Supplementary Tables (Manuscript Version 2017-07-06)

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Supplementary Table 1

Sample sizes and numbers of genetic variants in GWAS of 31 human phenotypes. For each trait, the number of "total" SNPs is the number of SNPs reported in the corresponding publication and/or summary statistics file, and the number of "analyzed" SNPs is the number of SNPs used in our analyses. Both columns are visualized in **Supplementary Figure 1**.

Phenotype (abbreviation)	PMID	Number of SNPs		Sample size (cases+controls)
		Total	Analyzed	
Neurological phenotypes				
Amyotrophic lateral sclerosis (ALS)	27455348	8,709,433	1,162,845	12,577+23,475
Depressive symptoms (DS)	27089181	6,524,474	1,119,108	161,460
Alzheimer's disease (LOAD)	24162737	7,055,881	1,136,997	17,008+37,154
Neuroticism (NEU)	27089181	6,524,432	1,119,108	170,911
Schizophrenia (SCZ)	25056061	9,444,230	1,113,442	152,805
Anthropometric traits				
Body mass index (BMI)	25673413	2,554,637	1,012,465	234,069
Height (HEIGHT)	25282103	2,550,858	1,064,575	253,288
Waist-to-hip ratio (WHR)	25673412	2,542,431	1,008,898	142,762
Immune-related traits				
Crohn's disease (CD)	26192919	12,276,505	1,064,533	5,956+14,927
Inflammatory bowel disease (IBD)	26192919	12,716,083	1,081,481	12,882+21,770
Rheumatoid arthritis (RA)	24390342	8,747,962	1,158,064	14,361+43,923
Ulcerative colitis (UC)	26192919	12,255,196	1,092,170	6,968+20,464
Metabolic phenotypes				
Age at natural menopause (ANM)	26414677	2,418,695	1,047,412	69,360
Coronary artery disease (CAD)	26343387	9,455,778	1,121,322	60,801+123,504
Fasting glucose (FG)	22581228	2,628,879	1,114,610	58,074
Fasting insulin (FI)	22581228	2,627,848	1,114,592	51,750
Gout (GOUT)	23263486	2,538,056	1,061,037	2,115+67,259
High-density lipoprotein (HDL)	20686565	2,692,429	1,032,214	99,900
Heart rate (HR)	23583979	2,516,789	1,066,168	92,355
Low-density lipoprotein (LDL)	20686565	2,692,564	1,030,397	95,454
Myocardial infarction (MI)	26343387	9,289,491	1,111,568	42,561+123,504
Type 2 diabetes (T2D)	22885922	2,473,441	1,047,618	12,171+56,862
Total cholesterol (TC)	20686565	2,692,413	1,032,272	100,184
Triglycerides (TG)	20686565	2,692,560	1,030,671	96,598
Serum urate (URATE)	23263486	2,450,547	1,050,253	110,347
Hematopoietic traits				
Haemoglobin (HB)	23222517	2,593,078	1,116,281	61,155
Mean cell HB (MCH)	23222517	2,586,784	1,114,901	51,711
Mean cell HB concentration (MCHC)	23222517	2,588,875	1,115,595	56,475
Mean cell volume (MCV)	23222517	2,591,132	1,116,066	58,114
Packed cell volume (PCV)	23222517	2,591,079	1,115,725	53,089
Red blood cell count (RBC)	23222517	2,589,454	1,115,397	53,661

Supplementary Table 2

Confounding adjustment in GWAS of 31 human phenotypes. Columns left to right: (1) phenotype and its abbreviation; (2) genomic control (GC) factor [1]; (3) LD score (LDSC) regression intercept [2]; (4) the number of top genotype-derived principal components (PCs) that were included as covariates in the single-SNP association testing [3]; (5) other covariates included in the single-SNP association testing. The genomic control factor λ_{GC} and the LD score regression intercept λ_{LDSC} are two measures of confounding biases such as population stratification. Values of $\lambda_{\mathrm{GC}} \approx 1$ or $\lambda_{\mathrm{LDSC}} \approx 1$ indicate little confounding effects, whereas $\lambda_{\mathrm{GC}} \geq 1$ or $\lambda_{\mathrm{LDSC}} \geq 1$ suggest possible existence of confounding biases. The "cohort" covariate denote all factors that are specific to study cohorts (e.g. genotyping array, study site).

Phenotype (abbreviation)	λ_{GC}	λ_{LDSC}	# of PCs	Other covariates
Neurological phenotypes				
Amyotrophic lateral sclerosis (ALS)	1.12	1.10	1-4	not shown
Depressive symptoms (DS)	1.17	1.01	4-15	sex, age, cohort
Alzheimer's disease (LOAD)	1.09	1.04	2-8	sex, age
Neuroticism (NEU)	1.32	1.00	4-15	sex, age, cohort
Schizophrenia (SCZ)	1.47	1.07	10	not shown
Anthropometric traits				
Body mass index (BMI)	1.08	1.02	not shown	sex, age, cohort
Height (HEIGHT)	1.94	1.05	not shown	sex, age, cohort
Waist-to-hip ratio (WHR)	1.01	0.93	not shown	sex, age, cohort, BMI
Immune-related traits				
Crohn's disease (CD)	1.13	1.03	10	not shown
Inflammatory bowel disease (IBD)	1.16	1.06	15	not shown
Rheumatoid arthritis (RA)	1.07	0.98	5-10	not shown
Ulcerative colitis (UC)	1.11	1.04	7	not shown
Metabolic phenotypes				
Age at natural menopause (ANM)	not shown	not shown	not shown	cohort
Coronary artery disease (CAD)	1.18	1.05	not shown	not shown
Fasting glucose (FG)	not shown	not shown	not shown	sex, age, cohort, BMI
Fasting insulin (FI)	1.07	1.02	not shown	sex, age, cohort, BMI
Gout (GOUT)	1.03	not shown	2-10	sex, age, cohort
High-density lipoprotein cholesterol (HDL)	1.14	1.01	not shown	sex, age, cohort
Heart rate (HR)	1.11	1.01	not shown	sex, age, cohort, BMI
Low-density lipoprotein cholesterol (LDL)	1.10	1.00	not shown	sex, age, cohort
Myocardial infarction (MI)	not shown	not shown	not shown	not shown
Type 2 diabetes (T2D)	1.10	1.03	not shown	cohort
Total cholesterol (TC)	1.11	1.01	not shown	sex, age, cohort
Triglycerides (TG)	1.12	1.00	not shown	sex, age, cohort
Serum urate (URATE)	1.12	1.01	2-10	sex, age, cohort
Hematopoietic traits				
Haemoglobin (HB)	1.10	not shown	2-10	sex, age, cohort
Mean cell HB (MCH)	1.13	not shown	2-10	sex, age, cohort
Mean cell HB concentration (MCHC)	1.08	not shown	2-10	sex, age, cohort
Mean cell volume (MCV)	1.14	not shown	2-10	sex, age, cohort
Packed cell volume (PCV)	1.10	not shown	2-10	sex, age, cohort
Red blood cell count (RBC)	1.14	not shown	2-10	sex, age, cohort

Supplementary Table 3

Grids of hyper-parameters used in genome-wide multiple-SNP analyses of 31 human phenotypes, assuming no pathways are enriched.

	Round 1 analysis		Round 2 analysis	
Phenotype (abbreviation)	h	θ_0	h	θ_0
Neurological phenotypes				
Amyotrophic lateral sclerosis (ALS)	(0.3:0.1:0.6)	(-6:0.25:-3)	(0.3:0.1:0.6)	(-6:0.05:-5)
Depressive symptoms (DS)	(0.3:0.1:0.6)	(-6:0.25:-2)	(0.3:0.1:0.6)	(-6:0.05:-5)
Alzheimer's disease (LOAD)	(0.3:0.1:0.6)	(-5.25:0.25:-3.25)	0.3	(-5.25:0.025:-4.75)
Neuroticism (NEU)	(0.3:0.1:0.6)	(-4.5:0.25:-2)	0.3	(-4.5:0.025:-4)
Schizophrenia (SCZ)	(0.3:0.1:0.6)	(-4:0.25:-1)	0.3	(-2.25:0.025:-1.75)
Anthropometric traits				
Body mass index (BMI)	(0.3:0.1:0.6)	(-5:0.25:-1)	0.3	(-4.25:0.025:-3.75)
Height (HEIGHT)	(0.3:0.1:0.6)	(-4:0.25:-1)	(0.3:0.1:0.4)	(-2.25:0.025:-1.75)
Waist-to-hip ratio (WHR)	(0.3:0.1:0.6)	(-6:0.25:-3)	(0.3:0.1:0.6)	(-6:0.05:-5)
Immune-related traits				
Crohn's disease (CD)	(0.3:0.1:0.6)	(-4:0.25:-2)	0.3	(-3.25:0.025:-2.75)
Inflammatory bowel disease (IBD)	(0.3:0.1:0.6)	(-4:0.25:-2)	0.3	(-3.25:0.025:-2.75)
Rheumatoid arthritis (RA)	(0.3:0.1:0.6)	(-4.5:0.25:-2)	0.3	(-3.5:0.025:-3)
Ulcerative colitis (UC)	(0.3:0.1:0.6)	(-4:0.25:-2)	0.3	(-3.25:0.025:-2.75)
Metabolic phenotypes				
Age at natural menopause (ANM)	(0.3:0.1:0.6)	(-6:0.25:-2)	0.4	(-5.75:0.025:-5.25)
Coronary artery disease (CAD)	(0.3:0.1:0.6)	(-5:0.25:-2)	0.3	(-4.25:0.25:-3.75)
Fasting glucose (FG)	(0.3:0.1:0.6)	(-6:0.25:-3)	0.6	(-6:0.05:-5)
Fasting insulin (FI)	(0.3:0.1:0.6)	(-6:0.25:-3)	0.6	(-6.25:0.025:-5.75)
Gout (GOUT)	(0.3:0.1:0.6)	(-5.5:0.25:-2)	(0.3:0.1:0.6)	(-5.5:0.05:-4.5)
High-density lipoprotein (HDL)	(0.3:0.1:0.6)	(-5:0.25:-2)	0.3	(-3.75:0.025:-3.25)
Heart rate (HR)	(0.3:0.1:0.6)	(-5:0.25:-2)	(0.3:0.1:0.4)	(-4.5:0.025:-4)
Low-density lipoprotein (LDL)	(0.3:0.1:0.6)	(-5:0.25:-2)	0.3	(-4:0.025:-3.5)
Myocardial infarction (MI)	(0.3:0.1:0.6)	(-5:0.25:-2)	0.3	(-4.5:0.025:-4)
Type 2 diabetes (T2D)	(0.3:0.1:0.6)	(-5:0.25:-2)	(0.3:0.1:0.6)	(-4.75:0.025:-4.25)
Total cholesterol (TC)	(0.3:0.1:0.6)	(-5:0.25:-2)	0.6	(-5:0.025:-4.5)
Triglycerides (TG)	(0.3:0.1:0.6)	(-6:0.25:-3)	0.5	(-6.25:0.025:-5.75)
Serum urate (URATE)	(0.3:0.1:0.6)	(-5.5:0.25:-2)	0.5	(-5.5:0.025:-5)
Hematopoietic traits				
Haemoglobin (HB)	(0.3:0.1:0.6)	(-6:0.25:-3)	0.6	(-6.25:0.025:-5.75)
Mean cell HB (MCH)	(0.3:0.1:0.6)	(-5:0.25:-2)	0.6	(-4.75:0.05:-3.75)
Mean cell HB concentration (MCHC)	(0.3:0.1:0.6)	(-6:0.25:-3)	(0.3:0.1:0.6)	(-6:0.05:-5)
Mean cell volume (MCV)	(0.3:0.1:0.6)	(-5:0.25:-2)	0.6	(-4.25:0.025:-3.75)
Packed cell volume (PCV)	(0.3:0.1:0.6)	(-5:0.25:-2)	0.6	(-5.25:0.025:-4.75)
Red blood cell count (RBC)	(0.3:0.1:0.6)	(-5:0.25:-2)	(0.3:0.1:0.6)	(-3.75:0.025:-3.25)

Supplementary Table 4

Grids of hyper-parameters used in genome-wide multiple-SNP analyses of 31 human phenotypes, assuming a candidate pathway are enriched.

	Round 1 analysis			Round 2 analysis		
Phenotype (abbreviation)	h	θ_0	θ	h	θ_0	θ
Neurological phenotypes						
Amyotrophic lateral sclerosis (ALS)	(0.3:0.1:0.6)	(-6:0.25:-5)	(0:0.6:6)	(0.3:0.1:0.6)	(-6:0.05:-5)	(0:0.1:4)
Depressive symptoms (DS)	(0.3:0.1:0.6)	(-6:0.25:-5)	(0:0.6:6)	(0.3:0.1:0.6)	(-6:0.05:-5)	(0:0.15:6)
Alzheimer's disease (LOAD)	0.6	-5	(0:0.025:5)	0.6	(-5.150:0.025:-5.075)	(0:0.01:4)
Neuroticism (NEU)	(0.3:0.1:0.4)	(-4.5:0.25:-4)	(0:0.1:4)	0.3	(-4.5:0.025:-4)	(0:0.037:3.7)
Schizophrenia (SCZ)	0.3	-2	(0:0.01:2)	0.3	(-2.2:0.025:-2.05)	(0:0.01:2)
Anthropometric traits						
Body mass index (BMI)	0.3	-4	(0:0.02:4)	0.3	(-4.2:0.025:-3.8)	(0:0.018:3.5)
Height (HEIGHT)	0.3	-2	(0:0.01:2)	0.3	(-2.075:0.025:-1.925)	(0:0.01:1)
Waist-to-hip ratio (WHR)	0.3	-3	(0:0.015:3)	0.3	(-3:0.025:-2.95)	(0:0.01:3)
Immune-related traits						
Crohn's disease (CD)	0.3	-3	(0:0.015:3)	0.3	-3	(0:0.01:2)
Inflammatory bowel disease (IBD)	0.3	-3	(0:0.015:3)	0.3	(-3:0.025:-2.8)	(0:0.02:2)
Rheumatoid arthritis (RA)	0.3	-3.25	(0:0.016:3.25)	0.3	(-3.25:0.025:-3.175)	(0:0.01:2)
Ulcerative colitis (UC)	0.3	-3	(0:0.015:3)	0.3	(-3.175:0.025:-2.775)	(0:0.025:2.5)
Metabolic phenotypes						
Age at natural menopause (ANM)	0.4	-5.5	(0:0.028:5.5)	0.4	(-5.75:0.025:-5.7)	(0:0.04:4.5)
Coronary artery disease (CAD)	0.3	-4	(0:0.02:4)	0.3	(-4.025:0.025:-3.775)	(0:0.035:3.5)
Fasting glucose (FG)	0.6	-5.25	(0:0.026:5.25)	0.6	(-6:0.05:-5.75)	(0.1:0.1:4.5)
Fasting insulin (FI)	0.6	-6	(0:0.03:6)	0.6	(-6.25:0.025:-6)	(0:0.019:3.8)
Gout (GOUT)	(0.3:0.1:0.6)	(-5.5:0.25:-4.75)	(0:0.46:5.5)	(0.3:0.1:0.6)	(-5.5:0.05:-4.6)	(0:0.1:5)
High-density lipoprotein (HDL)	0.3	-3.5	(0:0.018:3.5)	0.3	(-3.575:0.025:-3.5)	(0:0.01:3)
Heart rate (HR)	(0.3:0.1:0.4)	(-4.5:0.25:-4.25)	(0:(4.5/50):4.5)	(0.3:0.1:0.4)	(-4.5:0.025:-4.1)	(0:0.038:3.8)
Low-density lipoprotein (LDL)	0.3	-3.75	(0:0.019:3.75)	0.3	(-3.625:0.025:-3.55)	(0:0.01:3)
Myocardial infarction (MI)	0.3	(-4.5:0.25:-4)	(0:0.067:4.5)	0.3	(-4.475:0.025:-4)	(0:0.045:4.5)
Type 2 diabetes (T2D)	(0.4:0.1:0.6)	-4.5	(0:0.067:4.5)	(0.3:0.1:0.6)	(-4.75:0.025:-4.35)	(0:0.3:3)
Total cholesterol (TC)	0.6	-4.75	(0:0.024:4.75)	0.6	(-4.8:0.025:-4.55)	(0:0.02:4)
Triglycerides (TG)	0.5	-4	(0:0.03:4)	0.5	(-6.25:0.025:-6.1)	(0:0.02:5.2)
Serum urate (URATE)	0.5	-5.25	(0:0.026:5.25)	0.5	(-5.4:0.025:-5)	(0:0.1:4.7)
Hematopoietic traits						
Haemoglobin (HB)	0.6	-6	(0:0.03:6)	0.6	(-6.25:0.025:-5.9)	(0:0.04:4.4)
Mean cell HB (MCH)	0.6	-4	(0:0.02:4)	0.6	(-4.7:0.05:-4.35)	(0:0.015:3)
Mean cell HB concentration (MCHC)	(0.3:0.1:0.6)	(-6:0.25:-5.25)	(0:0.5:6)	(0.3:0.1:0.6)	(-6:0.05:-5)	(0:0.1:5)
Mean cell volume (MCV)	0.6	-4	(0:0.02:4)	0.6	(-4.225:0.025:-4.125)	(0:0.02:3)
Packed cell volume (PCV)	0.6	-5	(0:0.025:5)	0.6	(-5.25:0.025:-5.15)	(0:0.02:4.5)
Red blood cell count (RBC)	(0.3:0.1:0.6)	-3.5	(0:0.07:3.5)	(0.5:0.1:0.6)	(-3.7:0.025:-3.6)	(0:0.035:3.5)

References

1. Devlin B, Roeder K (1999) Genomic control for association studies. Biometrics 55: 997–1004.

2. Bulik-Sullivan BK, Loh P-R, Finucane HK, Ripke S, Yang J, et al. (2015) LD score regression distinguishes confounding from polygenicity in genome-wide association studies. Nature Genetics 47: 291–295.

3. Price AL, Patterson NJ, Plenge RM, Weinblatt ME, Shadick NA, et al. (2006) Principal components analysis corrects for stratification in genome-wide association studies. Nature Genetics 38: 904–909.