

Supplementary Materials

Integrating external controls by regression calibration for genome-wide association study

Lirong Zhu¹, Shijia Yan¹, Xuewei Cao¹, Shuanglin Zhang¹, Qiuying Sha^{1,*}

¹Department of Mathematical Sciences, Michigan Technological University, Houghton, Michigan, USA

*Corresponding author: Qiuying Sha, Department of Mathematical Sciences, Michigan Technological University, Houghton, Michigan 49931, USA. E-mail: qsha@mtu.edu

Table S1. Empirical type I error rates of iECAT-RC, compared with other three methods iECAT-N, Internal, and iECAT-Score at different significance levels, 0.05, 0.01, 10^{-3} and 10^{-4} with $DVS = 0.5$.

Model	Significance level	iECAT-RC	iECAT-N	Internal	iECAT-Score
Model 1	0.05	0.033	0.3895	0.05	0.0457
	0.01	0.0057	0.3285	0.0102	0.0077
	0.001	3×10^{-4}	0.2762	0.0012	9×10^{-4}
	1×10^{-4}	0	0.2386	2×10^{-4}	0
Model 2	0.05	0.0529	0.4083	0.0343	0.0449
	0.01	0.0109	0.357	0.0089	0.0111
	0.001	7×10^{-4}	0.3217	9×10^{-4}	0.0016
	1×10^{-4}	1×10^{-4}	0.2912	1×10^{-4}	0
Model 3	0.05	0.0464	0.1334	0.0139	0.0377
	0.01	0.0103	0.0829	0.0037	0.0066
	0.001	9×10^{-4}	0.0513	5×10^{-4}	8×10^{-4}
	1×10^{-4}	0	0.0364	0	0
Model 4	0.05	0.0323	0.4163	0.042	0.0407
	0.01	0.0052	0.3292	0.0089	0.0082
	0.001	6×10^{-4}	0.2608	0.0013	4×10^{-4}
	1×10^{-4}	2×10^{-4}	0.2231	3×10^{-4}	0
Model 5	0.05	0.0501	0.475	0.0327	0.0492
	0.01	0.0117	0.4002	0.0097	0.0087
	0.001	0.0016	0.3289	0.0011	0.0016
	1×10^{-4}	0	0.2775	1×10^{-4}	4×10^{-4}
Model 6	0.05	0.0453	0.1017	0.0139	0.0316
	0.01	0.0102	0.0546	0.0044	0.0072
	0.001	0.0012	0.028	8×10^{-4}	7×10^{-4}
	1×10^{-4}	0	0.0158	1×10^{-4}	0

Notes: Type I error rates are evaluated based on 5×10^5 simulations. The bold-faced values indicate the type I error rates beyond the upbound of the corresponding 95% confidence interval.

Table S2. The relative frequency of significant SNPs identified by each method using 10,000 repeated samples.

Chr	SNP	Base Position	iECAT-RC	iECAT-Score	Internal
22	rs62228062	46381234	95.3%	79.5%	37.4%
22	rs9330811	46362396	54.3%	38.8%	3.9%
22	rs28628653	46396925	34.7%	15.2%	1.1%
7	rs2290221	37987632	11.2%	1.8%	0.0%
22	rs9626908	46428306	8.3%	0.7%	0.2%
9	rs12685782	135320210	6.3%	0.2%	0.1%
22	rs28520003	46411969	5.0%	0.2%	0.1%

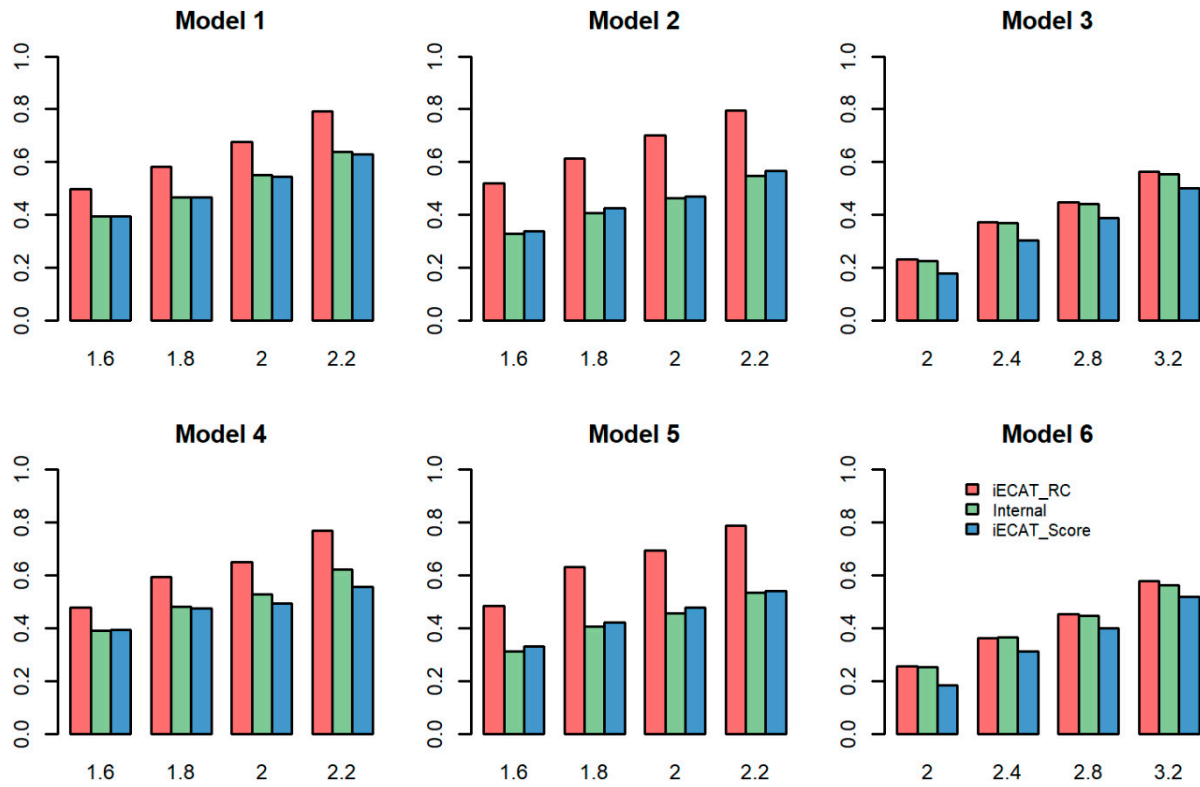


Figure S1. The power comparison of iECAT-RC, Internal, and iECAT-Score when $DVS = 0.5$ at the significance level of 5×10^{-8} . The horizontal axis represents the odds ratio, and the vertical axis represents power.