

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 generations, we would like to extend the analysis over time. If natural selection moves in the same direction over multiple generations, this 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.

This paper attempts 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. At the same time it suggests some answers to the questions above.

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 that 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 as 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, we show that the polygenic scores' raw effects on fertility are negatively correlated with their effects on income; on the other hand, when we control for age at first live birth, scores' effects on fertility and on household income

are positively correlated. These 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

Figure 1 plots mean polygenic scores by 5-year birth intervals, for the entire sample. Several scores show consistent increases or declines over this 30-year period, of the order of 5% of a standard deviation.

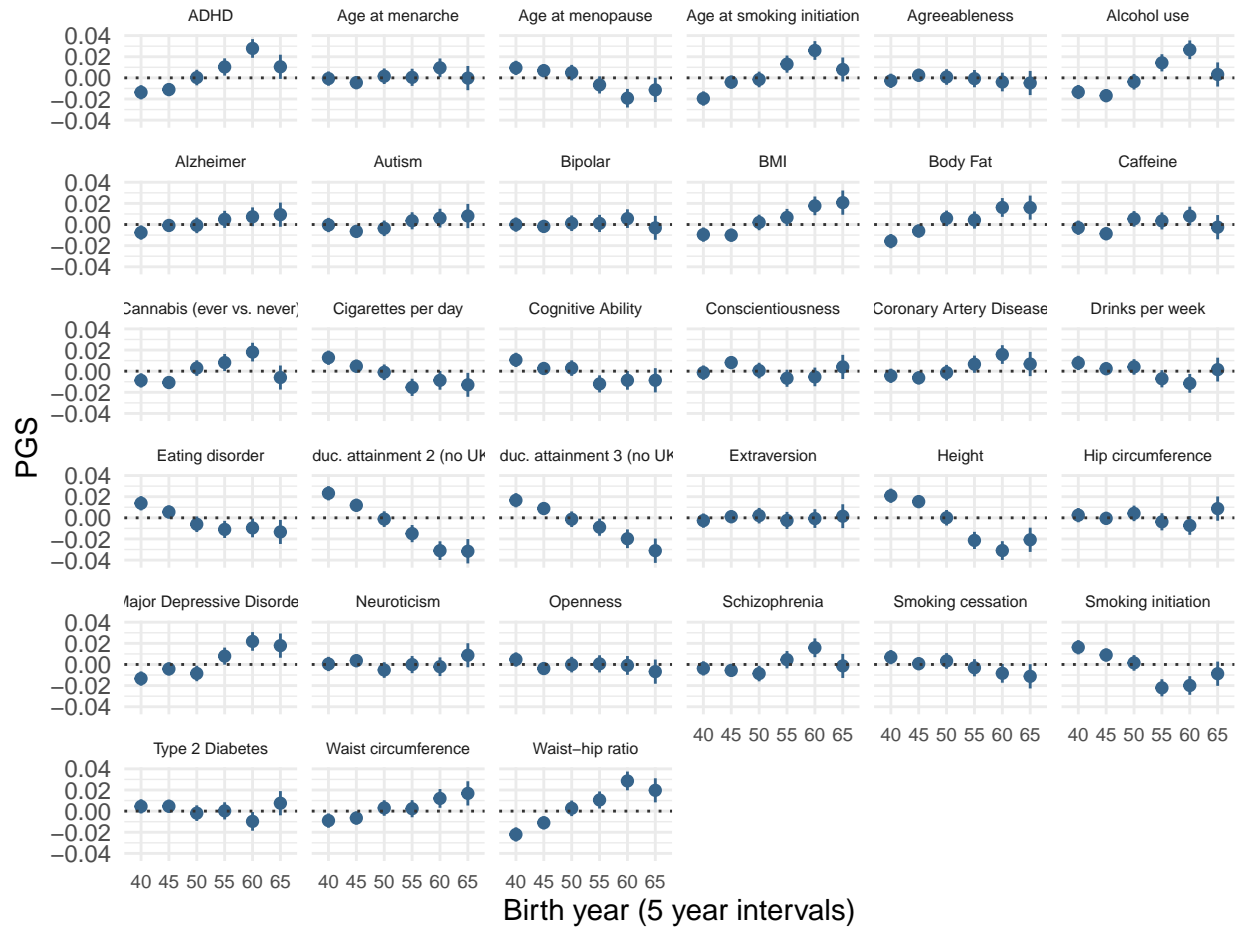


Figure 1: Mean polygenic scores by birth year in UK Biobank. Points are means for 5-year intervals. Lines are 95% confidence intervals.

These estimates may suffer from ascertainment bias within the UK Biobank 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).

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:

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

The effect size β measures the strength of natural selection within the sample (or a given subgroup). In fact, since polygenic scores are normalized to mean 0, β is the expected polygenic score among children of the sample or subgroup.

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 increase the age at which a respondent leaves school.

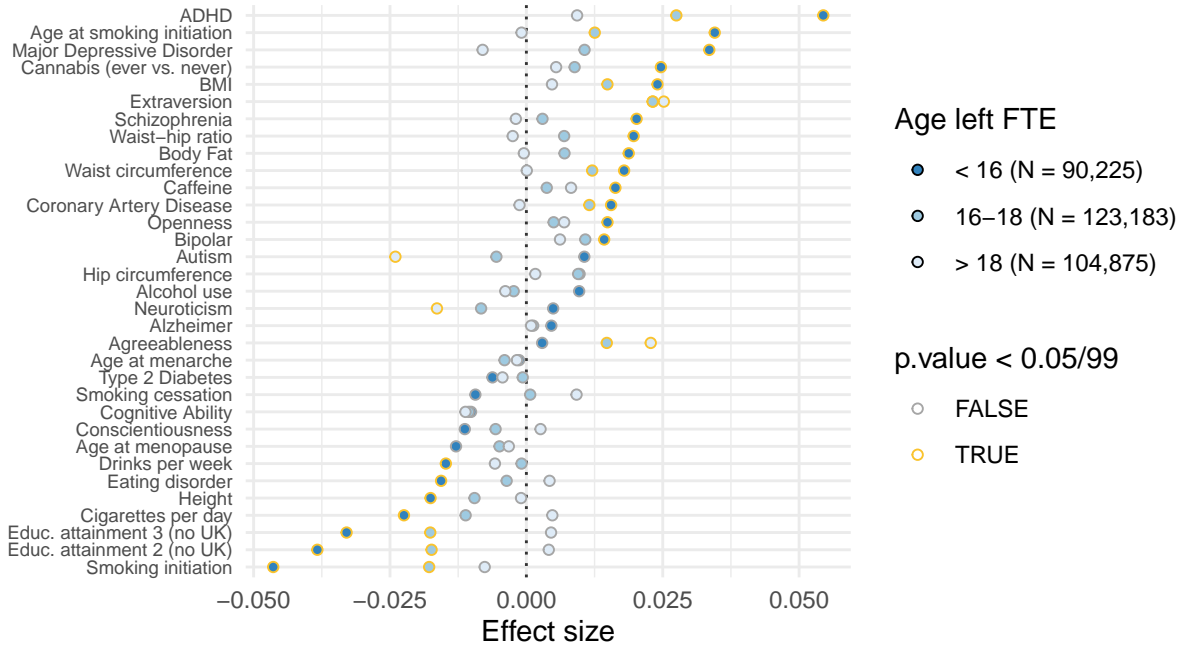


Figure 2: Effect sizes on number of children by age left full-time education

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.

When we split respondents up by other demographic variables, we get a more surprising result: the direction of natural selection is different among different subgroups.

Figure 5 shows effect sizes estimated separately for each tercile of age at first live birth. Several effects are strikingly different across terciles. ADHD and MDD are selected for amongst the youngest third of mothers,

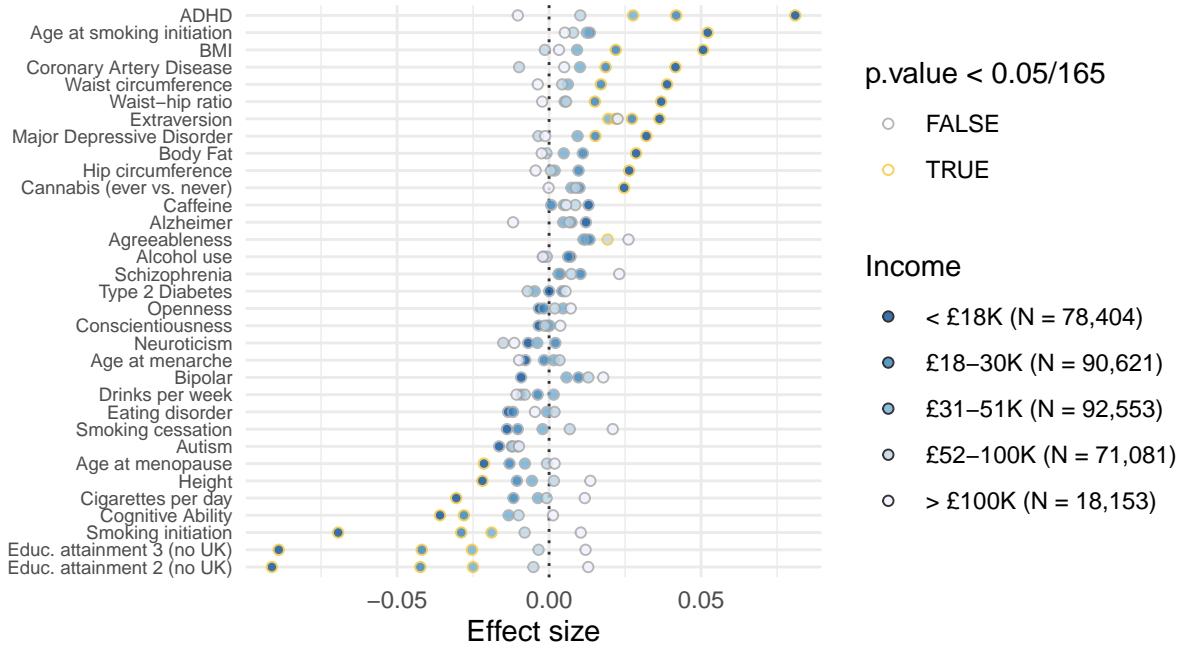


Figure 3: Effect sizes on number of children by household income

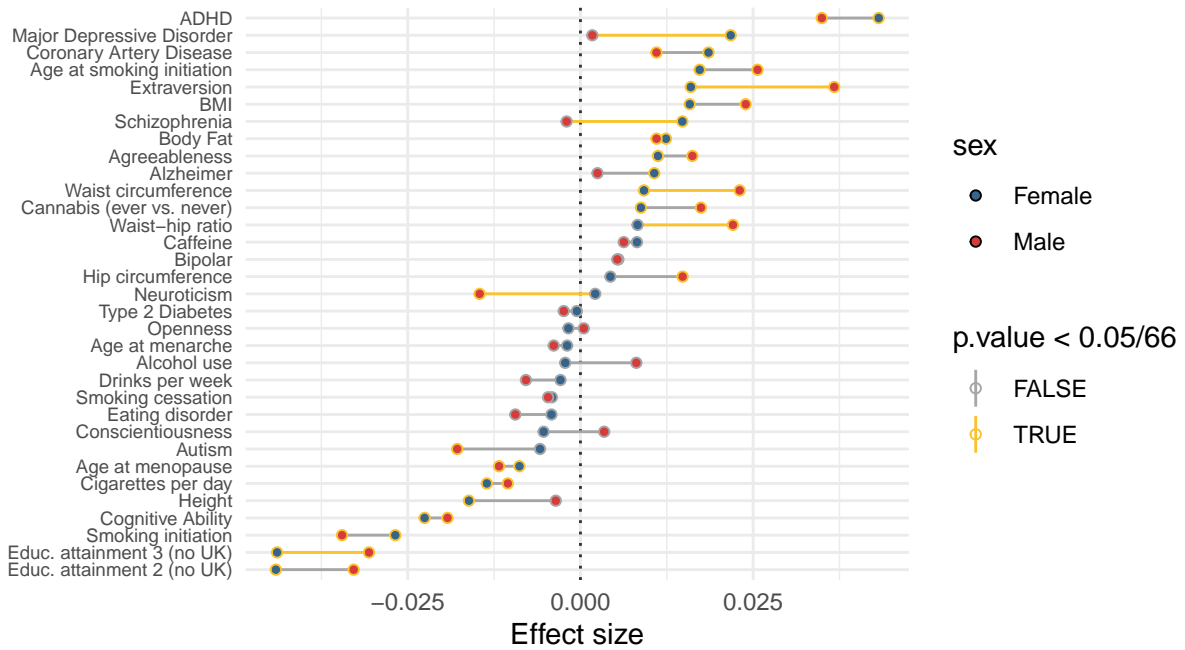


Figure 4: Effect sizes on number of children by sex. Lines show significant differences

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.

Figure 6 splits males and females by lifetime number of sexual partners, at the median value of 3. Again, selection effects are reversed across the groups. Among men and women with more than 3 sexual partners, for example, educational attainment is selected against; among those with 3 or fewer sexual partners, it is selected for.

Figure 7 splits respondents up by whether they were living with a spouse or partner at the time of interview. Effects are generally the same sign in both groups, but are much larger among those not living with a spouse or partner.

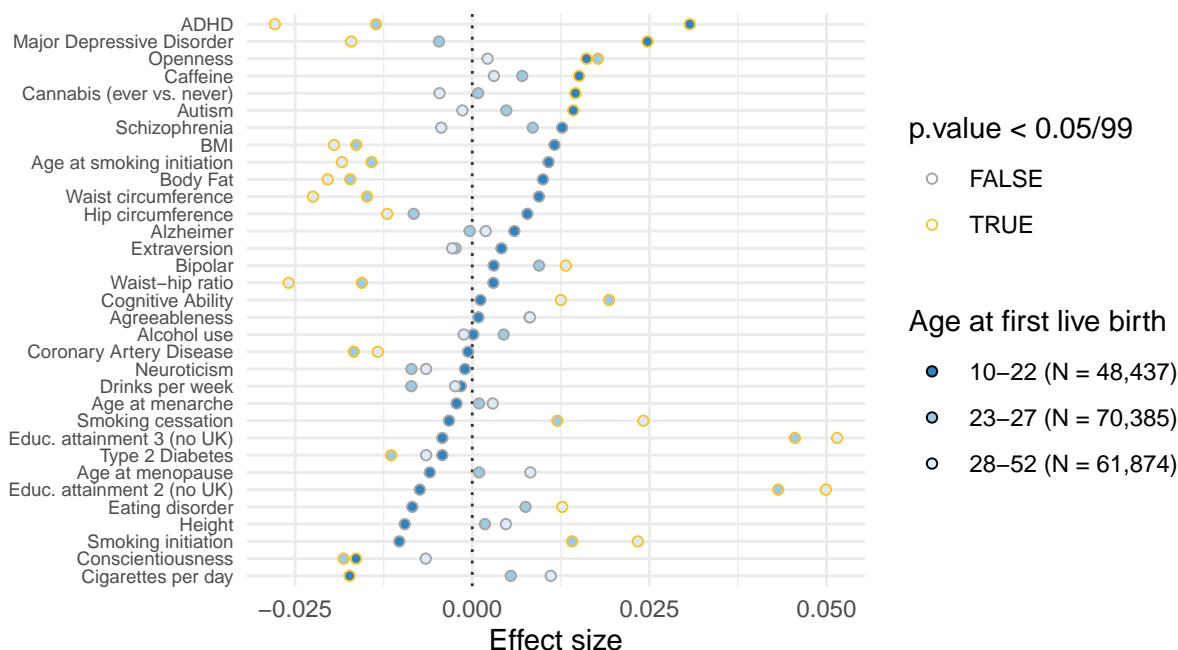


Figure 5: Effect sizes on number of children, by age at first live birth terciles

Figure 8 shows the results of regressions for women only, controlling for age at first live birth. Effect sizes are greatly reduced. This could be because the 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 age at first live birth, and raw effect sizes, is -0.75.

3.1 Weighted regressions

To compensate for ascertainment bias in the UK Biobank sample, 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).

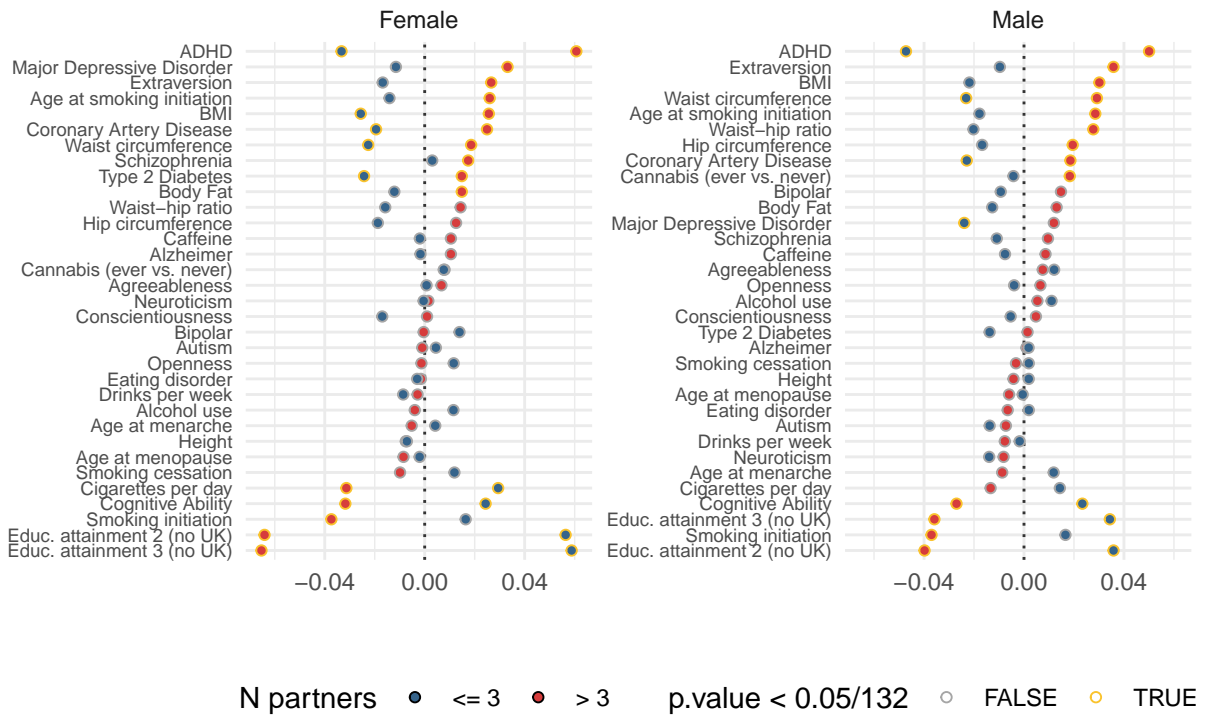


Figure 6: Effect sizes on number of children by number of sexual partners

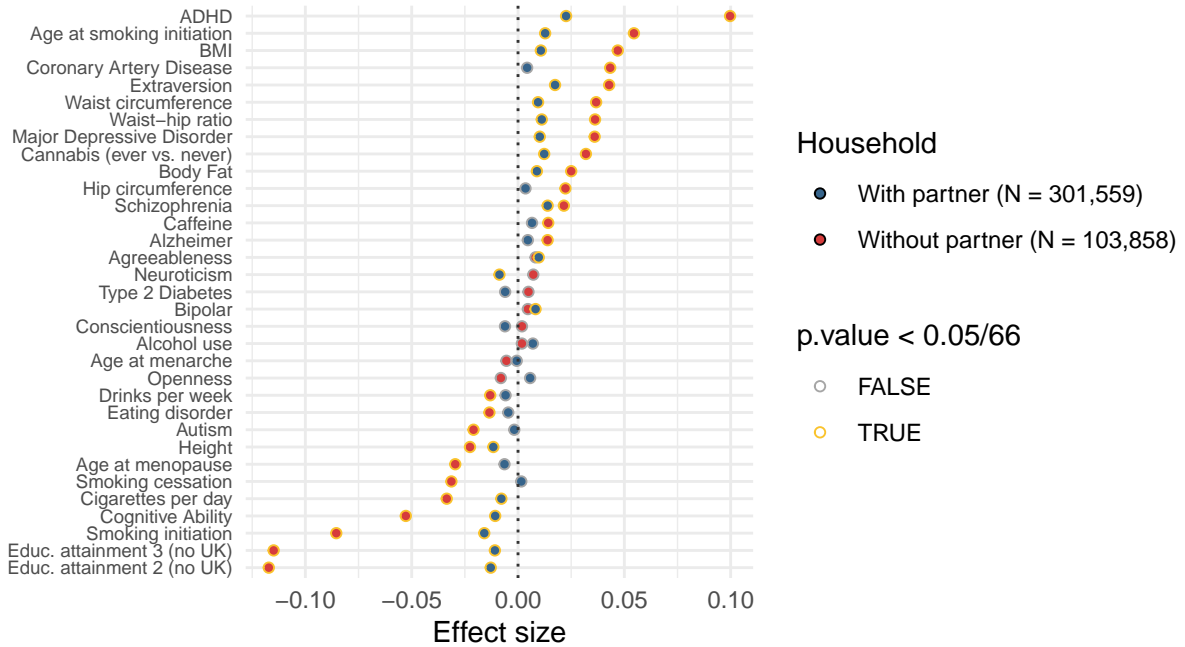


Figure 7: Effect sizes on number of children by household type

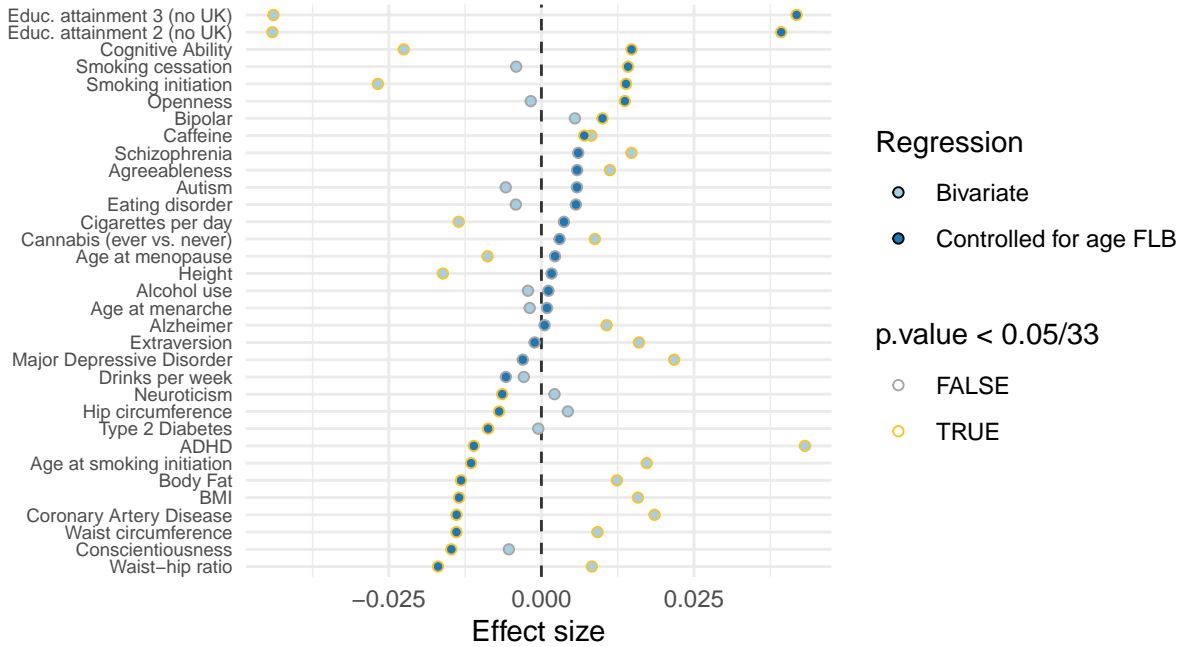


Figure 8: Effect sizes on number of children, controlling for age at first live birth (women only). Effect sizes for women without controls are shown for comparison

Figure 9 plots effect sizes among the entire sample, using these weighting schemes. We include unweighted regressions for comparison. Weighted effect sizes are significantly larger in absolute value. Table 1 gives effect sizes as a proportion of unweighted effect sizes for the census-based weightings.

Effect sizes are reasonably consistent across the geographical and age/qualification weights, but they are increased again when we weight by age at first live birth. 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 view our estimates as likely to be conservative.

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 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,

Table 1: Weighted effect sizes as a proportion of unweighted

PGS	Weighting		
	Geographical	Age/Qualification	Age/Qual/FLB
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/FLB as a proportion of unweighted regressions for females only.

but do not change over time within either dependent variable, the explanation may be due to remaining ascertainment bias within our sample.

3.3 Mechanisms behind modern natural selection

Why do selection effects have opposite signs across certain subgroups – for example, across older and younger mothers by age at first live birth, or across those with more and fewer lifetime sexual partners? 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

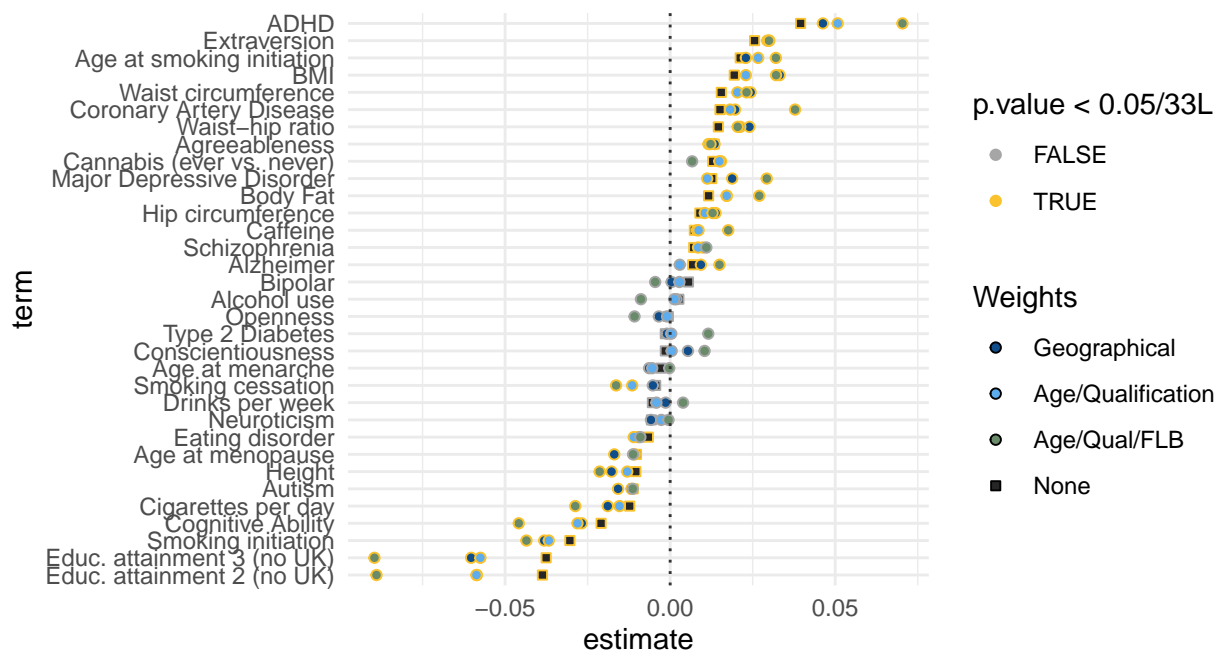


Figure 9: Effects of polygenic scores on fertility. Weighted regressions.

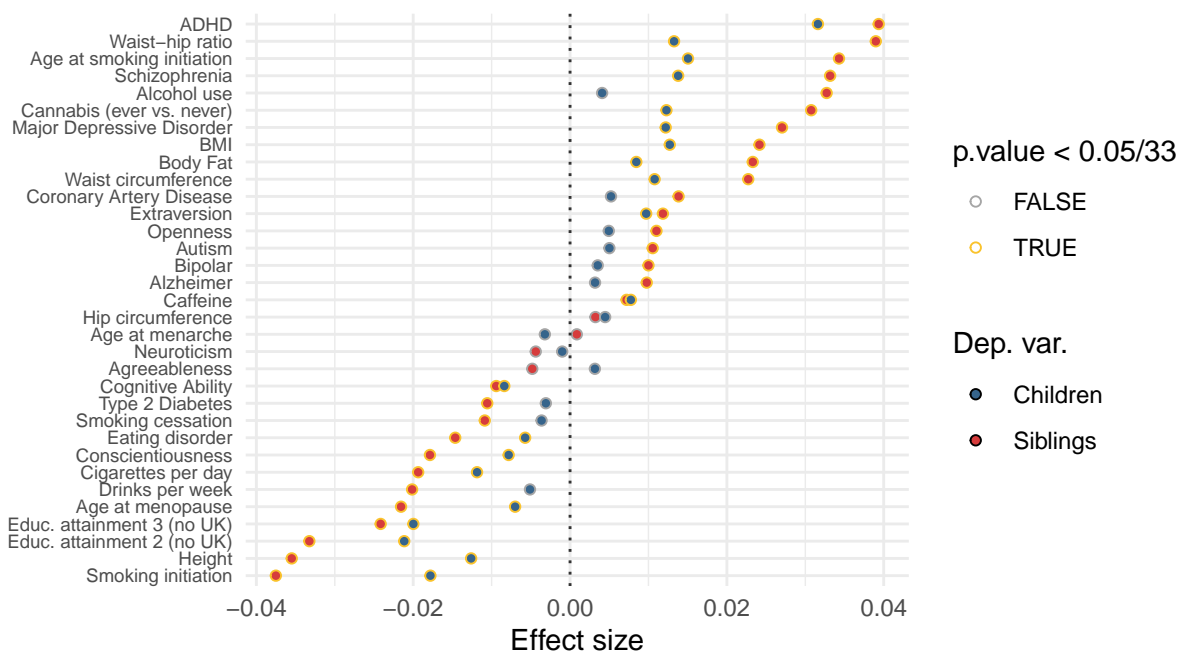


Figure 10: Effects of polygenic scores on fertility, respondents' parents vs. respondents

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 differently-signed effects 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. 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.

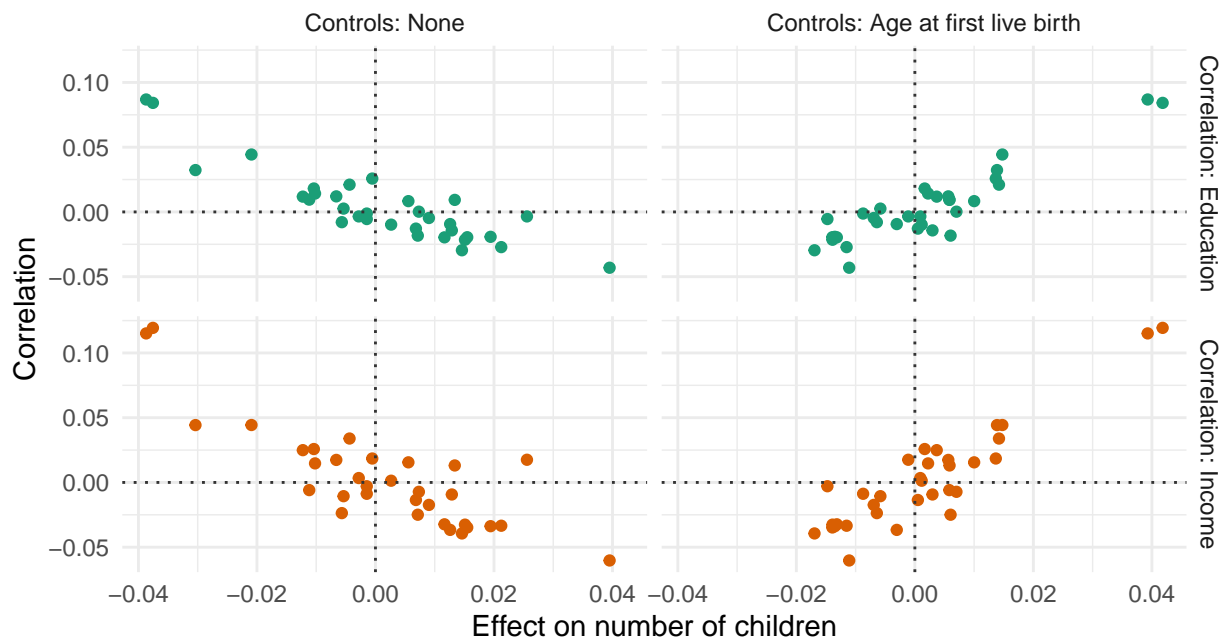


Figure 11: Effect sizes on number of children, with and without controls for age at first live birth, by correlations with income and education

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. Potentially, natural selection could increase the health burden on modern societies, but that depends on effect sizes. Existing work argues that these are small. However, as we show, estimates can be crucially affected by ascertainment bias in population samples. 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 impulsivity and low time discount rates, via the channel of early sexual behaviour. The data here provide some support for this: scores which might plausibly be linked to impulsivity, like ADHD and age at smoking initiation, are selected for. However, the “impulsivity” theory is less good at explaining variation in selection across the full range of scores, including e.g. waist-hip ratio and BMI. Impulsivity also does not explain the reversed sign of selection among e.g. older parents. Overall, then, the economic theory is probably 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).

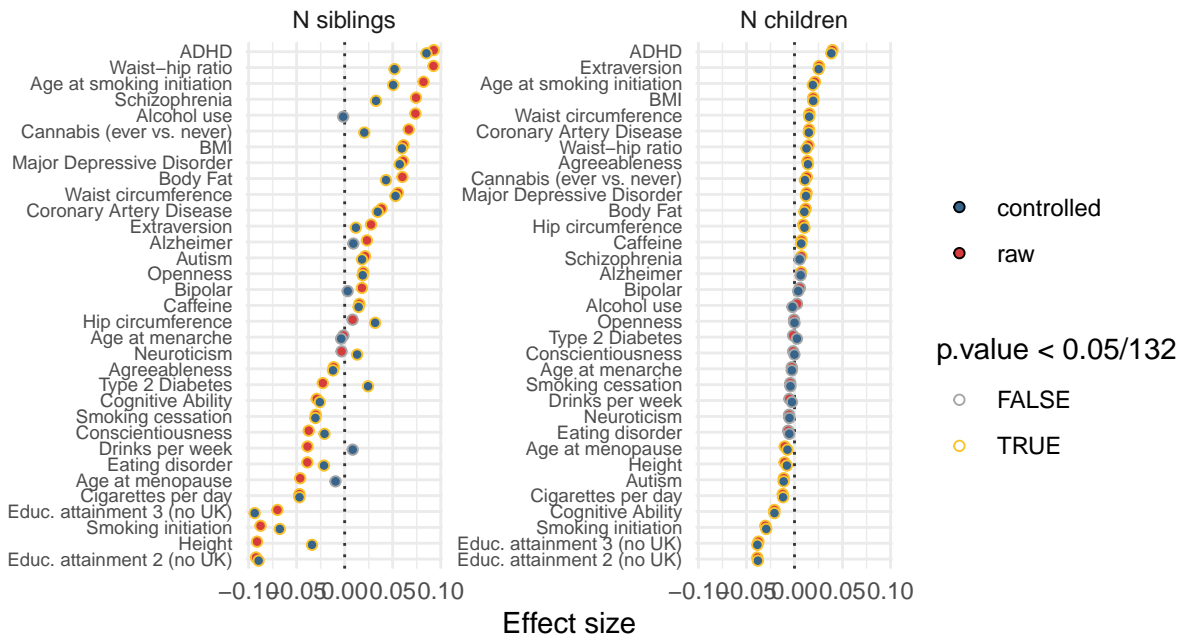


Figure 12: Effects of residualized polygenic scores on number of siblings/children.

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.

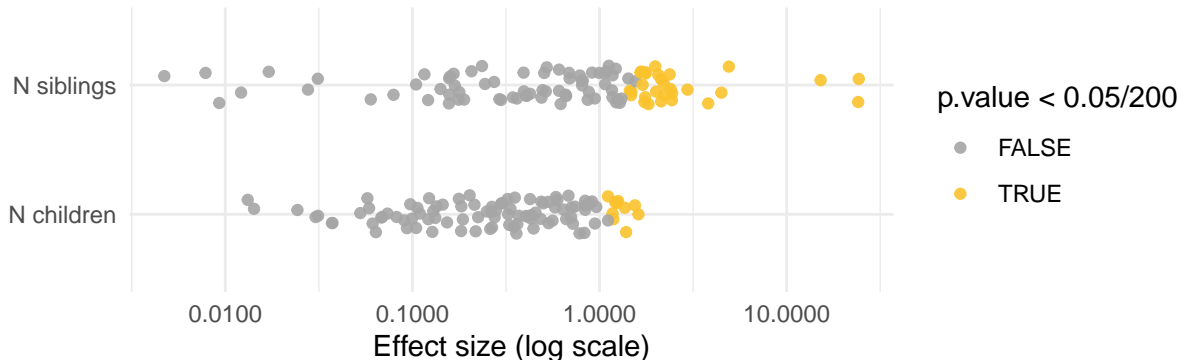


Figure 13: Effect of principal components of genetic data on number of siblings/children. Absolute effect sizes are plotted. Each dot represents one bivariate regression. Points are jittered on the Y axis.

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 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 14 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: $\rho = \text{cor_raw_moth}$).

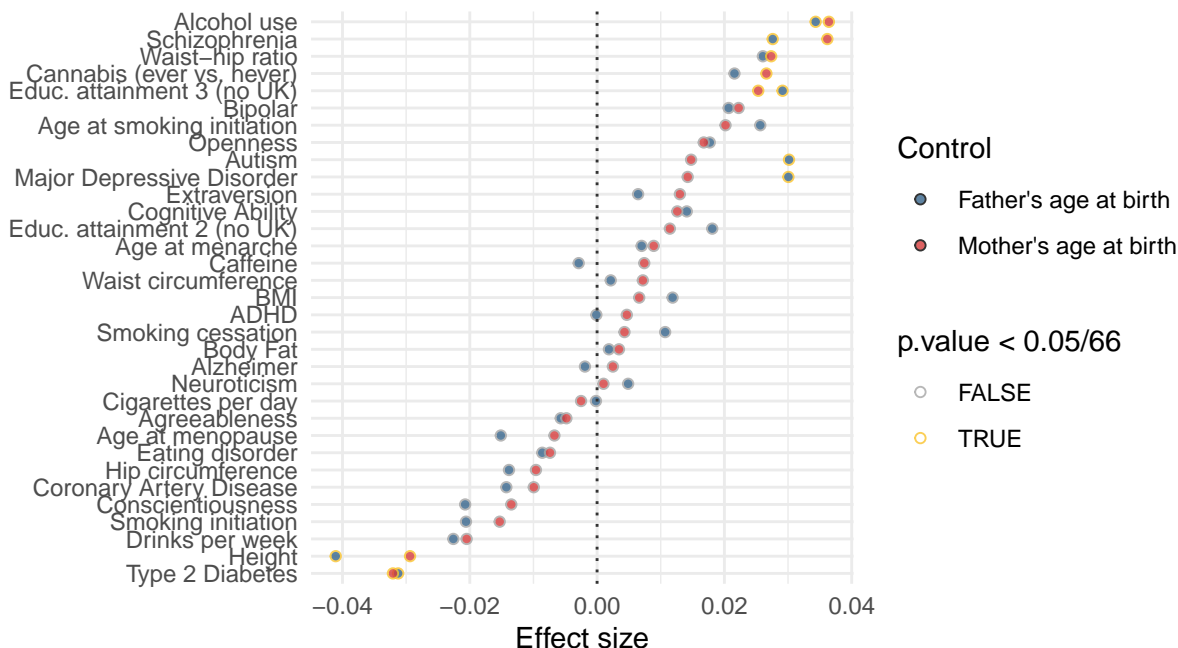


Figure 14: Effect sizes on number of siblings controlling for parents' age at birth, eldest siblings

5.4 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 15 plots estimated effect sizes from bivariate regressions for respondents, and Figure 16 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

5.5 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 17 shows this is so.

TODO: ref source of data.

5.6 Number of children

Figure 18 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.

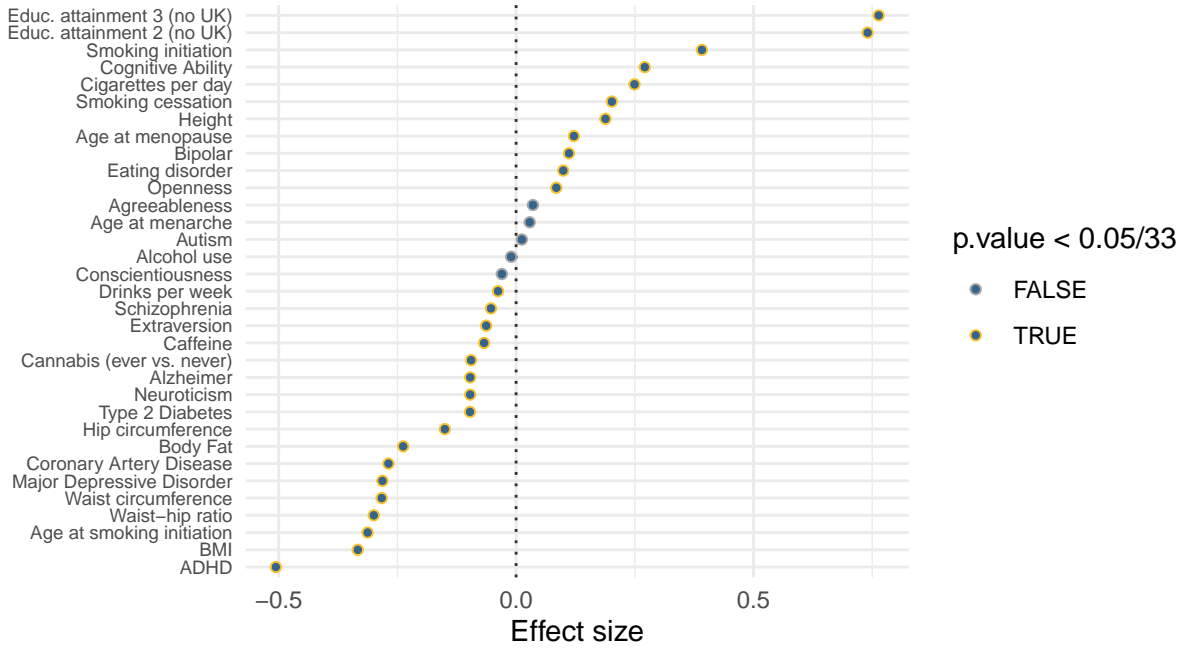


Figure 15: Effects of polygenic scores on age at first live birth

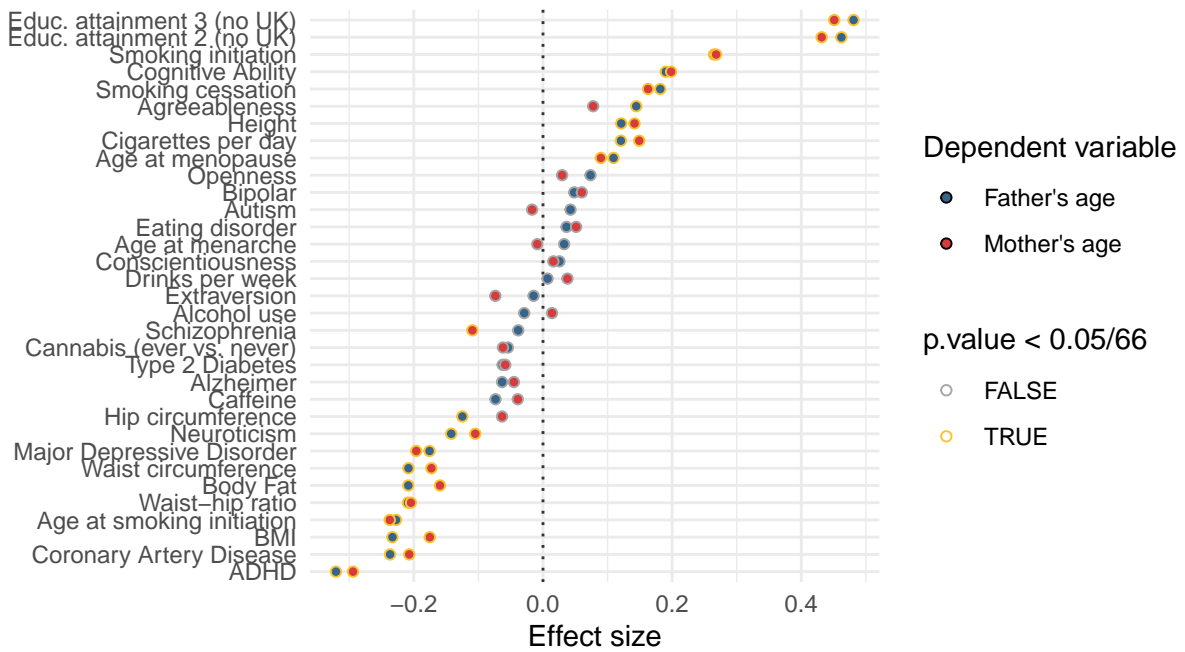


Figure 16: Effects of polygenic scores on parents' age at own birth, eldest siblings

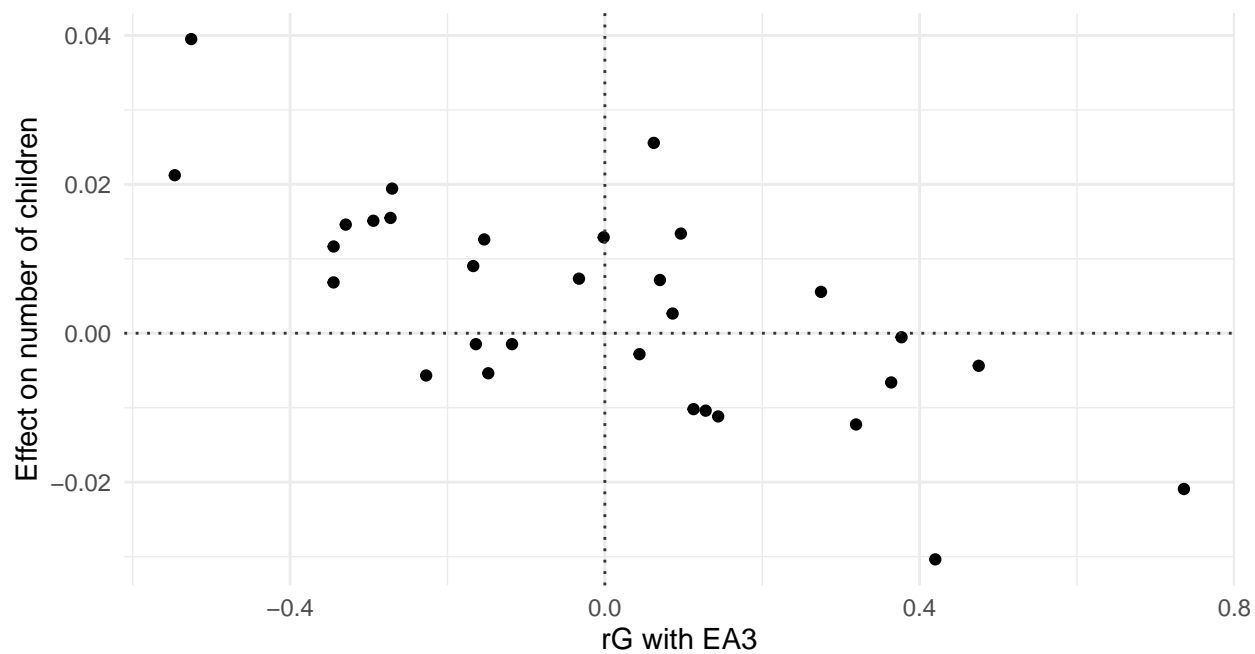


Figure 17: Effect size on n siblings by genetic correlation with EA3

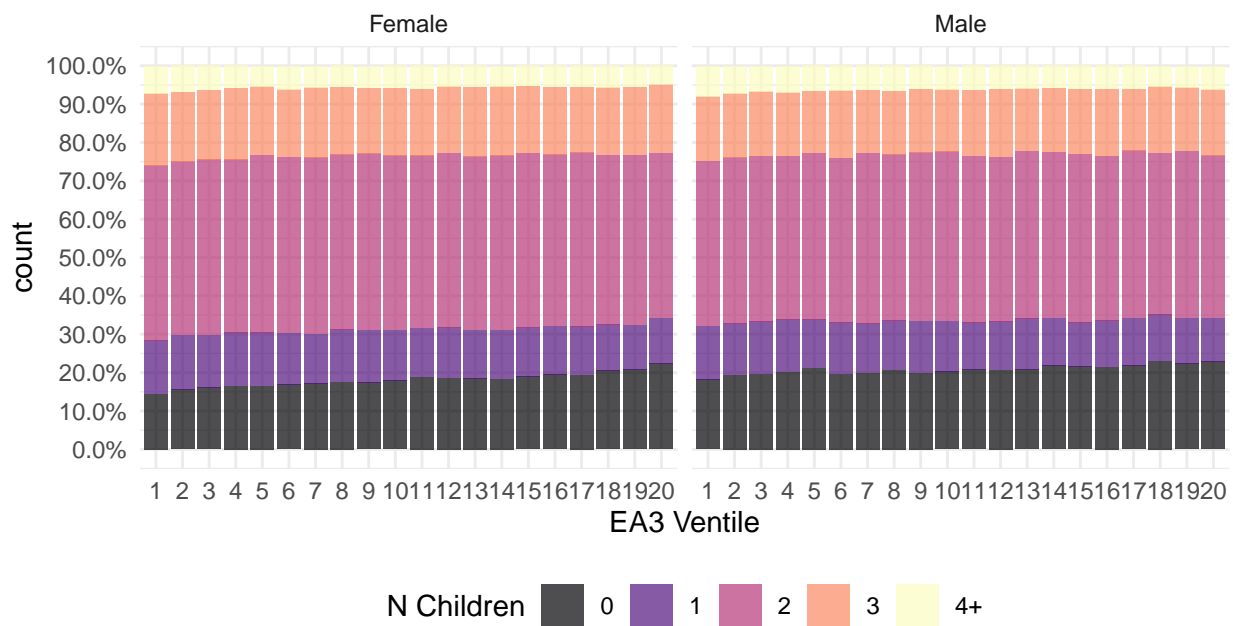


Figure 18: Number of children by ventiles of EA3 PGS

5.7 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 19 shows the results. Interestingly, several PGS remain independently significant, although effect sizes are reduced.

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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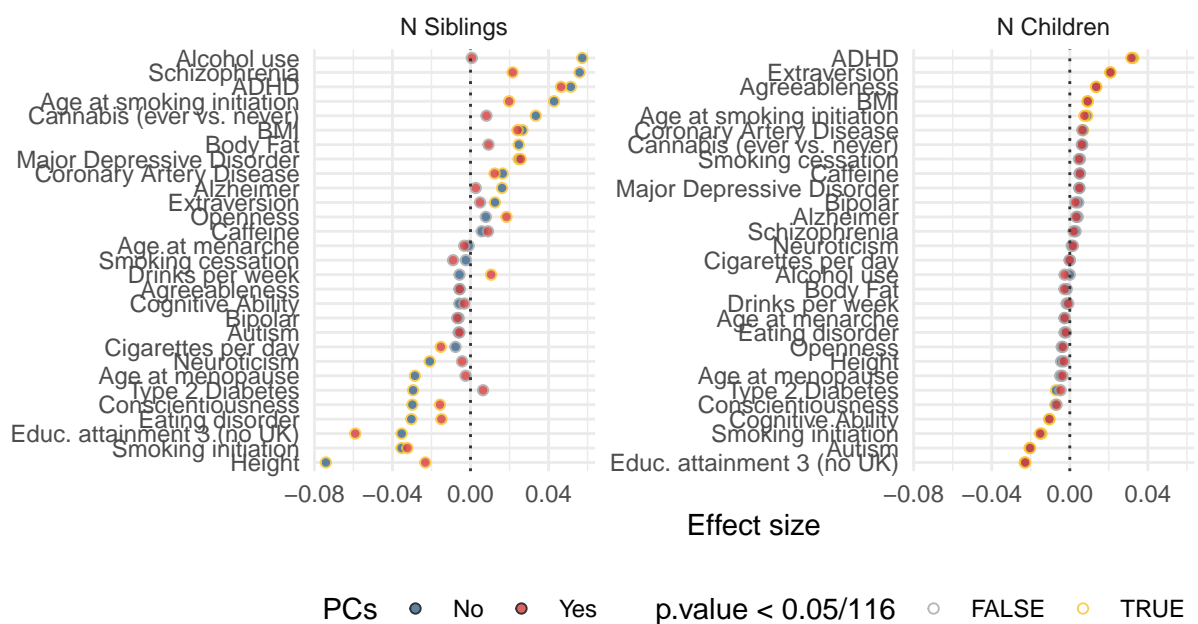


Figure 19: Partial correlations with number of children