

Supplementary Tables and Figures

Mendelian Randomisation study of the influence of eGFR on coronary heart disease

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GENE(s) in hit regions	Function (if known)	Marker SNPs
<i>NAT8, NAT8B, ALMS1, DUSP11, TPRKB</i>	acetylation enzyme, NAT8 expressed in tubular cells known monogenetic kidney disease: Alstrom unknown	rs10206899, rs15358
<i>DAB2</i> <i>C9</i>	Proximal tubular adaptor protein, links to megalin complement C9 locus	rs11959928
<i>SLC34A1</i>	Na Phosphate transporter, associated with stones	rs6420094
<i>DACH1</i>	involved in organogenesis, tubular epithelial cells	rs626277
<i>STC1</i>	Stanniocalcin 1, expressed in human nephron, involved in fish in calcium metabolism	rs1731274
<i>UMOD</i>	Tamm-Horsfall protein/Uromodulin, rare variants associated with medullary cystic kidney disease type 2, familial juvenile hyper-uricemic nephropathy, glomerulo-cystic kidney disease, known hypertension gene	rs12917707 rs4293393 rs13333226
<i>SLC7A9</i>	amino-acid transporter in tubular cells (including lysine), causes cystinuria, nephrolithiasis	rs4805834 rs8101881
<i>SOX11</i>	embryonal transcription factor	rs16864170
<i>VEGFA</i>	Vascular endothelial growth factor	rs881858
<i>PKRAG2</i>	rare variants associated with WPW, and cardiac changes	rs7805747

	and hypertrophy of kidney	
<i>ATXN2</i>	Associated with retinal vessel caliber, celiac disease, diabetes type 1, myocardial infarction, blood pressure variant	rs653178
<i>TBX2</i>	T-box transcription factors, no known kidney phenotype	rs8068318
<i>GCKR, IFT172, FNDC4</i>	Pleiotropic locus. Common variants in <i>GCKR</i> are associated with a variety of human traits in genetic association studies, including serum triglycerides, fasting glucose, C-reactive protein and uric acid as well as susceptibility to type 2 diabetes.	rs1260326
<i>ANXA9, FAM63A, PRUNE, BNIPL, LASS2, SETDB1</i>	Unknown	rs267734
<i>SYPL2, ATXN7L2, CYB561D1, PSMA5, AMIGO1, SORT1</i>	Unknown	rs1933182
<i>TFDP2</i>	Transcription factor involved in cell cycle	rs347685
<i>SHROOM3</i>	expressed in kidney, neuro-epithelial development, associated with low blood magnesium in genome-wide association study, and borderline association with UACR	rs17319721 rs9992101
<i>PIP5K1B</i>	Unknown	rs4744712
<i>RNASEH2C, KAT5, OVOL1</i>	<i>OVOL1</i> is zinc-finger transcription factor, downstream of WNT signalling	rs4014195
<i>UBE2Q2</i>	belongs to the ubiquitin-conjugating enzyme family, potentially involved in degradation of tubular transporter proteins, potential cancer suppressor gene	rs1394125
<i>MHC region</i>	HLA region known to be associated with autoimmune forms of kidney disease	rs3828890
<i>UNCX</i>	Associated with blood urea nitrogen in East Asians, encodes a paired-type homeobox transcription factor that has essential roles in skeleton formation and kidney development	rs10277115
<i>MPPED2-DCDC5</i>	Unknown Associated with blood urea nitrogen in East Asians, and with serum magnesium levels	rs963837
<i>BCAS3</i>	Unknown Associated with blood urea nitrogen and uric acid in East Asians	rs9895661
<i>WDR72</i>	Unknown Associated with blood urea nitrogen in East Asians	rs17730281 rs491567
<i>CUBN</i>	Cubilin - interacts with megalin and as a receptor for intrinsic factor-vitamin B12 complexes. Associated with low HDL, known CVD risk gene	rs1801239

S1 Table. Consistent and replicated SNP markers for CKD in European populations (Chambers et al., 2010, Gudbjartsson et al., 2010, Kottgen et al., 2009, Kottgen et al., 2010a, Kottgen et al., 2010b). All markers were associated with eGFR, except *CUBN*, which was associated with an incident urinary albumin/creatinine ratio. SNPs in genes that encode for synthesis or secretion of cystatin C and creatinine (blood markers for eGFR) are excluded.

snps used in our MR study (17 snps in total)
snps removed due to high LD
snps not available in Metabochip (UCLEB)

chr	reported eGFR SNPs	CARDIoGRAMplusC4D		
		CARDIoGRAM GWAS (22,233 CHD cases and 64,762 controls)	C4D GWAS (15,420 CHD cases and 15,062 controls)	CARDIoGRAMplusC4D Metabochip (63,746 CHD cases and 130,681 controls)
1	rs267734	y		y
1	rs1933182	y		
2	rs10206899	y		
2	rs16864170			
2	rs1260326	y	y	
3	rs347685			
4	rs17319721	y		
4	rs9992101			
5	rs11959928			
5	rs6420094	y	y	
6	rs881858	y		
6	rs3828890			
7	rs7805747	y	y	
7	rs10277115			
8	rs1731274			
9	rs4744712	y		y
10	rs1801239			
11	rs4014195	y		
11	rs963837			
12	rs653178	y	y	y
13	rs15358			
13	rs626277			
15	rs1394125			
15	rs17730281	y		
15	rs491567			
16	rs12917707	y		
16	rs4293393			
16	rs13333226			
17	rs8068318	y		
17	rs9895661			

19	rs4805834			
19	rs8101881	y	y	y

S2 Table. Selection of 17 SNPs and their availability in CARDIoGRAMplusC4D. Out of 32 SNPs listed in Supplementary Table I, 11 SNPs (brown boxes) are not available in UCLEB. A further 4 SNPs (light blue boxes) are shown as high LD SNPs ($r^2 > 0.7$). Hence the 17 remaining SNPs (dark blue box) are selected as potential instrumental variables. “y” represents the availability of SNPs across 3 data sets from CARDIoGRAMplusC4D.

Abbreviation	Description
sex	sex
age	age
whr	Waist to hip ratio
wcir	Waist circumference
bmi	Body mass index
pbfat	% body fat
ht	height
wt	Weight
sbp	Systolic blood pressure
dbp	Diastolic blood pressure
smoke	smoking (ever/never)
alcohol	Alcohol
Tc	TC
ldl	LDL
hdl	HDL
tg	Triglyceride
lpa	Lp(a)
hba1c	HbA1c
glucose	glucose
insulin	insulin
viscosity	Plasma viscosity
hct	Haematocrit
fact8	Factor VIII
fact9	Factor IX
aptt	Activated partial thromboplastin time
tpa	tPa
vwf	vW factor
ddimer	D-Dimer
fact7	Factor VII
wcc	WCC
fib	Fib

il6	IL-6
tnfalpa	TNF-alpha
platelet	Platelets
rbc	Red blood cell count
haemoglobin	Heamoglobin levels
mcv	Mean cell volume
mch	Mean call haemoglobin
mpv	Mean platelet count
neutrophil	Neutrophil
lympho	Lymphocytes
mono	Monocytes
eosinophil	Eosinophils
basinophil	Basinophils
mchc	Mean cellular Haemoglobin
crp	CRP
ferr	Ferritin
ggt	GGT
alt	ALT
alkphos	Alk Phos
albumin	Albumin
bilirubin	Bilirubin
ast	AST
creatinine	Creatinine
surea	Serum urea concentration
spotassium	Serum potassium concentration
ssodium	Serum sodium concentration
surate	Serum urate concentration
smagnesium	Serum magnesium concentration
scalcium	Serum calcium concentration
ccalcium	Corrected calcium concentration
sphosph	Serum phosphate concentration
sprotein	Total serum protein concentration
egfr	eGFR
pwave	ECG P wave
printerval	ECG PR interval
qtinterval	ECG QT interval
qtc	ECG QTc
qrsvoltsum	ECG QRS voltage sum
qrsvoltprod	ECG QRS voltage product
cornellprod	ECG Cornell product
sokolowlyon	ECG Sokolow Lyon
sclass	Social class
occup	Occupation
fev1	FEV1

fvc	FVC
pefr	Peak Expiratory Flow Rate
probnp	NT-proBNP
leptin	Leptin
igf1	IGF-1
vitc	Vitamin C
vite	Vitamin E
betacarot	Beta-carotene
adiponectin	Adiponectin
il18	IL-18
mmp9	MMP-9
scd401	sCD40L
cotinine	Cotinine

S3 Table. Phenotype descriptions in UCLEB

	eGFR-trait		CHD-trait		unweighted gene score-trait		internally-weighted gene score-trait	
	unadjusted	adjusted	unadjusted	adjusted	unadjusted	adjusted	unadjusted	adjusted
adiponectin	9.56E-01	9.57E-01	6.20E-01	6.89E-01	1.82E-02	3.57E-01	1.31E-02	2.56E-01
age*	8.45E-58	6.93E-56	1.05E-14	2.41E-13	8.77E-01	9.94E-01	8.12E-01	9.77E-01
albumin	1.65E-08	5.90E-08	4.22E-01	4.98E-01	2.99E-01	9.05E-01	4.94E-01	8.86E-01
alcohol*	7.91E-05	1.85E-04	1.46E-02	2.80E-02	5.23E-01	9.94E-01	2.36E-01	8.51E-01
alkphos	1.15E-02	2.20E-02	9.46E-02	1.45E-01	6.28E-01	9.94E-01	6.06E-01	9.25E-01
alt	1.78E-10	9.13E-10	7.31E-01	7.78E-01	5.73E-01	9.94E-01	9.54E-01	9.77E-01
apoa1	NA	NA	9.13E-06	3.50E-05	2.23E-01	9.05E-01	1.66E-01	7.63E-01
apob	NA	NA	2.49E-13	3.27E-12	8.79E-01	9.94E-01	1.12E-01	7.63E-01
apoe	NA	NA	2.31E-06	1.01E-05	9.54E-02	8.50E-01	2.72E-01	8.62E-01
aptt	9.56E-01	9.57E-01	7.38E-02	1.17E-01	7.44E-01	9.94E-01	3.87E-01	8.86E-01
ast	2.71E-02	4.63E-02	6.62E-01	7.25E-01	6.49E-01	9.94E-01	3.73E-01	8.86E-01
basinophil	6.03E-03	1.18E-02	1.31E-01	1.95E-01	8.72E-01	9.94E-01	8.54E-01	9.77E-01
betacarot	7.04E-01	7.49E-01	2.28E-02	4.11E-02	9.99E-01	9.99E-01	7.17E-01	9.77E-01
bilirubin	3.67E-01	4.55E-01	6.01E-02	9.88E-02	2.80E-01	9.05E-01	2.90E-01	8.62E-01
bmi*	1.26E-17	1.72E-16	7.28E-06	2.91E-05	8.77E-01	9.94E-01	3.56E-01	8.86E-01
ccalcium	1.38E-08	5.13E-08	1.49E-01	2.17E-01	1.80E-01	9.05E-01	1.81E-01	7.63E-01
cornellprod *	1.10E-03	2.38E-03	4.31E-07	2.09E-06	7.66E-01	9.94E-01	6.67E-01	9.76E-01
cotinine*	4.81E-03	9.62E-03	1.38E-04	3.63E-04	4.30E-01	9.65E-01	1.09E-01	7.63E-01
creatinine(**)	-	-	-	-	1.23E-10	6.02E-09	1.39E-17	6.83E-16
crp*	4.29E-09	1.85E-08	1.56E-05	5.51E-05	8.56E-01	9.94E-01	1.58E-01	7.63E-01

dbp	2.80E-01	3.58E-01	3.32E-03	7.11E-03	9.75E-01	9.97E-01	6.02E-01	9.25E-01
ddimer*	6.19E-16	6.35E-15	3.08E-05	1.01E-04	6.58E-01	9.94E-01	4.10E-01	8.86E-01
egfr(**)	-	-	-	-	2.01E-14	1.97E-12	3.37E-21	3.30E-19
eosinophil*	3.85E-12	3.16E-11	1.87E-03	4.42E-03	4.30E-01	9.65E-01	1.87E-01	7.63E-01
esel	NA	NA	1.73E-01	2.45E-01	4.35E-01	9.65E-01	4.13E-01	8.86E-01
fact7	1.94E-11	1.33E-10	2.08E-01	2.89E-01	8.79E-01	9.94E-01	9.35E-01	9.77E-01
fact8*	1.61E-20	3.30E-19	1.77E-09	1.36E-08	1.54E-01	9.05E-01	8.73E-01	9.77E-01
fact9*	1.24E-08	4.85E-08	3.94E-03	8.23E-03	3.47E-02	4.25E-01	1.17E-01	7.63E-01
ferr	NA	NA	3.11E-01	3.93E-01	4.43E-01	9.65E-01	5.88E-01	9.25E-01
fev1*	6.78E-05	1.64E-04	1.82E-11	1.67E-10	4.93E-01	9.94E-01	6.76E-02	7.63E-01
fib*	4.99E-17	5.84E-16	2.24E-13	3.27E-12	2.36E-01	9.05E-01	4.39E-01	8.86E-01
fvv*	1.63E-06	4.61E-06	1.97E-12	2.02E-11	2.69E-01	9.05E-01	1.94E-02	3.16E-01
ggt	3.41E-02	5.60E-02	1.19E-01	1.79E-01	5.47E-01	9.94E-01	5.25E-01	8.86E-01
glucose	4.39E-01	5.37E-01	1.65E-06	7.61E-06	3.29E-02	4.25E-01	5.40E-01	8.86E-01
haemoglobi n	4.51E-19	7.40E-18	3.12E-01	3.93E-01	9.50E-01	9.97E-01	5.15E-01	8.86E-01
hba1c	5.89E-01	6.70E-01	4.18E-08	2.41E-07	3.04E-01	9.05E-01	9.76E-01	9.86E-01
hct	3.38E-36	1.39E-34	4.13E-01	4.98E-01	9.84E-01	9.97E-01	9.26E-01	9.77E-01
hdl*	1.10E-10	6.02E-10	2.27E-39	2.09E-37	5.71E-01	9.94E-01	9.54E-01	9.77E-01
ht	1.59E-02	2.77E-02	7.75E-01	7.92E-01	2.89E-03	7.09E-02	4.81E-03	1.18E-01
icam	NA	NA	5.27E-01	6.06E-01	7.10E-01	9.94E-01	7.33E-01	9.77E-01
igf1	6.73E-01	7.26E-01	6.02E-01	6.84E-01	2.90E-01	9.05E-01	8.65E-01	9.77E-01
il18	7.76E-01	8.06E-01	6.21E-01	6.89E-01	7.80E-02	7.64E-01	9.11E-02	7.63E-01
il6*	6.93E-06	1.89E-05	3.24E-05	1.03E-04	4.95E-01	9.94E-01	9.57E-01	9.77E-01
insulin	5.85E-01	6.70E-01	6.09E-03	1.22E-02	1.69E-01	9.05E-01	4.50E-01	8.86E-01
ldl	1.53E-02	2.74E-02	6.00E-02	9.88E-02	1.10E-01	9.02E-01	7.42E-01	9.77E-01
leptin	1.03E-04	2.35E-04	8.57E-01	8.57E-01	9.51E-01	9.97E-01	9.11E-01	9.77E-01
lpa	NA	NA	4.07E-05	1.25E-04	3.20E-02	4.25E-01	1.56E-01	7.63E-01
lympho	3.43E-01	4.33E-01	7.29E-01	7.78E-01	3.11E-01	9.05E-01	3.55E-01	8.86E-01
mch	1.47E-02	2.68E-02	3.98E-02	7.04E-02	8.56E-01	9.94E-01	1.54E-01	7.63E-01
mchc	1.19E-02	2.22E-02	7.36E-01	7.78E-01	8.34E-01	9.94E-01	7.65E-01	9.77E-01
mcv	6.29E-01	7.06E-01	4.40E-01	5.12E-01	6.94E-01	9.94E-01	1.42E-01	7.63E-01
mmp9	2.46E-01	3.31E-01	1.26E-03	3.06E-03	3.05E-01	9.05E-01	1.64E-01	7.63E-01
mono	7.75E-02	1.16E-01	2.77E-08	1.70E-07	3.53E-01	9.50E-01	2.59E-01	8.62E-01
mpv	1.12E-01	1.61E-01	2.97E-03	6.67E-03	5.84E-01	9.94E-01	5.27E-01	8.86E-01
neutrophil*	2.50E-05	6.42E-05	1.43E-14	2.63E-13	9.01E-01	9.97E-01	8.93E-01	9.77E-01
occup	2.61E-07	7.92E-07	7.61E-02	1.19E-01	3.59E-01	9.50E-01	8.30E-01	9.77E-01
pbfat*	5.41E-05	1.34E-04	4.52E-05	1.34E-04	8.77E-01	9.94E-01	7.13E-01	9.77E-01
pefr*	1.32E-04	2.92E-04	1.54E-05	5.51E-05	8.80E-01	9.94E-01	2.19E-01	8.27E-01
platelet	1.51E-05	3.99E-05	1.72E-01	2.45E-01	1.76E-01	9.05E-01	8.40E-01	9.77E-01
printerval	2.88E-03	5.90E-03	5.34E-02	9.09E-02	8.36E-01	9.94E-01	9.33E-01	9.77E-01
probnp*	2.99E-08	1.02E-07	2.44E-09	1.73E-08	5.48E-01	9.94E-01	9.93E-01	9.93E-01
prothrombi n	NA	NA	7.69E-01	7.92E-01	9.62E-01	9.97E-01	7.82E-01	9.77E-01
pwave	9.57E-01	9.57E-01	4.20E-01	4.98E-01	6.58E-01	9.94E-01	6.14E-01	9.25E-01

qrsvoltprod	7.72E-01	8.06E-01	2.87E-04	7.33E-04	7.51E-01	9.94E-01	8.87E-01	9.77E-01
qrsvoltsum	2.73E-01	3.58E-01	1.50E-02	2.81E-02	9.66E-01	9.97E-01	8.95E-01	9.77E-01
qtc*	4.89E-13	4.46E-12	4.35E-09	2.86E-08	2.44E-01	9.05E-01	1.58E-01	7.63E-01
qtinterval*	5.46E-08	1.79E-07	8.32E-05	2.25E-04	3.23E-01	9.05E-01	5.30E-01	8.86E-01
rbc	2.53E-11	1.60E-10	3.07E-01	3.93E-01	7.94E-01	9.94E-01	8.74E-01	9.77E-01
sbp	2.77E-01	3.58E-01	6.81E-06	2.85E-05	9.06E-01	9.97E-01	5.05E-01	8.86E-01
scalcium	2.34E-01	3.20E-01	3.86E-01	4.80E-01	9.54E-01	9.97E-01	8.29E-01	9.77E-01
scd40l	6.52E-01	7.23E-01	3.09E-03	6.78E-03	3.19E-01	9.05E-01	4.51E-01	8.86E-01
sclass	6.66E-02	1.05E-01	5.09E-03	1.04E-02	4.36E-01	9.65E-01	2.01E-01	7.87E-01
sex*	9.24E-09	3.79E-08	1.04E-19	3.18E-18	8.82E-01	9.94E-01	4.73E-01	8.86E-01
smagnesium	6.99E-02	1.06E-01	2.32E-01	3.19E-01	7.56E-01	9.94E-01	7.53E-01	9.77E-01
smoke	1.41E-01	1.96E-01	5.08E-08	2.75E-07	6.94E-01	9.94E-01	7.84E-01	9.77E-01
sokolowlyon	9.53E-02	1.40E-01	7.38E-05	2.06E-04	2.47E-01	9.05E-01	5.26E-01	8.86E-01
sposph	4.46E-01	5.38E-01	2.59E-01	3.45E-01	4.34E-01	9.65E-01	2.43E-01	8.51E-01
spotassium	5.16E-02	8.30E-02	2.46E-01	3.32E-01	1.88E-01	9.05E-01	3.84E-01	8.86E-01
sprotein*	1.47E-07	4.63E-07	6.71E-03	1.31E-02	2.33E-01	9.05E-01	2.79E-01	8.62E-01
ssodium	6.70E-01	7.26E-01	7.47E-01	7.81E-01	7.39E-01	9.94E-01	6.67E-01	9.76E-01
surate(**)	-	-	-	-	9.87E-01	9.97E-01	1.71E-01	7.63E-01
surea(**)	-	-	-	-	3.00E-04	9.79E-03	9.55E-07	3.12E-05
tc	3.19E-02	5.35E-02	4.20E-01	4.98E-01	7.96E-01	9.94E-01	3.54E-01	8.86E-01
tg*	1.95E-03	4.10E-03	3.83E-11	3.20E-10	5.01E-02	5.45E-01	4.34E-02	6.08E-01
tnfalpha	1.69E-09	7.70E-09	6.33E-02	1.02E-01	7.55E-01	9.94E-01	4.85E-01	8.86E-01
tpa*	1.54E-11	1.15E-10	2.35E-05	8.01E-05	7.60E-01	9.94E-01	5.43E-01	8.86E-01
uric	NA	NA	2.43E-03	5.60E-03	8.07E-01	9.94E-01	7.88E-01	9.77E-01
vcam	NA	NA	8.12E-01	8.21E-01	3.15E-01	9.05E-01	1.67E-01	7.63E-01
viscosity	6.97E-02	1.06E-01	5.45E-04	1.36E-03	6.28E-01	9.94E-01	5.64E-01	9.07E-01
vitc	5.33E-07	1.56E-06	4.47E-02	7.75E-02	5.21E-01	9.94E-01	5.09E-01	8.86E-01
vite	5.67E-01	6.65E-01	2.99E-01	3.93E-01	2.21E-01	9.05E-01	1.59E-01	7.63E-01
vwf*	8.22E-25	2.25E-23	9.24E-08	4.72E-07	4.41E-01	9.65E-01	8.89E-01	9.77E-01
wcc	5.37E-01	6.38E-01	1.90E-02	3.49E-02	1.99E-01	9.05E-01	3.29E-01	8.86E-01
wcir*	3.49E-10	1.69E-09	7.11E-13	8.17E-12	5.75E-01	9.94E-01	7.29E-01	9.77E-01
whr	1.19E-01	1.68E-01	2.76E-22	1.27E-20	4.84E-01	9.94E-01	3.91E-01	8.86E-01
wt*	6.34E-11	3.71E-10	5.23E-05	1.50E-04	1.20E-01	9.03E-01	4.12E-01	8.86E-01

S4 Table. Unadjusted and Benjamini-Hochberg adjusted *P*-values for association of each trait with eGFR, CHD, unweighted gene score, and UCLEB internally weighted gene score. Twenty one traits (*) are potential confounding factors. NAs shown in eGFR-trait column are due to missing trait measurement on the samples with available eGFR. Kidney related phenotypes (**) are not considered as potential confounders, so eGFR-trait and CHD-trait associations are not calculated for those phenotypes.

	unweighted gene score-trait associations			weighted score-trait associations		
	beta	se	p-value	beta	se	p-value
adiponectin	-4.62E-01	1.96E-01	1.82E-02	-7.13E-01	2.87E-01	1.31E-02
age	-2.99E-03	1.93E-02	8.77E-01	-7.08E-03	2.97E-02	8.12E-01
albumin	-1.51E-02	1.45E-02	2.99E-01	-1.53E-02	2.24E-02	4.94E-01
alcohol	-7.38E-03	1.16E-02	5.23E-01	-2.09E-02	1.76E-02	2.36E-01
alkphos	1.71E-01	3.53E-01	6.28E-01	2.67E-01	5.17E-01	6.06E-01
alt	-3.42E-02	6.07E-02	5.73E-01	-5.40E-03	9.27E-02	9.54E-01
apoa1	-3.09E-03	2.54E-03	2.23E-01	-5.10E-03	3.69E-03	1.66E-01
apob	-3.28E-04	2.14E-03	8.79E-01	4.95E-03	3.12E-03	1.12E-01
apoe	2.16E-04	1.30E-04	9.54E-02	2.10E-04	1.91E-04	2.72E-01
aptt	1.47E-02	4.51E-02	7.44E-01	5.83E-02	6.73E-02	3.87E-01
ast	-2.87E-02	6.31E-02	6.49E-01	-8.57E-02	9.62E-02	3.73E-01
basinophil	-8.95E-05	5.57E-04	8.72E-01	-1.52E-04	8.26E-04	8.54E-01
betacarot	1.81E-05	2.32E-02	9.99E-01	-1.25E-02	3.45E-02	7.17E-01
bilirubin	-4.52E-02	4.18E-02	2.80E-01	-6.41E-02	6.06E-02	2.90E-01
bmi	2.46E-03	1.59E-02	8.77E-01	2.23E-02	2.42E-02	3.56E-01
ccalcium	1.19E-03	8.92E-04	1.80E-01	1.78E-03	1.33E-03	1.81E-01
cornellprod	1.28E-01	4.28E-01	7.66E-01	-2.76E-01	6.41E-01	6.67E-01
cotinine	6.71E-01	8.51E-01	4.30E-01	2.03E+00	1.27E+00	1.09E-01
creatinine	-5.52E-01	8.57E-02	1.23E-10	-1.08E+00	1.27E-01	1.39E-17
crp	-5.05E-03	2.78E-02	8.56E-01	-5.87E-02	4.16E-02	1.58E-01
dbp	1.28E-03	4.12E-02	9.75E-01	-3.23E-02	6.19E-02	6.02E-01
ddimer	-5.24E-01	1.18E+00	6.58E-01	-1.49E+00	1.80E+00	4.10E-01
egfr	4.97E-01	6.50E-02	2.01E-14	9.54E-01	1.01E-01	3.37E-21

eosinophil	9.49E-04	1.20E-03	4.30E-01	-2.35E-03	1.78E-03	1.87E-01
esel	-2.41E-01	3.08E-01	4.35E-01	-3.72E-01	4.54E-01	4.13E-01
fact7	2.22E-02	1.46E-01	8.79E-01	-1.81E-02	2.21E-01	9.35E-01
fact8	3.18E-01	2.23E-01	1.54E-01	5.52E-02	3.47E-01	8.73E-01
fact9	5.43E-01	2.57E-01	3.47E-02	6.01E-01	3.84E-01	1.17E-01
ferr	5.12E-01	6.68E-01	4.43E-01	5.61E-01	1.04E+00	5.88E-01
fev1	-2.13E-03	3.11E-03	4.93E-01	-8.77E-03	4.80E-03	6.76E-02
fib	3.30E-03	2.78E-03	2.36E-01	3.21E-03	4.16E-03	4.39E-01
fvf	-4.51E-03	4.08E-03	2.69E-01	-1.48E-02	6.33E-03	1.94E-02
ggt	1.65E-01	2.75E-01	5.47E-01	2.59E-01	4.08E-01	5.25E-01
glucose	-1.07E-02	5.04E-03	3.29E-02	-4.66E-03	7.60E-03	5.40E-01
haemoglobin	-9.00E-04	1.42E-02	9.50E-01	-1.20E-02	1.84E-02	5.15E-01
hba1c	-5.47E-03	5.32E-03	3.04E-01	2.33E-04	7.87E-03	9.76E-01
hct	-1.78E-04	8.66E-03	9.84E-01	-1.27E-03	1.36E-02	9.26E-01
hdl	-7.76E-04	1.37E-03	5.71E-01	-1.21E-04	2.08E-03	9.54E-01
ht	-8.91E-04	2.99E-04	2.89E-03	-1.28E-03	4.54E-04	4.81E-03
icam	-4.67E-01	1.26E+00	7.10E-01	-6.31E-01	1.85E+00	7.33E-01
igf1	-9.72E-01	9.18E-01	2.90E-01	-2.29E-01	1.35E+00	8.65E-01
il18	1.49E+01	8.43E+00	7.80E-02	2.10E+01	1.24E+01	9.11E-02
il6	9.51E-03	1.39E-02	4.95E-01	1.12E-03	2.09E-02	9.57E-01
insulin	-2.34E-01	1.70E-01	1.69E-01	-1.17E-01	1.55E-01	4.50E-01
ldl	-5.97E-03	3.74E-03	1.10E-01	-1.88E-03	5.70E-03	7.42E-01
leptin	2.93E-02	4.79E-01	9.51E-01	-7.88E-02	7.03E-01	9.11E-01
lpa	4.31E-01	2.01E-01	3.20E-02	4.15E-01	2.93E-01	1.56E-01
lympho	3.93E-02	3.88E-02	3.11E-01	5.32E-02	5.75E-02	3.55E-01

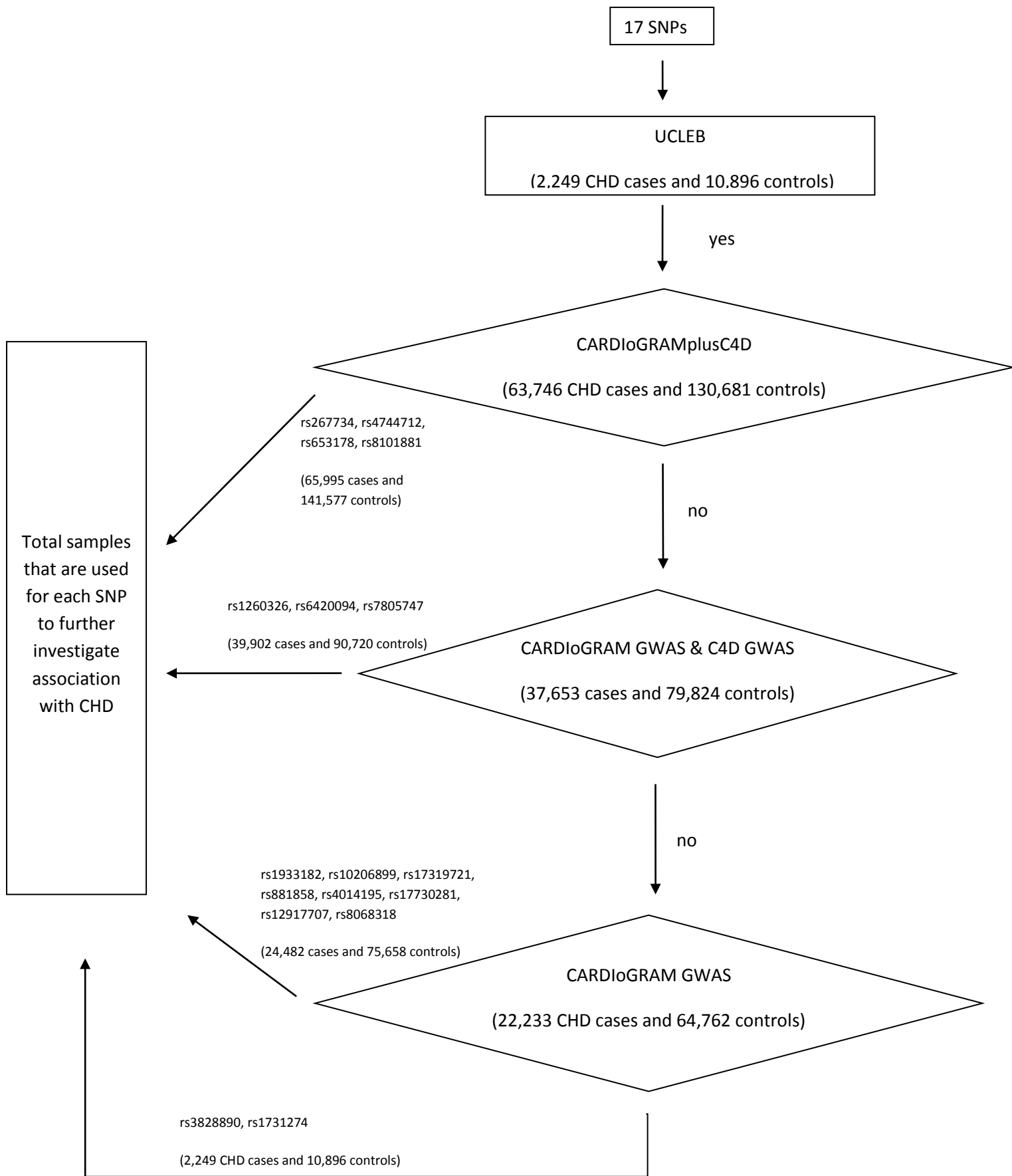
mch	-1.84E-03	1.01E-02	8.56E-01	-2.25E-02	1.58E-02	1.54E-01
mchc	2.32E-03	1.11E-02	8.34E-01	-4.18E-03	1.40E-02	7.65E-01
mcv	-1.02E-02	2.59E-02	6.94E-01	-5.86E-02	3.99E-02	1.42E-01
mmp9	3.88E+00	3.78E+00	3.05E-01	7.81E+00	5.61E+00	1.64E-01
mono	1.12E-03	1.20E-03	3.53E-01	2.02E-03	1.79E-03	2.59E-01
mpv	5.53E-03	1.01E-02	5.84E-01	9.81E-03	1.55E-02	5.27E-01
neutrophil	-1.46E-03	1.17E-02	9.01E-01	-2.34E-03	1.73E-02	8.93E-01
occup	3.13E-03	3.41E-03	3.59E-01	1.13E-03	5.29E-03	8.30E-01
pbfat	1.51E-02	9.71E-02	8.77E-01	5.23E-02	1.42E-01	7.13E-01
pefr	8.49E-02	5.63E-01	8.80E-01	-1.07E+00	8.68E-01	2.19E-01
platelet	4.88E-01	3.61E-01	1.76E-01	1.12E-01	5.58E-01	8.40E-01
printerval	-2.65E-02	1.28E-01	8.36E-01	1.58E-02	1.90E-01	9.33E-01
probnp	3.64E+00	6.05E+00	5.48E-01	-7.65E-02	8.99E+00	9.93E-01
prothrombin	-4.77E-08	1.01E-06	9.62E-01	-4.15E-07	1.50E-06	7.82E-01
pwave	-6.90E-02	1.56E-01	6.58E-01	-9.88E-02	1.96E-01	6.14E-01
qrsvoltprod	-9.82E-01	3.10E+00	7.51E-01	-6.65E-01	4.67E+00	8.87E-01
qrsvoltsum	-9.13E-01	2.13E+01	9.66E-01	4.26E+00	3.22E+01	8.95E-01
qtc	-1.54E-01	1.32E-01	2.44E-01	-2.79E-01	1.97E-01	1.58E-01
qtinterval	-1.78E-01	1.80E-01	3.23E-01	-1.70E-01	2.70E-01	5.30E-01
rbc	-5.47E-04	2.09E-03	7.94E-01	5.14E-04	3.24E-03	8.74E-01
sbp	8.36E-03	7.06E-02	9.06E-01	7.12E-02	1.07E-01	5.05E-01
scalcium	-4.31E-04	7.41E-03	9.54E-01	-8.43E-04	3.91E-03	8.29E-01
scd40l	3.86E-02	3.87E-02	3.19E-01	4.33E-02	5.75E-02	4.51E-01
sclass	-4.40E-03	5.65E-03	4.36E-01	-1.11E-02	8.70E-03	2.01E-01
sex	1.33E-03	9.00E-03	8.82E-01	9.70E-03	1.35E-02	4.73E-01

smagnesium	-1.63E-03	5.23E-03	7.56E-01	-8.55E-04	2.72E-03	7.53E-01
smoke	2.94E-03	7.49E-03	6.94E-01	-3.11E-03	1.13E-02	7.84E-01
sokolowlyon	-4.03E+00	3.48E+00	2.47E-01	-3.30E+00	5.21E+00	5.26E-01
sphosph	1.18E-03	1.50E-03	4.34E-01	2.62E-03	2.24E-03	2.43E-01
spotassium	-2.87E-02	2.18E-02	1.88E-01	-1.12E-02	1.29E-02	3.84E-01
sprotein	3.55E-02	2.98E-02	2.33E-01	5.00E-02	4.61E-02	2.79E-01
ssodium	6.21E-02	1.87E-01	7.39E-01	5.04E-02	1.17E-01	6.67E-01
surate	9.11E-06	5.48E-04	9.87E-01	-1.16E-03	8.50E-04	1.71E-01
surea	-3.39E-02	9.37E-03	3.00E-04	-7.16E-02	1.46E-02	9.55E-07
tc	-1.00E-03	3.89E-03	7.96E-01	5.48E-03	5.92E-03	3.54E-01
tg	8.58E-03	4.38E-03	5.01E-02	1.33E-02	6.58E-03	4.34E-02
tnfalpha	-4.97E-03	1.60E-02	7.55E-01	-1.64E-02	2.34E-02	4.85E-01
tpa	-8.32E-03	2.73E-02	7.60E-01	2.56E-02	4.21E-02	5.43E-01
uric	4.44E-03	1.82E-02	8.07E-01	7.24E-03	2.70E-02	7.88E-01
vcam	-1.82E+00	1.81E+00	3.15E-01	-3.68E+00	2.67E+00	1.67E-01
viscosity	-1.32E-03	2.73E-03	6.28E-01	-8.35E-04	1.45E-03	5.64E-01
vitc	1.74E-01	2.72E-01	5.21E-01	2.68E-01	4.05E-01	5.09E-01
vite	1.74E-01	1.42E-01	2.21E-01	2.98E-01	2.12E-01	1.59E-01
vwf	1.65E-01	2.14E-01	4.41E-01	-4.49E-02	3.22E-01	8.89E-01
wcc	2.74E-02	2.14E-02	1.99E-01	3.27E-02	3.35E-02	3.29E-01
wcir	-2.44E-02	4.36E-02	5.75E-01	2.29E-02	6.62E-02	7.29E-01
whr	2.02E-04	2.88E-04	4.84E-01	3.74E-04	4.37E-04	3.91E-01
wt	-7.74E-02	4.97E-02	1.20E-01	-6.18E-02	7.53E-02	4.12E-01

S5 Table. Summary statistics from regression analyses of unweighted and weighted gene scores on phenotypes.

	eGFR increasing allele	beta	se	p
rs653178*	T	0.016	0.224	9.42E-01
rs6420094*	A	0.054	0.326	8.67E-01
rs3828890	C	0.107	0.379	7.77E-01
rs17730281	A	0.11	0.338	7.44E-01
rs1933182	A	0.134	0.243	5.83E-01
rs7805747**	A	0.323	0.282	2.51E-01
rs881858**	A	0.336	0.264	2.03E-01
rs4744712*	C	0.341	0.226	1.32E-01
rs8101881	T	0.456	0.229	4.59E-02
rs8068318	C	0.499	0.256	5.10E-02
rs1260326*	T	0.603	0.231	8.92E-03
rs1731274	G	0.671	0.281	1.71E-02
rs4014195	G	0.763	0.251	2.38E-03
rs267734**	T	0.856	0.276	1.94E-03
rs17319721*	G	0.961	0.225	2.04E-05
rs12917707*	T	1.291	0.286	6.43E-06
rs10206899	T	1.837	0.76	1.57E-02

S6 Table. Internal weights estimated in UCLEB. Out of these 17 SNPs, 9 SNPs previously reported associations between eGFR-SNP in Olden et al., 2013 (*, **). Three of them are shown to have different effect direction from what we observed in UCLEB (**).



S1 Figure. A flowchart representing total samples that are used for each SNP to further investigate association with CHD

Supplementary Methods

Significance thresholds under multiple testing

We observed substantial correlation between some traits measured by UCLEB and therefore suspected that the Benjamini-Hochberg method might be too conservative. To assess this we considered family-wise type-1 error and applied a permutation approach to identify 5% significance thresholds across multiple traits tested. These were then compared to Bonferroni corrections.

To simulate the null hypothesis of no association between eGFR and any of the 94 traits available in UCLEB, eGFR values were randomly shuffled among subjects within each cohort, to break any association between eGFR and traits. Then the permuted eGFR was linearly regressed across all 94 traits, and the minimum p-value across 94 null p-values was recorded. This was repeated 10000 times to obtain an empirical distribution of the minimum p-value under the null. The 5% quantile of this distribution is an estimate of the significance threshold required to obtain family-wise type-1 error of 5%. We repeated this procedure using CHD as the outcome and logistic regression for analysis.

To simulate the null hypothesis of no association between gene scores and any of the 94 traits available in UCLEB (test of possible pleiotropic effect of gene score), a similar approach was performed with trait values randomly shuffled among subjects.

The estimated 5% family-wise error thresholds are shown in Supplementary table VII, and are seen to be very similar to the Bonferroni threshold of $0.05/94=5.32 \times 10^{-4}$. We concluded that the correlation could safely be ignored for family-wise error control, and assumed that the same could apply to false discovery rate control.

Association between	5% FWER
eGFR - 94 traits	3.85×10^{-4}
CHD - 94 traits	6.78×10^{-4}
unweighted gene score – 94 traits	5.05×10^{-4}
internally weighted gene score – 94 traits	4.34×10^{-4}

S7 Table. Significance thresholds for 5% FWER estimated from permutation testing.