Appendix table 1 Simulation results from scenario I assessing performance of different confounding adjustment methods with different events per coefficient*.

	10 EPC	5 EPC	2.5 EPC	1 EPC	0.5 EPC
Mean odds ratio					
LR	1.00	1.00	1.00	N/A#	$9.2*10^{118}$
PS	1.00	1.00	1.00	1.09	$1.2*10^{9}$
DRS1	1.01	1.03	1.05	1.10	1.15
DRS2	1.01	1.03	1.05	1.10	1.15
DRS3	1.01	1.03	1.05	1.10	1.15
DRS4	1.03	1.05	1.08	1.13	1.19
Relative bias					
LR	0.05	-0.06	-0.49	N/A#	$9.2*10^{120}$
PS	0.00	-0.12	-0.30	8.80	$1.2*10^{11}$
DRS1	1.38	2.57	4.57	9.53	14.70
DRS2	1.38	2.57	4.57	9.53	14.71
DRS3	1.39	2.59	4.61	9.56	14.72
DRS4	2.55	4.62	7.52	13.40	18.84
Coverage					
LR	0.946	0.936	0.920	0.651	1.000
PS	0.954	0.950	0.954	0.939	0.975
DRS1	0.951	0.949	0.945	0.926	0.898
DRS2	0.951	0.949	0.945	0.926	0.898
DRS3	0.950	0.949	0.945	0.927	0.898
DRS4	0.948	0.945	0.936	0.904	0.867
SMSE					
LR	0.22	0.25	0.30	$2.9*10^{14}$	$1.7*10^{4}$
PS	0.21	0.22	0.23	0.27	1317.99
DRS1	0.21	0.21	0.21	0.23	0.25
DRS2	0.21	0.21	0.21	0.23	0.25
DRS3	0.21	0.21	0.21	0.23	0.25
DRS4	0.21	0.21	0.22	0.24	0.25
Mean SE					
LR	0.22	0.25	0.27	$2.7*10^{6}$	$8.8*10^{6}$
PS	0.21	0.22	0.23	0.26	49.94
DRS1	0.21	0.21	0.21	0.21	0.21
DRS2	0.21	0.21	0.21	0.21	0.21
DRS3	0.21	0.21	0.21	0.21	0.21
DRS4	0.21	0.21	0.21	0.20	0.20
Empirical SE					
LR	0.22	0.25	0.30	$2.7*10^{14}$	$1.7*10^{4}$
PS	0.21	0.22	0.23	0.25	1317.98
DRS1	0.21	0.21	0.21	0.21	0.21
DRS2	0.21	0.21	0.21	0.21	0.21
DRS3	0.21	0.21	0.21	0.21	0.21
DRS4	0.21	0.21	0.21	0.20	0.21
Type 1 error					
LR	0.054	0.064	0.080	0.349	0.000
PS	0.046	0.050	0.046	0.061	0.025
DRS1	0.049	0.051	0.055	0.074	0.102
DRS2	0.049	0.051	0.055	0.074	0.102
DRS3	0.050	0.051	0.055	0.073	0.102
DRS4	0.052	0.055	0.064	0.096	0.133

* SMSE = square root of the mean squared error. # While all LR samples converged, the OR estimate was $\exp(5.42*10^{12})$ resulting in an error when calculating the mean OR and relative bias.

Appendix table 2 Simulation results from scenario II and III comparing different DRS models in the presence of an interaction effect in the training data*.

	LR	PS	DRS1	DRS2	DRS3	DRS4
Scenario II#						
Mean odds ratio	1.00	1.00	1.05	1.01	1.02	1.04
Relative bias	-0.16	-0.19	5.10	0.51	2.19	4.14
Coverage	0.950	0.956	0.947	0.954	0.954	0.949
RMSE	0.22	0.21	0.21	0.21	0.21	0.21
Mean SE	0.22	0.21	0.21	0.21	0.21	0.21
Empirical SE	0.22	0.21	0.21	0.21	0.21	0.21
Type 1 error	0.050	0.044	0.053	0.046	0.046	0.051
Scenario III^						
Mean odds ratio	1.00	1.00	1.09	1.17	1.02	1.03
Relative bias	0.27	0.23	9.22	16.94	1.87	3.25
Coverage	0.948	0.954	0.93	0.881	0.952	0.950
RMSE	0.22	0.21	0.22	0.26	0.21	0.21
Mean SE	0.22	0.21	0.21	0.20	0.21	0.21
Empirical SE	0.22	0.21	0.21	0.20	0.21	0.21
Type 1 error	0.052	0.046	0.070	0.119	0.048	0.050

* SMSE = square root of the mean squared error. # Treatment by confounder 1 interaction OR of 0.30.
^ Treatment by confounder 1 interaction OR of 3.0

Appendix table 3 Simulation results from scenario I comparing logistic regression (LR), propensity score (PS) and penalized logistic regression (PLR) models with different events per coefficient[#].

	10 EPC	5 EPC	2.5 EPC	1 EPC	0.5 EPC
Mean odds ratio					
LR	1.00	0.99	1.00	0.00	0.00
PS	1.00	1.00	1.00	1.09	0.01
PLR	1.00	1.00	1.00	1.00	0.91
Relative bias					
LR	0.10	-0.50	0.19	-100	-100
PS	0.04	-0.50	0.21.	8.75	-98.56
PLR	0.16	-0.39	0.21	-0.16	-9.13
Coverage					
LR	0.944	0.935	0.921	0.647	1.000
PS	0.953	0.951	0.953	0.942	0.973
PLR	0.956	0.957	0.963	0.931	1.000
SMSE					
LR	0.23	0.25	0.30	$2.8*10^{14}$	3900.28
PS	0.21	0.22	0.23	0.27	296.90
PLR	0.21	0.22	0.24	0.44	8.84
Mean SE					
LR	0.22	0.23	0.27	$2.7*10^{6}$	$5.2*10^{6}$
PS	0.21	0.22	0.23	0.26	29.52
PLR	0.22	0.23	0.25	0.39	30.67
Empirical SE					
LR	0.23	0.25	0.30	$2.8*10^{14}$	3899.93
PS	0.21	0.22	0.23	0.25	296.87
PLR	0.21	0.22	0.24	0.44	8.84
Type 1 error					
LR	0.056	0.065	0.079	0.353	0.00
PS	0.047	0.049	0.047	0.058	0.027
PLR	0.044	0.043	0.037	0.069	0.00

* SMSE = square root of the mean squared error . # All models converged. Defining extreme estimates as an estimate above 5 resulted in excluding 7248 (EPC 1.0) and 9433 (EPC 0.5) for the LR method, 4758 (EPC 0.5) for the PS method and 2524 (EPC 0.05) for the PLR model.