Supplementary data for “Exploring predictive biomarkers from clinical genome-wide association studies via multidimensional hierarchical mixture models”

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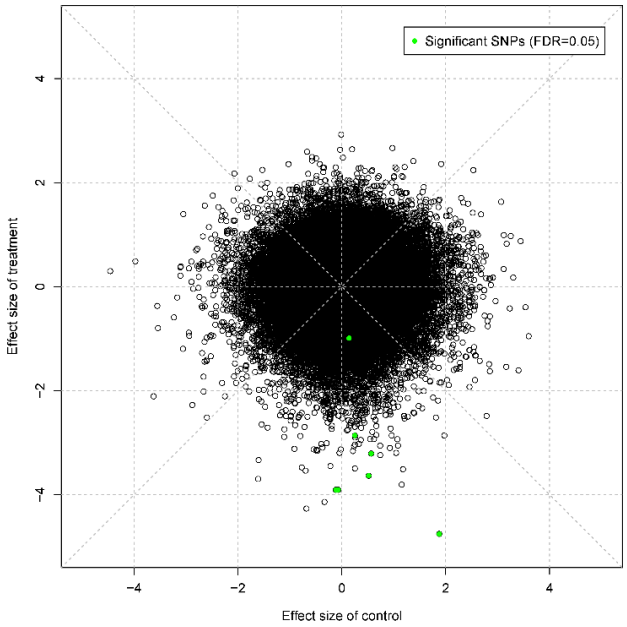
a.



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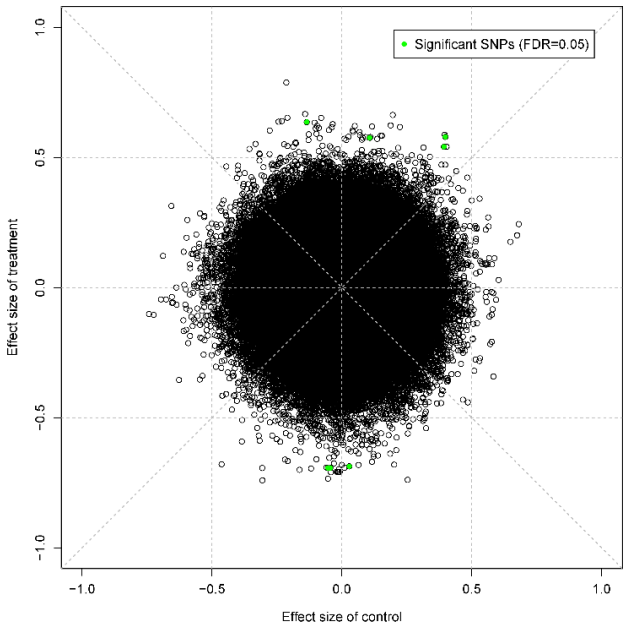
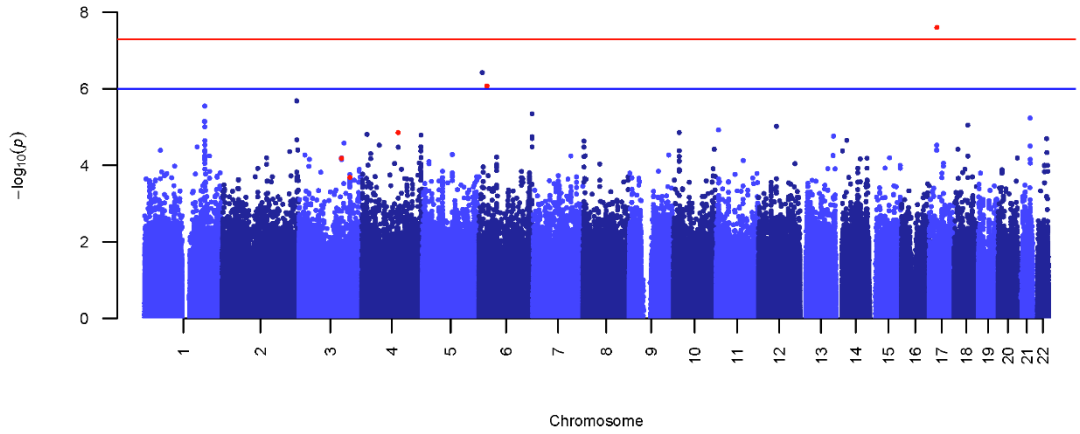


Figure S1. Plots of regression coefficients derived from maximum likelihood estimation for control and treatment groups. Two plots are shown, one from the stroke trial (a) and the other from the breast cancer trial (b). The *x* axis represents the effect size for the control group and the *y* axis represents the effect size for the treatment group. Green points indicate SNPs detected by the ODP (FDR<5%).

a.



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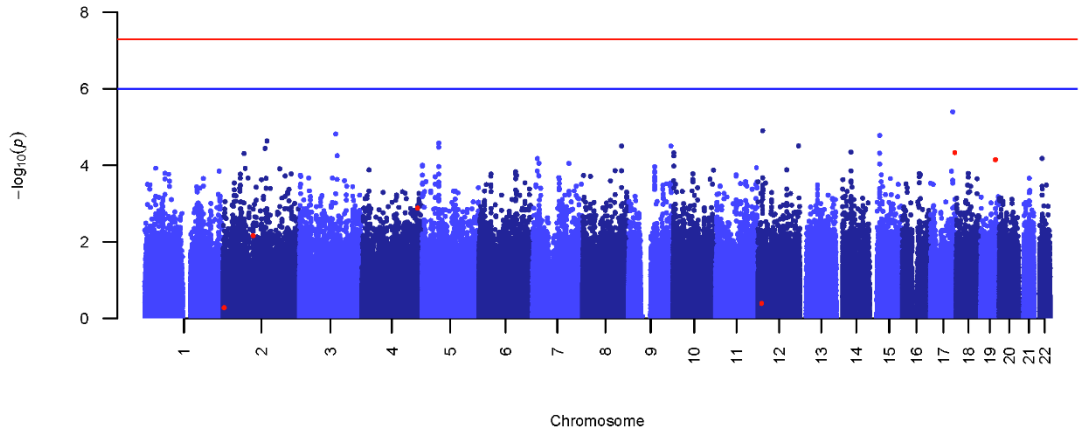
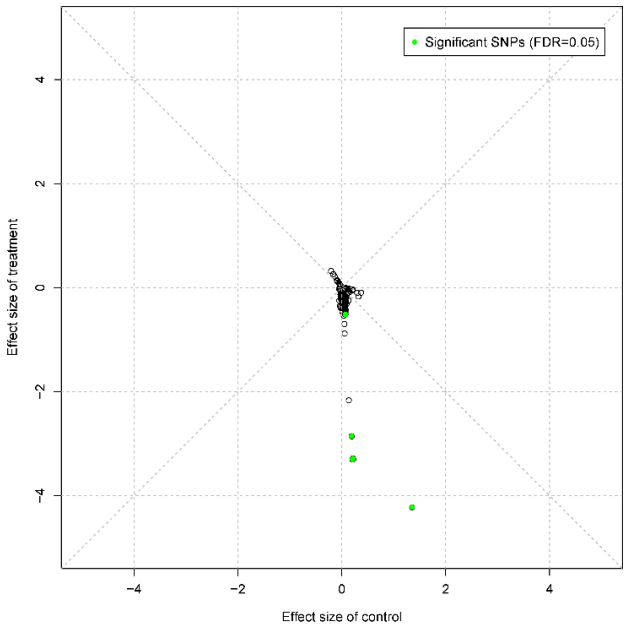


Figure S2. Manhattan plots from association tests using standard regression models with interaction terms. Two plots are shown, one from the stroke trial (a) and the other from the breast cancer trial (b). $-\log_{10} p$ for each SNP (y axis) are plotted by chromosomal position (x axis). Red lines denote the genome-wide significance level ($p = 5 \times 10^{-8}$), and blue lines denote the suggestive level ($p = 10^{-6}$). Red points denote p-values of SNPs that are detected by the ODP (FDR<5%) and that are not in LD.

a.



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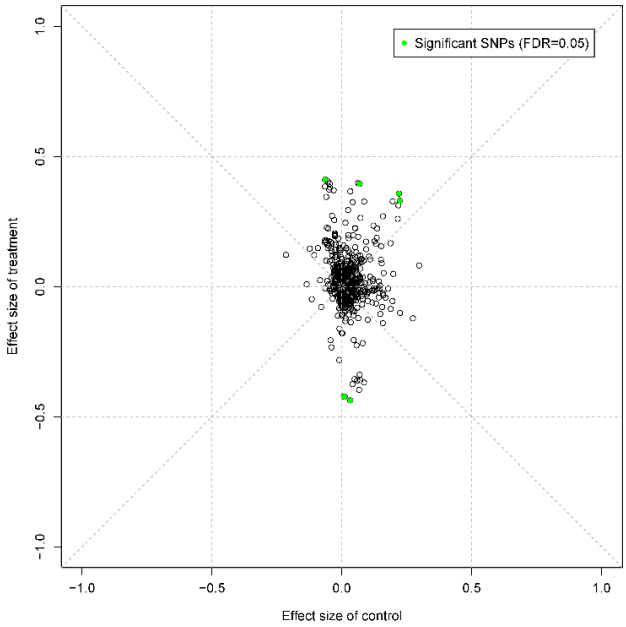

Figure S3. Plots of adjusted effect size estimates derived from the hierarchical mixture models. Two plots are shown, one from the stroke trial (a) and the other from the breast cancer trial (b). The *x* axis represents the effect size for the control group and the *y* axis represents the effect size for the treatment group. Green points indicate SNPs detected by the ODP (FDR<5%).

Table S1-S9. Summaries of genomic annotation for LD surrogates of SNPs detected by the ODP.

Please see supplemental Excel documents.

Table S10. Comparison of the number of significant SNPs detected by qvalue and ODP.

	Blood homocysteine levels		Breast cancer	
FDR	qvalue	ODP	qvalue	ODP
1%	0	5	0	1
5%	1	8	0	7
10%	1	12	0	25
20%	2	26	0	47

Note that the number of independently associated SNPs is likely to be much smaller since some SNPs are in LD.

Table S11. Average numbers of significant SNPs and true positives for the ODP and conventional methods in 200 simulations based on the stroke trial.

	Significant SNPs			True positives		
FDR	5%	10%	20%	5%	10%	20%
1533 subjects						
$\pi = 0.9$						
ODP	19009.0	26619.7	39667.4	18063.7	24016.4	32004.0
S_j	2683.7	4226.8	7888.2	2555.1	3823.9	6386.6
T_j	6652.1	10834.2	19261.6	6329.7	9785.8	15526.5
$\pi = 0.99$						
ODP	690.2	999.6	1567.7	652.8	897.2	1260.4
S_j	124.7	156.3	226.2	118.6	140.2	180.8
T_j	206.9	296.9	502.5	196.6	267.3	401.6
$\pi = 0.999$						
ODP	26.5	36.6	56.1	24.7	31.9	44.0
S_j	9.5	10.6	13.1	8.9	9.4	10.3
T_j	12.0	14.6	20.1	11.3	12.8	15.5
5000 subjects						
$\pi = 0.9$						
ODP	60675.2	68208.1	81789.3	57743.1	61572.3	65768.5
S_j	25913.3	32505.5	43760.8	24650.4	29340.9	35223.6
T_j	43936.3	51622.2	64646.5	41761.0	46521.2	51882.7
$\pi = 0.99$						
ODP	4808.8	5468.4	6636.3	4580.5	4944.0	5347.8
S_j	1439.1	1836.0	2524.5	1367.3	1652.1	2019.2
T_j	2964.9	3571.4	4592.2	2816.4	3213.4	3674.5
$\pi = 0.999$						
ODP	369.5	425.7	523.7	351.7	384.8	421.7
S_j	79.8	102.2	141.8	75.8	91.7	113.1
T_j	187.8	231.4	305.7	177.9	207.6	243.4

Table S12. Average numbers of significant SNPs and true positives for the ODP and conventional methods in 200 simulations based on the breast cancer trial.

	Significant SNPs			True positives		
FDR	5%	10%	20%	5%	10%	20%
3289 subjects						
$\pi = 0.9$						
ODP	8894.2	12009.7	17330.2	8460.9	10889.9	14203.6
S_j	3342.6	5025.3	8232.3	3184.9	4548.6	6666.0
T_j	4039.6	6018.2	9679.4	3847.1	5445.9	7836.0
$\pi = 0.99$						
ODP	374.1	515.4	757.7	353.3	462.7	614.1
S_j	106.1	163.5	270.8	100.6	147.0	217.3
T_j	126.7	196.1	329.2	120.0	175.6	261.8
$\pi = 0.999$						
ODP	14.7	21.2	32.6	13.6	18.4	25.1
S_j	3.6	5.6	9.1	3.4	4.9	7.0
T_j	4.2	6.6	11.2	3.9	5.7	8.5
5000 subjects						
$\pi = 0.9$						
ODP	15973.9	19549.9	25456.6	15266.9	17877.2	21160.8
S_j	7566.2	10083.7	14520.0	7201.3	9114.4	11731.4
T_j	8815.5	11586.6	16397.4	8392.1	10474.1	13245.4
$\pi = 0.99$						
ODP	927.6	1152.8	1529.3	883.6	1047.9	1257.6
S_j	357.9	479.6	698.7	340.0	432.3	560.4
T_j	424.8	571.2	826.1	402.8	512.9	659.5
$\pi = 0.999$						
ODP	51.9	65.6	88.5	49.1	59.0	71.2
S_j	17.0	22.5	33.1	16.1	20.2	26.3
T_j	19.8	26.9	40.1	18.7	24.0	31.4