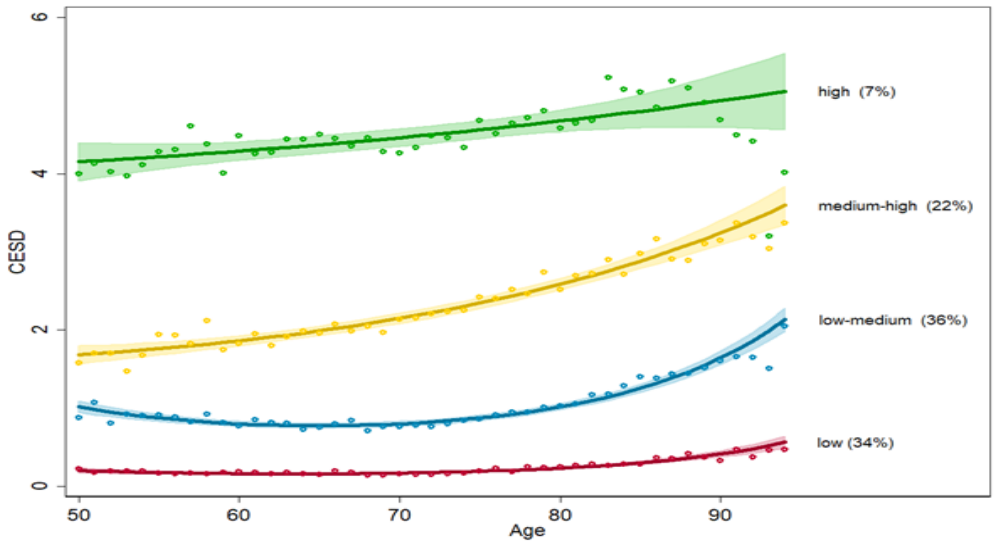
Table 2: Association of PGSs, Childhood SES and Schooling Attainment with BMI Trajectory Group Membership

	European Ancestry Sample				African American Ancestry Sample		
	P(Low)	P(low-Medium)	P(Medium)	P(High)	P(Low)	P(Medium)	P(High)
	(1)	(2)	(3)	(4)	(5)	(6)	(7)
Male	-0.102**	0.097***	0.021**	-0.016***	0.156***	-0.079**	-0.077***
	(0.009)	(0.010)	(0.008)	(0.004)	(0.027)	(0.027)	(0.012)
Education PGS	-0.007	-0.001	0.006	0.001	-0.010	0.003	0.007
	(0.005)	(0.005)	(0.004)	(0.002)	(0.014)	(0.014)	(0.006)
Smoking PGS	-0.011*	0.008	0.003	0.000	-0.012	0.004	0.008
	(0.005)	(0.005)	(0.005)	(0.002)	(0.013)	(0.013)	(0.005)
Depression PGS	0.006	-0.001	-0.004	-0.001	0.037**	-0.030*	-0.007
	(0.005)	(0.005)	(0.004)	(0.002)	(0.014)	(0.014)	(0.006)
BMI PGS	-0.071***	-0.002	0.051***	0.022***	-0.092***	0.071***	0.021*
	(0.005)	(0.005)	(0.004)	(0.002)	(0.018)	(0.018)	(0.008)
Wellbeing PGS	0.001	0.009	-0.009*	-0.002	0.022	-0.015	-0.006
	(0.005)	(0.005)	(0.004)	(0.002)	(0.014)	(0.014)	(0.005)
Cognition PGS	0.000	0.004	-0.002	-0.002	-0.002	0.004	-0.002
	(0.005)	(0.005)	(0.004)	(0.002)	(0.015)	(0.014)	(0.006)
Childhood SES	0.008	0.000	-0.006	-0.003	-0.018	0.018	0.001
	(0.005)	(0.005)	(0.004)	(0.002)	(0.014)	(0.014)	(0.007)
Grades of Schooling	0.023***	-0.001	-0.019***	-0.003	0.029*	-0.018	-0.012
	(0.005)	(0.005)	(0.004)	(0.002)	(0.015)	(0.014)	(0.006)

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, grades of schooling, year of birth indicators, cohort dummies, and the first 10 genetic principal components. The PGSs, childhood SES and grades of schooling are standardized to have mean of zero and standard deviation of one. Standard errors clustered at the household level. ***significant at 1% **significant at 5% *significant at 10%

Figure 3: Depressive Symptoms Trajectories

European Ancestry Sample



African American Ancestry Sample

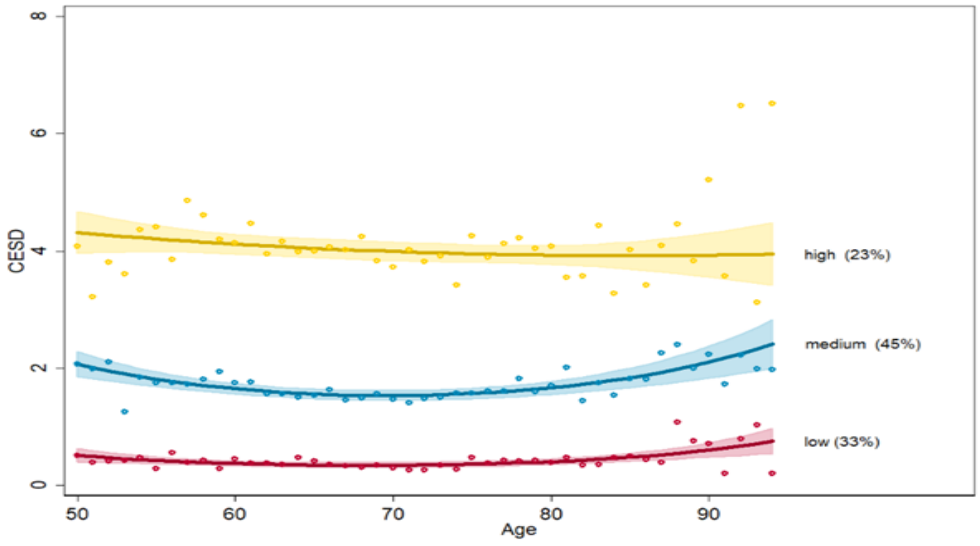


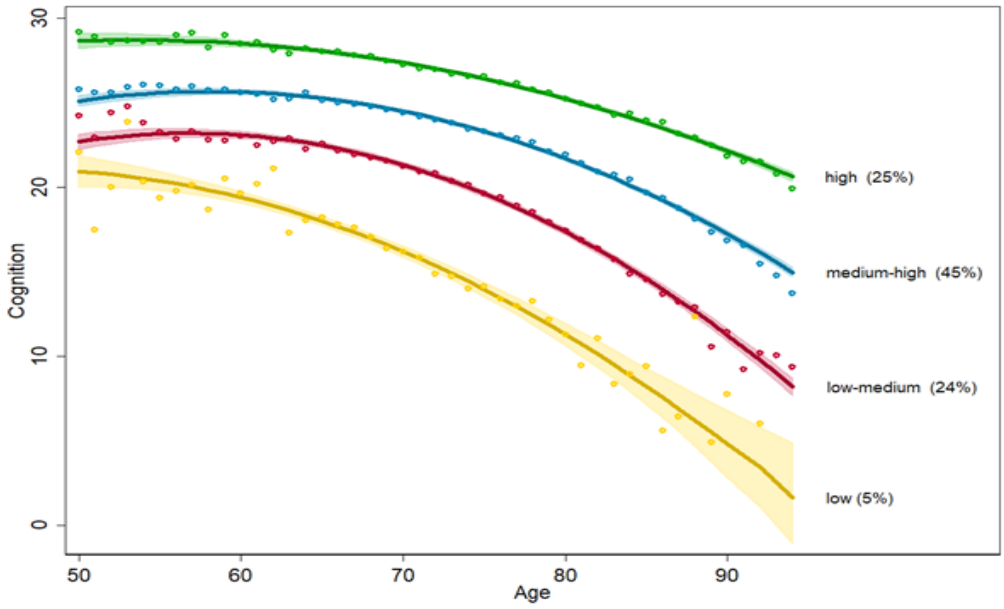
Table 3: Association of PGSs, Childhood SES and Schooling Attainment with Depressive Symptoms Trajectory Group Membership

	European Ancestry Sample				African American Ancestry Sample		
	P(Low)	P(Low-Medium)	P(Medium)	P(High)	P(Low)	P(Medium)	P(High)
	(1)	(2)	(3)	(4)	(5)	(6)	(7)
Male	0.114***	-0.000	-0.071***	-0.042***	0.099***	0.007	-0.105***
	(0.010)	(0.010)	(0.008)	(0.004)	(0.028)	(0.028)	(0.022)
Education PGS	0.005	0.004	-0.004	-0.005*	0.031*	-0.024	-0.007
	(0.006)	(0.005)	(0.005)	(0.003)	(0.014)	(0.015)	(0.012)
Smoking PGS	-0.001	-0.003	0.004	0.000	-0.013	0.015	-0.002
	(0.006)	(0.006)	(0.005)	(0.003)	(0.013)	(0.014)	(0.011)
Depression PGS	-0.028***	0.009	0.009	0.010***	-0.021	0.002	0.020
	(0.006)	(0.005)	(0.005)	(0.003)	(0.014)	(0.015)	(0.013)
BMI PGS	-0.009	-0.006	0.007	0.008**	0.031	-0.015	-0.016
	(0.006)	(0.005)	(0.005)	(0.003)	(0.018)	(0.019)	(0.016)
Wellbeing PGS	0.028***	-0.015**	-0.007	-0.006*	0.020	-0.018	-0.001
	(0.006)	(0.005)	(0.005)	(0.002)	(0.014)	(0.014)	(0.012)
Cognition PGS	0.005	0.002	-0.005	-0.001	-0.005	0.008	-0.003
	(0.006)	(0.006)	(0.005)	(0.003)	(0.015)	(0.015)	(0.012)
Childhood SES	0.042***	-0.003	-0.022***	-0.017***	0.031*	0.015	-0.047***
	(0.006)	(0.005)	(0.005)	(0.002)	(0.014)	(0.014)	(0.013)
Grades of Schooling	0.070***	0.003	-0.049***	-0.024***	0.152***	-0.070***	-0.083***
	(0.006)	(0.006)	(0.005)	(0.002)	(0.016)	(0.015)	(0.012)

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, grades of schooling, year of birth indicators, cohort dummies, and the first 10 genetic principal components. The PGSs, childhood SES and grades of schooling are standardized to have mean of zero and standard deviation of one. Standard errors clustered at the household level. ***significant at 1% **significant at 5% *significant at 10%

Figure 4: Cognition Trajectories

European Ancestry Sample



African American Ancestry Sample

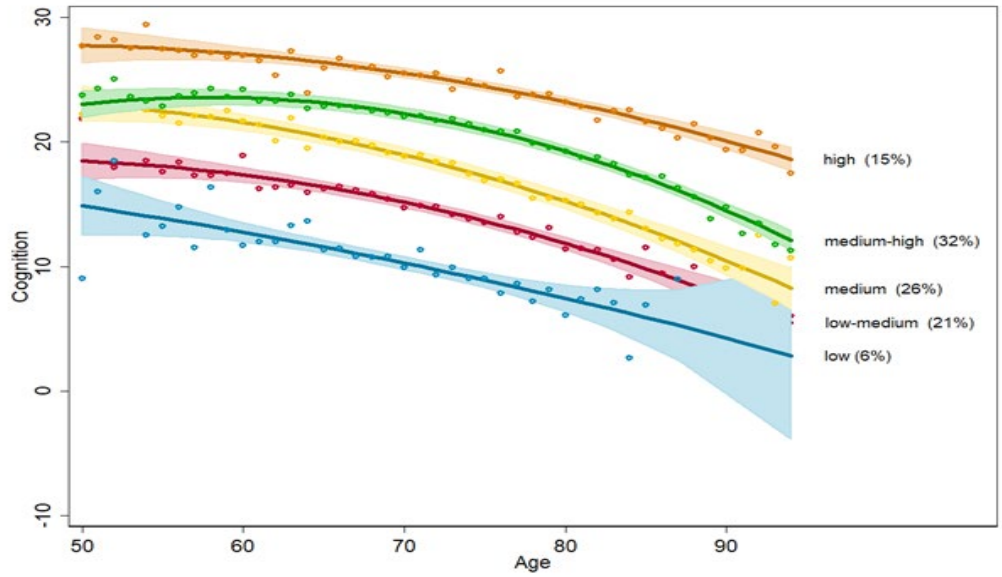


Table 4: Association of PGSs, Childhood SES and Schooling Attainment with Cognition Trajectory Group Membership

	European Ancestry Sample				African American Ancestry Sample				
	P(Low)	**P(Low-Medium)**	**P(Medium)**	**P(High)**	**P(Low)**	**P(Low-Medium)**	**P(Medium)**	**P(Medium-High)**	**P(High)**
	(1)	**(2)**	**(3)**	**(4)**	**(5)**	**(6)**	**(7)**	**(8)**	**(9)**
Male	0.012***	0.078***	0.010	-0.100***	0.002	-0.012	0.026	0.038	-0.054***
	(0.003)	(0.009)	(0.010)	(0.008)	(0.006)	(0.021)	(0.024)	(0.027)	(0.014)
Education PGS	-0.007***	-0.023***	0.008	0.022***	-0.005	-0.027*	0.007	0.024	0.001
	(0.002)	(0.005)	(0.005)	(0.005)	(0.003)	(0.011)	(0.012)	(0.013)	(0.008)
Smoking PGS	-0.002	0.003	-0.006	0.005	-0.003	0.009	0.010	-0.015	-0.001
	(0.001)	(0.005)	(0.005)	(0.005)	(0.003)	(0.010)	(0.012)	(0.012)	(0.007)
Depression PGS	0.002	-0.002	-0.002	0.002	0.002	-0.007	0.012	-0.009	0.003
	(0.002)	(0.005)	(0.005)	(0.005)	(0.003)	(0.011)	(0.012)	(0.012)	(0.007)
BMI PGS	-0.001	0.004	-0.002	-0.001	-0.000	-0.012	0.016	-0.005	0.001
	(0.002)	(0.005)	(0.005)	(0.005)	(0.004)	(0.015)	(0.015)	(0.017)	(0.009)
Wellbeing PGS	-0.000	-0.003	0.001	0.002	-0.003	-0.002	0.007	-0.005	0.003
	(0.002)	(0.005)	(0.005)	(0.005)	(0.003)	(0.010)	(0.012)	(0.012)	(0.007)
Cognition PGS	-0.002	-0.019***	-0.002	0.024***	0.001	0.009	-0.014	0.002	0.003
	(0.002)	(0.005)	(0.005)	(0.005)	(0.003)	(0.011)	(0.012)	(0.013)	(0.008)
Childhood SES	-0.003	-0.011*	-0.004	0.018***	0.001	0.000	0.001	0.002	-0.003
	(0.002)	(0.005)	(0.005)	(0.005)	(0.003)	(0.011)	(0.012)	(0.013)	(0.007)
Grades of Schooling	-0.030***	-0.114***	0.027***	0.118***	-0.039***	-0.167***	-0.049***	0.135***	0.121***
	(0.002)	(0.006)	(0.006)	(0.005)	(0.006)	(0.015)	(0.015)	(0.018)	(0.010)

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, grades of schooling, year of birth indicators, cohort dummies, and the first 10 genetic principal components. The PGSs, childhood SES and grades of schooling are standardized to have mean of zero and standard deviation of one. Standard errors clustered at the household level. ***significant at 1% **significant at 5% *significant at 10%

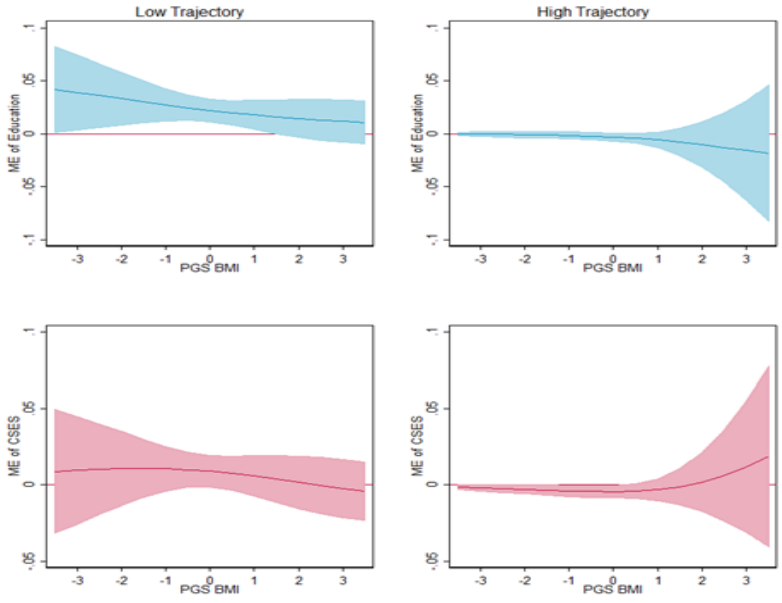
Table 5: Summary of Association of PGS, Childhood SES and Schooling Attainment with Good Health Trajectory Membership

Sample	European	African American	European	African American	European	African American
Outcome	BMI	BMI	Depressive Symptoms	Depressive Symptoms	Cognition	Cognition
Trajectory Group	Low	Low	Low	Low	High	High
Trajectory Proportion	32	50	34%	33%	25%	15%
Trajectory Description	BMI in normal weight range over age 50-90	BMI in overweight range up to age 70 and BMI in normal weight range thereafter	Persistently low depressive symptoms over ages 50-90	Persistently low depressive symptoms over ages 50-90	High initial cognition, decreasing over age 50-90	High initial cognition, decreasing over age 50-90
Predictors						
Male						
Education PGS	—	—	—			—
Smoking PGS	—	—	—	—	—	—
Depression PGS	—			—	—	—
BMI PGS			—	—	—	—
Wellbeing PGS	—	—		—	—	—
Cognition PGS	—	—	—	—		—
Childhood SES	—	—			—	—
Grades of Schooling						

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.

Figure 5: Marginal Effects of Schooling and Childhood SES with BMI Trajectory Group Membership by BMI PGS

European Ancestry Sample



African American Ancestry Sample

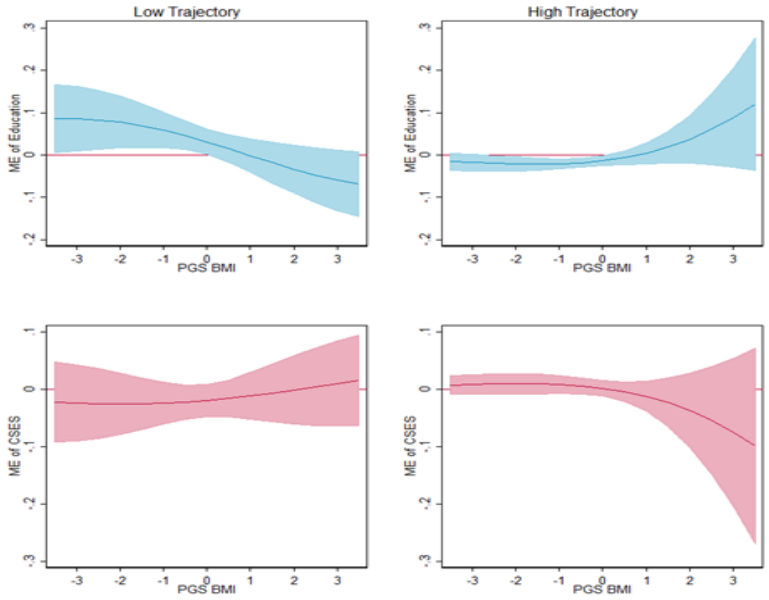
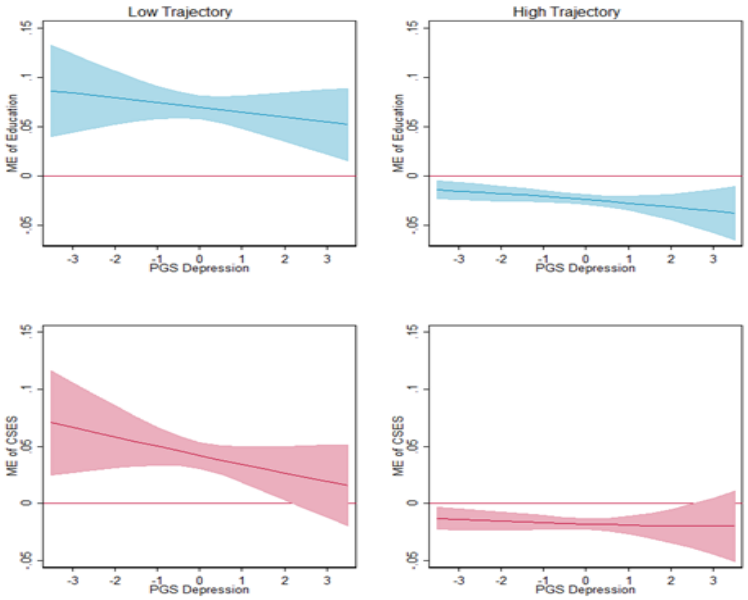


Figure 6: Marginal Effects of Schooling and Childhood SES with Depressive Symptoms Trajectory Group Membership by Depression PGS

European Ancestry Sample



African American Ancestry Sample

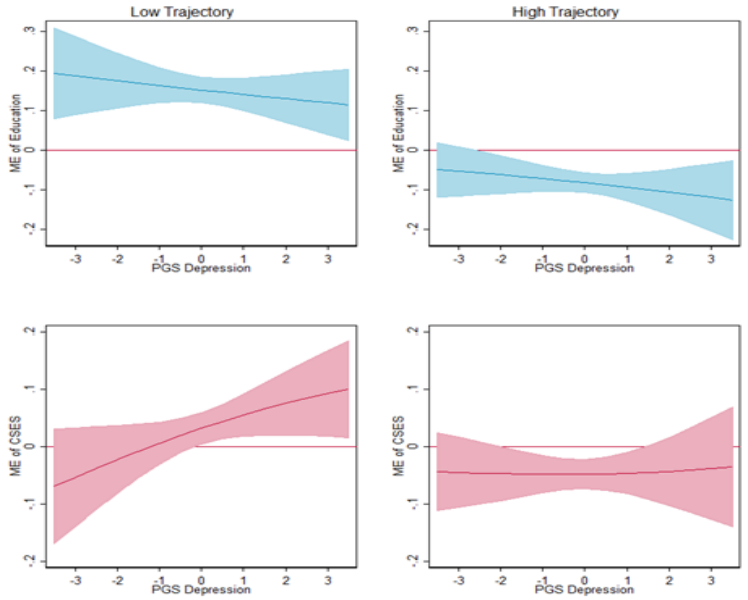
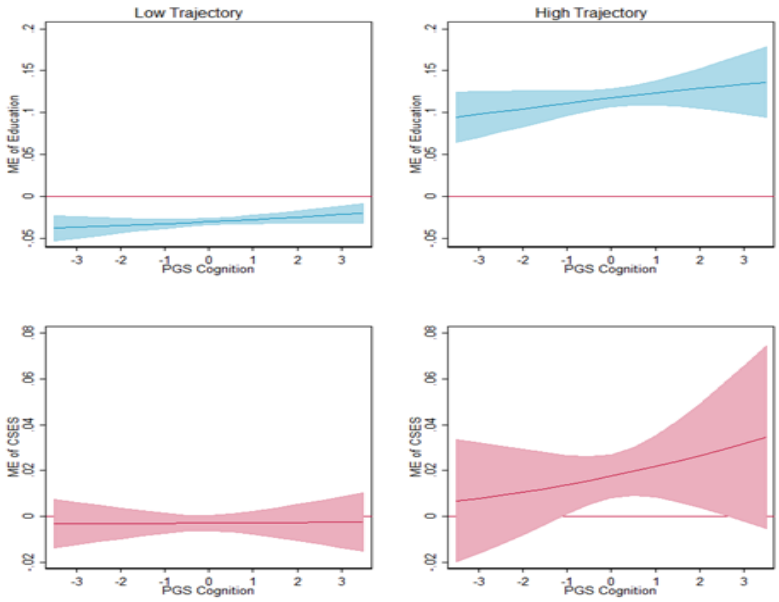
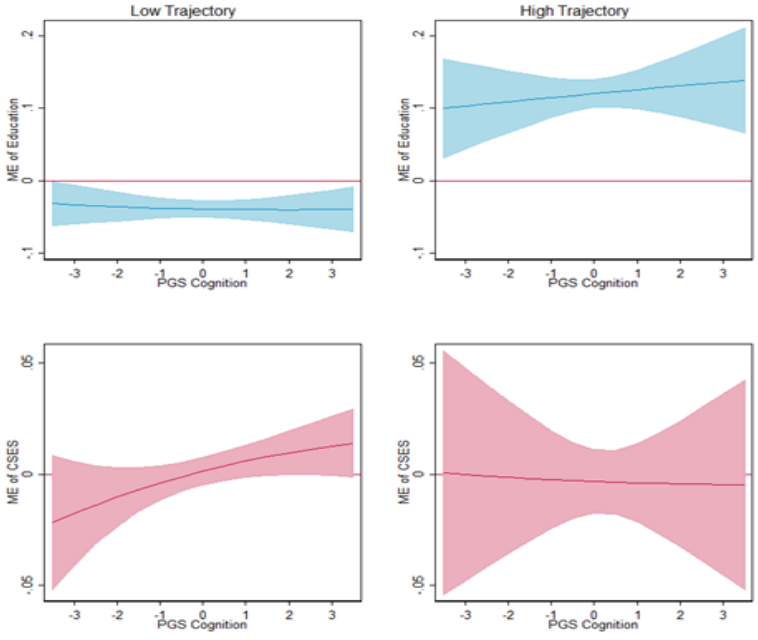


Figure 7: Marginal Effects of Schooling and Childhood SES with Cognition Trajectory Group Membership by Cognition PGS

European Ancestry Sample



African American Ancestry Sample



Appendix Table A1: Association of PGSs, Childhood SES and Schooling Attainment with BMI Trajectory Group Membership from FML models with Childhood SES and Grades of Schooling Interacted with BMI PGS

	European Ancestry Sample				African American Ancestry Sample		
	P(Low)	P(low-Medium)	P(Medium)	P(High)	P(Low)	P(Medium)	P(High)
	(1)	(2)	(3)	(4)	(5)	(6)	(7)
Male	-0.102***	0.097***	0.021**	-0.016***	0.154***	-0.079**	-0.075***
	(0.009)	(0.010)	(0.008)	(0.004)	(0.027)	(0.027)	(0.012)
Education PGS	-0.007	-0.001	0.006	0.001	-0.010	0.003	0.007
	(0.005)	(0.005)	(0.004)	(0.002)	(0.014)	(0.014)	(0.006)
Smoking PGS	-0.011*	0.008	0.003	0.000	-0.012	0.004	0.008
	(0.005)	(0.005)	(0.005)	(0.002)	(0.013)	(0.013)	(0.005)
Depression PGS	0.006	-0.001	-0.004	-0.001	0.038**	-0.030*	-0.008
	(0.005)	(0.005)	(0.004)	(0.002)	(0.014)	(0.014)	(0.006)
BMI PGS	-0.070***	-0.002	0.051***	0.022***	-0.093***	0.072***	0.021**
	(0.005)	(0.005)	(0.004)	(0.002)	(0.018)	(0.018)	(0.008)
Wellbeing PGS	0.001	0.009	-0.009*	-0.002	0.021	-0.016	-0.006
	(0.005)	(0.005)	(0.004)	(0.002)	(0.014)	(0.014)	(0.005)
Cognition PGS	0.000	0.004	-0.002	-0.002	-0.002	0.005	-0.003
	(0.005)	(0.005)	(0.004)	(0.002)	(0.015)	(0.014)	(0.006)
Childhood SES	0.009	0.002	-0.006	-0.004*	-0.020	0.017	0.002
	(0.005)	(0.005)	(0.004)	(0.002)	(0.014)	(0.014)	(0.007)
Grades of Schooling	0.022***	-0.001	-0.018***	-0.003	0.031*	-0.017	-0.014*
	(0.005)	(0.005)	(0.004)	(0.002)	(0.015)	(0.014)	(0.006)

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, grades of schooling, year of birth indicators, cohort dummies, and the first 10 genetic principal components. The PGSs, childhood SES and grades of schooling are standardized to have mean of zero and standard deviation of one. Standard errors clustered at the household level. ***significant at 1% **significant at 5% *significant at 10

Appendix Table A2: Association of PGSs, Childhood SES and Schooling Attainment with Depressive Symptoms Trajectory Group Membership from FML models with Childhood SES and Grades of Schooling Interacted with Depression PGS

	European Ancestry Sample				African American Ancestry Sample		
	P(Low)	P(Low-Medium)	P(Medium)	P(High)	P(Low)	P(Medium)	P(High)
	(1)	(2)	(3)	(4)	(5)	(6)	(7)
Male	0.114***	-0.001	-0.071***	-0.042***	0.099***	0.006	-0.105***
	(0.010)	(0.010)	(0.008)	(0.004)	(0.028)	(0.029)	(0.022)
Education PGS	0.005	0.004	-0.004	-0.005*	0.032*	-0.025	-0.007
	(0.006)	(0.005)	(0.005)	(0.003)	(0.014)	(0.015)	(0.012)
Smoking PGS	-0.001	-0.003	0.004	0.000	-0.012	0.014	-0.002
	(0.006)	(0.006)	(0.005)	(0.003)	(0.013)	(0.014)	(0.011)
Depression PGS	-0.026***	0.008	0.008	0.011***	-0.022	0.003	0.019
	(0.006)	(0.006)	(0.005)	(0.003)	(0.014)	(0.015)	(0.013)
BMI PGS	-0.009	-0.006	0.007	0.008**	0.031	-0.015	-0.016
	(0.006)	(0.005)	(0.005)	(0.003)	(0.018)	(0.019)	(0.016)
Wellbeing PGS	0.027***	-0.014**	-0.007	-0.006*	0.020	-0.019	-0.002
	(0.006)	(0.005)	(0.005)	(0.002)	(0.014)	(0.014)	(0.012)
Cognition PGS	0.005	0.002	-0.005	-0.001	-0.005	0.008	-0.003
	(0.006)	(0.006)	(0.005)	(0.003)	(0.015)	(0.015)	(0.012)
Childhood SES	0.042***	-0.002	-0.022***	-0.018***	0.032*	0.016	-0.048***
	(0.006)	(0.005)	(0.005)	(0.002)	(0.014)	(0.014)	(0.013)
Grades of Schooling	0.069***	0.004	-0.049***	-0.024***	0.152***	-0.071***	-0.081***
	(0.006)	(0.006)	(0.005)	(0.002)	(0.016)	(0.015)	(0.012)

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, grades of schooling, year of birth indicators, cohort dummies, and the first 10 genetic principal components. The PGSs, childhood SES and grades of schooling are standardized to have mean of zero and standard deviation of one. Standard errors clustered at the household level. ***significant at 1% **significant at 5% *significant at 10

Appendix Table A3: Association of PGSs, Childhood SES and Schooling Attainment with Cognition Trajectory Group Membership from FML models with Childhood SES and Grades of Schooling Interacted with Cognition PGS

	European Ancestry Sample				African American Ancestry Sample				
	P(Low)	P(Low-Medium)	P(Medium)	P(High)	P(Low)	P(Low-Medium)	P(Medium)	P(Medium-High)	P(High)
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)
Male	0.012***	0.078***	0.010	-0.100***	0.003	-0.012	0.025	0.038	-0.055***
	(0.003)	(0.009)	(0.010)	(0.008)	(0.006)	(0.021)	(0.024)	(0.027)	(0.014)
Education PGS	-0.007***	-0.023***	0.008	0.022***	-0.005	-0.027*	0.007	0.024	0.001
	(0.002)	(0.005)	(0.005)	(0.005)	(0.003)	(0.011)	(0.012)	(0.013)	(0.008)
Smoking PGS	-0.002	0.003	-0.006	0.005	-0.004	0.009	0.010	-0.015	-0.001
	(0.002)	(0.005)	(0.005)	(0.005)	(0.002)	(0.010)	(0.012)	(0.012)	(0.007)
Depression PGS	0.001	-0.002	-0.002	0.002	0.001	-0.007	0.012	-0.009	0.003
	(0.002)	(0.005)	(0.005)	(0.005)	(0.003)	(0.011)	(0.012)	(0.012)	(0.007)
BMI PGS	-0.001	0.004	-0.002	-0.001	-0.000	-0.012	0.016	-0.005	0.001
	(0.002)	(0.005)	(0.005)	(0.005)	(0.004)	(0.015)	(0.015)	(0.016)	(0.009)
Wellbeing PGS	-0.000	-0.003	0.001	0.002	-0.003	-0.002	0.007	-0.005	0.003
	(0.002)	(0.005)	(0.005)	(0.005)	(0.003)	(0.010)	(0.011)	(0.012)	(0.008)
Cognition PGS	0.001	-0.020***	-0.003	0.022***	-0.002	0.010	-0.012	0.005	-0.001
	(0.002)	(0.005)	(0.006)	(0.005)	(0.003)	(0.011)	(0.012)	(0.013)	(0.010)
Childhood SES	-0.003	-0.010*	-0.004	0.018***	0.001	0.001	0.000	0.001	-0.003
	(0.002)	(0.005)	(0.005)	(0.005)	(0.003)	(0.011)	(0.012)	(0.013)	(0.007)
Grades of Schooling	-0.030***	-0.114***	0.027***	0.118***	-0.039***	-0.168***	-0.049***	0.135***	0.120***
	(0.002)	(0.006)	(0.006)	(0.005)	(0.006)	(0.015)	(0.015)	(0.018)	(0.010)

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, grades of schooling, year of birth indicators, cohort dummies, and the first 10 genetic principal components. The PGSs, childhood SES and grades of schooling are standardized to have mean of zero and standard deviation of one. Standard errors clustered at the household level. ***significant at 1% **significant at 5% *significant at 10