Figure S1: Tuning Parameter Optimization: Tuning parameter optimization for the large GWAS based breast cancer PRS with Lassosum (A and B) and "P&T" approach (C & D) for MGI (A & C) and UKB (B & D).
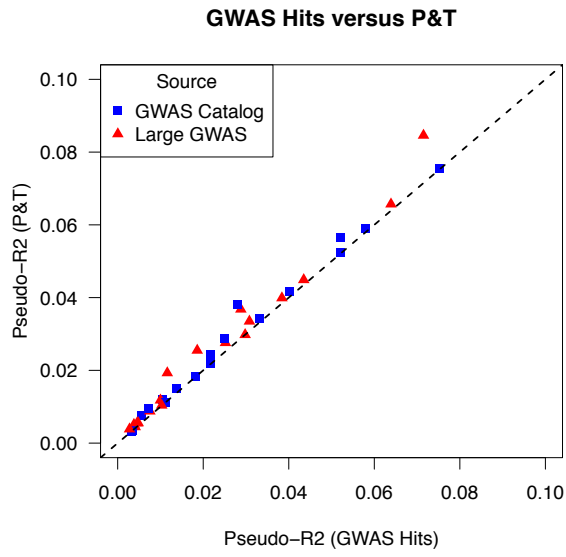
Figure S2: P&T versus GWAS Catalog hits. Pairwise comparison of the two PRS methods P&T and "GWAS hits" (P <= 5x10-8) using GWAS Catalog entries as input. 36 PRS for 20 cancer traits (18 MGI PRS and 18 UKB PRS) are shown. Dashed line: identity line.
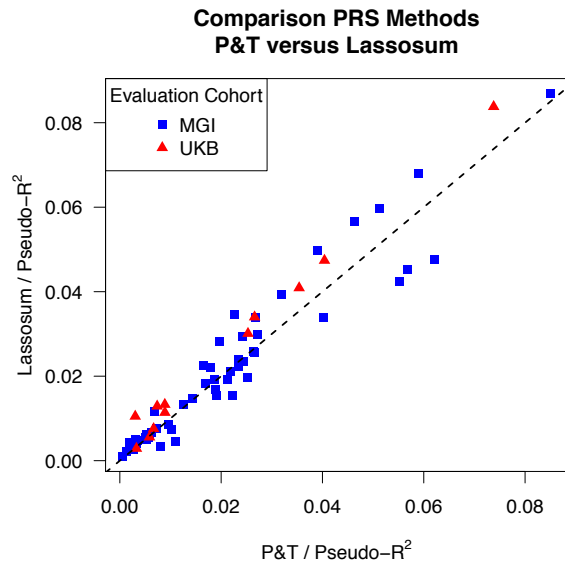
Comparison PRS Methods
P&T versus Lassosum

Figure S3: "P&T versus Lassosum". Pairwise comparison of the two PRS methods P&T and Lassosum using pseudo-R^2. 70 GWAS sources where P&T and Lassosum-based PRS were positively and nominally significant associated with their cancer trait in MGI (blue; 58 PRS) and UKB (red; 12 PRS) are shown. Dashed line: identity line.
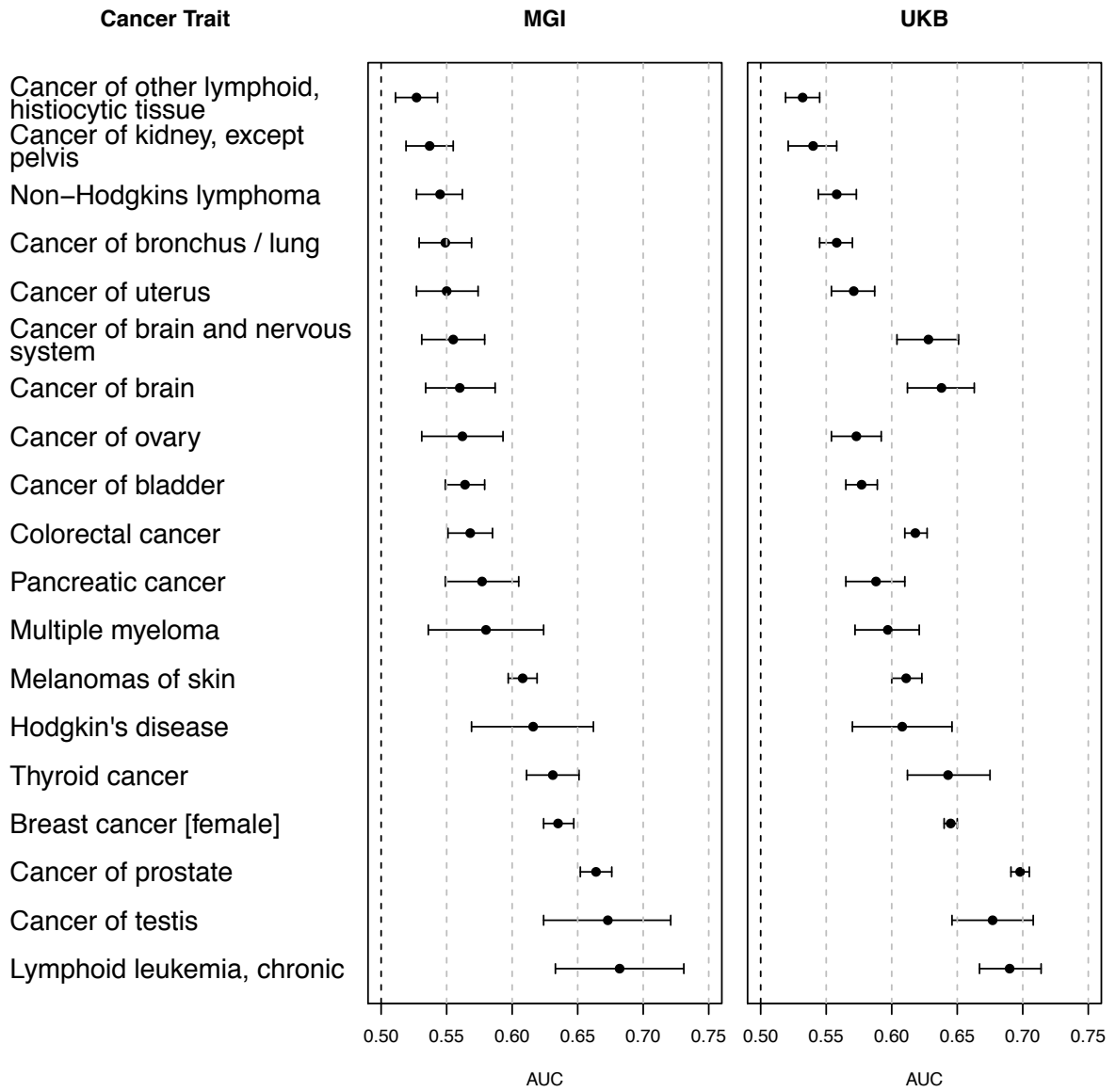
Figure S4: AUC of the top ranked PRS for 19 cancers that were present for MGI (left) and UKB (right). AUC values (dots) and their 95% confidence intervals are shown.
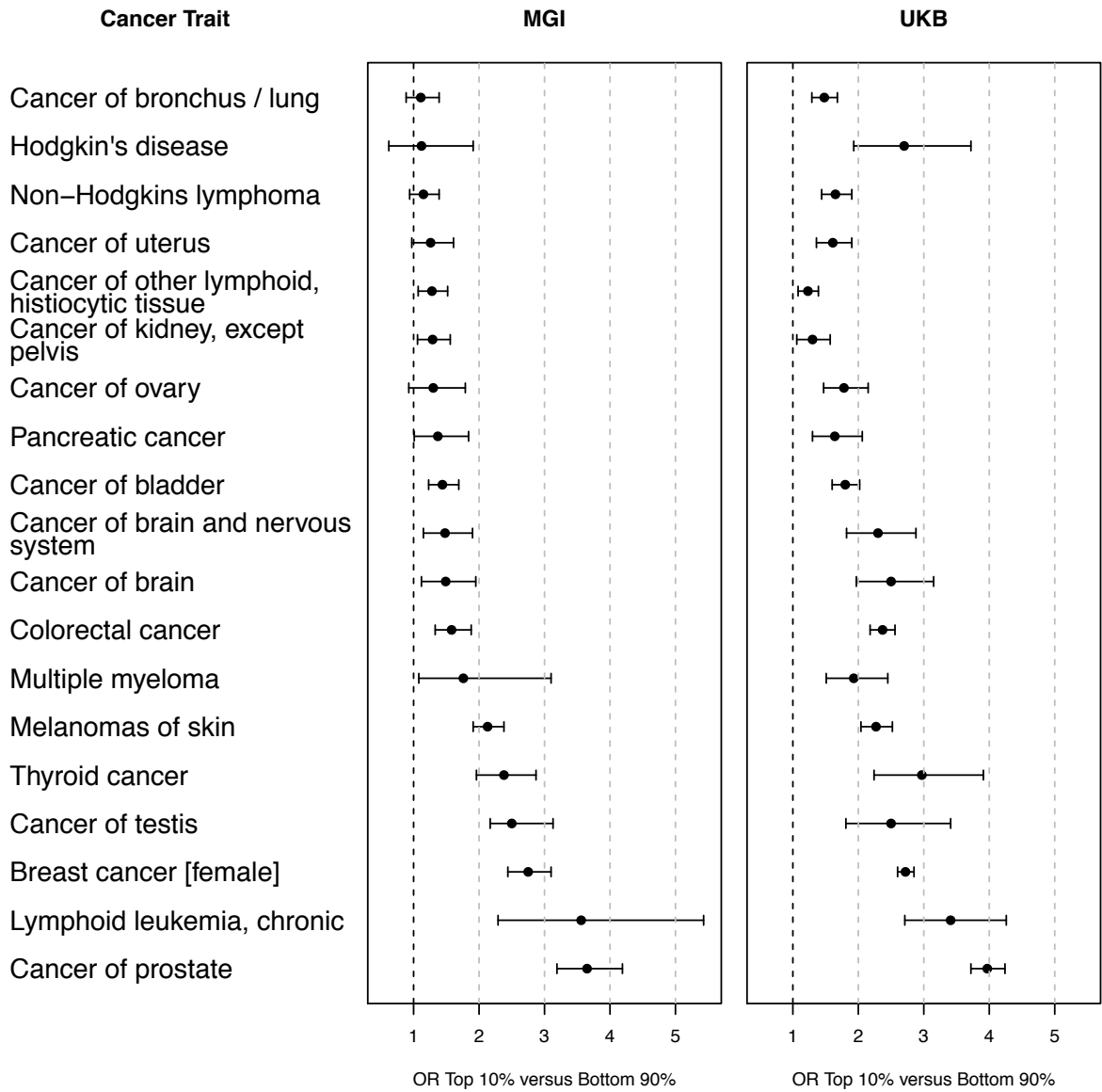
Figure S5: Case enrichment of the top ranked PRS for 19 cancers that were present for MGI (left) and UKB (right). Odds ratios (OR, top 10% versus bottom 90% of PRS distribution) and their 95% confidence intervals are shown.
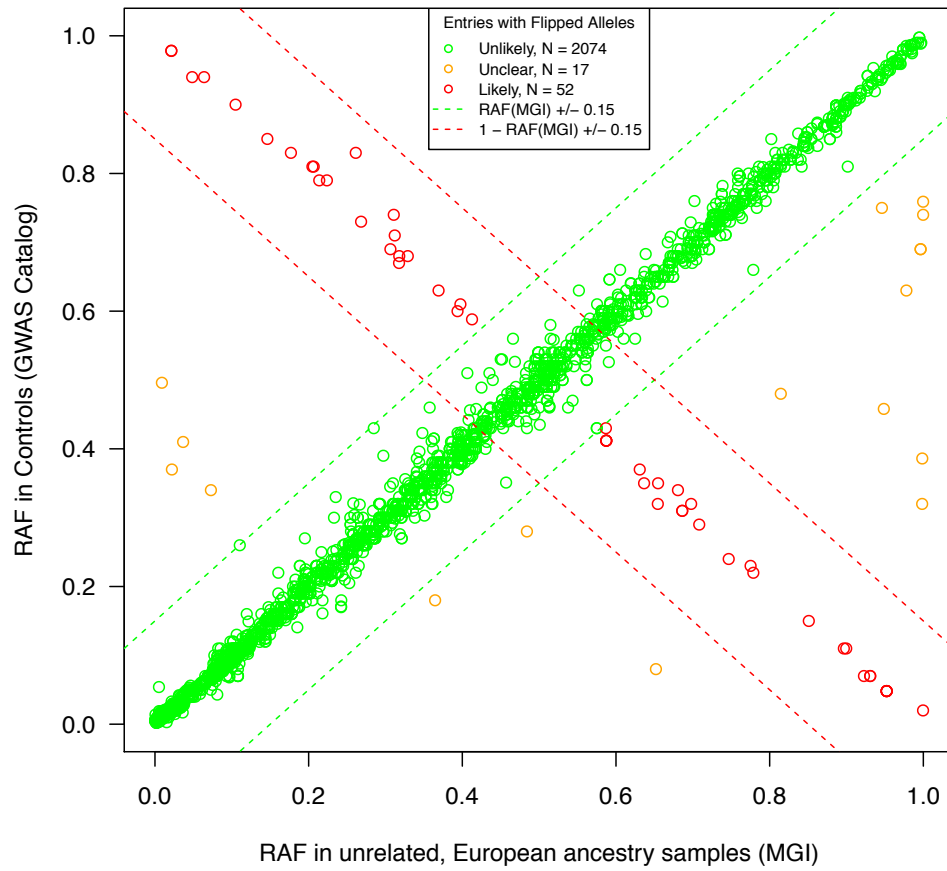
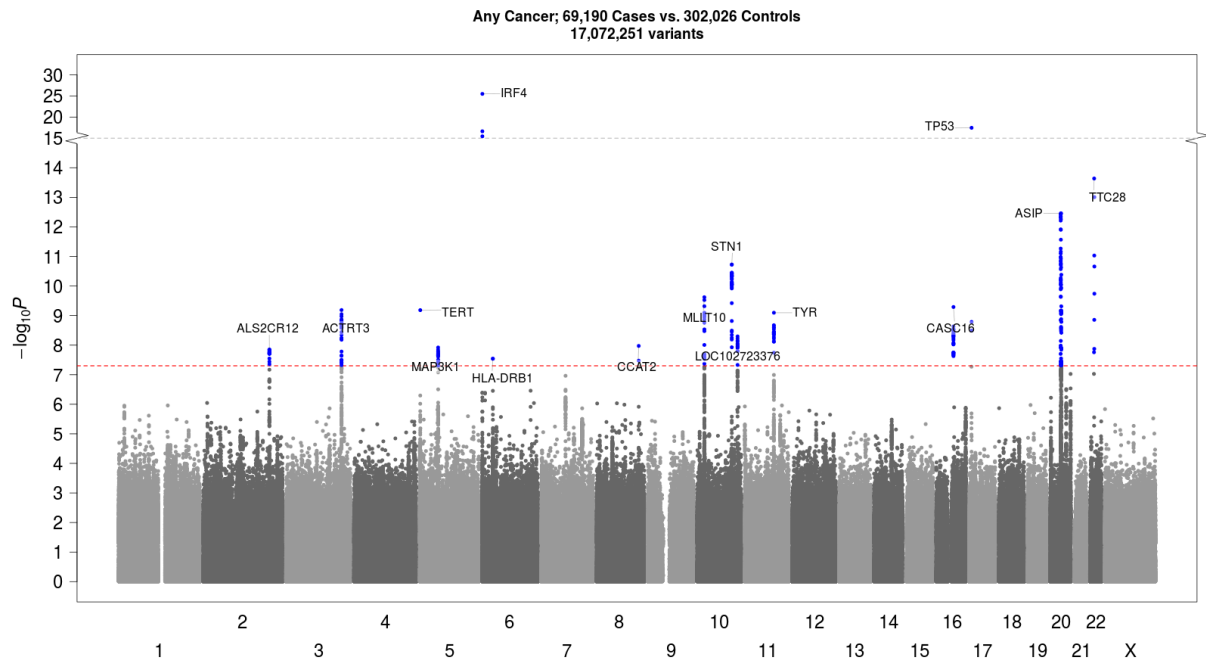**Figure S6** Comparison of the Risk Allele Frequencies in the GWAS Catalog vs. MGI

Figure S7: Manhattan plot of UKB GWAS on 69,190 cases with any cancer versus 302,026 controls. SNPs with P < 5x10-8 are highlighted in blue. Candidate loci are named after the nearest gene closest to the strongest signal.
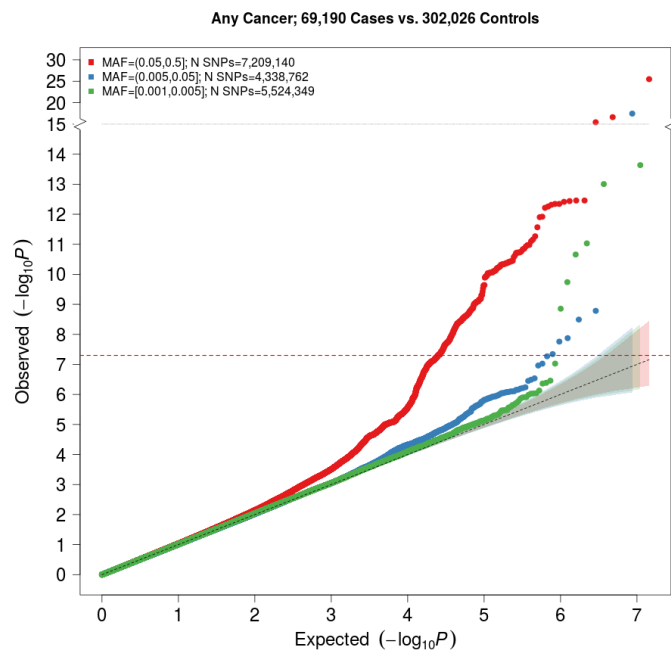
Figure S8: QQ plot of UKB GWAS on 69,190 cases with any cancer versus 302,026 controls. -log10(P-values) are stratified by minor allele frequency (MAF) bins.
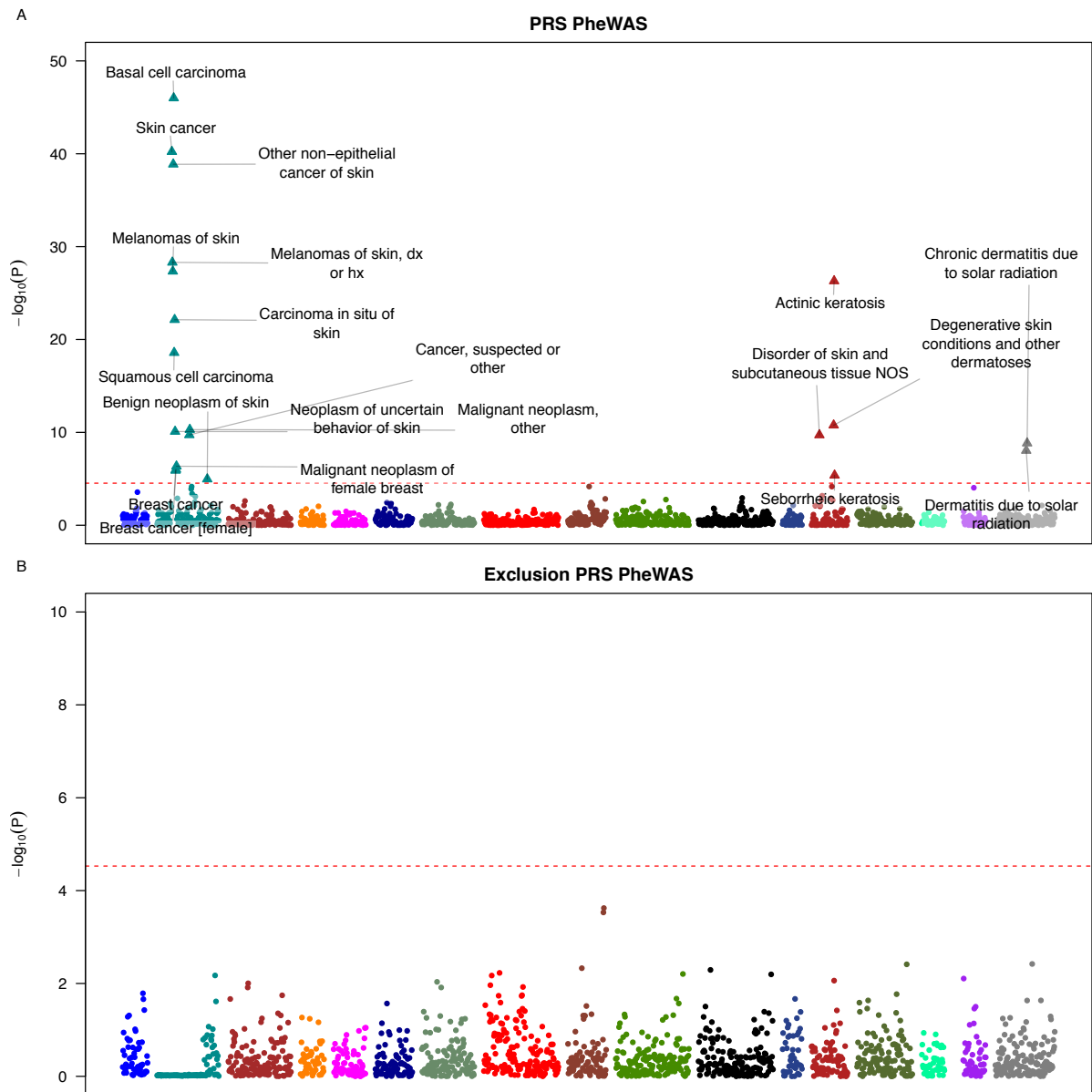
Figure S9: PRS PheWAS plot of the 'any cancer' lassosum PRS in MGI before (top) and after (bottom) excluding 20,751 MGI individuals with 'any cancer'.