Eight blood pressure loci identified by genome-wide association study of 34,433 people of European ancestry

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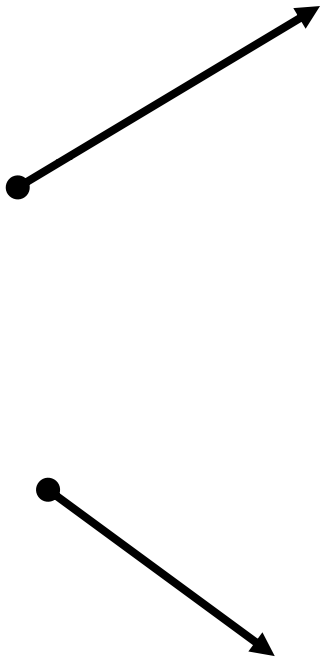
Supplementary Figures

Supplementary Figure 1. Study design**.** Meta analysis of genome-wide association data was performed in stage 1 across all the cohorts listed. Twenty SNPs representing loci most associated with SBP or DBP were selected for follow up (stage 2). Twelve SNPs were directly genotyped (2a), all twenty SNPs were tested for replication in silico (2b).

Stage 1
Genome wide association studies
n=34,433 European ancestry

Population-based cohorts
BLSA (n=708)
B58C-T1DGC (n=2,580)
B58C-WTCCC (n=1,473)
CoLaus (n=4,969)
EPIC-Norfolk (n=2,100)
Fenland (n=1,401)
InCHIANTI (n=562)
KORA (n=1,644)
NFBC1966 n=4,761)
SardiNIA (n=3,998)
SHIP (n=3,310)
SUVIMAX (n=1,823)
TwinsUK (n=873)

Controls from case-control series
DGI (n=1,277)
FUSION (n=1,038)
MIGen (n=1,121)
PROCARDIS (n=795)



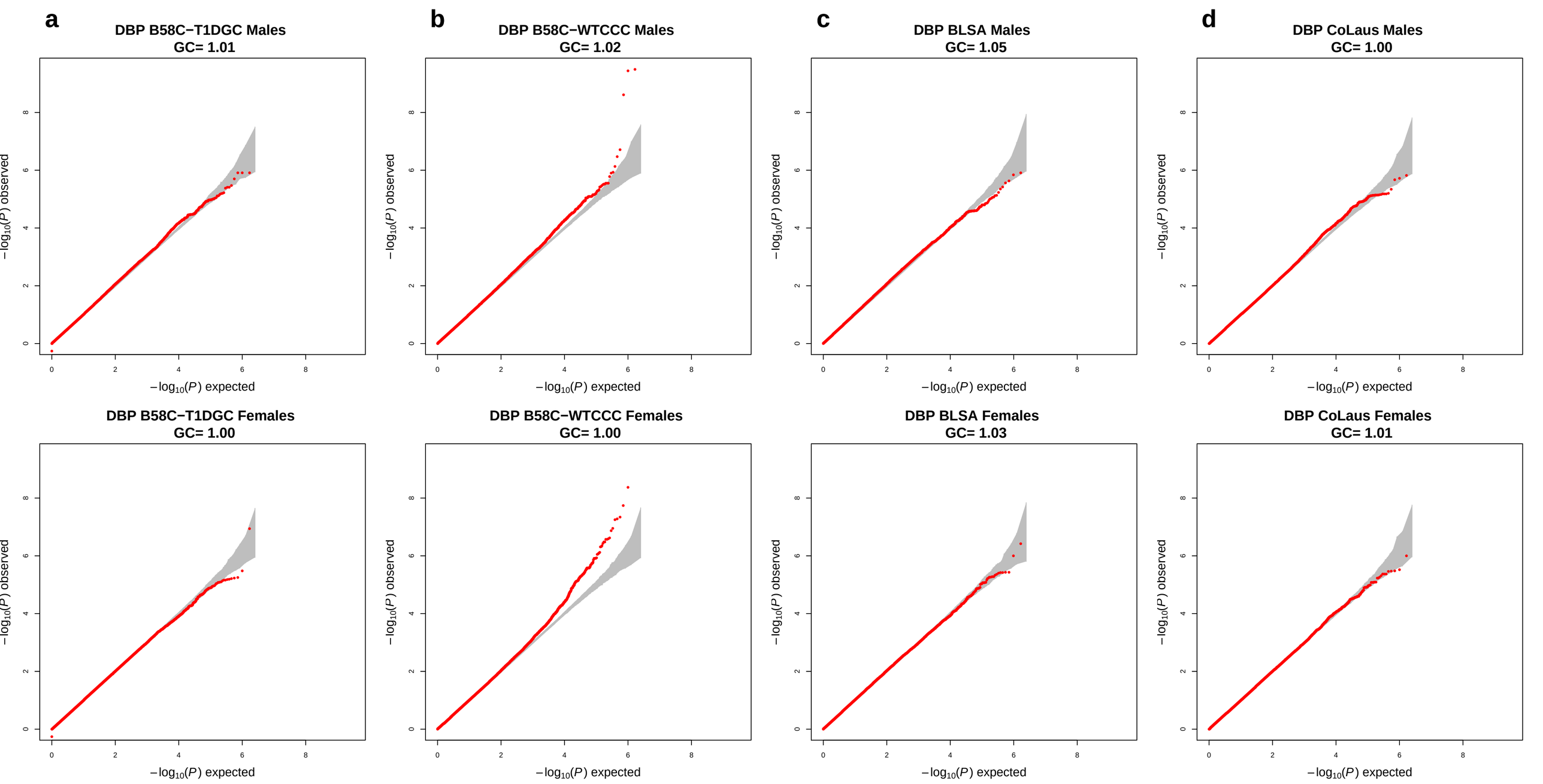
Stage 2a
Genotyping in population or case-control series
n≤71,225 European, n≤12,889 Indian Asian

ARYA (n=736)
BRIGHT-HTN (n=2,445)
BRIGHT-NT (n=673)
EPIC-Italy (n=3,909)
EPIC-Norfolk-REP (n=15,858)
Finrisk97 (n=7,023)
FUSION2 (n=1,162)
Lolipop-Eur (n=6,006)
Lolipop IA (n=12,823)
MDC-CC (n=5,330)
METSIM (n=5,934)
MPP (n=14,249)
PREVEND (n=7,272)
Prospect-EPIC (n=1,680)
Utrecht Health Project (n=2,829)

Stage 2b
In silico replication samples
n=29,122 European ancestry

CHARGE consortium

Supplementary Figure 2. **Panel A**. Quantile-quantile plots of association results by cohort and overall. Meta-analysis of 2,497,993 autosomal SNPs in 34,433 individuals was performed using inverse variance weighting after cohort-specific genomic control. Shown are plots of $-\log_{10}(P)$ of association tests for diastolic and systolic blood pressure for each cohort in gender-specific analysis and for overall meta-analysis results. λ_{GC} before genomic control was 1.08 for systolic and 1.07 for diastolic blood pressure for the overall meta-analysis. **Panel B**. Association results for systolic and diastolic blood pressure. Plotted are the $-\log_{10}(P)$ of results for 2,497,993 SNPs after genomic control of meta-analysis results for 34,433 individuals for systolic (a) and diastolic blood pressure (b). Red squares denote SNPs that achieved genome-wide significance in final meta-analysis of results from stages, 1, 2a, 2b. Note that loci 10q21 and 15q24 show genome-wide significant SNPs that are not the strongest SNPs at the locus. These SNPs were selected for validation genotyping at an interim analysis and are shown throughout the text for consistency. Note that two independent loci on 17q21 are associated with blood pressure, one with SBP and one with DBP.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GC= 1.01
b
DBP B58C−WTCCC Males
GC= 1.02
c
DBP BLSA Males
GC= 1.05
d
DBP CoLaus Males
GC= 1.00
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GC= 1.00
DBP BLSA Females
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−log10(P) expected
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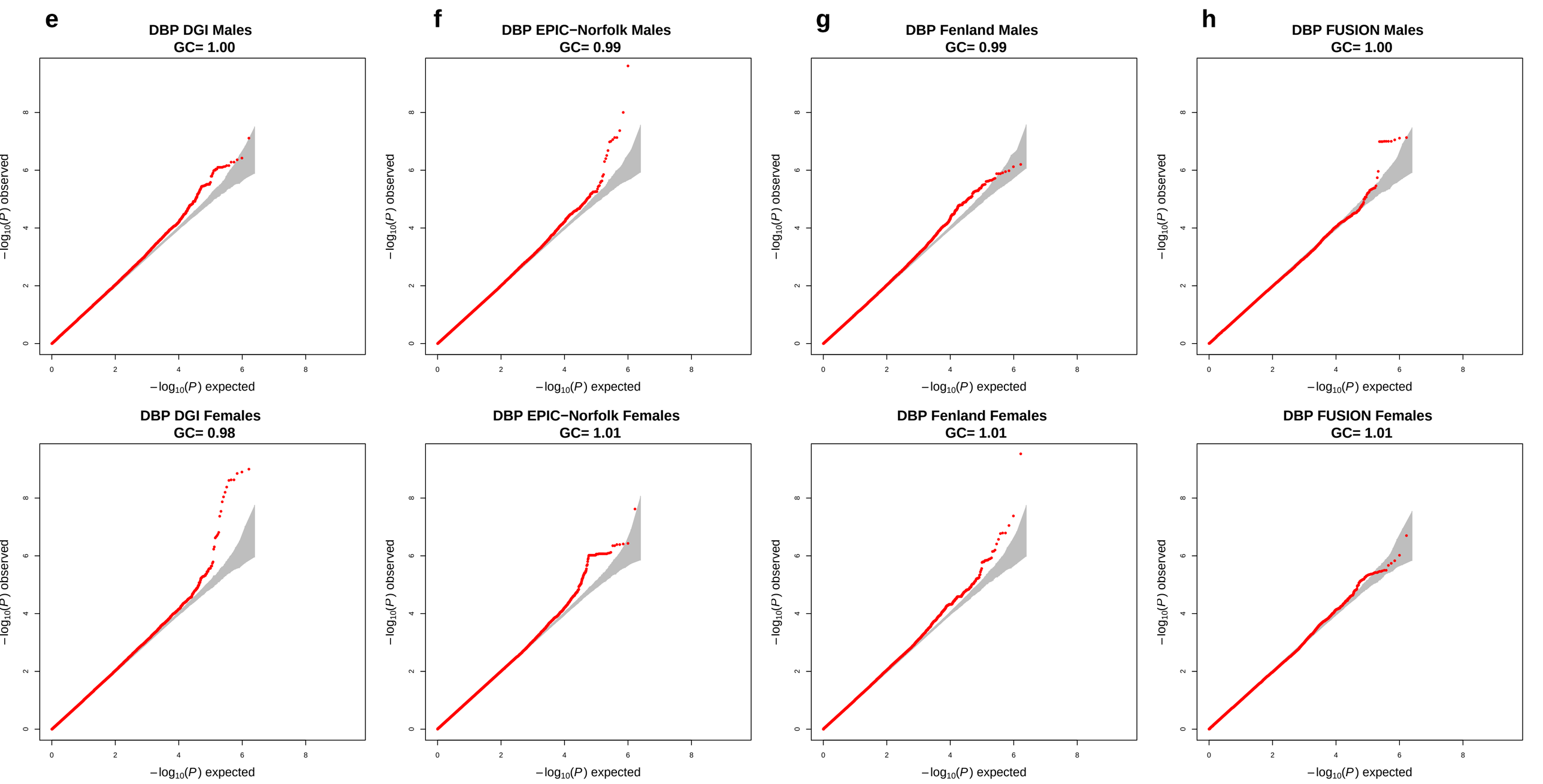
2
4
6
8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f
DBP EPIC−Norfolk Males
GC= 0.99
g
DBP Fenland Males
GC= 0.99
h
DBP FUSION Males
GC= 1.00
DBP DGI Females
GC= 0.98
DBP EPIC−Norfolk Females
GC= 1.01
DBP Fenland Females
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−log10(P) expected
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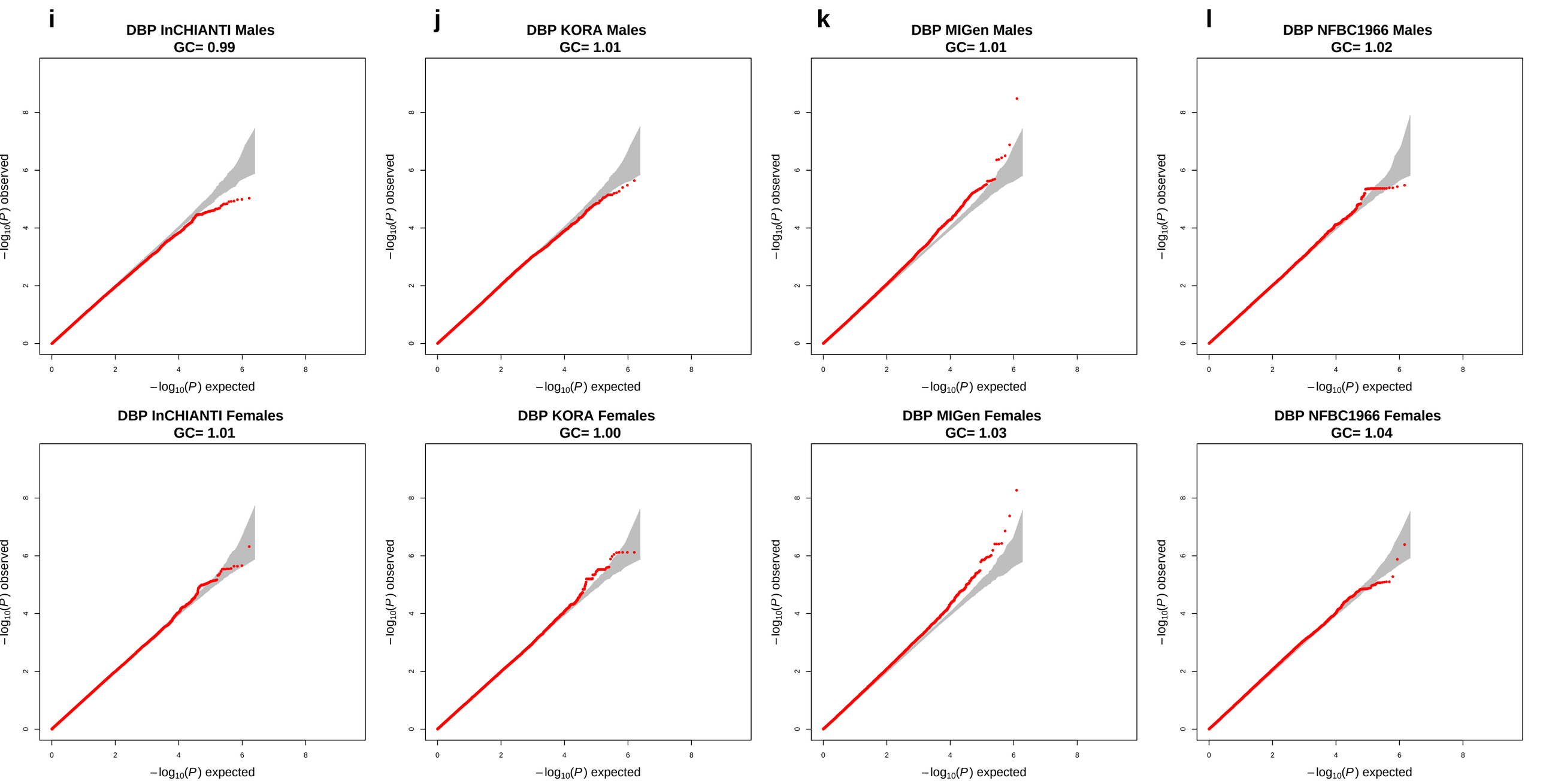
2
4
6
8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GC= 1.01
k
DBP MIGen Males
GC= 1.01
l
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GC= 1.02
DBP InCHIANTI Females
GC= 1.01
DBP KORA Females
GC= 1.00
DBP MIGen Females
GC= 1.03
DBP NFBC1966 Females
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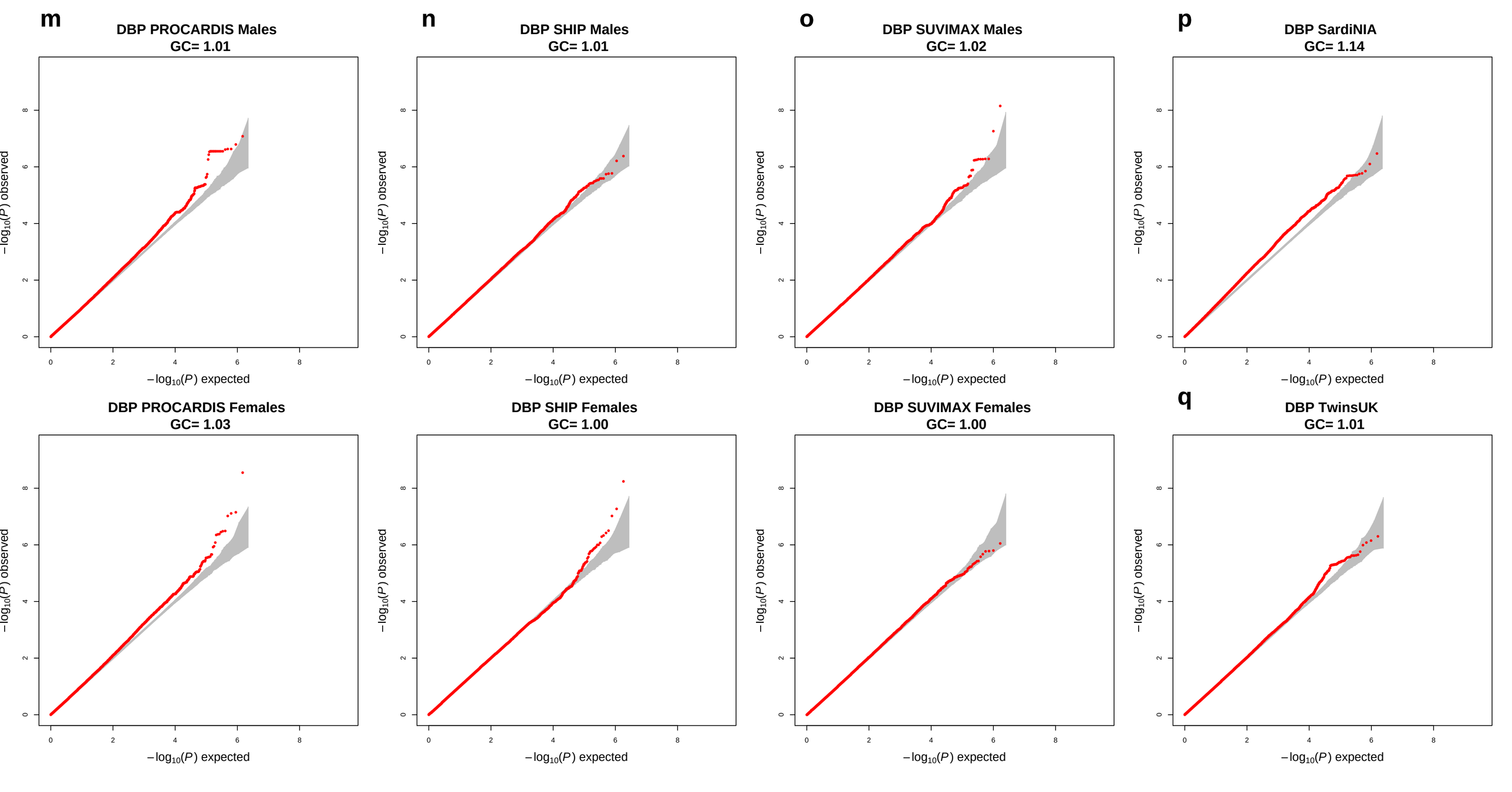
−log10(P) observed
−log10(P) expected
0
2
4
6
8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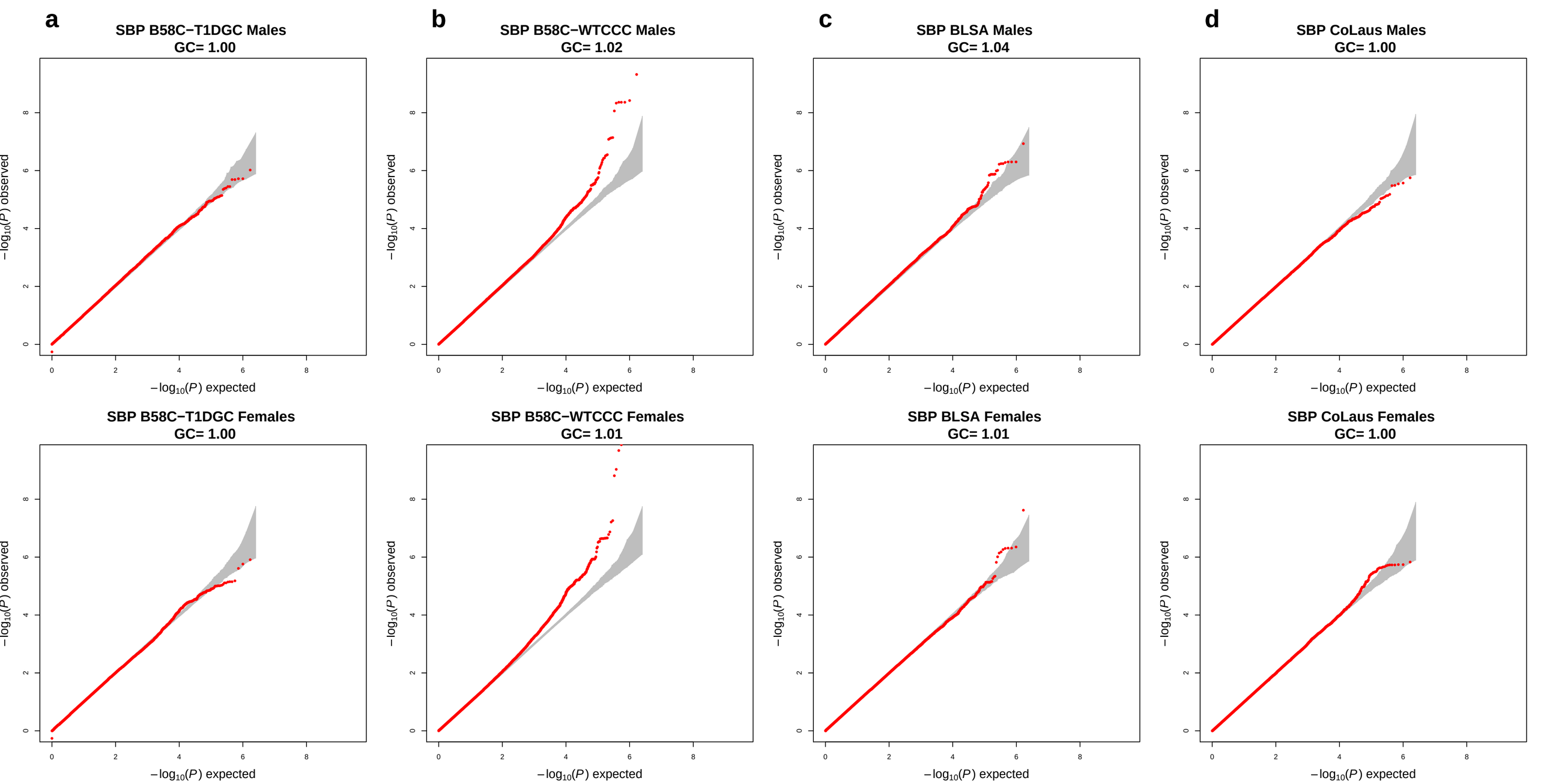
n
DBP SHIP Males
GC= 1.01
o
DBP SUVIMAX Males
GC= 1.02
p
DBP SardiNIA
GC= 1.14
DBP PROCARDIS Females
GC= 1.03
DBP SHIP Females
GC= 1.00
DBP SUVIMAX Females
GC= 1.00
q
DBP TwinsUK
GC= 1.01
−log10(P) observed
−log10(P) expected
0
2
4
6
8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GC= 1.02
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d
SBP CoLaus Males
GC= 1.00
SBP B58C−T1DGC Females
GC= 1.00
SBP B58C−WTCCC Females
GC= 1.01
SBP BLSA Females
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GC= 1.00
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−log10(P) expected
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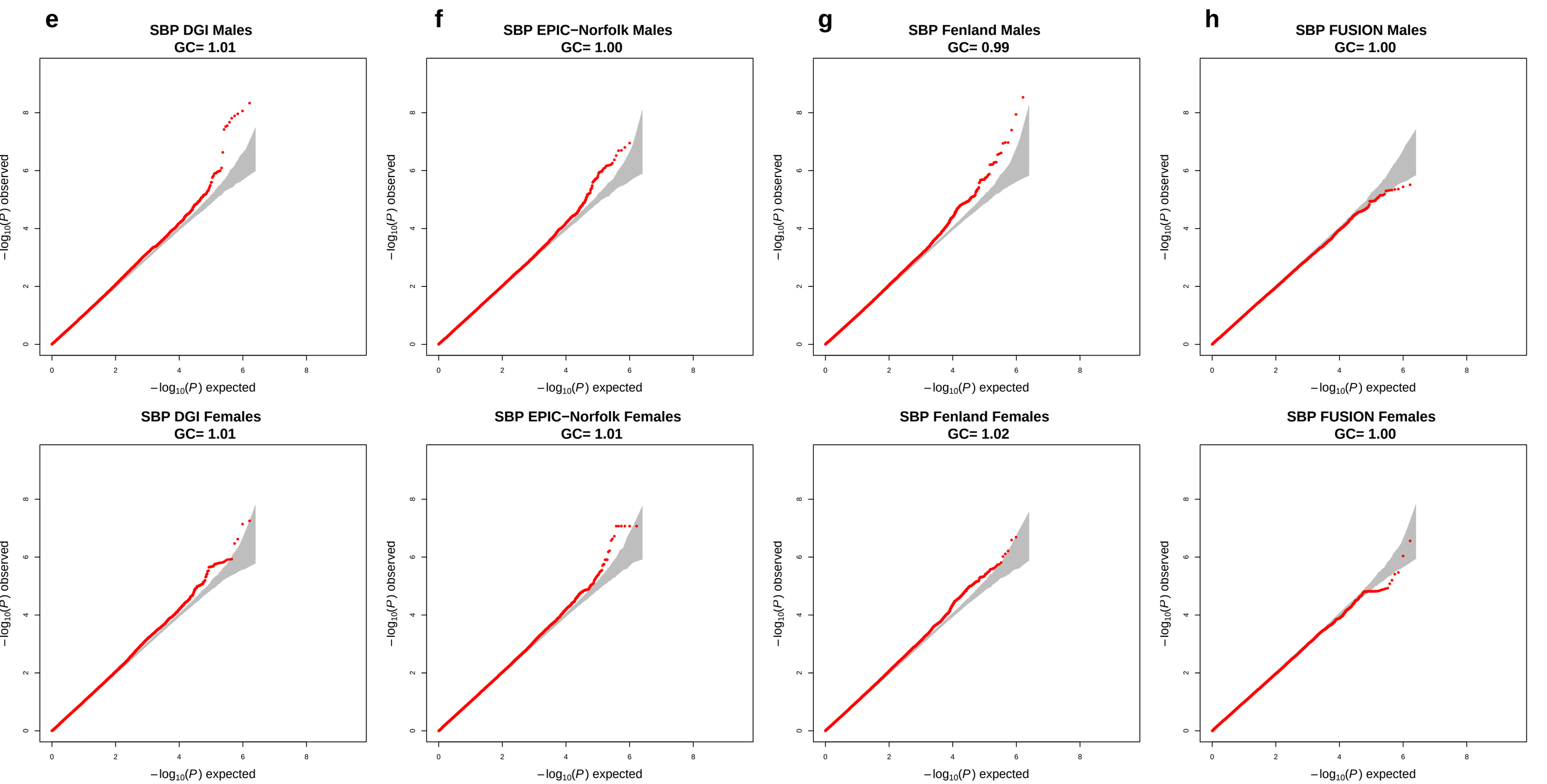
4
6
8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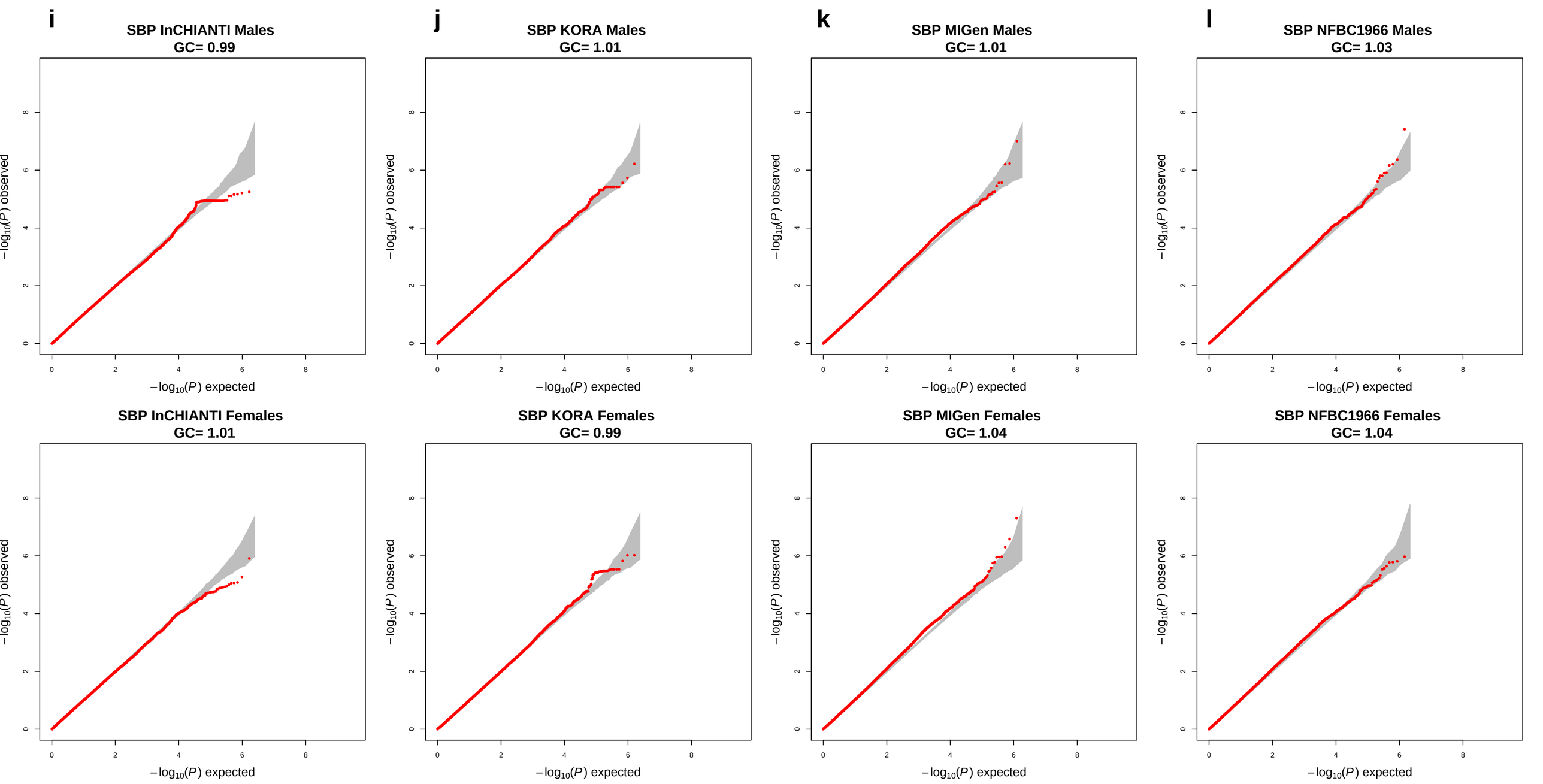
GC= 1.01
f
SBP EPIC−Norfolk Males
GC= 1.00
g
SBP Fenland Males
GC= 0.99
h
SBP FUSION Males
GC= 1.00
SBP DGI Females
GC= 1.01
SBP EPIC−Norfolk Females
GC= 1.01
SBP Fenland Females
GC= 1.02
SBP FUSION Females
GC= 1.00
−log10(P) observed
−log10(P) expected
0
2
4
6
8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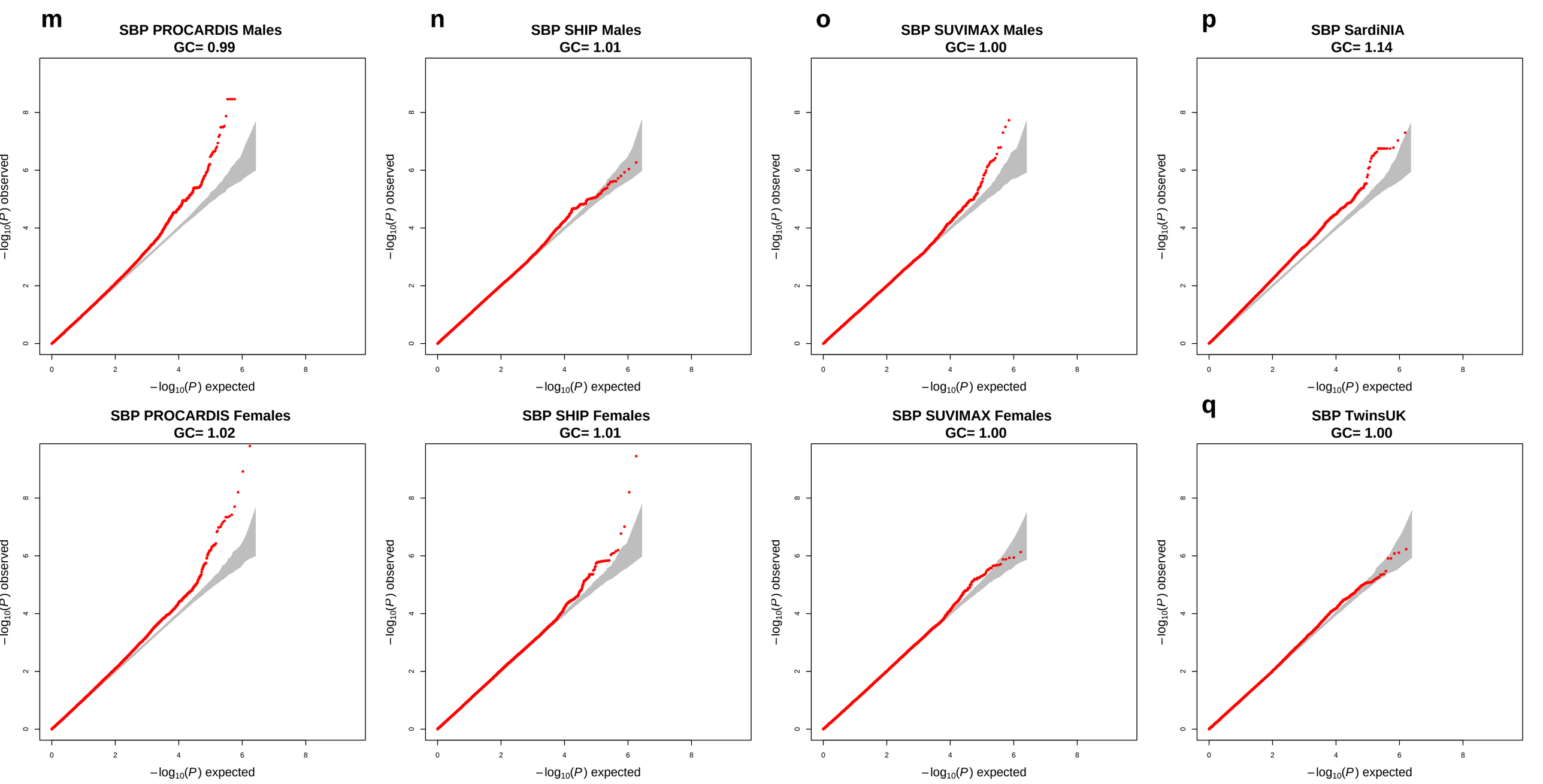
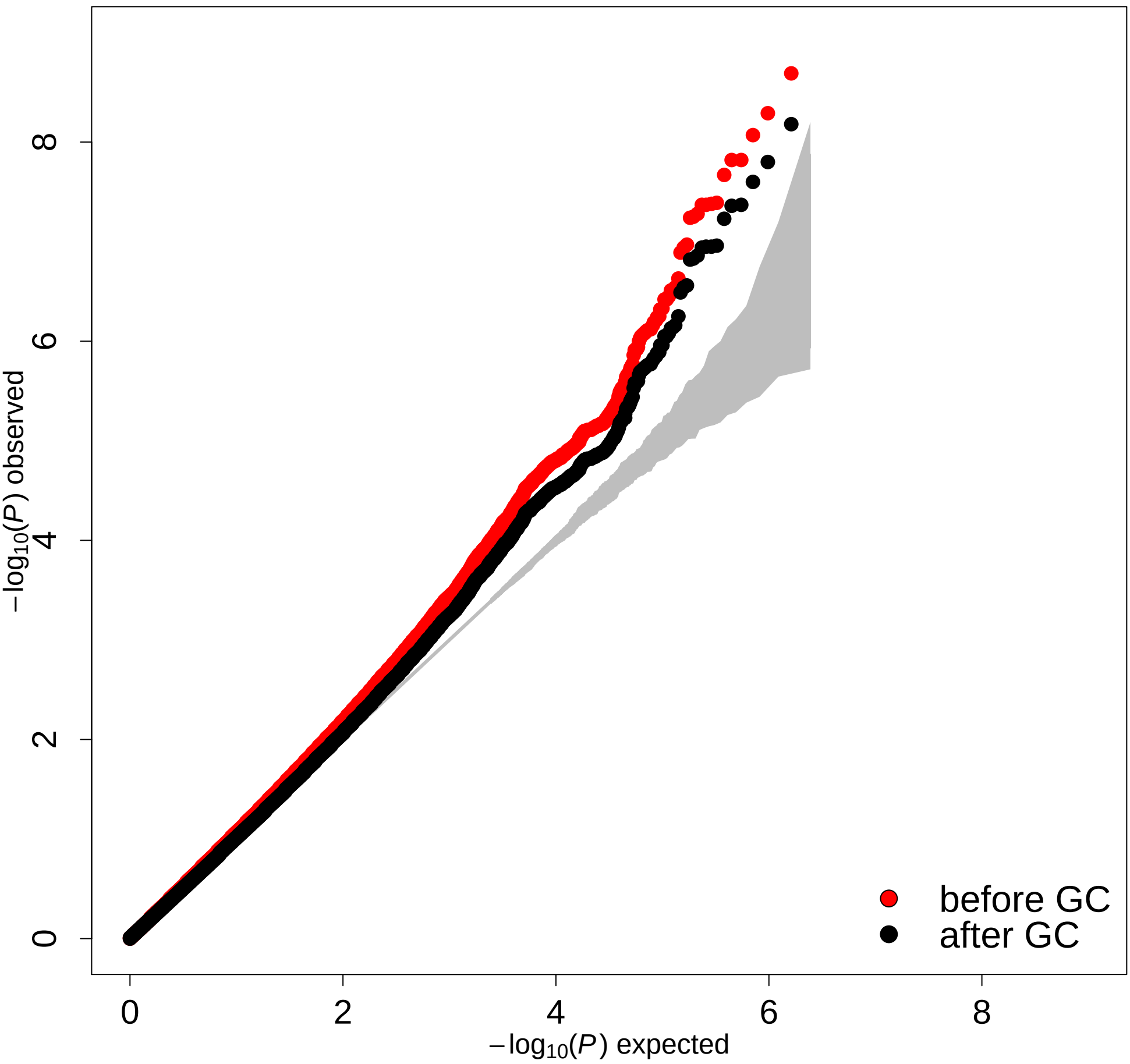
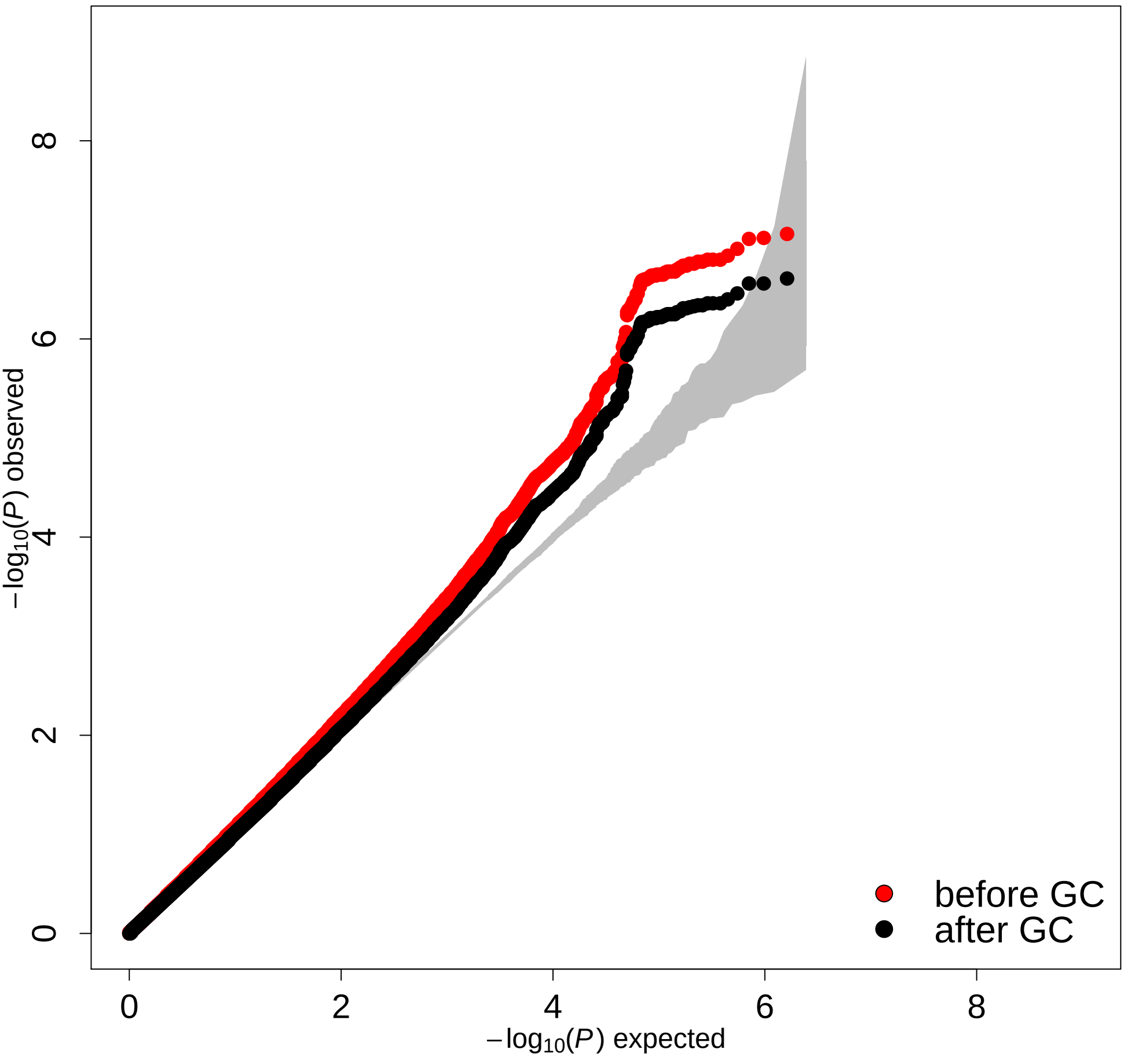
GC= 0.99
j
SBP KORA Males
GC= 1.01
k
SBP MIGen Males
GC= 1.01
l
SBP NFBC1966 Males
GC= 1.03
SBP InCHIANTI Females
GC= 1.01
SBP KORA Females
GC= 0.99
SBP MIGen Females
GC= 1.04
SBP NFBC1966 Females
GC= 1.04
−log10(P) observed
−log10(P) expected
0
2
4
6
8

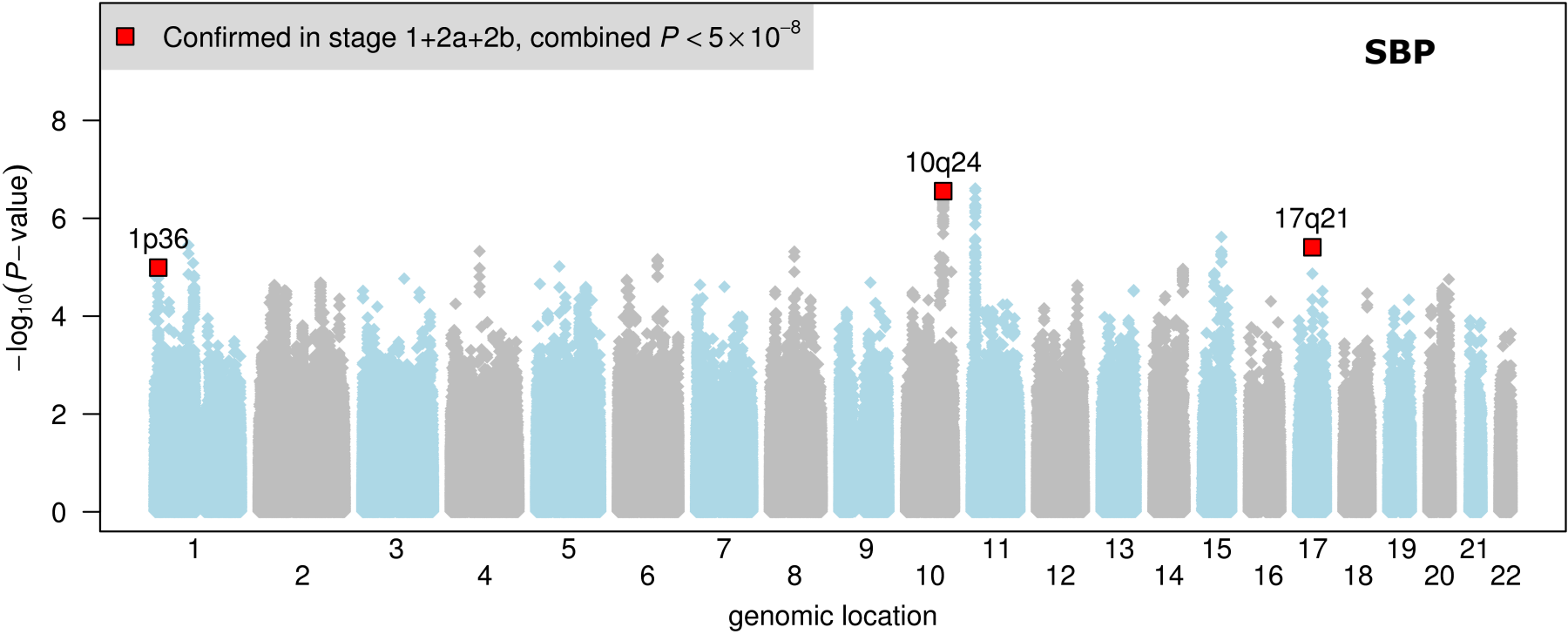

m
SBP PROCARDIS Males
GC= 0.99
n
SBP SHIP Males
GC= 1.01
o
SBP SUVIMAX Males
GC= 1.00
p
SBP SardiNIA
GC= 1.14
SBP PROCARDIS Females
GC= 1.02
SBP SHIP Females
GC= 1.01
SBP SUVIMAX Females
GC= 1.00
q
SBP TwinsUK
GC= 1.00
−log10(P) observed
−log10(P) expected

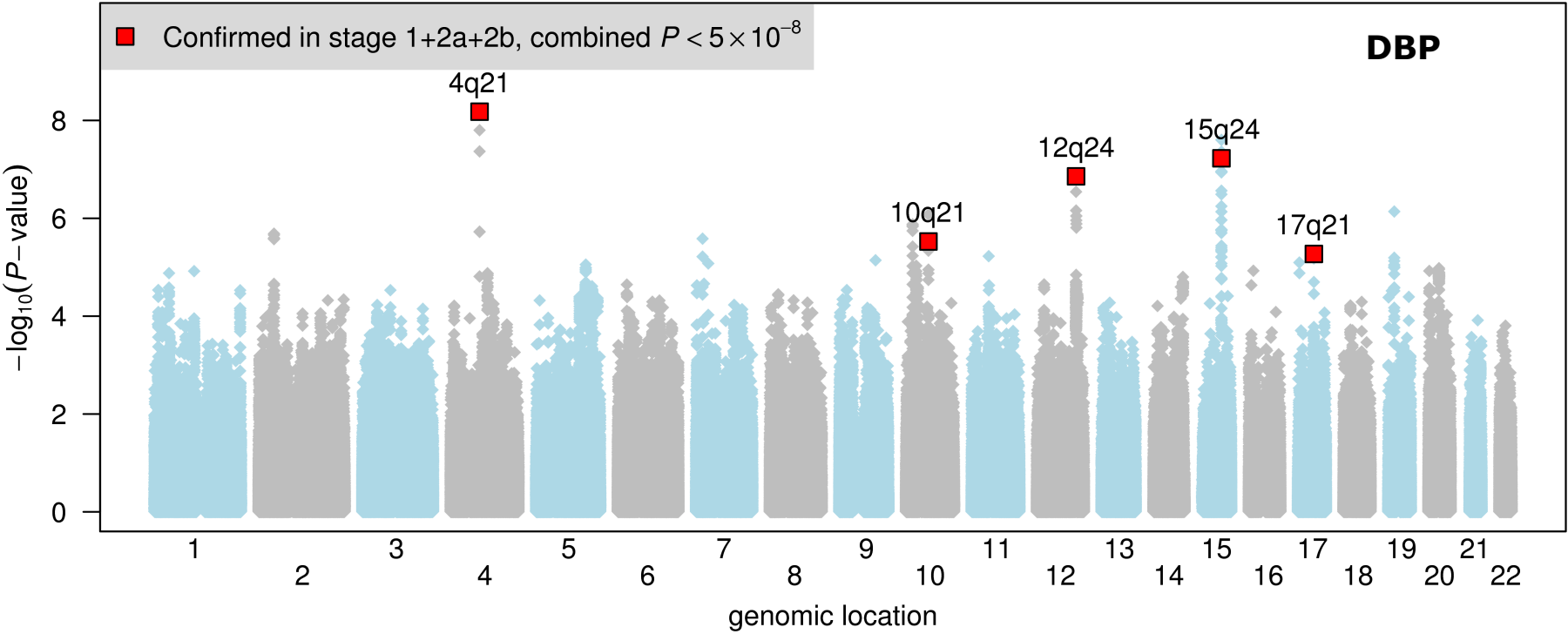
DBP


−log10(P) observed
0
2
4
6
8
−log10(P) expected
0
2
4
6
8
before GC
after GC

SBP


−log10(P) observed
0
2
4
6
8
−log10(P) expected
0
2
4
6
8
before GC
after GC


Confirmed in stage 1+2a+2b, combined $P < 5 \times 10^{-8}$
SBP
1p36
10q24
17q21
$-\log_{10}(P-\text{value})$
0
2
4
6
8
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
genomic location


Confirmed in stage 1+2a+2b, combined $P < 5 \times 10^{-8}$
DBP
4q21
10q21
12q24
15q24
17q21
$-\log_{10}(P-\text{value})$
0
2
4
6
8
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
genomic location

Supplementary Table 1. **Global BPgen Stage 1 genome-wide genotyping, imputation and genotype-phenotype analysis by cohort**. Shown are the genotyping platforms, filters applied to individuals and SNPs (if any) before imputation, imputation software and genotype-phenotype association software. Lambda estimates are shown for SBP and DBP in cases (not analyzed in stage 1) and controls separately for men and women. All individual cohort association results underwent genomic control before meta-analysis.

Cohort	Platform	Calling algorithm	Indiv Callrate Before Imp'n	SNP Callrate Before Imp'n	SNP HWE Before Imp'n	SNP MAF Before Imp'n	Other filter	# SNPs For Imp'n	Imputation software	NCBI; HapMap CEU	Genotype-phenotype software	Lambda SBP men/women controls	Lambda SBP men/women cases	Lambda DBP men/women controls	Lambda DBP men/women cases
B58C-WTCCC	Affymetrix 500K	CHIAMO	>0.97	>0.95 MAF>0.05 >0.99 MAF<0.05	5.7E-7	none	NA	490,032	IMPUTE	35; v21	SNPTEST	1.017/1.007	NA	1.015/1.000	NA
B58C-T1DGC	Illumina 550K	ILLUMINUS	>0.98	none	none	none	SNPs mapping to >1 locus in the genome	539,548	MACH V1.0.13	35; v21	ProbABEL v0.0-5b	1.00/1.00	NA	1.01/1.00	NA
BLSA	Illumina 550K	Beadstudio	>0.97	>0.99	>1E-4	>0.01	NA	501,764	MACH v1.0.15	35; v21	Merlin offline	1.037/1.012	NA	1.054/1.029	NA
CoLaus	Affymetrix 500K	BRLMM	>0.95	>0.70	>1E-7	>0	NA	390,631	IMPUTE v0.2	35; v21	custom C++	0.998/0.998	NA	1.001/1.006	NA
DGI	Affymetrix 500K	BRLMM	NA	>0.95	>1E-6 in controls	≥0.01	SNPs mapping to >1 locus in the genome	378,860	MACH v1.0.9	35; V21	SNPTEST	1.012/1.005	0.985/0.988	1.001/0.985	0.989/0.995
EPIC-Norfolk-GWAS	Affymetrix 500K	BRLMM	≥0.94	≥0.90	>1E-6	≥0.01	NA	397,438	IMPUTE	35; v21	SNPTEST	1.001/1.008	0.996/1.011	0.989/1.010	0.976/1.002
Fenland	AffymetrixSNP 5.0	BRLMM	≥0.94	≥0.90	>1E-6	≥0.01	NA	362,059	IMPUTEv0.4.2	36; V22	SNPTEST	NA	NA	NA	NA
FUSION	Illumina HumanHap 300	Beadstudio, clustering with FUSION	>0.975	≥0.90	>1E-6	>0.01	>3 Mendel or duplicate errors	304,581	MACH	35; v21	Merlin	0.998/1.002	1.018/0.989	1.002/1.005	1.007/1.009
InCHIANTI	Illumina 550K	Beadstudio	>0.97	>0.99	>1E-4	>0.01	NA	484,115	MACH v1.0.15	35; v21	Merlin offline	0.995/1.007	NA	0.992/1.010	NA
KORA	Affymetrix 500K	BRLMM	>0.93 each chip	>0.90		≥0.01	NA		MACH v1.0.9	35; v21	PLINK	1.014/0.992	NA	1.009/1.004	NA
MIGen	Affymetrix 6.0	BirdSuite1	≥0.95	≥0.95	≥1E-6	≥0.01	close	750,407	MACH v1.013	36; v22	SNPTEST	0.999/1.036	NA	0.992/1.017	NA

	(1M)						relatives								
NFBC66	Illumina 370	Beadstudio	NA	>0.95	>1E-4	≥0.01	NA	328,007	IMPUTE	35; v21	SNPTEST	1.02/1.03	NA	1.01/1.03	NA
PROCARDIS	Illumina 1M	Bead studio	>0.95	>0.95	>1E-3	None	NA	882,598	IMPUTE v0.3.2	36; v22	SNPTEST	0.997/1.025	0.999/1.008	0.988/1.020	1.007/0.999
SardiNIA	Affymetrix 500	BRLMM	>0.95	>0.95	>1E-6	>0.01	NA	356,359	MACH v1.0.15	35; v21	Merlin offline	1.14	NA	1.14	NA
SHIP	Affymetrix SNP6.0	BirdsuiteV2	>0.92	NA	NA	NA	QC CR ≥0.86	869,224	IMPUTE v0.5.0	36; v22	SNPTEST	NA	NA	NA	NA
SUVIMAX	Illumina 317K	Beadstudio	>0.94	NA	NA	NA	NA	302,607	IMPUTE v0.3.2	35; v21	Custom C++	1.005/0.998	NA	1.017/0.996	NA
TWINS UK	Illumina 317K	Beadstudio	NA	>0.95	>1E-6 in controls	≥0.01	SNPs mapping >1 loci		Impute V 0.4.2	36; CEU v22	SNPTEST	NA/1.000	NA	NA/1.006	NA

Supplementary Table 2. Follow up genotyping in up to 71,225 European ancestry individuals from 13 cohort samples and up to 12,889 Indian Asians. Shown are results for the SNPs selected for follow up genotyping in stage 2a. See Methods and Supplementary Methods for details on individual replication studies. The cohorts are: The Utrecht Atherosclerosis Risk in Young Adults (AYRA), British Genetics of Hypertension study normotensive controls (BRIGHT NT), EPIC-Italy, EPIC-Norfolk-replication cohort (EPIC-Norfolk-REP), Finrisk97, FUSION2, London Life Sciences Population (LOLIPOP)-European ancestry (-EA) or -Indian Asian ancestry (-IA), Malmö Diet and Cancer Cardiovascular Cohort (MDC), Malmö Preventive Project (MPP), Metabolic syndrome in Men (METSIM), Prevention of REnal and Vascular ENd stage Disease (PREVEND), PROSPECT-EPIC cohort and Utrecht Health Project (UHP). Bold indicates the meta-analysis results across all European ancestry samples using inverse variance weighting.

SNP ID	Cohort	Coded allele frequency	Effect (mmHg)	SE	*P*	N
rs17367504	ARYA	0.17	-0.80	0.82	0.33	688
MTHFR/NPPA	BRIGHT NT	0.17	-0.69	0.47	0.14	1,937
SBP	LOLIPOP-EA	0.16	-0.63	0.45	0.16	5,939
Coded allele: G	PREVEND	0.16	-1.25	0.40	0.002	7,091
Noncoded allele: A	PROSPECT-EPIC	0.17	-0.03	1.00	0.97	1,585
	UHP	0.16	-1.69	0.68	0.01	2,511
	Pooled European ancestry	**0.16**	**-0.93**	**0.22**	**$2x10^{-5}$**	**19,751**
	LOLIPOP-IA	0.17	-0.52	0.31	0.09	12,756
rs11191548	ARYA	0.94	0.47	1.26	0.71	729
CYP17A1	EPIC-Italy	0.90	1.57	0.62	0.01	3,680
SBP	EPIC-Norfolk-REP	0.92	1.42	0.36	$1x10^{-4}$	14,854
Coded allele: T	Finrisk97	0.92	1.82	0.54	$7x10^{-4}$	7,019
Noncoded allele: C	FUSION2	0.92	2.48	1.50	0.10	2,477
	LOLIPOP-EA	0.92	-0.40	0.61	0.51	6,024
	MDC-CC	0.89	1.80	0.58	$2x10^{-3}$	5,332
	METSIM	0.93	1.37	0.60	0.02	6,161
	MPP	0.89	1.04	0.27	$1x10^{-4}$	13,585
	PREVEND	0.92	0.90	0.52	0.09	7,204
	PROSPECT-EPIC	0.92	1.24	1.36	0.36	1,621
	UHP	0.92	1.38	0.91	0.13	2,539
	Pooled European ancestry	**0.91**	**1.19**	**0.15**	**$9x10^{-15}$**	**71,225**

	LOLIPOP-IA	0.79	0.76	0.29	0.008	12,889
rs12946454	ARYA	0.23	-0.37	0.75	0.62	700
PLCD3	LOLIPOP-EA	0.27	0.33	0.37	0.37	5,981
SBP	PREVEND	0.24	0.56	0.35	0.11	7,082
Coded allele: T	PROSPECT-EPIC	0.25	1.23	0.84	0.14	1,598
Noncoded allele: A	UHP	0.24	0.40	0.57	0.49	2,516
	Pooled European ancestry	**0.25**	**0.43**	**0.21**	**0.045**	**17,877**
	LOLIPOP-IA	0.29	0.21	0.26	0.42	12,776
rs6544619	ARYA	0.45	0.17	0.44	0.71	708
HAAO	LOLIPOP-EA	0.43	-0.23	0.19	0.24	6,002
DBP	PREVEND	0.44	-0.54	0.21	0.01	7,091
Coded allele: T	PROSPECT-EPIC	0.44	0.07	0.42	0.88	1,569
Noncoded allele: C	UHP	0.42	-0.17	0.32	0.59	2,516
	Pooled European ancestry	**0.44**	**-0.27**	**0.12**	**0.02**	**17,886**
	LOLIPOP-IA	0.49	-0.03	0.14	0.82	12,877
rs1918974	ARYA	0.56	0.03	0.42	0.94	700
MDS1	BRIGHT NT	0.55	0.04	0.24	0.86	1,956
DBP	Finrisk97	0.57	-0.41	0.18	0.02	7,014
Coded allele: T	LOLIPOP-EA	0.54	-0.16	0.22	0.47	4,522
Noncoded allele: C	PREVEND	0.53	-0.18	0.15	0.22	7,161
	PROSPECT-EPIC	0.55	-0.01	0.41	0.98	1,599
	UHP	0.52	-0.17	0.32	0.59	2,513
	Pooled European ancestry	**0.55**	**-0.18**	**0.08**	**0.04**	**26,910**
	LOLIPOP-IA	0.49	-0.30	0.14	0.03	12,757
rs16998073	ARYA	0.31	0.65	0.47	0.16	722
FGF5	BRIGHT NT	0.27	0.19	0.27	0.48	1,943
DBP	EPIC-Italy	0.25	0.09	0.26	0.74	3,701
Coded allele: T	EPIC-Norfolk-REP	0.29	0.39	0.14	0.01	15,013
Noncoded allele: A	Finrisk97	0.28	1.14	0.20	$2x10^{-8}$	7,023
	FUSION2	0.31	0.32	0.44	0.47	2,477
	LOLIPOP-EA	0.30	0.38	0.21	0.07	6,017
	MDC-CC	0.35	0.38	0.20	0.06	5,321
	PREVEND	0.30	0.67	0.17	$7x10^{-5}$	7,159
	PROSPECT-EPIC	0.28	0.81	0.46	0.08	1,610
	UHP	0.29	0.29	0.35	0.41	2,522
	Pooled European ancestry	**0.29**	**0.50**	**0.07**	**$6x10^{-13}$**	**53,508**

	LOLIPOP-IA	0.28	0.54	0.16	$5x10^{-4}$	12,881
rs10156056	ARYA	0.89	0.04	0.67	0.95	726
IL6	FUSION2	0.81	0.78	0.50	0.12	2,477
DBP	LOLIPOP-EA	0.88	0.26	0.30	0.39	6,023
Coded allele: G	METSIM	0.78	-0.16	0.22	0.46	6,161
Noncoded allele: C	PREVEND	0.88	0.15	0.23	0.53	7,212
	PROSPECT-EPIC	0.89	-0.18	0.66	0.78	1,604
	UHP	0.89	-0.14	0.49	0.77	2,539
	Pooled European ancestry	**0.85**	**0.07**	**0.13**	**0.57**	**26,742**
	LOLIPOP-IA	0.89	0.07	0.22	0.75	12,853
rs7098454	ARYA	0.74	0.13	0.49	0.79	726
ADRB1	FUSION2	0.76	-0.16	0.46	0.73	2,477
DBP	LOLIPOP-EA	0.75	-0.09	0.22	0.70	6,006
Coded allele: T	MDC-CC	0.76	-0.37	0.22	0.09	5,308
Noncoded allele: A	METSIM	0.76	-0.32	0.21	0.13	6,161
	PREVEND	0.68	-0.24	0.18	0.17	7,173
	PROSPECT-EPIC	0.75	-0.64	0.47	0.17	1,621
	UHP	0.74	-0.04	0.36	0.92	2,538
	Pooled European ancestry	**0.74**	**-0.24**	**0.09**	**0.01**	**32,010**
	LOLIPOP-IA	0.72	0.13	0.15	0.47	12,823
rs1530440	ARYA	0.19	0.10	0.56	0.85	703
C10orf107	BRIGHT NT	0.19	0.35	0.31	0.26	1,948
DBP	Finrisk97	0.20	-0.27	0.23	0.22	7,021
Coded allele: T	LOLIPOP-EA	0.18	-0.74	0.29	0.01	5,966
Noncoded allele: C	PREVEND	0.17	-0.51	0.20	0.01	7,149
	PROSPECT-EPIC	0.17	0.43	0.55	0.43	1,590
	UHP	0.18	0.16	0.41	0.69	2,528
	Pooled European ancestry	**0.18**	**-0.21**	**0.11**	**0.05**	**26,905**
	LOLIPOP-IA	0.15	0.03	0.19	0.87	12,781
rs653178	ARYA	0.50	-1.07	0.43	0.01	687
ATXN2/SH2B3	BRIGHT NT	0.52	0.23	0.24	0.35	1,912
DBP	LOLIPOP-EA	0.52	-0.91	0.19	$2x10^{-6}$	5,939
Coded allele:	PREVEND	0.56	-0.47	0.15	0.002	7,106
	PROSPECT-EPIC	0.53	0.04	0.43	0.92	1,544
	UHP	0.53	0.30	0.31	0.33	2,501
	Pooled European ancestry	**0.54**	**-0.40**	**0.10**	**$3x10^{-5}$**	**19,689**

	LOLIPOP-IA	0.89	0.18	0.22	0.40	12,760
rs1378942	ARYA	0.35	0.65	0.45	0.14	726
CYP1A2	EPIC-Italy	0.38	0.24	0.23	0.30	3,720
DBP	EPIC-Norfolk-REP	0.33	0.29	0.14	0.04	13,936
Coded allele: C	Finrisk97	0.45	0.38	0.18	0.04	7,019
Noncoded allele: A	FUSION2	0.44	0.57	0.79	0.47	2,477
	LOLIPOP-EA	0.34	0.50	0.20	0.01	5,994
	MDC-CC	0.31	0.40	0.20	0.05	5,311
	METSIM	0.44	0.92	0.33	0.005	6,161
	MPP	0.32	0.24	0.11	0.03	14,436
	PREVEND	0.25	0.72	0.16	$1x10^{-5}$	7,168
	PROSPECT-EPIC	0.33	0.53	0.44	0.22	1,611
	UHP	0.31	0.77	0.33	0.02	2,527
	Pooled European ancestry	**0.35**	**0.41**	**0.06**	**$2x10^{-12}$**	**71,086**
	LOLIPOP-IA	0.77	0.22	0.16	0.17	12,858
rs16948048	ARYA	0.36	0.29	0.45	0.51	694
ZNF652/PHB	BRIGHT NT	0.37	0.43	0.26	0.10	1,937
DBP	LOLIPOP-EA	0.37	-0.15	0.20	0.46	5,958
Coded allele: G	PREVEND	0.37	0.35	0.16	0.03	7,080
Noncoded allele: A	PROSPECT-EPIC	0.38	0.78	0.43	0.07	1,591
	UHP	0.37	0.11	0.33	0.73	2,492
	Pooled European ancestry	**0.37**	**0.23**	**0.10**	**0.02**	**19,752**
	LOLIPOP-IA	0.16	-0.17	0.19	0.37	12,779

Supplementary Table 3. Results of *in silico* exchange of 10 SBP and 10 DBP Global BPgen results with CHARGE. Shown are the top SNPs at each locus with association results in Global BPgen and in CHARGE for the same coded allele. The pooled test of association was determined using inverse variance weighted meta-analysis. The coded allele is the allele to which the beta (effect) estimate refers; for a SNP coded AA=0, AG=1, GG=2, G is the coded allele. SNPs in bold were selected for validation genotyping. The SNP rs1918974 at the locus containing *MDS1* was selected for genotyping at an interim analysis at which the strength of association in Global BPgen was stronger and was retained in the list despite weaker association in the final stage 1 meta-analysis, displacing the 10th SNP for DBP. Loci that overlap between CHARGE and Global BPgen top ten lists are indicated with asterisks.

SNP ID	Chr	Position NCBI35	Genes of interest	Coded allele	Non-coded allele	Coded Allele freq	Effect (SE) mmHg	*P*	N	Coded allele freq	Effect (SE) mmHg	*P*	N	Effect (SE) mmHg	*P*	N
Systolic blood pressure						**Global BPgen**				**CHARGE**				**Pooled**		
rs7112413	11	10,222,076	*ADM*	T	C	0.20	0.80 (0.16)	$2x10^{-7}$	34,076	0.19	0.18 (0.19)	0.33	28,856	0.55 (0.12)	$4x10^{-6}$	62,932
rs11191548	10*	104,836,168	*CYP17A1*	T	C	0.91	1.17 (0.23)	$3x10^{-7}$	33,123	0.92	1.05 (0.27)	$9x10^{-5}$	28,204	1.12 (0.17)	$1x10^{-10}$	61,326
rs12725199	1	97,005,813	*PTBLP, DPYD*	C	A	0.74	0.68 (0.15)	$4x10^{-6}$	33,826	0.74	0.07 (0.17)	0.67	28,692	0.42 (0.11)	$2x10^{-4}$	62,518
rs12946454	17	40,563,647	*PLCD3*	T	A	0.28	0.68 (0.15)	$4x10^{-6}$	32,120	0.27	0.50 (0.17)	$4x10^{-3}$	27,693	0.60 (0.11)	$7x10^{-8}$	59,813
rs12676935	8	69,047,290	*DEPDC2*	G	C	0.50	0.60 (0.13)	$5x10^{-6}$	30,563	0.53	0.14 (0.15)	0.37	27,285	0.40 (0.10)	$5x10^{-5}$	57,848
rs932764	10	95,885,930	*PLCE1*	G	A	0.43	0.58 (0.13)	$6x10^{-6}$	33,920	0.43	0.36 (0.15)	0.02	28,796	0.49 (0.10)	$6x10^{-7}$	62,716
rs6930230	6	112,170,175	*FYN*	T	C	0.55	0.58 (0.13)	$7x10^{-6}$	33,288	0.58	0.12 (0.15)	0.44	28,105	0.39 (0.10)	$8x10^{-5}$	61,393
rs11581614	1	110,041,045	*EPS8L3*	T	C	0.84	-0.80 (0.18)	$8x10^{-6}$	33,275	0.84	-0.12 (0.21)	0.56	27,646	-0.51 (0.14)	$2x10^{-4}$	60,920
rs3121685	5	65,697,889	*SFRS12, MAST4*	T	C	0.50	-0.57 (0.13)	$1x10^{-5}$	32,321	0.49	-0.21 (0.15)	0.16	28,013	-0.42 (0.10)	$2x10^{-5}$	60,333
rs17367504	1	11,797,044	*MTHFR, NPPA*	G	A	0.14	-0.79 (0.18)	$1x10^{-5}$	34,158	0.16	-0.85 (0.20)	$3x10^{-5}$	29,064	-0.81 (0.13)	$1x10^{-9}$	63,222
Diastolic blood pressure						**Global BPgen**				**CHARGE**				**Pooled**		

rs16998073	4	81,541,520	*FGF5*	T	A	0.21	0.65 (0.11)	$7x10^{-9}$	26,106	0.24	0.36 (0.12)	$3x10^{-3}$	22,009	0.51 (0.08)	$4x10^{-10}$	48,115
rs1378942	15*	72,864,420	*CYP1A2*	C	A	0.36	0.48 (0.09)	$6x10^{-8}$	34,126	0.33	0.43 (0.09)	$3x10^{-6}$	29,046	0.46 (0.06)	$1x10^{-12}$	63,172
rs653178	12*	110,470,476	*ATXN2*	T	C	0.53	-0.46 (0.09)	$1x10^{-7}$	30,853	0.52	-0.50 (0.09)	$2x10^{-8}$	29,119	-0.48 (0.06)	$1x10^{-14}$	59,972
rs7246865	19	17,080,105	*MYO9B*	G	A	0.75	-0.51 (0.10)	$7x10^{-7}$	28,918	0.74	-0.01 (0.11)	0.92	26,129	-0.27 (0.07)	$3x10^{-4}$	55,046
rs1530440	10	63,194,597	*C10orf107*	T	C	0.19	-0.51 (0.11)	$3x10^{-6}$	32,718	0.19	-0.44 (0.12)	$1x10^{-4}$	27,651	-0.48 (0.08)	$1x10^{-9}$	60,369
rs16916925	10*	18,508,217	*CACNB2*	G	A	0.14	0.58 (0.12)	$1x10^{-6}$	33,584	0.15	0.12 (0.13)	0.36	28,265	0.36 (0.09)	$4x10^{-5}$	61,849
rs6544619	2	43,096,380	*HAAO*	T	C	0.44	-0.41 (0.09)	$2x10^{-6}$	33,922	0.44	-0.22 (0.09)	0.01	28,829	-0.32 (0.06)	$3x10^{-7}$	62,752
rs13231835	7	18,338,298	*HDAC9*	T	C	0.62	-0.45 (0.10)	$3x10^{-6}$	26,277	0.60	-0.13 (0.10)	0.16	25,718	-0.29 (0.07)	$2x10^{-5}$	51,995
rs16948048	17	44,795,465	*ZNF652, PHB*	G	A	0.39	0.40 (0.09)	$5x10^{-6}$	34,052	0.37	0.29 (0.09)	$2x10^{-3}$	28,637	0.34 (0.06)	$5x10^{-8}$	62,688
rs1918974	3*	170,648,590	*MDS1*	T	C	0.54	-0.28 (0.09)	$1x10^{-3}$	32,674	0.53	-0.35 (0.09)	$8x10^{-5}$	28,307	-0.32 (0.06)	$3x10^{-7}$	60,981

Supplementary Table 4. **Gender-specific results for 8 confirmed blood pressure loci.** Shown are the Global BPgen gender-specific association results for the top SNP at each genome-wide significant blood pressure locus. The *P* value for interaction between the SNP-blood pressure trait association and gender is shown. The coded allele is the allele to which the beta (effect) estimate refers; for a SNP coded AA=0, AG=1, GG=2, G is the coded allele. The effective sample size is shown (see methods for description) in each subsample. Note that the SardiNIA sample is not included as this was analyzed in a gender-pooled analysis only with adjustment for gender because of its family structure.

Trait	SNP ID	Chr	Position NCBI35	Coded allele	Effect (SE) mmHg men	*P* men	N men	Effect (SE) mmHg women	*P* women	N women	*P* interaction
SBP	rs17367504	1	11,797,044	G	-0.96 (0.25)	$1x10^{-4}$	14,199	-0.67 (0.24)	$5x10^{-3}$	15,962	0.54
SBP	rs11191548	10	104,836,168	T	1.10 (0.33)	$8x10^{-4}$	13,542	1.16 (0.31)	$2x10^{-4}$	15,584	0.66
SBP	rs12946454	17	40,563,647	T	0.59 (0.21)	$5x10^{-3}$	13,400	0.81 (0.20)	$4x10^{-5}$	15,102	0.30
DBP	rs16998073	4	81,541,520	T	0.47 (0.16)	$4x10^{-3}$	10,910	0.83 (0.15)	$3x10^{-8}$	12,349	0.03
DBP	rs1530440	10	63,194,597	T	-0.49 (0.16)	$2x10^{-3}$	13,699	-0.52 (0.14)	$3x10^{-4}$	15,439	0.54
DBP	rs653178	12	110,470,476	T	-0.59 (0.13)	$3x10^{-6}$	13,121	-0.36 (0.12)	$2x10^{-3}$	14,812	0.37
DBP	Rs1378942	15	72,864,420	C	0.32 (0.13)	$1x10^{-2}$	14,199	0.62 (0.12)	$1x10^{-7}$	15,947	0.03
DBP	Rs16948048	17	44,795,465	G	0.37 (0.13)	$4x10^{-3}$	14,147	0.43 (0.12)	$2x10^{-4}$	15,908	0.43

Supplementary Methods

Population-based GWAS samples, phenotype measurement.

This section describes study-specific characteristics that are not presented in the tables. All participants provided written informed consent and studies were approved by local Research Ethics Committees and/or Institutional Review boards.

The Baltimore Longitudinal Study of Aging (BLSA) is an ongoing prospective study of human aging which started in 1958[1]. The study recruited volunteers predominantly from Washington DC and Baltimore MD, USA. Healthy volunteers aged >17 years were recruited; there were no exclusion criteria. Only European-origin individuals were included in the analysis. Blood pressure was measured using a mercury sphygmomanometer in the seated position, the average of the 2nd and 3rd readings were recorded for both the right and left arm.

The British 1958 Birth cohort – Type 1 Diabetes Genetics Consortium (B58C-T1DGC) is a sample from the national population-based sample followed periodically from birth to age 44-45 years http://www.b58cgene.sgul.ac.uk/collection.php); 2,580 individuals were included in this analysis. Blood pressure was recorded using the Omron 705CP machine three times, seated. The average of three readings was used for the analysis.

The British 1958 Birth cohort –Wellcome Trust Case Control Consortium (B58C-WTCCC) is a second sample from the national population-based sample followed periodically from birth to age 44-45 years (http://www.b58cgene.sgul.ac.uk/collection.php); 1,473 individuals were included in the analysis and are distinct from individuals included in the B58C-T1DGC cohort. Blood pressure was recorded using the Omron 705CP machine three times, seated. The average of three readings was used for the analysis.

Cohorte Lausannoise (CoLaus) is a population-based study aimed at assessing the prevalence and molecular determinants of cardiovascular risk factors in the Caucasian population of Lausanne, Switzerland[2]. Participants in the study (4,969) were randomly selected from the population register of Lausanne in 2003 (n=56,694, aged 35-75 years). All individuals were of Caucasian origin, defined as having both parents and grandparents born in a defined list of European countries. Blood pressure was measured using the Omron HEM-907 machine, in the seated position. Three measures were taken on the left arm; the mean of the last two measures was used in the analyses.

The European Prospective Investigation of Cancer- Norfolk-Genome Wide Association Study (EPIC-Norfolk-GWAS) study includes 3,847 participants with genome-wide genotyping data nested within the EPIC-Norfolk Study, a population-based cohort study of 25,663 Europid men and women aged 39-79 years recruited in Norfolk, UK between 1993 and 1997[3,4]. The 2,100 non-obese individuals were included in stage 1. Blood pressure was measured using the Accutorr oscillometric BP machine; the mean of two readings was taken and used in the analysis.

The Fenland Study is an ongoing population-based cohort study designed to investigate the association between genetic and lifestyle environmental factors and the risk of obesity, insulin sensitivity, hyperglycemia and related metabolic traits in

men and women aged 30 to 55 yrs. Volunteers were recruited from General Practice sampling frames in the Fenland, Ely and Cambridge areas of the Cambridgeshire Primary Care Trust in the U.K. The study currently comprises more than 3,000 participants; 1,500 volunteers were genotyped and included in the current analyses. Blood pressure was measured using an Accutorr automated sphygmomanometer; the average of three measurements made at one minute intervals in the seated position was used for this analysis.

The Invecchiare in Chianti (InCHIANTI) study is a representative population-based study of older people living in the Chianti area of Tuscany, Italy[5]. All participants were >21 years of age and of white European origin. Blood pressure was measured using a mercury sphygmomanometer in the supine position; the average of the 2nd and 3rd readings was used for the analysis.

Kooperative Gesundheitsforschung in der Region Augsburg (KORA) (third survey: S3/F3) is an epidemiological cohort recruited from the general population of Augsburg, Germany in 1994-1995[6,7]. A subset of this survey (1,644 subjects) participated in this study (http://epi.helmholtz-muenchen.de/kora-gen/). Subjects with BMI<35 kg/m^2 were included; diabetics were excluded. Blood pressure was measured using a random zero sphygmomanometer in the seated position at the first examination cycle; the mean of two readings was used.

The North Finland Birth Cohort of 1966 (NFBC1966, n=12,058 live born) was designed to study factors affecting preterm birth, low birth weight, and subsequent morbidity and mortality (http://kelo.oulu.fi/NFBC/). The longitudinal data collection includes clinical examination and blood sampling at age 31 years, from which data in the current study are drawn. The attendees in the follow-up (71% response rate) were adequately representative of the original cohort[8] as is the final study sample in the present analyses. Blood pressure was measured using a mercury sphygmomanometer, seated, from the right arm after 15 minutes rest. The average of two readings taken 5 minutes apart was used for the analyses. Both questionnaire and national medication reimbursement data were used for anti-hypertensive medication information.

The SardiNIA study is a longitudinal study examining age-related quantitative traits in individuals from the Ogliastra region of Sardinia, Italy[9]. The SardiNIA GWAS examined 4,305 related individuals (age >14 years), of whom 3,998 individuals were included in this study. Blood pressure was measured using a mercury sphygmomanometer; the average of the second and third reading was used for the analyses.

The Study of Health in Pomerania (SHIP) study is a population-based survey in West Pomerania, the north-east area of Germany[10]. A sample from the adult population aged 20 to 79 years was drawn based on population registries of cities and towns in the region. SHIP finally comprised 4,310 participants (corresponding to a final response rate of 68.8%). 3,310 individuals with GWAS data were included in this study. Blood pressure was measured three times, seated, after 5 minutes of rest, using a digital blood pressure monitor (HEM-705CP, Omron Corporation, Tokyo, Japan), after a rest period of 3 minutes for each measurement. The mean of the second and third measurements was used in the analyses.

The Supplementation en Vitamines et Mineraux Antioxydants (SU.VI.MAX) study is a longitudinal study performed on a national sample of healthy volunteers from France between 1996 and 2001. 1,823 individuals, aged 35-65 years at baseline were included in this study[11]. Blood pressure was measured using a mercury sphygmomanometer in the seated position; the average of three readings taken from the first examination (1996) was used in the analysis.

The TwinsUK Study comprises a sample of 1,195 healthy female Caucasians recruited through the TwinsUK registry in London (http://www.twin-research.ac.uk/indexscience.html). All participants were recruited from the general population without presence or interest in any particular disease or trait through national media campaigns. One of each twin pair was selected, with ages ranging from 18 to 76 years. Blood pressure was measured using the Omron HEM-907 machine, seated. Three readings were taken, the first was discarded and the average of the other two was used in the analyses.

Control GWAS samples from case-control studies, phenotype measurement.

The Diabetes Genetics Initiative (DGI) is a type 2 diabetes (T2D) case-control study of Swedish and Finnish individuals matched on age, gender and BMI[12]. The 1,467 normoglycemic male and female controls were included in the stage 1 Global BPgen analysis. Blood pressure traits were the average of two seated measurements using a mercury sphygmomanometer.

The Finland-United States Investigation of NIDDM Genetics (FUSION) study aims to discover variants predisposing to T2D and T2D-related quantitative traits (http://fusion.sph.umich.edu/)[13,14]. The FUSION GWAS sample includes 1,161 Finnish T2D cases and 1,174 normal glucose tolerant (NGT) controls and 122 offspring of case/control pairs (1T2D, 119 NGT, 2 with impaired glucose tolerance). The controls and NGT offspring were used in stage 1 of the Global BPgen analysis. The blood pressure trait was the average of two seated measurements using a mercury sphygmomanometer after 5 minutes of rest[15]. FUSION analyses were adjusted for birth province.

The Myocardial Infarction Genetics Consortium (MIGen) cohort is composed of a subset of the controls of a case-control study aimed at identifying genetic variants associated with early-onset myocardial infarction. Most of the controls are selected from population based cross-sectional or cohort studies and come from five different studies: Heart Attack Risk in Puget Sound (Seattle, USA), REGICOR (Girona, Spain), MGH Premature Coronary Artery Disease Study (Boston, USA), FINRISK (Finland); Malmö Diet and Cancer Study (Malmö, Sweden). For the majority of studies, blood pressure was measured twice using calibrated sphygmomanometers, in the seated position after at least 5 minutes of rest; the mean of the two measurements was used in the analysis.

The Precocious Coronary Artery Disease (PROCARDIS, www.procardis.org) study is a European consortium investigating the genetics of precocious coronary artery disease (CAD) in German, Italian, Swedish and British CAD patients and controls[16]. Country of origin was a covariate in all analyses. The controls included in

this study had no personal history of CAD, hypertension or diabetes. Blood pressure was measured twice using various sphygmomanometers, in the seated position after at least 5 minutes of rest; the mean of the two measurements was used.

Stage 2a Replication samples and phenotype measurement.

The Utrecht Atherosclerosis Risk in Young Adults (ARYA) study is a cross sectional population-based birth cohort designed to assess predictors of cardiovascular events in young adults[17]. It includes 750 young adults, born in 1970-1973 in Utrecht, The Netherlands. Blood pressure was measured using a Dinamap machine. An average of 4 seated readings (two from the first visit and two from a second visit, mean 20 days apart) was used for the analysis.

The BRIGHT study is a hypertension case-control study (www.brightstudy.ac.uk)[18]. 2,445 hypertensive cases and 673 normotensive controls were included in this study. Case inclusion criterion was a diagnosis of hypertension prior to 50 years of age (BRIGHT-HTN). Exclusion criteria included BMI>35, diabetes, secondary hypertension or a co-existing illness. Normotensive controls (BRIGHT-NT) had blood pressure recordings of SBP ≤120mmHg and DBP≤ 85mmHg and were not taking any anti-hypertensive medications. Blood pressure was measured in both cohorts using the OMRON-705CP blood pressure monitor, the mean of three blood pressure recordings in the seated position was used in the analysis.

The EPIC-Italy study is a longitudinal cohort of 10,603 volunteers, aged 35-64 years at baseline, from the Turin area, Italy[19]. Individuals were excluded if they had anamnesis of cancer. Blood pressure was measured using a mercury sphygmomanometer, seated, in the left arm. 4,111 healthy subjects of both genders were included in this study.

The European Prospective Investigation of Cancer-Norfolk-replication cohort (EPIC-Norfolk-REP) includes 15,858 participants who were not part of the genome-wide scan in EPIC-Norfolk. These individuals were used for stage 2a follow-up; cohort details and blood pressure measurements are the same as described above for EPIC-Norfolk-GWAS.

The Finland-United States Investigation of NIDDM Genetics (FUSION2) controls (n=1,162) are an independent sample from the FUSION study, these were used for stage 2a follow-up genotyping; cohort details and blood pressure measurements are same as described above for the FUSION study.

Finrisk97 is a population-based, cross-sectional survey conducted in 1997 designed to study the prevalence of cardiovascular risk factors in Finland. Genotypes were available in 7,023 men and women free of exclusions. Blood pressures in Finrisk97 were averaged from 2 measures using a mercury column sphygmomanometer in seated participants resting for at least 5 minutes[15].

The London Life Sciences Population (LOLIPOP) study is an ongoing population-based cohort study of ~30,000 individuals (18,000 Indian Asians and 12,000 European white men and women), aged 35-75 years and recruited from the lists of 58 General Practitioners in West London, United Kingdom[20,21]. In the present study,

DNA was available for 18,829 participants. Blood pressure was measured using an Omron 705CP sphygmomanometer (mean of 3 measurements) with the subject seated. Indian Asian analyses were adjusted for self-reported religion.

The Malmö Diet and Cancer (MDC) study is a community-based prospective epidemiologic cohort of 28,449 persons recruited for a baseline examination between 1991 and 1996. From this cohort, 6,103 persons were randomly selected to participate in the Cardiovascular Cohort (MDC-CC), which seeks to investigate risk factors for cardiovascular disease[22]. Blood pressure was measured using a mercury sphygmomanometer once after 10 minutes of rest in the supine position.

The METabolic Syndrome In Men (METSIM) study includes men aged 45–72 years, randomly selected from the population of the town of Kuopio, Eastern Finland, Finland (population 95,000)[23,24]. The present analysis is based on the first ~6,200 subjects examined for METSIM. Blood pressure was measured in the seated position after 5 minutes rest using a mercury sphygmomanometer. The average of 3 measurements was used in the analysis.

The Malmö Preventive Project (MPP) is a screening program for cardiovascular risk factors and comprises 33,346 Swedish subjects (22,444 men and 10,902 women) from the city of Malmö in southern Sweden[25]. There are 14,600 with DNA after removing subjects who were also participants in MDC-CC (see above). Blood pressure was measured using a mercury sphygmomanometer (mean of 2 measurements) after 10 minutes of rest supine.

The Prevention of REnal and Vascular ENd stage Disease (PREVEND) study, is an ongoing prospective study investigating the natural course of increased levels of urinary albumin excretion and its relation to renal and cardiovascular disease. Inhabitants 28 to 75 years of age (n=85,421) in the city of Groningen, The Netherlands were asked to complete a short questionnaire; 47% responded, and individuals were then selected with a urinary albumin concentration of at least 10 mg/L (n = 7,768) and a randomly selected control group with a urinary albumin concentration less than 10 mg/L (n = 3,395). Details of the protocol have been described elsewhere[26,27]. Blood pressure was measured in the supine position every minute for 10 and 8 minutes, respectively, with an automatic DINAMAP XL Model 9300 series monitor (Critikon, Tampa, Florida). Systolic and diastolic blood pressures were calculated as the mean of the last two measurements at the two visits.

The Prospect-EPIC cohort is one of the two Dutch contributions to the European Prospective Investigation into Cancer and Nutrition (EPIC)[28]. Participants were recruited between 1993 and 1997 among women living in Utrecht and its vicinity and who attended the regional population-based breast cancer screening program. A total of 17,357 women aged 49-70 years were included. For laboratory analysis a 10% random sample of 1,736 samples was taken. Blood pressure was measured using an automated and calibrated Oscillomat (Bosch & Son, Jungingen, Germany); the average of two readings after 10 minutes rest in the seated position was used for the analysis.

The Utrecht Health Project (UHP) is a prospective cohort of 2,829 individuals conducted in a newly developed residential area in the Netherlands (Leidsche

Rijn)[29]. Blood pressure was measured using an Omron M4 machine, in the seated position; the average of 2 readings was used in the current analysis.

Stage 2a follow-up genotyping. For cohorts EPIC-Italy, MPP, MDC-CC, and EPIC-Norfolk-REP we used Taqman assays. For Finrisk97, FUSION2 and METSIM samples genotyping was performed using the iPLEX Sequenom MassARRAY platform. For all remaining studies we performed genotyping at KBiosciences using the KASPAR assay. All SNPs were in Hardy-Weinberg equilibrium (p>0.001) with call rate >90%.

Annotation of top results. We used a variety of tools including: UCSC genome browser (http://genome.ucsc.edu), HapMap (http://www.hapmap.org), OMIM (Online Mendelian Inheritance in Man), Medline, GeneCards (http://www.genecards.org), and Genesniffer (http://www.genesniffer.org).

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Atherosclerosis Risk in Young Adults. Investigators: Michiel L Bots, Cuno S Uiterwaal. Project conception and design, and data acquisition: M.L.B., C.S.U. The ARYA study was funded by the Health Research and Development Council of the Netherlands (ZON) (#2100.0008 and #2100.0042). Genotyping for this project was funded through an Incentive Grant from the Board of the UMC Utrecht.

Baltimore Longitudinal Study of Aging. Investigators: Luigi Ferrucci, Toshiko Tanaka. Conceived and designed experiments: L.F. Data analysis: T.T. A portion of that support was through a R&D contract with MedStar Research Institute. This research was supported in part by the Intramural Research Program of the NIH, National Institute on Aging.

British 1958 Birth Cohort – T1DGC. Investigators: David P Strachan, David Hadley, Wendy L McArdle, Simon Heath. Data analysis: S.H., D.P.S., D.H. This research utilizes resources provided by the Type 1 Diabetes Genetics Consortium, a collaborative clinical study sponsored by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), National Institute of Allergy and Infectious Diseases (NIAID), National Human Genome Research Institute (NHGRI), National Institute of Child Health and Human Development (NICHD), and Juvenile Diabetes Research Foundation International (JDRF) and supported by U01 DK062418. T1DGC GWAS data were deposited by the Diabetes and Inflammation Laboratory, Cambridge Institute for Medical Research (CIMR), University of Cambridge (John Todd, Helen Stevens and Neil Walker), which is funded by Juvenile Diabetes Research Foundation International, the Wellcome Trust and the National Institute for Health Research Cambridge Biomedical Research Centre; the CIMR is in receipt of a Wellcome Trust Strategic Award (079895). We acknowledge use of the DNA from the British 1958 Birth Cohort collection, funded by the Medical Research Council and Wellcome Trust. We thank the Avon Longitudinal Study of Parents and Children laboratory in Bristol and the British 1958 Birth Cohort team, including S. Ring, R. Jones, M. Pembrey, W. McArdle, D. Strachan and P. Burton for preparing and providing the control DNA samples.

British 1958 Birth Cohort - WTCCC. Investigators: Paul R Burton, David Hadley, Wendy L McArdle, Konstantinos Papadakis, David P Strachan, Martin D Tobin, Wellcome Trust Case Control Consortium. Oversight of fieldwork: D.P.S. DNA handling and Quality control: W.L.M. Data handling: D.H., K.P., D.P.S. Data analysis: D.H., K.P., D.Strachan, M.D.T. Supported analysis: P.R.B. The British 1958 Birth Cohort DNA collection was funded by the Medical Research Council grant G0000934 and the Wellcome Trust grant 068545/Z/02. Genotyping for the Wellcome Trust Case Control Consortium was funded by the Wellcome Trust grant 076113/B/04/Z. M.D.T. holds an MRC Clinician Scientist Fellowship (G0501942).

British Genetics of Hypertension study. Investigators: Morris Brown, Mark Caulfield, John M Connell, Anna Dominiczak, Martin Farrall, G Mark Lathrop, Patricia B Munroe, Stephen J Newhouse, Nilesh J Samani, Chris Wallace, John Webster, Wellcome Trust Case Control Consortium, Eleftheria Zeggini. Study establishment:

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Cohorte Lausannoise (CoLaus) study. Investigators: Jacques S Beckmann, Sven Bergmann, Murielle Bochud, Toby Johnson, Noha Lim, Vincent Mooser, Kijoung Song, Peter Vollenweider, Gerard Waeber, Dawn M Waterworth, Xin Yuan. Principal Investigators: V.M., P.Vollenweider. Study design: J.S.B., V.M., P.Vollenweider, G.W., D.M.W. Assembly of the cohort: G.W. Data analysis: S.Bergmann, M.Bochud, T.J., N.L., K.S., X.Y. Project management: J.S.B., S.Bergmann, M.Bochud, V.M., P.Vollenweider, D.M.W. T.J. was supported by a MRC-GSK pilot programme grant (ID 85374) and by the Giorgi-Cavaglieri Foundation. J.S.B. was supported by UNIL and by a grant from the Swiss National Science Foundation (310030-112552). S.Bergmann is supported by the Giorgi-Cavaglieri Foundation and the Swiss National Science Foundation (Grant # 3100AO-116323/1). M.Bochud was supported by the Swiss National Science Foundation(PROSPER 3200BO-111362/1 and 3233BO-111361/1). P.Vollenweider and G.W. received financial support from GlaxoSmithKline to build the CoLaus study. This work has been supported by GlaxoSmithKline, the Swiss National Science foundation (33CSO-122661) and and the Faculty of Biology and Medicine of Lausanne, Switzerland.

Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications. Investigators: Shelley B Bull, Ian de Boer, Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications Research Group, Andrew D Paterson, Daryl Waggott. Study design: S.B.B. Ascertainment of BP: I.d.B. Provision of GWAS data: A.D.P. Data analysis: S.B.B., D.W. S.B.B. held a Canadian Institutes of Health Research (CIHR) Senior Investigator award (2002-7). A.D.P. holds a Canada Research Chair in the Genetics of Complex Diseases. This work has received support from National Institute of Diabetes and Digestive and Kidney Diseases Contract N01-DK-6-2204, National Institute of Diabetes and Digestive and Kidney Diseases Grant R01-DK-077510 and support from the Canadian Network of Centres of Excellence in Mathematics. A complete list of investigators and members of the Research Group appears in N Engl J Med 2005; 353(25):2643-53. The content of this article is solely the responsibility of the authors and does not necessarily represent the official views of the National Institute of Diabetes and Digestive and Kidney Diseases or the National Institutes of Health.

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EPIC-Norfolk-replication. Investigators: Sheila A Bingham, Kay-Tee Khaw, Ruth JF Loos, Robert N Luben, Nicholas J Wareham. Genotyping, Data analysis: S.A.B., K.-T.K., R.J.F.L., R.N.L., N.J.W. The EPIC Norfolk Study is funded by Cancer Research United Kingdom, the Medical Research Council and the Wellcome Trust (077016/Z/05/Z).

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the international level by Elio Riboli (IARC, Lyon and Imperial College, London) and supported by the European Unit.

Fenland Study. Investigators: Ruth JF Loos Nicholas J Wareham Nita G. Forouhi, Jian'an Luan. Study design: R.J.F.L., N.J.W., N.G. F. Data analysis J.L. We are grateful to all the volunteers for their time and help, and to the General Practitioners and practice staff for help with recruitment. We thank the Fenland Study co-ordination team and the Field Epidemiology team of the MRC Epidemiology Unit for recruitment and clinical testing. The Fenland Study is funded by the Wellcome Trust and the Medical Research Council, as well as by the Support for Science Funding programme and CamStrad.

Finland-United States Investigation of NIDDM Genetics. Investigators: Richard N Bergman, Michael Boehnke, Lori L Bonnycastle, Francis S Collins, Anne U Jackson, Karen L Mohlke, Mario A Morken, Laura J Scott, Heather M Stringham, Jaakko Tuomilehto, Timo T Valle, Cristen J Willer. Study design: M Boehnke, F.S.C., K.L.M., L.J.S., T.V., J.T., R.N.B. Sample collection and phenotyping: J.T., T.V. DNA sample co-ordination and genotyping: L.L.B., M.A.M. Analysis: A.U.J., L.J.S., H.M.S., C.J.W. C.J.W. was supported by a postdoctoral fellowship award from the American Diabetes Association. Support for the FUSION cohort and genotyping was provided by NIH grants DK062370 (M.Boehnke), DK072193 (K.L.M.), U54 DA021519, National Human Genome Research Institute intramural project number 1 Z01 HG000024 (F.S.C.).

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Invecchiare in Chianti. Investigators: Stefania Bandinelli, Luigi Ferrucci, Toshiko Tanaka. Conceived and designed experiments: S.Bandinelli., L.F. Data analysis: T.T. This research was supported in part by the Intramural Research Program of the NIH, National Institute on Aging. The InCHIANTI Study was supported as a "targeted project" (ICS 110.1RS97.71) by the Italian Ministry of Health, by the U.S. National Institute on Aging (Contracts N01-AG-916413, N01-AG-821336 and Contracts 263 MD 9164 13 and 263 MD 821336) and in part by the Intramural Research Program, National Institute on Aging, NIH, USA

Kooperative Gesundheitsforschung in der Region Augsburg (KORA). Investigators: Angela Döring, Susana Eyheramendy, Christian Gieger, Thomas Illig, Maris Laan, Thomas Meitinger, Elin Org, Arne Pfeufer. Principal investigator: H Erich Wichmann. Study design: A.Döring, C.G., T.I., M.L., T.M., E.O. Phenotyping: A.Döring. Genotyping: T.I., T.M., E.O., A.P. Provision of GWA data: H.E.W. Data

management: C.G. Quality control: T.I., A.P. Data analysis: S.E., C.G. Interpretation: M.L., E.O., A.P. Study coordination: M.L., H.E.W. KORA 500K Blood Pressure project was supported by: Wellcome Trust International Senior Research Fellow (grant no. 070191/Z/03/Z) in Biomedical Science in Central Europe and Estonian Ministry of Education and Science core grant no. 0182721s06 (to M.L.), and Alexander-von-Humboldt Foundation partnership grant V-Fokoop-1113183 (to M.L. and T.M.). The KORA Augsburg studies were financed by the Helmholtz Zentrum München, German Research Center for Environmental Health, Neuherberg, Germany and supported by grants from the German Federal Ministry of Education and Research (BMBF). The KORA study group consists of H-E. Wichmann (speaker), A. Peters, C. Meisinger, T. Illig, R. Holle, J. John and co-workers who are responsible for the design and conduct of the KORA studies. Part of this work was financed by the German National Genome Research Network (NGFN, T.M.).

London Life Sciences Population study. Investigators: John C Chambers, Paul Elliott, Jaspal S Kooner. Principal investigator: J.S.K. Co-Principal Investigators: J.C.C., P.E. Data analysis: J.C.C. Project management: P.E. LOLIPOP is supported by the British Heart Foundation Grant SP/04/002.

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MIGen Study. Investigators:Gavin Lucas, Isaac Subirana, Sekar Kathiresan, Christopher J. O'Donnell, Veikko Salomaa, Stephen M. Schwartz, Jaume Marrugat, David S. Siscovick, Roberto Elosua. Other investigators: Benjamin F. Voight, Olle Melander, David Altshuler. Study design, sample collection and phenotyping: S.M.S., D.S.S., R.E., O.M., J.M., C.J.O., S.K., V.S., D.A. Data assembly: R.E., G.L., I.S., S.K., S.M.S. Data Analysis: G.L., I.S., B.F.V., R.E. The MIGen study was funded by the U.S. National Institutes of Health (NIH) and National Heart, Lung, and Blood Institute's STAMPEED genomics research program through a grant to D.A. S.K. is supported by a Doris Duke Charitable Foundation Clinical Scientist Development Award, a charitable gift from the Fannie E. Rippel Foundation, the Donovan Family Foundation, a career development award from the NIH, and institutional support from the Department of Medicine and Cardiovascular Research Center at Massachusetts General Hospital. Genotyping was partially funded by The Broad Institute Center for Genotyping and Analysis, which is supported by grant U54 RR020278 from the National Center for Research Resources. V.S. was

supported by the Sigrid Juselius Foundation and the Finnish Foundation for Cardiovascular Research. The REGICOR study was partially funded by the Ministerio de Sanidad y Consumo, Instituto de Salud Carlos III (Red HERACLES RD06/0009), the CIBER Epidemiología y Salud Pública, the FIS (CP05/00290), and AGAUR (SGR 2005/00577). The HARPS study was supported by grants and contracts from the US NIH (R01HL056931, P30ES007033, N01-HD-1-3107).

Metabolic Syndrome in Men. Investigators: Johanna Kuusisto, Markku Laakso. Project conception and design, and data acquisition: J.K. and M.L. Support for METSIM was provided by grant 124243 from the Academy of Finland (ML).

Northern Finland Birth Cohort of 1966. Investigators: Lachlan Coin, Paul Elliott, Nelson B Freimer, Anna-Liisa Hartikainen, Marjo-Riitta Jarvelin, Mark I McCarthy, Paul F O'Reilly, Leena Peltonen, Anneli Pouta. Data collection: A.-L.H., M.-R.J., A.P. Provision of GWA data: P.E., N.B.F., M.-R.J., M.I.M., L.P. Data analysis: L.C., P.F.O. Project oversight and management: P.E., M.-R.J. We acknowledge the support of NHLBI grant 5R01HL087679-02 through the STAMPEED program, the MRC of the UK, EURO-BLCS, QLG1-CT-2000-01643, Biocenter of University of Oulu, ENGAGE project and grant agreement HEALTH-F4-2007-201413, Academy of Finland, and NIMH grant 1RL1MH083268-01.

PREVEND. Investigators: Paul E de Jong, Gerjan Navis, Harold Snieder, Pim van der Harst, Wiek H van Gilst. Coordination of genetic studies: G.N., W.H.v.G. Principal investigator: P.E.d.J. Study establishment: P.E.d.J., G.N., W.H.v.G. Data acquisition: P.E.d.J., G.N., P.v.d.H., W.H.v.G. Genotyping: P.v.d.H. Data analysis: H.S., P.v.d.H. PREVEND genetics is supported by the Dutch Kidney Foundation (Grant E033), EU project grant GENECURE (FP-6 LSHM CT 2006 037697), and NWO VENI (grant number 916.76.170).

PROCARDIS. Investigators: Robert Clarke, Martin Farrall, Anuj Goel, Anders Hamsten, Simon C Heath, G Mark Lathrop, John F Peden, Udo Seedorf, Ann-Christine Syvänen, Giovanni Tognoni, Hugh Watkins. Principal investigator for project: H.W. Principal investigators for collection centre: R.C., A.H., U.S., G.T. Genotyping: S.C.H., G.M.L., A.-C.S. Quality control: S.C.H. Data analysis: M.F., A.G., J.F.P. Project management: J.F.P., H.W. We are grateful to the participants and to the medical and nursing staff who assisted in this project. This work was funded by the British Heart Foundation, EC Sixth Framework Programme (LSHM-CT-2007-037273), AstraZeneca AB, the Swedish Research Council (8691), the Swedish Heart-Lung Foundation, the Stockholm County Council (562183) and the Knut and Alice Wallenberg Foundation. See www.procardis.org for full membership of PROCARDIS consortium.

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Supplementation en Vitamines et Minéraux Antioxydants. Investigators: Pilar Galan, Ivo G Gut, Simon C Heath, Serge Hercberg, Toby Johnson, G Mark Lathrop, Pierre Meneton, Diana Zeleneka. Created the cohort: P.G., S.H. Genotyping: S.C.H., G.M.L., I.G.G., D.Z. Quality control: S.C.H. Data analysis: S.C.H., T.J., P.M. Project coordination: P.M. This work has been supported by the Commissariat à l'Energie Atomique, the Institut National de la Santé et de la Recherche Médicale, the Institut National de la Recherche Agronomique and the Conservatoire National des Arts et Métiers.

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Appendix A: WTCCC Membership and affiliations

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MIGen consortium

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References

1. Shock, N.W., Greulich, R. & Andres, R. Normal Human Aging: The Baltimore Study of Aging. (US Department of Health and Human Services, Washington, DC, 1984).
2. Firmann, M. et al. The CoLaus study: a population-based study to investigate the epidemiology and genetic determinants of cardiovascular risk factors and metabolic syndrome. *BMC Cardiovasc Disord* **8**, 6 (2008).
3. Day, N. et al. EPIC-Norfolk: study design and characteristics of the cohort. European Prospective Investigation of Cancer. *Br J Cancer* **80 Suppl 1**, 95-103 (1999).
4. Loos, R.J. et al. Common variants near MC4R are associated with fat mass, weight and risk of obesity. *Nat Genet* **40**, 768-75 (2008).
5. Ferrucci, L. et al. Subsystems contributing to the decline in ability to walk: bridging the gap between epidemiology and geriatric practice in the InCHIANTI study. *J Am Geriatr Soc* **48**, 1618-25 (2000).
6. Wichmann, H.E., Gieger, C. & Illig, T. KORA-gen--resource for population genetics, controls and a broad spectrum of disease phenotypes. *Gesundheitswesen* **67 Suppl 1**, S26-S30 (2005).
7. Heid, I.M. et al. Association of the 103I MC4R allele with decreased body mass in 7937 participants of two population based surveys. *J Med Genet* **42**, e21 (2005).
8. Jarvelin, M.R. et al. Early life factors and blood pressure at age 31 years in the 1966 northern Finland birth cohort. *Hypertension* **44**, 838-46 (2004).
9. Pilia, G. et al. Heritability of cardiovascular and personality traits in 6,148 Sardinians. *PLoS.Genet* **2**, e132- (2006).
10. John, U. et al. Study of Health In Pomerania (SHIP): a health examination survey in an east German region: objectives and design. *Soz Praventivmed* **46**, 186-94 (2001).
11. Hercberg, S. et al. Background and rationale behind the SU.VI.MAX Study, a prevention trial using nutritional doses of a combination of antioxidant vitamins and minerals to reduce cardiovascular diseases and cancers. SUpplementation en VItamines et Mineraux AntioXydants Study. *Int J Vitam Nutr Res* **68**, 3-20 (1998).
12. Saxena, R. et al. Genome-wide association analysis identifies loci for type 2 diabetes and triglyceride levels. *Science* **316**, 1331-1336 (2007).
13. Valle, T. et al. Mapping genes for NIDDM. Design of the Finland-United States Investigation of NIDDM Genetics (FUSION) Study. *Diabetes Care* **21**, 949-58 (1998).
14. Scott, L.J. et al. A genome-wide association study of type 2 diabetes in Finns detects multiple susceptibility variants. *Science* **316**, 1341-1345 (2007).
15. Kastarinen, M.J. et al. Trends in blood pressure levels and control of hypertension in Finland from 1982 to 1997. *Journal of Hypertension* **16**, 1379-1387 (1998).
16. Broadbent, H.M. et al. Susceptibility to coronary artery disease and diabetes is encoded by distinct, tightly linked SNPs in the ANRIL locus on chromosome 9p. *Hum Mol Genet* **17**, 806-14 (2008).
17. Oren, A. et al. The Atherosclerosis Risk in Young Adults (ARYA) study: rationale and design. *Eur J Epidemiol* **18**, 715-27 (2003).
18. Caulfield, M. et al. Genome-wide mapping of human loci for essential hypertension. *Lancet* **361**, 2118-23 (2003).
19. Palli, D. et al. A molecular epidemiology project on diet and cancer: the EPIC-Italy Prospective Study. Design and baseline characteristics of participants. *Tumori* **89**, 586-93 (2003).
20. Kooner, J.S. et al. Genome-wide scan identifies variation in MLXIPL associated with plasma triglycerides. *Nat Genet* **40**, 149-51 (2008).
21. Chambers, J.C. et al. Common genetic variation near MC4R is associated with waist circumference and insulin resistance. *Nat Genet* **40**, 716-8 (2008).

22. Berglund, G., Elmstahl, S., Janzon, L. & Larsson, S.A. The Malmo Diet and Cancer Study. Design and feasibility. *J.Intern.Med.* **233**, 45-51 (1993).
23. Wang, J. et al. Variants of transcription factor 7-like 2 (TCF7L2) gene predict conversion to type 2 diabetes in the Finnish Diabetes Prevention Study and are associated with impaired glucose regulation and impaired insulin secretion. *Diabetologia* **50**, 1192-200 (2007).
24. Zeggini, E. et al. Meta-analysis of genome-wide association data and large-scale replication identifies additional susceptibility loci for type 2 diabetes. *Nat Genet* **40**, 638-45 (2008).
25. Berglund, G. et al. Cardiovascular risk groups and mortality in an urban swedish male population: the Malmo Preventive Project. *J Intern Med* **239**, 489-97 (1996).
26. Pinto-Sietsma, S.J. et al. Urinary albumin excretion is associated with renal functional abnormalities in a nondiabetic population. *J Am Soc Nephrol* **11**, 1882-8 (2000).
27. Hillege, H.L. et al. Urinary albumin excretion predicts cardiovascular and noncardiovascular mortality in general population. *Circulation* **106**, 1777-82 (2002).
28. Boker, L.K. et al. Prospect-EPIC Utrecht: study design and characteristics of the cohort population. European Prospective Investigation into Cancer and Nutrition. *Eur J Epidemiol* **17**, 1047-53 (2001).
29. Grobbee, D.E. et al. The Utrecht Health Project: optimization of routine healthcare data for research. *Eur J Epidemiol* **20**, 285-7 (2005).