Supporting Information

The genetic risk for hypertension is lower among the Hungarian Roma population compared to the general population

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Supplementary Figure 1. Details of the systematic review search according to the PRISMA Statement

A) The keywords were used for the literature search:

PubMed:

(„essential hypertension" OR „blood pressure") AND

(„molecular genetics" OR „genomics" OR „genes") AND

(„single-nucleotide polymorphism" OR „genetic variants" OR „gene polymorphism" OR „common gene variants") AND

(„genome-wide association study" OR „GWAS" OR „candidate gene study" OR „case-control study" OR „meta-analysis" OR „review" OR „association")

filters: Humans, English

time frame: 11/30/2015 or earlier

Huge Navigator/Literature Finder:

(„essential hypertension" OR „blood pressure") AND

(„molecular genetics" OR „genomics" OR „genes") AND

(„single-nucleotide polymorphism" OR „genetic variants" OR „gene polymorphism" OR „common gene variants") AND

(„genome-wide association study" OR „GWAS" OR „candidate gene study" OR „case-control study" OR „meta-analysis" OR „review" OR „association")

filters: disease-->hypertension

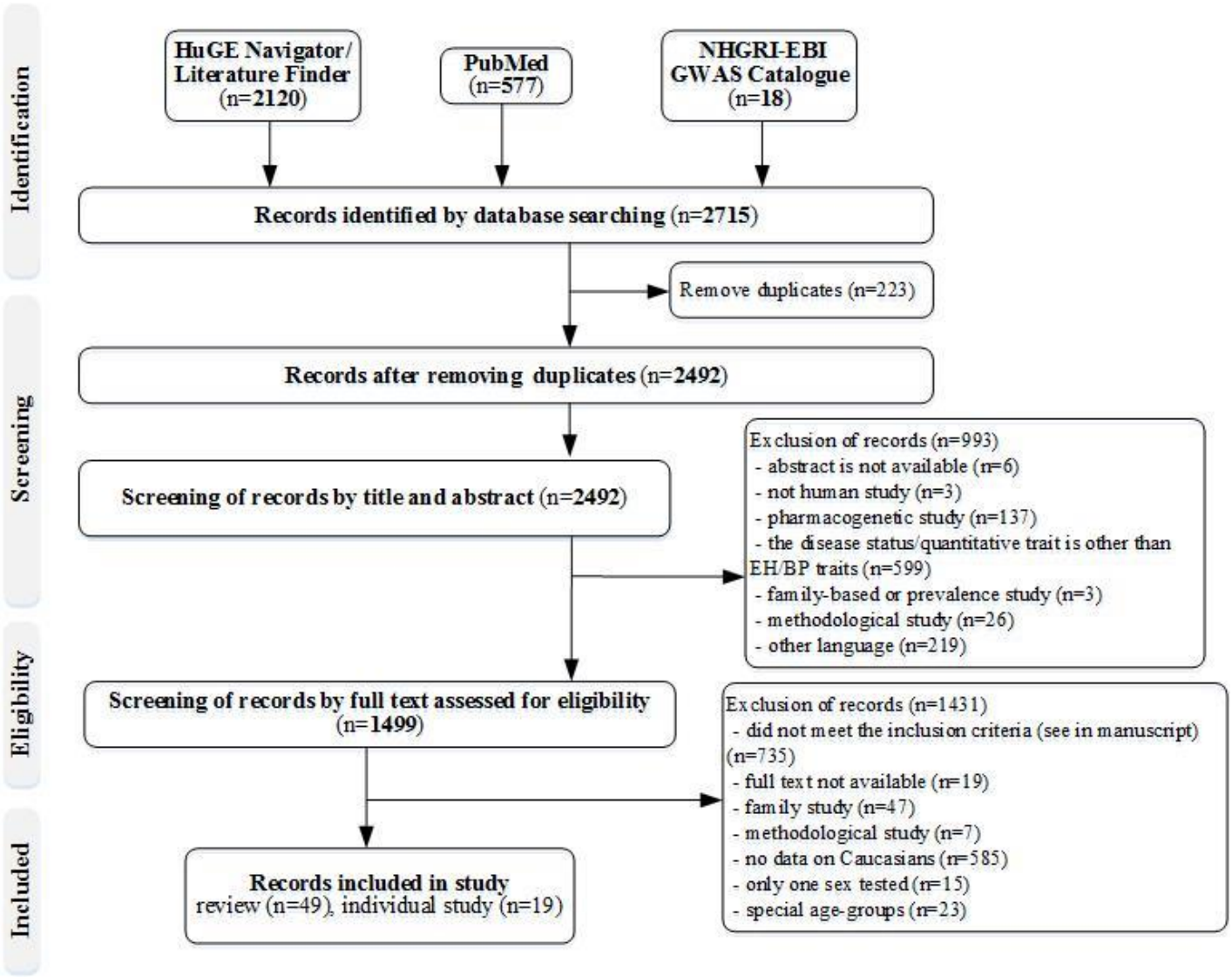
time frame: 11/30/2015 or earlier

NHGRI-EBI GWAS Catalog

filter: disease-->hypertension

time frame: 11/30/2015 or earlier

B) The flow-chart of the systematic search according to the PRISMA Statement



From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). *P*referred *R*eporting *I*tems for *S*ystematic Reviews and *M*eta-*A*nalyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

Supplementary Table 1. Selection process of the SNPs included in the study

Step 1.

SNPs chosen after literature review				
Number	SNP	Locus	Gene name(s)	Reference
1	rs4305	*ACE*	Angiotensin I converting enzyme	[1]
2	rs4341	*ACE*	Angiotensin I converting enzyme	[2] [3]
3	rs4961	*ADD1*	Adducin 1	[4] [5]
4	rs1801253	*ADRB1*	Adrenoceptor beta 1	[1]
5	rs2004776	*AGT*	Angiotensinogen	[1] [6] [7] [8]
6	rs699	*AGT*	Angiotensinogen	[9] [10]
7	rs4762	*AGT*	Angiotensinogen	[10] [11]
8	rs5049	*AGT*	Angiotensinogen	[11]
9	rs5186	*AGTR1*	Angiotensin II receptor type 1	[12]
10	rs17249754	*ATP2B1*	ATPase plasma membrane Ca2+ transporting 1	[8] [13]
11	rs2681472	*ATP2B1*	ATPase plasma membrane Ca2+ transporting 1	[8] [14]
12	rs4590817	*C10orf107*	Chromosome 10 open reading frame 107	[13]
13	rs11014166	*CACNB2*	Calcium voltage-gated channel auxiliary subunit beta 2	[7] [8] [14]
14	rs1813353	*CACNB2(3')*	Calcium voltage-gated channel auxiliary subunit beta 2	[8] [13]
15	rs4373814	*CACNB2(5')*	Calcium voltage-gated channel auxiliary subunit beta 2	[13]
16	rs1799998	*CYP11B2*	Cytochrome P450 family 11 subfamily B member 2	[15]
17	rs1378942	*CYP1A1-ULK3*	Cytochrome P450 family 1 subfamily A member 1; Unc-51 like kinase 3	[8] [13] [16]
18	rs2266782	*FMO3*	Flavin containing monooxygenase 3	[17]
19	rs6015450	*GNAS-EDN3*	GNAS complex locus; Endothelin 3	[8] [13]
20	rs5443	*GNB3*	G protein subunit beta 3	[18]
21	rs17367504	*MTHFR-NPPB*	Methylenetetrahydrofolate reductase; Natriuretic peptide B	[7] [8] [13] [16]
22	rs1799983	*NOS3*	Nitric oxide synthase 3	[19]
23	rs2070744	*NOS3*	Nitric oxide synthase 3	[19]
24	rs3918226	*NOS3*	Nitric oxide synthase 3	[6] [7] [19]
25	rs5068	*NPPA*	Natriuretic peptide A	[20] [21]
26	rs198358	*NPPA-AS1*	NPPA antisense RNA 1	[20]
27	rs1173771	*NPR3-C5orf23*	Natriuretic peptide receptor 3; Chromosome 5 open reading frame 23	[7] [8] [13]
28	rs932764	*PLCE1*	Phospholipase C epsilon 1	[7] [8] [13]
29	rs3754777	*STK39*	Serine/threonine kinase 39	[22]
30	rs13333226	*UMOD*	Uromodulin	[8] [23]

Step 2.

	SNPs included based on assay design	
Number	SNP	Locus
1	rs4341	*ACE*
2	rs4961	*ADD1*
3	rs699	*AGT*
4	rs4762	*AGT*
5	rs5049	*AGT*
6	rs5186	*AGTR1*
7	rs2681472	*ATP2B1*
8	rs1813353	*CACNB2(3')*
9	rs4373814	*CACNB2(5')*
10	rs1799998	*CYP11B2*
11	rs1378942	*CYP1A1-ULK3*
12	rs2266782	*FMO3*
13	rs6015450	*GNAS-EDN3*
14	rs5443	*GNB3*
15	rs17367504	*MTHFR-NPPB*
16	rs1799983	*NOS3*
17	rs2070744	*NOS3*
18	rs3918226	*NOS3*
19	rs5068	*NPPA*
20	rs198358	*NPPA-AS1*
21	rs1173771	*NPR3-C5orf23*
22	rs932764	*PLCE1*
23	rs13333226	*UMOD*

	SNPs excluded during assay design	
Number	SNP	Locus
1	rs4305	*ACE*
2	rs1801253	*ADRB1*
3	rs2004776	*AGT*
4	rs17249754	*ATP2B1*
5	rs4590817	*C10orf107*
6	rs11014166	*CACNB2*
7	rs3754777	*STK39*

Step 3.

	SNPs included in the study (allele frequency comparison, GRS computation)	
Number	SNP	Locus
1	rs4961	*ADD1*
2	rs699	*AGT*
3	rs4762	*AGT*
4	rs5049	*AGT*
5	rs5186	*AGTR1*
6	rs2681472	*ATP2B1*
7	rs1813353	*CACNB2(3')*
8	rs4373814	*CACNB2(5')*
9	rs1378942	*CYP1A1-ULK3*
10	rs2266782	*FMO3*
11	rs6015450	*GNAS-EDN3*
12	rs5443	*GNB3*
13	rs17367504	*MTHFR-NPPB*
14	rs1799983	*NOS3*
15	rs2070744	*NOS3*
16	rs5068	*NPPA*
17	rs198358	*NPPA-AS1*
18	rs1173771	*NPR3-C5orf23*
19	rs932764	*PLCE1*
20	rs13333226	*UMOD*

	SNPs were not recommended		
Number	SNP	Gene	Reason for exclusion
1	rs4341	*ACE*	Did not work. Wrong genotypes called due to poor cluster separation, and too many heterozygots called.
2	rs1799998	*CYP11B2*	Deviation from HWE in our analysis.
3	rs3918226	*NOS3*	Deviation from HWE in our analysis.

Step 4.

	SNPs have effect size estimates publicly available	
Number	SNP	Locus
1	rs4961	*ADD1*
2	rs699	*AGT*
3	rs4762	*AGT*
4	rs5049	*AGT*
5	rs5186	*AGTR1*
6	rs2681472	*ATP2B1*
7	rs1813353	*CACNB2(3')*
8	rs4373814	*CACNB2(5')*
9	rs1378942	*CYP1A1-ULK3*
10	rs6015450	*GNAS-EDN3*
11	rs5443	*GNB3*
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14	rs2070744	*NOS3*
15	rs5068	*NPPA*
16	rs198358	*NPPA-AS1*
17	rs1173771	*NPR3-C5orf23*
18	rs932764	*PLCE1*
19	rs13333226	*UMOD*

	SNPs without available effect size	
Number	SNP	Locus
1	rs2266782	*FMO3*

Step 5.

	SNPs included in wGRS analyses	
Number	SNP	Locus
1	rs4961	*ADD1*
2	rs699	*AGT*
3	rs4762	*AGT*
4	rs5049	*AGT*
5	rs5186	*AGTR1*
6	rs2681472	*ATP2B1*
7	rs1813353	*CACNB2(3')*
8	rs4373814	*CACNB2(5')*
9	rs1378942	*CYP1A1-ULK3*
10	rs6015450	*GNAS-EDN3*
11	rs5443	*GNB3*
12	rs17367504	*MTHFR-NPPB*
13	rs1799983	*NOS3*
14	rs2070744	*NOS3*
15	rs5068	*NPPA*
16	rs198358	*NPPA-AS1*
17	rs1173771	*NPR3-C5orf23*
18	rs932764	*PLCE1*
19	rs13333226	*UMOD*

Step 1. On the basis of the systematic literature review altogether 30 SNPs associated with hypertension were identified.

Step 2. During the assay design different SNP pools were created by the service provider. Our decision on the set of SNPs on which the assay was carried out was based on the representation of SNPs with strong (susceptible or protective) influence on the investigated phenotype. In this set suitable for simultaneous genotyping in iPLEX Gold chemistry 23 SNPs were included.

Step 3. In the early stage of genotyping process 1 SNP were not recommended for further analysis by the service provider for the following reason: in case of the rs4341 SNP the assay failed, the observed wrong genotypes called due to poor cluster separation, and too many heterozygotes called. Further 2 SNPs, the 1799998 and rs3918226 deviated from Hardy-Weinberg Equilibrium in the Hungarian general population ($p<0.05$) according to our analyses. The remaining 20 SNPs were involved in comparison of allele frequencies and computation of unweighted GRS.

Step 4. Effect size estimates from association studies were available for 19 SNPs in the literature, consequently only these SNPs could be considered in computation of weighted GRS.

Step 5. Based on the LD pattern none of the pairwise LD of the studied SNPs reached the r^2 threshold of ≥0.8, there were not observed multicollinearity between the polymorphisms, thus it was not necessary to prune SNP from the analysis. Finally, 19 SNPs could be included in the wGRS computation.

Supplementary Table 2. Distribution of study populations by wGRS quintiles (p=0.029)

	Hungarian general population (%)	Hungarian Roma population (%)
1st quintile of wGRS (-0.54 - ≤0.85)	18.51	21.51
2nd quintile of wGRS (0.85 - ≤1.25)	18.77	21.26
3rd quintile of wGRS (1.25 - ≤1.63)	19.54	20.49
4th quintile of wGRS (1.64 - ≤2.08)	21.59	18.37
5th quintile of wGRS (2.09 - ≤4.92)	21.59	18.37

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