

SUPPLEMENTARY DATA

Supplementary Table 1. Characteristics of participants in UK Biobank.

N Individuals	120286
Age \pm SD, years	56.9 \pm 7.9
Male, n (%)	56936 (47.3%)
UK BiLEVE Array, n (%)	41397 (34.4%)
SBP \pm SD, mm Hg*	143.6 \pm 21.8 mm Hg
DBP \pm SD, mm Hg*	84.5 \pm 11.8 mm Hg
BMI \pm SD, kg/m ²	27.5 \pm 4.8 kg/m ²
Waist-to-Hip Ratio \pm SD	0.88 \pm 0.091
Diabetes Mellitus, n (%)	6148 (5.1%)
Coronary Heart Disease, n (%)	4831 (4.0%)

*Reported measurements are after adjustment for treatment (addition of 15 mm Hg to SBP and 10 mm Hg to DBP)

Abbreviations: SBP, systolic blood pressure; DBP, diastolic blood pressure; BP, blood pressure; SD, standard deviation; BMI, body mass index.

UK BiLEVE Array refers to participants who were genotyped using the UK BiLEVE array rather than the UK Biobank Axiom Array.

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Supplementary Table 2 Characteristics of genome wide association studies included in this study.

Consortium	Outcome/Trait	Sample Size	Genotyping
MAGIC(1)	Fasting glucose Fasting insulin Two hour glucose HbA1c	Up to 133 010 individuals	Various arrays, imputation to 2.5 million SNPs using HapMap reference panel
GIANT(2,3)	Waist-to-hip ratio Waist circumference Hip circumference Body mass index	Up to 322,154 individuals	Various arrays, imputation to 2.5 million SNPs using HapMap reference panel
CARDIoGRAM Exome Consortium(4)	Coronary heart disease	Up to 72868 cases/ 120770 controls	Illumina OmniExome Chip and Illumina HumanExome BeadChip
DIAGRAM(5)	Diabetes	Up to 34 840 cases/ 114 981 controls	37 studies using MetaboChip, 23 studies various arrays, imputation to 2.5 million SNPs using HapMap reference panel

Abbreviations: CARDIoGRAM, Coronary ARtery Disease Genome wide Replication and Meta-analysis; DIAGRAM, DIAbetes Genetics Replication And Meta-analysis; GIANT, Genetic Investigation of ANthropometric Traits; MAGIC, Meta-Analyses of Glucose and Insulin-related traits Consortium; SNPs, single nucleotide polymorphism; LDL cholesterol, low-density lipoprotein cholesterol; HDL cholesterol, high-density lipoprotein cholesterol.

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Supplementary Table 3. Definitions of outcomes

Outcome	Definition (UK Biobank unless otherwise specified)
Coronary heart disease	Inverse variance weighted fixed effects meta-analysis of CARDIOGRAM Exome Consortium(4) outcome (coronary heart disease) and UK Biobank outcome: (1) Myocardial infarction (MI), coronary artery bypass grafting, or coronary artery angioplasty documented in medical history at time of enrollment by a trained nurse or (2) Hospitalization for ICD-10 code for acute myocardial infarction (I21.0, I21.1, I21.2, I21.4, I21.9) or (3) Hospitalization for OPCS-4 coded procedure: coronary artery bypass grafting (K40.1-40.4, K41.1-41.4, K45.1-45.5) or (4) Hospitalization for OPCS-4 coded procedure: coronary angioplasty ± stenting (K49.1-49.2, K49.8-49.9, K50.2, K75.1-75.4, K75.8-75.9)
Atrial fibrillation/flutter	History of atrial fibrillation or flutter during verbal interview with trained nurse or hospitalization for ICD code I48
Heart failure	History of heart failure during verbal interview with trained nurse or hospitalization for ICD code I50
Stroke	History of stroke, ischaemic stroke, or subarachnoid hemorrhage during verbal interview with trained nurse or hospitalization for ICD codes I60-I64
Peripheral vascular disease	History of peripheral vascular disease or intermittent claudication during verbal interview with trained nurse or hospitalization for ICD code I74 or I1739
Venous thromboembolism	History of venous thromboembolism, deep vein thrombosis or pulmonary embolism during verbal interview with trained nurse or hospitalization for ICD code I26 or I80-I82
Aortic stenosis	History of aortic stenosis during verbal interview with trained nurse or hospitalization for ICD code I350
Type 2 Diabetes	Inverse variance weighted fixed effects meta-analysis of DIAGRAM Exome Consortium outcome (type 2 diabetes) and UK Biobank (history of diabetes unspecified, type 2 diabetes during verbal interview with trained nurse or current use of insulin medication)
Chronic kidney disease	Chronic Kidney Disease Genetics Consortium outcome(6) (creatinine estimated glomerular filtration rate <60 ml/min)
Inflammatory bowel disease	History of inflammatory bowel disease, Crohn's disease or ulcerative colitis during verbal interview with trained nurse
Gastric reflux	History of gastric reflux during verbal interview with trained nurse
Irritable bowel syndrome	History of irritable bowel syndrome during verbal interview with trained nurse
Gallstone	History of gallstones during verbal interview with trained nurse
Hyperthyroidism	History of hyperthyroidism during verbal interview with trained nurse
Hypothyroidism	History of hypothyroidism during verbal interview with trained nurse

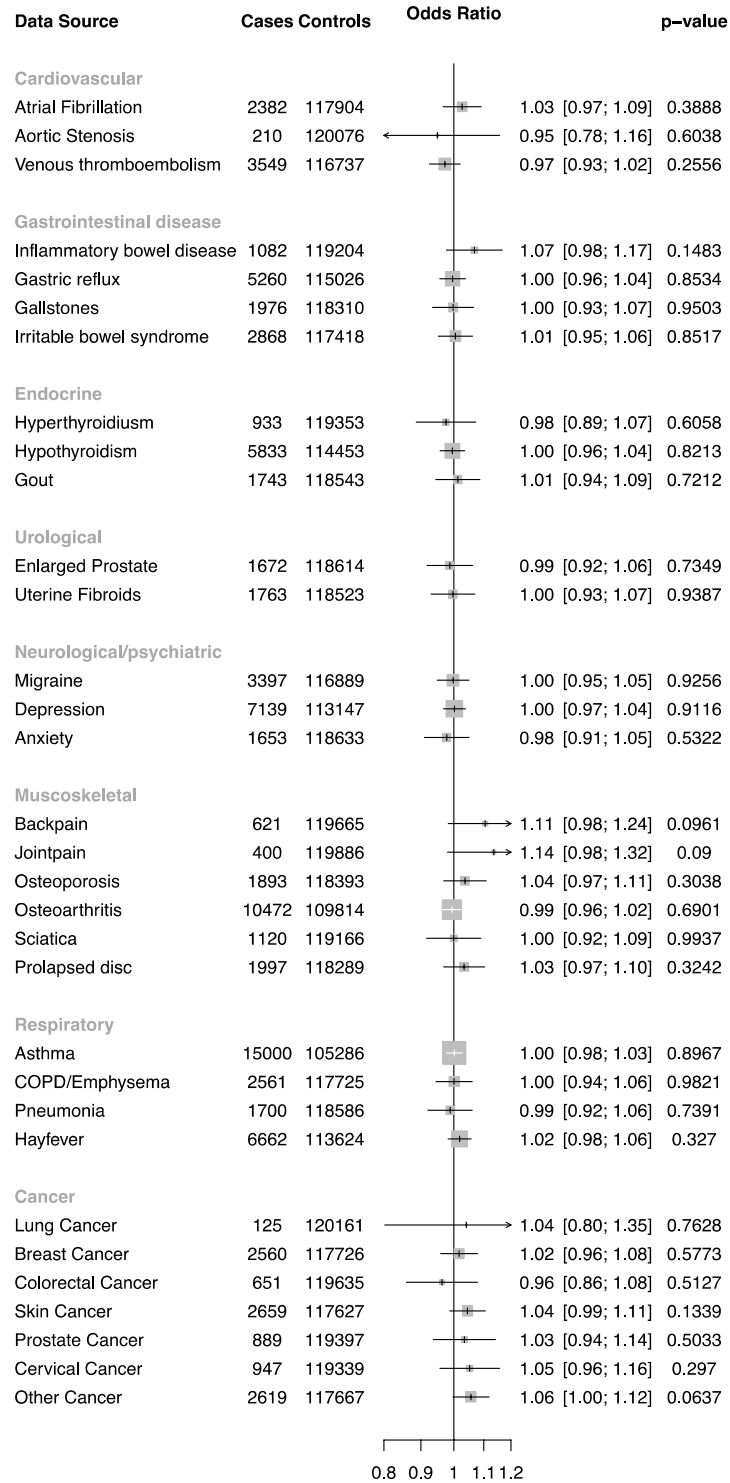
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Gout	History of gout during verbal interview with trained nurse
Enlarged prostate	History of enlarged prostate during verbal interview with trained nurse
Uterine fibroids	History of uterine fibroids during verbal interview with trained nurse
Migraine	History of migraine during verbal interview with trained nurse
Depression	History of depression during verbal interview with trained nurse
Anxiety	History of anxiety/panic attacks during verbal interview with trained nurse
Osteoporosis	History of osteoporosis during verbal interview with trained nurse
Osteoarthritis	History of osteoarthritis during verbal interview with trained nurse
Sciatica	History of sciatica during verbal interview with trained nurse
Prolapsed disc	History of prolapsed disc/slipped disc during verbal interview with trained nurse
Asthma	History of asthma during verbal interview with trained nurse
COPD/Emphysema	History of chronic obstructive airways disease, emphysema/chronic bronchitis or emphysema during verbal interview with trained nurse
Pneumonia	History of pneumonia during verbal interview with trained nurse
Hayfever	History of hayfever during verbal interview with trained nurse
Breast cancer	History of breast cancer during verbal interview with trained nurse
Colorectal cancer	History of large bowel cancer/colorectal cancer, colon cancer/sigmoid cancer or rectal cancer during verbal interview with trained nurse
Skin cancer	History of skin cancer, malignant melanoma, non-melanoma skin cancer, basal cell carcinoma or squamous cell carcinoma during verbal interview with trained nurse
Prostate cancer	History of prostate cancer during verbal interview with trained nurse
Cervical cancer	History of cervical cancer or cin cells at the cervix during verbal interview with trained nurse
Other cancer	History of any other cancer than lung cancer, breast cancer, colorectal cancer, skin cancer, prostate cancer or cervical malignancy during verbal interview with trained nurse

Abbreviations: COPD, chronic obstructive pulmonary disease; ICD, international classification of disease

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Supplementary Figure 1. Association of ABCC8 A1369S variant with a range of diseases. Estimates were derived in UK Biobank using logistic regression, adjusted for age, sex, ten principal components and array type. Abbreviations: OR, odds ratio; SD, standard deviation; COPD, chronic obstructive pulmonary disease.



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