

**Supplementary Information for “Genome-wide meta-analysis of problematic alcohol use
in 435,563 individuals yields insights into biology and relationships with other traits”**

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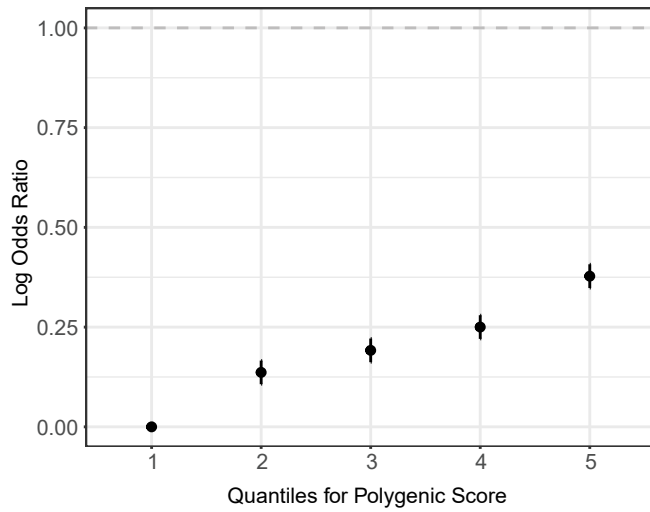
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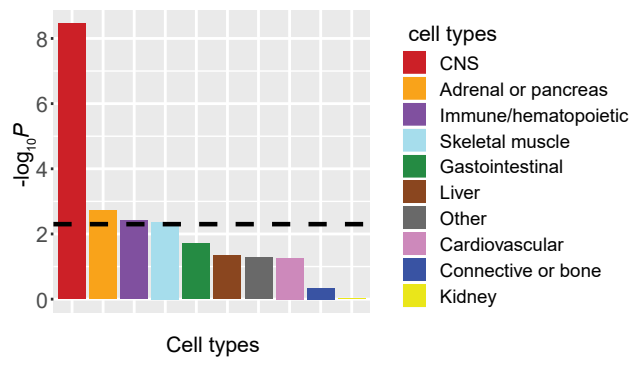
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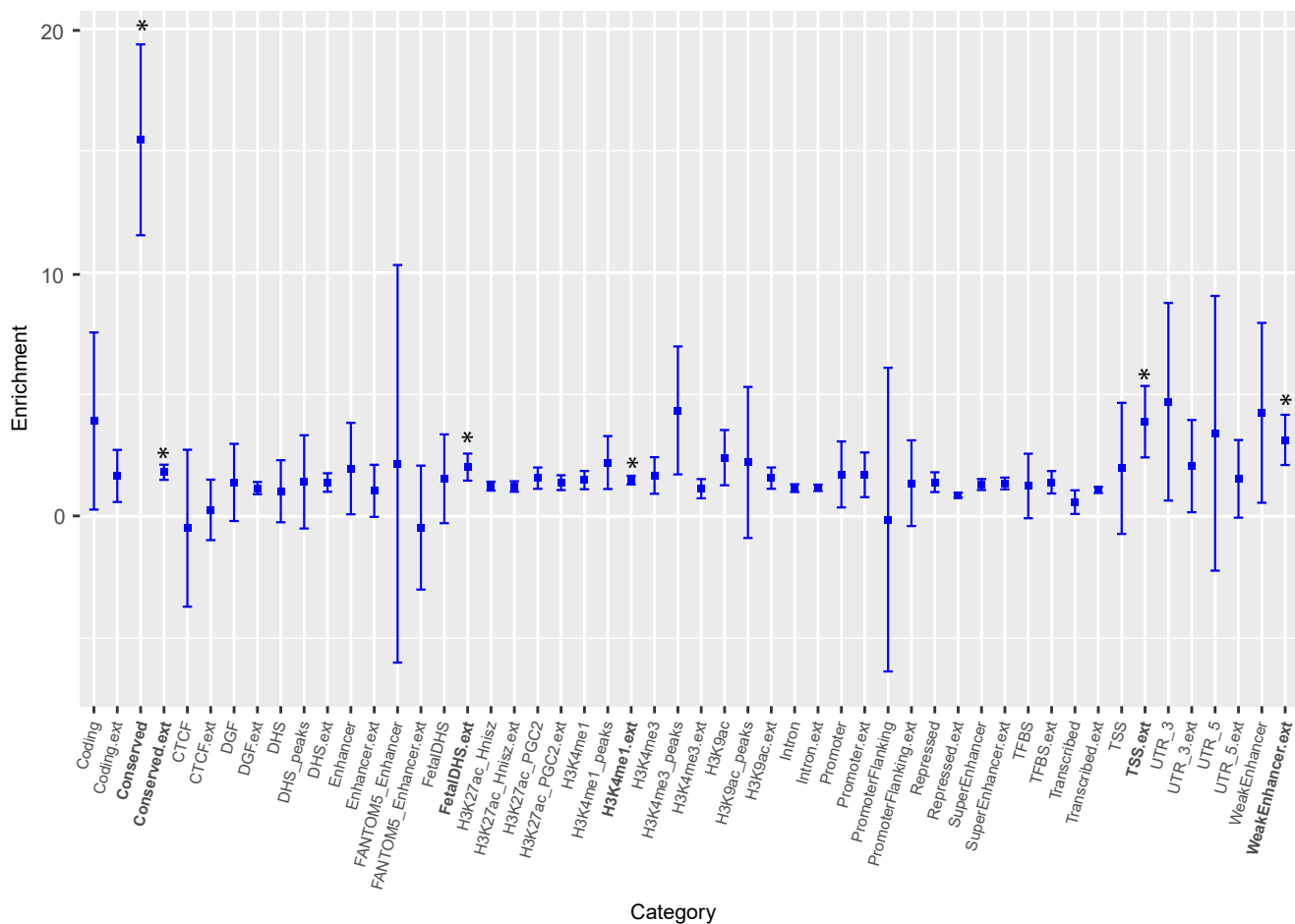
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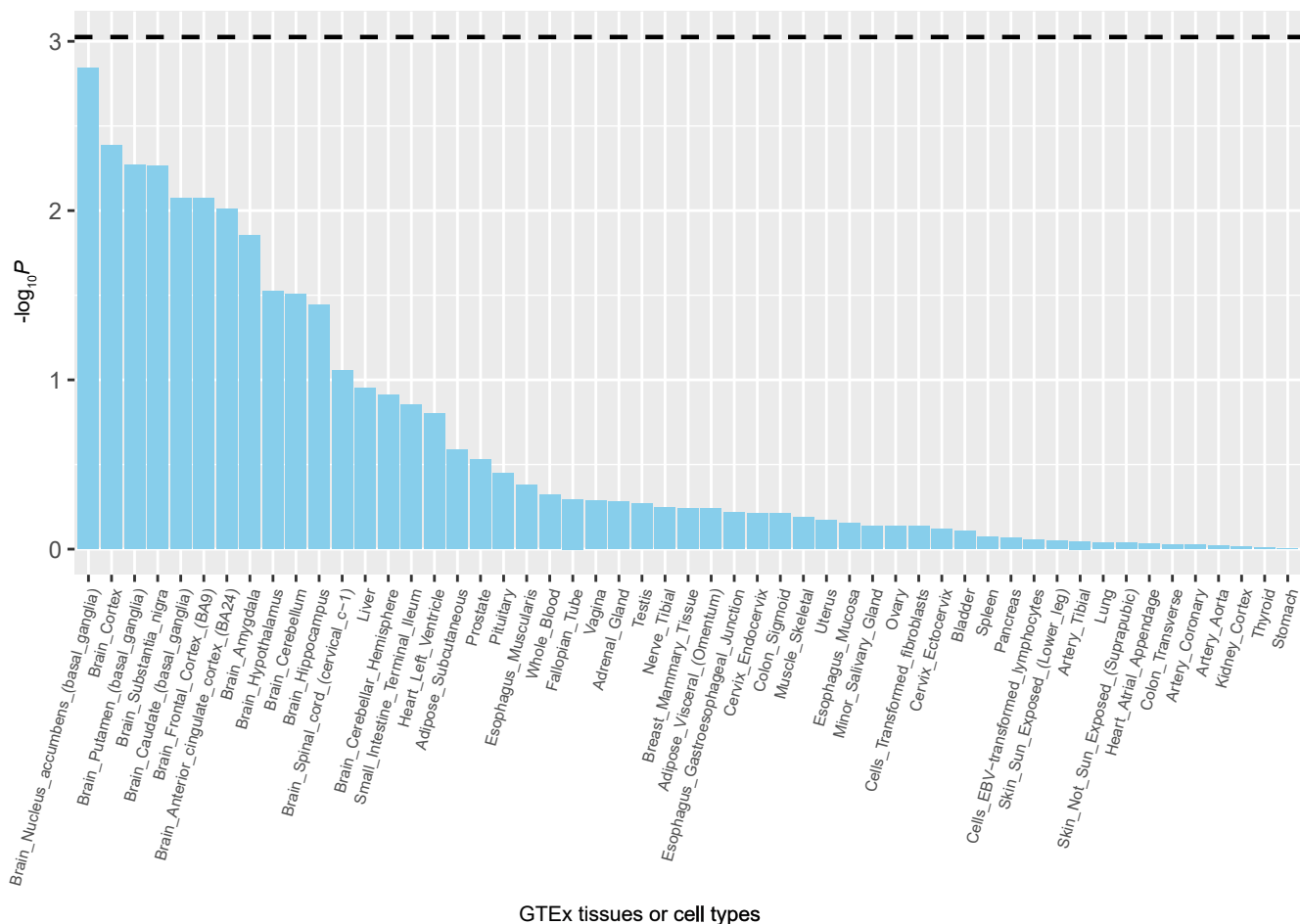
Supplementary Figure 1. Quantiles for PRS of AUD meta-analysis associated with AUDIT-P in UKB. Polygenic scores for AUD were calculated in 82,930 participants using PRSice-2, then split into 5 quantiles. Linear regression was applied to test the effect of increasing PRS on predicted risk of AUDIT-P (set quantile #1 as reference). The centre values are the coefficient and error bars are 95% confidence intervals.



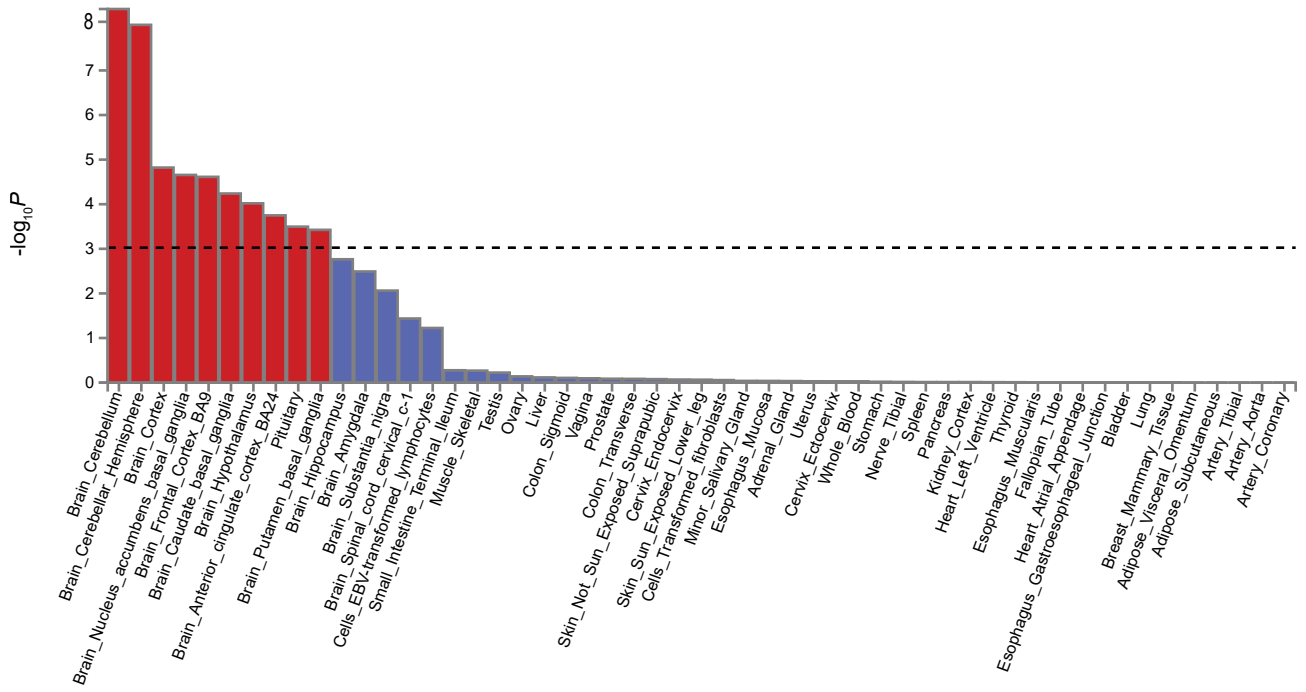
Supplementary Figure 2. Cell type group partitioning heritability enrichment for PAU using LDSC. The dashed line is the cutoff for Bonferroni-corrected significance ($p < 0.005$). CNS: central nervous system.



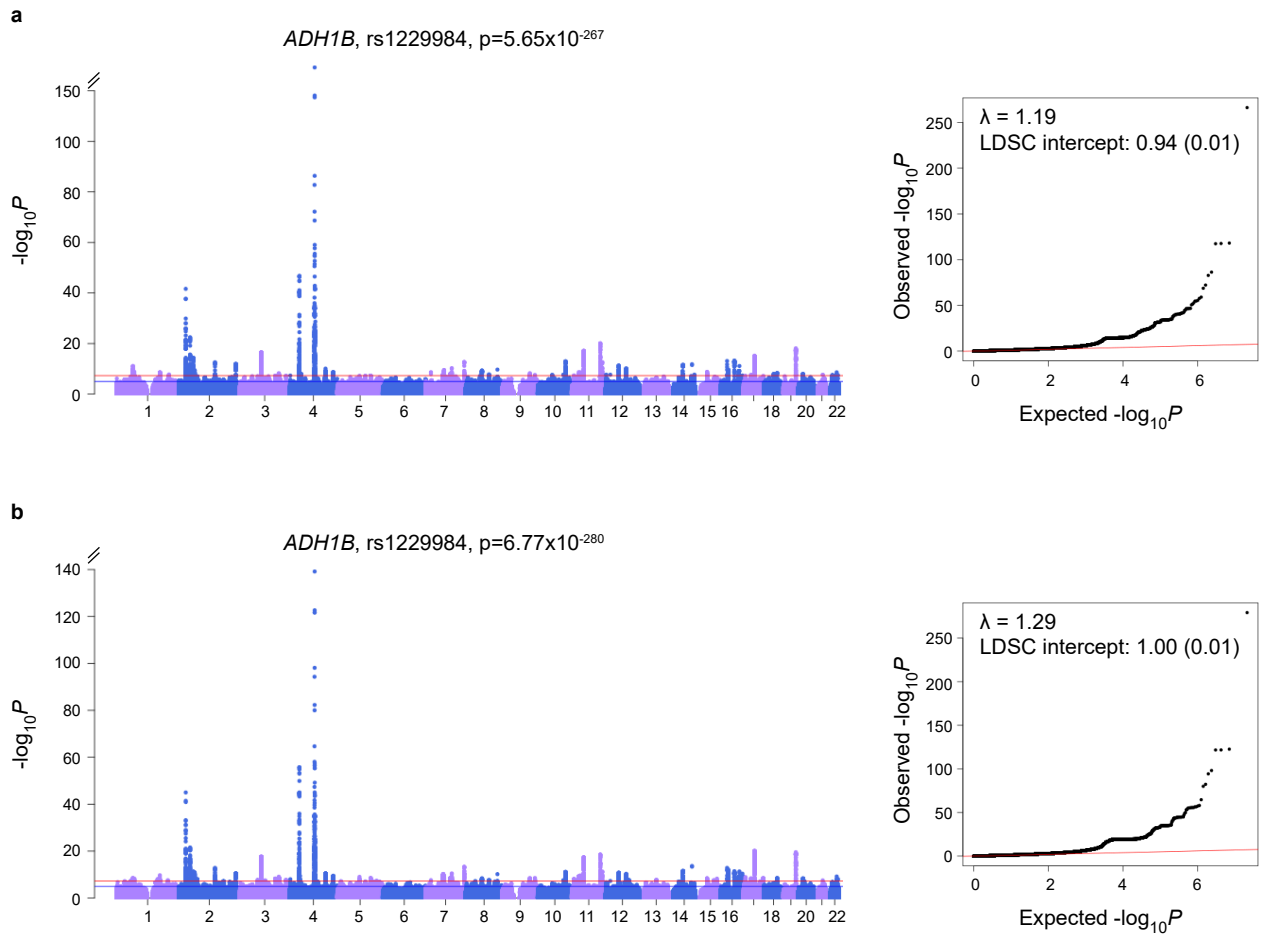
Supplementary Figure 3. Functional category partitioning heritability enrichment for PAU using LDSC baseline model. The categories labeled by asterisks are significant after Bonferroni correction ($p < 9.62 \times 10^{-4}$). For each of the 24 main annotations, there is an annotation extended 500 bp (ext) from the original one. There are 4 annotations with 100bp windows around the peaks (peaks) from the original ones. Centre values are the enrichments and error bars indicate 95% confidence intervals.



Supplementary Figure 4. GTEx tissues or cell types partitioning heritability enrichment for PAU using LDSC. The dashed line is the cutoff for Bonferroni-corrected significance ($p < 9.43 \times 10^{-4}$).



Supplementary Figure 5. GTEx tissue expression enrichment using MAGMA. The dashed line is the cutoff for Bonferroni-corrected significance ($p < 9.43 \times 10^{-4}$).



Supplementary Figure 6. Manhattan and QQ plots for MTAG analysis. Summary statistics from PAU ($n=435,563$, $n_{\text{effective}}=300,789$) and DrnkWk ($n=537,352$) were analyzed by MTAG. Red lines indicate GWS after correction for multiple testing ($p < 5 \times 10^{-8}$). a. MTAG results for PAU; b. MTAG results for DrnkWk.