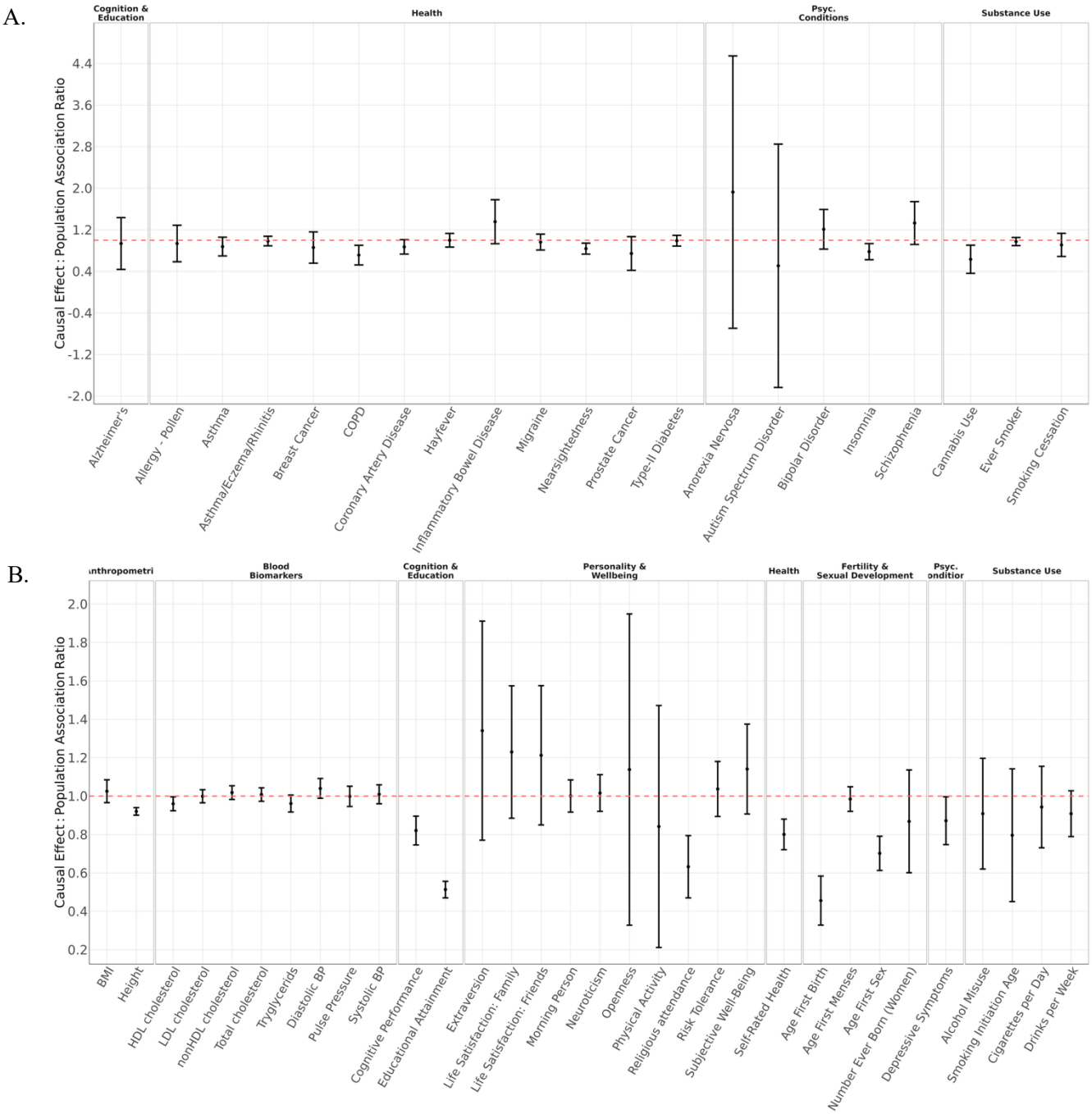
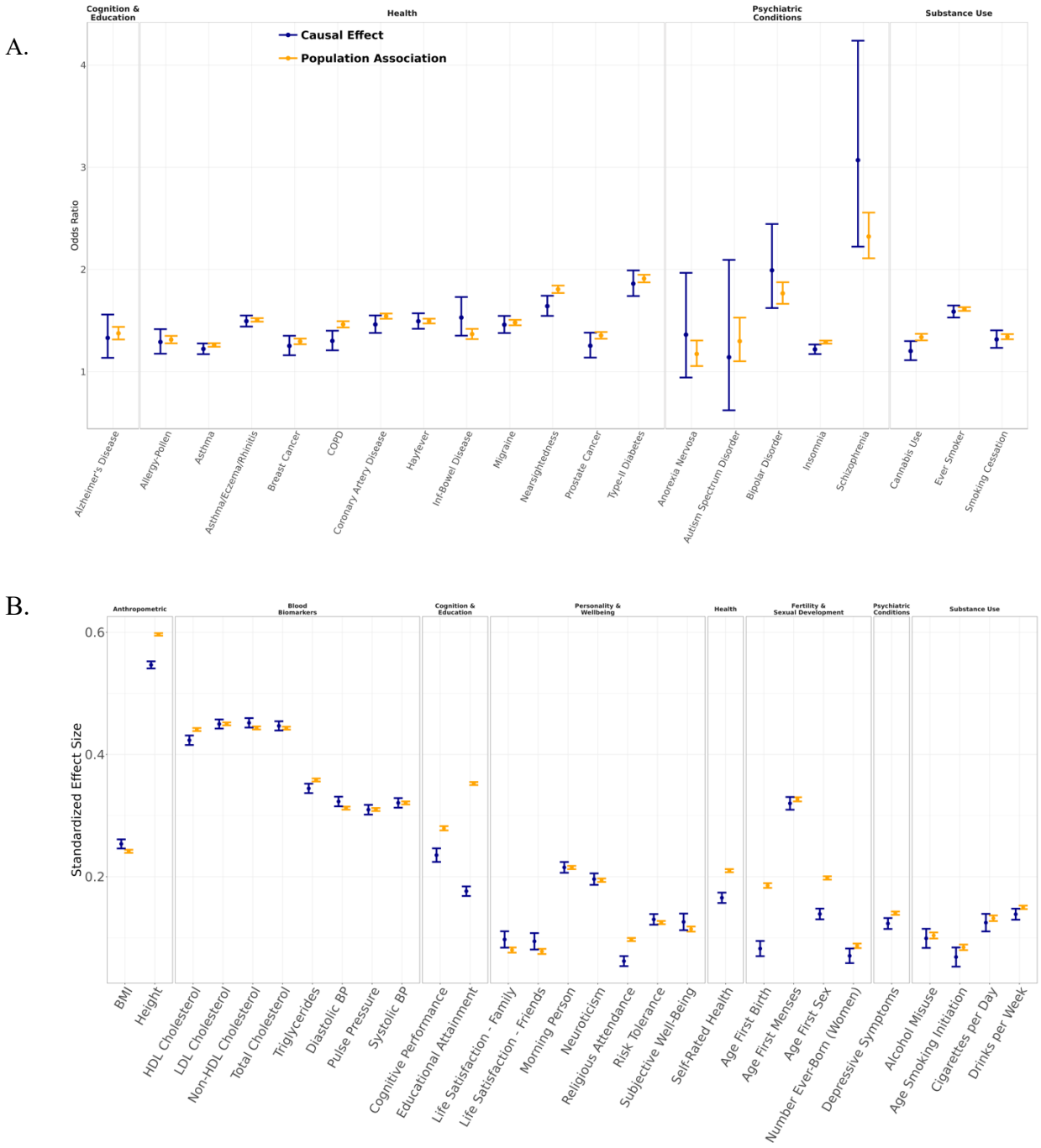
Supplementary Figure 1. Ratio of causal effects of PGIs to their population associations meta-analyzed across UKB and WLS



Notes: Ratio of causal effects of PGIs to their population associations among binary (Panel A) and quantitative (Panel B) phenotypes. The causal effects were estimated in a sample of first-degree relatives, while the population associations were estimated in a sample of unrelated individuals in the third partition (UKB3). The ratios were calculated by dividing the direct effects by the population associations. Error bars represent 95% confidence intervals. Standard errors were computed using the delta method (Methods).

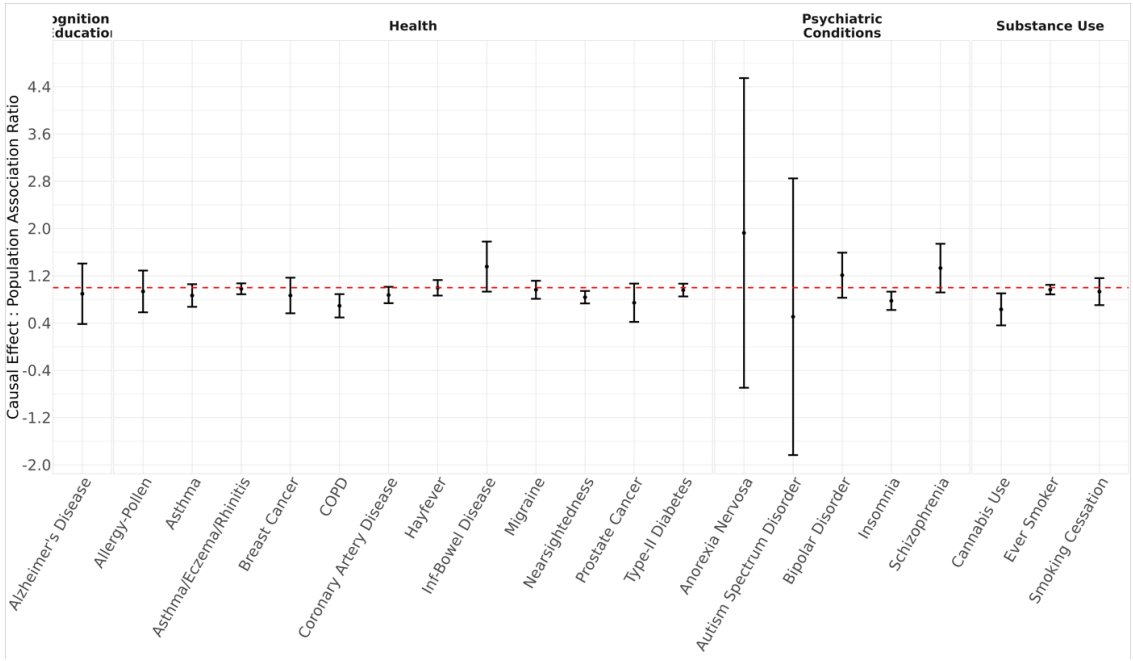
Supplementary Figure 2. Causal effects of PGIs versus their population associations in UKB



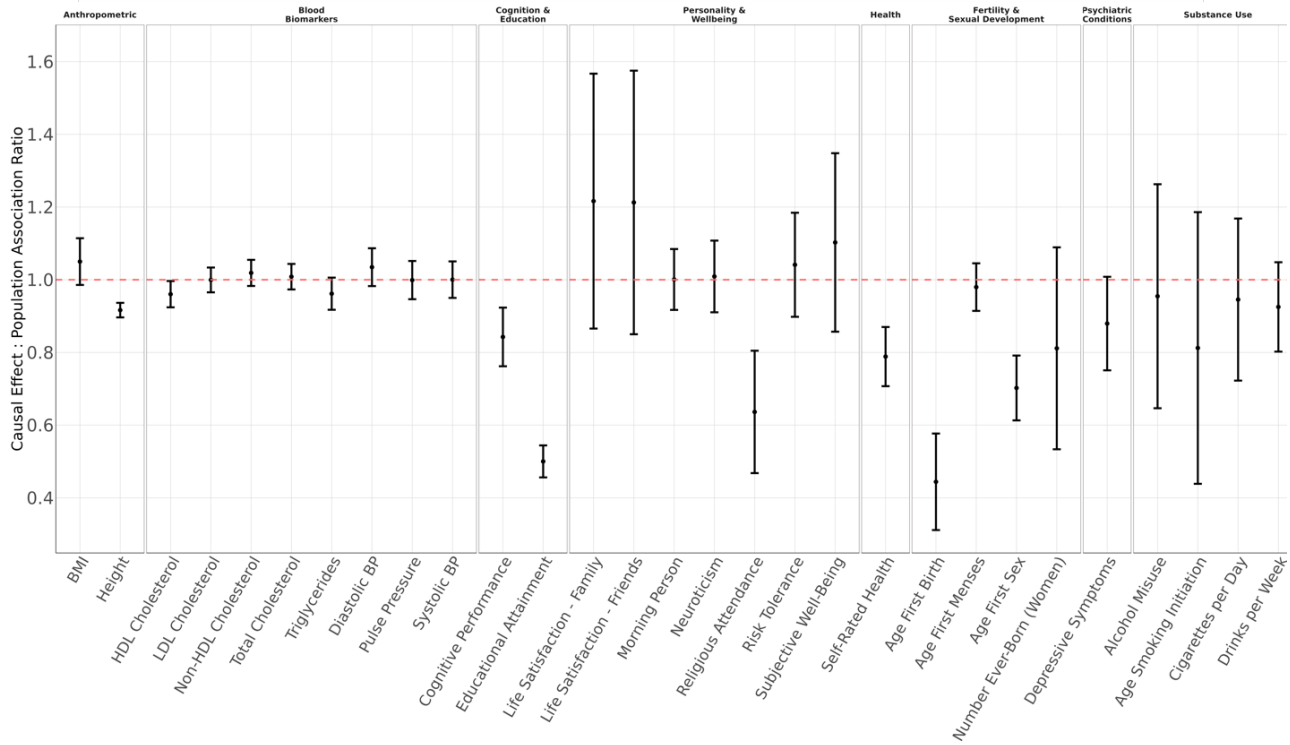
Notes: Causal effects and population associations of PGIs in UKB. Causal effects were estimated in the sample of first-degree relatives, and population associations in a sample of unrelated individuals (third partition of UKB). For binary phenotypes, population associations were estimated using logistic regression and causal effects were estimated using a generalized mixed linear model with logistic link function in order to account for residual correlations between siblings (Panel A). For quantitative phenotypes, population associations were estimated using linear regression, and causal effects were obtained from a mixed linear model (Panel B). Error bars represent 95% confidence intervals.

Supplementary Figure 3. Ratio of causal effects of PGIs to their population associations in UKB

A.



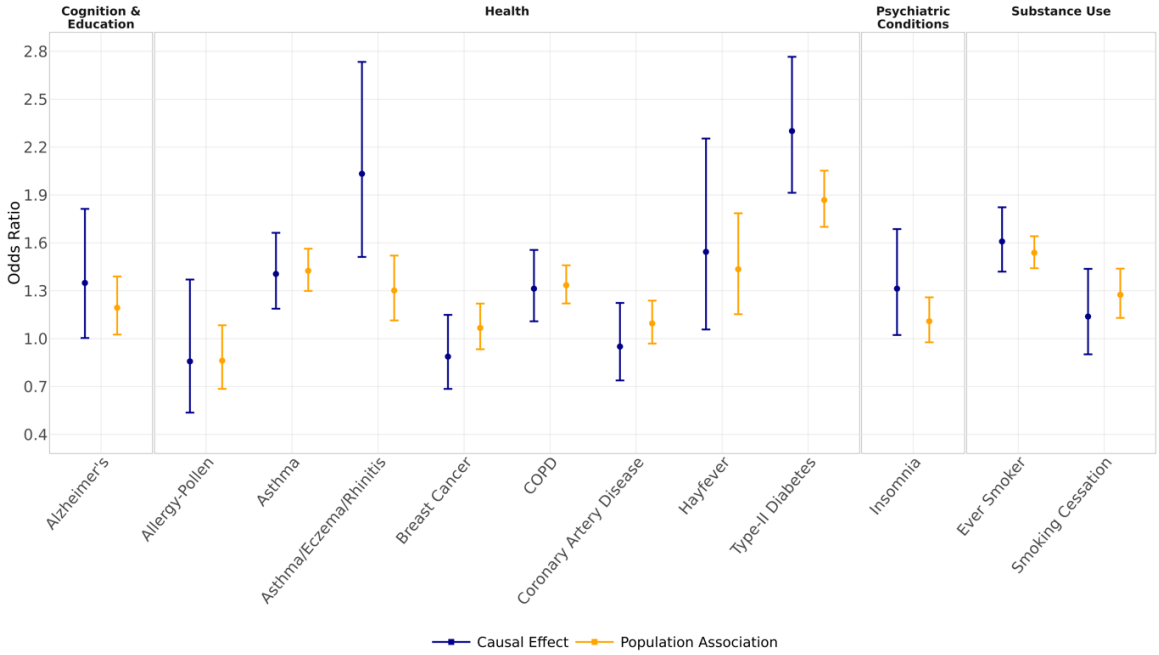
B.



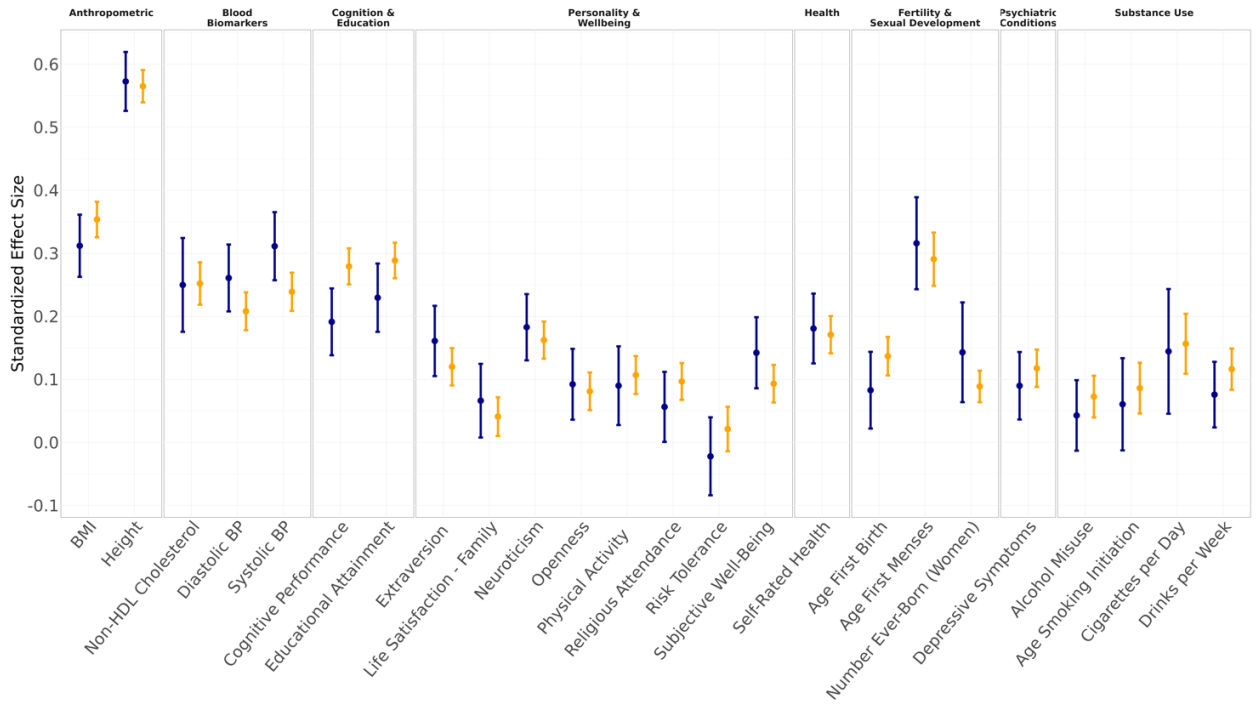
Notes: Ratio of causal effects of PGIs to their population associations among binary (Panel A) and quantitative (Panel B) phenotypes. The causal effects were estimated in a sample of first-degree relatives, while the population associations were estimated in a sample of unrelated individuals in the third partition (UKB3). The ratios were calculated by dividing the direct effects by the population associations. Error bars represent 95% confidence intervals. Standard errors were computed using the delta method (Methods).

Supplementary Figure 4. Causal effects of PGIs versus their population associations in WLS

A.



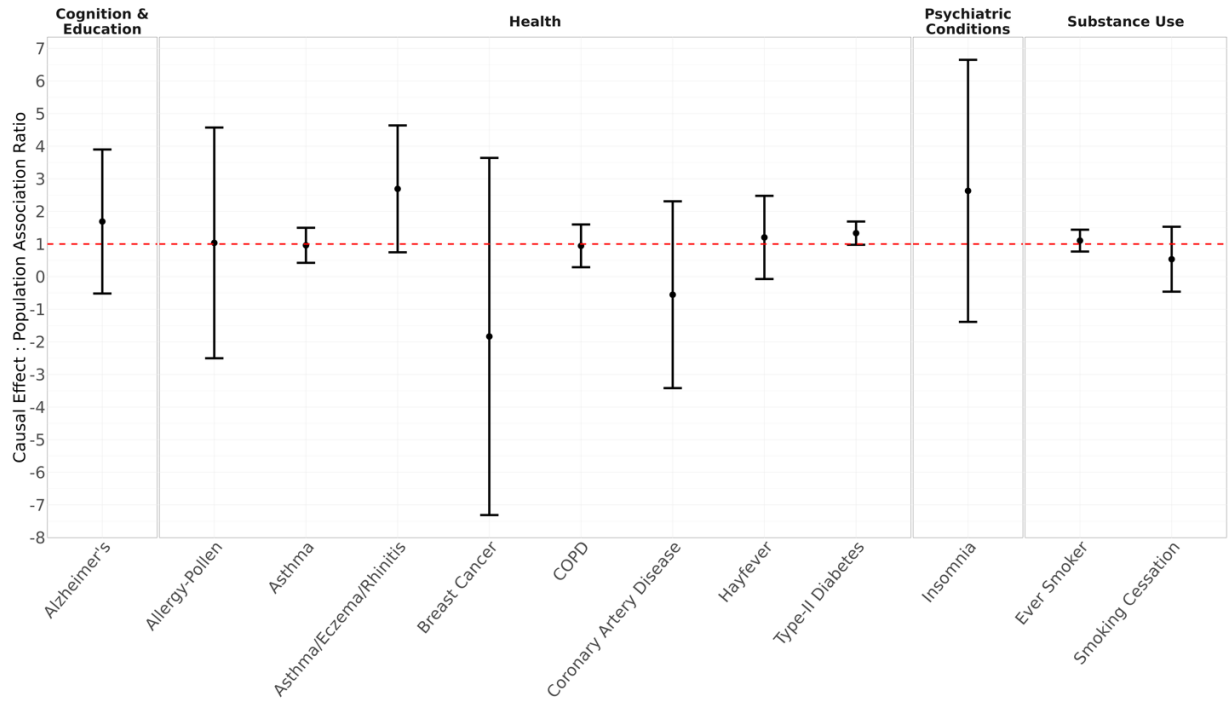
B.



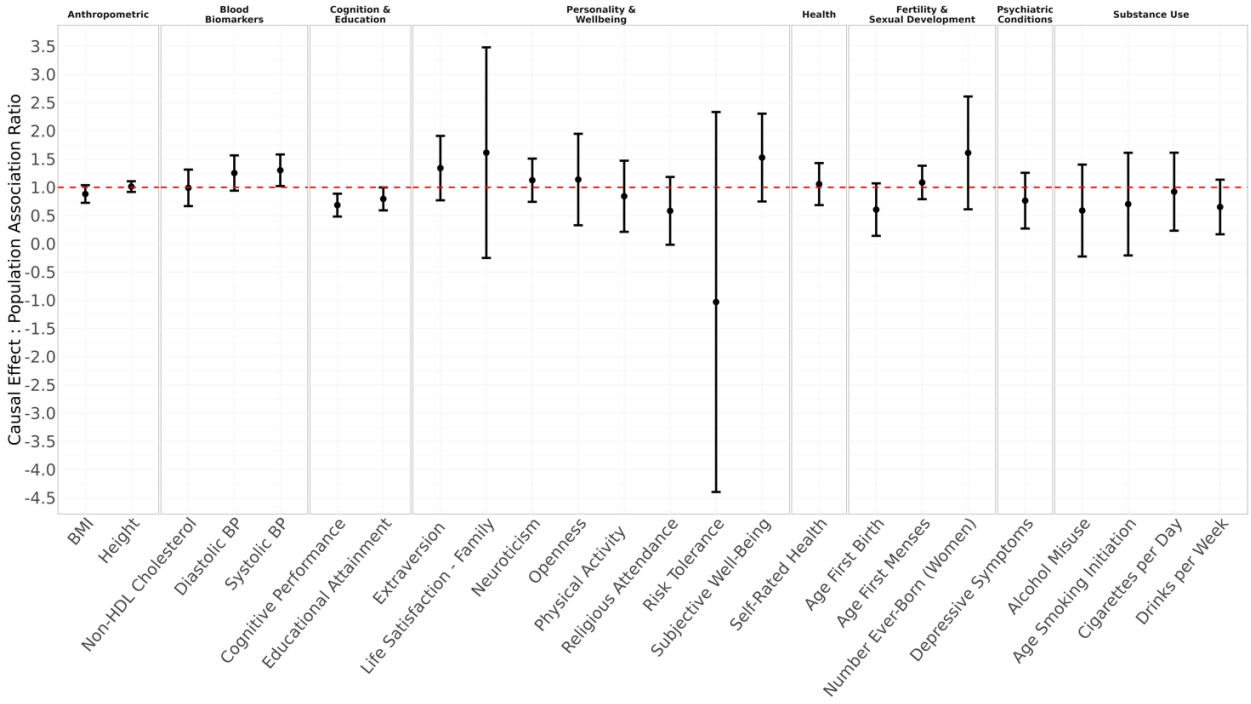
Notes: Causal effects of PGIs versus their population associations in the WLS cohort. Causal effects were estimated using first-degree relatives (those with sibling genotype data), and population associations were estimated in the sample of unrelated individuals. For binary phenotypes, population associations were estimated using logistic regression and causal effects were estimated using a generalized mixed linear model with logistic link function in order to account for residual correlations between siblings (Panel A). For quantitative phenotypes, population associations were estimated using linear regression, and causal effects were obtained from a mixed linear model (Panel B). Error bars represent 95% confidence intervals.

Supplementary Figure 5. Ratio of causal effects of PGIs to their population associations in WLS

A.

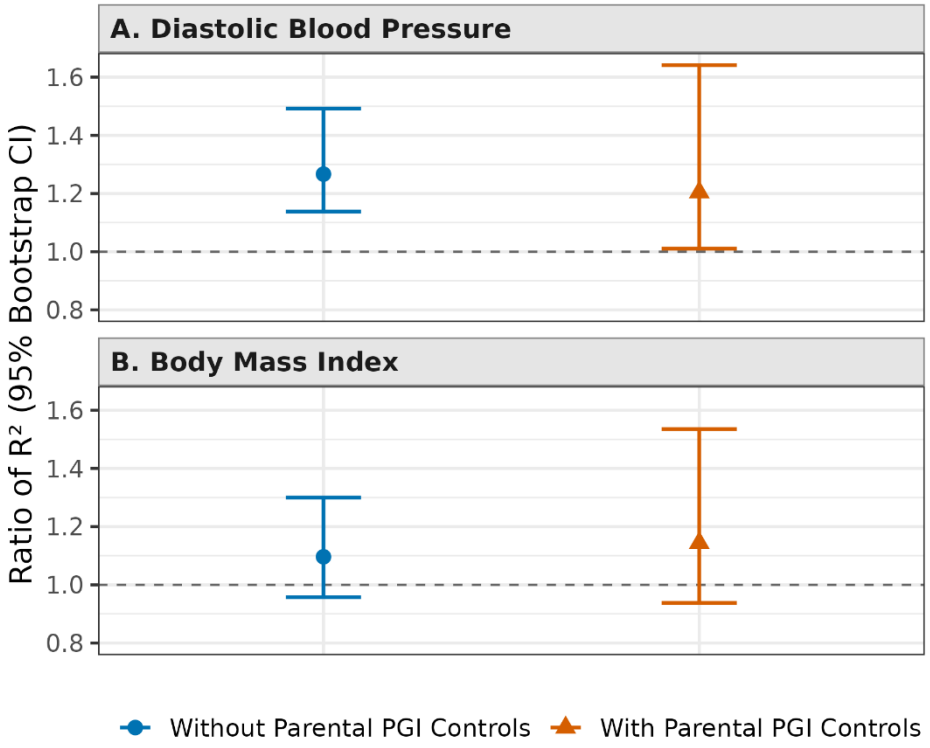


B.



Notes: Ratio of causal effect to population association of PGIs among binary (Panel A) and quantitative (Panel B) phenotypes. Causal effects were estimated using first-degree relatives (those with sibling genotype data), and population associations were estimated in the sample of unrelated individuals. Ratios were obtained by dividing the estimates of causal effects by those of population association effects. Error bars represent 95% confidence intervals. Standard errors were computed using the delta method (Methods).

Supplementary Figure 6. Ratios of incremental R^2 between subgroups, with and without parental PGI controls



Notes: Ratio of PGI predictive accuracy (incremental R^2) in subgroups of UKB for two traits, comparing models without parental PGI controls (blue circles) to models with parental PGI controls (orange triangles). Panel A shows the female / male incremental R^2 ratio for diastolic blood pressure; Panel B shows the younger / older incremental R^2 ratio for body mass index. Error bars are 95% confidence intervals obtained by the percentile method from 1,000 non-parametric bootstrap resamples of families within each subgroup. The dashed horizontal line at 1 indicates equal predictive accuracy across subgroups. Full model and bootstrap details are provided in the Methods.