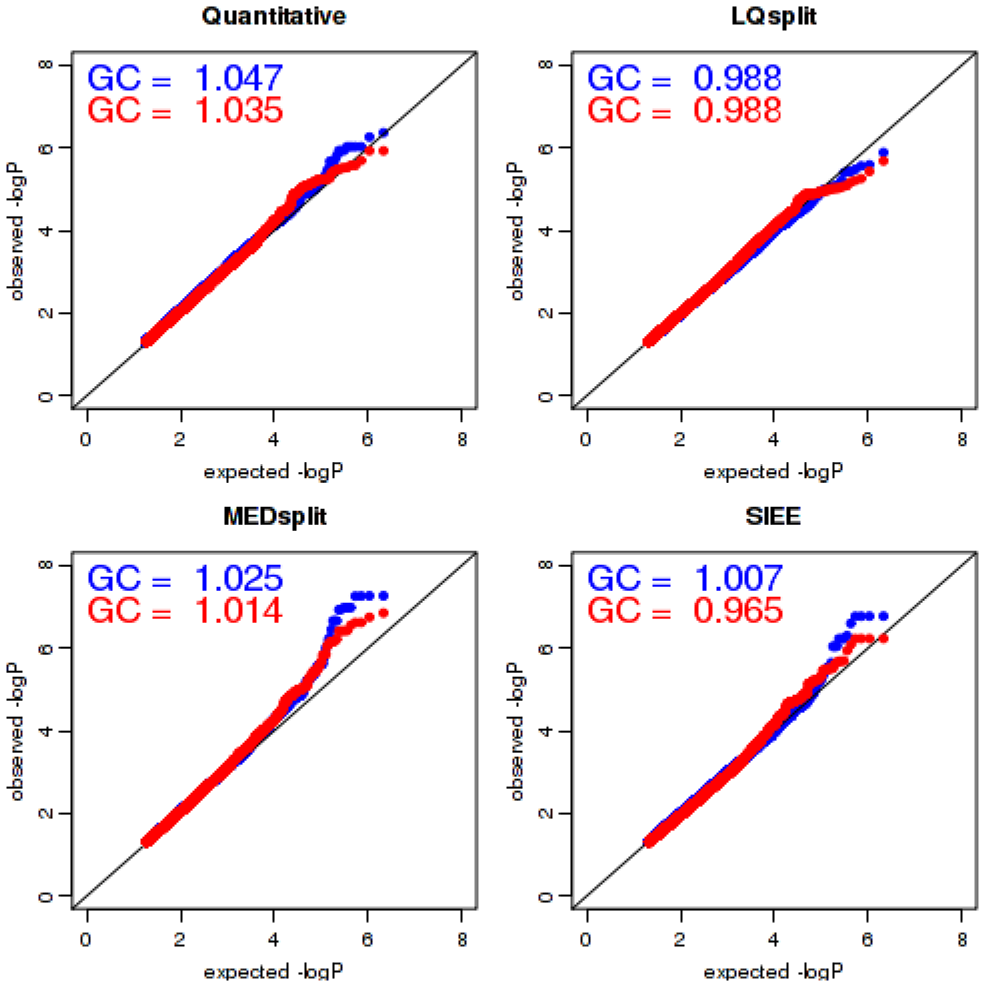

Figure S1. QQ plots by PA variables for SBP. Log$_{10}$ *P*-values from the 1 DF interaction test are shown in blue and the 2 DF joint test are shown in red. Genomic control lambda (GC; same as λ) is generally well controlled. See Table S6 for definition of abbreviations.

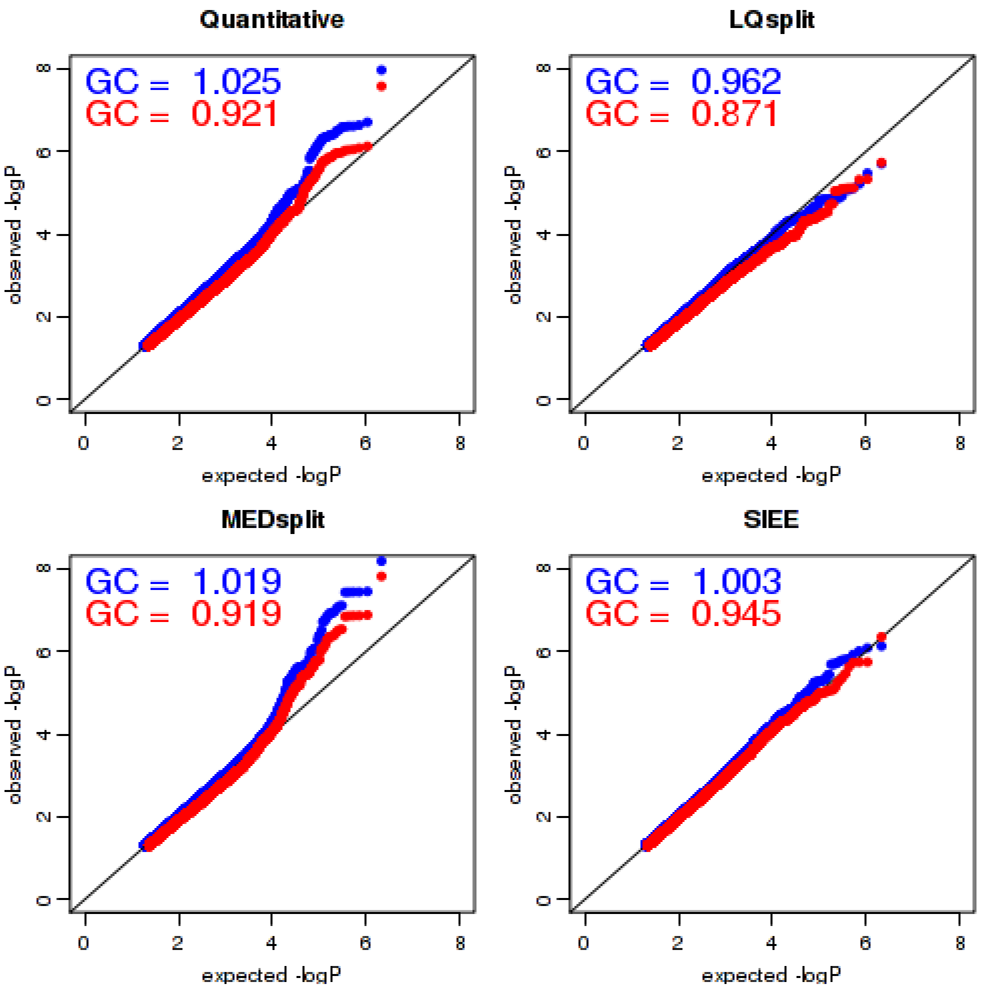

Figure S2. QQ plots by PA variables for DBP. Log_{10} *P*-values from the 1 DF interaction test are shown in blue and the 2 DF joint test are shown in red. Genomic control (GC) for the 2DF test is moderately deflated for the LQsplit PA variable. See Table S6 for definition of abbreviations.

Table S1. Total number of SNPs in sets used in the 4 analyses for each phenotype.

Phenotype	Quantitative	LQsplit	MEDsplit	SIEE
SBP	2,144,171	2,144,171	2,144,143	2,144,462
DBP	2,144,169	2,144,169	2,144,141	2,144,462

Abbreviations: SBP, systolic blood pressure; DBP, diastolic blood pressure;

LQsplit, created by splitting Quantitative by the lower quartile of its distribution;

MEDsplit, created by splitting Quantitative by the median of its distribution;

SIEE, created by selecting individuals with Quantitative values in the lower and upper quartiles and excluding individuals intermediate between the lower and upper quartile.

Table S2. Top SNP hits for SBP detected using 2 DF joint test in all four analyses defined by PA variable.

Chr:Position†	Loci Tag	EAF	Imputation	β_G	β_{GE}	*P*_β_{GE}	Joint 2-DF	PA variable	Effect direction
1:192857024	9	0.3136	0.9375	0.5007	1.5730	3.93E-03	6.16E-06	LQsplit	SYN
1:192857024	9	0.3097	0.9375	0.5170	0.7636	1.17E-02	2.49E-06	SIEE	SYN
2:197062178	11	0.9424	0.9886	2.6580	-2.8310	3.19E-03	6.73E-06	LQsplit	ANT
2:197062178	11	0.9417	0.9886	3.6060	-1.9190	1.63E-04	3.36E-06	SIEE	SYN
2:197062178	11	0.9424	0.9886	0.0512	0.2921	4.88E-03	3.02E-06	Quantitative	NA
2:206880872	21	0.4030	0.9648	1.0530	-0.2396	6.53E-06	6.51E-06	Quantitative	NA
2:206969101	21	0.3625	0.8692	-1.8270	1.4060	2.92E-06	7.07E-06	SIEE	SYN
2:218367315	19	0.0851	0.7696	-3.2550	3.1210	9.11E-04	5.66E-06	MEDsplit	SYN
3:34818945	23	0.8573	0.9807	2.3930	-1.6070	3.62E-05	6.96E-06	SIEE	SYN
4:157688802	8	0.4569	0.8888	-0.9336	2.3790	8.75E-07	2.06E-06	MEDsplit	ANT
4:75035707	15	0.1780	0.7205	2.0620	-1.9980	1.16E-02	3.71E-06	LQsplit	SYN
5:124653679	13	0.9128	0.8282	-3.6490	2.4700	2.25E-06	3.37E-06	SIEE	SYN
5:1845474	28	0.0929	0.9862	-1.7770	3.9530	8.72E-06	9.65E-06	LQsplit	ANT
5:1845474	28	0.0929	0.9862	-2.4490	3.5090	8.34E-06	9.07E-06	MEDsplit	ANT
5:35044449	26	0.1237	0.7612	-3.0880	0.4229	4.39E-06	8.61E-06	Quantitative	NA
6:32328375	16	0.8522	0.9546	0.1765	2.0100	2.29E-03	5.33E-06	MEDsplit	SYN
6:32514451	16	0.8021	0.9976	2.1960	-0.1737	6.03E-03	5.49E-06	Quantitative	NA
7:130493617	2	0.0572	0.9714	0.1025	-3.4720	3.34E-04	1.79E-07	MEDsplit	ANT
7:130493617	2	0.0572	0.9714	-3.9620	0.3704	1.57E-03	3.06E-06	Quantitative	NA
7:155831233	5	0.2567	0.7040	1.8910	-3.3010	1.14E-07	6.73E-07	MEDsplit	ANT
7:20608418	25	0.5390	0.4167	0.9551	-0.3127	8.08E-05	8.47E-06	Quantitative	NA
7:43335541	6	0.2687	0.8381	2.2240	-2.7660	1.82E-06	9.07E-07	MEDsplit	ANT
7:43335541	6	0.2687	0.8381	-0.9940	0.2841	8.28E-06	2.03E-06	Quantitative	NA
8:68259006	10	0.8670	0.3169	-4.4120	0.6899	4.29E-07	2.66E-06	Quantitative	NA
9:128252235	17	0.8785	0.9144	2.3460	-1.5360	3.36E-02	8.47E-06	MEDsplit	SYN
9:128252235	17	0.8803	0.9144	2.6600	-0.7072	9.54E-02	5.41E-06	SIEE	SYN
9:128274132	17	0.1298	0.9994	-0.6771	-0.1305	6.50E-02	5.63E-06	Quantitative	NA
9:13620162	3	0.1937	0.9150	-2.1030	1.8350	1.69E-07	5.86E-07	SIEE	SYN
9:13621427	3	0.1911	0.9153	2.1630	-0.3375	9.38E-07	5.94E-06	Quantitative	NA
9:13621992	3	0.1912	0.9157	-1.6120	3.2460	5.40E-08	3.79E-07	MEDsplit	ANT
10:4618784	18	0.4122	0.9625	0.9921	-2.4980	1.29E-06	5.56E-06	LQsplit	ANT
10:82575930	14	0.0607	0.9823	3.4420	-0.6237	2.86E-01	3.48E-06	SIEE	SYN

10:97298997	24	0.9475	0.9197	-1.3290	4.5030	1.36E-05	8.23E-06	MEDsplit	ANT
12:71678350	12	0.2599	0.9759	0.4874	-2.1890	4.69E-05	3.11E-06	MEDsplit	ANT
12:73799585	7	0.0949	0.9745	-2.6010	4.0060	5.54E-07	1.49E-06	MEDsplit	ANT
12:93573610	27	0.3999	0.9307	-0.2573	-0.1205	2.53E-02	8.80E-06	Quantitative	NA
14:75651645	1	0.1075	0.8972	3.2580	-3.9240	6.21E-07	1.41E-07	MEDsplit	ANT
14:75651645	1	0.1086	0.8972	3.4880	-2.0590	5.98E-06	1.15E-06	SIEE	SYN
14:75651645	1	0.1075	0.8972	-1.2910	0.4073	7.62E-06	1.18E-06	Quantitative	NA
14:92288711	20	0.8803	0.5242	3.5470	-2.2650	1.52E-05	5.91E-06	SIEE	SYN
19:52704281	22	0.1334	0.8932	2.4380	-3.3430	5.05E-06	6.70E-06	MEDsplit	ANT
19:8012521	4	0.4171	0.4590	-1.9050	0.6698	3.57E-01	2.07E-06	LQsplit	SYN
19:8012521	4	0.4171	0.4590	-2.3400	1.1840	7.99E-02	6.05E-07	MEDsplit	SYN
19:8012521	4	0.4171	0.4590	-1.1340	-0.0954	2.16E-01	1.18E-06	Quantitative	NA

Abbreviations and symbols:

†Genome build: NCBI build 36.

EAF: effect allele frequency

β_G	is the genetic main effect
β_{GE}	is the GxPA interaction effect
P_β_{GE}	is the 1-DF test *P*-value

Joint 2-DF refers to *P*-values from the Wald 2-DF joint test for β_G and β_{GE}

Effect direction: based on the similarity in the direction of β_G

and the sum of β_G and β_{GE} to get an estimate of effect size in the exposed group

SYN indicates same effect direction between exposure groups

ANT indicates opposite effect direction between exposure groups

Table S3. Top SNP hits for SBP detected using 1 DF interaction test in all four analyses defined by PA variable.

Chr:Position†	Loci Tag	EAF	Imputation	β_G	β_{GE}	P_β_{GE}	PA variable	Effect direction
1:117395987	20	0.3962	0.4295	1.2540	-3.3810	8.31E-06	LQsplit	ANT
1:224575268	21	0.3041	0.8441	1.3400	-2.4030	9.38E-06	MEDsplit	ANT
2:206880872	12	0.4030	0.9648	1.0530	-0.2396	6.53E-06	Quantitative	NA
2:206975861	12	0.3625	0.8528	-1.8310	1.4200	2.87E-06	SIEE	SYN
2:68014962	11	0.3215	0.8689	0.8404	-2.6820	2.57E-06	LQsplit	ANT
4:157688802	6	0.4569	0.8888	-0.9336	2.3790	8.75E-07	MEDsplit	ANT
5:124653679	9	0.9128	0.8282	-3.6490	2.4700	2.25E-06	SIEE	SYN
5:1845474	19	0.0929	0.9862	-1.7770	3.9530	8.72E-06	LQsplit	ANT
5:1845474	19	0.0929	0.9862	-2.4490	3.5090	8.34E-06	MEDsplit	ANT
5:1845474	19	0.0955	0.9862	-1.9490	2.0510	8.07E-06	SIEE	ANT
5:35044449	15	0.1237	0.7612	-3.0880	0.4229	4.39E-06	Quantitative	NA
6:39163494	14	0.0972	0.8389	0.9100	-3.7340	4.06E-06	LQsplit	ANT
7:155831233	2	0.2567	0.7040	1.8910	-3.3010	1.14E-07	MEDsplit	ANT
7:155842801	2	0.2277	0.6765	-1.9650	0.3401	3.62E-06	Quantitative	NA
7:17656736	22	0.2609	0.9657	-1.4440	0.2601	9.55E-06	Quantitative	NA
7:43402308	7	0.0965	0.7328	3.2690	-4.5770	1.00E-06	MEDsplit	ANT
7:43402308	7	0.0965	0.7328	-2.2680	0.5051	3.20E-06	Quantitative	NA
8:68259006	3	0.8670	0.3169	-4.4120	0.6899	4.29E-07	Quantitative	NA
9:13621992	1	0.1912	0.9157	2.1630	-0.3374	9.36E-07	Quantitative	NA
9:13622110	1	0.1912	0.9158	-1.6120	3.2450	5.39E-08	MEDsplit	ANT
9:13622110	1	0.1938	0.9158	-2.1030	1.8340	1.68E-07	SIEE	SYN
10:4618581	8	0.4501	0.9366	1.1870	-1.2770	3.98E-06	SIEE	ANT
10:4618784	8	0.4122	0.9625	0.9921	-2.4980	1.29E-06	LQsplit	ANT
10:84414058	13	0.7458	0.9719	1.6940	-1.4760	3.60E-06	SIEE	SYN
12:73799585	4	0.0949	0.9745	-2.6010	4.0060	5.54E-07	MEDsplit	ANT
14:75602180	5	0.8477	0.9997	1.4240	-0.3240	5.64E-06	Quantitative	NA
14:75651645	5	0.1075	0.8972	3.2580	-3.9240	6.21E-07	MEDsplit	ANT
14:75651645	5	0.1086	0.8972	3.4880	-2.0590	5.98E-06	SIEE	SYN
14:76167428	17	0.8312	0.9663	2.0200	-1.6800	6.81E-06	SIEE	SYN
15:85878957	16	0.1718	0.9992	-1.0120	2.9950	6.26E-06	LQsplit	ANT
19:17647792	18	0.2830	0.3661	2.2570	-0.3987	7.08E-06	Quantitative	NA
19:52739090	10	0.1094	0.9866	2.2130	-3.5300	2.44E-06	MEDsplit	ANT

Abbreviations and symbols:

†Genome build: NCBI build 36.

EAF: effect allele frequency

β_{G}	is the genetic main effect
β_{GE}	is the GxPA interaction effect
P_β_{GE}	is the 1-DF test *P*-value

Effect direction: based on the similarity in the direction of β_{G} and the sum of β_{G} and β_{GE} to get an estimate of beta for the exposed group

SYN indicates same effect direction between exposure groups

ANT indicates opposite effect direction between exposure groups

Table S4. Top SNP hits for DBP detected using 2 DF joint test in all four analyses defined by PA variable. Significant hit at threshold of $P \leq 5 \times 10^{-8}$ in bold.

Chr:Position[†]	Loci Tag	EAF	Imputation	β_G	β_{GE}	P_β_{GE}	Joint 2-DF	PA variable	Effect direction
2:118667087	6	0.9247	0.7308	-1.2450	2.7230	5.27E-07	2.51E-06	MEDsplit	ANT
2:25474404	5	0.7346	0.9786	-0.6980	-0.1155	7.28E-01	4.72E-06	LQsplit	SYN
2:25474404	5	0.7346	0.9786	-0.5615	-0.3410	2.48E-01	2.30E-06	MEDsplit	SYN
2:25474404	5	0.7346	0.9786	-0.8520	0.0193	5.66E-01	4.28E-06	Quantitative	NA
3:64324928	11	0.1721	0.3103	2.1870	-0.3231	1.01E-06	6.35E-06	Quantitative	NA
3:85454090	8	0.5263	1.0039	0.2553	-1.3020	2.00E-06	7.99E-06	LQsplit	ANT
3:85454090	8	0.5216	1.0039	0.5050	-0.7458	1.49E-06	4.46E-06	SIEE	ANT
6:33398525	12	0.5016	0.9764	-0.4698	1.1920	2.47E-06	6.44E-06	MEDsplit	ANT
6:36351472	10	0.2535	0.9864	-0.8762	0.8814	8.25E-07	5.12E-06	SIEE	ANT
7:11418729	2	0.6360	0.9754	0.9183	-1.1980	4.10E-06	1.58E-06	MEDsplit	ANT
8:29307602	4	0.0521	0.6711	-1.1900	-1.3260	6.69E-02	1.86E-06	LQsplit	SYN
10:8828265	7	0.0762	0.4406	-1.0660	0.3404	8.29E-05	2.76E-06	Quantitative	NA
12:646358	9	0.1710	0.9624	-1.4340	0.1805	5.07E-06	4.86E-06	Quantitative	NA
13:47846570	3	0.2595	0.9863	0.4536	-0.8531	2.02E-06	1.81E-06	SIEE	ANT
18:13477861	13	0.8419	0.5154	-0.7617	1.2640	7.57E-06	8.96E-06	SIEE	ANT
21:46484473	1	0.6957	0.9903	-1.0380	1.5830	6.48E-09	1.52E-08	MEDsplit	ANT
21:46484473	1	0.6970	0.9903	-1.1930	0.8155	1.18E-06	4.44E-07	SIEE	SYN
21:46484473	1	0.6957	0.9903	0.9487	-0.1884	1.07E-08	2.63E-08	Quantitative	NA

Abbreviations and symbols:

[†]Genome build: NCBI build 36.

EAF: effect allele frequency

β_G	is the genetic main effect
β_{GE}	is the GxPA interaction effect
*P*_β_{GE}	is the 1-DF test *P*-value

Joint 2-DF refers to *P*-values from the Wald 2-DF joint test for β_G and β_{GE}

Effect direction: based on the similarity in the direction of β_G

and the sum of β_G and β_{GE} to get an estimate of beta for the exposed group

SYN indicates same effect direction between exposure groups

ANT indicates opposite effect direction between exposure groups

Table S5. Top SNP hits for DBP detected using 1 DF interaction test in all four analyses defined by PA variable. Significant hit at threshold of $P \leq 5 \times 10^{-8}$ in bold.

Chr:Position†	Loci Tag	EAF	Imputation	β_G	β_{GE}	P_β_{GE}	PA variable	Effect direction
1:63897567	16	0.223	0.989	0.577	-0.857	5.50E-06	SIEE	ANT
1:63897660	16	0.227	0.989	-1.128	0.158	8.34E-06	Quantitative	NA
1:71550136	9	0.192	0.967	0.522	-1.586	3.37E-06	LQsplit	ANT
2:118667087	2	0.925	0.731	-1.245	2.723	5.27E-07	MEDsplit	ANT
2:9914074	21	0.163	0.998	0.961	-0.168	7.69E-06	Quantitative	NA
3:64324928	4	0.172	0.310	-1.196	2.655	9.00E-06	MEDsplit	ANT
3:64324928	4	0.172	0.310	2.187	-0.323	1.01E-06	Quantitative	NA
3:85454090	5	0.526	1.004	0.255	-1.302	2.00E-06	LQsplit	ANT
3:85454090	5	0.522	1.004	0.505	-0.746	1.49E-06	SIEE	ANT
3:99639402	24	0.558	0.873	-0.812	0.132	9.15E-06	Quantitative	NA
4:125514882	19	0.710	0.665	-0.730	1.522	7.41E-06	MEDsplit	ANT
4:181903298	17	0.103	0.974	-1.125	0.209	6.05E-06	Quantitative	NA
4:34911652	23	0.817	0.845	-1.243	0.175	8.81E-06	Quantitative	NA
4:38025631	13	0.115	0.915	-1.304	1.167	4.78E-06	SIEE	SYN
5:113072300	8	0.077	0.843	1.426	-0.232	3.08E-06	Quantitative	NA
6:33366421	7	0.507	0.974	-0.489	1.204	1.97E-06	MEDsplit	ANT
6:36351472	3	0.254	0.986	-0.876	0.881	8.25E-07	SIEE	ANT
6:7417981	26	0.073	0.755	1.848	-0.284	9.40E-06	Quantitative	NA
7:11411026	12	0.629	0.922	0.875	-1.217	4.03E-06	MEDsplit	ANT
7:155835300	10	0.645	0.565	0.878	-1.619	3.59E-06	MEDsplit	ANT
7:93067389	27	0.575	0.988	-0.667	0.131	9.44E-06	Quantitative	NA
9:135834384	25	0.557	0.771	-0.979	0.141	9.17E-06	Quantitative	NA
9:14819767	18	0.287	0.436	0.770	-2.102	6.20E-06	LQsplit	ANT
11:40180006	14	0.949	0.680	1.475	-3.109	4.81E-06	MEDsplit	ANT
11:7951172	22	0.919	0.911	-1.453	1.352	8.16E-06	SIEE	SYN
12:653611	15	0.169	0.950	-1.436	0.182	5.00E-06	Quantitative	NA
13:47872743	6	0.263	0.985	0.485	-0.851	1.92E-06	SIEE	ANT
14:54249771	11	0.809	0.916	0.694	-1.485	3.85E-06	MEDsplit	ANT
18:13477861	20	0.842	0.515	-0.762	1.264	7.57E-06	SIEE	ANT

Chr:Position[†]	**Loci Tag**	**EAF**	**Imputation**	**β_G**	**β_{GE}**	**P_β_{GE}**	**PA variable**	**Effect direction**
21:46479105	1	0.557	0.982	0.837	-0.772	7.46E-07	SIEE	SYN
21:46484473	1	0.696	0.990	-1.038	1.583	6.48E-09	MEDsplit	ANT
21:46484473	1	0.696	0.990	0.949	-0.188	1.07E-08	Quantitative	NA

Abbreviations and symbols:

[†] Genome build: NCBI build 36.

EAF: effect allele frequency

β_G	is the genetic main effect
β_{GE}	is the GxPA interaction effect
P_β_{GE}	is the 1-DF test *P*-value

Effect direction: based on the similarity in the direction of β_G

and the sum of β_G and β_{GE} to get an estimate of beta for the exposed group

SYN indicates same effect direction between exposure groups

ANT indicates opposite effect direction between exposure groups

Table S6. Overlap in genetic loci detected by gene-physical activity interaction (GxPA) analysis that differed in physical activity (PA) variable using the 1 DF interaction test. Overlap is the sum of loci detected by at least two different GxPA analyses that differed in PA variable.

Phenotype	**PA variable**	**Total**	**Unique**	**Overlap including Quantitative**	**Overlap with dichotomous only**
SBP	Quantitative	9	4	NA	5
	LQsplit	6	4	0	2
	MEDsplit	9	4	4	1
	SIEE	8	3	3	2
DBP	Quantitative	12	9	NA	3
	LQsplit	3	2	0	1
	MEDsplit	9	7	2	0
	SIEE	8	5	2	1

Abbreviations: SBP, systolic blood pressure; DBP, diastolic blood pressure;

LQsplit, created by splitting Quantitative by the lower quartile of its distribution;

MEDsplit, created by splitting Quantitative by the median of its distribution;
SIEE, created by selecting individuals with Quantitative values in the lower and upper quartiles and excluding individuals intermediate between the lower and upper quartile.