

Fig. S1. Distribution of GWAS samples and birth year IMR. (A) Number of GWAS samples ($N = 330,340$ in total) in each birth year cohort colored by sex. **(B)** Distribution density of birth year IMR in GWAS samples. **(C)** Violin plots of birth year IMR in each year of birth.

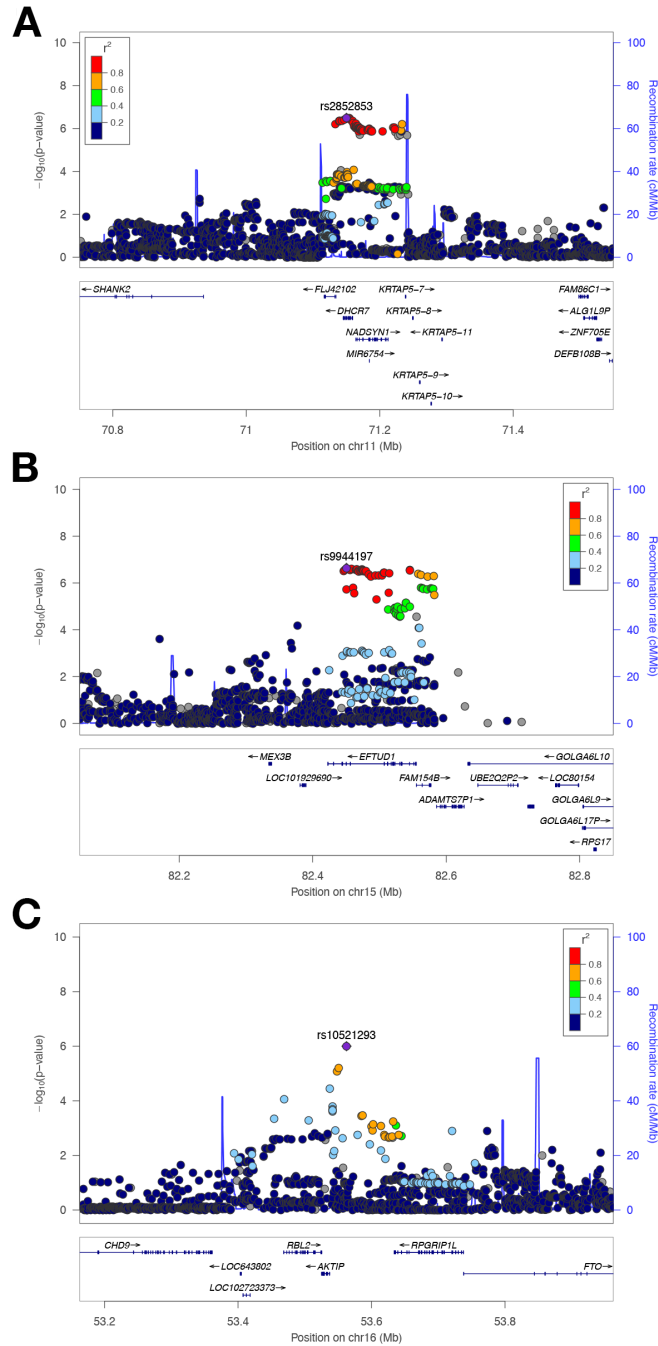


Fig. S2. Genetic associations with birth year IMR at the *DHCR7/NADSYN1* locus on chromosome 11, *EFTUD1* (a.k.a. *EFL1*) locus on chromosome 15, and *RPRIP1L/FTO* locus on chromosome 16.

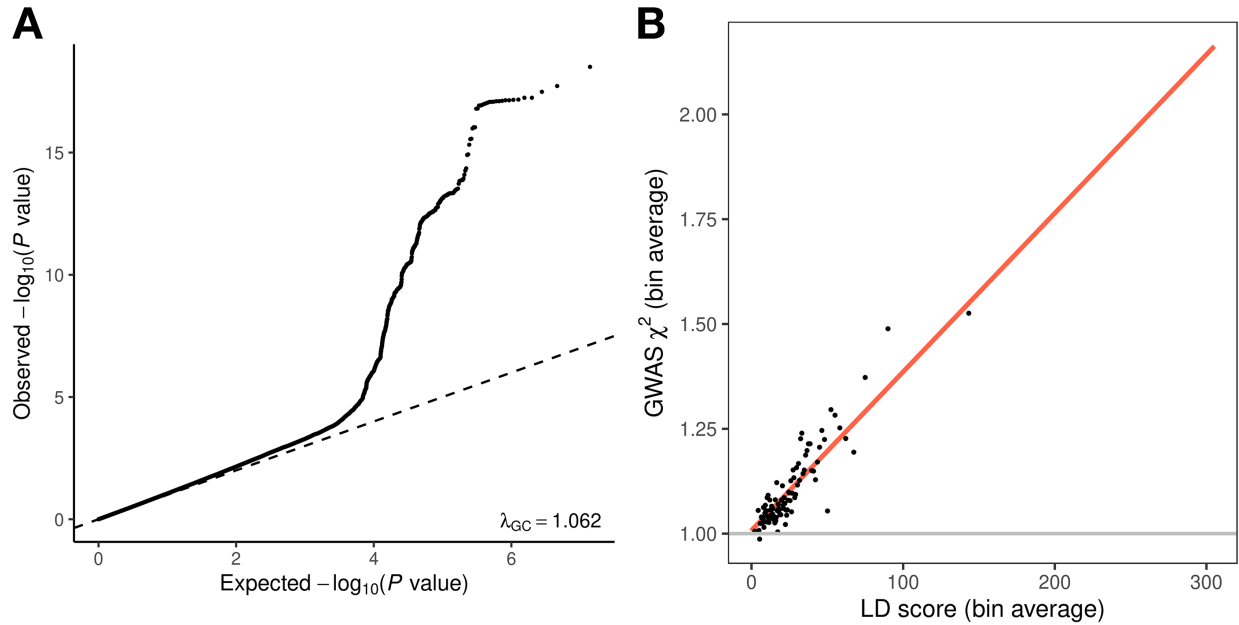


Fig. S3. Polygenic genetic basis of birth year IMR. (A) QQ plot for GWAS of birth year IMR. **(B)** LD score regression suggests a positive heritability of birth year IMR. We grouped SNPs into 100 bins based on LD scores. Each point in the plot shows the average LD score and the average GWAS chi-square statistics in a bin. Only HapMap 3 SNPs were included in this analysis.

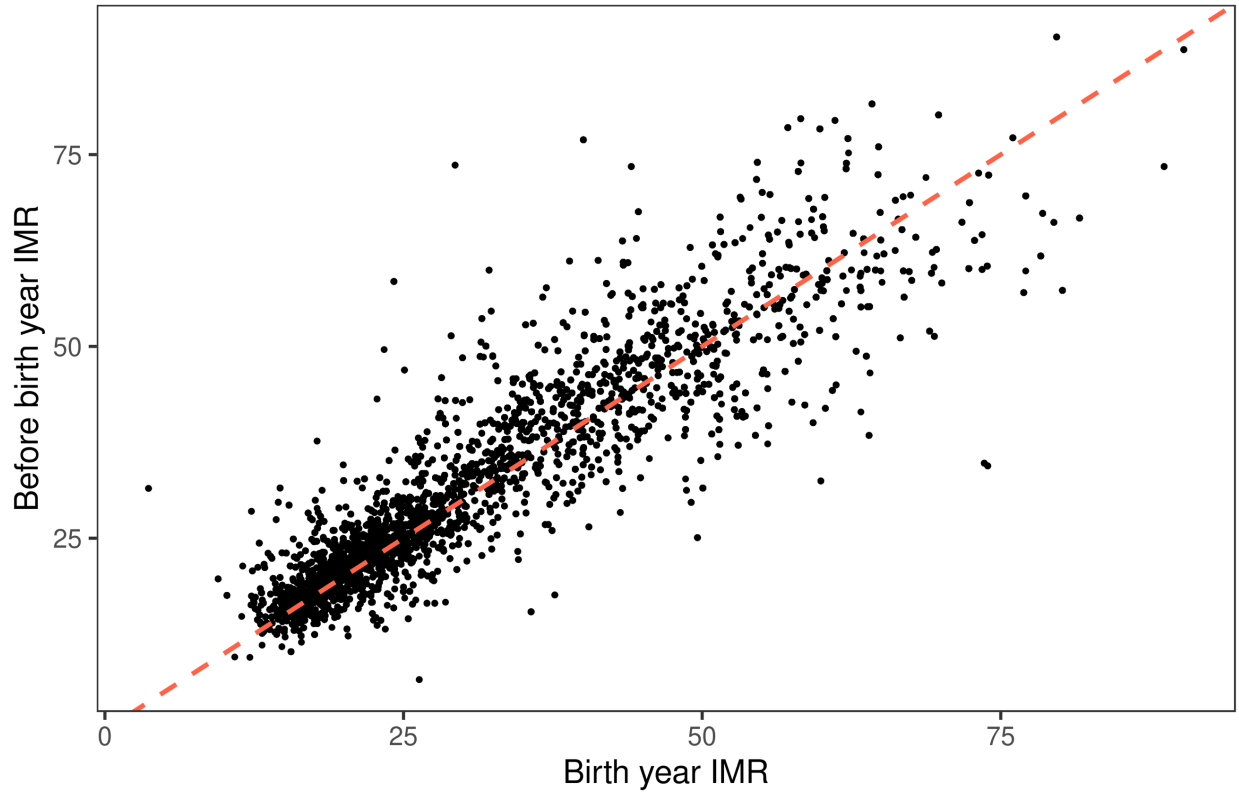


Fig. S4. Correlation between birth year IMR and lagged-IMR in UKB samples.

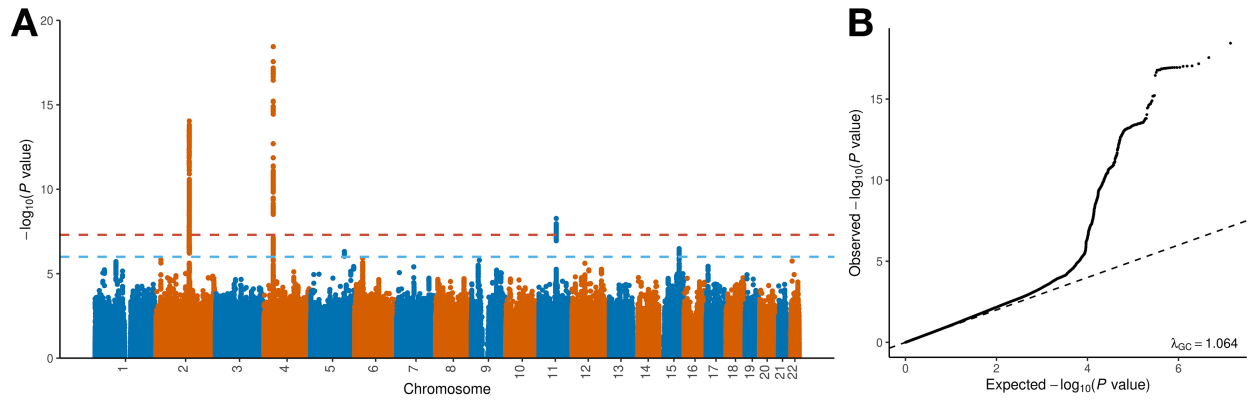


Fig. S5. Genetic associations with IMR of the year before birth. (A) Manhattan plot for the lagged IMR. The horizontal lines mark the genome-wide significance cutoff of $5.0e-8$ and a suggestive cutoff of $1.0e-6$, respectively. **(B)** QQ plot for GWAS of lagged-IMR.

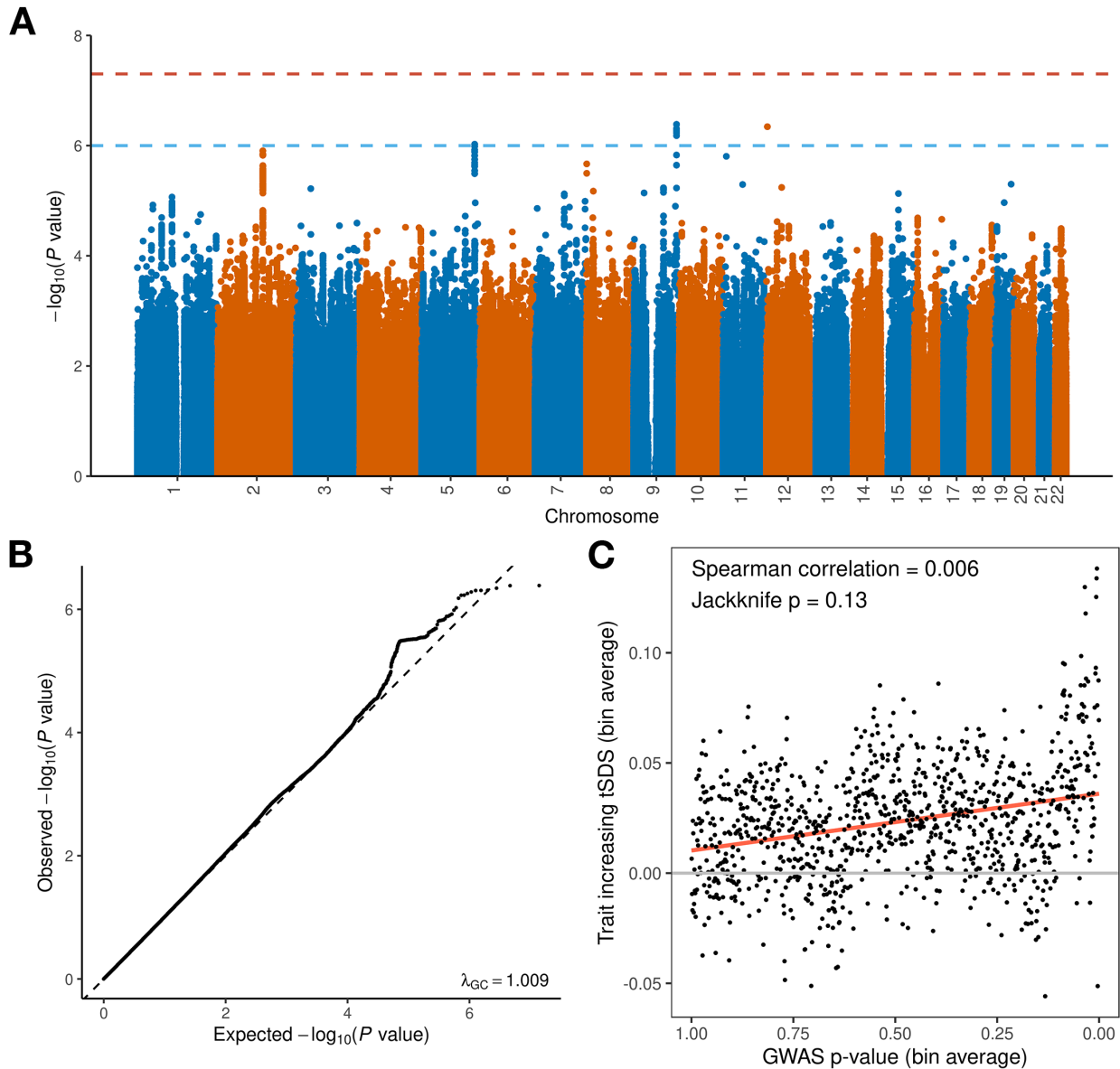


Fig. S6. Genetic associations with birth year IMR after randomly shuffling county of birth. (A) Manhattan plot for region-shuffled IMR. The horizontal lines mark the genome-wide significance cutoff of 5.0×10^{-8} and a suggestive cutoff of 1.0×10^{-6} , respectively. (B) QQ plot for GWAS of county-shuffled IMR. (C) Correlation between GWAS associations of county-shuffled birth year IMR and SDS matched with IMR-associated alleles.

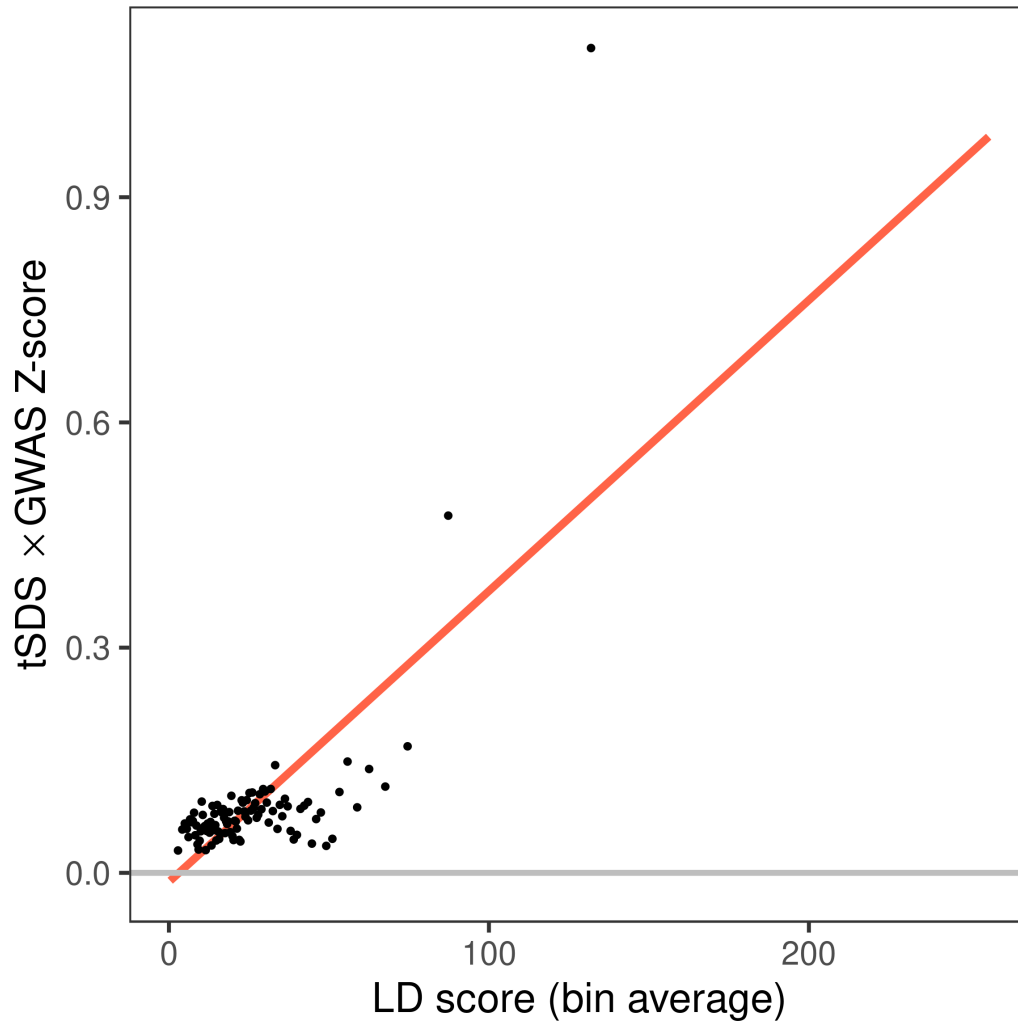


Fig. S7. Bivariate LD score regression confirms correlation between IMR associations and SDS. We grouped SNPs into 100 bins based on LD scores. Each point in the plot shows the average LD score and the average product of z-scores in a bin. Only HapMap 3 SNPs were included in the analysis.

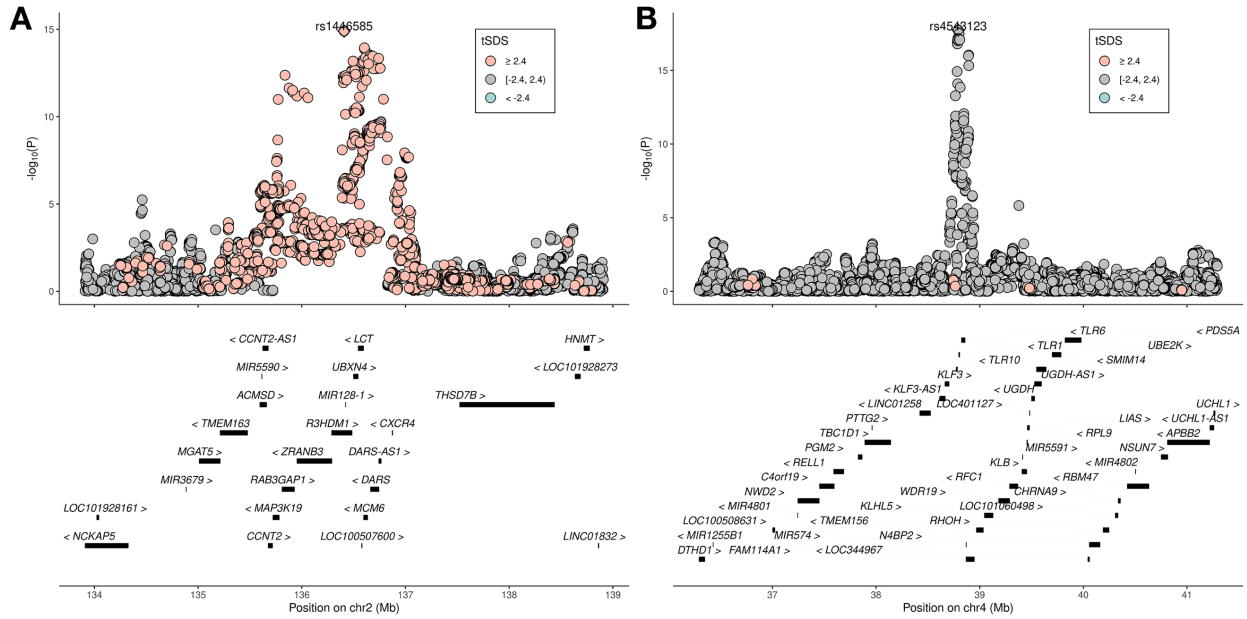


Fig. S8. SDS values at the (A) *LCT* and (B) *TLR1/6/10* loci. The x-axis shows hg19 genome coordinates. The top SNP (rs5743618) does not exist in the SDS data, and we used the SNP rs4543123 with the 2nd smallest p-value in the locus in (B).

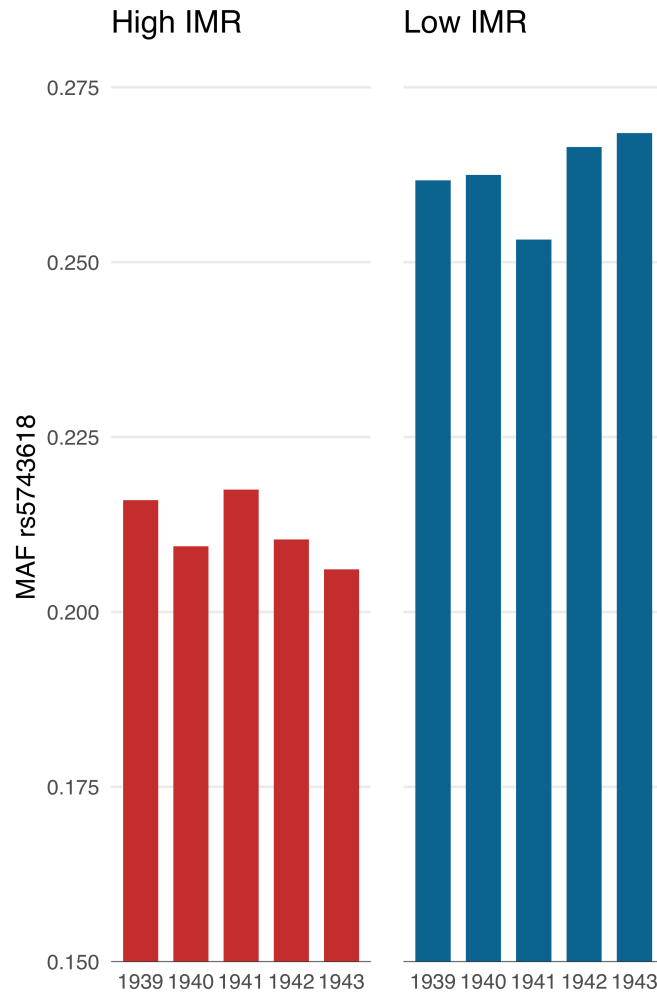


Fig. S9. Minor allele frequency of rs5743618 in UKB birth cohort in 1939-1943. Major allele at this locus is known to associate with resistance to leprosy.

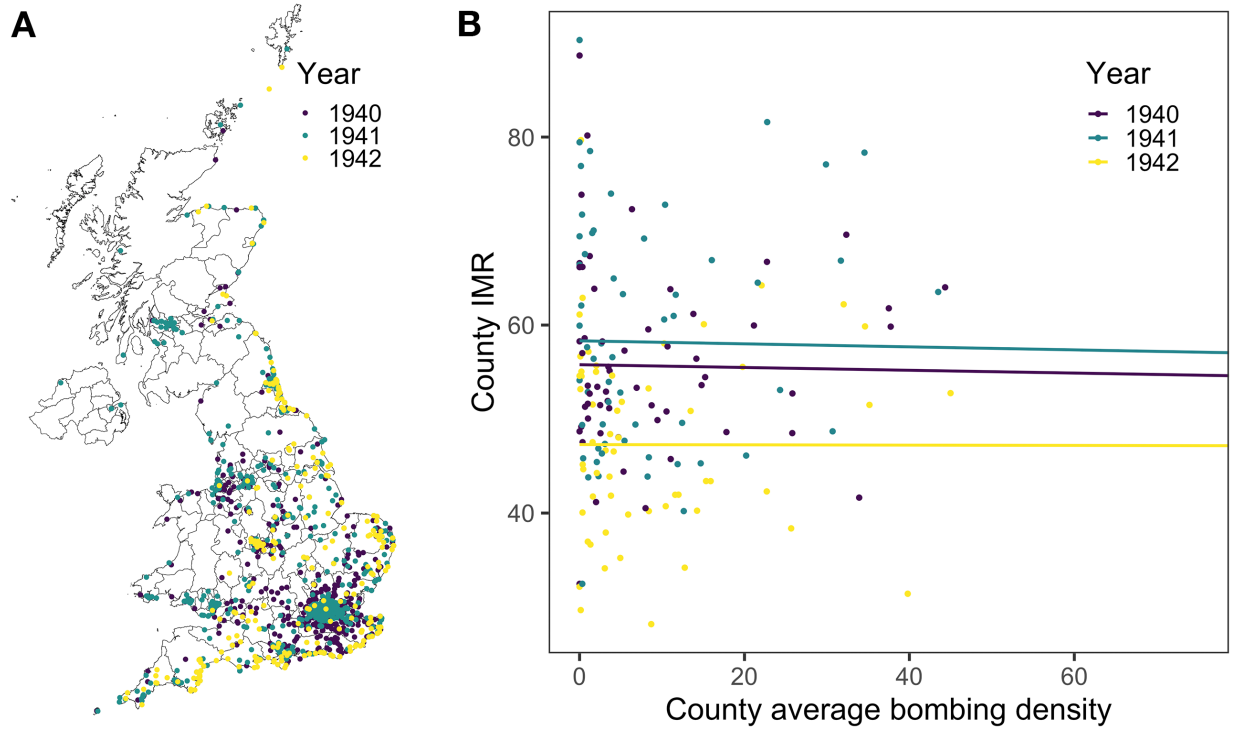


Fig. S10. A lack of correlation between bombing density and county-level IMR during the war. (A) Location of bombing with casualty during 1940-1942 in the UK. **(B)** Scatter plot for county-level IMR and average bombing density in 1940 and 1941. Bombing density for each UKB participant was defined as the number of bombing events with casualty in the participant's year of birth and within a 10-kilometer radius of the participant's place of birth. Values shown on the x-axis are the average bombing density for the 1940-1942 birth cohorts for each county. Five counties were omitted from the plot due to very high bombing densities.

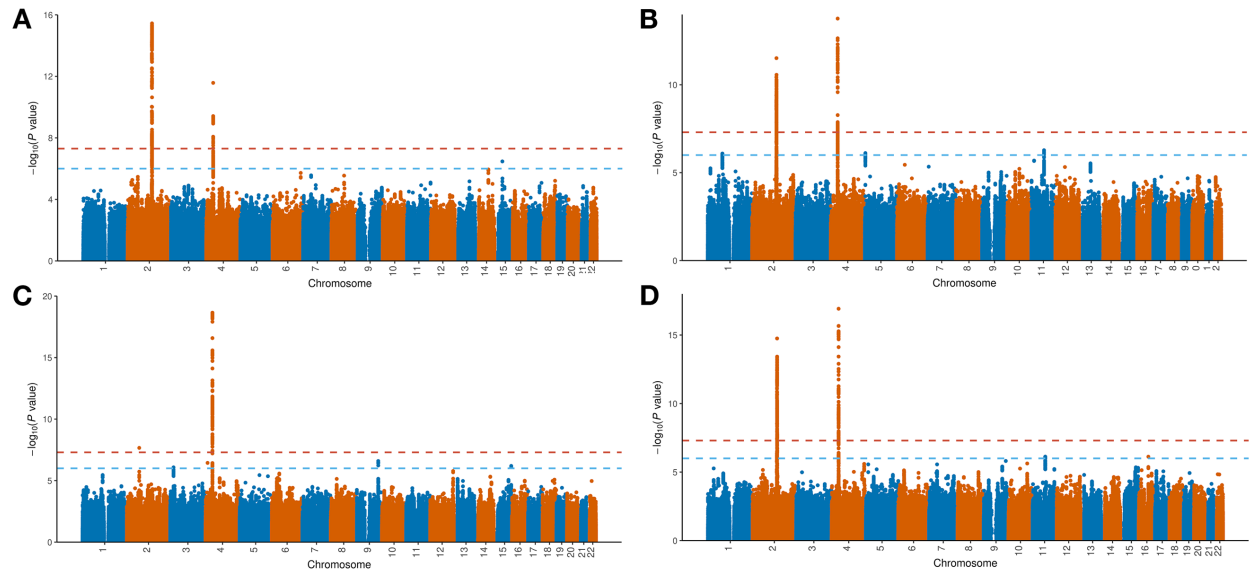


Fig. S11. Genetic associations with birth year IMR (A) in participants of the MHQ questionnaire, (B) in non-participants of the MHQ questionnaire, (C) in NA-participants of the MHQ questionnaire, and (D) after controlling for a latent factor for participation activity. The horizontal lines mark the genome-wide significance cutoff of 5.0×10^{-8} and a suggestive cutoff of 1.0×10^{-6} , respectively.

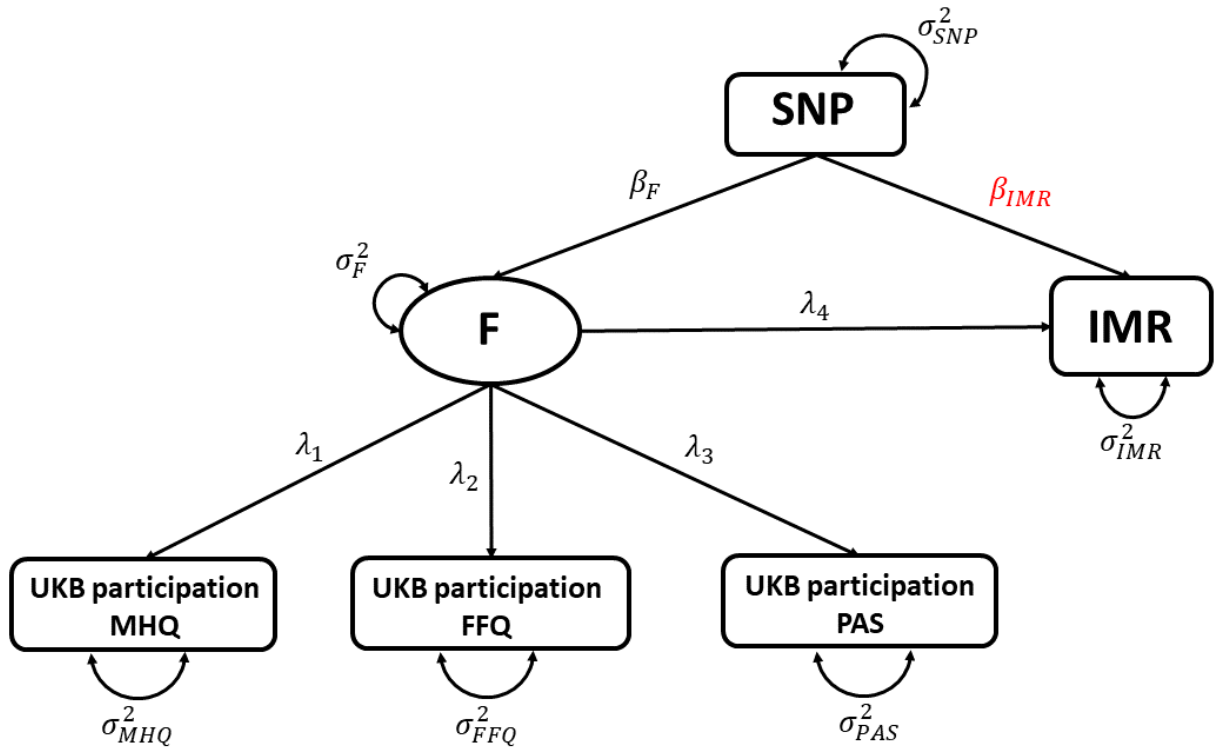


Fig. S12. Accounting for a latent factor for participation in the GWAS of birth year IMR. GSEM was used to fit the model for each SNP separately. The parameter of interest is highlighted in red.

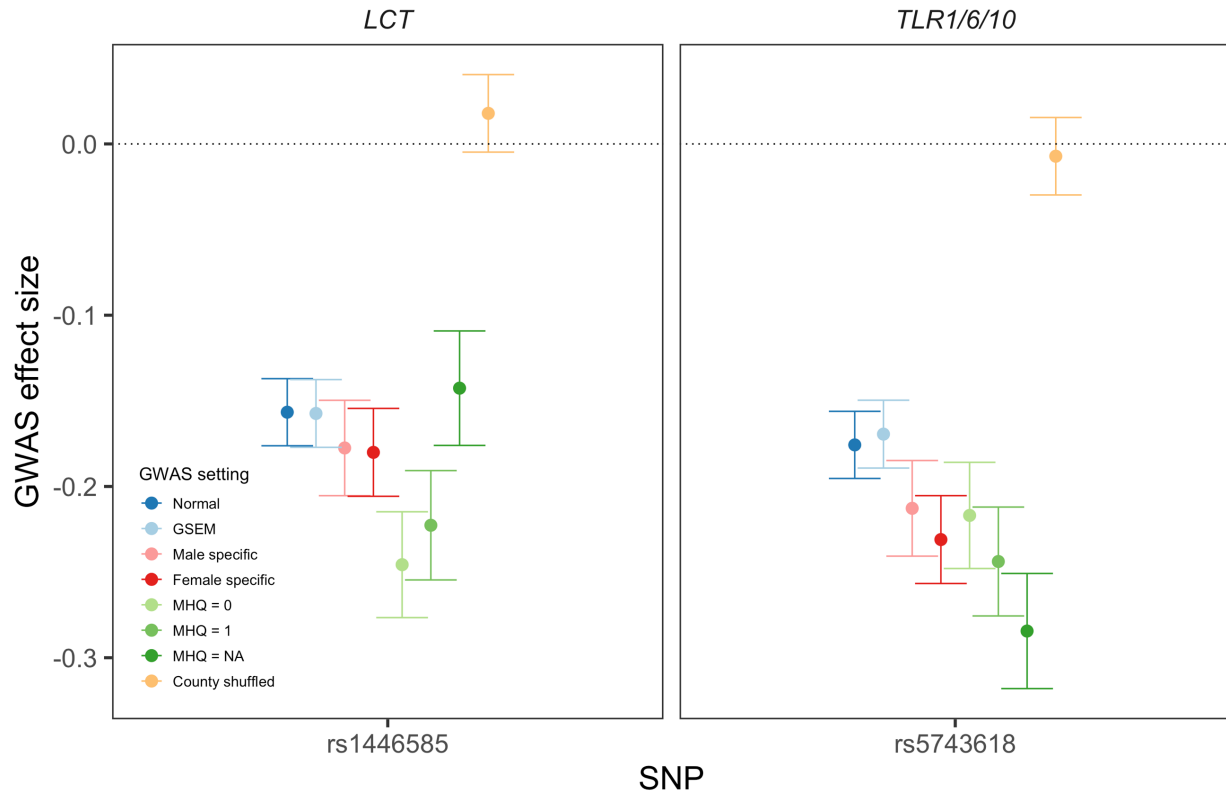


Fig. S13. Effect size of lead SNPs at *LCT* and *TLR1/6/10* loci. The intervals indicate point estimates and standard errors of SNP-IMR associations in the primary GWAS (dark blue), in GSEM-based analysis adjusting for participation (light blue), in sex-specific analyses (red), in analyses conditioning on participation status of the MHQ questionnaire (green), and in GWAS with county-shuffled IMR phenotype (yellow).

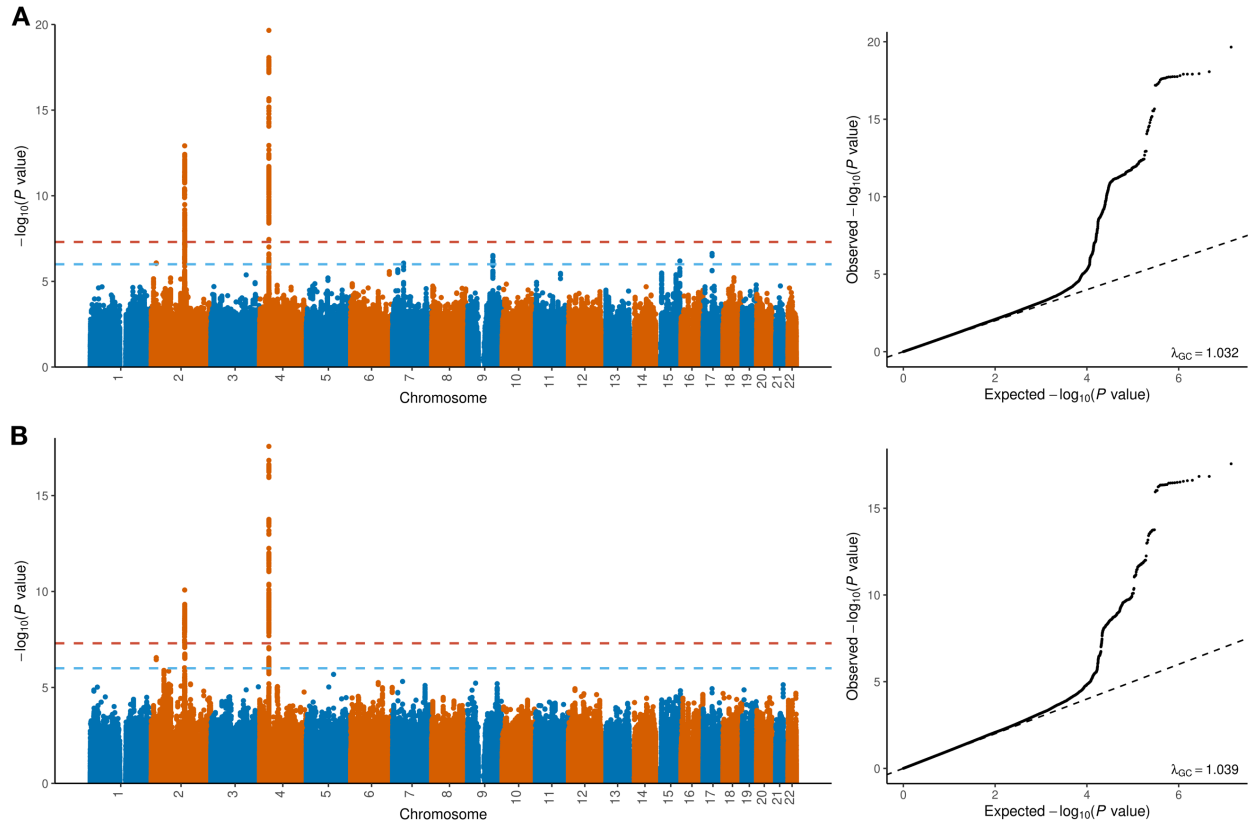


Fig. S14. Manhattan and QQ plots for the IMR GWAS using (A) counties of birth with at least 5000 participants (N = 269,085) or (B) using samples whose region of birth is identical to the region of current address (N = 209,852).

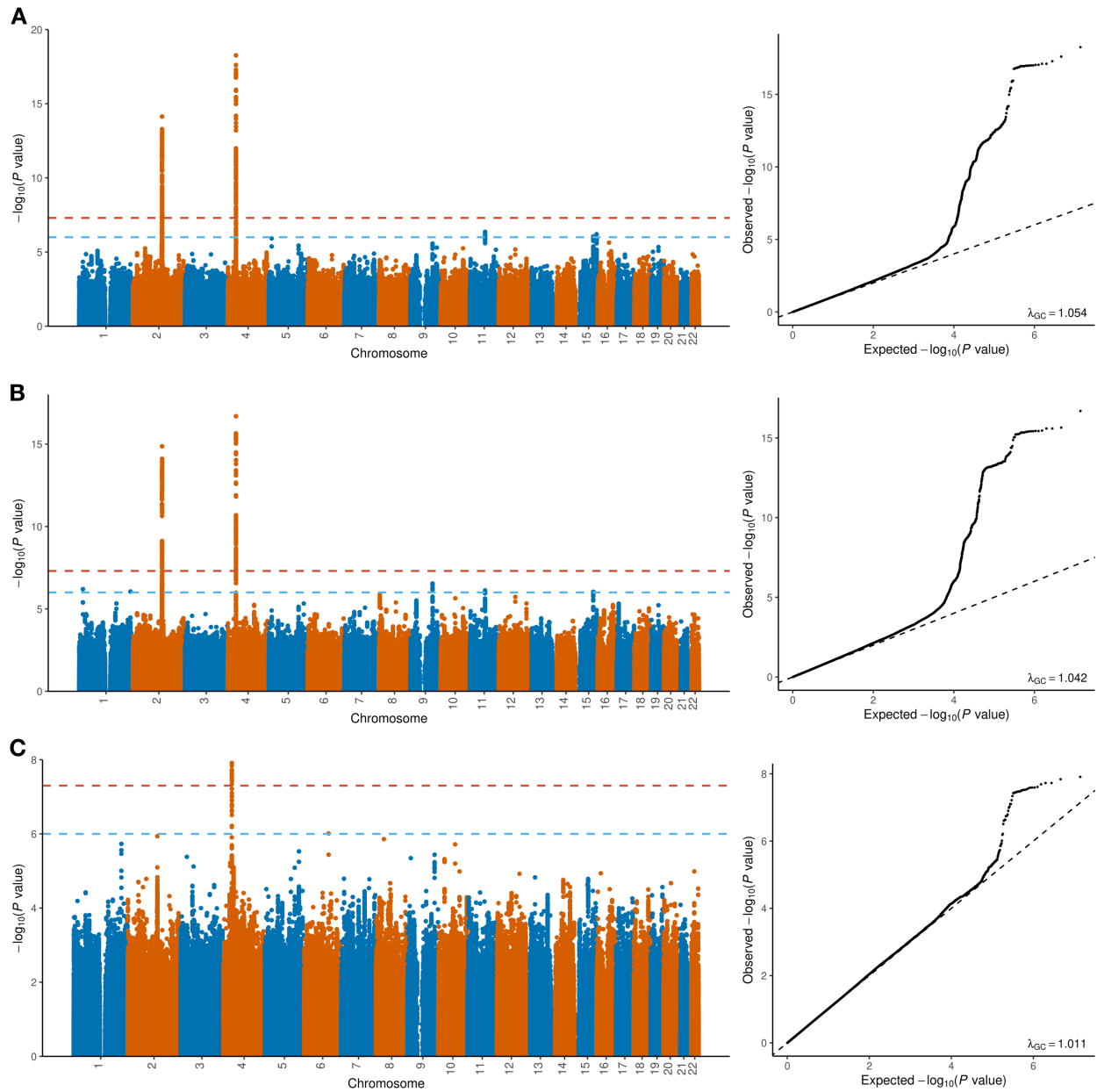


Fig. S15. Manhattan and QQ plots of birthyear IMR GWAS after adjusting for (A) household income, (B) educational attainment, or (C) lagged IMR.

LDSC genetic correlation between IMR vs. 50 traits

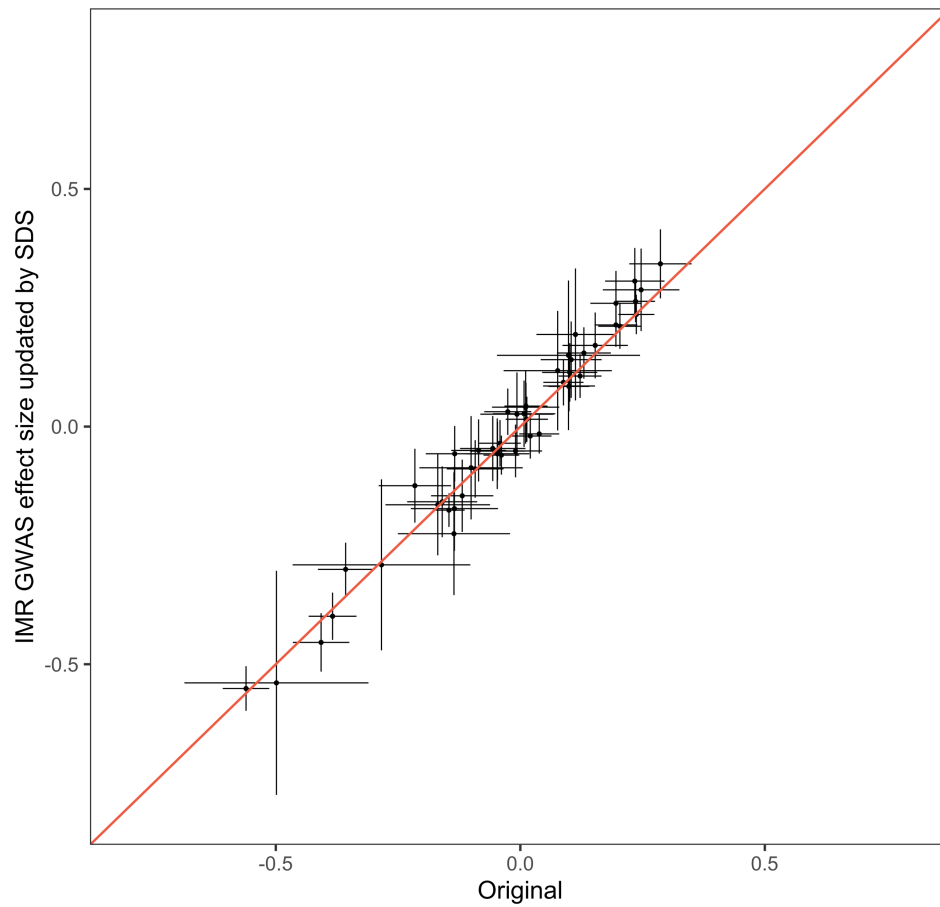


Fig. S16. Comparison of LDSC genetic correlations. We first updated SNP effect sizes by regressing out SDS, then used the updated effect sizes to compute the genetic correlations with 50 complex traits. The scatter plot shows the comparison of LDSC genetic correlations between the SDS-updated vs. original results. Dots and intervals are the point estimates and plus/minus one standard error.

LDSC genetic correlations between IMR and 50 complex traits

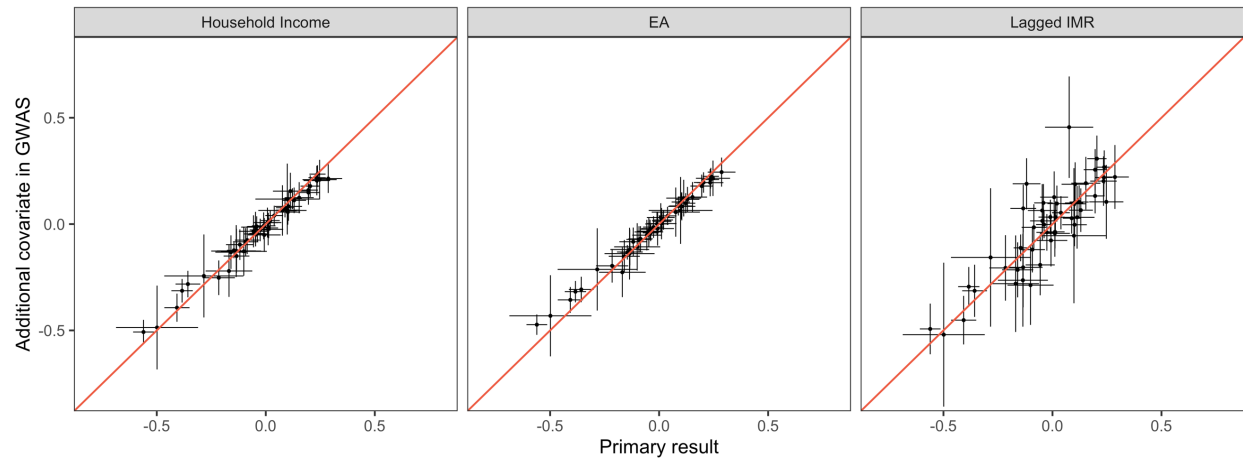


Fig. S17. LDSC genetic correlation comparisons between primary results vs. including additional covariates (household income, EA, or lagged IMR) in the IMR GWAS.