

# Natural Selection in the 20th Century

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## 1 Introduction

Geneticists have long hypothesized that natural selection is taking place in modern human populations. Recent work confirms this using genome-wide analysis (Barban et al. 2016; Beauchamp 2016; Kong et al. 2017; Sanjak et al. 2018). In particular, genetic variants associated with higher educational attainment are being selected against, although effect sizes appear small.

Several gaps in our knowledge remain. First, while existing work examines contemporary populations, we would like to extend the analysis over time, since natural selection in the same direction over multiple generations could lead to significant effects in the long run. Second, there are concerns about ascertainment bias in the samples used. This could potentially bias estimates of the magnitude of natural selection. Lastly, we know little about the mechanisms behind natural selection in contemporary populations.

Here we attempt to answer these questions, using data from UK Biobank. We use questions on respondents' number of children, and their number of siblings, to reconstruct two generations of family size. We then relate these to 33 different polygenic scores for a variety of characteristics. This analysis provides a broader picture of natural selection in the UK than has previously been available.

Our key results are as follows. First, comparing natural selection across the two generations, there are few signs of change in size or direction over time. Most polygenic scores are selected in the same direction in both generations. We also see little evidence of changes across birth cohorts within either generation.

Second, natural selection is concentrated among population subgroups which are under-represented in the sample, including less-educated people and poorer households. When we weight the sample to correct for ascertainment bias, many effect sizes are larger, sometimes much larger. We emphasize that our weights are only a partial solution to ascertainment bias in the sample. As a result, much uncertainty remains about the strength of natural selection in the UK population, but we can be reasonably sure that it is larger than naïve estimates suggest.

Lastly, patterns in natural selection give us clues to the underlying mechanism. In particular, among mothers who were older at their first birth, and among parents with fewer sexual partners, the direction of natural selection is reversed: for example, among these subgroups, higher polygenic scores (PGS) for educational attainment are associated with having more offspring, rather than fewer. The effects of PGS can be decomposed into two channels: an effect on age at first live birth, and an opposite-signed effect on number of children conditional on age at first live birth.

This pattern can be explained by economic theories of fertility (Becker 1960). In these, higher potential earnings have two opposite effects on fertility: a fertility-increasing income effect (higher income makes children more affordable), and a fertility-lowering substitution effect (time spent on childrearing has a higher cost in foregone earnings). Among couples who can take advantage of coordination in childcare activities, the income effect dominates; among single parents, or those in unstable relationships, the substitution effect dominates. Supporting this explanation, polygenic scores' raw effects on fertility are negatively correlated with their effects on income; on the other hand, controlling for age at first live birth, scores' effects on fertility and on household income are positively correlated. These two results are compatible with the substitution effect and the income effect respectively.

## 2 Data

Data is taken from UK Biobank. Polygenic scores were normalized to mean 0, variance 1.

## 3 Results

We first show raw changes in polygenic scores over birth years, within the entire UK Biobank sample. Figure 1 plots mean polygenic scores by 5-year birth intervals. Several scores show consistent increases or declines over this 30-year period, of the order of 5% of a standard deviation.

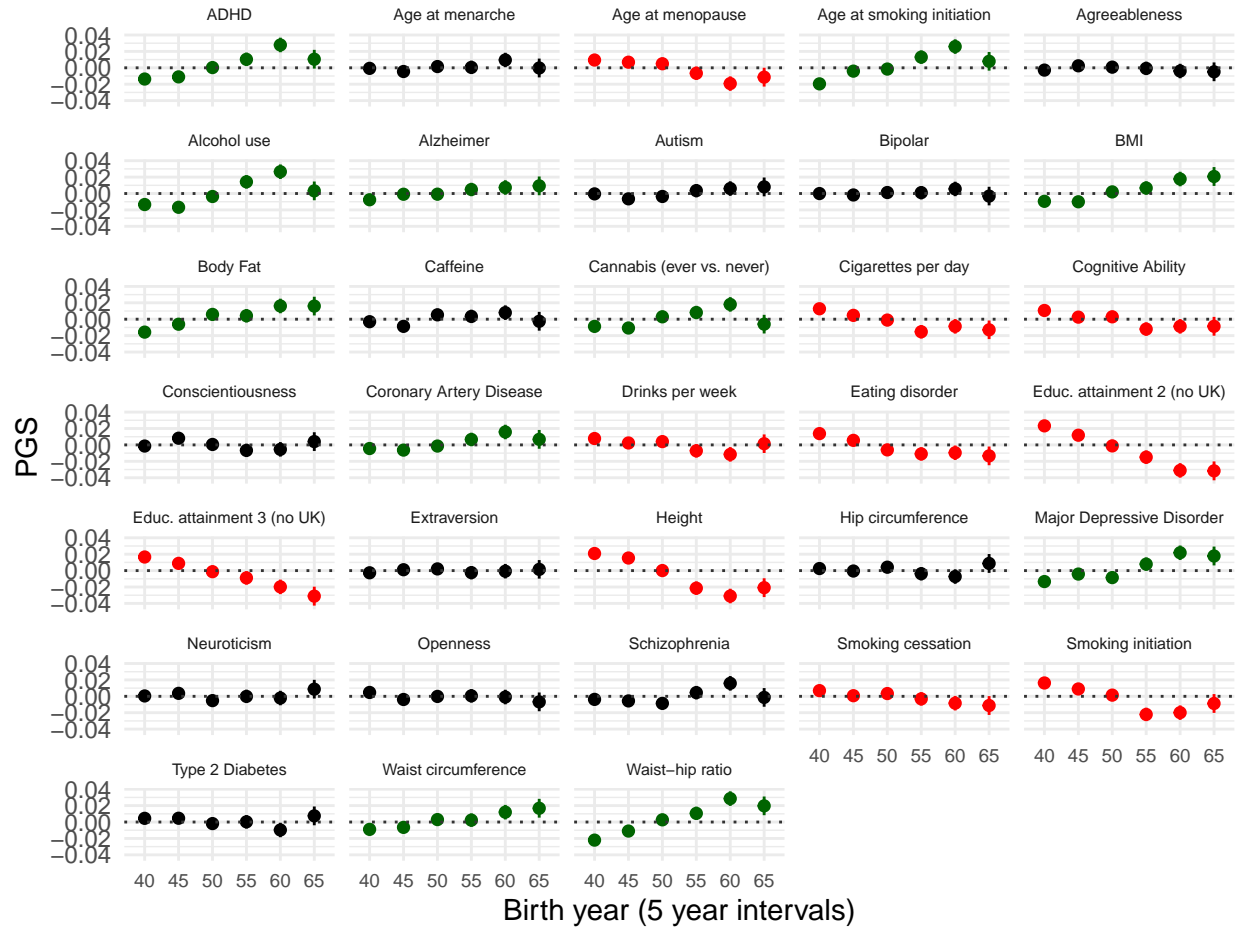


Figure 1: Mean polygenic scores by birth year in UK Biobank. Points are means for 5-year intervals. Lines are 95% confidence intervals. Green lines show a significant increase over time ( $p < 0.05$ ). Red lines show a significant decrease.

These changes could reflect either natural selection within the UK population, or ascertainment bias within the sample. Respondents are higher income and better educated than the UK population, and they may also differ on other unobserved characteristics (Fry et al. 2017). Since richer and educated people also live longer, this bias might also increase with age.

To examine the effects of sampling, we start by measuring the strength of natural selection within different subgroups. To do this we regress respondents' polygenic scores on their number of children ( $y_i$ ):

$$y_i = \alpha + \beta \text{PGS}_i + \varepsilon_i$$

The effect size  $\beta$  measures the strength of natural selection within the sample or a given subgroup. In fact, since polygenic scores are normalized to mean 0,  $\beta$  is the expected polygenic score among children of the sample or subgroup (Beauchamp 2016). We begin with basic demographic variables including education, income and sex. These are all potential sources of ascertainment bias: as well as the ascertainment for income and education, mentioned above, the sample sex ratio skews 54.05% female.

Figures 2 and 3 plot effect sizes for each polygenic score. Figure 2 groups respondents by age of completing full-time education. Figure 3 groups respondents by household income. Effect sizes are larger and more significant for the lowest income category, and for the lowest education category. Note that the overall effect is not a simple average of the effect among the different subgroups, because polygenic scores may also shift respondents between the subgroups. For example, a high PGS for educational attainment may correlate with fewer children among early school leavers, but may also increase the age at which a respondent leaves school.

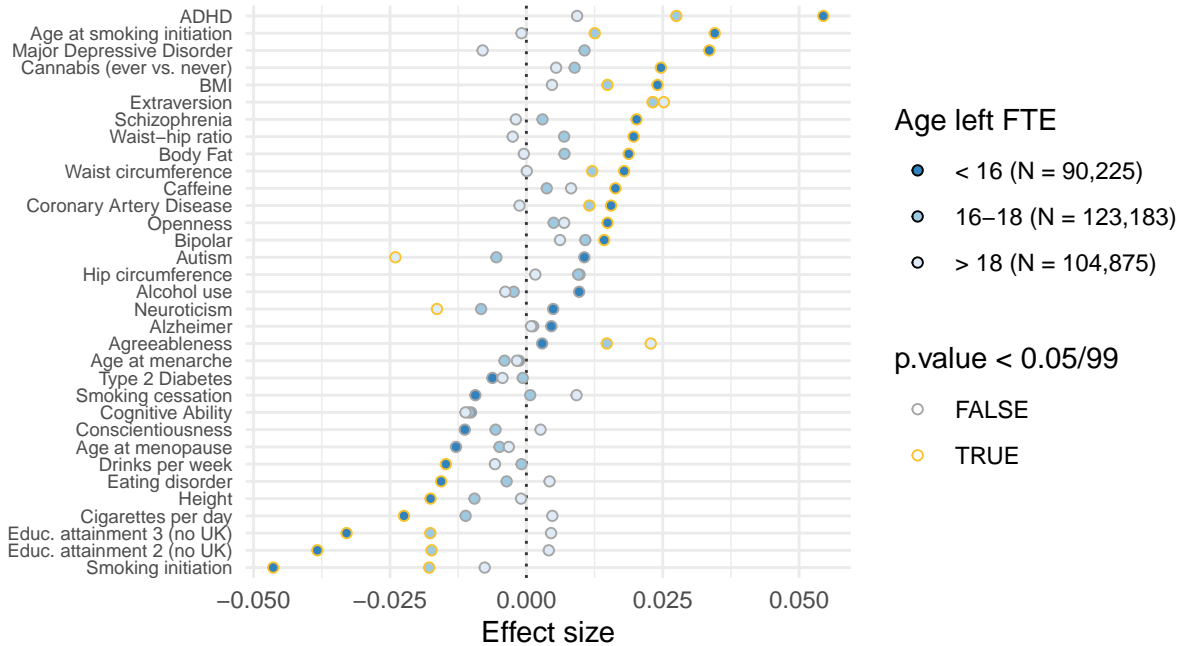


Figure 2: Effect sizes on number of children by age left full-time education

These results could be driven by age, if older respondents are poorer and less educated, and also more subject to selection on polygenic scores. However, if we rerun the regressions, interacting the polygenic score with income category and also with a quadratic in age, the interaction with income remains significant at 0.05/33 for 21 out of 33 regressions. Similarly if we interact the PGS with age of leaving full time education and a quadratic in age, the interaction with age leaving FTE remains significant at 0.05/33 for 17 out of 33 regressions.

Figure 4 shows effect sizes of PGS on number of children separately for males and females. Differences are particularly large for educational attainment, height and MDD. Several PGS for mental illness and personality traits are more selected for (or less against) among women, including major depressive disorder (MDD), schizophrenia and neuroticism, while extraversion is more selected for among men. Waist circumference and waist-hip ratio are less selected for among women, and educational attainment is more selected against, though the difference is only significant for EA3.

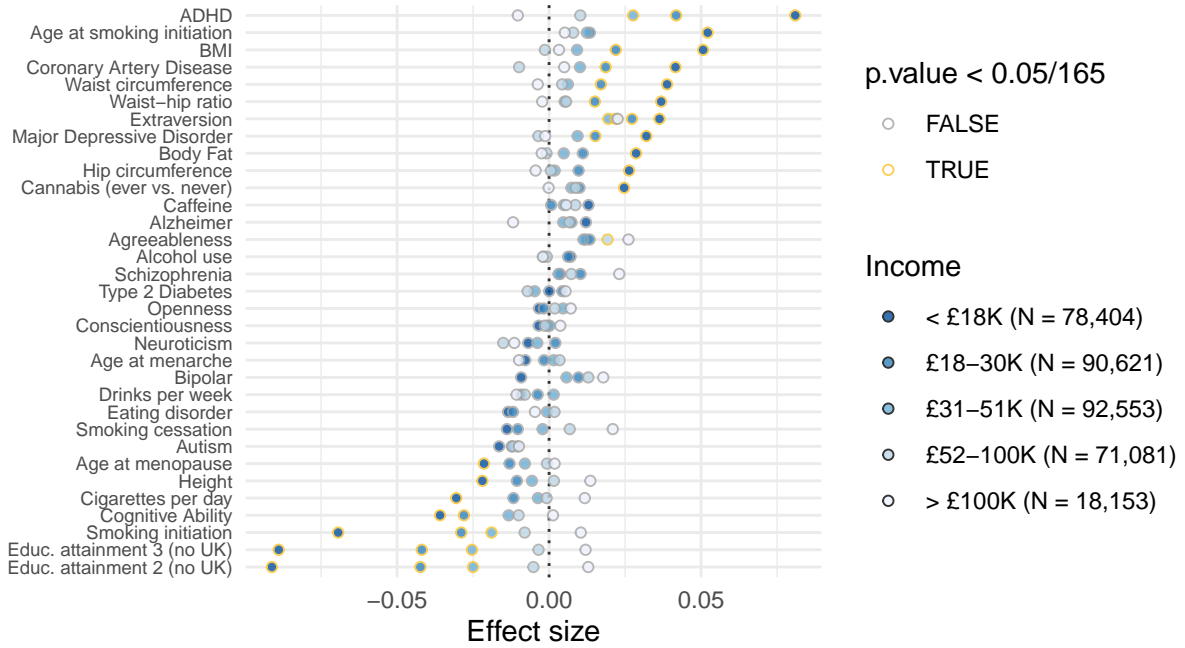


Figure 3: Effect sizes on number of children by household income

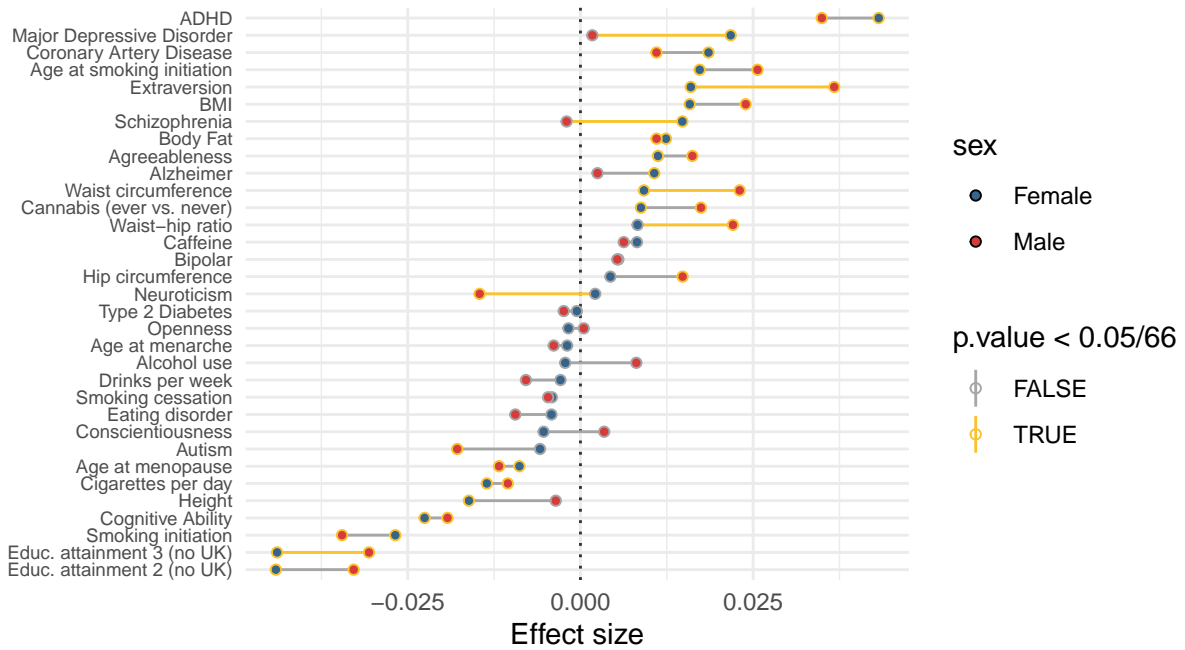


Figure 4: Effect sizes on number of children by sex. Lines show significant differences

These results show that ascertainment within UK Biobank could bias estimates of the size of natural selection towards zero. We now focus in on variables specifically related to marriage markets and raising children. Whatever processes give rise to natural selection, these variables are likely to be involved; at the same time, they may also be ascertained within the sample.

Figure 5 splits males and females by lifetime number of sexual partners, at the median value of 3. For both sexes, effects are larger and more significant among those with more than 3 partners. Results are unchanged if we control for respondents' age (Figure 14 in the appendix). Figure 6 splits respondents up by whether they were living with a spouse or partner at the time of interview. Again, effects are larger among those not living with a spouse or partner.

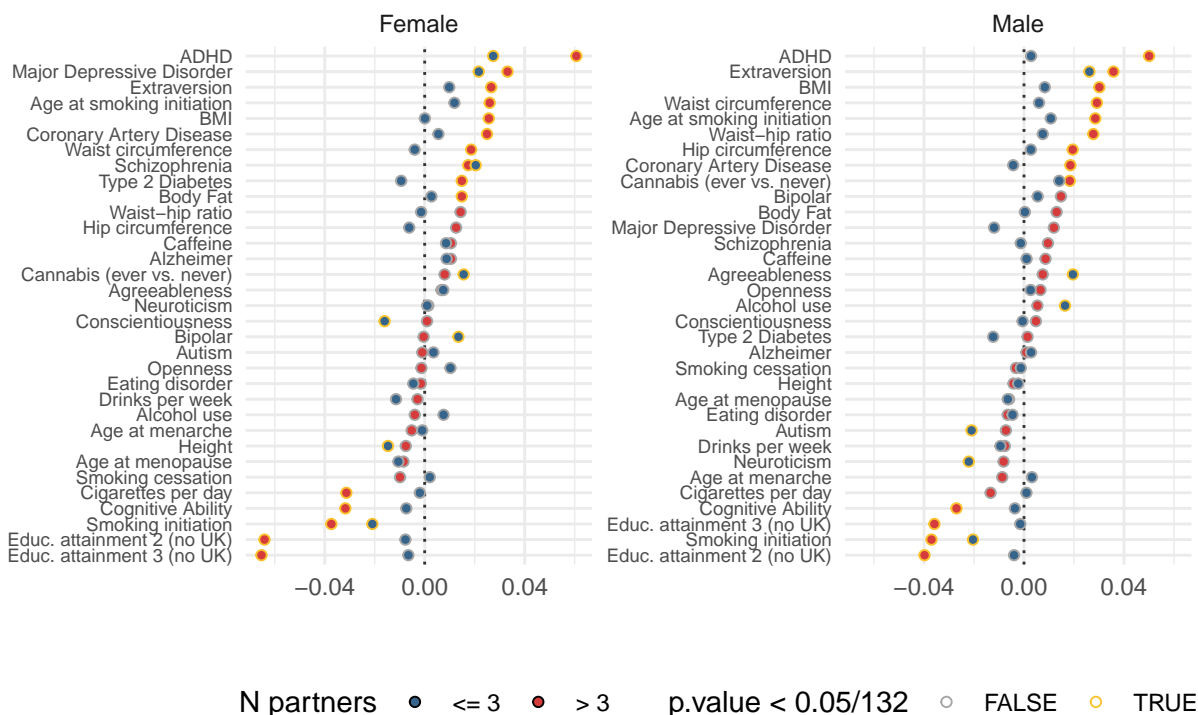


Figure 5: Effect sizes on number of children by number of sexual partners

Our final variable is age at first live birth (AFLB), for females only. There is evidence for genetic effects on AFLB (Barban et al. 2016). There is also a close link between this variable and number of children born.

Figure 7 shows effect sizes estimated separately for each tercile of AFLB. Several effects are strikingly different across terciles. ADHD and MDD are selected for amongst the youngest third of mothers, but selected against among the oldest two-thirds. Educational attainment is selected for among the oldest two-thirds of mothers, but is not significantly selected among the youngest third. Similarly, several PGS of body measurements are selected against only among older mothers. The correlation between effect sizes for the youngest and oldest terciles is -0.54. As before, recall that PGS may have two effects: they may change the number of children within categories, but may also shift respondents between categories.

To investigate this further, we regress number of children on PGS controlling for AFLB. Figure 8 shows the results, along with raw effect sizes for comparison. Controlling for AFLB greatly reduces effect sizes. This could be because the controlled regressions exclude childless women. However, in 24 out of 33 cases, effects actually change sign when controls are added. The correlation between effect sizes controlling for AFLB, and raw effect sizes, is -0.75. So, natural selection “effects” seem to come through two channels: an effect on AFLB, and an effect on number of children controlling for AFLB. Moreover, these channels often push in opposite directions.

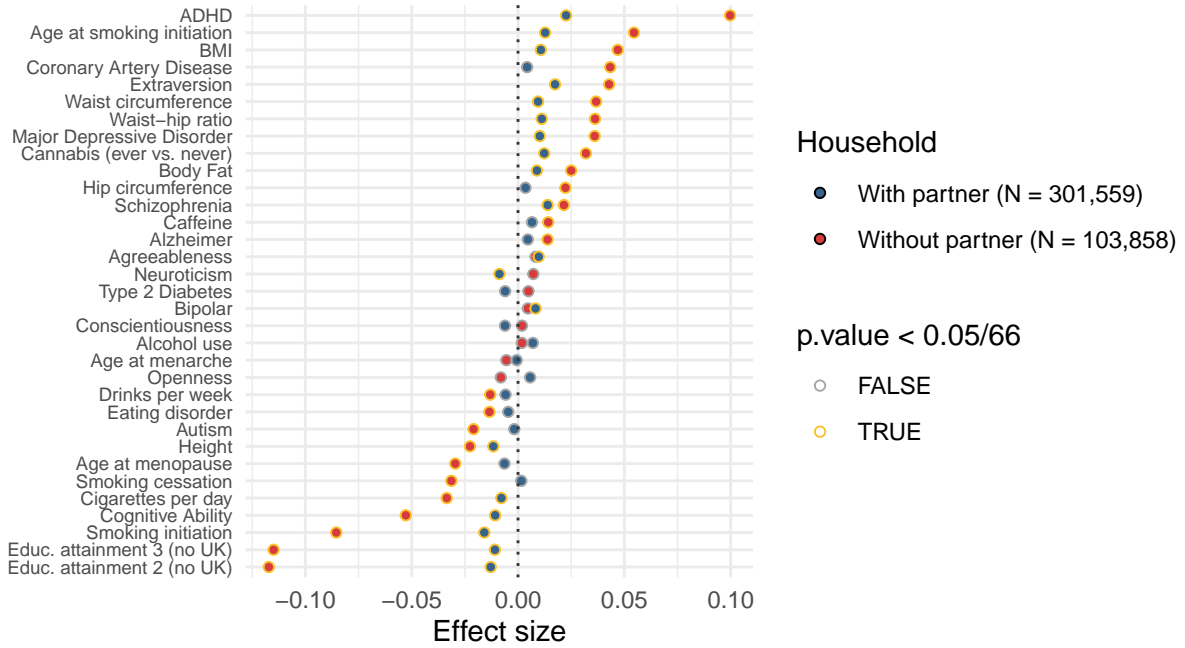


Figure 6: Effect sizes on number of children by household type

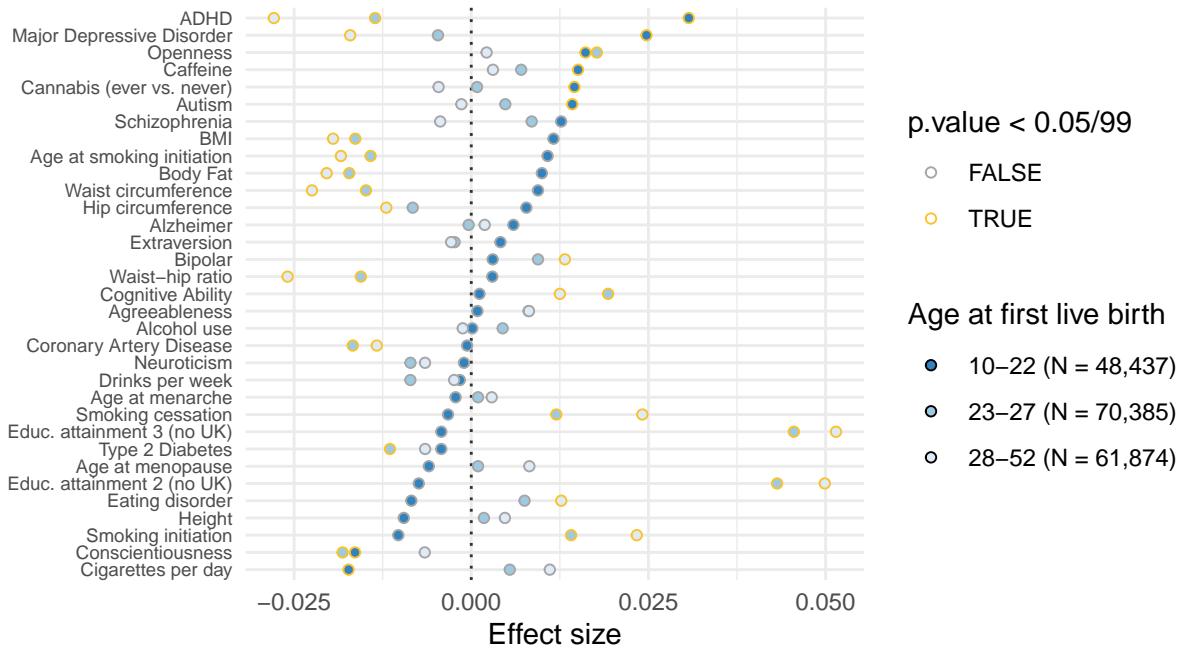


Figure 7: Effect sizes on number of children, by age at first live birth terciles

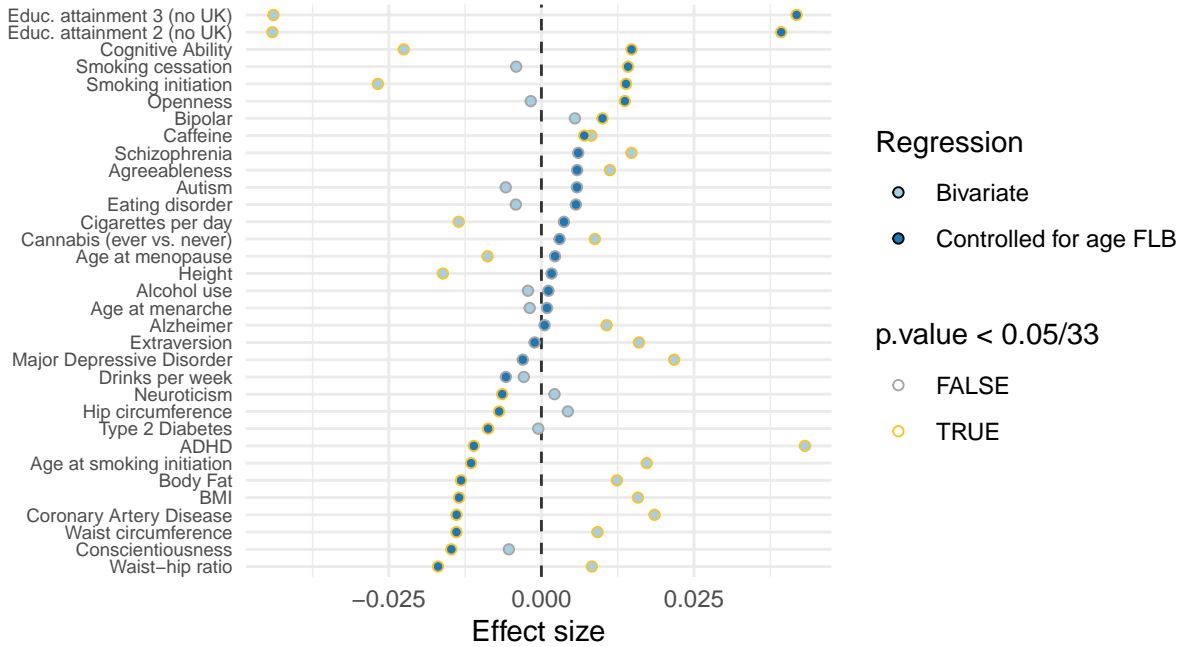


Figure 8: Effect sizes on number of children, controlling for age at first live birth (women only). Effect sizes for women without controls are shown for comparison

### 3.1 Weighted regressions

These results show that there may be ascertainment bias in estimates of natural selection derived from UK Biobank. One way to compensate for this is by survey weighting. Weighting is not guaranteed to lead to unbiased estimates, because as well as ascertainment on characteristics which we measure and weight for, there may also be ascertainment on other, unmeasured characteristics. But the exercise will give us a rough sense of the direction and magnitude of bias. We weight participants using data from the 2011 Census and from the 2006 General Household Survey (GHS). We try three alternative weighting schemes:

- Geographical weighting by census MSOA, age and presence/absence of a partner;
- Weighting by age and highest educational qualification;
- Weighting by age, highest qualification, and age at first live birth, using GHS data (women only).

Figure 9 plots effect sizes among the entire sample, using these weighting schemes. We include unweighted regressions for comparison. Table 1 gives effect sizes as a proportion of the unweighted effect size. As expected, weighting generally increases estimated effect sizes. Sizes are reasonably similar across the geographical and age/qualification weights, but they are increased further when we weight by AFLB. This suggests that estimates might be further affected by weighting on other demographic variables. Given that the Biobank sample seems to be ascertained in ways that reduce estimates of natural selection, we suspect that these weighted estimates are still conservative.

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### 3.2 Change over time

The UK Biobank data contains information on respondents' number of siblings. Since respondents' polygenic scores are equal in expectation to their parents' mean scores, we can use this to look at natural selection in

Table 1: Weighted effect sizes as a proportion of unweighted

PGS	Weighting		
	Geographical	Age/Qualification	Age/Qual/AFLB
Height	1.71	1.25	1.32
BMI	1.71	1.18	2.03
Age at menopause	1.66	1.06	1.27
Waist-hip ratio	1.65	1.46	2.47
Educ. attainment 3 (no UK)	1.6	1.53	2.04
Waist circumference	1.57	1.31	2.52
Cigarettes per day	1.54	1.25	2.12
Hip circumference	1.52	1.16	2.96
Educ. attainment 2 (no UK)	1.51	1.52	2.02
Major Depressive Disorder	1.49	0.891	1.35
Eating disorder	1.48	1.67	2.15
Body Fat	1.47	1.47	2.18
Autism	1.41	1.05	1.94
Schizophrenia	1.39	1.18	0.744
Alzheimer	1.36	0.429	1.4
Coronary Artery Disease	1.3	1.2	2.04
Cognitive Ability	1.28	1.34	2.03
Smoking initiation	1.26	1.21	1.62
Cannabis (ever vs. never)	1.19	1.15	0.761
Extraversion	1.17	1.15	1.87
ADHD	1.17	1.28	1.63
Caffeine	1.11	1.18	2.15
Age at smoking initiation	1.08	1.26	1.86
Agreeableness	1.01	0.868	1.09
<i>Mean</i>	1.4	1.21	1.82
<i>Median</i>	1.44	1.21	1.98

Only consistent and significant (when unweighted) estimates are shown.

Age/Qual/AFLB as a proportion of unweighted regressions for females only.

the parents' generation. The dependent variable is now number of siblings (including the respondent him- or herself).

The parents' generation has a second source of ascertainment bias, beyond the sampling bias of the survey. Sampling parents of respondents inherently overweights parents who have many children. For instance, parents of three children will have, on average, three times more children as respondents in UK Biobank than parents of one child. Parents of no children will not be represented at all, by definition.

To compensate for this, we reweight our preferred weightings (Age/Qualification) by the inverse of number of siblings. We then regress this on PGS. Figure 10 shows the results. For comparison, we show regressions on number of children, where we have excluded respondents with no children.

Effect sizes appear larger in the parents' generation, i.e. for number of siblings. However, we treat this result cautiously, because when we split respondents up by year of birth, we find few differences in effect sizes between early- and late-born respondents, whether our dependent variable is number of siblings or number of children. In other words, since estimated effect sizes change when we change the dependent variable, but do not change over time within either dependent variable, the explanation may be due to remaining



Figure 9: Effects of polygenic scores on fertility. Weighted regressions.

ascertainment bias within our sample.

### 3.3 Mechanisms behind modern natural selection

Why do selection effects have opposite signs across older and younger mothers at first live birth, and opposite signs when AFLB is controlled for? A possible answer is given by the economic theory of fertility (Becker 1960). According to this, increases in potential earned income affect fertility via two opposing channels. There is an “income effect” by which children become more affordable, like any other good. Since childrearing has a cost in time, there is also a substitution effect: the opportunity cost of childrearing increases if one’s market wage is higher. The income effect would lead higher earners to have more children. The substitution effect would lead higher earners to have fewer children. It is often assumed that the substitution effect will dominate for lone parents, since they have less opportunity to share childcare responsibilities, while the income effect will dominate for couples who are able to reap the gains from specialization.

If so, then genetic characteristics which affect one’s earnings potential in the labour market may lead to opposing effects on fertility. Genetic variants which improve one’s earnings may increase fertility among couples, but decrease fertility among single parents. They may also decrease the likelihood of becoming a young mother, if this is correlated with single motherhood. Lastly, if lifetime number of sexual partners predicts single parent versus two-parent status, the theory could also explain the different effect sizes across people with more and fewer sexual partners.

This explanation predicts that the strength of polygenic scores’ effects on fertility will correlate with the strength of their relationship with earnings. To test this, we measure the correlation of each PGS with household income, as well as with education level, a phenotype which predicts earnings. We then relate these measurements to effect sizes on number of children. There is a clear negative relationship between a score’s effect on fertility, and its correlation with income or education (Figure 11). If we control for age at first live birth, the relationship changes sign and becomes positive.

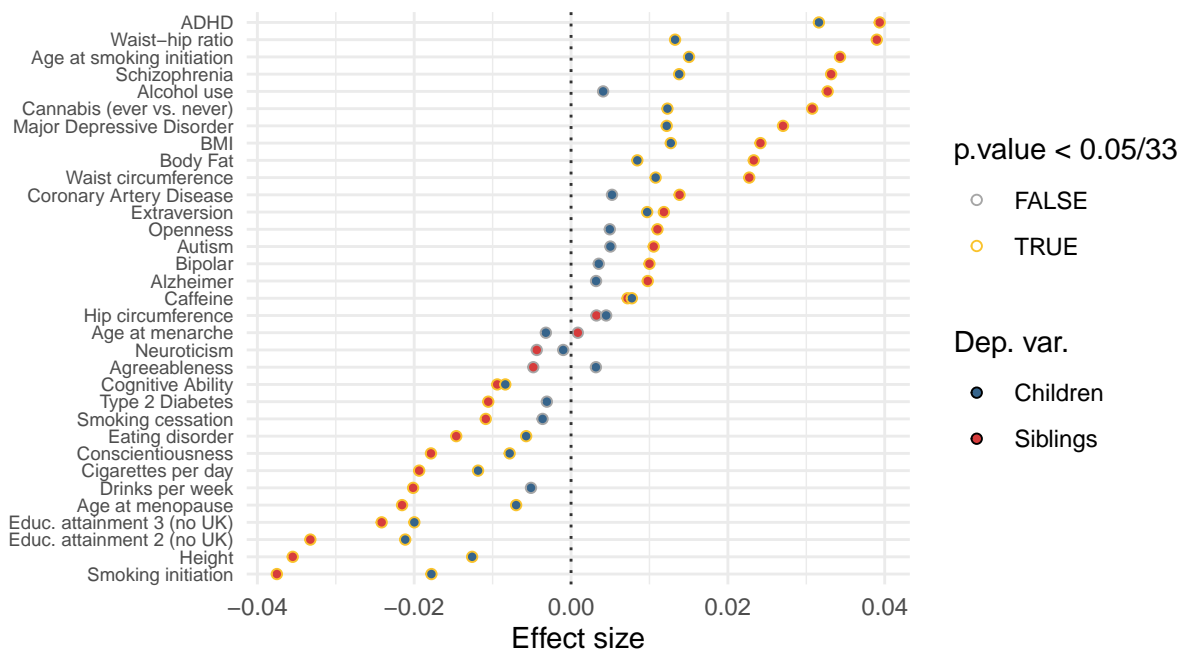


Figure 10: Effects of polygenic scores on fertility, respondents' parents vs. respondents

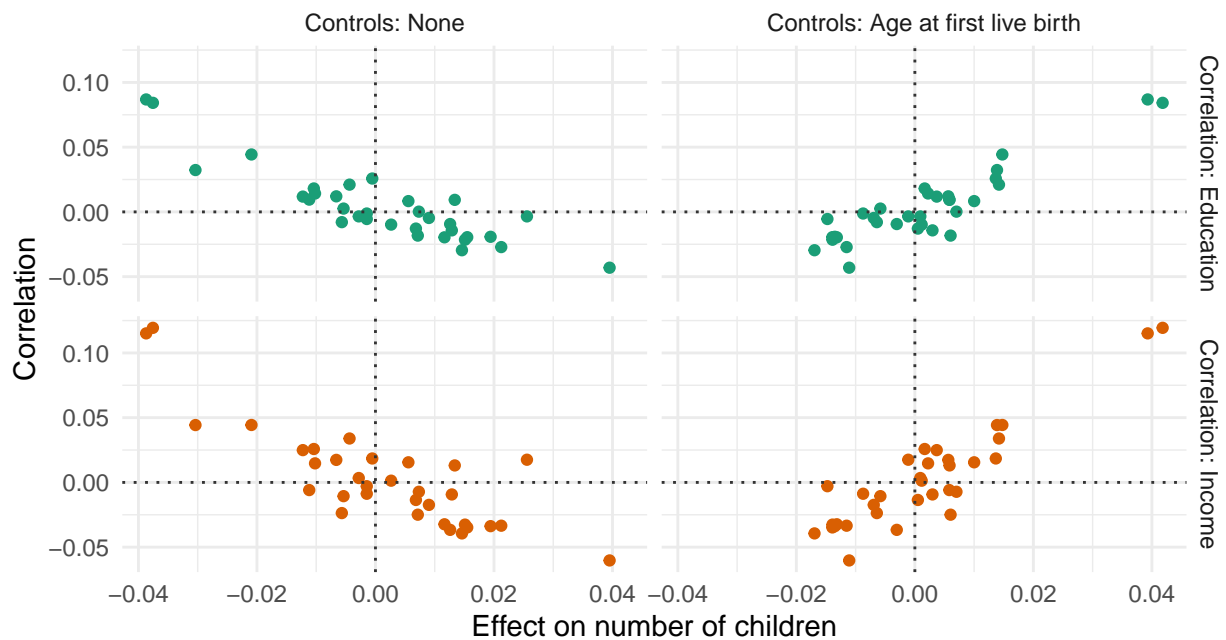


Figure 11: Effect sizes on number of children, with and without controls for age at first live birth, by correlations with income and education

## 4 Conclusion

Natural selection is taking place in modern populations on variants underlying many polygenic scores. In a loose sense, phenotypes relating to scores which are selected for (against) would be seen as undesirable (desirable) by many people. For example, most people would probably prefer to have high educational attainment, a low risk of major depressive disorder, and a low risk of coronary artery disease, but PGS underlying these traits are being selected for. In addition, the size of selection on PGS is negatively correlated with the score’s correlation with household income. Potentially, natural selection could increase the health burden on modern societies, but that depends on effect sizes. Existing work argues that these are small (Beauchamp 2016).

However, as we show, estimates can be crucially affected by ascertainment bias in population samples. This problem may be less serious in other surveys, such as the US Health and Retirement Study, which explicitly aims to be representative (as the UK Biobank does not). Nevertheless, ascertainment bias can still be a problem, since not all respondents consent to the collection of genetic data: for instance, completion rates were around 80-85% for HRS genotype data (HRS, n.d.).

In addition, we do not know whether estimated effect sizes of natural selection will increase or decrease as more accurate polygenic scores are produced. We are also unsure about whether polygenic scores for new phenotypes will show a similar pattern of natural selection as existing ones. In short, it is probably too early to tell whether modern natural selection is substantively important or not.

Previous work has documented natural selection in modern populations (Beauchamp 2016; Kong et al. 2017; Sanjak et al. 2018) but has not explained its underlying causes. The economic theory of fertility provides a parsimonious explanation for which traits are selected, and for why the direction of selection is reversed among certain subgroups. An alternative theory is that traits selected for are linked to externalizing behaviour and low time discount rates, via the channel of early sexual behaviour (Mills et al. 2020). The data here provide some support for this: scores which might plausibly be linked to externalizing behaviour, like ADHD and age at smoking initiation, are selected for. However, this theory is less good at explaining variation in selection across the full range of scores, including for example waist-hip ratio and BMI. Externalizing behaviour also does not explain the reversed sign of selection among older parents. Overall, we believe that the economic theory is the leading explanation at present.

## 5 Appendix

### 5.1 Controlling for principal components

Polygenic scores could capture effects that are really due to population stratification, although would not change our results for natural selection of the scores. In 12 we show results for selection on polygenic scores residualized for the top 100 principal components of the genetic data, calculated within the UK Biobank population. (TODO Abdel details.)

In siblings regressions, effect sizes are smaller when residualizing for principal components – sometimes much smaller, as in the case of height. 25 out of 33 “controlled” effect sizes have a smaller absolute value than the corresponding “raw” effect size. The median proportion between raw and controlled effect sizes is 0.89. Among the children regressions, this no longer holds. Effect sizes are barely affected by controlling for principal components.

Overall, 78.79 per cent of effect sizes are consistently signed across all four regressions (on children and siblings, and with and without residualization).

To get a further insight into this we regress `siblings` and `children` on individual principal components. As Figure 13 shows, effects are larger and more significant in siblings regressions. 29 principal components significantly predicted number of siblings, while only 10 significantly predicted number of children.

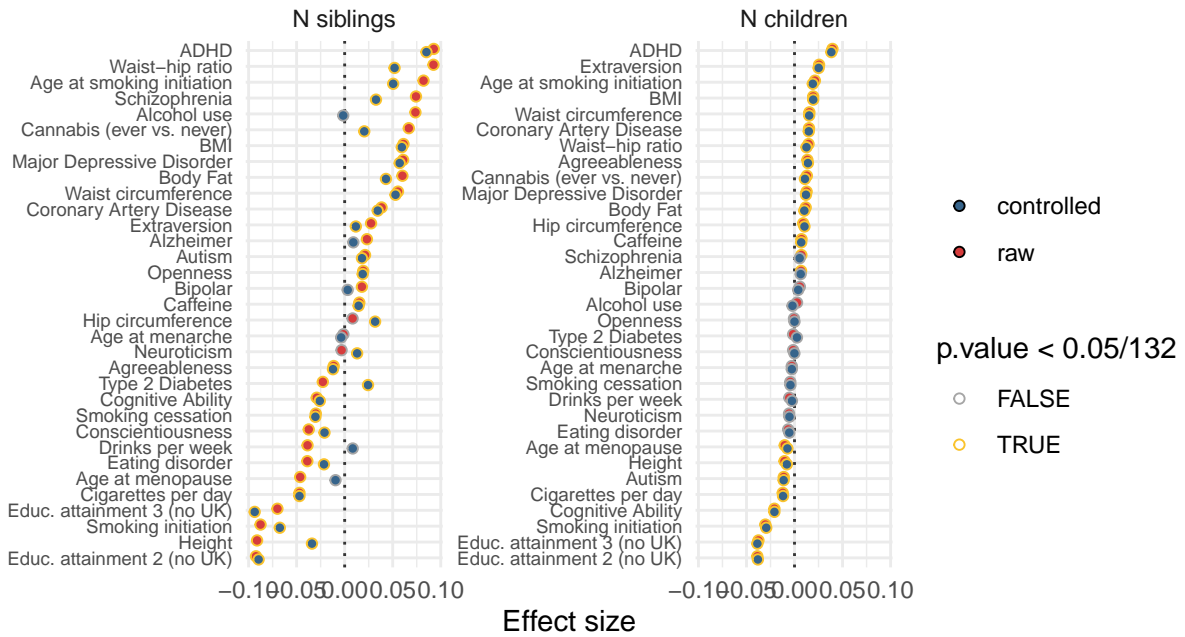


Figure 12: Effects of residualized polygenic scores on number of siblings/children.

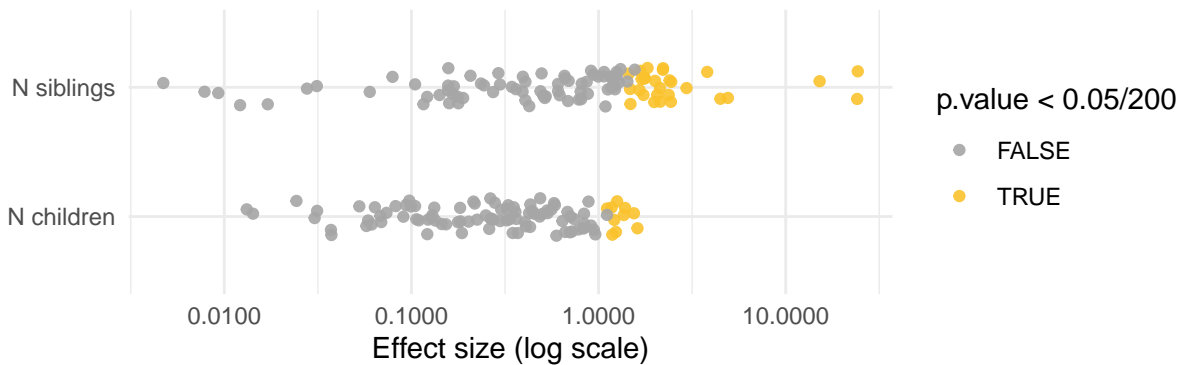


Figure 13: Effect of principal components of genetic data on number of siblings/children. Absolute effect sizes are plotted. Each dot represents one bivariate regression. Points are jittered on the Y axis.

## 5.2 Selection over time

To check whether effect sizes were changing over time, we ran regressions interacting PGS with birth year, median split at 1950 (“early born” versus “late born”). We use both number of children and number of siblings as a dependent variable. We weight using age/qualification cells, and further adjust for selection in the parents’ generation (see above).

Tables 2 and 3 summarize the results. There is no change in natural selection in the parents’ generation. In the respondents’ generation, effect sizes were larger in absolute size among the late born for five PGS: autism, cognitive ability, EA2, EA3 and extraversion. Three PGS showed significant changes in sign: alcohol use (positive to negative); conscientiousness (negative to positive); and type II diabetes (negative to positive).

Table 2: Change in effect sizes between parents of early and late born respondents (regressions on number of siblings)

Change	Number of scores
Insignificant	33
Significance is measured at $p < 0.05/66$	

Table 3: Change in effect sizes between early and late born respondents (regressions on number of children)

Change	Number of scores
Change sign	3
Insignificant	25
Size increasing	5
Significance is measured at $p < 0.05/66$	

## 5.3 Selection by number of partners, controlling for age

Figure 14 shows selection effects by lifetime number of sexual partners. Age, age squared, and interactions of age and age squared with PGS are controlled for.

## 5.4 Selection controlling for age at first live birth: respondents’ parents

Among the parents’ generation, we can control for age at first live birth using the subsets of respondents who reported their mother’s or father’s age, and who had no elder siblings. We run regressions on number of siblings on these subsets, controlling for either parent’s age at their birth. Figure 15 shows the results. Effect sizes are very similar, whether controlling for father’s or mother’s age. Unlike for the respondents’ generation, effect sizes are positively correlated with the effect sizes from bivariate regressions without the age at birth control (father’s age at birth:  $\rho$  0.51; mother’s age at birth:  $\rho$  `r_cor_raw_moth`).

## 5.5 Effects of PGS on age at first live birth

Our results suggest that polygenic scores may directly correlate with age at first live birth. Figure 16 plots estimated effect sizes from bivariate regressions for respondents, and Figure 17 does the same for their parents. Effect sizes are reasonably large. They are also very highly correlated across generations. Effect sizes of PGS on father’s age at own birth, and on own age at first live birth, have a correlation of 0.98; for mother’s age and own age it is 0.98

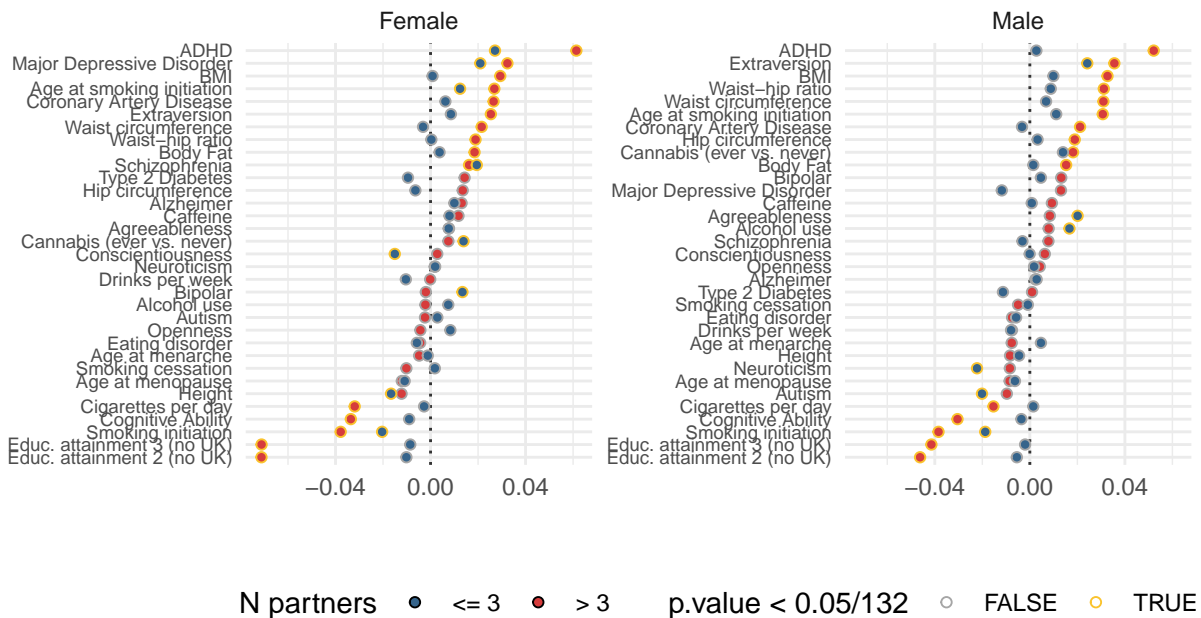


Figure 14: Effect sizes on number of siblings interacted with number of sexual partners (median split at 3), respondent's age and age squared.

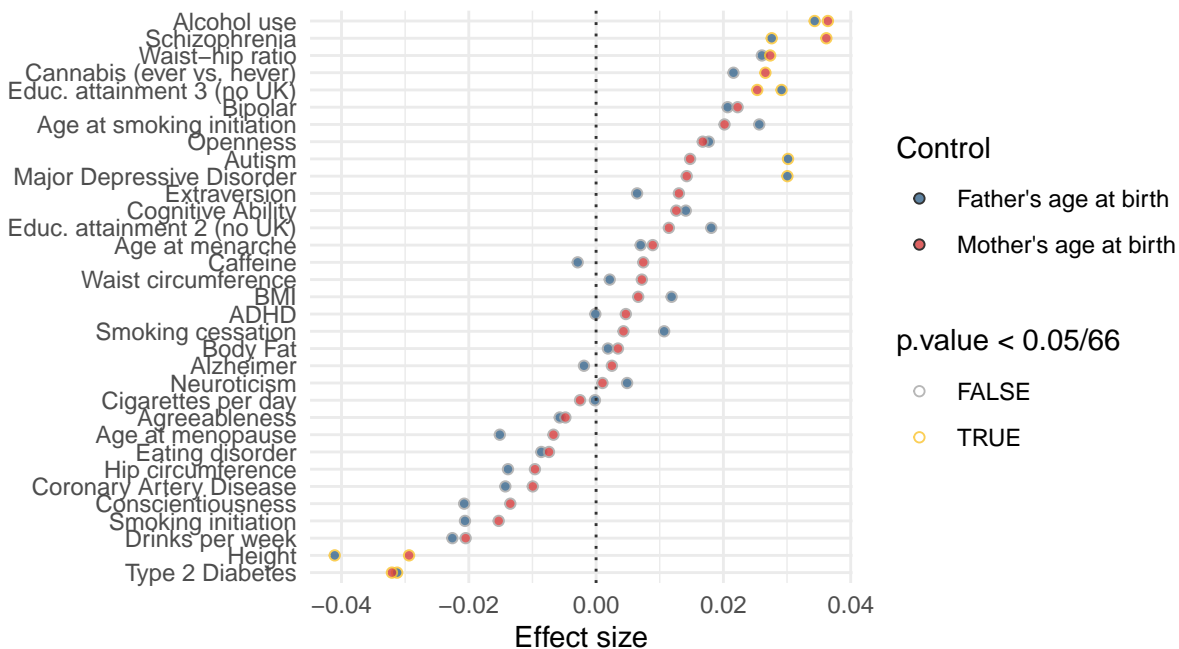


Figure 15: Effect sizes on number of siblings controlling for parents' age at birth, eldest siblings

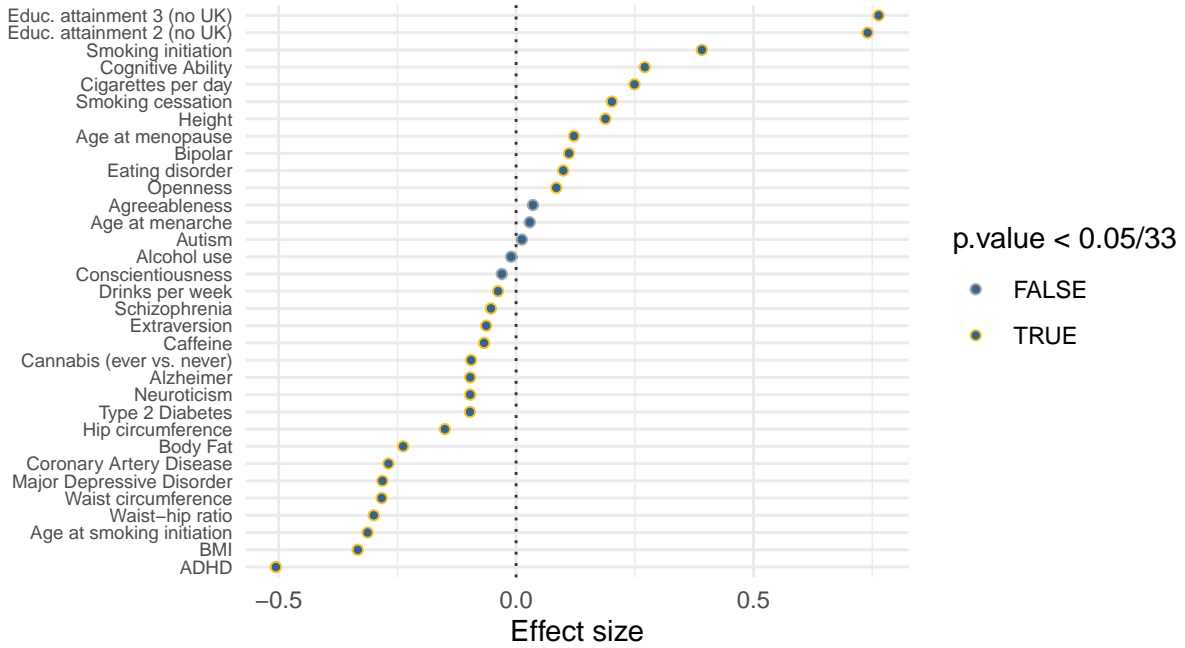


Figure 16: Effects of polygenic scores on age at first live birth

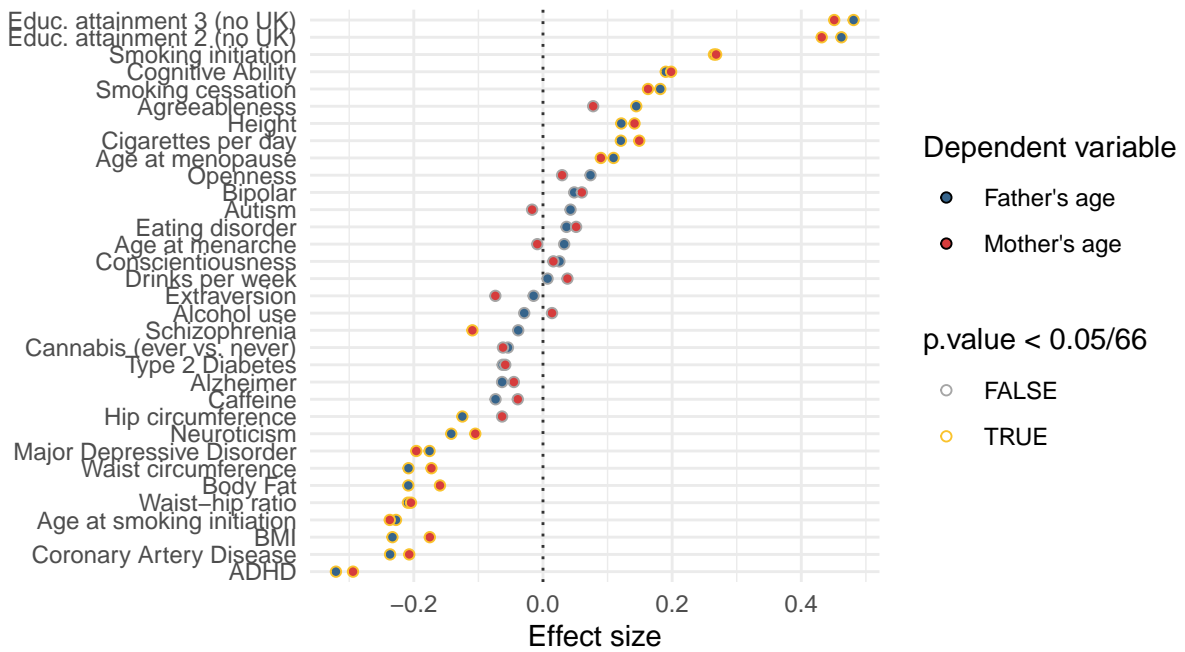


Figure 17: Effects of polygenic scores on parents' age at own birth, eldest siblings

## 5.6 Genetic correlations with EA3

Another way to examine the “earnings” theory of natural selection is to compare effect sizes of PGS with their genetic correlation with educational attainment (EA3). Since EA3 strongly predicts earnings, if earnings drives differences in fertility, we’d expect a correlation between the two sets of results. Figure 18 shows this is so.

TODO: ref source of data.

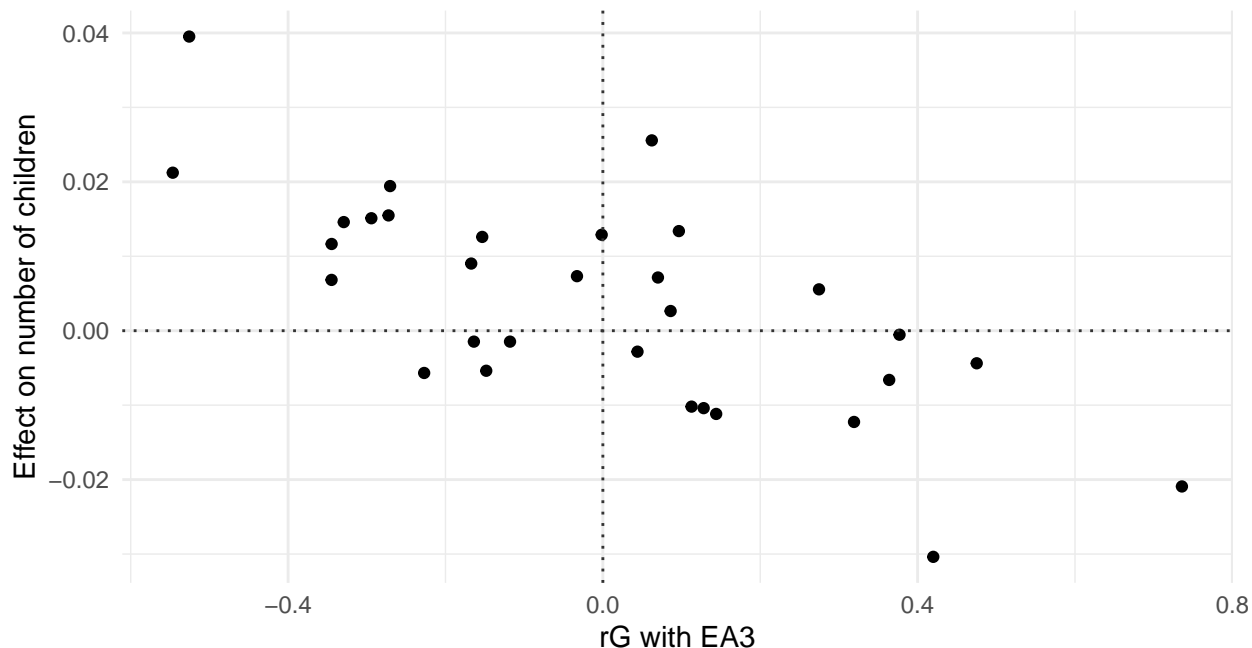


Figure 18: Effect size on n siblings by genetic correlation with EA3

## 5.7 Number of children

Figure 19 shows the full distribution of number of children born for different ventiles of the EA3 polygenic score. The strongest relationship seems to be for having 0 children versus 1 or more.

## 5.8 Causality

Different polygenic scores are correlated. Table 4 shows the top correlations in the sample. Because of this, bivariate correlations between PGS and number of children might be driven by other genetic scores. To explore which polygenic scores are driving negative selection, we run a single omnibus regression of number of children on all the PGS. We exclude EA2, waist-hip ratio, waist-circumference, and “Hip combined” since they are highly correlated with other scores, which could make our estimates unstable. Figure 20 shows the results. Interestingly, several PGS remain independently significant, although effect sizes are reduced.

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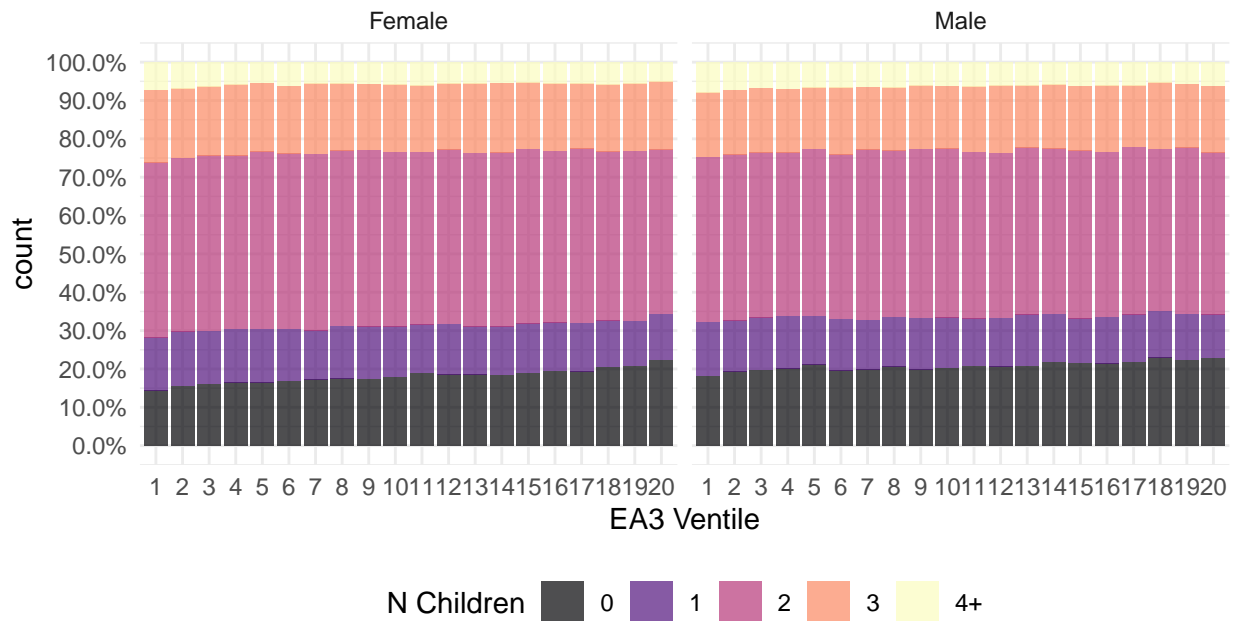


Figure 19: Number of children by ventiles of EA3 PGS

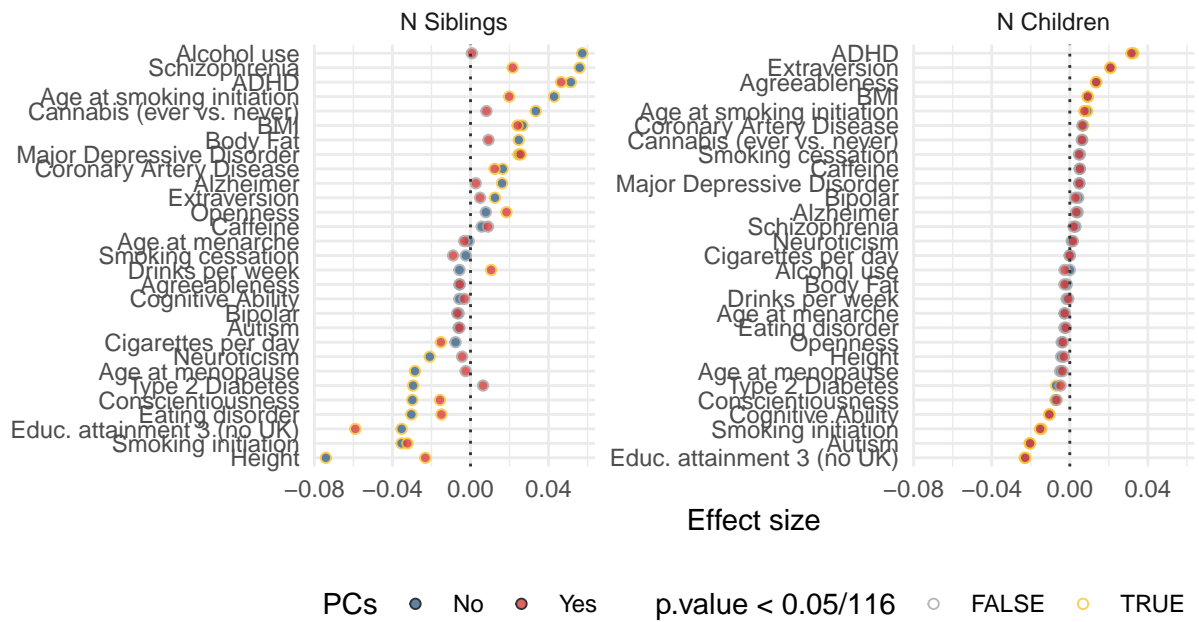


Figure 20: Partial correlations with number of children

Table 4: Top 10 correlations between polygenic scores

PGS	PGS	Correlation
Educ. attainment 2 (no UK)	Educ. attainment 3 (no UK)	0.89
Hip circumference	Waist circumference	0.807
BMI	Waist circumference	0.753
Waist circumference	Waist-hip ratio	0.711
BMI	Hip circumference	0.697
Body Fat	Waist circumference	0.435
BMI	Body Fat	0.425
BMI	Waist-hip ratio	0.425
Body Fat	Hip circumference	0.385
ADHD	Autism	0.328

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