

a

UKB SAIGE Analysis Proportion of Associations Expected to be False at $p \leq 5 \times 10^{-8}$ (N = 1,418)			
MAF Category	Primary GWAS: Number of Independent Associations	Single Permutation GWAS: Number of Independent Associations	Expected FDR
MAF \geq 0.05	3,183	77	2%
0.01 \leq MAF < 0.05	469	85	18%
0.001 \leq MAF < 0.01	355	237	67%
0.0001 \leq MAF < 0.001	1,272	1,053	83%
Overall	5,279	1,452	28%

b

MGI SAIGE Analysis Proportion of Associations Expected to be False at $p \leq 5 \times 10^{-8}$ (N = 1,659)					
MAF Category	Number of Independent GWAS Associations			Expected FDR	
	Primary	Single Permutation	Average Permutation (Range)	Single Permutation	Average Permutation (Range)
MAF \geq 0.05	373	81	85 (78-90)	22%	23% (21-24%)
0.01 \leq MAF < 0.05	137	70	73 (69-77)	51%	53% (50-56%)
0.001 \leq MAF < 0.01	240	208	221 (208-250)	87%	92% (87-100%)
0.0001 \leq MAF < 0.001	650	521	556 (522-584)	80%	86% (80-90%)
Overall	1,400	880	935 (880-989)	63%	67% (63-71%)

Supplementary Table 1. Proportion of significant ($p \leq 5 \times 10^{-8}$) independent associations expected to be false in the SAIGE analyses by minor allele frequency and p-value category. *N* is the number of phenotypes analyzed. a) Results for a single permutation of 1,418 UKB phenotypes by MAF category. b) Results for a single permutation and an average of five permutations of 1,659 MGI phenotypes by MAF category.

a

UKB SAIGE Analysis Proportion of Associations Expected to be False Across P-value Categories (N = 1,418)			
P-value Category	Primary GWAS: Number of Independent Associations	Single Permutation GWAS: Number of Independent Associations	Expected FDR
$p \leq 5 \times 10^{-8}$	5,279	1,452	28%
$p \leq 5 \times 10^{-9}$	2,892	141	5%
$p \leq 5 \times 10^{-10}$	2,182	14	1%
$p \leq 5 \times 10^{-11}$	1,794	0	0%
$p \leq 5 \times 10^{-12}$	1,495	0	0%

b

MGI SAIGE Analysis Proportion of Associations Expected to be False Across P-value Categories (N = 1,659)					
P-Value Category	Number of Independent GWAS Associations			Expected FDR	
	Primary	Single Permutation	Average Permutations (Range)	Single Permutation	Average Permutation (Range)
$p \leq 5 \times 10^{-8}$	1,400	880	935 (880-989)	63%	67% (63-71%)
$p \leq 5 \times 10^{-9}$	391	80	92 (80-105)	20%	24% (20-27%)
$p \leq 5 \times 10^{-10}$	237	5	8 (5-11)	2%	3% (2-5%)
$p \leq 5 \times 10^{-11}$	185	1	1 (0-2)	1%	<1% (<1%)
$p \leq 5 \times 10^{-12}$	159	0	0 (0-1)	<1%	<1% (<1%)

Supplementary Table 2. Proportion of significant ($p \leq 5 \times 10^{-8}$) independent associations expected to be false in the SAIGE analyses by minor allele frequency and p-value category. *N* is the number of phenotypes analyzed. a) Results for a single permutation of 1,418 UKB phenotypes by p-value category. b) Results for a single permutation and an average of five permutations of 1,659 MGI phenotypes by p-value category.

a

UKB SAIGE Analysis Proportion of Associations Expected to be False at $p \leq 5 \times 10^{-8}$ (N = 1,418)			
MAC Category	Primary GWAS: Number of Independent Associations	Single Permutation GWAS: Number of Independent Associations	Expected FDR
MAC \geq 10,000	3,569	144	4%
5,000 \leq MAC < 10,000	157	41	26%
1,000 \leq MAC < 5,000	223	176	79%
0 \leq MAC < 1,000	1,330	1,091	82%
Overall	5,279	1,452	28%

b

MGI SAIGE Analysis Proportion of Associations Expected to be False at $p \leq 5 \times 10^{-8}$ (N = 1,659)					
MAC Category	Number of Independent GWAS Associations			Expected FDR	
	Primary	Single Permutation	Average Permutation (Range)	Single Permutation	Average Permutation (Range)
MAC \geq 10,000	244	44	51 (44-60)	18%	21% (18-25%)
5,000 \leq MAC < 10,000	107	20	21 (16-24)	19%	19% (15-22%)
1,000 \leq MAC < 5,000	113	69	65 (60-69)	61%	57% (53-61%)
0 \leq MAC < 1,000	938	748	799 (748-862)	80%	85% (80-92%)
Overall	1,402	881	935 (881-989)	63%	67% (63-71%)

Supplementary Table 3. Proportion of significant ($p \leq 5 \times 10^{-8}$) independent associations expected to be false in the SAIGE analyses by minor allele count. *N* is the number of phenotypes analyzed.

a) Results for a single permutation of 1,418 UKB phenotypes by MAC category. b) Results for a single permutation and an average of five permutations of 1,659 MGI phenotypes by MAC category.

a

MGI fastGWA Analysis Proportion of Associations Expected to be False at $p \leq 5 \times 10^{-8}$ (N = 1,659)			
MAF Category	Primary GWAS: Number of Independent Associations	Single Permutation GWAS: Number of Independent Associations	Expected FDR
MAF ≥ 0.05	343	66	19%
$0.01 \leq \text{MAF} < 0.05$	529	444	84%
$0.001 \leq \text{MAF} < 0.01$	42,725	42,566	>99%
$0.0001 \leq \text{MAF} < 0.001$	4,553,448	4,485,583	99%
Overall	4,597,051	4,528,660	99%

b

MGI fastGWA Analysis Proportion of Common Variant Independent Associations (MAF ≥ 0.05) Expected to be False Across P-value Categories (N = 1,659)				
P-value Category	Primary GWAS: Number of Independent Associations	Single Permutation GWAS: Number of Independent Associations	Expected FDR	Analogous FDR from SAIGE Analysis
$p \leq 5 \times 10^{-8}$	343	66	19%	23%
$p \leq 5 \times 10^{-9}$	224	8	4%	4%
$p \leq 5 \times 10^{-10}$	177	1	<1%	<1%
$p \leq 5 \times 10^{-11}$	149	0	<1%	<1%
$p \leq 5 \times 10^{-12}$	125	0	<1%	<1%

c

MGI fastGWA Analysis Proportion of Associations Expected to be False Across P-value Categories (N = 1,659)			
P-value Category	Primary GWAS: Number of Independent Associations	Single Permutation GWAS: Number of Independent Associations	Expected FDR
$p \leq 5 \times 10^{-8}$	4,597,051	4,528,660	99%
$p \leq 5 \times 10^{-9}$	3,695,848	3,640,179	98%
$p \leq 5 \times 10^{-10}$	3,011,004	2,957,145	98%
$p \leq 5 \times 10^{-11}$	2,479,366	2,432,045	98%
$p \leq 5 \times 10^{-12}$	2,042,671	2,003,497	98%

Supplementary Table 4. Proportion of significant ($p \leq 5 \times 10^{-8}$) independent associations expected to be false in the fastGWA analysis by minor allele frequency and p-value category. *N* is the number of phenotypes analyzed. a) Results for a single permutation of 1,659 MGI phenotypes by MAF category. b) Results for a single permutation of 1,659 MGI phenotypes for associations with $\text{MAF} \geq 0.05$ by p-value category. c) Results for a single permutation of 1,659 MGI phenotypes by p-value category.