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Supplemental Data

Blood Pressure Loci Identified with a Gene-Centric Array

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Contents

1 Supplemental Figures

List of Figures

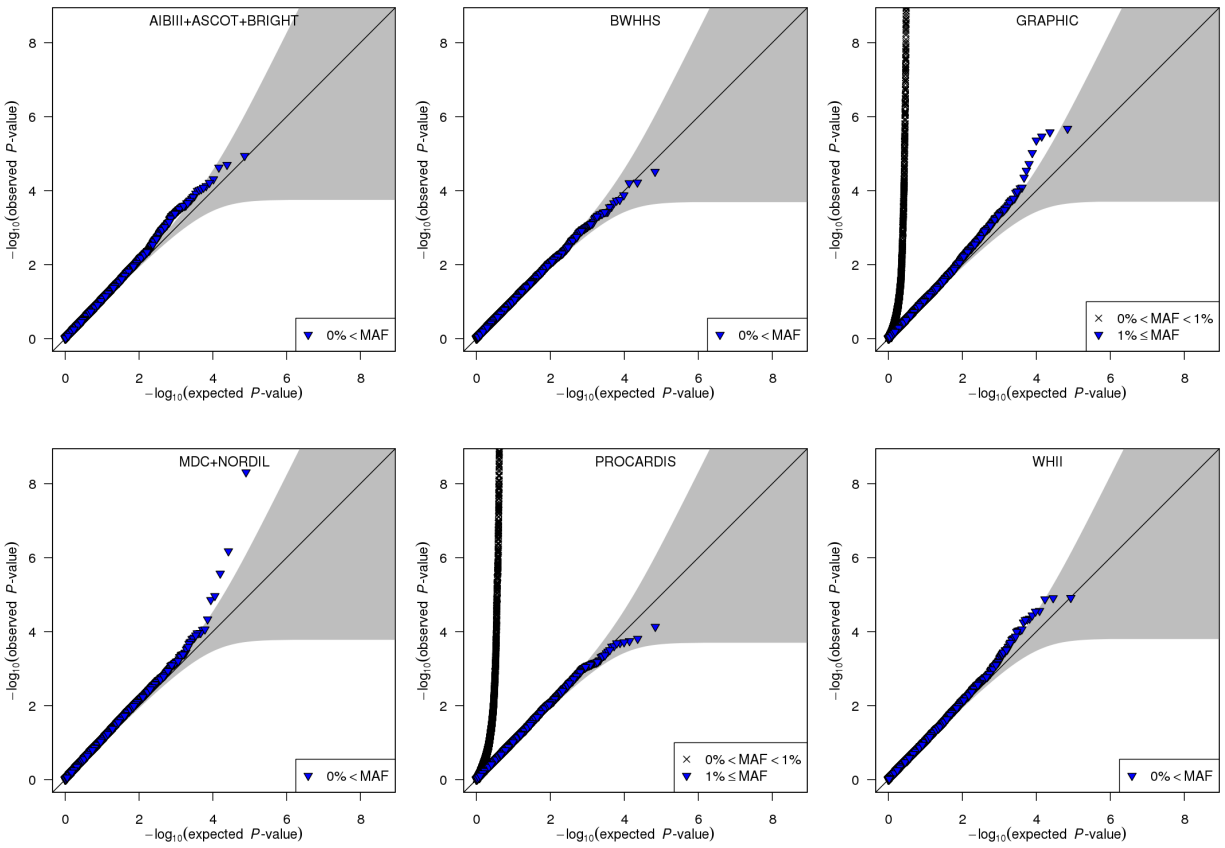

Fig. S1: **QQ plots for DBP by study** after exclusion of SNPs on basis of Hardy-Weinberg proportions ($P < 10^{-6}$), missingness (call rate < 0.98 for single cohort studies and call rate < 0.9975 for studies combining case and control cohorts), and differential missingness ($P < 10^{-6}$). Grey shaded regions are 99% probability envelopes for no association. Inspection of these plots indicated that, in cohorts with related individuals (GRAPHIC and PROCARDIS), SNPs with MAF < 0.01 should be excluded because they showed gross departure from null expectations, whereas in studies with unrelated individuals no exclusion on the basis of MAF was necessary.

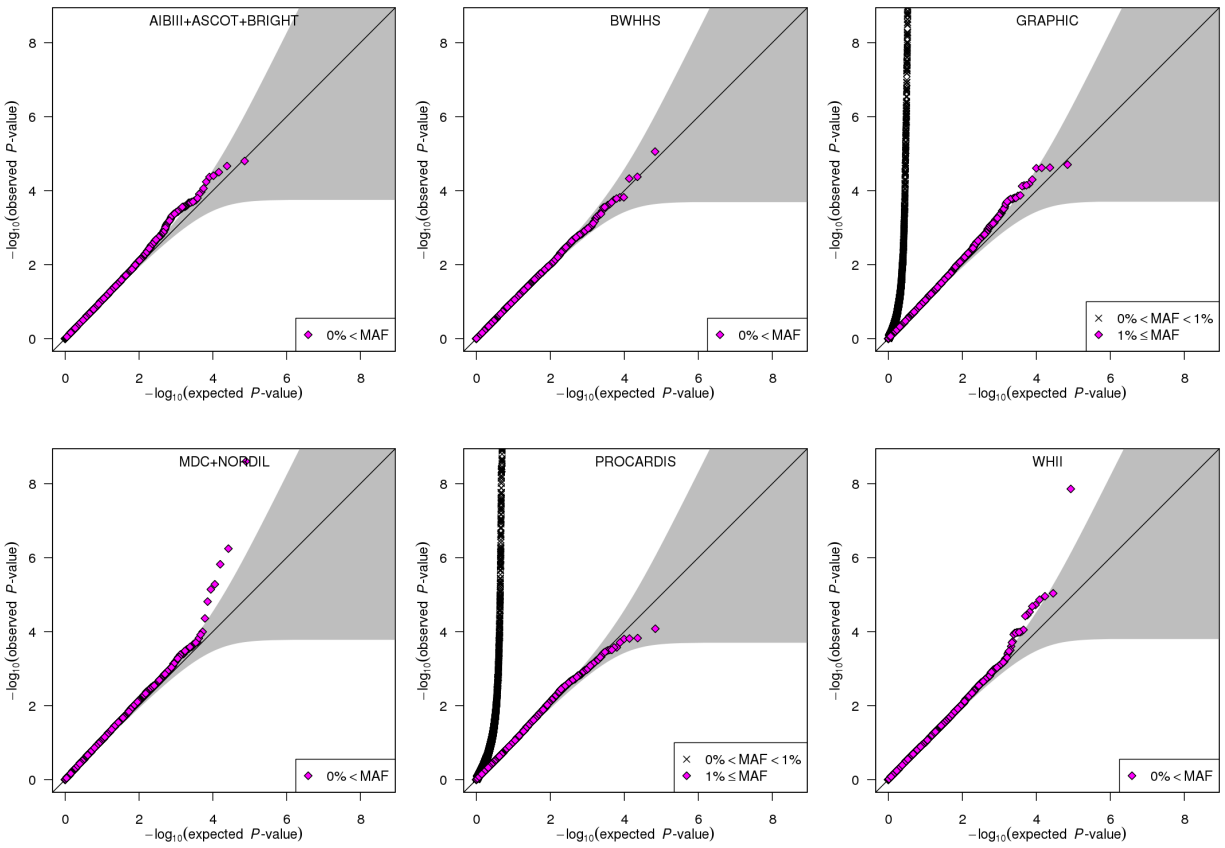

Fig. S2: **QQ plots for MAP by study** after exclusion of SNPs on basis of Hardy-Weinberg proportions ($P < 10^{-6}$), missingness (call rate < 0.98 for single cohort studies and call rate < 0.9975 for studies combining case and control cohorts), and differential missingness ($P < 10^{-6}$). Grey shaded regions are 99% probability envelopes for no association. Inspection of these plots indicated that, in cohorts with related individuals (GRAPHIC and PROCARDIS), SNPs with MAF < 0.01 should be excluded because they showed gross departure from null expectations, whereas in studies with unrelated individuals no exclusion on the basis of MAF was necessary.

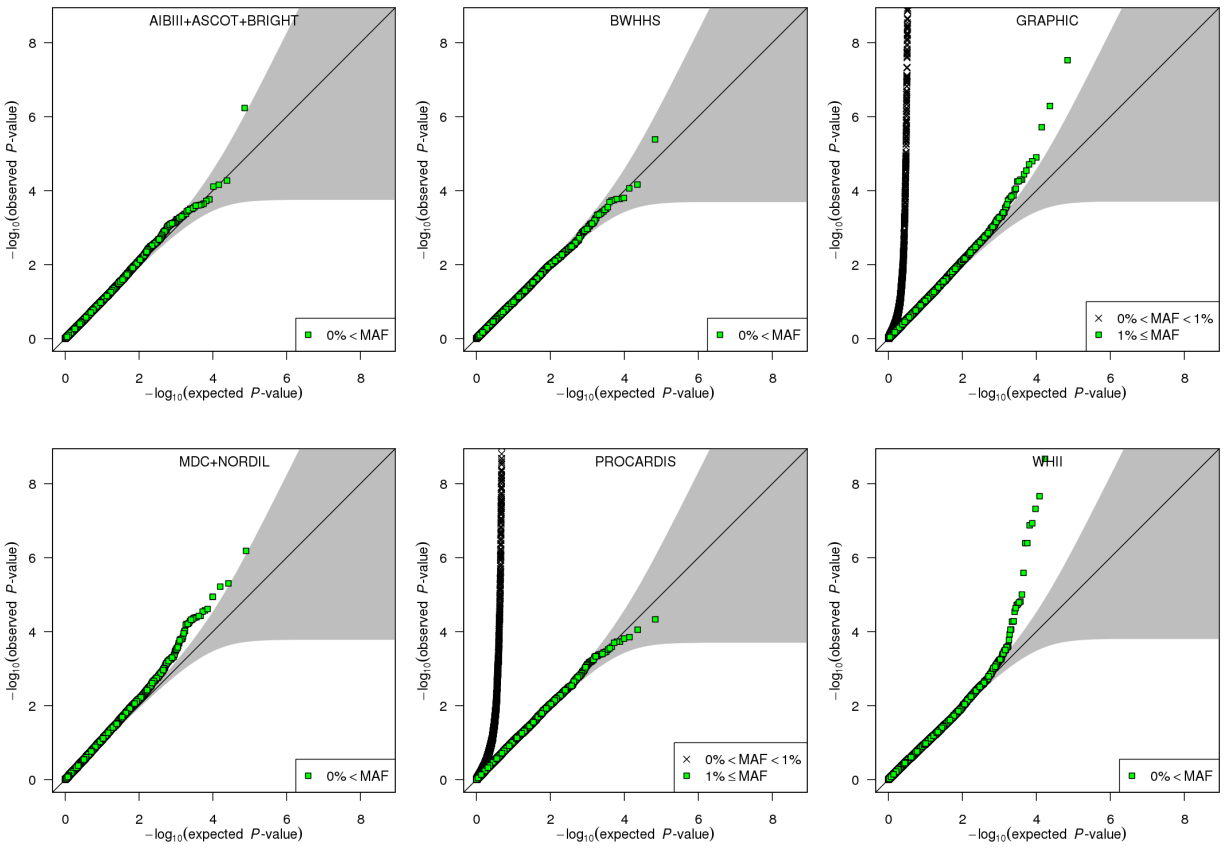

Fig. S3: **QQ plots for PP by study** after exclusion of SNPs on basis of Hardy-Weinberg proportions ($P < 10^{-6}$), missingness (call rate < 0.98 for single cohort studies and call rate < 0.9975 for studies combining case and control cohorts), and differential missingness ($P < 10^{-6}$). Grey shaded regions are 99% probability envelopes for no association. Inspection of these plots indicated that, in cohorts with related individuals (GRAPHIC and PROCARDIS), SNPs with MAF < 0.01 should be excluded because they showed gross departure from null expectations, whereas in studies with unrelated individuals no exclusion on the basis of MAF was necessary.

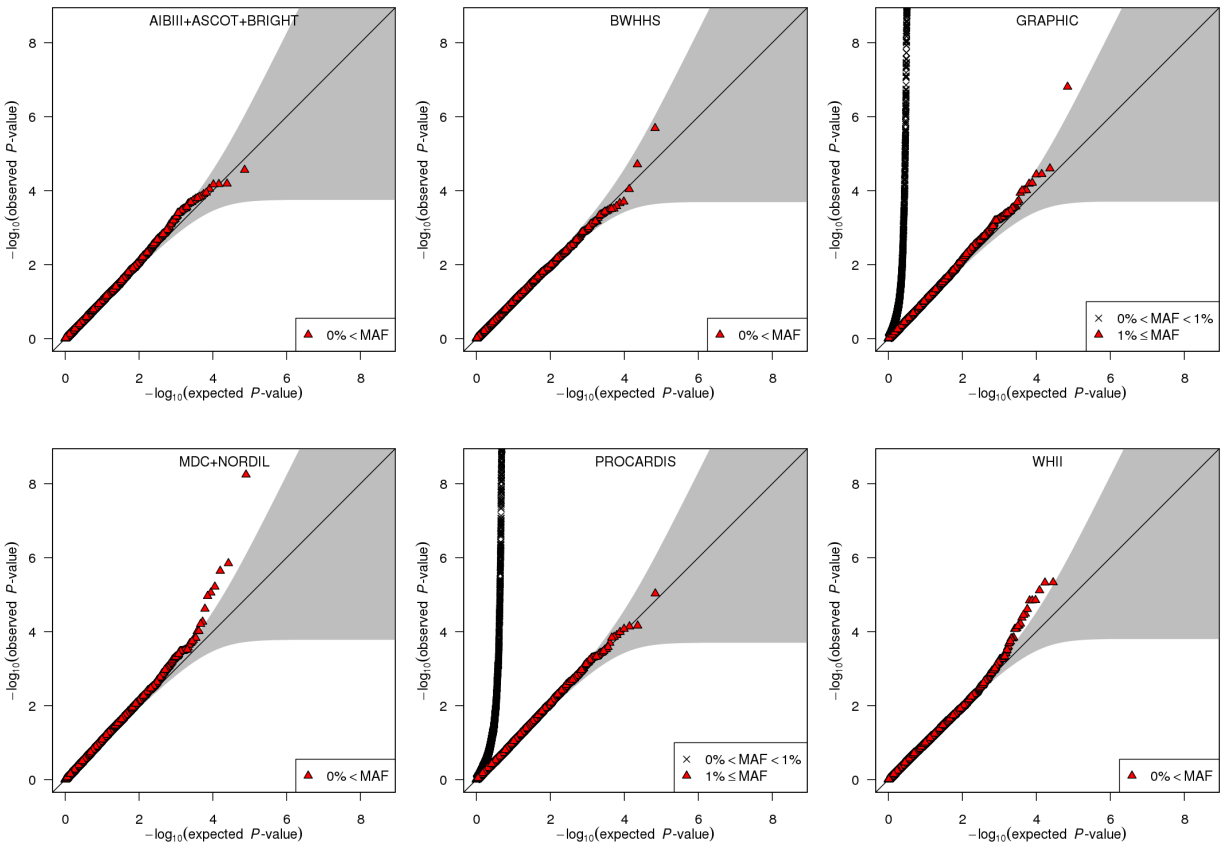

Fig. S4: **QQ plots for SBP by study** after exclusion of SNPs on basis of Hardy-Weinberg proportions ($P < 10^{-6}$), missingness (call rate < 0.98 for single cohort studies and call rate < 0.9975 for studies combining case and control cohorts), and differential missingness ($P < 10^{-6}$). Grey shaded regions are 99% probability envelopes for no association. Inspection of these plots indicated that, in cohorts with related individuals (GRAPHIC and PROCARDIS), SNPs with MAF < 0.01 should be excluded because they showed gross departure from null expectations, whereas in studies with unrelated individuals no exclusion on the basis of MAF was necessary.

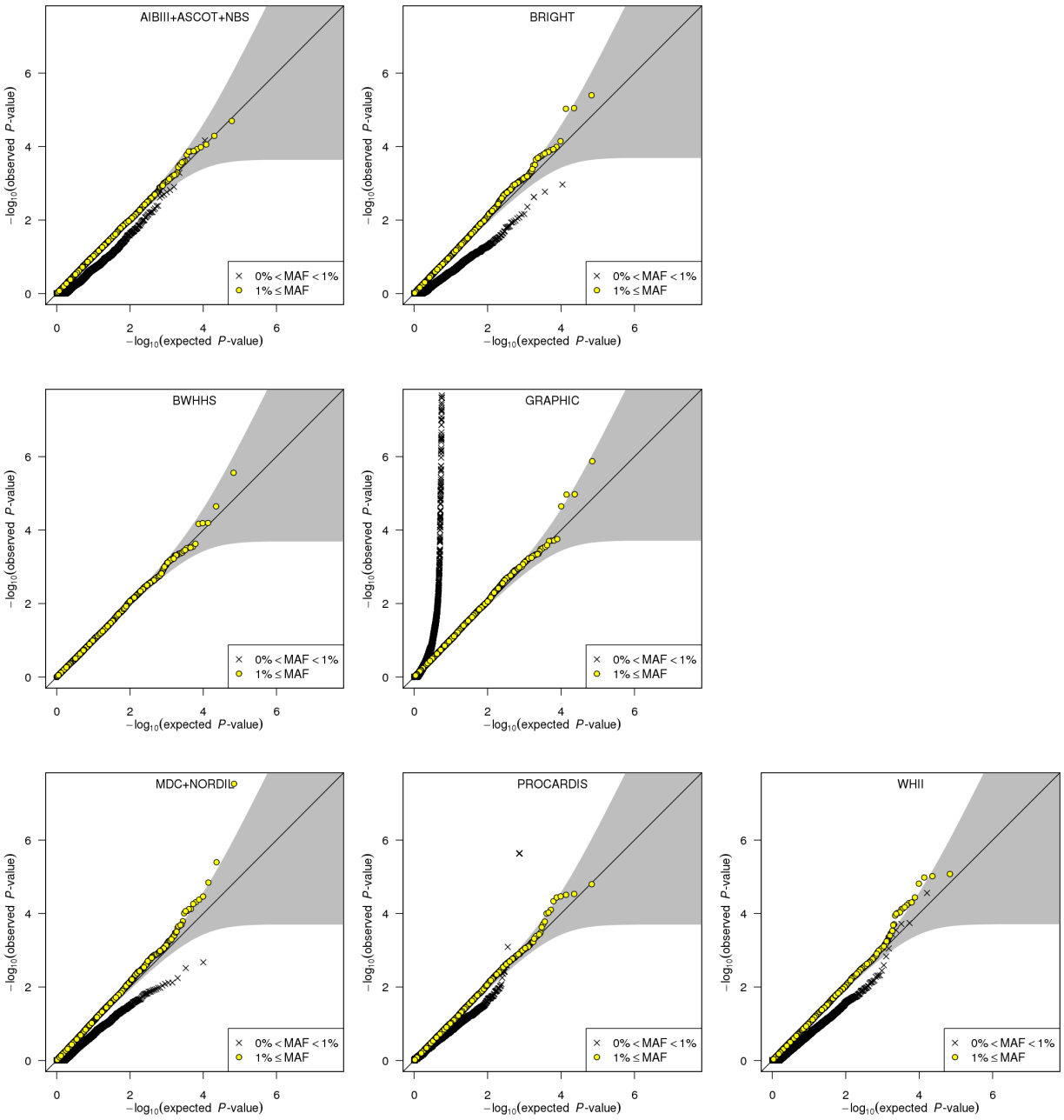

Fig. S5: **QQ plots for dichotomous hypertension (HTN) by study** after exclusion of SNPs on basis of Hardy-Weinberg proportions ($P < 10^{-6}$), missingness (call rate < 0.98 for single cohort studies and call rate < 0.9975 for studies combining case and control cohorts), and differential missingness ($P < 10^{-6}$). Grey shaded regions are 99% probability envelopes for no association. We decided *a priori* to exclude SNPs with MAF < 0.01 from analyses for HTN because the normal null test statistic distribution for logistic regression analyses applies only asymptotically.

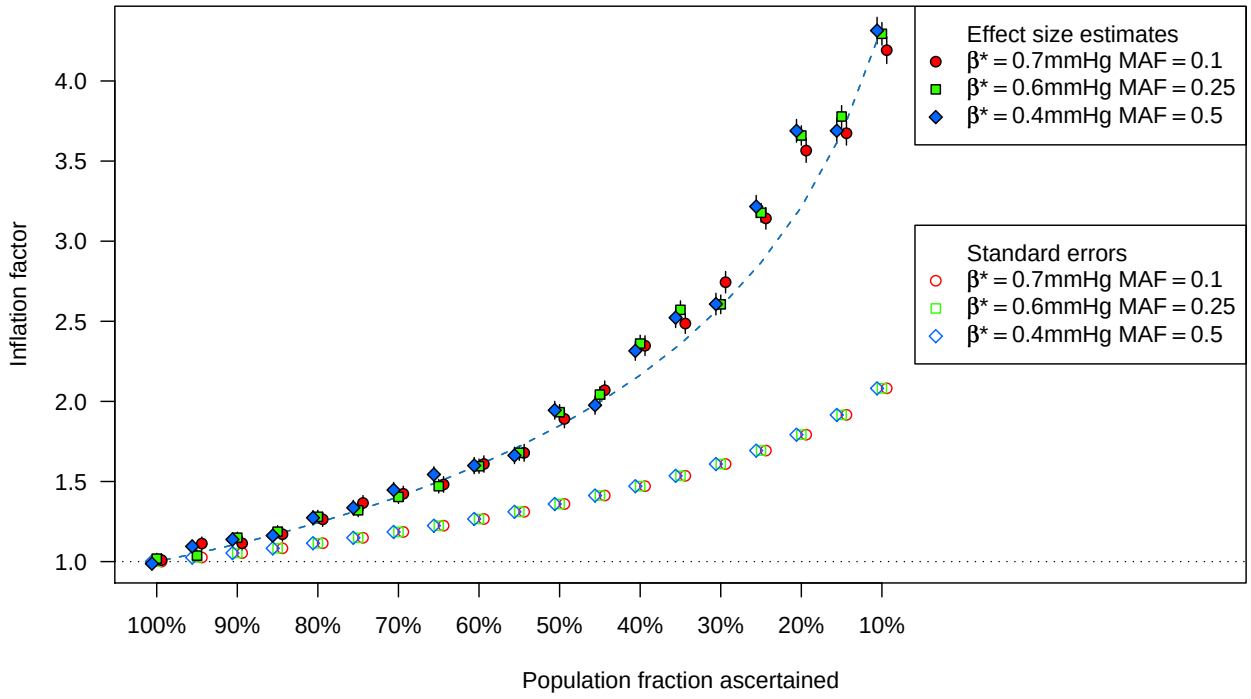

Fig. S6: **Effect size estimate inflation and phenotypic variance inflation in ascertained samples**, plotted as functions of the population fraction satisfying the sample ascertainment criteria (x-axis; 100% means no ascertainment). For each parameter combination, averages from 1000 replicate simulations are plotted, with vertical bars to show associated standard errors. For each replicate a large population was simulated and association statistics were calculated in an ascertained sample drawn from that population. Filled points show the inflation of the effect size estimate obtained in an ascertained sample, relative to the true per-allele effect size in the population from which the sample was drawn ($\beta^\star$). As the degree of ascertainment increases, the effect size estimate inflation increases faster than the standard error inflation (open points), and hence power increases. Although direct estimation of the effect size estimate inflation is sensitive to precise details of the ascertainment scheme (not shown), we observed that for all parameter combinations and ascertainment schemes simulated, the effect size estimate inflation is robustly estimated by the inflation in phenotypic variance in an ascertained sample, relative to the phenotypic variance in the population from which the sample was drawn (dashed curves; indistinguishable for the different $\beta^\star$ and MAF combinations).

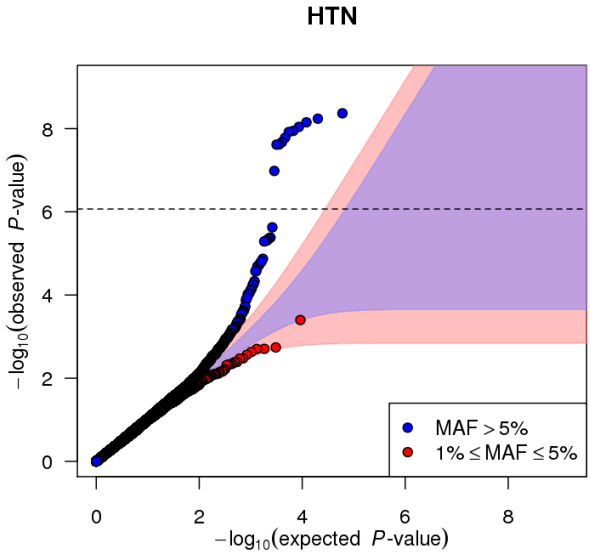

Fig. S7: **QQ plots of meta-analysis results for dichotomous hypertension (HTN).** The plot shows common (MAF $>$ 5%; blue) and some low-frequency (1% $<$ MAF $\leq$ 5%; red) SNPs separately. SNPs with MAF $\leq$ 1% were not analysed for HTN; see Fig. S5. Shaded regions are 99% probability envelopes for no association, which depend on the number of SNPs and hence are different sizes for common and low-frequency SNPs. The horizontal dashed line indicates our overall study-specific significance threshold $P < 8.56 \times 10^{-7}$.

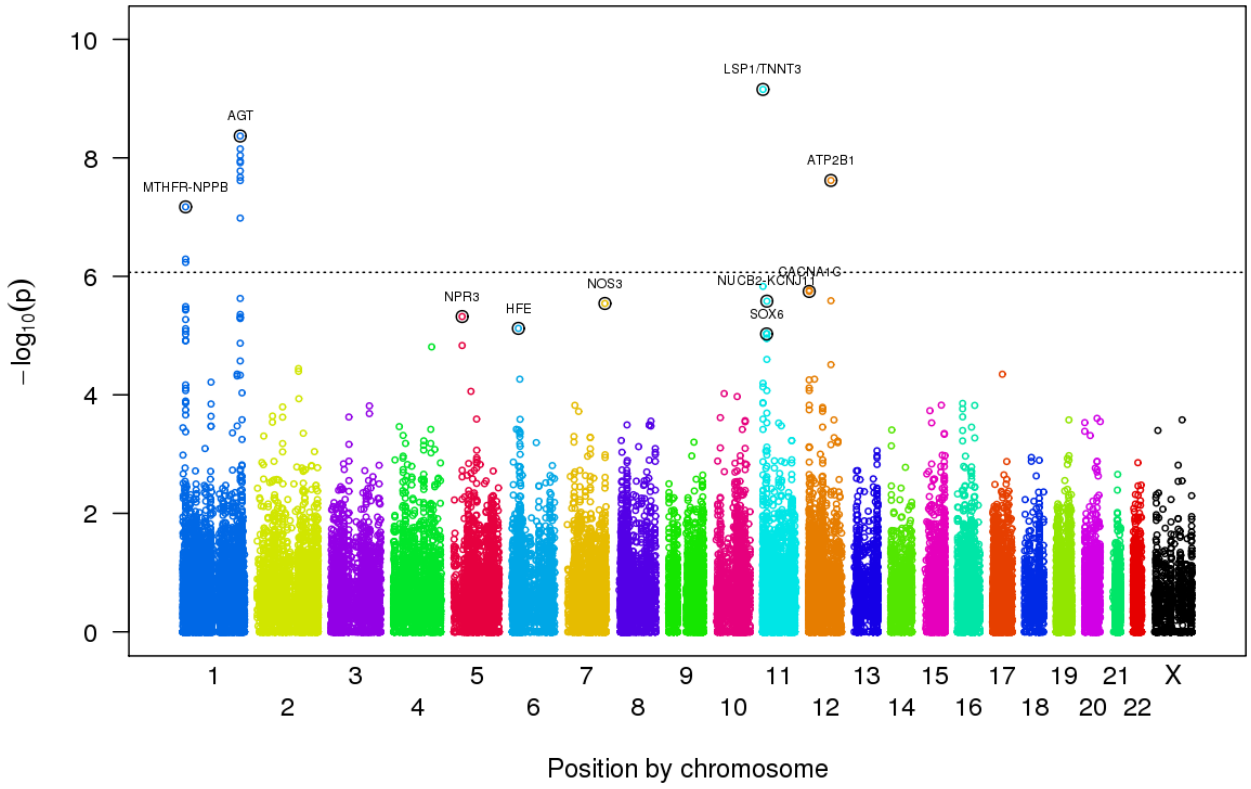

Fig. S8: **Manhattan plot showing the best P value over the five phenotypes studied.** The plot shows the best P value over association analyses for DBP, MAP, PP, SBP and HTN, for each SNP in the discovery meta-analysis. Although these "best" P values do not have a standard distribution (uniform on the $[0, 1]$ interval) under the null hypothesis of no association, we estimated an appropriate significance threshold $P < 8.56 \times 10^{-7}$ (horizontal dashed line) taking into account multiple testing over the five phenotypes and over the $49,452$ SNPs on the HumanCVD BeadChip, to control the overall study-wise false positive rate (FWER) at 5%. The ten SNPs targeted for followup analysis are labelled.

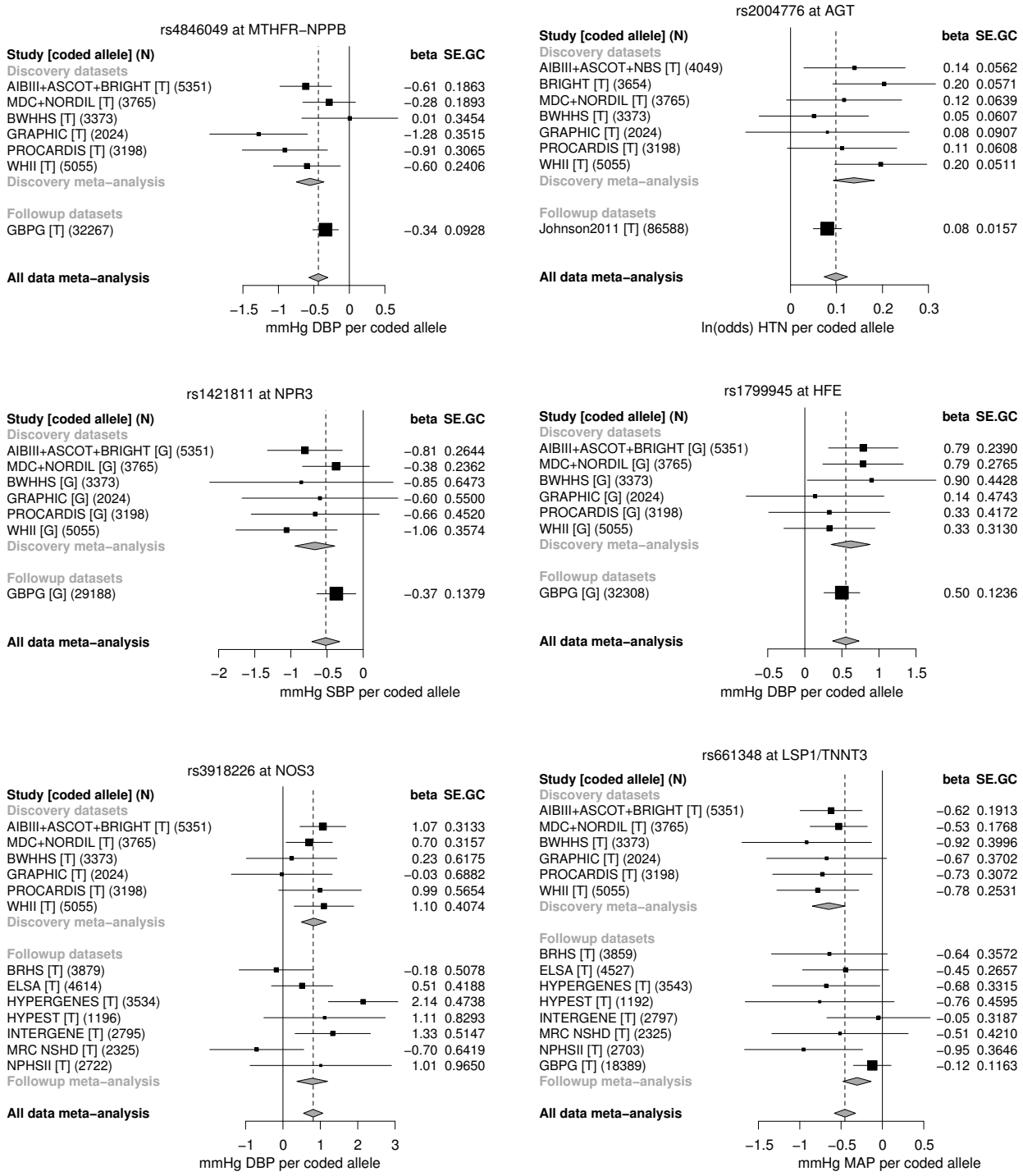

Fig. S9: **Forest plots for 10 SNPs followed up** (continued and with legend on next page).

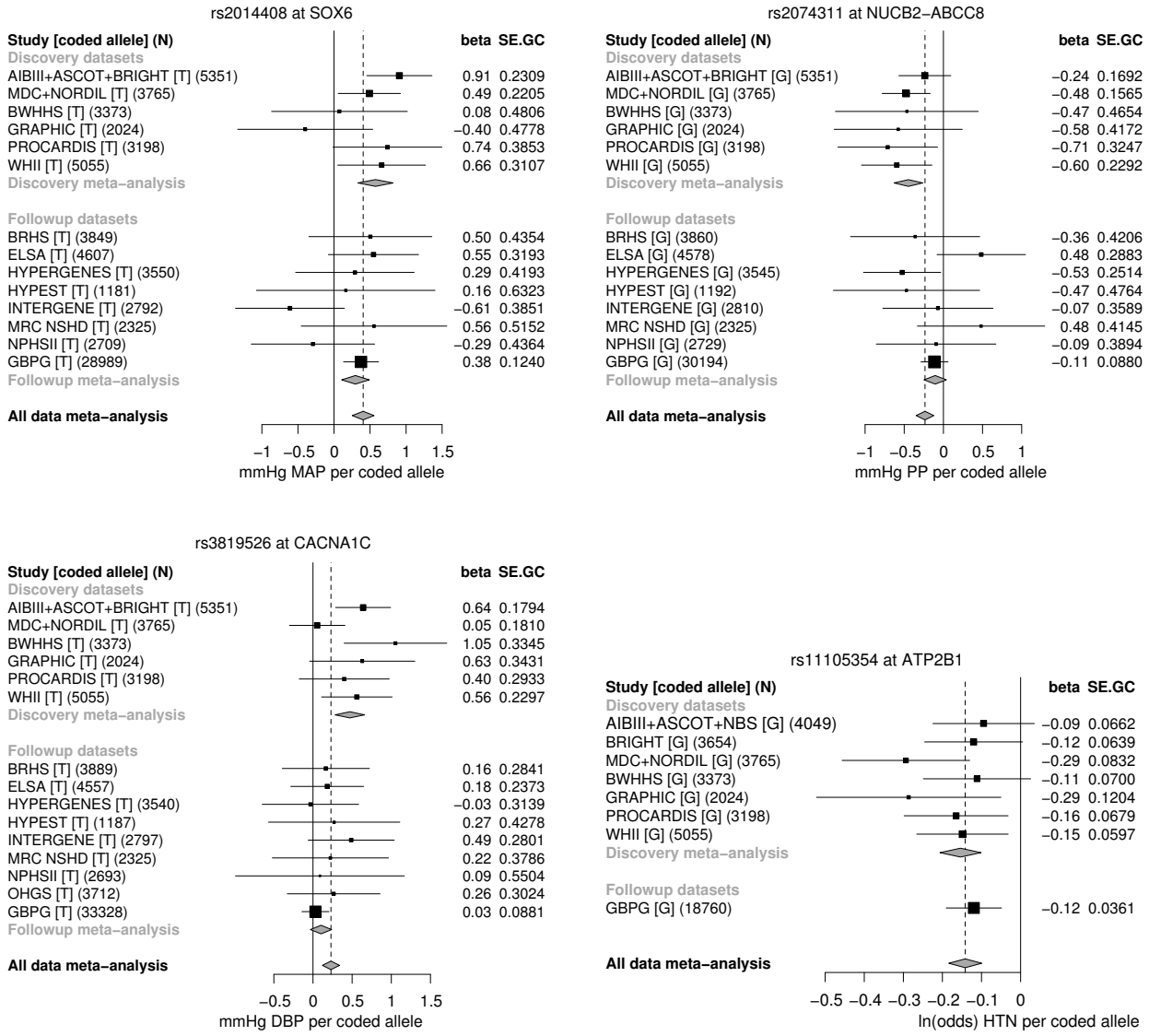

Fig. S9: **Forest plots for 10 SNPs followed up** (continued from previous page). For each of the 10 SNPs targeted for followup, allelic effect sizes and 95% confidence intervals are plotted for each study analysed. Meta-analyses for discovery studies combined, for followup studies combined, and for all studies combined, are plotted as diamond symbols, with a vertical dashed line for the effect size estimate from all studies combined. Numerical values for the allelic effect size (beta) and standard error after genomic control was applied (SE.GC) are given. Results are shown only for the primary phenotype for each SNP.

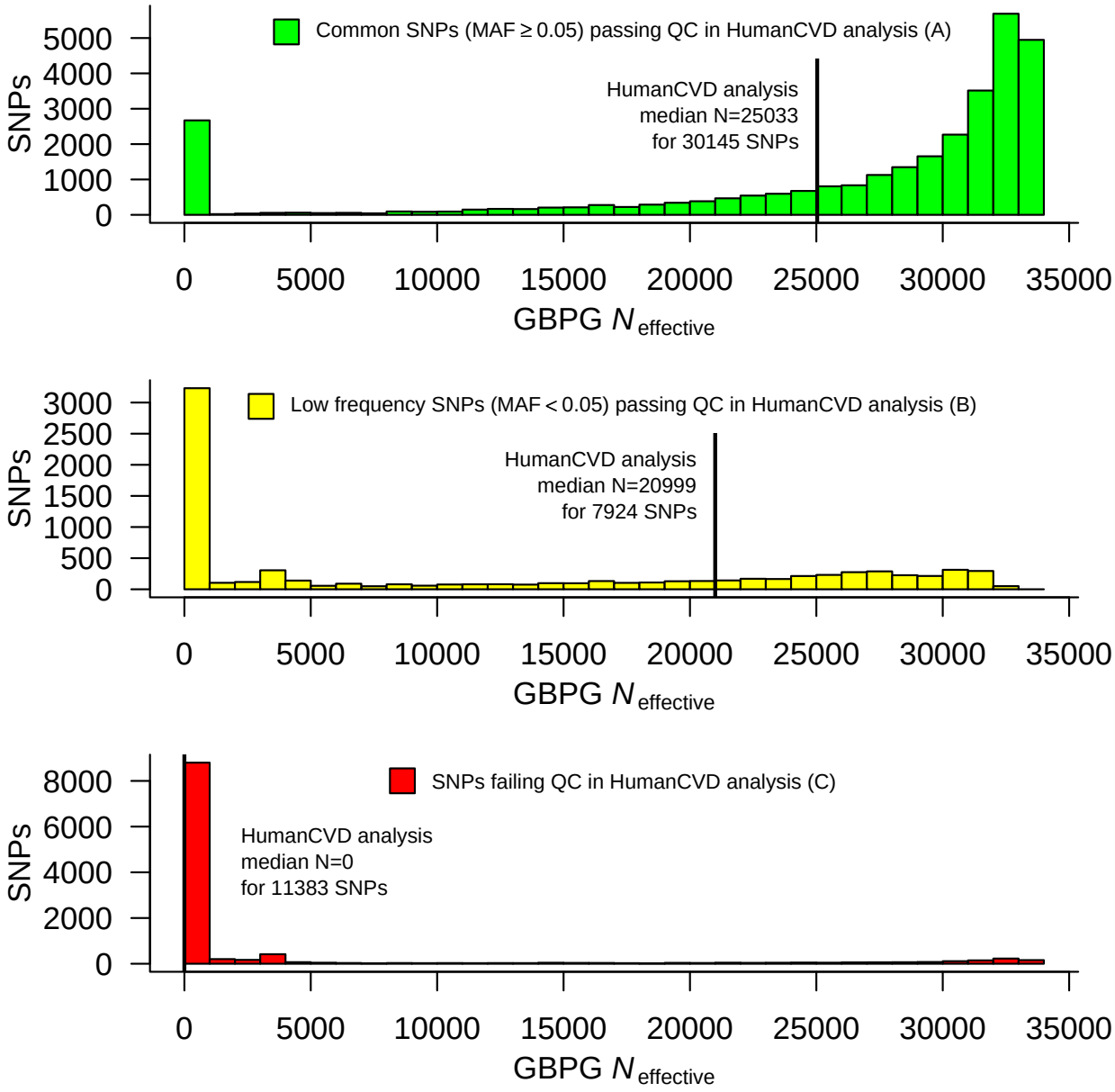

Fig. S10: **Coverage of HumanCVD BeadChip content by standard GWAS meta-analysis.** Coverage of the 49,452 SNPs genotyped on the HumanCVD BeadChip was measured using the Global BPgen (GBPG; Newton-Cheh *et al.* 2009) meta-analysis effective sample size ($N_{\text{effective}}$), which is typical of standard GWAS meta-analyses. SNPs that are on the HumanCVD BeadChip but were not analysed by GBPG because they are not present in the HapMap versions used for genotype imputation have GBPG $N_{\text{effective}} = 0$. Common SNPs successfully genotyped on the HumanCVD BeadChip (median $N = 25,033$) are mostly well-covered by standard GWAS meta-analysis (panel A; 86% have GBPG $N_{\text{effective}} \geq 0.5N_{\text{total}}$). Low frequency SNPs successfully genotyped on the HumanCVD BeadChip (median $N = 20,999$) are not well-covered by standard GWAS meta-analysis (panel B; 39% have GBPG $N_{\text{effective}} \geq 0.5N_{\text{total}}$). SNPs failing QC in our analysis (median $N = 0$) are not well-covered by standard GWAS meta-analysis (panel C), mostly because they are monomorphic in populations of European ancestry.

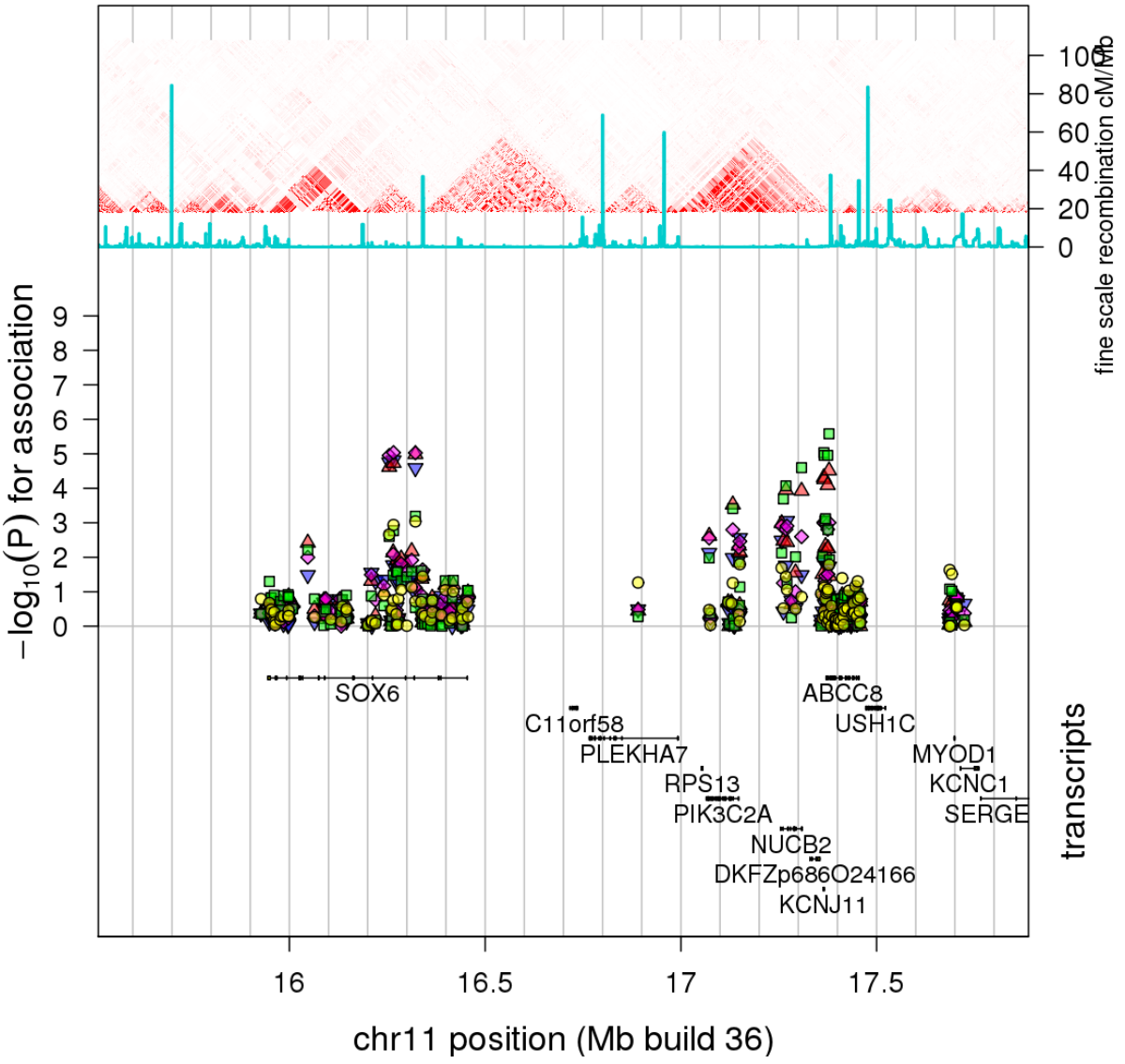

Fig. S11: **Regional association plot for chromosomal region 11p15.2-11p15.1.** The previously reported association at the PLEKHA7 locus (Levy *et al.* 2009) was rs381815 at 16,858,844 Mb, in a different LD block to the signals at the SOX6 and NUCB2-ABCC8 loci identified in our discovery analysis. (Note only the signal at the SOX6 locus was significant in combined discovery and followup data). See legend to main Figure 2 for further explanation of figure elements.

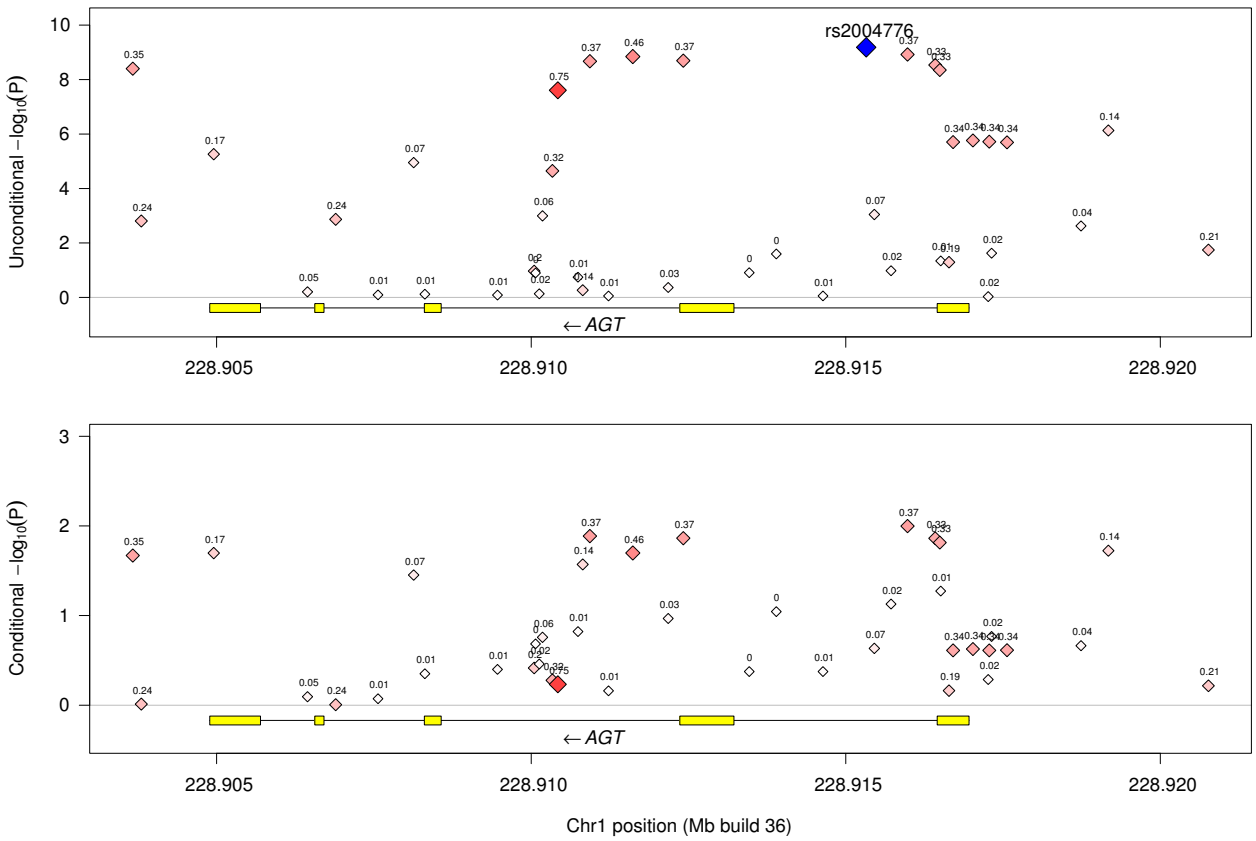

Fig. S12: **Regional association plot at the AGT locus.** Individual SNP association P-values are plotted for analyses without (upper panel) and with (lower panel) conditioning on the most significantly associated SNP at this locus. For SNPs in the local region around the *AGT* transcript (shown for reference, with exons drawn as yellow blocks), we performed a conditional analysis for dichotomous hypertension (the most significantly associated phenotype), conditioning on the most significantly associated SNP in our discovery meta-analysis, rs2004776 (plotted in blue in upper panel). The conditional meta-analysis was identical to unconditional discovery meta-analysis, except that each study included rs2004776 genotype as an additional covariate (coded 0/1/2). In both panels, symbols for each SNP are coloured and annotated according to the pairwise LD with rs2004776 ($r^2 = 0$ white; $r^2 = 1$ red). There are 41 SNPs excluding rs2004776 that passed QC in our discovery analysis in this local region, and in the conditional analysis no SNPs reached a significance threshold $P < 0.05/41 = 0.0012$ at which we could declare a significant secondary signal at this locus.

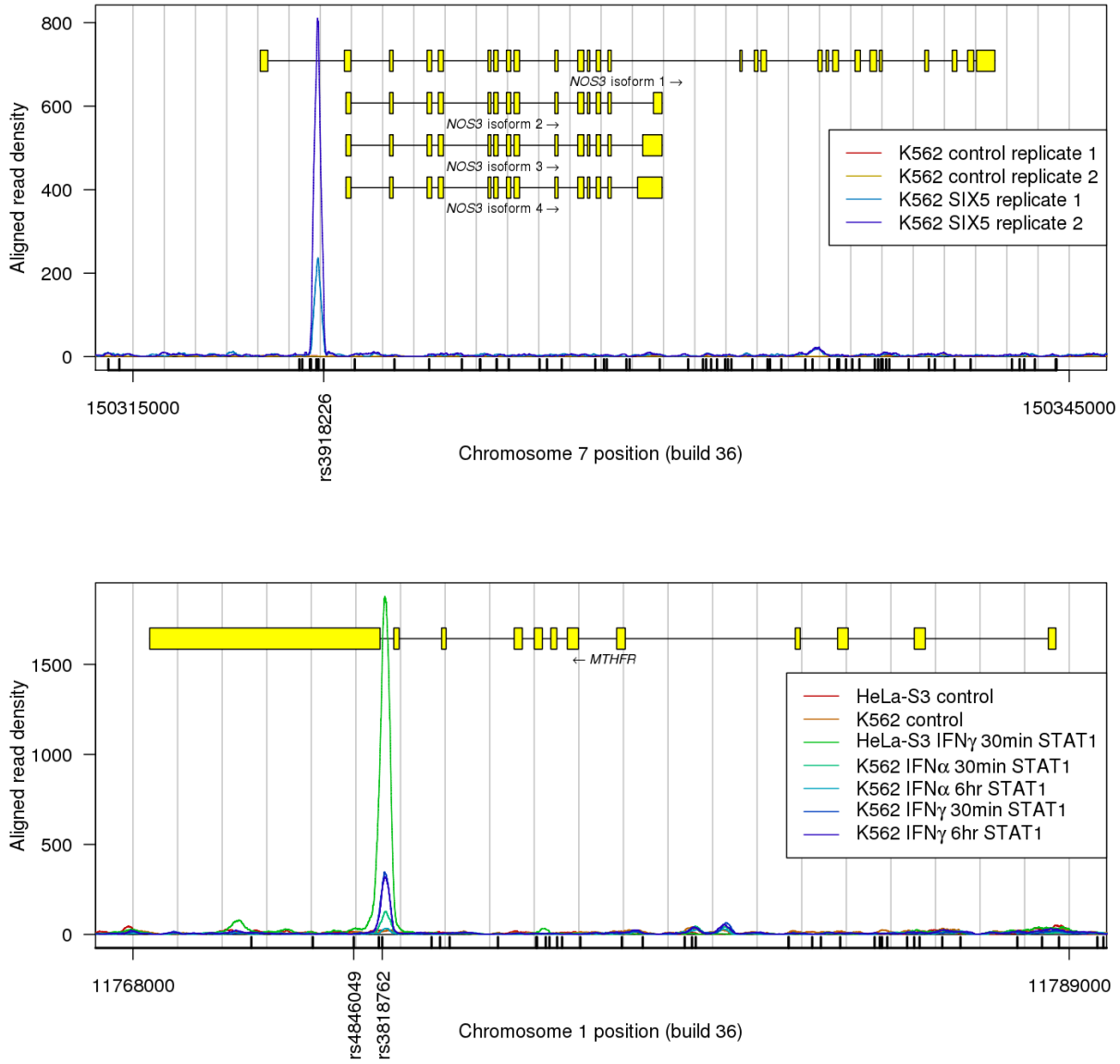

Fig. S13: **Density of aligned reads from ChIP-Seq experiments.** The density of aligned reads from chromatin immunoprecipitation followed by tag sequencing (ChIP-Seq) is plotted in the context of SNPs significantly associated with BP, and gene structure with exons (coding and untranslated) drawn as yellow blocks. Grey vertical lines are plotted every 1Kb and small ticks above the x-axis represent all SNPs on the HumanCVD BeadChip. The upper panel shows data from experiments in K562 cell lines, for controls with no IP and for experiments using an antibody against the *SIX5* transcription factor (Euskirchen *et al.* 2007, Rozowsky *et al.* 2009), relative to the only significantly associated SNP at this locus in our data (rs3918226). Note the first exon of *NOS3* isoform 1 is untranslated. The lower panel shows data from experiments in HeLa-S3 and K562 cell lines, for controls with no IP and for experiments with IFNα and IFNγ growth factor treatments and using an antibody against the growth factor responsive *STAT1* transcription activator (Johnson *et al.* 2007, Valouev *et al.* 2008, Zhang *et al.* 2008), relative to the most significantly associated SNP at this locus in our data (rs4846049; $P = 6.7 \times 10^{-8}$ for DBP) and a less significantly associated SNP (rs3818762; $P = 5.8 \times 10^{-7}$ for DBP).

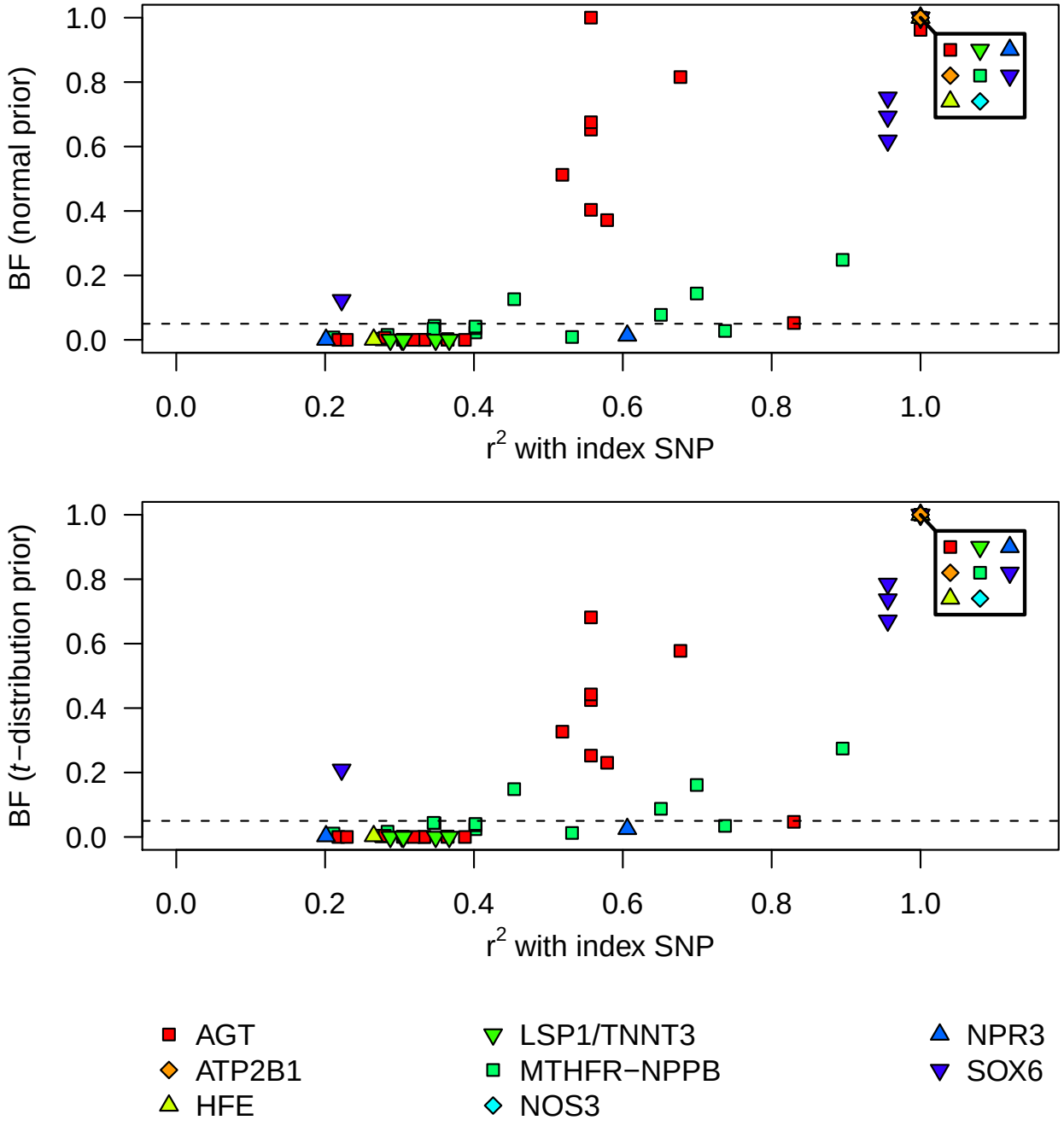

Fig. S14: **Relationship between Bayes Factors and pairwise LD.** SNPs in Table S13 at the eight loci discovered here are plotted by Bayes Factor (BF) and by pairwise LD (r^2) with the index SNP at their locus, with the BF calculated assuming a normal prior (upper panel) and assuming a t-distribution prior (lower panel) on effect sizes. For each locus there is (at least) one SNP with BF $\simeq 1$ and $r^2 = 1$. The BF is a model based, theoretically sound and interpretable criterion for excluding that SNPs cannot credibly be the sole causal variant at each locus. We use BF < 0.05 (horizontal dashed line) as our operational criterion. Pairwise r^2 is widely used as a criterion for similar purposes but is not theoretically well grounded. In our data we see SNPs with pairwise r^2 as low as 0.2 that have BF high enough that they cannot credibly be excluded as potential causal variants.

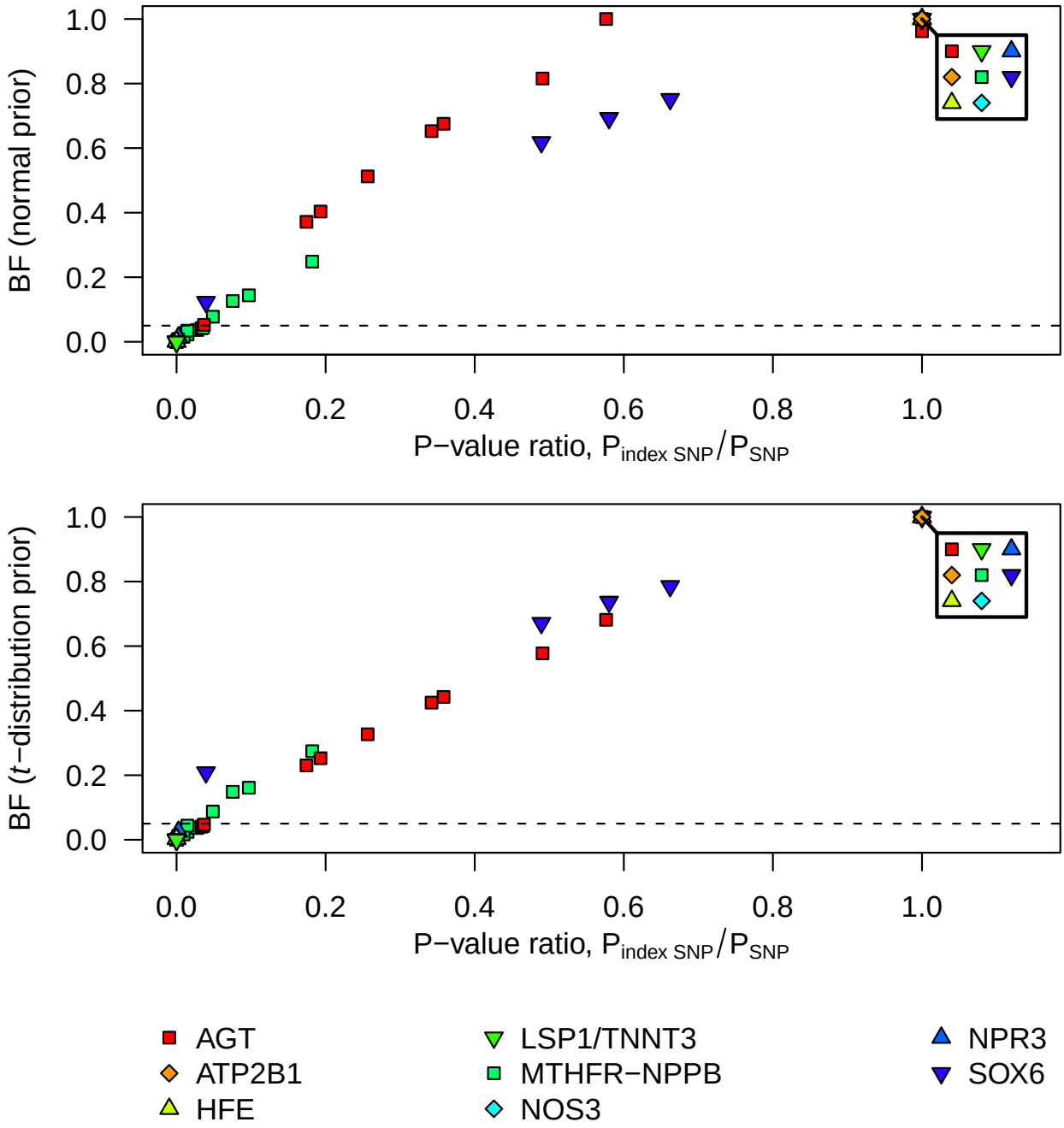

Fig. S15: **Relationship between Bayes Factors and P values.** SNPs in Table S13 at the eight loci discovered here are plotted by Bayes Factor (BF) and by P-value ratio relative to the index SNP at their locus, with the BF calculated assuming a normal prior (upper panel) and assuming a t-distribution prior (lower panel) on effect sizes. For the t-distribution prior the relationship is roughly linear, and hence our operational criterion for excluding that SNPs cannot credibly be the sole causal variant at each locus, BF < 0.05 (horizontal dashed line), is roughly equivalent to excluding SNPs with P-values $> 20\times$ greater (less significant) than the index SNP, when data from the same individuals (and hence same total N) are analysed for all SNPs at each locus.

2 Supplemental Tables

List of Tables

Table S1: **Demographic data for discovery and followup cohorts.**

Cohort[a]	N [b]	Female [%]	Age [years]	(SD)	BMI [kg/m^2]	(SD)	SBP [mmHg]	(SD)	DBP [mmHg]	(SD)	MAP [mmHg]	(SD)	PP [mmHg]	(SD)	BP med.[c] [%]	HTN[d] [%]
Discovery studies, *Ascertained cohorts*																
AIBIII (controls)	458	54.4	52.8	(9.2)	25.7	(3.6)	119.9	(13.7)	75.4	(7.6)	90.2	(8.8)	44.5	(10.3)	0	10.3
ASCOT (cases)	1239	18.1	63.0	(8.1)	29.1	(4.6)	161.4	(17.8)	92.9	(9.9)	115.7	(10.6)	68.5	(16.1)	89.2	100
BRIGHT (cases)	1919	59.6	58.0	(10.3)	27.4	(3.8)	154.3	(21.1)	93.9	(11.3)	114.0	(13.3)	60.4	(15.7)	92.5	100
BRIGHT (controls)	1735	62.7	58.7	(8.9)	25.3	(3.3)	123.0	(10.5)	76.4	(7.2)	91.9	(7.5)	46.7	(8.3)	0	0
MDC (controls)	1846	58.2	57.8	(5.9)	24.3	(3.3)	115.6	(5.8)	73.6	(5.3)	87.6	(4.7)	42.0	(6.0)	0	0
NBS (controls)	2352	50.3	41.4	(12.4)	NA		NA		NA		NA		NA		NA	NA
NORDIL (cases)	1919	51.0	56.0	(4.0)	28.3	(4.6)	177.3	(14.6)	105.9	(5.5)	129.7	(7.1)	71.5	(13.6)	0[e]	100
Discovery studies, *Non-ascertained (population) cohorts*																
BWHHS	3373	100	68.9	(5.5)	27.3	(6.0)	146.5	(26.6)	79.2	(12.9)	102.0	(15.0)	67.6	(19.0)	30.2	61.4
GRAPHIC	2024	49.6	39.3	(14.5)	26.1	(4.6)	127.1	(17.8)	79.1	(11.0)	95.1	(12.5)	48.0	(11.9)	6.7	28.5
PROCARDIS	3198	51.1	59.3	(9.9)	26.8	(4.4)	130.8	(17.1)	79.6	(10.0)	96.7	(11.2)	51.1	(13.4)	19.3	43.9
WHII	5055	36.5	60.9	(6.0)	26.7	(4.3)	128.1	(16.7)	74.6	(10.5)	92.4	(11.8)	53.5	(11.2)	22.8	39.0
Followup studies, *Ascertained cohorts*																
HYPERGENES (cases)	1828	33.5	48.5	(9.6)	27.2	(3.9)	150.8	(15.4)	96.6	(10.2)	116.4	(9.4)	54.9	(11.0)	14.8	100
HYPERGENES (controls)	1722	40.1	60.9	(8.8)	25.6	(3.6)	123.4	(9.0)	77.5	(6.2)	92.8	(6.3)	45.9	(7.7)	0	0
HYPEST (cases)	715	59.6	50.8	(13.2)	27.6	(3.8)	149.3	(17.5)	91.1	(10.4)	114.6	(11.6)	59.9	(14.0)	35.1	100
HYPEST (controls)	489	74.6	38.7	(9.1)	24.4	(3.3)	126.9	(7.9)	79.5	(5.7)	95.3	(5.7)	47.4	(6.7)	0	0
OHGS (cases)	2234	35.9	52.1	(7.2)	29.7	(5.4)	138.0	(18.7)	82.7	(11.9)	NA		NA		53.1	59.4
OHGS (controls)	1522	47.8	72.6	(5.2)	25.8	(4.0)	124.5	(10.0)	73.5	(7.7)	NA		NA		0	0
Followup studies, *Non-ascertained (population) cohorts*																
BRHS	3945	0	68.8	(5.5)	26.9	(3.7)	149.1	(24.2)	85.2	(11.2)	106.5	(14.2)	64.0	(18.4)	28.0	73.5
EAS	904	50.4	64.3	(5.6)	25.5	(3.8)	143.0	(23.5)	77.1	(12.2)	99.1	(14.3)	65.8	(18.9)	12.5	54.1
ELSA	4643	54.4	66.2	(9.1)	27.8	(4.7)	134.9	(18.5)	75.3	(10.9)	95.2	(12.0)	59.6	(14.9)	14.0	45.0
INTERGENE	2845	53.6	51.0	(13.5)	26.0	(4.0)	131.7	(21.5)	82.2	(10.5)	98.7	(12.9)	49.5	(16.6)	12.23	41.4
MRC NSHD	2269	49.4	53.0	(0)	27.3	(4.5)	136.2	(19.7)	84.6	(12.1)	103.4	(14.9)	52.3	(13.9)	13.8	49.9
NPHSII	2775	0	56.1	(3.4)	26.5	(3.5)	138.5	(19.1)	84.6	(11.2)	102.5	(12.9)	53.8	(14.3)	8.5	52.9

Notes: **a.** Demographics are presented by cohort, identified by the short names defined in Table S2. For the ascertained studies demographics are presented separately for hypertensive case cohorts and for control cohorts, but for the non-ascertained studies each consisting of a single cohort, demographics are presented for all individuals combined. **b.** Number of samples analysed, i.e. with both genotype and phenotype data. **c.** Percentage of individuals taking antihypertensive or BP lowering medication, when BP was measured. **d.** Percentage of hypertensive individuals (defined as SBP $\geq$ 140mmHg, or DBP $\geq$ 90mmHg, or taking antihypertensive or BP lowering medication for any reason). **e.** No medication for two weeks prior to when BP was measured.

Table S2: **Recruitment, ascertainment and phenotyping.** We describe criteria used to ascertain individuals on the basis of BP values (including age limits at which the values must have been observed), other ascertainment criteria, and methods of BP measurement.

Study	Details
AIBIII: Controls from the **A**llied **I**rish **B**ank (AIBIII) study	
BP ascertainment:	$\leq$ 160mmHg SBP and $\leq$ 90mmHg DBP.
Other ascertainment:	Current and retired bank employees and spouses; 18–80 years of age; recruited between June 2003 and June 2004; had suffered no cardiovascular events; were not taking any vasoactive medication; Caucasian; Irish.
BP measurement:	Sitting clinic BP, measured from the right arm using a regularly calibrated validated Omron HEM-705CP instrument (Omron Healthcare Inc., Vernon Hills, IL); measured in the brachial artery 3 times at 5 minute intervals; the mean of the last 2 measurements was used for this work.
ASCOT: Hypertensive cases from the **A**nglo-**S**candinavian **C**ardiac **O**utcomes **T**rial	
BP ascertainment:	$\geq$ 160mmHg SBP or $\geq$ 100mmHg DBP untreated; or $\geq$ 140mmHg SBP or $\geq$ 90mmHg DBP treated with one or more antihypertensive therapy.
Other ascertainment:	ASCOT participants recruited in UK and Ireland; $\geq$ 40 years of age; $\geq$ 3 additional cardiovascular risk factors (Sever *et al.* 2001).
Exclusions:	As detailed by Sever *et al.* (2001), including: contraindications to antihypertensive therapies; secondary or malignant hypertension; previous clinical myocardial infarction or current treated angina; cerebrovascular event within previous 3 months; heart failure; uncontrolled arrhythmias; clinically important haematological or biochemical abnormalities.
BP measurement:	Measured seated, 3 times using an Omron HEM-705CP instrument at the trial randomisation visit; the mean of the 2nd and 3rd measurements was used for this work.
References:	Sever *et al.* (2001, 2003), Dahlöf *et al.* (2005)
BRIGHT: Hypertensive cases from the **BRI**tish **G**enetics of **H**yper**T**ension study	
BP ascertainment:	$\geq$ 150mmHg SBP and $\geq$ 100mmHg DBP for a single reading; or $\geq$ 145mmHg SBP and $\geq$ 95mmHg DBP for 3 consecutive readings on a single visit; prior to 50 years of age.
Other ascertainment:	From families with more than 1 hypertensive affected sibling (by definition above); 1 individual from each family was used for this work; recruited from 6 UK geographical regions.
Exclusions:	BMI $>$ 35; diabetes; secondary hypertension; co-existing illness.
BP measurement:	Clinic BP was measured in triplicate by trained research nurses, in the seated position, after at least 5 minutes rest and having refrained from smoking and exercise, using an Omron HEM-705CP instrument with an appropriate size cuff applied on the non-dominant arm, with an interval of at least 3 minutes between readings. The mean of the 2nd and 3rd readings was used in this work.
References:	Caulfield *et al.* (2003), Wellcome Trust Case Control Consortium (2007)
BRIGHT: Controls from the **BRI**tish **G**enetics of **H**yper**T**ension study	
BP Ascertainment:	$\leq$ 140mmHg SBP and $\leq$ 90mmHg DBP and not taking any antihypertensive medications.
Other ascertainment:	From similar UK geographical regions as the BRIGHT hypertensive cases
BP measurement:	Identically as for the BRIGHT cases (above).
References:	Newhouse *et al.* (2009)

Study	Details
MDC: Controls from the **M**almö **D**iet and **C**ancer study	
BP ascertainment:	$\leq$ 120mmHg SBP and $\leq$ 80mmHg DBP and not on any antihypertensive medication.
Other ascertainment:	At least 50 years of age; free from cardiovascular events (coronary events and stroke) during 10 years of followup.
BP measurement:	In the recumbent position, after 5–10 minutes rest, using a manual spyhgmanometer.
References:	Berglund *et al.* (1993), Kathiresan *et al.* (2008)
NBS: Controls from the **N**ational **B**lood **S**ervice	
BP ascertainment:	None (no measures available).
Other ascertainment:	Blood donors in the UK.
NORDIL: Hypertensive cases from the **NOR**dic **DIL**tiazem trial	
BP ascertainment:	$\geq$ 160mmHg SBP and $\geq$ 100mmHg DBP, for at least 2 consecutive measurements, at less than 63 years of age.
Other ascertainment:	NORDIL trial participants.
BP measurement:	Measured at the trial randomisation visit (1992–1999), after antihypertensive medication had been withdrawn for a 2 week period.
References:	Hansson *et al.* (2000)
BWHHS: The **B**ritish **W**omens **H**eart and **H**ealth **S**tudy	
BP ascertainment:	None.
Other ascertainment:	Female; Consent for genetic testing.
Exclusions:	Defined by the examining nurse as non-white.
BP measurement:	A Dinamap 1846SX vital signs monitor was used. Arm circumference was measured and the appropriate cuff size was used. Measurements were taken twice in succession, using the right arm, with the participant seated and the arm supported on a cushion. Since the Dinamap 1846SX is known to systematically overestimate SBP by 8mmHg, this was subtracted from values before analysis.
References:	`http://www.lshtm.ac.uk/eph/ncde/research/bwhhs`
GRAPHIC: The **G**enetic **R**egulation of **A**rterial **P**ressure of **H**umans **I**n the **C**ommunity cohort	
BP ascertainment:	None
Other ascertainment:	Through general practices in Leicestershire (UK); nuclear families that consisted of both parents (aged 40–60 years) and two adult offspring (18 years); white European.
Exclusions:	Previous history of chronic kidney disease.
BP measurement:	Clinic BP was measured in triplicate by trained research nurses using an Omron HEM-705CP instrument with an appropriate size cuff applied on the non-dominant arm, with an interval of at least 3 minutes between readings. The mean of the 2nd and 3rd readings was used in this work.
References:	Tobin *et al.* (2008)
PROCARDIS: The **PR**ec**O**cious **C**oronary **AR**tery **DIS**ease study	
BP ascertainment:	None.
Other ascertainment:	CAD free controls from CAD case-control study; German, Italian, Swedish and British.
BP measurement:	Measured twice using various sphygmomanometers, in the seated position after at least 5 minutes rest; the second of the 2 measurements was used in this work.
References:	Clarke *et al.* (2009), `http://www.procardis.org`

Study	Details
WHII: The **W**hite**H**all **II** study	
BP ascertainment:	None.
Other ascertainment:	Recruited between 1985 and 1989, from 20 London (UK) based civil service departments.
BP measurement:	Measures from phase 7 (2003–2004) of the longitudinal study; measured 3 times with participant in a seated position following a 10 minute rest period, by a nurse using an OMRON HEM-907 instrument; the mean of 3 measurements was used for this work.
HYPERGENES: Hypertensive cases from the HYPERGENES European Network for Genetic-Epidemiological Studies	
BP ascertainment:	$>$ 140mmHg SBP or $>$ 90mmHg DBP or taking antihypertensive treatment, before 50 years of age.
Other ascertainment:	North European, Sardinian and South European.
BP measurement:	Using a sphygmomanometer for 3–5 times per visit for more than 1 visit; for this work, where available the last off-medication measurement was used, otherwise an on-medication measurement adjusted by +15mmHg SBP and +10mmHg DBP was used.
References:	`http://www.hypergenes.eu`
HYPERGENES: Controls from the HYPERGENES European Network for Genetic-Epidemiological Studies	
BP ascertainment:	$\leq$ 130mmHg SBP and $\leq$ 85mmHg DBP for all measurements during 10 years (average) followup.
Other ascertainment:	Healthy subjects older than 55 years of age; North European, Sardinian and South European (matched to the HYPERGENES Hypertensive cases).
BP measurement:	Using a sphygmomanometer for 3–5 times per visit for more than 1 visit; for this work the earliest measurement available after age 55 was used.
References:	`http://www.hypergenes.eu`
HYPEST: The **HYP**ertension in **EST**onia study	
BP ascertainment:	Mixed hypertensive individuals and general population sample; essential hypertension patients selected based on the clinical diagnosis and profile of BP specialists during the patients ambulatory visits or hospitalization at the North Estonia Medical Center, Centre of Cardiology, or at the Cardiology Clinic, Tartu University Hospital.
Other ascertainment:	Recruited in Estonia between 2004 and 2007; general population sample were long-term blood donors.
BP measurement:	After resting in the seated position, measured by a trained clinician using a standard mercury column sphygmomanometer with arm circumference adjusted cuffs; median value over multiple readings (on average 4.3 per individual over a mean of 3.2 years) was used for this work
References:	Org *et al.* (2009)
OHGS: Hypertensive cases from the **O**ttawa **H**eart **G**enomic **S**tudy	
BP ascertainment:	$\geq$ 140mmHg SBP, or $\geq$ 90mmHg DBP, or taking antihypertensive or BP lowering medication, before 65 years of age.
BP measurement:	Using a Philips IntelliVue MP5 at the time of consent (before any angiography was performed) or as close to the consenting date as possible.
OHGS: Controls from the **O**ttawa **H**eart **G**enomic **S**tudy	
BP ascertainment:	Not hypertensive and not currently receiving prescribed medication for hypertension, $\geq$ 65 years of age.
BP measurement:	Using a Philips IntelliVue MP5 at the time of consent (before any angiography was performed) or as close to the consenting date as possible.

Study	Details
BRHS: The **B**ritish **R**egional **H**eart **S**tudy	
BP ascertainment:	None.
Other ascertainment:	Male; recruited from general practices across Great Britain from 1978-1980.
BP measurement:	At re-examination in 1998-2000 (20 years after recruitment); measured twice in succession on the right arm, with the subject seated and the arm supported, using a Dinamap 1846 oscillometric BP recorder; the mean of 2 readings was used for this work; over-reading of SBP by the instrument was corrected in the analysis and readings were adjusted for observer variation within each town
References:	`http://www.ucl.ac.uk/pcph/research-groups-themes/brhs-pub`
EAS: The **E**dinburgh **A**rtery **S**tudy	
BP ascertainment:	None.
Other ascertainment:	Age stratified random sample of men and women, 55-74 years of age; selected between August 1987 and September 1988 from age-sex registers of ten general practices with a geographical and socio-economical catchment population spread throughout the city of Edinburgh, UK.
Exclusions:	Unfit to participate (e.g. due to severe mental illness or terminal disease); excluded individuals were replaced by other randomly sampled subjects.
BP measures:	Performed by specially trained research nurses, using standardised operating procedures. Systolic and diastolic (phase V) BP was recorded once in the right arm, after 10 minutes rest in the supine position, using a Hawksley random zero sphygmomanometer.
ELSA: The **E**nglish **L**ongitudinal **S**tudy of **A**geing	
BP ascertainment:	None.
Other ascertainment:	Over 50 years of age; recruited from the Health Surveys for England in 1998, 1999, and 2001. Genetic data were collected at wave 2 of the study (2004/5); the phenotype measurements taken at wave 2 were used for this study.
BP measurement:	Participants were visited in the home; heavy physical activity, smoking, and alcohol use were avoided for 30 minutes prior to measurement; 3 measurements in the seated position following 10 minutes of rest were takentaken using an OMRON HEM-907 instrument by a nurse; the mean was used for this work.
GBPG: The **G**lobal **BP G**enetics consortium meta-analysis	
BP ascertainment:	None.
BP measurement:	As described by Newton-Cheh *et al.* (2009); dichotomous hypertension (HTN) analyses were conducted using individuals with $\geq$ 140mmHg SBP or $\geq$ 90mmHg DBP or taking antihypertensive medication as cases, and using individuals with $\leq$ 120mmHg SBP and $\leq$ 85mmHg DBP and not taking antihypertensive medication as controls, and excluding individuals not matching either definition.
References:	(Newton-Cheh *et al.* 2009)

Study	Details
INTERGENE: The study of the **INTER**play between **GENE**tic susceptibility and environmental factors for the risk of chronic diseases	
BP ascertainment:	None.
Other ascertainment:	Randomly sampled women and men 25-74 years of age and living in the Västra Götaland region of Western Sweden, between 2001 and 2004, were invited to participate.
BP measurement:	Measured twice in the sitting position after a 5 minute rest by trained research nurses, with a validated OMROM 711 Automatic IS intrument (Golara *et al.* 2002); the mean of 2 valid measurements was used for this work.
References:	Berg *et al.* (2009), Strandhagen *et al.* (2010)
MRC NSHD: The **M**edical **R**esearch **C**ouncil **N**ational **S**urvey of **H**ealth and **D**evelopment	
BP ascertainment:	None.
Other ascertainment:	Birth cohort study consisting of a stratified random sample of all births in England, Scotland and Wales in 1 week in March 1946
BP measurement:	In 1999 when cohort members were 53 years of age; measured twice, seated and after 5 minutes of rest, in their own homes by research nurses using an Omron HEM-705 instrument; the 2nd reading was used for this work.
References:	Wadsworth *et al.* (2006), `http://www.nshd.mrc.ac.uk`
NPHSII: The **N**orthwick **P**ark **H**eart **S**tudy	
BP ascertainment:	None.
Other ascertainment:	Prospective study of healthy middle-aged men, 50-64 years of age at recruitment; sampled from nine United Kingdom general practices between 1989 and 1994
Exclusions:	History of unstable angina or acute myocardial infarction; a major Q wave on the ECG; regular antiplatelet or anticoagulant therapy; cerebrovascular disease; life-threatening malignancy.
BP measures:	Recorded with a random-zero sphygmomanometer (average of 2 measurements) at study baseline.
References:	Cooper *et al.* (2000)
Whole blood and tissue panel	
Samples:	Combination of $N = 1469$ peripheral whole blood samples, and tissue panel from $N = 85$ individuals with subcutaneous and visceral adipose tissue, liver tissue and muscle tissue; all samples from unrelated individuals of European ancestry.
RNA measurement:	Complementary RNA hybridized to Illumina HumanRef-8 v2 arrays ($N = 229$ peripheral blood samples) or to Illumina HumanHT-12 arrays ($N = 1,240$ peripheral blood samples, $N = 83$ subcutaneous adipose samples, $N = 77$ visceral adipose samples, $N = 74$ liver samples, $N = 62$ muscle samples), and scanned on the Illumina BeadArray Reader.
Normalisation:	Raw probe intensities extracted using Illumina BeadStudio Gene Expression module v3.2 (no background correction applied, no probes with low expression removed); HumanRef-8 and HumanHT-12 datasets quantile normalized separately to the median distribution; expression values $\log_2$ transformed then affinely scaled to have zero mean and unit variance.
Batch effects:	HumanRef-8 and HumanHT-12 datasets separately analysed using PCA; residual expression levels calculated by regressing onto 50 PCs that strongly affect gene expression levels but reflect among others technical (batch) effects; for each individual in the tissue panel, residuals then averaged over tissues.

Study	Details
Monocytes	
Samples:	Monocytes from $N = 758$ individuals, comprising $N = 395$ healthy blood donors (recruited from one Centre) and $N = 363$ patients with premature myocardial infarction (recruited from 4 centres), assembled by the Cardiogenics consortium; all subjects of white European descent.
RNA measurement:	RNA extracted from monocytes isolated from whole blood with CD14 micro beads (AutoMacs Pro, Miltenyi); mRNA amplified and labelled using Illumina Total Prep RNA Amplification Kit (Ambion, Inc., Austin, TX); hybridized to Illumina HumanRef-8 arrays, and scanned using the Illumina BeadArray Reader.
Normalisation:	Probe intensities extracted using the Illumina Bead Studio Gene Expression module. Variance Stabilization Transformation (VST) was applied to the raw intensities and quantile normalization was performed in the R statistical environment (R Development Core Team 2004) using the Lumi and Beadarray packages.
Level quantification:	Transcripts were categorised according to whether expression was within the top 20%, the bottom 20% or between 20-80% of genes expressed to give an indication of the relative level of expression (high, low or medium, respectively) for that gene in monocytes.

Table S3: **Genotyping, quality control and association analyses.**

Study	Details
AIBIII, ASCOT, BRIGHT cases and controls, MDC, NBS and NORDIL	
Genotyping:	Illumina HumanCVD BeadChip (Illumina, San Diego, CA) following manufacturer's protocol.
Genotype calling:	Intensity data normalised using Illumina BeadStudio; genotypes called using Illuminus (Teo *et al.* 2007) in two batches, corresponding to UK/Irish ancestry (AIBIII, ASCOT, BRIGHT and NBS) and to Nordic ancestry (MDC and NORDIL), for a total of $N = 12420$ samples.
Sample call rate:	Excluded samples on whole/half plates with low call rate ($N = 204$); excluded samples with genotyping rate < 0.98 (taken over SNPs with good clustering, defined as Illuminus perturbation score > 0.9; $N = 116$).
Sample duplicates:	Merged genotypes for deliberate duplicate pairs ($N = 17$); excluded samples with inconsistent data across duplicates ($N = 2$); excluded accidental duplicates ($N = 144$).
Sample relatedness:	Excluded lower-call-rate samples from first degree relative pairs ($N = 87$).
Sample ancestry:	Ancestry PCA (Price *et al.* 2006) in two batches corresponding to UK/Irish ancestry and to Nordic ancestry, using an LD-pruned set of $\sim 14,000$ SNPs; excluded outliers (defined as > 6 standard deviations from the mean in any of the first 10 dimensions) over 5 iterated rounds of ancestry PCA ($N = 220$).
Sample sex checks:	Excluded samples with X chromosome heterozygosity inconsistent with phenotypic sex ($N = 153$).
SNP exclusions:	Separately for UK/Irish ancestry and for Nordic ancestry samples: Excluded SNPs with call rate < 0.9975; excluded SNPs with Hardy–Weinberg $P < 10^{-6}$ in either cases alone, controls alone, or cases and controls combined; excluded SNPs with differential missingness between cases and controls at $P < 10^{-6}$; excluded SNPs with MAF < 0.01 for dichotomous hypertension analyses.
Association analyses:	Normal linear model and logistic regression using PLINK (Purcell *et al.* 2007); analysed as 3 groups (ASCOT vs. AIBIII+NBS, BRIGHT cases vs. controls, NORDIL vs. MDC) for dichotomous hypertension; analysed as 2 groups (AIBIII+ASCOT+BRIGHT, MDC+NORDIL) for continuous trait analyses to maintain approximate balance between high and low BP individuals because no BP phenotype data for NBS; first 10 PCs from ancestry PCA used as covariates.
BWHHS	
Genotyping:	Illumina HumanCVD BeadChip following manufacturer's protocol (Illumina, San Diego, CA).
Genotype calling:	Intensity data normalised and genotypes called using Illumina BeadStudio (v3) Genotyping Module.
Sample ancestry:	Ancestry PCA Price *et al.* (2006) confirmed self-reported ethnicity; excluded individuals on the basis of non-European ancestry ($N = 32$).
SNP exclusions:	Excluded SNPs with call rate < 0.98; excluded SNPs with Hardy–Weinberg $P < 10^{-6}$ in combined sample. excluded SNPs with MAF < 0.01 for dichotomous hypertension analyses.
Association analyses:	Normal linear model and logistic regression using PLINK (Purcell *et al.* 2007); age, age^2 and BMI used as covariates.
GRAPHIC	
Genotyping:	Illumina HumanCVD BeadChip following manufacturer's protocol (Illumina, San Diego, CA).
Genotype calling:	Intensity data normalised and genotypes called using Illumina BeadStudio (v3) Genotyping Module.

Study	Details
Sample call rate:	Excluded individuals with < 0.90 overall genotyping call rate ($N = 13$).
SNP exclusions:	Excluded SNPs with call rate < 0.98; excluded SNPs with Hardy–Weinberg $P < 10^{-6}$ in combined sample. excluded SNPs with MAF < 0.01 for all analyses.
Association analyses:	Normal linear regression and logistic regression, fitted using generalized estimating equations with exchangeable correlation structure to account for familial correlations; sex, age, age^2 and BMI used as covariates.
PROCARDIS	
Genotyping:	Illumina HumanCVD BeadChip following manufacturer's protocol (Illumina, San Diego, CA).
Genotype calling:	Intensity data normalised and genotypes called using Illumina BeadStudio (v3) Genotyping Module.
Sample call rate:	Excluded individuals with < 0.95 call rate ($N = 2$).
Sample duplicates:	Excluded duplicate samples ($N = 6$).
Sample relatedness:	Identity-by-state (IBS) analysis identified cryptically closely-related individuals as well as providing information to confirm or revise self-reported full/half-sib relationships between some (21%) individuals.
Sample sex checks:	Sex codes revised to genotype sex for 20 individuals. Males with heterozygous X-chromosome genotypes were excluded (on a marker by marker basis).
SNP exclusions:	Excluded SNPs with call rate < 0.98; excluded SNPs with Hardy–Weinberg $P < 10^{-6}$ in combined sample. excluded SNPs with MAF < 0.01 for all analyses.
Association analyses:	Normal linear model and logistic regression, with robust sandwich estimators of variance (Williams 2000) to allow for familial clustering (full and half-siblings), calculated using Stata (version 10.1); country-of-origin used as a categorical covariate; sex, age, age^2 and BMI used as covariates.
WHII	
Genotyping:	DNA was stored from over 6,000 participants that provided a blood sample at phase 7; Illumina HumanCVD BeadChip following manufacturer's protocol (Illumina, San Diego, CA).
Genotype calling:	Intensity data normalised and genotypes called using Illumina BeadStudio (v3) Genotyping Module.
Sample call rate:	Excluded samples with call rate < 0.80.
Sample ancestry:	Excluded outliers in a multidimensional scaling analysis based on the genome-wide identity-by-state, as implemented in PLINK (Purcell *et al.* 2007).
SNP exclusions:	Excluded SNPs with call rate < 0.98; excluded SNPs with Hardy–Weinberg $P < 10^{-6}$ in combined sample. excluded SNPs with MAF < 0.01 for dichotomous hypertension analyses.
Association analyses:	Normal linear model and logistic regression using PLINK (Purcell *et al.* 2007); sex, age, age^2 and BMI used as covariates.
BRHS, ELSA, INTERGENE and MRC NSHD	
Genotyping:	KASPAR assay at KBiosciences.
Genotype calling:	By KBiosciences.
SNP exclusions:	Excluded SNPs with call rate < 0.95; excluded SNPs with Hardy–Weinberg $P < 0.005$.
Association analyses:	Analysed by cohort; normal linear regression and logistic regression using PLINK (Purcell *et al.* 2007) and R (R Development Core Team 2004); sex, age, age^2 and BMI used as covariates when not invariant.
EAS, HYPEST and NPHSII	
Genotyping:	KASPAR assay at Bart's and the London Genome Center.

Study	Details
Genotype calling:	Image processing and genotype calling using SDS (Applied Biosystems); genotype calling using Autocaller (Applied Biosystems); genotypes discrepant between the two calling algorithms manually inspected and corrected.
SNP exclusions:	Excluded SNPs with call rate < 0.95; excluded SNPs with Hardy–Weinberg $P < 0.005$.
Association analyses:	Analysed by cohort; normal linear regression and logistic regression; sex, age, age^2 and BMI used as covariates for population cohorts (EAS and NPHSII).
HYPERGENES cases and controls	
Genotyping:	Human 1M-duo BeadChip (Illumina Inc, San Diego, CA, USA).
Sample call rate:	Excluded if call rate ≤ 0.95.
Sample ancestry:	25 outliers excluded in ancestry PCA (Price *et al.* 2006).
SNP exclusions:	Excluded if call rate < 0.99 or Hardy-Weinberg $P < 10^{-8}$ or MAF < 0.01.
SNP imputation:	Not needed because the Human 1M-duo BeadChip includes all SNPs on the HumanCVD BeadChip.
Association analyses:	Normal linear regression and logistic regression; first 10 PCs from ancestry PCA used as covariates.
OHGS cases and controls	
Genotyping:	Genechip® Human Mapping 500K Array set (Affymetrix, Santa Clara, CA); Genome-Wide Human SNP Array 6.0 (Affymetrix, Santa Clara, CA)
Genotype calling:	Dynamic module algorithm and BRLMM algorithm for 500K Array set; Birdseed algorithm for 6.0 Array.
Sample call rate:	All samples > 0.93 for dynamic module algorithm, > 0.98 for BRLMM algorithm; mean call rate 0.993 for Birdseed algorithm.
Sample ancestry:	Outliers excluded in ancestry PCA (Price *et al.* 2006).
SNP exclusions:	Only 482,251 SNPs common between 500K Array set and 6.0 Arrays were used; SNPs excluded if call rate < 0.95; or if Hardy-Weinberg $P < 10^{-4}$; or if MAF < 0.01.
SNP imputation:	Using IMPUTE (version 0.5.0; Marchini *et al.* 2007) and a HapMap CEU reference panel International HapMap Consortium (2007).
Association analyses:	Normal linear model and logistic regression, using the "-proper" option in SNPTEST to account for uncertainty in imputed genotypes (Marchini *et al.* 2007); first 10 PCs from ancestry PCA used as covariates.
GBPG	
Genotyping etc.:	Genotyping, QC, and SNP imputation have all been described previously (Newton-Cheh *et al.* 2009).
Association analyses:	Normal linear regression and logistic regression by individual cohorts (Newton-Cheh *et al.* 2009). To avoid double counting of samples, we reran the GBPG meta-analyses, excluding results from $N = 795$ individuals from the PROCARDIS study that had been genotyped on the Illumina Human1M-Duo BeadChip, and that partly overlap with the $N = 3,198$ individuals from the PROCARDIS study genotyped on the HumanCVD BeadChip and used in our discovery analysis.
Whole blood and tissue panel	
SNP Genotyping:	Using HumanHap300, HumanHap370, Human 610-Quad, and Omni1-Quad BeadChips (Illumina, San Diego, USA), according to standard protocols from Illumina.
SNP exclusions:	Analysis confined to 294,757 SNPs that are genotyped by all the genotyping arrays used; excluded SNPs with call rate < 0.95, Hardy–Weinberg $P < 0.001$, or MAF < 0.05.
SNP imputation:	Using IMPUTE (v2.0; Marchini *et al.* 2007) and phased haplotypes from the HapMap II release 22 CEU reference panel (International HapMap Consortium 2007).

Study	Details
Association analysis:	Meta-analysis of all samples (final sample size $N = 1,554$) performed for association with each transcript in turn, using normal linear regression models and testing all SNPs within a window extending 500kb either side of the probe centre.
Multiple testing:	False discovery rate (FDR) controlled at 5%, by permuting the data 100 times using the average of the expression of the four tissues in the panel (Tusher *et al.* 2001), giving significance threshold $P < 10^{-3}$ for *cis*-acting eSNPs.
***Trans*-analysis:**	For the SOX6 index SNP we searched for *trans*-acting effects using an identical analysis except that all probes were tested for association, and applied FDR control separately for this analysis because of the larger multiple testing burden.
Monocytes	
SNP genotyping:	Genomic DNA was extracted from peripheral blood by standard procedures. Whole-genome genotyping was carried out using either the Human Custom 1.2M or the Human Quad Custom 670 arrays from Illumina.
Proxy SNPs:	Where the index SNP was not directly genotyped, proxy SNPs (with $r^2 > 0.9$) were used where available: rs1801131 ($r^2 = 0.93$ with rs4846048 at MTHFR-NPPB); rs129128 ($r^2 = 1$ with rs1799945 at HFE); rs2681472 ($r^2 = 1$ with rs11105354 at ATP2B1); no good proxy was available for rs3918226 at NOS3 or rs661348 at LSP1/TNNT3.
Association analyses:	*cis*-associations tested for all transcripts within 1 Mb of each index SNP; association tested using additive regression models adjusted for age, gender and centre status using Stata (version 11).
Multiple testing:	Raw (unadjusted) association P-values for all transcripts were reported; in the text we refer only to associations wtih $P \leq 10^{-4}$.

Table S4: **Estimates of non-ascertained phenotypic SDs for ascertained studies.**

Study	Phenotypic SD	— Phenotype —			
		DBP	MAP	PP	SBP
AIBIII+ASCOT+BRIGHT					
	Ascertained (observed data)	16.09	19.77	17.50	29.32
	Nonascertained (estimated[a])	12.02	13.86	12.31	19.71
	Ratio[b]	1.34	1.43	1.42	1.49
MDC+NORDIL					
	Ascertained (observed data)	16.99	21.87	18.13	32.80
	Nonascertained (estimated[a])	11.79	13.32	11.28	18.41
	Ratio[b]	1.44	1.64	1.61	1.78
HYPERGENES					
	Ascertained (observed data)	12.86	14.27	10.54	18.82
	Nonascertained (estimated[a])	12.81	14.46	12.75	20.18
	Ratio[b,c]	1.00	0.99	0.83	0.93
OHGS					
	Ascertained (observed data)	11.35			17.12
	Nonascertained (estimated[a])	11.94			19.72
	Ratio[b,c]	0.95			0.87

Notes: **a.** For each ascertained study, the SD of the corresponding population or non-ascertained BP trait distribution was estimated, using the following linear regression models that were estimated in a non-ascertained cohort (WHII):

$$\begin{aligned}
\text{DBP} &= \text{const} - 2.36 \times \text{SEX} + 1.03 \times \text{AGE} - 0.00678 \times \text{AGE}^2 + 0.933 \times \text{BMI} + E \\
\text{MAP} &= \text{const} - 2.60 \times \text{SEX} + 0.682 \times \text{AGE} - 0.00212 \times \text{AGE}^2 + 1.01 \times \text{BMI} + E \\
\text{PP} &= \text{const} - 0.746 \times \text{SEX} - 1.05 \times \text{AGE} + 0.0140 \times \text{AGE}^2 + 0.220 \times \text{BMI} + E \\
\text{SBP} &= \text{const} - 3.10 \times \text{SEX} - 0.019 \times \text{AGE} + 0.00721 \times \text{AGE}^2 + 1.153 \times \text{BMI} + E
\end{aligned}$$

We assume the population phenotypic variance can be decomposed into a component for the specific demographic composition of each ascertained study (calculated using coefficients estimated in a non-ascertained sample; for SEX coded 1 for males and 2 for females; AGE in years; and BMI in kg/m^2), and a further independent component (again estimated in a non-ascertained sample; with SD(E) = 10.9mmHg for DBP; 12.3mmHg for MAP; 10.8mmHg for PP; and 17.2mmHg for SBP). **b.** As illustrated in Figure S6, we estimated each inflation correction factor r_i as the ratio of phenotypic variances, i.e. the square of the ratio of phenotypic SDs. For non-ascertained studies $r_i = 1$. If $\hat{\beta}_i$ and s_i are the effect size estimate and standard error for the i-th study, standard inverse variance weighted (IVW) meta-analysis gives

$$\hat{\beta}_{\text{IVW}} = \sum_i \hat{\beta}_i s_i^{-2} \Big/ \sum_i s_i^{-2} \qquad \text{with} \quad s_{\text{IVW}} = \sqrt{1 \Big/ \sum_i s_i^{-2}}$$

Our alternatively weighted (AW) meta-analysis replaces $\hat{\beta}_i$ by $\hat{\beta}_i / r_i$, and therefore replaces s_i by s_i / r_i, and thus gives

$$\hat{\beta}_{\text{AW}} = \sum_i r_i \hat{\beta}_i s_i^{-2} \Big/ \sum_i r_i^2 s_i^{-2} \qquad \text{with} \quad s_{\text{AW}} = \sqrt{1 \Big/ \sum_i r_i^2 s_i^{-2}}$$

Note that our alternative weighting does not affect the false positive rate (because a well calibrated standard error can be calculated for any linear combination of the $\hat{\beta}_i$, assuming well calibrated s_i and independence of the $\hat{\beta}_i$), and that it maximises power when all studies (ascertained and non-ascertained) are unbiasedly estimating equivalent population parameters after rescaling. **c.** Because we have estimated the ratio of phenotypic SDs using a demographic model with coefficients estimated in a convenience population, and not from the actual populations from which the ascertained samples were drawn, the estimated ratio can be less than one due to imprecision or bias. In these cases we used no inflation correction i.e. we used $r_i = 1$.

Table S5: **Inter-trait test statistic correlation matrix.**

— Spearman correlation —[a]

	DBP	SBP	MAP	PP	HTN
DBP	1	0.83[b]	0.96[c]	0.45	0.67[d]
SBP		1	0.95[c]	0.86[c]	0.70[d]
MAP			1	0.66	0.72[d]
PP				1	0.53[d]
HTN					1

— Eigenvalues —

3.96	0.64	0.39	0.015	0.0012 [e]

— Effective number of tests —

$M_{\text{eff}} = 2.7577$ [f]

Notes: **a.** We calculated the Spearman correlation (ρ) between meta-analysis association statistics (for our full discovery dataset) for each pairwise combination of phenotypes, over all SNPs analysed. For clarity only the upper triangle of the correlation matrix is shown. The Spearman correlation is relatively robust to "outliers" caused by true positive associations, and when association statistics for most SNPs follow the multivariate normal null distribution, it provides a robust estimate of the Pearson correlation (r) between null test statistics. Extremely similar results were observed when we calculated the correlations only over SNPs with meta-analysis sample sizes $> 50\%$ of the maximum sample size (not shown). **b.** The correlation between DBP and SBP is higher than the phenotypic correlation typically observed in general population samples, because of the inclusion of samples ascertained from the extremes of the BP distribution in our analysis. **c.** As expected, there is a strong correlation between MAP and both DBP and SBP, and between PP and SBP. Thus, testing these four continuous BP phenotypes in parallel will have at best a minor power advantage over simply testing DBP and SBP as in most previous studies, and would potentially incur a power disadvantage unless the inter-phenotype correlations are taken into account when correcting for multiple testing. **d.** The weaker correlation with dichotomous hypertension (HTN) arises in part because of the additional cohort (NBS) used in that analysis, and hence in our study the correlation is lower than would be observed if a common set of individuals were used for all analyses. **e.** The near rank deficiency of the 5×5 correlation matrix is expected because the PP and MAP phenotype vectors are linear combinations of the DBP and SBP phenotype vectors, and hence normal linear model association test statistics for PP and MAP are linear combinations of the association test statistics for DBP and SBP, and so the 5×5 Pearson correlation matrix for association test statistics computed for a single study with unrelated individuals has rank 3. **f.** The generally high inter-trait correlations imply that the effective number of tests is $M_{\text{eff}} = 2.7577$ when all 5 traits are tested in parallel, using the estimate of Nyholt (2004). For small correlation matrices, we prefer the method of Nyholt (2004) because it gives an effective number of tests that is an analytically continuous function of the Eigenvalues of the correlation matrix, whereas the method of Li and Ji (2005) is extremely sensitive to any individual Eigenvalue changing from slightly-above to slightly-below any integer value.

Table S6: **Effective number of tests by chromosome.**

Chromosome	— BRIGHT —[a]			— NORDIL+MDC —[b]		
	#SNPs[c]	— M_{eff} —[d]		#SNPs[c]	— M_{eff} —[d]	
		Nyholt	Li and Ji[e]		Nyholt	Li and Ji[e]
1	5078	5072.75	2284.34	5002	4996.78	2259.20
2	2821	2816.96	1476.75	2812	2807.83	1448.33
3	2062	2058.49	1135.90	2037	2033.48	1120.43
4	1939	1934.34	1027.98	1894	1889.27	996.64
5	2030	2025.75	1076.77	2035	2030.58	1067.17
6	2538	2531.06	1212.77	2549	2541.86	1210.64
7	2003	1998.71	1064.69	2010	2005.65	1066.37
8	2126	2118.93	990.93	2108	2100.75	980.14
9	1576	1571.88	874.47	1574	1569.8	871.38
10	2084	2079.16	1061.63	2064	2059.11	1046.21
11	2760	2755.97	1394.61	2717	2712.97	1374.25
12	2520	2515.44	1288.66	2518	2513.25	1259.52
13	909	905.99	540.88	899	895.91	532.26
14	853	849.87	523.89	850	846.75	512.08
15	1383	1378.25	712.53	1381	1376.1	697.21
16	1461	1456.8	768.54	1451	1446.67	756.90
17	1839	1835.6	1026.95	1825	1821.61	1009.50
18	570	567.46	365.40	566	563.36	358.67
19	1633	1630.05	960.81	1603	1600.08	951.42
20	990	987.49	611.05	965	962.51	598.38
21	639	632.89	326.28	632	625.62	316.55
22	752	749.22	454.58	735	732.12	435.11
Totals	40566	40473.06	21180.41	40227	40132.04	20868.36

Notes: **a.** Genotype data from the N=3,657 BRIGHT cases and controls, which we assumed was representative of allele frequencies and LD patterns in European ancestry samples in general. **b.** Genotype data from the $N = 3,771$ NORDIL/MDC cases and controls, which gives very similar results to the BRIGHT data. **c.** Number of polymorphic SNPs. **d.** We found that it was computationally efficient to compute the Eigenvalues of the genotype correlation matrix for each chromosome directly from the singular value decomposition (SVD) of the normalised genotype matrix, thus avoiding the steps of explicitly calculating or decomposing the correlation matrix. **e.** For large correlation matrices, the method of Li and Ji (2005) has been shown in simulation tests to estimate the effective number of tests more accurately and less conservatively than the method of Nyholt (2004). The sensitivity mentioned in Table S5 note f. is less important because it averages out over the very large number of Eigenvalues.

Table S7: **Discovery results for top 10 SNPs and 5 BP phenotypes.**

Locus and SNP[a]	Phenotype	Alleles coded/ noncoded	— Discovery analysis — N	Coded freq.	β_{SNP}(SE)	P value
	DBP[b]	T/C	22693	0.08	0.8263(0.1766)	2.87×10^{-6}
NOS3	SBP	T/C	22693	0.08	0.7151(0.2570)	5.40×10^{-3}
	MAP	T/C	22693	0.08	0.7470(0.1920)	1.00×10^{-4}
rs3918226	PP	T/C	22693	0.08	0.0572(0.1701)	7.37×10^{-1}
	HTN	T/C	25050	0.08	0.1325(0.0367)	3.01×10^{-4}
	DBP	T/C	22684	0.57	-0.5743(0.0962)	2.36×10^{-9}
LSP1/TNNT3	SBP	T/C	22684	0.57	-0.8414(0.1425)	3.57×10^{-9}
	MAP[b]	T/C	22684	0.57	-0.6502(0.1055)	7.00×10^{-10}
rs661348	PP	T/C	22684	0.57	-0.3992(0.0945)	2.42×10^{-5}
	HTN	T/C	25042	0.57	-0.1183(0.0203)	5.78×10^{-9}
	DBP	T/C	22690	0.21	0.4979(0.1184)	2.59×10^{-5}
SOX6	SBP	T/C	22690	0.21	0.7771(0.1762)	1.03×10^{-5}
	MAP[b]	T/C	22690	0.21	0.5763(0.1301)	9.38×10^{-6}
rs2014408	PP	T/C	22690	0.21	0.3983(0.1168)	6.46×10^{-4}
	HTN	T/C	25048	0.21	0.0821(0.0248)	9.13×10^{-4}
	DBP	G/A	22659	0.58	-0.2282(0.0970)	1.86×10^{-2}
NUCB2-ABCC8	SBP	G/A	22659	0.58	-0.5982(0.1435)	3.05×10^{-5}
	MAP	G/A	22659	0.58	-0.3497(0.1062)	9.94×10^{-4}
rs2074311	PP[b]	G/A	22659	0.58	-0.4468(0.0951)	2.62×10^{-6}
	HTN	G/A	25017	0.58	-0.0488(0.0203)	1.64×10^{-2}
	DBP[b]	T/C	22662	0.61	0.4703(0.0985)	1.80×10^{-6}
CACNA1C	SBP	T/C	22662	0.61	0.5889(0.1453)	5.07×10^{-5}
	MAP	T/C	22662	0.61	0.4925(0.1077)	4.85×10^{-6}
rs3819526	PP	T/C	22662	0.61	0.2511(0.0963)	9.12×10^{-3}
	HTN	T/C	25020	0.61	0.0765(0.0208)	2.31×10^{-4}
	DBP[b]	T/G	22659	0.33	-0.5536(0.1025)	6.73×10^{-8}
MTHFR-NPPB	SBP	T/G	22659	0.33	-0.6930(0.1517)	4.91×10^{-6}
	MAP	T/G	22659	0.33	-0.5803(0.1123)	2.39×10^{-7}
rs4846049	PP	T/G	22659	0.33	-0.2671(0.1006)	7.90×10^{-3}
	HTN	T/G	25014	0.33	-0.0924(0.0217)	2.01×10^{-5}
	DBP	T/C	22686	0.24	0.5605(0.1123)	5.94×10^{-7}
AGT	SBP	T/C	22686	0.24	0.7299(0.1661)	1.11×10^{-5}
	MAP	T/C	22686	0.24	0.5972(0.1230)	1.21×10^{-6}
rs2004776	PP	T/C	22686	0.24	0.3000(0.1100)	6.40×10^{-3}
	HTN[b]	T/C	25042	0.24	0.1379(0.0235)	4.28×10^{-9}
	DBP	G/C	22662	0.39	-0.3903(0.0985)	7.39×10^{-5}
NPR3	SBP[b]	G/C	22662	0.39	-0.6683(0.1461)	4.77×10^{-6}
	MAP	G/C	22662	0.39	-0.4761(0.1080)	1.04×10^{-5}
rs1421811	PP	G/C	22662	0.39	-0.3737(0.0968)	1.13×10^{-4}
	HTN	G/C	25018	0.39	-0.0895(0.0208)	1.66×10^{-5}
	DBP[b]	G/C	22677	0.15	0.6164(0.1377)	7.56×10^{-6}
HFE	SBP	G/C	22677	0.15	0.6408(0.2048)	1.75×10^{-3}
	MAP	G/C	22677	0.15	0.5949(0.1513)	8.43×10^{-5}
rs1799945	PP	G/C	22677	0.15	0.1605(0.1354)	2.36×10^{-1}
	HTN	G/C	25034	0.15	0.1089(0.0284)	1.25×10^{-4}
	DBP	G/A	22671	0.16	-0.6615(0.1319)	5.30×10^{-7}
ATP2B1	SBP	G/A	22671	0.16	-1.0013(0.1963)	3.37×10^{-7}
	MAP	G/A	22671	0.16	-0.7607(0.1449)	1.54×10^{-7}
rs11105354	PP	G/A	22671	0.16	-0.4644(0.1298)	3.48×10^{-4}
	HTN[b]	G/A	25029	0.16	-0.1538(0.0276)	2.41×10^{-8}

Notes: **a.** Results are shown for the 10 SNPs followed up in additional samples. **b.** Primary phenotype, which for each SNP is defined as the phenotype with smallest discovery analysis association P value.

Table S8: **Followup results for top 10 SNPs and 5 BP phenotypes.**

Locus and SNP	Phenotype	Alleles coded/ noncoded	— Followup analysis — N	Coded freq.	β_{SNP}(SE)	P value[a] one-tailed	Heterogeneity Q	P
	DBP[b]	T/C	21065	0.09	0.7820(0.2096)	9.53×10^{-5} ***	18.96	0.0042
NOS3	SBP	T/C	21065	0.09	1.3059(0.3065)	1.02×10^{-5}	12.31	0.0554
	MAP	T/C	21065	0.09	0.9727(0.2312)	1.30×10^{-5}	17.01	0.0093
rs3918226	PP	T/C	21065	0.09	0.3066(0.2265)	8.80×10^{-2}	5.23	0.5145
	HTN	T/C	21065	0.09	0.1560(0.0375)	1.58×10^{-5}	17.79	0.0068
	DBP	T/C	39325	0.55	-0.2245(0.0794)	2.35×10^{-3}	9.12	0.17
LSP1/TNNT3	SBP	T/C	39345	0.55	-0.4293(0.1162)	1.11×10^{-4}	8.72	0.19
	MAP[b]	T/C	39335	0.55	-0.3067(0.0868)	2.04×10^{-4} **	9.97	0.13
rs661348	PP	T/C	39335	0.55	-0.1498(0.0819)	3.37×10^{-2}	5.21	0.52
	HTN	T/C	32115	0.55	-0.0260(0.0179)	7.37×10^{-2}	6.06	0.42
	DBP	T/C	53754	0.19	0.2628(0.0866)	1.21×10^{-3}	9.62	0.21
SOX6	SBP	T/C	53750	0.19	0.3298(0.1287)	5.19×10^{-3}	7.03	0.43
	MAP[b]	T/C	50002	0.19	0.2979(0.0980)	1.19×10^{-3} *	8.94	0.18
rs2014408	PP	T/C	50002	0.19	-0.0044(0.0899)	5.19×10^{-1}	5.87	0.44
	HTN	T/C	42165	0.19	0.0526(0.0196)	3.70×10^{-3}	8.46	0.29
	DBP	G/A	51239	0.58	-0.1713(0.0721)	8.75×10^{-3}	11.11	0.09
NUCB2-ABCC8	SBP	G/A	51228	0.58	-0.2401(0.1063)	1.19×10^{-2}	17.01	0.01
	MAP	G/A	51233	0.58	-0.1890(0.0791)	8.41×10^{-3}	15.35	0.02
rs2074311	PP[b]	G/A	51233	0.58	-0.1048(0.0731)	7.58×10^{-2} NS	9.96	0.13
	HTN	G/A	38444	0.58	-0.0246(0.0168)	7.08×10^{-2}	9.35	0.15
	DBP[b]	T/C	58028	0.61	0.1026(0.0692)	6.91×10^{-2} NS	3.43	0.84
CACNA1C	SBP	T/C	58024	0.61	0.1479(0.1024)	7.43×10^{-2}	6.32	0.50
	MAP	T/C	54314	0.61	0.1148(0.0780)	7.06×10^{-2}	4.55	0.60
rs3819526	PP	T/C	54314	0.61	0.0735(0.0721)	1.54×10^{-1}	4.13	0.66
	HTN	T/C	43673	0.61	0.0155(0.0159)	1.65×10^{-1}	4.62	0.71
	DBP[b]	T/G	32267	0.31	-0.3353(0.0928)	1.52×10^{-4} **	NA[c]	
MTHFR-NPPB	SBP	T/G	32263	0.31	-0.4831(0.1380)	2.33×10^{-4}	NA[c]	
	MAP	T/G	32265	0.31	-0.3840(0.1017)	7.98×10^{-5}	NA[c]	
rs4846049	PP	T/G	32265	0.31	-0.0933(0.0902)	1.50×10^{-1}	NA[c]	
	HTN	T/G	18479	0.31	-0.0740(0.0274)	3.48×10^{-3}	NA[c]	
	DBP	T/C	86588	0.23	0.3200(0.0587)	2.50×10^{-8}	NA[c]	
AGT	SBP	T/C	86588	0.23	0.4200(0.0909)	1.90×10^{-6}	NA[c]	
	MAP	T/C	32586	0.23	0.1014(0.1132)	1.85×10^{-1}	NA[c]	
rs2004776	PP	T/C	32586	0.23	0.0213(0.1000)	4.16×10^{-1}	NA[c]	
	HTN[b]	T/C	86588	0.23	0.0800(0.0157)	1.85×10^{-7} ***	NA[c]	
	DBP	G/C	29220	0.38	-0.1560(0.0928)	4.64×10^{-2}	NA[c]	
NPR3	SBP[b]	G/C	29188	0.38	-0.3715(0.1379)	3.53×10^{-3} *	NA[c]	
	MAP	G/C	29204	0.38	-0.2372(0.1016)	9.79×10^{-3}	NA[c]	
rs1421811	PP	G/C	29204	0.38	-0.2185(0.0903)	7.78×10^{-3}	NA[c]	
	HTN	G/C	16907	0.38	-0.0733(0.0277)	4.05×10^{-3}	NA[c]	
	DBP[b]	G/C	32308	0.14	0.4998(0.1236)	2.62×10^{-5} ***	NA[c]	
HFE	SBP	G/C	32294	0.14	0.6619(0.1858)	1.83×10^{-4}	NA[c]	
	MAP	G/C	32301	0.14	0.5653(0.1363)	1.67×10^{-5}	NA[c]	
rs1799945	PP	G/C	32301	0.14	0.1774(0.1191)	6.82×10^{-2}	NA[c]	
	HTN	G/C	18451	0.14	0.1516(0.0369)	1.96×10^{-5}	NA[c]	
	DBP	G/A	33024	0.15	-0.3433(0.1199)	2.09×10^{-3}	NA[c]	
ATP2B1	SBP	G/A	33021	0.15	-0.5942(0.1815)	5.30×10^{-4}	NA[c]	
	MAP	G/A	33022	0.15	-0.4273(0.1328)	6.44×10^{-4}	NA[c]	
rs11105354	PP	G/A	33022	0.15	-0.2425(0.1152)	1.76×10^{-2}	NA[c]	
	HTN[b]	G/A	18760	0.15	-0.1196(0.0361)	4.55×10^{-4} **	NA[c]	

Notes: **a.** Only the primary phenotype for each SNP was tested, using a one-tailed test with effect direction pre-specified by the discovery analysis. With Bonferroni correction for 10 independent tests, results are annotated * $P \leq 0.05/10$; ** $P \leq 0.01/10$; *** $P < 0.001/10$. **b.** Primary phenotype (see Table S7). **c.** Heterogeneity test not performed when followup data were from existing meta-analysis results.

Table S9: **Discovery and followup combined results for top 10 SNPs and 5 BP phenotypes**

Locus and SNP	Phenotype	Alleles coded/ noncoded	— Combined[a] analysis — N	β_{SNP}(SE)	P value
	DBP[b]	T/C	43758	0.8079(0.1350)	2.19×10^{-9}
NOS3	SBP	T/C	43758	0.9590(0.1970)	1.12×10^{-6}
	MAP	T/C	43758	0.8391(0.1477)	1.34×10^{-8}
rs3918226	PP	T/C	43758	0.1472(0.1360)	2.79×10^{-1}
	HTN	T/C	46115	0.1440(0.0262)	3.95×10^{-8}
	DBP	T/C	62009	-0.3663(0.0612)	2.22×10^{-9}
LSP1/TNNT3	SBP	T/C	62029	-0.5938(0.0901)	4.32×10^{-11}
	MAP[b]	T/C	62019	-0.4454(0.0670)	2.98×10^{-11}
rs661348	PP	T/C	62019	-0.2567(0.0619)	3.37×10^{-5}
	HTN	T/C	57157	-0.0664(0.0134)	7.86×10^{-7}
	DBP	T/C	76444	0.3448(0.0699)	8.11×10^{-7}
SOX6	SBP	T/C	76440	0.4855(0.1039)	2.99×10^{-6}
	MAP[b]	T/C	72692	0.3987(0.0783)	3.52×10^{-7}
rs2014408	PP	T/C	72692	0.1455(0.0712)	4.11×10^{-2}
	HTN	T/C	67213	0.0640(0.0154)	3.20×10^{-5}
	DBP	G/A	73898	-0.1916(0.0579)	9.29×10^{-4}
NUCB2-ABCC8	SBP	G/A	73887	-0.3669(0.0854)	1.73×10^{-5}
	MAP	G/A	73892	-0.2463(0.0634)	1.03×10^{-4}
rs2074311	PP[b]	G/A	73892	-0.2319(0.0580)	6.33×10^{-5}
	HTN	G/A	63461	-0.0344(0.0129)	7.81×10^{-3}
	DBP[b]	T/C	80690	0.2242(0.0566)	7.53×10^{-5}
CACNA1C	SBP	T/C	80686	0.2942(0.0837)	4.40×10^{-4}
	MAP	T/C	76976	0.2447(0.0632)	1.08×10^{-4}
rs3819526	PP	T/C	76976	0.1373(0.0577)	1.74×10^{-2}
	HTN	T/C	68693	0.0381(0.0126)	2.57×10^{-3}
	DBP[b]	T/G	54926	-0.4336(0.0688)	2.96×10^{-10}
MTHFR-NPPB	SBP	T/G	54922	-0.5782(0.1021)	1.48×10^{-8}
	MAP	T/G	54924	-0.4724(0.0754)	3.71×10^{-10}
rs4846049	PP	T/G	54924	-0.1708(0.0671)	1.10×10^{-2}
	HTN	T/G	43493	-0.0853(0.0170)	5.20×10^{-7}
	DBP	T/C	109274	0.3716(0.0520)	9.03×10^{-13}
AGT	SBP	T/C	109274	0.4914(0.0797)	7.10×10^{-10}
	MAP	T/C	55272	0.3288(0.0833)	7.92×10^{-5}
rs2004776	PP	T/C	55272	0.1474(0.0740)	4.64×10^{-2}
	HTN[b]	T/C	111630	0.0979(0.0131)	6.74×10^{-14}
	DBP	G/C	51882	-0.2662(0.0675)	8.09×10^{-5}
NPR3	SBP[b]	G/C	51850	-0.5113(0.1003)	3.41×10^{-7}
	MAP	G/C	51866	-0.3494(0.0740)	2.36×10^{-6}
rs1421811	PP	G/C	51866	-0.2907(0.0660)	1.07×10^{-5}
	HTN	G/C	41925	-0.0837(0.0166)	4.80×10^{-7}
	DBP[b]	G/C	54985	0.5518(0.0920)	1.97×10^{-9}
HFE	SBP	G/C	54971	0.6523(0.1376)	2.12×10^{-6}
	MAP	G/C	54978	0.5786(0.1013)	1.10×10^{-8}
rs1799945	PP	G/C	54978	0.1701(0.0894)	5.73×10^{-2}
	HTN	G/C	43485	0.1248(0.0225)	2.89×10^{-8}
	DBP	G/A	55695	-0.4872(0.0887)	3.95×10^{-8}
ATP2B1	SBP	G/A	55692	-0.7818(0.1332)	4.43×10^{-9}
	MAP	G/A	55693	-0.5794(0.0979)	3.25×10^{-9}
rs11105354	PP	G/A	55693	-0.3402(0.0862)	7.86×10^{-5}
	HTN[b]	G/A	43789	-0.1412(0.0219)	1.14×10^{-10}

Notes: **a.** Our combined analysis was performed using all discovery and followup data. **b.** Primary phenotype (see Table S7).

Table S10: **Low frequency variant associations tested using gene dosage model.**

Gene[a]	–Num RV[b]–		–Mean RV[c]–		–SD RV[c]–		Best	–Association P value–		
	AABN	MN	AABN	MN	AABN	MN	pheno[d]	AABN	MN	Combined
TGFBR2	43	37	0.86	0.75	1.28	1.05	MAP	1.3×10^{-3}	0.43	1.9×10^{-3}
SCP2	21	22	0.58	0.63	1.3	1.35	DBP	0.14	0.06	0.02
IGF1R	73	73	2.85	3.33	4.76	5.55	MAP	0.05	0.20	0.02
PCSK6	31	31	0.63	0.75	0.89	1.08	HTN	0.16	0.09	0.03
NFKB1	35	26	1.04	0.58	1.66	0.92	MAP	0.02	0.82	0.03
TRAF2	24	21	0.42	0.46	1	1.02	HTN	0.08	0.34	0.04
UMOD[e]	1	1	0.10	0.01	0.31	0.12	DBP	0.07	0.41	0.05
LRP2	27	26	0.59	0.8	1.04	1.24	HTN	0.08	0.32	0.05
PPARD	46	48	1.36	1.38	2.77	3.25	DBP	0.19	0.15	0.05
ABCA4	24	24	1.02	1.1	1.45	1.7	DBP	0.63	0.02	0.05
NRG3	140	113	4.98	3.81	4.77	3.91	HTN	0.04	0.81	0.05
CD36	30	33	0.9	0.9	2.28	2.63	SBP	0.89	0.01	0.06
NPPB[e]	5	4	0.18	0.2	0.41	0.43	PP	0.06	0.45	0.06
IL1R1	21	22	0.37	0.34	0.78	0.77	PP	0.57	0.03	0.06
F5	39	33	0.74	0.79	0.9	1.05	PP	0.03	0.66	0.07
RYR2	65	69	1.92	2.29	2.23	2.39	PP	0.40	0.08	0.07
FLT1	22	21	0.46	0.62	0.81	0.88	PP	0.07	0.52	0.08
CYP1A2[e]	3	3	0.14	0.13	0.45	0.45	HTN	0.08	0.59	0.08
PCSK5	22	26	0.99	0.83	1.22	1.14	PP	0.19	0.28	0.09
ADRB1	11	11	0.37	0.38	0.66	0.68	SBP	0.39	0.13	0.10
RUNX1	30	27	0.78	0.69	1.41	1.31	SBP	0.12	0.52	0.11
NPR3[e]	1	2	0	0	0.04	0.03	DBP	0.39	0.13	0.11
SORCS1	50	50	1.24	1.41	2	2.28	DBP	0.13	0.48	0.11
ABCC4	34	25	0.9	0.66	1.59	0.98	PP	0.36	0.12	0.12
NOS1	52	55	0.69	0.56	1.22	1.07	PP	0.22	0.38	0.13
PON1	21	23	0.3	0.56	1	1.1	HTN	0.14	0.62	0.14
LTB	20	21	0.39	0.7	0.65	1.2	HTN	0.03	0.98	0.14
CUBN	36	34	1.06	1.4	1.77	2.41	DBP	0.94	0.05	0.14
TFPI	24	20	0.53	0.87	0.98	1.23	DBP	0.02	0.93	0.15
IGF1	29	21	0.82	1.03	1.53	1.75	DBP	0.16	0.54	0.15
TNNI3K	23	22	0.49	0.82	0.92	1.26	PP	0.03	0.95	0.15
CPA6	21	20	0.49	0.64	1.09	1.23	DBP	0.36	0.27	0.15
PCSK9	32	30	1.08	1.2	1.99	1.97	HTN	0.36	0.28	0.18
FTO	65	62	2.22	2.5	2.63	2.9	PP	0.22	0.52	0.18
MSRA	26	26	0.83	0.87	1.32	1.42	PP	0.85	0.03	0.19
PRKCB	24	20	0.59	0.61	0.85	0.84	PP	0.86	0.03	0.20
AGT	24	17	0.78	0.8	1.14	1.12	HTN	0.11	0.84	0.21
CDKN2BAS	26	31	0.24	0.23	0.84	0.88	HTN	0.08	0.74	0.22
SOX6[e]	14	13	0.16	0.23	0.65	0.87	DBP	0.32	0.45	0.22
SLC12A3[f]	6	7	0.2	0.21	0.44	0.45	SBP	0.39	0.39	0.23
TNF	20	21	0.38	0.72	0.62	1.21	HTN	0.06	0.98	0.23
VDR	26	20	0.67	0.62	1.16	1.09	PP	0.54	0.25	0.23
LSP1[e]	2	1	0.17	0.07	0.48	0.26	PP	0.41	0.28	0.23
LDLR	24	23	0.48	0.65	0.75	0.87	PP	0.92	0.08	0.25
GATA4[e]	9	9	0.08	0.06	0.36	0.32	HTN	0.14	0.80	0.25
ARHGAP6	35	43	2.22	2.61	6.05	6.95	DBP	0.32	0.54	0.25
PDE4B	39	40	0.75	1.26	1.72	2.17	SBP	0.51	0.35	0.26
PDE11A	20	20	0.34	0.33	0.67	0.6	HTN	0.34	0.58	0.27
CHUK	26	28	0.89	1.02	1.45	1.46	HTN	0.03	0.18	0.27
ACOT11	21	21	0.73	0.79	1.57	1.52	PP	0.51	0.01	0.28

Gene[a]	–Num RV[b]–		–Mean RV[c]–		–SD RV[c]–		Best	–Association P value–		
	AABN	MN	AABN	MN	AABN	MN	pheno[d]	AABN	MN	Combined
PPARA	31	28	0.39	0.5	0.85	0.82	PP	0.60	0.30	0.29
SCARB1	25	24	0.53	0.62	1.39	1.76	PP	0.78	0.11	0.31
NRG1	103	82	1.99	2.52	3.68	4.04	DBP	0.07	0.66	0.32
ESR1	79	82	2.13	2.34	2.5	2.9	HTN	0.36	0.71	0.34
ALOX5AP	27	29	0.97	1	1.34	1.22	DBP	0.93	0.16	0.34
TMEM117	22	29	0.69	0.97	1.44	1.62	HTN	0.20	0.88	0.34
CLCN6[e]	4	5	0.08	0.27	0.27	0.64	HTN	0.45	0.53	0.35
ABCA1	25	21	0.77	1.04	1.29	1.51	DBP	0.59	0.46	0.36
NOS3	21	24	0.14	0.17	0.38	0.41	MAP	0.94	0.18	0.39
LIPC	35	30	0.84	0.94	1.41	1.69	DBP	0.83	0.34	0.40
RXRA	49	44	0.84	1.13	1.08	1.44	HTN	0.42	0.74	0.40
SLC12A1[f]	5	14	0.15	0.29	0.53	0.81	HTN	0.35	0.83	0.40
TCF7L2	21	20	0.35	0.33	0.6	0.61	PP	0.83	0.36	0.45
KCNH8	29	32	0.66	0.86	1.36	1.72	PP	0.12	0.67	0.45
NPPA[e]	3	2	0.1	0.12	0.32	0.34	PP	0.21	0.84	0.45
VLDLR	40	29	0.84	0.8	1.56	1.63	HTN	0.31	0.86	0.45
TNFRSF1B	41	31	1.18	1.31	2.29	2.38	DBP	0.85	0.37	0.46
GAS7	34	33	0.63	0.68	1.06	1.11	HTN	0.32	0.84	0.47
RIPK1	32	32	1.03	1.06	2.15	2.1	MAP	0.05	0.17	0.49
STARD13	23	20	0.46	0.64	1.05	1.3	PP	0.66	0.60	0.49
CDKAL1	39	44	1.37	1.63	1.75	2.23	PP	0.45	0.83	0.50
FDFT1[e]	6	4	0.12	0.05	0.45	0.24	HTN	0.79	0.18	0.50
NOS2	27	23	0.53	0.63	0.86	0.91	PP	0.46	0.87	0.51
APOB	47	38	0.64	0.78	0.88	0.93	PP	0.45	0.91	0.52
BCL2	67	54	1.95	2.03	2.3	2.09	HTN	0.54	0.83	0.52
MTHFR[e]	5	7	0.01	0.27	0.08	0.64	HTN	0.91	0.53	0.52
AGTR1	28	21	0.54	0.41	1.14	0.86	PP	0.64	0.68	0.54
CACNA1C	70	63	2.31	2.31	2.72	2.68	HTN	0.84	0.13	0.55
CYP1A1[e]	3	5	0.05	0.17	0.23	0.4	PP	0.79	0.41	0.59
TNNT3[e]	1	1	0.02	0.02	0.13	0.15	HTN	0.33	0.67	0.60
GPR98	28	30	0.82	0.73	1.34	1.3	HTN	0.67	0.76	0.61
CYP17A1[e]	1	1	0	0	0.03	0.04	DBP	0.58	0.25	0.62
KCNQ1	35	28	1.13	0.8	1.62	1.06	PP	0.71	0.74	0.62
MSR1	31	39	0.5	1.32	0.91	2.82	PP	0.42	0.87	0.66
FAS	22	20	0.29	0.38	0.63	0.73	DBP	0.29	0.66	0.66
APP	52	51	1.87	2.48	4.77	5.77	HTN	0.29	0.47	0.66
F13A1	23	22	0.6	0.6	0.83	0.85	HTN	0.65	0.93	0.67
LRP1	37	36	1.17	1.04	1.33	1.17	PP	0.29	0.49	0.67
FURIN[e]	3	3	0.01	0	0.11	0.07	HTN	0.69	0.94	0.69
NOS1AP	51	51	2.16	2.02	3.12	2.96	HTN	0.24	0.21	0.70
PPARG	28	25	0.48	0.6	0.98	1.19	DBP	0.43	0.22	0.72
TBXAS1	40	37	1.02	1.02	1.49	1.66	HTN	0.52	0.65	0.78
ATP2B1[e]	5	5	0.22	0.17	0.57	0.7	SBP	0.77	0.91	0.90

Notes: **a.** We tested all genes with $\geq$ 20 low frequency ($0 < \text{MAF} \leq 0.05$) variants genotyped on the HumanCVD BeadChip, plus genes where either rare or common variant associations had been reported previously. **b.** For each gene, "Num RV" is the number of low frequency SNPs (extending 50kb from transcript ends), reported separately for the UK/Irish ancestry (AIBIII+ASCOT+BRIGHT+NBS; "AABN") and Nordic ancestry (MDC+NORDIL; "MN") datasets. **c.** "Mean RV" and "SD RV" are the mean and SD of low frequency allele dosage (count) over individuals. **d.** For each gene we tested association between each BP phenotype and the low frequency allele dosage. For testing five phenotypes and 93 genes, we use a significance threshold $P < 0.05/(2.758 \times 93) = 1.9 \times 10^{-4}$ to control the FWER at 5%. Because no associations were significant at this threshold, we present association results only for the most significantly associated phenotype ("best pheno"). **e.** Gene included because nearby common variant association discovered here (Table 1) or previously (Table S12). **f.** Gene included because rare variant association reported previously (Ji *et al.* 2008).

Table S11: **CNV tag-SNP results** for eight index SNPs.

Locus	Index SNP	Tag SNP[a]	–r^2–[b]		CNV	–CNV–		
			index:tag	tag:CNV	Name	Start	End	Type
MTHFR-NPPB	rs4846049	NA						
AGT	rs2004776	NA						
NPR3	rs1421811	NA						
HFE	rs1799945	NA						
NOS3	rs3918226	NA						
LSP1/TNNT3	rs661348	rs3817197[c]	0.24	1.00	CNVR5019.1	1862691	1864048	gain
SOX6	rs2014408	NA						
ATP2B1	rs11105354	NA						

Notes: **a.** We obtained lists of CNV-tSNPS from four sources: (i) 261 CNV-tSNPs, which tag CNVs at $r^2 > 0.8$, generated at the Broad Institute by typing HapMap samples on the Affymetrix 6.0 array. (ii) 2,174 CNV-tSNPs, which tag CNVs at $r^2 > 0.8$, made available by the Genomic Structural Variation consortium and based largely on typing 450 HapMap samples on a custom-made Agilent 105K array that is capable of genotyping $\sim 3,320$ CNVs in HapMap CEU. (iii) 3,113 CNV-tSNPs, generated using HapMap phase III samples genotyped using Affymetrix 6.0 and Illumina 1M arrays, generated by the HapMap 3 project. (iv) 2,905 CNV-tSNPs, generated using $\sim 19,000$ samples of European ancestry genotyped by the Wellcome Trust Case Control Consortium (3,000 controls and 2,000 cases for each of 8 diseases) using the same custom-made Agilent 105K array as used in (ii). Because these CNV-tSNP lists were derived using HapMap data but only list the best tagging SNP for each CNV, we first identified all $r^2 > 0.2$ proxies for our eight index SNPs using HapMap CEU r22, and then searched for all index SNPs plus these proxy SNPs in the CNV-tSNP lists. **b.** For tag SNPs thus identified we report the r^2 between the BP index SNP and the tag SNP, and the r^2 between the tag SNP and the CNV itself. **c.** The only CNV-tSNP identified was rs3817197, which is an almost perfect tag ($r^2 > 0.99$) for CNVR5019.1 and therefore we considered CNV-tSNP genotype to be equivalent to the genotype at the CNV itself. However, the CNV-tSNP rs3817197 is in relatively weak LD with our index SNP rs661348 at the LSP1/TNNT3 locus. The CNV-tSNP rs3817197 shows substantially weaker association with BP in our discovery data ($P = 3 \times 10^{-4}$ for MAP, compared with $P = 7 \times 10^{-10}$ for the index SNP, BF $< 10^{-4}$, see Table S13) such that the CNV-tSNP genotype (and therefore CNV genotype itself) cannot credibly explain the observed association at the LSP1/TNNT3 locus.

Table S12: **Association results for previously reported SNPs.**

Publication[a]	Locus	Reported SNP	Proxy[b] SNP(r^2)	–N–[c] cont./ HTN	Best[d] pheno	Best P value
Wang2008	STK39	rs6749447	—(1)	17354/21000	PP	0.125
Org2009	CDH13	rs11646213	NA			
Newhouse2009	WNK1	rs765250	rs6489752(0.67)	22693/25050	SBP	0.328
Newhouse2009	WNK1	rs765250	rs7980163(0.67)	18969/21327	SBP	0.082
Newhouse2009	WNK1	rs765250	rs10774464(0.59)	0/ 0		NA
Newhouse2009	WNK1	rs765250	rs10849559(0.57)	0/ 0		NA
Cho2009	ATP2B1	rs17249754	rs11105354(1)	22671/25029	HTN	2.41×10^{-8}
NewtonCheh2009a	NPPA/NPPB	rs5068	—(1)	22663/25021	DBP	8.48×10^{-5}
NewtonCheh2009a	NPPA/NPPB	rs5068	rs17375901(0.87)	1988/ 1988		NA
NewtonCheh2009b	MTHFR-NPPB	rs17367504	—(1)	22672/25030	DBP	3.56×10^{-6}
NewtonCheh2009b	MTHFR-NPPB	rs17367504	rs17037390(1)	22692/25049	DBP	3.71×10^{-6}
NewtonCheh2009b	MTHFR-NPPB	rs17367504	rs13306561(0.80)	22665/25023	DBP	3.24×10^{-6}
NewtonCheh2009b	MTHFR-NPPB	rs17367504	rs17037425(0.77)	22686/25044	DBP	1.22×10^{-5}
NewtonCheh2009b	MTHFR-NPPB	rs17367504	rs1537514(0.66)	22688/25046	DBP	1.36×10^{-4}
NewtonCheh2009b	MTHFR-NPPB	rs17367504	rs17037396(0.66)	22688/25046	DBP	1.81×10^{-4}
NewtonCheh2009b	MTHFR-NPPB	rs17367504	rs2066470(0.66)	22690/25048	DBP	7.74×10^{-5}
NewtonCheh2009b	MTHFR-NPPB	rs17367504	rs13306556(0.55)	22698/25056	DBP	1.27×10^{-4}
NewtonCheh2009b	MTHFR-NPPB	rs17367504	rs198358(0.55)	22648/25006	DBP	6.36×10^{-3}
NewtonCheh2009b	CYP17A1-NT5C2	rs11191548	NA			
NewtonCheh2009b	PLCD3	rs12946454	rs12603813(0.64)	0/ 0		NA
NewtonCheh2009b	FGF5	rs16998073	NA			
NewtonCheh2009b	C10orf107	rs1530440	NA			
NewtonCheh2009b	SH2B3	rs653178	rs3184504(1)	17334/20981	DBP	6.98×10^{-3}
NewtonCheh2009b	CYP1A1-CSK	rs1378942	rs2472304(0.83)	22663/25021	SBP	0.010
NewtonCheh2009b	CYP1A1-CSK	rs1378942	rs7085(0.79)	22691/25049	PP	0.024
NewtonCheh2009b	CYP1A1-CSK	rs1378942	rs2472300(0.63)	22669/25026	SBP	0.022
NewtonCheh2009b	CYP1A1-CSK	rs1378942	rs762551(0.63)	22687/25044	SBP	0.026
NewtonCheh2009b	ZNF652	rs16948048	NA			
Levy2009	CYP17A1	rs1004467	rs3824755(1)	22690/25047	SBP	3.84×10^{-4}
Levy2009	PLEKHA7	rs381815	NA			
Levy2009	ATP2B1	rs2681492	rs11105354(0.92)	22671/25029	HTN	2.41×10^{-8}
Levy2009	SH2B3	rs3184504	—(1)	17334/20981	DBP	6.98×10^{-3}
Levy2009	ULK4	rs9815354	NA			
Levy2009	CACNB2	rs11014166	NA			
Levy2009	ATP2B1	rs2681472	rs11105354(1)	22671/25029	HTN	2.41×10^{-8}
Levy2009	TBX3-TBX5	rs2384550	NA			
Levy2009	CSK-ULK3	rs6495122	NA			
Padmanabhan2010	UMOD	rs13333226	—(1)	22691/25049	SBP	1.39×10^{-4}
Padmanabhan2010	UMOD	rs13333226	rs11647727(0.65)	22688/25046	MAP	1.72×10^{-4}
Padmanabhan2010	UMOD	rs13333226	rs4297685(0.51)	22657/25015	DBP	4.00×10^{-4}
Takeuchi2010	CASZ1	rs880315	NA			
Johnson2011	ADRB1	rs1801253	—(1)	22675/25031	HTN	2.85×10^{-4}
Johnson2011	ADRB1	rs1801253	rs7076938(0.93)	22676/25034	HTN	2.72×10^{-4}
Johnson2011	AGT	rs2004776	—(1)	22686/25042	HTN	4.28×10^{-9}
Johnson2011	AGT	rs2004776	rs6687360(0.66)	22642/24998	HTN	9.09×10^{-9}
Johnson2011	AGT	rs11122587	rs2004776(0.56)	22686/25042	HTN	4.28×10^{-9}
Tomazewski2011	MTHFR	rs13306560	—(1)	22687/25045	MAP	0.027
Li2010	FURIN	rs2071410	—(1)	17324/20962	HTN	1.04×10^{-3}
Li2010	FURIN	rs2071410	rs6227(1)	2009/ 2009		NA
Li2010	FURIN	rs2071410	rs4932370(0.86)	22678/25036	DBP	5.41×10^{-3}

Publication[a]	Locus	Reported SNP	Proxy[b] SNP(r^2)	–N–[c] cont./ HTN	Best[d] pheno	Best P value
Li2010	FURIN	rs2071410	rs4932178(0.84)	22665/25023	DBP	5.33×10^{-3}
Li2010	FURIN	rs2071410	rs4932371(0.80)	22662/25020	DBP	3.78×10^{-3}
Ho2011	BLK-GATA4	rs2898290	rs9329221(0.57)	22663/25020	HTN	0.010
Ho2011	BLK-GATA4	rs2898290	rs6999466(0.55)	22676/25034	MAP	5.91×10^{-3}
Ho2011	BLK-GATA4	rs2898290	rs4433149(0.54)	22667/25024	HTN	0.013
Ho2011	BLK-GATA4	rs2898290	rs11249996(0.53)	22623/24981	MAP	0.022
Ho2011	BLK-GATA4	rs2898290	rs7005363(0.52)	17344/20990	HTN	0.026
Ho2011	BLK-GATA4	rs2898290	rs7459532(0.51)	22678/25035	DBP	0.018
Ho2011	BLK-GATA4	rs2898290	rs1986972(0.51)	22685/25042	MAP	0.015
Hong2011	AKAP13	rs11638762	rs745191(0.55)	17353/20998	SBP	0.224
Kato2011	ST7L-CAPZA1	rs17030613	rs3737136(0.95)	22686/25043	MAP	0.205
Kato2011	FIGN-GRB14	rs16849225	NA			
Kato2011	ENPEP	rs6825911	NA			
Kato2011	NPR3	rs1173766	rs1173743(0.85)	22670/25025	HTN	5.77×10^{-3}
Kato2011	RPL6-ALDH2	rs11066280	NA			
Kato2011	TBX3	rs35444	NA			
Zhu2011	SUB1-NPR3	rs7726475	NA			
Ehret2011	MTHFR-NPPB	rs17367504	—(1)	22672/25030	DBP	3.56×10^{-6}
Ehret2011	MTHFR-NPPB	rs17367504	rs17037390(1)	22692/25049	DBP	3.71×10^{-6}
Ehret2011	MTHFR-NPPB	rs17367504	rs13306561(0.80)	22665/25023	DBP	3.24×10^{-6}
Ehret2011	MTHFR-NPPB	rs17367504	rs17037425(0.77)	22686/25044	DBP	1.22×10^{-5}
Ehret2011	MTHFR-NPPB	rs17367504	rs1537514(0.66)	22688/25046	DBP	1.36×10^{-4}
Ehret2011	MTHFR-NPPB	rs17367504	rs17037396(0.66)	22688/25046	DBP	1.81×10^{-4}
Ehret2011	MTHFR-NPPB	rs17367504	rs2066470(0.66)	22690/25048	DBP	7.74×10^{-5}
Ehret2011	MTHFR-NPPB	rs17367504	rs13306556(0.55)	22698/25056	DBP	1.27×10^{-4}
Ehret2011	MTHFR-NPPB	rs17367504	rs198358(0.55)	22648/25006	DBP	6.36×10^{-3}
Ehret2011	MOV10	rs2932538	NA			
Ehret2011	SLC4A7	rs13082711	NA			
Ehret2011	ULK4	rs3774372	NA			
Ehret2011	MECOM	rs419076	NA			
Ehret2011	FGF5	rs1458038	NA			
Ehret2011	SLC39A8	rs13107325	NA			
Ehret2011	GUCY1A3-GUCY1B3	rs13139571	NA			
Ehret2011	NPR3-C5orf23	rs1173771	rs1173743(0.76)	22670/25025	HTN	5.77×10^{-3}
Ehret2011	EBF1	rs11953630	NA			
Ehret2011	HFE	rs1799945	—(1)	22677/25034	DBP	7.56×10^{-6}
Ehret2011	BAT2-BAT5	rs805303	rs805301(0.96)	22675/25033	HTN	5.44×10^{-5}
Ehret2011	BAT2-BAT5	rs805303	rs805304(0.69)	22676/25034	HTN	6.71×10^{-4}
Ehret2011	BAT2-BAT5	rs805303	rs7029(0.61)	22669/25027	HTN	3.05×10^{-3}
Ehret2011	BAT2-BAT5	rs805303	rs2763979(0.54)	22643/25000	DBP	0.012
Ehret2011	CACNB2(5')	rs4373814	NA			
Ehret2011	CACNB2(3')	rs1813353	NA			
Ehret2011	C10orf107	rs4590817	NA			
Ehret2011	PLCE1	rs932764	NA			
Ehret2011	CYP17A1-NT5C2	rs11191548	NA			
Ehret2011	ADM	rs7129220	NA			
Ehret2011	PLEKHA7	rs381815	NA			
Ehret2011	FLJ32810-TMEM133	rs633185	NA			
Ehret2011	ATP2B1	rs17249754	rs11105354(1)	22671/25029	HTN	2.41×10^{-8}
Ehret2011	SH2B3	rs3184504	—(1)	17334/20981	DBP	6.98×10^{-3}
Ehret2011	TBX5-TBX3	rs10850411	NA			
Ehret2011	CYP1A1-ULK3	rs1378942	rs2472304(0.83)	22663/25021	SBP	9.71×10^{-3}
Ehret2011	CYP1A1-ULK3	rs1378942	rs7085(0.79)	22691/25049	PP	0.024
Ehret2011	CYP1A1-ULK3	rs1378942	rs2472300(0.63)	22669/25026	SBP	0.022

Publication[a]	Locus	Reported SNP	Proxy[b] SNP(r^2)	–N–[c] cont./ HTN	Best[d] pheno	Best P value
Ehret2011	CYP1A1-ULK3	rs1378942	rs762551(0.63)	22687/25044	SBP	0.026
Ehret2011	FURIN-FES	rs2521501	rs2071410(0.83)	17324/20962	HTN	1.04×10^{-3}
Ehret2011	FURIN-FES	rs2521501	rs6227(0.83)	2009/ 2009	NA	
Ehret2011	FURIN-FES	rs2521501	rs4932370(0.77)	22678/25036	DBP	5.41×10^{-3}
Ehret2011	FURIN-FES	rs2521501	rs4932178(0.75)	22665/25023	DBP	5.33×10^{-3}
Ehret2011	FURIN-FES	rs2521501	rs4932371(0.71)	22662/25020	DBP	3.78×10^{-3}
Ehret2011	GOSR2	rs17608766	NA			
Ehret2011	ZNF652	rs12940887	NA			
Ehret2011	JAG1	rs1327235	NA			
Ehret2011	GNAS-EDN3	rs6015450	NA			
Wain2011	FIGN	rs13002573	NA			
Wain2011	FIGN	rs1446468	NA			
Wain2011	MAP4	rs319690	NA			
Wain2011	CHIC2	rs871606	NA			
Wain2011	NOV	rs2071518	NA			
Wain2011	PIK3CG	rs17477177	NA			
Wain2011	ADRB1	rs2782980	NA			
Wain2011	ADAMTS8	rs11222084	NA			

Notes: **a.** We considered previously reported, distinct genetic variants robustly associated with BP (defined by us as $P < 5{\times}10^{-8}$ in an analysis of multiple independent samples, either GWAS meta-analysis or discovery and followup data combined; main text references 4-15), and also for some genetic variants reported to be associated with BP in recent GWAS or candidate gene studies (Wang *et al.* 2008, Newhouse *et al.* 2009, Org *et al.* 2009, Li *et al.* 2010, Hong *et al.* 2011, Zhu *et al.* 2011). **b.** We determined whether the previously reported index SNP or any $r^2 > 0.5$ proxy was present on the HumanCVD BeadChip. "—" means the reported SNP was itself genotyped (and hence $r^2 = 1$), and "NA" means neither the reported SNP not any $r^2 > 0.5$ proxy was genotyped on the HumanCVD BeadChip. **c.** For genotyped SNPs and proxies, we report our discovery meta-analysis sample sizes ("N cont." for continuous BP traits and "N HTN" for HTN). **d.** For SNPs where $> 50\%$ of the total sample size was analysed, we report the most significantly associated phenotype "Best pheno" and corresponding association P value in our discovery dataset.

Table S13: **Identification of credibly causal SNPs.**

SNP[a]	r^2	Function[b]	Alleles coded/ noncoded	Coded freq.	— Meta-analysis —[c] $\hat{\beta}$ (SE) P-value	—Bayes Factor—[d] normal prior	t-dist. prior
MTHFR-NPPB locus			**DBP; PROCARDIS excluded** [e]				
⋆rs72640208	0.28	TFBS			NA		
⋆rs11586659	0.48	TFBS			NA		
⋆rs55867221	0.28	TFBS			NA		
⋆rs2151654	0.28	TFBS			NA		
⋆rs59375726	0.30	TFBS			NA		
rs1537514	0.28		G/C	0.89	0.507 (0.163) 0.0018	0.00	0.00
⋆rs4846049[f]	1	TFBS	T/G	0.33	-0.512 (0.106) 1.5×10^{-6}	1	1
⋆rs3818762	0.70	TFBS	G/C	0.72	0.473 (0.110) 1.6×10^{-5}	0.14	0.16
rs13306556	0.28		T/C	0.11	-0.510 (0.163) 0.0017	0.00	0.00
rs1476413	0.74		T/C	0.27	-0.426 (0.111) 0.00012	0.03	0.03
⋆rs1801131	0.90	*MTHFR* E429A	T/G	0.68	0.477 (0.107) 8.4×10^{-6}	0.25	0.27
⋆rs12121543	0.65		C/A	0.75	0.476 (0.114) 3.2×10^{-5}	0.08	0.09
rs1994798	0.53		G/A	0.41	-0.351 (0.102) 0.00056	0.01	0.01
rs17421511	0.30	TFBS	G/A	0.83	0.256 (0.132) 0.052	0.00	0.00
⋆rs45449597	0.30	TFBS			NA		
⋆rs45608437	0.30	TFBS			NA		
⋆rs4846052	0.55	TFBS			NA		
rs17037388	0.40	TFBS	G/A	0.16	-0.53 (0.136) 1.0×10^{-4}	0.02	0.02
⋆rs17421560	0.28	TFBS			NA		
⋆rs45504202	0.30	TFBS			NA		
rs13306553	0.28		G/A	0.11	-0.507 (0.162) 0.0017	0.00	0.00
rs17037390	0.40		G/A	0.84	0.55 (0.136) 5.5×10^{-5}	0.04	0.04
rs17037396	0.28		T/C	0.11	-0.497 (0.162) 0.0022	0.00	0.00
rs17367504	0.40	TFBS	G/A	0.16	-0.557 (0.137) 4.6×10^{-5}	0.04	0.04
rs2066470	0.28	TFBS	G/A	0.89	0.534 (0.163) 0.0011	0.00	0.00
⋆rs3753588	0.24	TFBS			NA		
⋆rs3753584	0.35	TFBS			NA		
⋆rs17367629	0.21	TFBS			NA		
⋆rs3753582	0.24	TFBS			NA		
rs13306561	0.35	TFBS	G/A	0.16	-0.557 (0.136) 4.3×10^{-5}	0.04	0.04
rs17037425	0.28		G/A	0.85	0.537 (0.142) 0.00016	0.02	0.02
⋆rs6669371	0.37	TFBS			NA		
⋆rs1023252	0.73	TFBS			NA		
rs17350396	0.3		G/A	0.17	-0.27 (0.132) 0.041	0.00	0.00
rs198375	0.35		T/C	0.6	0.395 (0.102) 0.00011	0.03	0.04
rs198388	0.21		T/C	0.43	-0.341 (0.101) 0.00071	0.01	0.01
⋆rs198389	0.28	TFBS			NA		
⋆rs6668659	0.45		T/G	0.65	0.446 (0.105) 2.0×10^{-5}	0.13	0.15
AGT locus			**HTN; no studies excluded** [e]				
⋆rs2493126	0.54	TFBS			NA		
⋆rs12059975	0.29	TFBS			NA		
⋆rs66946803	0.29	TFBS			NA		
⋆rs943580	0.56		G/A	0.40	0.116 (0.021) 2.1×10^{-8}	0.40	0.25
rs11122573	0.33	TFBS	T/C	0.08	0.110 (0.037) 0.0026	0.00	0.00
⋆rs10864770	0.33	TFBS			NA		
⋆rs10864771	0.33	TFBS			NA		
rs11122575	0.33		G/A	0.08	0.112 (0.037) 0.0023	0.00	0.00
rs2493132	0.22	TFBS	T/C	0.71	-0.070 (0.022) 0.0017	0.00	0.00

SNP[a]	r^2	Function[b]	Alleles coded/ noncoded	Coded freq.	— Meta-analysis —[c] $\hat{\beta}$ (SE) P-value	—Bayes Factor—[d] normal prior	t-dist. prior
⋆rs3789669	0.75	TFBS			NA		
AGT locus continued			**HTN; no studies excluded** [e]				
rs3789670	0.36	TFBS	T/C	0.11	0.131 (0.032) 5.4×10^{-5}	0.00	0.00
⋆rs3789671	0.83	TFBS	T/G	0.19	0.135 (0.026) 1.1×10^{-7}	0.05	0.05
⋆rs2493133	0.56	TFBS			NA		
⋆rs2478543	0.56	TFBS	T/C	0.59	-0.118 (0.021) 1.2×10^{-8}	0.65	0.42
⋆rs2478539	0.56	TFBS			NA		
⋆rs6687360	0.68	TFBS	T/C	0.36	0.122 (0.021) 8.2×10^{-9}	0.82	0.58
⋆rs699	0.56	*AGT* M268T	G/A	0.41	0.118 (0.021) 1.1×10^{-8}	0.68	0.44
⋆rs2004776[f]	1		T/C	0.24	0.139 (0.024) 4.0×10^{-9}	0.96	1
rs3889728	0.32		T/C	0.25	0.074 (0.023) 0.0016	0.00	0.00
⋆rs2493134	0.56		T/C	0.60	-0.120 (0.021) 7.0×10^{-9}	1	0.68
⋆rs3827750	0.36	TFBS			NA		
⋆rs3789678	0.36	TFBS			NA		
⋆rs3789679	0.36	TFBS			NA		
⋆rs2148582	0.52	TFBS	G/A	0.40	0.117 (0.021) 1.6×10^{-8}	0.51	0.33
⋆rs5051	0.58	TFBS	T/C	0.40	0.116 (0.021) 2.3×10^{-8}	0.37	0.23
rs5049	0.36	TFBS	T/C	0.11	0.145 (0.032) 5.9×10^{-6}	0.00	0.00
rs5046	0.36	TFBS	G/A	0.89	-0.146 (0.032) 5.2×10^{-6}	0.00	0.00
rs2071405	0.36		T/C	0.11	0.145 (0.032) 5.7×10^{-6}	0.00	0.00
rs2071404	0.36		C/A	0.89	-0.145 (0.032) 6.0×10^{-6}	0.00	0.00
rs2493137	0.23		T/C	0.70	-0.064 (0.022) 0.0038	0.00	0.00
rs1977414	0.28		T/C	0.27	0.107 (0.023) 2.4×10^{-6}	0.01	0.00
rs4028824	0.39		G/A	0.90	-0.075 (0.033) 0.024	0.00	0.00
⋆rs2493141	0.74	TFBS			NA		
⋆rs4847008	0.67	TFBS			NA		
⋆rs2478525	0.54	TFBS			NA		
NPR3 locus			**SBP; no studies excluded** [e]				
⋆rs72740637	0.63	TFBS			NA		
⋆rs1421811[f]	1		G/C	0.39	-0.668 (0.146) 4.8×10^{-6}	1	1
rs10057069	0.61		T/C	0.73	0.499 (0.160) 0.0019	0.01	0.03
rs976576	0.20		T/C	0.25	0.151 (0.163) 0.35	0.00	0.00
HFE locus			**DBP; no studies excluded** [e]				
⋆rs56027330	0.24	*SLC17A3* G201R,G279R			NA		
⋆rs72834630	0.78	TFBS			NA		
⋆rs72834647	0.85	TFBS			NA		
⋆. . .[g]	. . .[g]	TFBS			NA		
⋆rs1799945[f]	1	*HFE* H40D,H63D	G/C	0.15	0.616 (0.138) 7.6×10^{-6}	1	1
rs2071303	0.27		T/C	0.66	-0.139 (0.104) 0.18	0	0
⋆rs198851	0.85	TFBS			NA		
⋆rs129128	0.92	TFBS			NA		
⋆rs41266821	0.32	*HIST1H4G* V3A			NA		
NOS3 locus			**DBP; no studies excluded** [e]				
⋆rs3918226[f]	1	TFBS	T/C	0.08	0.826 (0.177) 2.9×10^{-6}	1	1
LSP1/TNNT3 locus			**MAP; no studies excluded** [e]				
⋆rs7113809	0.24	TFBS			NA		
⋆rs10769814	0.25	TFBS			NA		
⋆rs2137320	0.34	TFBS			NA		
⋆rs673791	0.24	TFBS			NA		
rs592373	0.30		G/A	0.37	-0.491 (0.110) 7.5×10^{-6}	0.00	0.00
rs2271439	0.29		C/A	0.84	-0.386 (0.143) 0.0069	0.00	0.00
⋆rs621679	0.57	*LSP1* A38T,A100T			NA[h]		

SNP[a]	r^2	Function[b]	Alleles coded/ noncoded	Coded freq.	— Meta-analysis —[c] $\hat{\beta}$ (SE) P-value	—Bayes Factor—[d] normal prior	t-dist. prior
⋆rs661348[f]	1		T/C	0.57	-0.650 (0.105) 7.0×10^{-10}	1	1
LSP1/TNNT3 locus continued			**MAP; no studies excluded** [e]				
rs3817197	0.35		G/A	0.53	-0.381 (0.106) 0.00031	0.00	0.00
rs3817198	0.31		T/C	0.68	0.348 (0.114) 0.0022	0.00	0.00
⋆rs517101	0.34	TFBS			NA		
⋆rs542605	0.30	TFBS			NA		
⋆rs576603	0.47	TFBS			NA		
⋆rs810021	0.50	TFBS			NA		
⋆rs1092608	0.25	TFBS			NA		
⋆rs28971510	0.23	TFBS			NA		
rs909116	0.37		T/C	0.52	-0.393 (0.105) 0.00018	0.00	0.00
SOX6 locus			**MAP; AIBIII+ASCOT+BRIGHT excluded** [e]				
⋆rs2351958	0.32	TFBS			NA		
⋆rs16932862	0.96		T/C	0.20	0.429 (0.154) 0.0054	0.75	0.79
⋆rs12799126	0.96		T/G	0.20	0.413 (0.154) 0.0073	0.62	0.67
⋆rs1401455	0.96		T/C	0.80	-0.420 (0.153) 0.0061	0.69	0.74
⋆rs1155685	0.96	TFBS			NA		
⋆rs7101502	0.87	TFBS			NA		
⋆rs297346	0.22		G/A	0.64	0.219 (0.129) 0.090	0.12	0.21
⋆rs2014408[f]	1		T/C	0.21	0.443 (0.152) 0.0036	1	1
ATP2B1 locus			**HTN; no studies excluded** [e]				
⋆rs11105273	0.23	TFBS			NA		
⋆rs11105310	0.45	TFBS			NA		
⋆rs10777184	0.45	TFBS			NA		
⋆rs10858896	0.45	TFBS			NA		
⋆rs10858899	0.45	TFBS			NA		
⋆rs11105319	0.45	TFBS			NA		
⋆rs10858906	0.45	TFBS			NA		
⋆rs2681492	0.91	TFBS			NA		
⋆rs11105354[f]	1		G/A	0.16	-0.155 (0.028) 2.2×10^{-8}	1	1
⋆rs2280715	0.22	TFBS			NA		

Notes: **a.** For the eight significantly associated index SNPs in our combined discovery and followup analysis ($P < 8.56 \times 10^{-7}$; Table S9), we used 120 phased CEU haplotypes at approx. 6.9M called SNPs from the June 2010 early release of resequencing data from the 1000 Genomes Project Consortium (2010) to non-stringently identify all SNPs in pairwise LD at $r^2 > 0.2$ with each index SNP. SNPs inferred to be credibly causal are annotated with a star (⋆). **b.** We defined as potentially functional any SNP that was not annotated only as "`--`", "`intronic`", "`UTR`", "`non-coding`", or encoding a synonymous amino acid substitution with respect to known transcripts. In addition, we defined as potentially functional all SNPs within transcription factor binding site (TFBS) peak regions defined by the ENCODE project for a set of 55 transcription factors (The ENCODE Project Consortium 2007, Raney *et al.* 2010), which are listed in detail in Table S15. Here we present data for only 159 of 860 such SNPs, which are (i) SNPs for which we have association data (regardless of functional annotation), plus (ii) SNPs that are potentially functional (regardless of whether we have association data). **c.** NAindicates association meta-analysis not available because the SNP was not genotyped on the HumanCVD BeadArray or failed QC in $> 50\%$ of total sample size.

See following page for notes **d.**–**h.**

Table S13 notes continued: **d.** We calculated marginal likelihoods assuming a prospective regression model, and following Wakefield (2009) we used a large sample normal approximation to the likelihood function, $\hat{\beta} \sim \mathcal{N}(\beta, \mathrm{SE}^2)$, where $\hat{\beta}$ is the effect size estimate (for the phenotype most significantly associated with the index SNP), β is the true effect size, and SE is the standard error (assumed known and fixed). Wakefield (2009) derived closed form expressions for the marginal likelihood, assuming a normal prior for β. However, a normal prior may not be sufficiently heavy tailed in the sense that it cannot simultaneously allow a high prior density near zero, a small prior mean effect size, and a flatness in the tails that allows data strongly supporting a large effect size to dominate the prior (Hoggart *et al.* 2008, Stephens and Balding 2009). We therefore computed results for two different priors: A normal prior where $\beta \sim \mathcal{N}(0, W)$ as assumed by Wakefield (2009), and a heavy tailed prior where β was t-distributed with 1 d.f. and scale chosen such that the central 80% probability interval was the same as the normal prior. We chose prior variance $W = (0.25\mathrm{mmHg})^2$ for continuous traits, and $W = (0.05)^2$ on a ln(odds) scale for dichotomous hypertension. These priors were motivated by an assumption that associations discovered previously (Levy *et al.* 2009, Newton-Cheh *et al.* 2009) were in the tails of the distribution of effect sizes for all truly associated SNPs, the observation that studies powered for OR around 1.2 did not discover loci for hypertension (Wellcome Trust Case Control Consortium 2007), and that effect sizes scale approximately like 0.2 ln(odds) per mmHg for previously discovered loci (Newton-Cheh *et al.* 2009). **e.** We analysed the primary BP trait for the index SNP at each locus (Table S7). For model comparison, a fixed set of observed data are necessary. Because all studies filtered at call rate $\geq 98\%$, for practical purposes this means a fixed set of studies must be used to compare support for different SNPs at each locus. Meta-analysis results reported here therefore exclude (on a locus-by-locus basis) studies that fail SNP QC for any SNPs that (i) were in $r^2 \geq 0.8$ with the index SNP and (ii) pass QC for $\geq 50\%$ of total sample size. **f.** Index SNP at each locus. **g.** 33 SNPs (rs2032444, rs198855, rs198823, rs11755618, rs11751062, rs41266811, chr6:26325824, chr6:26332322, chr6:26332356, chr6:26332382, chr6:26340330, rs16891464, chr6:26348453, rs3734534, rs11751286, chr6:26358008, chr6:26358012, rs11753610, rs11759682, rs3823157, rs11754168, chr6:26392649, rs41266829, rs41266831, chr6:26394705, chr6:26394727, rs11756428, rs57145038, rs34434694, rs73399394, rs11754384, rs6938696, rs73401236, rs61213538, rs61625476) in modest LD ($0.24 \leq r^2 \leq 0.47$) with index SNP. **h.** See Table S14 for association results from directly genotyping this SNP in the BRIGHT case and control samples.

Table S14: ***LSP1* p.[Ala38Thr, Ala100Thr] non-synonymous SNP.**

SNP	Alleles coded/ noncoded	–Single SNP analysis–[a] β_{SNP} (SE)	*P*-value	–Multiple SNP analysis–[a] β_{SNP} (SE)	*P*-value	–Pairwise LD (r^2)–[a] rs621679
rs661348	T/C	-1.551 (0.495)	1.76×10^{-3}	-0.891 (0.710)	0.209 [b]	0.513
rs621679[c]	G/A[d]	-1.531 (0.486)	1.66×10^{-3} [e]	-0.904 (0.697)	0.194 [b]	

Notes: **a.** Association with MAP, and pairwise LD, estimated using data on 3108 individuals from BRIGHT (1475 cases and 1633 controls) that were successfully genotyped for both SNPs. **b.** Neither SNP is significantly associated when added to a multivariate regression model that includes the other SNP. **c.** rs621679 genotyped using a KASPAR assay with call rate 97% and Hardy–Weinberg $P = 1.5 \times 10^{-5}$. Despite significant heterozygote deficit we infer the genotype calls are mostly correct because of the observed correlation with rs661348 matches the correlation in 1000G data. **d.** G/A alleles at nsSNP rs621679 correspond respectively to Ala/Thr residues, at either position 38 or position 100 depending on the *LSP1* transcript. This amino acid substitution is predicted to be benign by PolyPhen (Ramensky *et al.* 2002). **e.** The nsSNP rs621679 shows only slightly stronger association and therefore it is not surprising that both SNPs are credibly causal. Using the same approach as for Table S13 we obtain a BF for rs661348 vs rs621679 of 0.96 for the normal prior and 0.97 for the t-distribution prior.

Table S15: **Individual TFBS containing credibly causal SNPs.**

TFBS peak region[a]	Names[b] (scores[c])	Credibly causal SNPs (BF if not NA)[d]
MTHFR-NPPB locus		
chr1:11760–11761kb	HNF4A (1000)	rs72640208
chr1:11767–11768kb	BAF155 (767)	rs11586659, rs55867221, rs2151654, rs59375726
chr1:11768–11768kb	BAF170 (1000)	rs11586659, rs55867221
chr1:11772–11774kb	STAT1 (1000)[e]	rs4846049 (1.00), rs3818762 (0.16)
chr1:11773–11774kb	BAF155 (531), BAF170 (556)	rs3818762 (0.16)
chr1:11774–11774kb	c-Fos (510)	rs3818762 (0.16)
chr1:11780–11781kb	Brg1 (614), PU.1 (1000)	rs45449597, rs45608437, rs4846052, rs17421560, rs45504202
chr1:11781–11782kb	Max (1000)	rs45504202
chr1:11786–11787kb	BAF155 (682), HEY1 (1000), BAF170 (603)	rs3753588
chr1:11787–11789kb	HEY1 (1000)	rs3753584, rs17367629, rs3753582
chr1:11788–11790kb	Max (1000)	rs17367629, rs3753582
chr1:11788–11789kb	TAF1 (1000), BAF155 (648), BAF170 (850), SREBP1 (1000), FOSL2 (1000), GABP (886), JunD (1000), p300 (1000), c-Fos (581)	rs17367629, rs3753582
chr1:11804–11805kb	c-Jun (783)	rs6669371
chr1:11821–11822kb	Rad21 (618), CTCF (1000)	rs1023252
chr1:11841–11843kb	NRSF (1000)	rs198389
chr1:11842–11842kb	Ini1 (734)	rs198389
AGT locus		
chr1:228897–228898kb	FOSL2 (879)	rs2493126, rs12059975, rs66946803
chr1:228904–228907kb	FOSL2 (1000)	rs10864770, rs10864771
chr1:228910–228911kb	HEY1 (1000)	rs3789669, rs3789671 (0.05), rs2493133, rs2478543 (0.65), rs2478539
chr1:228911–228912kb	BAF155 (662), CEBPB (505), RXRA (695)	rs2493133, rs2478543 (0.65), rs2478539, rs6687360 (0.82)
chr1:228911–228911kb	p300 (1000), BHLHE40 (629)	rs2478543 (0.65)
chr1:228916–228917kb	TAF1 (512), JunD (1000), Sin3Ak-20 (822), FOSL2 (520), p300 (1000), RXRA (1000), BAF170 (758)	rs3827750, rs3789678, rs3789679, rs2148582 (0.51), rs5051 (0.37)
chr1:228931–228932kb	HNF4A (789)	rs2493141, rs4847008, rs2478525
NPR3 locus		
chr5:32746–32746kb	BAF170 (517)	rs72740637
chr5:32746–32747kb	BAF155 (542)	rs72740637
HFE locus		
chr6:26133–26136kb	HEY1 (1000)	rs72834630
chr6:26151–26155kb	HEY1 (1000)	rs72834647, rs2032444
chr6:26151–26153kb	POU2F2 (1000)	rs72834647
chr6:26211–26213kb	JunD (1000)	rs198855, rs198851
chr6:26212–26214kb	HEY1 (1000)	rs198851
chr6:26212–26213kb	RXRA (629), POU2F2 (1000), PAX5-N19 (628)	rs198851
chr6:26230–26236kb	HEY1 (1000)	rs198823, rs129128
chr6:26231–26233kb	TAF1 (1000)	rs198823
chr6:26322–26326kb	HEY1 (1000)	rs11755618, rs11751062, rs41266811, chr6:26325824

TFBS peak region[a]	Names[b] (scores[c])	Credibly causal SNPs (BF if not NA)[d]
chr6:26324–26326kb	POU2F2 (1000), TAF1 (1000)	rs11755618, rs11751062, rs41266811, chr6:26325824
chr6:26324–26324kb	PAX5-C20 (1000)	rs11755618, rs11751062
chr6:26324–26325kb	PAX5-N19 (1000), PAX5-C20 (614), BCL3 (694)	rs41266811
chr6:26325–26325kb	SP1 (1000), TCF12 (1000), IRF4 (583)	rs41266811
chr6:26332–26333kb	HEY1 (634), TAF1 (936)	chr6:26332322, chr6:26332356, chr6:26332382
chr6:26340–26343kb	HEY1 (1000)	chr6:26340330, rs16891464
chr6:26341–26343kb	POU2F2 (1000), BCL3 (1000)	rs16891464
chr6:26341–26344kb	TAF1 (1000)	rs16891464
chr6:26342–26343kb	ZBTB33 (1000)	rs16891464
chr6:26348–26350kb	POU2F2 (1000), TAF1 (1000)	chr6:26348453, rs3734534, rs11751286
chr6:26349–26350kb	PAX5-N19 (1000), PAX5-C20 (1000)	rs11751286
chr6:26358–26359kb	HEY1 (1000), POU2F2 (1000), PAX5-N19 (502), Pbx3 (927), TAF1 (1000), BCL3 (795)	chr6:26358008, chr6:26358012
chr6:26359–26360kb	SP1 (522)	rs11753610
chr6:26360–26360kb	c-Fos (536), TAF1 (1000)	rs11753610
chr6:26378–26380kb	POU2F2 (1000), BCL11A (659), Pbx3 (604)	rs11759682
chr6:26379–26380kb	TAF1 (1000), c-Fos (607)	rs3823157
chr6:26392–26394kb	HEY1 (1000)	rs11754168, chr6:26392649, rs41266829, rs41266831
chr6:26393–26394kb	POU2F2 (1000), TAF1 (1000), JunD (933), IRF4 (541), SP1 (547), Pbx3 (591), PAX5-N19 (1000), TCF12 (575), p300 (932), NRSF (911), Sin3Ak-20 (851), PAX5-C20 (1000)	rs41266829, rs41266831
chr6:26393–26395kb	c-Myc (561)	rs41266829, rs41266831, chr6:26394705, chr6:26394727
chr6:26395–26395kb	HSF1 (1000), CEBPB (616)	chr6:26394705, chr6:26394727
chr6:26413–26413kb	BAF155 (553)	rs11756428
chr6:26419–26420kb	HSF1 (583)	rs57145038
chr6:26428–26428kb	PU.1 (1000)	rs34434694
chr6:26430–26431kb	Max (782)	rs73399394, rs11754384
chr6:26431–26431kb	USF-1 (1000), BAF170 (624)	rs11754384
chr6:26436–26437kb	HSF1 (1000), CEBPB (552), Pol3 (699)	rs6938696
chr6:26436–26436kb	BAF170 (525)	rs6938696
chr6:26440–26440kb	Ini1 (815)	rs73401236
chr6:26445–26446kb	BAF155 (649)	rs61213538, rs61625476
chr6:26445–26445kb	Brg1 (514)	rs61213538, rs61625476
NOS3 locus		
chr7:150321–150321kb	SIX5 (1000)[e]	rs3918226 (1)
LSP1/TNNT3 locus		
chr11:1830–1834kb	NFKB (653)	rs7113809, rs10769814
chr11:1830–1833kb	POU2F2 (1000)	rs7113809
chr11:1841–1841kb	BAF155 (1000), Ini1 (588)	rs2137320
chr11:1841–1842kb	BAF155 (1000), Max (514), c-Jun (511), Ini1 (1000)	rs673791
chr11:1868–1869kb	POU2F2 (993)	rs517101, rs542605
chr11:1869–1869kb	BCL3 (989)	rs542605
chr11:1870–1871kb	BCL3 (935)	rs576603

TFBS peak region[a]	Names[b] (scores[c])	Credibly causal SNPs (BF if not NA)[d]
chr11:1871–1872kb	BCL3 (924)	rs810021, rs1092608, rs28971510
SOX6 locus		
chr11:16204–16205kb	GR (1000)	rs2351958
chr11:16271–16272kb	Ini1 (573), Brg1 (601)	rs1155685
chr11:16305–16305kb	Ini1 (946), Brg1 (1000)	rs7101502
ATP2B1 locus		
chr12:88311–88312kb	Brg1 (768), Ini1 (657)	rs11105273
chr12:88442–88444kb	Ini1 (552), BAF155 (584)	rs11105310, rs10777184, rs10858896
chr12:88442–88443kb	BAF170 (596)	rs11105310
chr12:88443–88443kb	CTCF (508)	rs11105310
chr12:88444–88444kb	SRF (859), SP1 (1000)	rs10777184, rs10858896
chr12:88448–88448kb	Rad21 (704), CTCF (956)	rs10858899
chr12:88451–88452kb	NRSF (1000)	rs11105319
chr12:88451–88451kb	BAF170 (599)	rs11105319
chr12:88458–88459kb	Brg1 (691)	rs10858906
chr12:88459–88459kb	GR (658)	rs10858906
chr12:88537–88537kb	c-Jun (575), c-Fos (723)	rs2681492
chr12:88625–88628kb	Max (543), BAF155 (727)	rs2280715
chr12:88625–88629kb	Ini1 (745)	rs2280715
chr12:88626–88628kb	TAF1 (1000), HEY1 (1000)	rs2280715
chr12:88627–88628kb	TCF12 (1000), PAX5-C20 (1000), SP1 (1000), PAX5-N19 (1000), Brg1 (570)	rs2280715

Notes: **a.** Transcription factor binding site (TFBS) peak region start and stop coordinates were rounded to the nearest kilobase before condensing identical regions into single table rows. **b.** Name of the antibody to a target transcription factor (from a set of 55; using the ENCODE controlled vocabulary) used in ChIP-Seq experiment data reported by the ENCODE consortium(The ENCODE Project Consortium 2007, Raney *et al.* 2010). **c.** Only TFBS peak regions with an ENCODE-defined score ≥ 500 are reported here. The score combines peaks called from processed data from multiple cell lines and experimental conditions into an overall measure of support for the region, on a 0–1000 scale. To approximately calibrate the observed overlap between these TFBS peak regions and BP associated SNPs, we noted that of all 38,122 SNPs on the HumanCVD BeadChip for which we had association test statistics with $\geq 50\%$ of our full sample size, only 3445 SNPs (9.04% of the total) occur within ENCODE defined TFBS peak regions with score ≥ 500. **d.** Credibly causal SNPs either have no association data and are in $r^2 > 0.2$ with the index SNP, or have association data and Bayes Factor BF > 0.05. Here we report the maximum of the BF from the normal prior and the t-distribution prior, see Table S13 for details. **e.** After identifying which of our credibly causal SNPs were within ENCODE defined TFBS peak regions, we examined the raw (aligned read density) signal data from the underlying ChIP-Seq experiments (Johnson *et al.* 2007, Rozowsky *et al.* 2009), to confirm the signal strength relative to control experiments, and to determine more precisely the position of the SNPs relative to the signal peak. Figure S13 illustrates two TFBS peak regions where the underlying raw data showed striking enrichment of aligned read density near our BP associated SNPs. For some other ENCODE defined TFBS we were not able to identify such visually clear signal enrichment by simply plotting the underlying raw signal data, and further analyses using more sophisticated normalization and peak identification algorithms (Valouev *et al.* 2008, Zhang *et al.* 2008, Rozowsky *et al.* 2009) are required to confirm the evidence for each TFBS along with their precise locations relative to the BP-associated SNPs.

Table S16: **eSNP analyses in monocytes and the whole blood and tissue panel.**

Locus	Index SNP[a]	(r^2)	Tissue	Transcript[b]	— Index SNP — P-value	P adj.[d]	Top eSNP[c]	(r^2)	— Top eSNP — P-value	P adj.[e]
MTHFR-NPPB	rs1801131	(0.93)	monocytes	*MTHFR*(−)[f]	3.1×10^{-36}	0.15	rs1476413	(0.73)	1.7×10^{-45}	1.9×10^{-11}
MTHFR-NPPB	rs4846049	(≡ 1)	blood/tissue	*MTHFR*(−)[f]	1.9×10^{-82}	0.12	rs3818762	(0.69)	3.2×10^{-99}	1.4×10^{-6}
MTHFR-NPPB	rs4846049	(≡ 1)	blood	*MTHFR*(−)[f]	2.9×10^{-19}	0.76	rs3818762	(0.69)	1.3×10^{-25}	0.021
MTHFR-NPPB	rs4846049	(≡ 1)	blood/tissue	*CLCN6*(−)[f]	1.6×10^{-8}	1.0×10^{-3}	rs3818762	(0.69)	8.8×10^{-15}	5.1×10^{-10}
HFE	rs129128	(1.00)	monocytes	*HIST1H2BK*(+)[g]	8.5×10^{-5}	NA	rs129128	(≡ 1)	8.5×10^{-5}	NA
HFE	rs1799945	(≡ 1)	blood/tissue	*HIST1H2AA*(+)[g]	2.9×10^{-4}	0.70	rs129128	(1.00)	8.1×10^{-5}	0.61
ATP2B1	rs2681472	(1.00)	monocytes	*GALNT4*(+)[h]	2.3×10^{-11}	0.92	rs3958726	(0.09)	6.4×10^{-171}	2.7×10^{-160}

Notes: **a.** Association between transcript levels and SNP genotypes was tested in monocytes for 6 index SNPs (the SNPs most significantly associated with BP, or where available $r^2 \geq 0.9$ proxies for the SNPs most significantly associated with BP), and in the whole blood and tissue panel for 8 index SNPs (the SNPs most significantly associated with BP at 8 loci, indicated by $r^2 \equiv 1$ because proxies were not used). **b.** We report the transcripts significantly associated with index SNPs, as described in Table S3, along with a (+) or (−) symbol according to whether the index SNP allele associated with higher blood pressure is associated with higher or lower transcript level. **c.** To determine whether the BP and transcript association signals were coincident, we followed the approach of Voight *et al.* (2010). We first identified the top eSNP for each transcript (the SNP with the most significant *cis*- association for the transcript) and report the pairwise LD (r^2) between the top eSNP and the index SNP, writing $r^2 \equiv 1$ when they are the same SNP. When the index SNP and the top eSNP are not the same, two conditional analyses were then performed: **d.** Association between transcript level and index SNP genotype, including the top eSNP genotype as a covariate; **e.** Association between transcript level and top eSNP genotype, including the index SNP genotype as a covariate. We interpret the results of these conditional analyses as follows: **f.** The BP and transcript association signals for the *MTHFR* and *CLCN6* transcripts are coincident: The index SNPs tag top eSNPs that are more strongly associated with transcript levels, with both conditional analyses showing attenuated significance and P adj.[e] more significant. The top eSNP rs3818762 shows similar strength of association with BP as the index SNP (Table S13). **g.** The BP and transcript association signals for the *HIST1H2BK* and *HIST1H2AA* transcripts are perfectly coincident: For *HIST1H2BK* the SNPs are the same ($r^2 \equiv 1$) and hence no conditional analyses were performed, and for *HIST1H2AA* either perfectly tags the other and hence both conditional analyses are non-significant. **h.** The BP and transcript association signals for the *GALNT4* transcripts are not coincident: The index SNP is a poor tag for the much-more-significantly-associated top eSNP.

Table S17: **MTHFR-NPPB locus conditional analysis.**

SNP[a]	alleles coded/ noncoded	–Single SNP analyses–[b] β_{SNP} (SE[c])	P value[c]	–Multiple SNP analyses–[b] β_{SNP} (SE[c])	P value[c]	–Pairwise LD (r^2)– rs17367504	rs5068
rs4846049	T/G	−0.5411 (0.0963)	1.92×10^{-8}	−0.3865 (0.1208)	1.37×10^{-3}	0.333	0.076
rs17367504	G/A	−0.6009 (0.1237)	1.20×10^{-6}	−0.1547 (0.1751)	0.38		0.258
rs5068	G/A	−0.8083 (0.1943)	3.18×10^{-5}	−0.3895 (0.2326)	0.094		

Notes: **a.** Conditional analyses were performed for three SNPs at the MTHFR-NPPB locus that showed strong association with DBP in our meta-analysis but that were in weak/moderate pairwise LD. **b.** Effect size estimates (β_{SNP}), standard errors and P-values for single SNP regression analyses, and for an otherwise identical three-SNP multiple regression analysis, meta-analysed over all studies in our discovery analysis. For each SNP in the multi-SNP regression performed within each study, the effect size estimate and confidence interval for a partial t-test correspond to an association analysis for the given SNP with other SNPs included as covariates, and hence were combined over studies using a standard inverse variance weighted meta-analysis with our modified weighting scheme for ascertained and non-ascertained studies. **c.** Because genomic control cannot be applied in the multiple regression analysis, we present all results in this table without genomic control.

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4 Internet resources

On 12 October 2011 we verified the internet resource URLs for the detailed study and reagent descriptions, for public releases of genotype and sequence data, for data annotation, and for software used for this work:

- Birdseed genotype calling algorithm
  `http://www.broadinstitute.org/mpg/birdsuite/birdseed.html`
- BRItish Genetics of HyperTension (BRIGHT) study
  `http://www.brightstudy.ac.uk`
- British Regional Heart Study (BRHS)
  `http://www.ucl.ac.uk/pcph/research-groups-themes/brhs-pub`
- British Womens Heart and Health Study (BWHHS)
  `http://www.lshtm.ac.uk/eph/ncde/research/bwhhs`
- Cardiogenics consortium
  `https://www.cardiogenics.org`
- ENCODE project ChIP-Seq raw signal data and TFBS peak regions
  `http://genome.ucsc.edu/cgi-bin/hgTables`
- ENCODE project controlled vocabulary for antibodies used for ChIP-Seq
  `http://genome.ucsc.edu/cgi-bin/hgEncodeVocab?ra=encode/cv.ra&type=Antibody`
- HYPERGENES European network for genetic-epidemiological studies
  `http://www.hypergenes.eu`
- Illumina HumanCVD BeadChip genotyping array
  `http://www.illumina.com/products/humancvd_whole_genome_genotyping_kits.ilmn`
- Illuminus genotype calling algorithm
  `http://homepages.lshtm.ac.uk/tgclark/downloads`
- International HapMap project
  `http://hapmap.ncbi.nlm.nih.gov`
- KASPAR genotyping systems
  `http://www.kbioscience.co.uk/reagents/KASP.html`
- Medical Research Council National Survey of Health and Development (MRC NSHD)
  `http://www.nshd.mrc.ac.uk`
- National Human Genome Resource Institute catalog of published GWAS
  `http://www.genome.gov/gwastudies`
- Online Mendelian Inheritance in Man (OMIM)
  `http://www.omim.org`
- PLINK genetic analysis software
  `http://pngu.mgh.harvard.edu/~purcell/plink`
- PRecOcious Coronary ARtery DISease (PROCARDIS) study
  `http://www.procardis.org`
- R software for statistical computing and graphics
  `http://www.r-project.org`
- SNPTEST genetic association analysis software
  `https://mathgen.stats.ox.ac.uk/genetics_software/snptest/snptest.html`
- Thousand genomes (1000G) project
  `http://www.1000genomes.org`
- Thousand genomes (1000G) project June 2010 early release data
  `http://sph.umich.edu/csg/abecasis/MACH/download/1000G-2010-06.html`

5 Author contributions

T.J. and P.B.M. designed the study and wrote analysis plans. T.J. performed statistical analyses. T.J. and P.B.M. interpreted the results and wrote the paper. All authors revised and approved the manuscript.

Additional contributions for specific cohorts were as follows.

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Global BPgen Consortium: Contributions are described in full elsewhere (Newton-Cheh *et al.* 2009)

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