Table S1. Ratios of the empirical type I error rates to the significance levels ($R = \hat{\alpha}/\alpha$) for the ST_{EVSD} and GLM methods, given an exposure rate of 0.5 and an extreme proportion of 0.2.

Effect size		**Model**	***R*(α = 0.05)**			***R*(α = 0.01)**		
Expos.-PO (β_1)	**SO-PO (β_3)**		**ST_{EVSD}**	**GLM_{2c} (GLM_{2b})**	**GLM_{1c_EVSD}**	**ST_{EVSD}**	**GLM_{2c} (GLM_{2b})**	**GLM_{1c_EVSD}**
−0.6	−0.6	**Continuous SO**	1	**20**	0.96	1	**100**	0.93
	−0.3	**Continuous SO**	0.96	**20**	0.95	0.9	**100**	0.85
	0.3	**Continuous SO**	1	**19**	1	1	**99**	1
	0.6	**Continuous SO**	1.1	**20**	1	0.98	**100**	1.1
−0.3	−0.6	**Continuous SO**	1	**20**	0.95	1.1	**99**	0.91
	−0.3	**Continuous SO**	0.98	**18**	1	1	**82**	1.2
	0.3	**Continuous SO**	0.99	**14**	0.98	1	**50**	0.92
	0.6	**Continuous SO**	0.95	**19**	1	0.84	**86**	0.92
0.3	−0.6	**Continuous SO**	0.95	**20**	1.1	0.96	**99**	1
	−0.3	**Continuous SO**	1	**18**	1	1	**83**	1
	0.3	**Continuous SO**	0.96	**14**	1	0.87	**50**	1.1
	0.6	**Continuous SO**	1	**19**	1	0.78	**86**	0.99
0.6	−0.6	**Continuous SO**	0.91	**20**	0.99	0.94	**100**	1.1
	−0.3	**Continuous SO**	1.1	**20**	0.95	1.1	**100**	0.9
	0.3	**Continuous SO**	0.96	**19**	0.97	0.92	**99**	0.98
	0.6	**Continuous SO**	1	**20**	0.98	1.1	**100**	0.92
−0.6	−0.6	**Binary SO**	1	**20**	—	1	**100**	—
	−0.3	**Binary SO**	0.96	**18**	—	0.94	**77**	—
	0.3	**Binary SO**	1	**18**	—	0.96	**78**	—
	0.6	**Binary SO**	1	**20**	—	0.9	**100**	—

−0. 3	−0. 6	**Binary SO**	0.96	**18**	**—**	0.88	**76**	**—**
	−0. 3	**Binary SO**	0.95	**7.7**	**—**	0.94	**18**	**—**
	0. 3	**Binary SO**	0.95	**7.9**	**—**	1	**18**	**—**
	0. 6	**Binary SO**	1	**18**	**—**	1.2	**78**	**—**
0. 3	−0. 6	**Binary SO**	1	**18**	**—**	1	**76**	**—**
	−0. 3	**Binary SO**	1	**7.7**	**—**	1	**18**	**—**
	0. 3	**Binary SO**	0.99	**7.7**	**—**	0.94	**18**	**—**
	0. 6	**Binary SO**	1	**18**	**—**	1	**78**	**—**
0. 6	−0. 6	**Binary SO**	0.97	**20**	**—**	0.86	**100**	**—**
	−0. 3	**Binary SO**	1	**18**	**—**	0.99	**77**	**—**
	0. 3	**Binary SO**	1	**18**	**—**	1.1	**78**	**—**
	0. 6	**Binary SO**	1	**20**	**—**	0.97	**100**	**—**

Expos.-PO: the effect size ($\boldsymbol{\beta_1}$) of exposure on the primary outcome (PO); **SO-PO**: the effect size ($\boldsymbol{\beta_3}$) of the secondary outcome (SO) on the primary outcome (PO); **GLM_{2c} (GLM_{2b})**: the GLM method for directly analyzing the continuous (binary) SO without taking into consideration the issue of EVSD; **GLM_{1c_EVSD}**: the GLM method in a new retrospective study with EVSD for continuous SOs.

Table S2. The mean of $\widehat{\gamma_1}$, the mean estimated standard error of $\widehat{\gamma_1}$, and the standard deviation of $\widehat{\gamma_1}$ for the ST_{EVSD} method and the GLM methods (GLM_{2b} and GLM_{1b_case}) for the binary secondary outcome, given $\gamma_1 = 0$ and 0.08, an exposure rate of 0.3, and an extreme proportion of 0.1 based on 10 000 simulations.

Effect size		$\overline{\lvert\widehat{\gamma_1}\rvert}$			$sd(\widehat{\gamma_1})$			$\overline{\widehat{se}(\widehat{\gamma_1})}$			$\overline{\lvert\widehat{\gamma_1}\rvert}/\overline{\widehat{se}(\widehat{\gamma_1})}$		
β_1	β_3	ST_{EVSD}	GLM_{2b}	GLM_{1b_case}	ST_{EVSD}	GLM_{2b}	GLM_{1b_case}	ST_{EVSD}	GLM_{2b}	GLM_{1b_case}	ST_{EVSD}	GLM_{2b}	GLM_{1b_case}
$\gamma_1 = 0$													
−0.6	−0.6	0.000	0.307	0.000	0.046	0.044	0.045	0.046	0.044	0.045	0.009	6.989	0.007
	−0.3	0.000	0.155	0.001	0.046	0.044	0.045	0.045	0.044	0.044	0.001	3.535	0.015
	0.3	0.000	0.156	0.000	0.048	0.046	0.045	0.048	0.046	0.045	0.003	3.414	0.002
	0.6	0.001	0.313	0.000	0.052	0.047	0.045	0.052	0.047	0.045	0.012	6.625	0.001
−0.3	−0.6	0.000	0.158	0.000	0.045	0.044	0.045	0.045	0.044	0.045	0.003	3.596	0.007
	−0.3	0.000	0.080	0.000	0.045	0.044	0.045	0.045	0.044	0.045	0.004	1.811	0.007
	0.3	0.000	0.082	0.000	0.048	0.046	0.045	0.048	0.046	0.045	0.009	1.767	0.001
	0.6	0.001	0.165	0.000	0.052	0.048	0.045	0.052	0.048	0.045	0.019	3.456	0.003
0.3	−0.6	0.000	0.272	0.000	0.031	0.043	0.054	0.032	0.042	0.054	0.011	6.436	0.006
	−0.3	0.000	0.158	0.000	0.045	0.044	0.045	0.044	0.044	0.045	0.007	3.618	0.004
	0.3	0.000	0.085	0.000	0.048	0.047	0.045	0.049	0.047	0.045	0.000	1.815	0.002
	0.6	0.001	0.173	0.000	0.053	0.048	0.045	0.053	0.048	0.044	0.016	3.610	0.003
0.6	−0.6	0.000	0.303	0.000	0.045	0.044	0.045	0.046	0.044	0.044	0.002	6.908	0.004
	−0.3	0.001	0.157	0.000	0.045	0.044	0.045	0.045	0.044	0.045	0.011	3.563	0.007
	0.3	0.001	0.166	0.000	0.050	0.046	0.045	0.050	0.046	0.045	0.019	3.598	0.007
	0.6	0.000	0.339	0.000	0.055	0.048	0.045	0.055	0.048	0.045	0.002	7.106	0.006

Effect size		$\lvert\overline{\widehat{\gamma_1}}\rvert$			$sd(\widehat{\gamma_1})$			$\overline{\widehat{se}(\widehat{\gamma_1})}$			$\lvert\overline{\widehat{\gamma_1}}\rvert/\overline{\widehat{se}(\widehat{\gamma_1})}$		
β_1	β_3	ST_{EVSD}	GLM_{2b}	GLM_{1b_case}	ST_{EVSD}	GLM_{2b}	GLM_{1b_case}	ST_{EVSD}	GLM_{2b}	GLM_{1b_case}	ST_{EVSD}	GLM_{2b}	GLM_{1b_case}
$\gamma_1 = 0.08$													
−0.3	−0.6	0.081	0.241	0.192	0.045	0.044	0.045	0.032	0.042	0.054	1.766	5.401	1.782
	−0.3	0.080	0.161	0.192	0.045	0.045	0.045	0.034	0.037	0.054	1.768	3.595	1.791
	0.3	0.081	0.002	0.192	0.048	0.046	0.045	0.034	0.036	0.054	1.703	0.044	1.816
	0.6	0.081	0.086	0.193	0.051	0.048	0.045	0.032	0.039	0.053	1.562	1.803	1.813
0.1	−0.6	0.080	0.028	0.192	0.045	0.044	0.045	0.031	0.043	0.054	1.802	0.654	1.796
	−0.3	0.079	0.053	0.192	0.045	0.045	0.045	0.034	0.038	0.054	1.771	1.185	1.792
	0.3	0.080	0.107	0.192	0.048	0.047	0.045	0.034	0.036	0.053	1.638	2.248	1.807
	0.6	0.080	0.135	0.193	0.052	0.048	0.045	0.032	0.039	0.054	1.521	2.779	1.786
0.2	−0.3	0.080	0.027	0.192	0.045	0.045	0.045	0.034	0.037	0.054	1.767	0.604	1.804
	0.3	0.080	0.133	0.193	0.048	0.047	0.045	0.034	0.036	0.053	1.671	2.845	1.816
	0.6	0.080	0.186	0.192	0.051	0.048	0.045	0.032	0.039	0.053	1.558	3.830	1.782
	1.0	0.081	0.254	0.193	0.058	0.050	0.045	0.031	0.043	0.054	1.400	5.122	1.824
0.4	−0.3	0.080	0.025	0.192	0.045	0.045	0.045	0.034	0.037	0.054	1.752	0.553	1.814
	0.3	0.080	0.183	0.192	0.048	0.046	0.045	0.034	0.036	0.054	1.669	3.943	1.839
	0.6	0.080	0.285	0.192	0.051	0.047	0.045	0.032	0.039	0.054	1.577	5.996	1.830
	1.0	0.081	0.417	0.192	0.058	0.050	0.045	0.031	0.042	0.054	1.383	8.275	1.790

The prevalence of binary secondary outcome is close to 0.3. **GLM_{2b}**: the GLM method for directly analyzing the binary SO without taking into consideration the issue of EVSD; **GLM_{1c_case}**: the GLM method in a new retrospective case-control study for binary SOs.

Figure S1. The power of the ST_{EVSD} method and the GLM methods (GLM_{2b} and GLM_{2c}) as a function of the effect size γ_1, given that the exposure rate is 0.1 and the effect size $\beta_1 = 0.1$

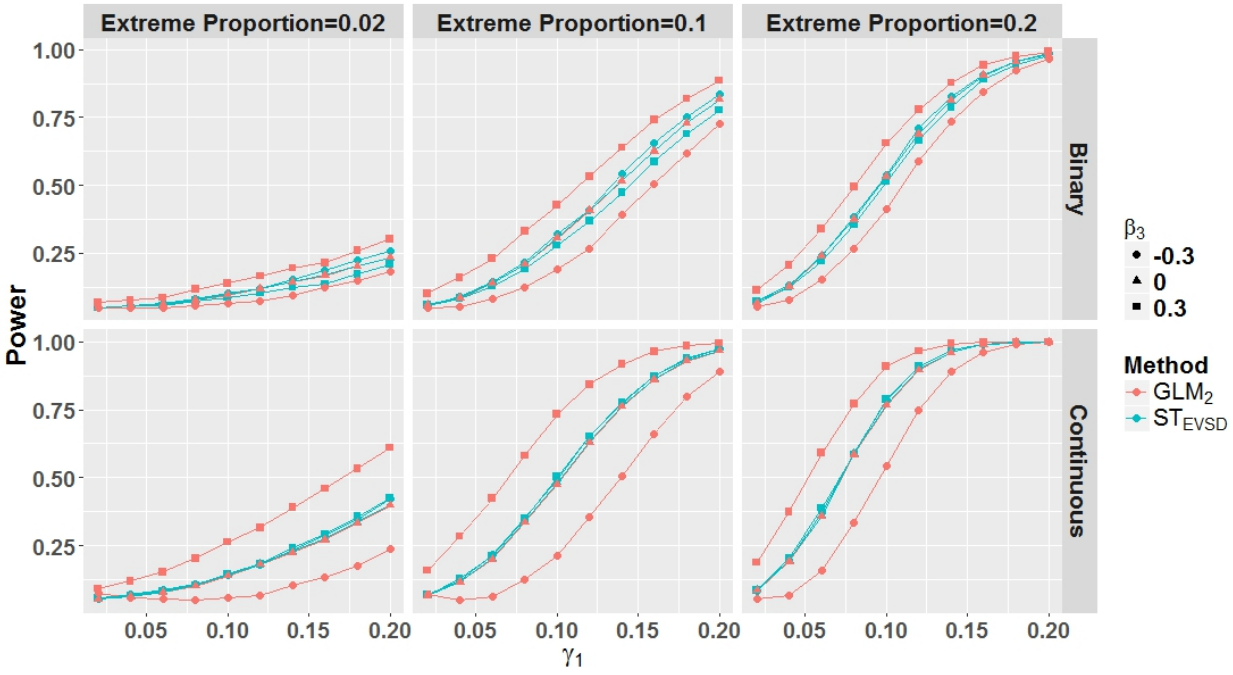

Figure S2. The power of the ST_{EVSD} method and the GLM methods (GLM_{2b} and GLM_{2c}) as a function of the effect size γ_1, given that the exposure rate is 0.5 and the effect size $\beta_1 = 0.1$

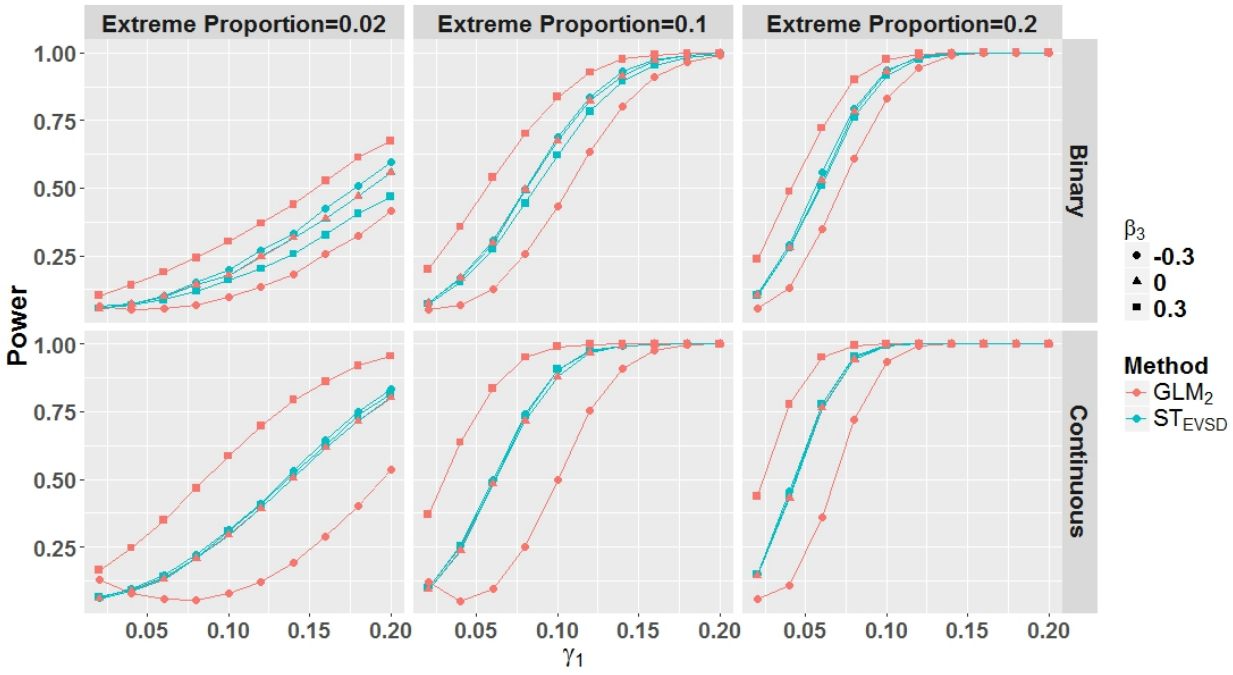

Figure S3. The power of the ST_{EVSD} method and the GLM methods (GLM_{2b} and GLM_{2c}) as a function of the effect size β_1, given that the extreme proportion is 0.1 and the effect size $\gamma_1 = 0.1$.

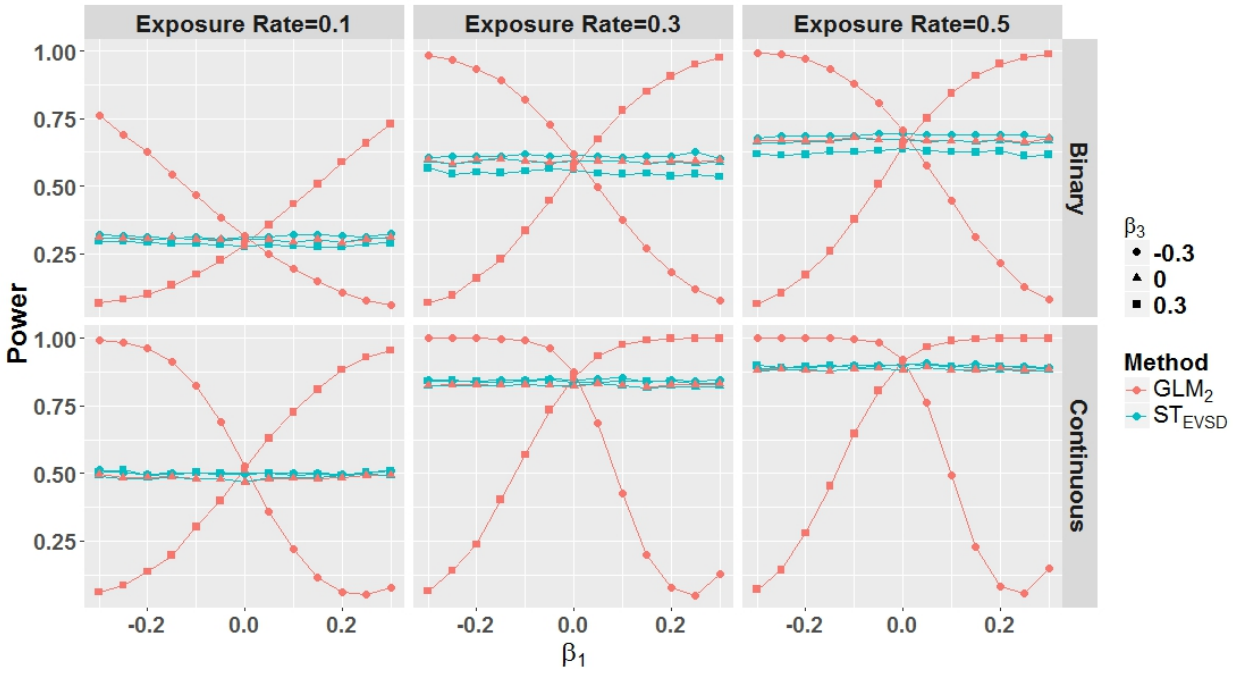

Figure S4. The power of the ST_{EVSD} method and the GLM methods (GLM_{2b} and GLM_{2c}) as a function of the extreme proportion ρ, given that the effect size $\beta_1 = 0.1$ and the effect size $\gamma_1 = 0.1$.

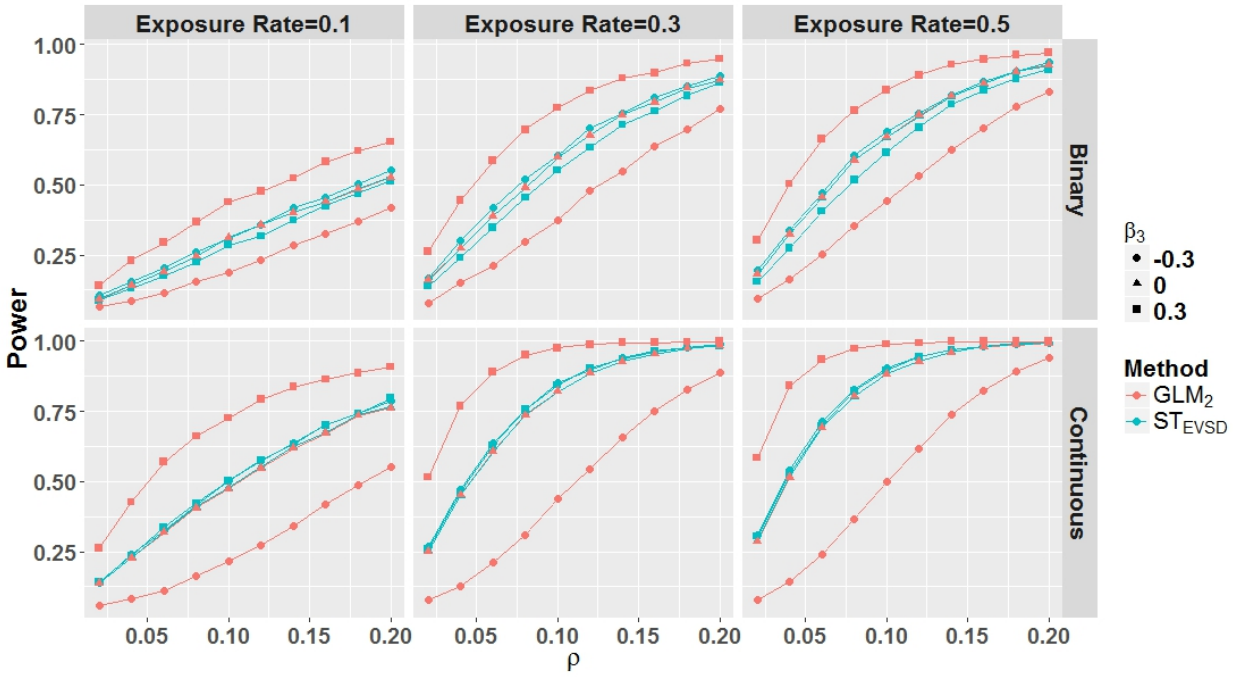

Figure S5. The power of the ST_{EVSD} method and the GLM_1 methods (GLM_{1b_case} and GLM_{1b_rand}) as a function of the correlation between two outcomes β_3, the correlation between the exposure and the primary outcome β_1, and the effect size γ_1 from 0.02 to 0.2, given that the extreme proportion $\rho = 0.1$ and there is a prevalence of $D = 0.3$ for the binary outcome.