

TABLE 26.2. How replicable are association studies?

Associated Gene, Phenotype	Number of Studies (Total)	Number of Studies ($p < 0.05$) Same Direction as Original Report	Number of Studies ($p < 0.05$) Opposite Direction as Original Report
<i>ABCC8</i> , type 2 diabetes ^a	9	1	1
<i>ABCC8</i>, type 2 diabetes^a	4	2	0
<i>ADD1</i>, hypertension	18	5	2
<i>APOE</i> , schizophrenia	12	0	1
<i>BLMH</i> , Alzheimer's disease	5	0	0
<i>COL1A1</i>, osteoporotic fracture	12	5	0
<i>COMT</i> , bipolar disorder	12	0	0
<i>COMT</i> , schizophrenia	9	0	1
<i>CTLA4</i>, type 1 diabetes	20	8	0
<i>DRD2</i>, schizophrenia	8	2	1
<i>DRD3</i>, schizophrenia	48	5	2
<i>GSTM1</i> , breast cancer	15	0	0
<i>GSTM1</i>, head/neck cancer	25	3	1
<i>GYS1</i> , type 2 diabetes	3	0	1
<i>HTR2A</i>, schizophrenia	28	3	1
<i>INSR</i> , type 2 diabetes	4	1	0
<i>INSR</i> , type 2 diabetes	4	0	0
<i>KCNJ11</i> , type 2 diabetes	6	0	0
<i>NTF3</i> , schizophrenia	7	0	0
<i>PON1</i>, coronary artery disease	14	5	0
<i>PPARG</i>, type 2 diabetes	14	4	1
<i>SERPINE1</i> , myocardial infarction	13	1	0
<i>SLCA1</i>, type 2 diabetes	3	2	0
<i>SLCA2</i> , type 2 diabetes	3	0	0
<i>TPH</i> , bipolar disorder	5	0	0
Total	301	47	12

From Table 1 of Lohmueller K.E. et al. 2003. *Nat. Genet.* **33**: 177–182 (© Macmillan Publishers, www.nature.com).

^aThe two entries for *ABCC8* in the first and second rows are for variants in the intron and exon, respectively.

A survey of 25 associations between markers and complex diseases found a total of 301 follow-up studies. Of these, 59 were significant at the 5% level, far higher than the number expected if the initial reports had been “false positives” ($301 \times 0.05 \sim 15$), but still a minority. Moreover, many of the subsequent significant findings were in the opposite direction. The significant replications were concentrated among 11 of the associations (in bold type), which suggests that about one-half of these associations actually exist.