

Supplementary materials for “Stable  
computational methods for additive binomial  
models with application to adjusted risk  
differences” by M. W. Donoghoe and  
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## **Web Appendix A**

The following Web Tables summarise the simulation results comparing the adjusted treatment effect estimates from the additive binomial to alternative methods. Web Tables 1–6 compare the additive binomial to the misspecified regression methods, Web Tables 7–12 compare the additive binomial to weighted methods, and Web Tables 13–18 compare the additive binomial to approximate methods. Relative MSE is mean squared error relative to the binomial method. For the regression methods, “Valid” is the percentage of simulations in which all fitted risks were within  $[0, 1]$ .

Web Table 1: Additive binomial versus regression methods, with 5% treatment effect and 0.15% age effect.

Risk range	$n$	Method	Bias (%)	Standard deviation	Relative MSE	Valid (%)
0.44-0.56	100	Binomial MLE	2.95	0.0988	1	100
		Poisson	3.38	0.1002	1.027	99.7
		Least squares	3.13	0.0988	1.000	99.8
	500	Binomial MLE	0.82	0.0444	1	100
		Poisson	0.90	0.0446	1.010	100
		Least squares	0.82	0.0444	1.000	100
	5000	Binomial MLE	-0.20	0.0141	1	100
		Poisson	-0.17	0.0141	1.001	100
		Least squares	-0.20	0.0141	1.000	100
0-0.12	100	Binomial MLE	-8.60	0.0459	1	100
		Poisson	-8.17	0.0460	1.005	99.7
		Least squares	-3.85	0.0461	1.003	37.2
	500	Binomial MLE	-1.93	0.0205	1	100
		Poisson	-1.84	0.0205	1.002	100
		Least squares	0.20	0.0206	1.005	50.3
	5000	Binomial MLE	0.50	0.0065	1	100
		Poisson	0.52	0.0065	0.999	100
		Least squares	1.01	0.0068	1.082	49.4
0.88-1	100	Binomial MLE	-4.95	0.0471	1	100
		Poisson	1.52	0.0478	1.026	36.7
		Least squares	0.56	0.0472	1.001	36.0
	500	Binomial MLE	-2.72	0.0205	1	100
		Poisson	-0.20	0.0207	1.021	50.4
		Least squares	-0.37	0.0206	1.011	50.1
	5000	Binomial MLE	-0.60	0.0064	1	100
		Poisson	0.04	0.0067	1.092	49.0
		Least squares	0.02	0.0066	1.082	47.3

Web Table 2: Additive binomial versus regression methods, with 5% treatment effect and 0.3% age effect.

Risk range	$n$	Method	Bias (%)	Standard deviation	Relative MSE	Valid (%)
0.41-0.59	100	Binomial MLE	9.54	0.1006	1	100
		Poisson	9.14	0.1023	1.035	99.9
		Least squares	9.14	0.1005	0.997	99.8
	500	Binomial MLE	0.98	0.0440	1	100
		Poisson	1.25	0.0443	1.012	100
		Least squares	0.94	0.0440	1.001	100
	5000	Binomial MLE	-0.83	0.0147	1	100
		Poisson	-0.83	0.0148	1.009	100
		Least squares	-0.83	0.0147	1.000	100
0-0.19	100	Binomial MLE	-3.33	0.0539	1	100
		Poisson	-3.19	0.0543	1.012	100
		Least squares	3.47	0.0568	1.107	45.9
	500	Binomial MLE	-4.60	0.0241	1	100
		Poisson	-4.57	0.0242	1.006	100
		Least squares	-0.93	0.0252	1.079	49.2
	5000	Binomial MLE	-1.68	0.0073	1	100
		Poisson	-1.66	0.0073	1.004	100
		Least squares	-0.68	0.0076	1.086	50.5
0.82-1	100	Binomial MLE	-5.61	0.0566	1	100
		Poisson	-1.04	0.0608	1.154	47.1
		Least squares	-1.56	0.0597	1.111	46.8
	500	Binomial MLE	-6.42	0.0246	1	100
		Poisson	-1.68	0.0260	1.102	50.8
		Least squares	-1.90	0.0256	1.074	49.9
	5000	Binomial MLE	-1.17	0.0076	1	100
		Poisson	-0.29	0.0083	1.192	51.7
		Least squares	-0.32	0.0083	1.166	50.2

Web Table 3: Additive binomial versus regression methods, with 5% treatment effect and 0.6% age effect.

Risk range	$n$	Method	Bias (%)	Standard deviation	Relative MSE	Valid (%)
0.34–0.66	100	Binomial MLE	7.25	0.0989	1	100
		Poisson	9.51	0.1017	1.058	99.4
		Least squares	6.74	0.0987	0.996	99.5
	500	Binomial MLE	-1.72	0.0445	1	100
		Poisson	-1.15	0.0449	1.021	100
		Least squares	-1.57	0.0444	0.998	100
	5000	Binomial MLE	-1.15	0.0141	1	100
		Poisson	-1.12	0.0143	1.022	100
		Least squares	-1.16	0.0141	0.999	100
0–0.32	100	Binomial MLE	-6.95	0.0678	1	100
		Poisson	-6.68	0.0678	1.002	100
		Least squares	2.07	0.0745	1.205	47.8
	500	Binomial MLE	-6.43	0.0285	1	100
		Poisson	-6.64	0.0287	1.009	100
		Least squares	-0.36	0.0307	1.140	49.5
	5000	Binomial MLE	-1.51	0.0089	1	100
		Poisson	-1.42	0.0089	0.999	100
		Least squares	-0.48	0.0100	1.252	47.9
0.68–1	100	Binomial MLE	-5.31	0.0669	1	100
		Poisson	6.32	0.0745	1.242	47.7
		Least squares	5.04	0.0719	1.156	48.7
	500	Binomial MLE	-7.74	0.0300	1	100
		Poisson	-1.48	0.0338	1.248	49.4
		Least squares	-1.61	0.0329	1.188	48.4
	5000	Binomial MLE	-1.12	0.0093	1	100
		Poisson	-0.22	0.0104	1.252	52.3
		Least squares	-0.13	0.0102	1.195	51.0

Web Table 4: Additive binomial versus regression methods, with 15% treatment effect and 0.15% age effect.

Risk range	$n$	Method	Bias (%)	Standard deviation	Relative MSE	Valid (%)
0.39-0.61	100	Binomial MLE	0.33	0.0977	1	100
		Poisson	1.24	0.0991	1.030	99.8
		Least squares	0.08	0.0974	0.994	99.9
	500	Binomial MLE	-1.13	0.0441	1	100
		Poisson	-0.94	0.0442	1.006	100
		Least squares	-1.14	0.0441	1.000	100
	5000	Binomial MLE	0.20	0.0140	1	100
		Poisson	0.24	0.0140	1.001	100
		Least squares	0.20	0.0140	1.000	100
0-0.22	100	Binomial MLE	-3.58	0.0616	1	100
		Poisson	-3.38	0.0617	1.003	100
		Least squares	-2.05	0.0610	0.976	30.8
	500	Binomial MLE	0.14	0.0274	1	100
		Poisson	0.21	0.0274	1.000	100
		Least squares	0.46	0.0274	0.999	46.6
	5000	Binomial MLE	-0.18	0.0085	1	100
		Poisson	-0.17	0.0085	1.000	100
		Least squares	-0.04	0.0085	1.014	48.8
0.78-1	100	Binomial MLE	-2.29	0.0589	1	100
		Poisson	0.11	0.0587	0.991	33.7
		Least squares	-0.89	0.0580	0.969	34.4
	500	Binomial MLE	-0.38	0.0276	1	100
		Poisson	0.19	0.0277	1.008	48.8
		Least squares	-0.01	0.0276	0.997	48.8
	5000	Binomial MLE	0.02	0.0086	1	100
		Poisson	0.13	0.0087	1.027	51.0
		Least squares	0.11	0.0087	1.020	48.4

Web Table 5: Additive binomial versus regression methods, with 15% treatment effect and 0.3% age effect.

Risk range	$n$	Method	Bias (%)	Standard deviation	Relative MSE	Valid (%)
0.36-0.64	100	Binomial MLE	1.34	0.1073	1	100
		Poisson	2.55	0.1091	1.036	99.2
		Least squares	1.15	0.1070	0.995	99.9
	500	Binomial MLE	-0.46	0.0443	1	100
		Poisson	-0.31	0.0445	1.010	100
		Least squares	-0.48	0.0443	1.001	100
	5000	Binomial MLE	0.34	0.0136	1	100
		Poisson	0.34	0.0136	1.005	100
		Least squares	0.34	0.0136	1.000	100
0-0.29	100	Binomial MLE	-2.13	0.0688	1	100
		Poisson	-1.87	0.0691	1.008	100
		Least squares	0.28	0.0683	0.983	45.1
	500	Binomial MLE	-1.53	0.0307	1	100
		Poisson	-1.40	0.0307	0.998	100
		Least squares	-0.87	0.0314	1.037	48.5
	5000	Binomial MLE	-0.43	0.0095	1	100
		Poisson	-0.41	0.0095	1.000	100
		Least squares	-0.33	0.0096	1.027	53.1
0.72-1	100	Binomial MLE	-1.46	0.0683	1	100
		Poisson	0.99	0.0694	1.033	47.0
		Least squares	0.13	0.0682	0.997	46.9
	500	Binomial MLE	-0.56	0.0306	1	100
		Poisson	0.61	0.0310	1.024	49.9
		Least squares	0.37	0.0308	1.010	50.1
	5000	Binomial MLE	-0.31	0.0094	1	100
		Poisson	-0.11	0.0097	1.065	52.8
		Least squares	-0.13	0.0096	1.048	52.0

Web Table 6: Additive binomial versus regression methods, with 15% treatment effect and 0.6% age effect.

Risk range	$n$	Method	Bias (%)	Standard deviation	Relative MSE	Valid (%)
0.29-0.71	100	Binomial MLE	-1.79	0.1038	1	100
		Poisson	-0.51	0.1054	1.030	99.2
		Least squares	-1.87	0.1036	0.997	99.1
	500	Binomial MLE	1.14	0.0443	1	100
		Poisson	1.42	0.0443	1.002	100
		Least squares	1.13	0.0443	0.999	100
	5000	Binomial MLE	-0.05	0.0144	1	100
		Poisson	-0.04	0.0145	1.014	100
		Least squares	-0.05	0.0144	1.000	100
0-0.42	100	Binomial MLE	-5.62	0.0799	1	100
		Poisson	-5.22	0.0806	1.015	100
		Least squares	-2.20	0.0807	1.009	51.1
	500	Binomial MLE	-2.27	0.0339	1	100
		Poisson	-2.18	0.0339	1.002	100
		Least squares	-0.87	0.0352	1.069	49.6
	5000	Binomial MLE	-0.14	0.0104	1	100
		Poisson	-0.11	0.0104	1.003	100
		Least squares	0.09	0.0109	1.097	51.2
0.58-1	100	Binomial MLE	-5.91	0.0806	1	100
		Poisson	-1.34	0.0849	1.097	54.0
		Least squares	-2.31	0.0820	1.024	54.2
	500	Binomial MLE	-3.44	0.0356	1	100
		Poisson	-1.50	0.0374	1.083	49.9
		Least squares	-1.72	0.0365	1.036	49.9
	5000	Binomial MLE	-0.61	0.0105	1	100
		Poisson	-0.28	0.0112	1.137	50.2
		Least squares	-0.30	0.0109	1.081	49.8

Web Table 7: Additive binomial versus weighted methods, with 5% treatment effect and 0.15% age effect.

Risk range	$n$	Method	Bias (%)	Standard deviation	Relative MSE
0.44–0.56	100	Binomial MLE	2.95	0.0988	1
		CMH	4.29	0.1008	1.041
		Böhning-Sarol	8.02	0.1097	1.234
		Inverse variance	9.05	0.1083	1.202
		Null-weighted	2.63	0.1000	1.023
		Greenland-Holland	0.59	0.0974	0.972
		Minimum risk	4.96	0.1017	1.060
	5000	Binomial MLE	-0.20	0.0141	1
		CMH	-0.19	0.0141	1.002
		Böhning-Sarol	-0.64	0.0147	1.088
		Inverse variance	-0.01	0.0141	1.007
		Null-weighted	-0.18	0.0141	1.003
		Greenland-Holland	-0.27	0.0141	1.001
		Minimum risk	-0.15	0.0141	1.003
0-0.12	100	Binomial MLE	-8.60	0.0459	1
		CMH	-4.03	0.0467	1.031
		Böhning-Sarol	-2.54	0.0506	1.209
		Inverse variance	-21.57	0.0415	0.865
		Null-weighted	-24.41	0.0405	0.844
		Greenland-Holland	-20.13	0.0419	0.874
		Minimum risk	-9.38	0.0450	0.963
	5000	Binomial MLE	0.50	0.0065	1
		CMH	1.01	0.0068	1.078
		Böhning-Sarol	1.33	0.0073	1.248
		Inverse variance	-0.69	0.0066	1.033
		Null-weighted	-0.82	0.0066	1.028
		Greenland-Holland	1.00	0.0068	1.081
		Minimum risk	0.73	0.0067	1.051
0.88-1	100	Binomial MLE	-4.95	0.0471	1
		CMH	0.51	0.0481	1.039
		Böhning-Sarol	2.18	0.0520	1.214
		Inverse variance	-17.52	0.0431	0.870
		Null-weighted	-20.27	0.0420	0.839
		Greenland-Holland	-16.68	0.0430	0.861
		Minimum risk	-4.96	0.0464	0.971
	5000	Binomial MLE	-0.60	0.0064	1
		CMH	0.01	0.0067	1.084
		Böhning-Sarol	0.02	0.0071	1.226
		Inverse variance	-1.24	0.0064	1.026
		Null-weighted	-1.36	0.0064	1.027
		Greenland-Holland	0.00	0.0067	1.086
		Minimum risk	-0.21	0.0066	1.058



Web Table 8: Additive binomial versus weighted methods, with 5% treatment effect and 0.3% age effect.

Risk range	$n$	Method	Bias (%)	Standard deviation	Relative MSE
0.41-0.59	100	Binomial MLE	9.54	0.1006	1
		CMH	7.36	0.1022	1.032
		Böhning-Sarol	11.34	0.1098	1.192
		Inverse variance	12.01	0.1120	1.240
		Null-weighted	5.73	0.1015	1.016
		Greenland-Holland	3.46	0.0983	0.954
		Minimum risk	7.77	0.1032	1.051
	5000	Binomial MLE	-0.83	0.0147	1
		CMH	-0.85	0.0147	1.000
		Böhning-Sarol	-0.60	0.0158	1.154
		Inverse variance	-0.69	0.0148	1.004
		Null-weighted	-0.85	0.0147	1.000
		Greenland-Holland	-0.93	0.0147	0.998
		Minimum risk	-0.82	0.0147	1.001
0-0.19	100	Binomial MLE	-3.33	0.0539	1
		CMH	4.87	0.0585	1.175
		Böhning-Sarol	4.03	0.0614	1.295
		Inverse variance	-8.66	0.0526	0.956
		Null-weighted	-12.17	0.0510	0.905
		Greenland-Holland	-1.11	0.0560	1.078
		Minimum risk	1.78	0.0569	1.114
	5000	Binomial MLE	-1.68	0.0073	1
		CMH	-0.71	0.0076	1.089
		Böhning-Sarol	-0.67	0.0082	1.250
		Inverse variance	-2.26	0.0075	1.090
		Null-weighted	-2.41	0.0075	1.093
		Greenland-Holland	-0.72	0.0076	1.091
		Minimum risk	-0.97	0.0075	1.060
0.82-1	100	Binomial MLE	-5.61	0.0566	1
		CMH	-1.02	0.0600	1.123
		Böhning-Sarol	1.10	0.0639	1.271
		Inverse variance	-12.94	0.0533	0.898
		Null-weighted	-16.23	0.0514	0.842
		Greenland-Holland	-6.77	0.0569	1.011
		Minimum risk	-3.68	0.0584	1.064
	5000	Binomial MLE	-1.17	0.0076	1
		CMH	-0.31	0.0083	1.168
		Böhning-Sarol	-0.44	0.0089	1.366
		Inverse variance	-1.20	0.0077	1.032
		Null-weighted	-1.35	0.0077	1.033
		Greenland-Holland	-0.33	0.0083	1.170
		Minimum risk	-0.45	0.0081	1.127

Web Table 9: Additive binomial versus weighted methods, with 5% treatment effect and 0.6% age effect.

Risk range	$n$	Method	Bias (%)	Standard deviation	Relative MSE
0.34–0.66	100	Binomial MLE	7.25	0.0989	1
		CMH	6.88	0.1001	1.023
		Böhning-Sarol	6.73	0.1069	1.167
		Inverse variance	12.95	0.1092	1.222
		Null-weighted	4.66	0.1003	1.027
		Greenland-Holland	2.87	0.0964	0.949
		Minimum risk	6.83	0.1013	1.048
	5000	Binomial MLE	-1.15	0.0141	1
		CMH	-1.17	0.0141	1.002
		Böhning-Sarol	-1.17	0.0151	1.144
		Inverse variance	-1.02	0.0141	1.004
		Null-weighted	-1.18	0.0141	1.002
		Greenland-Holland	-1.24	0.0141	1.001
		Minimum risk	-1.14	0.0141	1.002
0–0.32	100	Binomial MLE	-6.95	0.0678	1
		CMH	1.88	0.0765	1.272
		Böhning-Sarol	0.47	0.0821	1.462
		Inverse variance	-6.60	0.0717	1.118
		Null-weighted	-10.85	0.0680	1.012
		Greenland-Holland	-1.02	0.0744	1.203
		Minimum risk	0.41	0.0755	1.237
	5000	Binomial MLE	-1.51	0.0089	1
		CMH	-0.45	0.0100	1.258
		Böhning-Sarol	-0.18	0.0108	1.470
		Inverse variance	-1.24	0.0094	1.107
		Null-weighted	-1.39	0.0093	1.105
		Greenland-Holland	-0.47	0.0100	1.261
		Minimum risk	-0.58	0.0098	1.206
0.68–1	100	Binomial MLE	-5.31	0.0669	1
		CMH	4.18	0.0740	1.224
		Böhning-Sarol	5.45	0.0781	1.364
		Inverse variance	-0.76	0.0694	1.076
		Null-weighted	-6.03	0.0655	0.960
		Greenland-Holland	0.69	0.0718	1.153
		Minimum risk	3.25	0.0729	1.186
	5000	Binomial MLE	-1.12	0.0093	1
		CMH	-0.07	0.0102	1.196
		Böhning-Sarol	-0.03	0.0109	1.380
		Inverse variance	-0.11	0.0097	1.083
		Null-weighted	-0.25	0.0096	1.078
		Greenland-Holland	-0.12	0.0102	1.198
		Minimum risk	-0.04	0.0100	1.157

Web Table 10: Additive binomial versus weighted methods, with 15% treatment effect and 0.15% age effect.

Risk range	$n$	Method	Bias (%)	Standard deviation	Relative MSE
0.39–0.61	100	Binomial MLE	0.33	0.0977	1
		CMH	-0.14	0.0996	1.040
		Böhning-Sarol	-0.56	0.1046	1.147
		Inverse variance	7.02	0.1103	1.287
		Null-weighted	-0.64	0.0999	1.046
		Greenland-Holland	-3.91	0.0961	0.971
		Minimum risk	1.02	0.1012	1.074
	5000	Binomial MLE	0.20	0.0140	1
		CMH	0.21	0.0140	1.002
		Böhning-Sarol	0.32	0.0149	1.136
		Inverse variance	0.38	0.0140	1.006
		Null-weighted	0.21	0.0140	1.001
		Greenland-Holland	0.13	0.0140	1.000
		Minimum risk	0.24	0.0140	1.002
0-0.22	100	Binomial MLE	-3.58	0.0616	1
		CMH	-2.19	0.0615	0.990
		Böhning-Sarol	-1.80	0.0669	1.172
		Inverse variance	-12.84	0.0600	1.039
		Null-weighted	-16.39	0.0583	1.046
		Greenland-Holland	-11.92	0.0570	0.934
		Minimum risk	-4.48	0.0609	0.982
	5000	Binomial MLE	-0.18	0.0085	1
		CMH	-0.06	0.0086	1.017
		Böhning-Sarol	-0.02	0.0090	1.134
		Inverse variance	-0.58	0.0086	1.026
		Null-weighted	-0.70	0.0086	1.035
		Greenland-Holland	0.00	0.0086	1.020
		Minimum risk	-0.15	0.0085	1.014
0.78-1	100	Binomial MLE	-2.29	0.0589	1
		CMH	-0.85	0.0588	0.996
		Böhning-Sarol	-1.26	0.0632	1.150
		Inverse variance	-11.24	0.0590	1.082
		Null-weighted	-14.54	0.0579	1.102
		Greenland-Holland	-10.22	0.0554	0.949
		Minimum risk	-3.09	0.0587	0.996
	5000	Binomial MLE	0.02	0.0086	1
		CMH	0.12	0.0087	1.020
		Böhning-Sarol	0.20	0.0092	1.148
		Inverse variance	-0.28	0.0087	1.011
		Null-weighted	-0.41	0.0087	1.017
		Greenland-Holland	0.15	0.0087	1.022
		Minimum risk	0.05	0.0087	1.015

Web Table 11: Additive binomial versus weighted methods, with 15% treatment effect and 0.3% age effect.

Risk range	$n$	Method	Bias (%)	Standard deviation	Relative MSE
0.36-0.64	100	Binomial MLE	1.34	0.1073	1
		CMH	0.37	0.1086	1.024
		Böhning-Sarol	0.65	0.1153	1.154
		Inverse variance	6.55	0.1188	1.234
		Null-weighted	-0.92	0.1079	1.012
		Greenland-Holland	-3.34	0.1045	0.951
		Minimum risk	1.16	0.1097	1.045
	5000	Binomial MLE	0.34	0.0136	1
		CMH	0.34	0.0136	0.999
		Böhning-Sarol	0.33	0.0146	1.161
		Inverse variance	0.50	0.0136	1.004
		Null-weighted	0.34	0.0136	0.999
		Greenland-Holland	0.26	0.0136	0.997
		Minimum risk	0.37	0.0136	1.000
0-0.29	100	Binomial MLE	-2.13	0.0688	1
		CMH	0.32	0.0698	1.027
		Böhning-Sarol	-0.24	0.0728	1.117
		Inverse variance	-6.50	0.0696	1.041
		Null-weighted	-10.72	0.0678	1.022
		Greenland-Holland	-3.76	0.0673	0.961
		Minimum risk	-0.96	0.0702	1.041
	5000	Binomial MLE	-0.43	0.0095	1
		CMH	-0.33	0.0096	1.026
		Böhning-Sarol	-0.30	0.0101	1.137
		Inverse variance	-0.66	0.0095	1.010
		Null-weighted	-0.80	0.0095	1.014
		Greenland-Holland	-0.25	0.0096	1.030
		Minimum risk	-0.39	0.0096	1.016
0.72-1	100	Binomial MLE	-1.46	0.0683	1
		CMH	-0.23	0.0693	1.031
		Böhning-Sarol	0.75	0.0760	1.238
		Inverse variance	-6.94	0.0688	1.039
		Null-weighted	-11.17	0.0661	0.996
		Greenland-Holland	-4.09	0.0672	0.976
		Minimum risk	-1.70	0.0689	1.020
	5000	Binomial MLE	-0.31	0.0094	1
		CMH	-0.14	0.0096	1.052
		Böhning-Sarol	-0.20	0.0103	1.202
		Inverse variance	-0.42	0.0094	1.007
		Null-weighted	-0.55	0.0094	1.012
		Greenland-Holland	-0.08	0.0097	1.059
		Minimum risk	-0.18	0.0096	1.039

Web Table 12: Additive binomial versus weighted methods, with 15% treatment effect and 0.6% age effect.

Risk range	$n$	Method	Bias (%)	Standard deviation	Relative MSE
0.29-0.71	100	Binomial MLE	-1.79	0.1038	1
		CMH	-2.03	0.1054	1.032
		Böhning-Sarol	-2.55	0.1144	1.217
		Inverse variance	3.92	0.1120	1.167
		Null-weighted	-2.90	0.1043	1.011
		Greenland-Holland	-5.47	0.1020	0.972
		Minimum risk	-1.35	0.1060	1.044
	5000	Binomial MLE	-0.05	0.0144	1
		CMH	-0.05	0.0144	1.002
		Böhning-Sarol	-0.09	0.0153	1.118
		Inverse variance	0.10	0.0145	1.006
		Null-weighted	-0.07	0.0144	1.003
		Greenland-Holland	-0.13	0.0144	1.001
		Minimum risk	-0.03	0.0145	1.003
0-0.42	100	Binomial MLE	-5.62	0.0799	1
		CMH	-1.91	0.0823	1.050
		Böhning-Sarol	-1.72	0.0868	1.168
		Inverse variance	-4.81	0.0816	1.039
		Null-weighted	-9.90	0.0773	0.959
		Greenland-Holland	-4.74	0.0805	1.011
		Minimum risk	-2.41	0.0820	1.042
	5000	Binomial MLE	-0.14	0.0104	1
		CMH	0.10	0.0109	1.103
		Böhning-Sarol	0.16	0.0119	1.309
		Inverse variance	-0.13	0.0106	1.050
		Null-weighted	-0.28	0.0107	1.054
		Greenland-Holland	0.20	0.0109	1.112
		Minimum risk	0.07	0.0108	1.083
0.58-1	100	Binomial MLE	-5.91	0.0806	1
		CMH	-2.30	0.0830	1.049
		Böhning-Sarol	-1.55	0.0882	1.185
		Inverse variance	-5.18	0.0833	1.065
		Null-weighted	-9.98	0.0778	0.955
		Greenland-Holland	-5.34	0.0811	1.010
		Minimum risk	-2.88	0.0827	1.043
	5000	Binomial MLE	-0.61	0.0105	1
		CMH	-0.30	0.0109	1.083
		Böhning-Sarol	-0.28	0.0115	1.188
		Inverse variance	-0.49	0.0107	1.031
		Null-weighted	-0.63	0.0106	1.031
		Greenland-Holland	-0.23	0.0110	1.091
		Minimum risk	-0.33	0.0108	1.065

Web Table 13: Additive binomial versus approximate methods, with 5% treatment effect and 0.15% age effect.

Risk range	n	Method	Bias (%)	Standard deviation	Relative MSE
0.44–0.56	100	Binomial MLE	2.95	0.0988	1
		Fitted logistic	3.11	0.0988	1.000
		Pseudo likelihood	3.13	0.0988	1.000
		IPW2 prop. score	2.94	0.0987	0.997
		DR prop. score	2.99	0.0988	1.000
	5000	Binomial MLE	-0.20	0.0141	1
		Fitted logistic	-0.20	0.0141	1.000
		Pseudo likelihood	-0.20	0.0141	1.000
		IPW2 prop. score	-0.20	0.0141	1.000
		DR prop. score	-0.20	0.0141	1.000
0-0.12	100	Binomial MLE	-8.60	0.0459	1
		Fitted logistic	-3.71	0.0463	1.011
		Pseudo likelihood	-3.85	0.0461	1.003
		IPW2 prop. score	-3.98	0.0461	1.005
		DR prop. score	-2.49	0.0464	1.016
	5000	Binomial MLE	0.50	0.0065	1
		Fitted logistic	1.01	0.0068	1.083
		Pseudo likelihood	1.01	0.0068	1.082
		IPW2 prop. score	1.01	0.0068	1.082
		DR prop. score	1.01	0.0068	1.082
0.88-1	100	Binomial MLE	-4.95	0.0471	1
		Fitted logistic	0.86	0.0473	1.007
		Pseudo likelihood	0.56	0.0472	1.001
		IPW2 prop. score	0.58	0.0472	1.002
		DR prop. score	-0.77	0.0477	1.022
	5000	Binomial MLE	-0.60	0.0064	1
		Fitted logistic	0.02	0.0066	1.083
		Pseudo likelihood	0.02	0.0066	1.082
		IPW2 prop. score	0.02	0.0066	1.082
		DR prop. score	0.01	0.0066	1.082

Web Table 14: Additive binomial versus approximate methods, with 5% treatment effect and 0.3% age effect.

Risk range	n	Method	Bias (%)	Standard deviation	Relative MSE
0.41–0.59	100	Binomial MLE	9.54	0.1006	1
		Fitted logistic	9.07	0.1004	0.996
		Pseudo likelihood	9.14	0.1005	0.997
		IPW2 prop. score	8.99	0.1004	0.996
		DR prop. score	9.13	0.1005	0.997
	5000	Binomial MLE	-0.83	0.0147	1
		Fitted logistic	-0.83	0.0147	1.000
		Pseudo likelihood	-0.83	0.0147	1.000
		IPW2 prop. score	-0.83	0.0147	1.000
		DR prop. score	-0.82	0.0147	1.000
0-0.19	100	Binomial MLE	-3.33	0.0539	1
		Fitted logistic	4.06	0.0571	1.122
		Pseudo likelihood	3.47	0.0568	1.107
		IPW2 prop. score	3.50	0.0569	1.112
		DR prop. score	4.37	0.0569	1.113
	5000	Binomial MLE	-1.68	0.0073	1
		Fitted logistic	-0.67	0.0076	1.088
		Pseudo likelihood	-0.68	0.0076	1.086
		IPW2 prop. score	-0.68	0.0076	1.086
		DR prop. score	-0.68	0.0076	1.085
0.82-1	100	Binomial MLE	-5.61	0.0566	1
		Fitted logistic	-1.15	0.0598	1.114
		Pseudo likelihood	-1.56	0.0597	1.111
		IPW2 prop. score	-1.48	0.0597	1.111
		DR prop. score	-2.56	0.0600	1.124
	5000	Binomial MLE	-1.17	0.0076	1
		Fitted logistic	-0.31	0.0083	1.167
		Pseudo likelihood	-0.32	0.0083	1.166
		IPW2 prop. score	-0.32	0.0083	1.166
		DR prop. score	-0.31	0.0083	1.166

Web Table 15: Additive binomial versus approximate methods, with 5% treatment effect and 0.6% age effect.

Risk range	n	Method	Bias (%)	Standard deviation	Relative MSE
0.34–0.66	100	Binomial MLE	7.25	0.0989	1
		Fitted logistic	6.72	0.0987	0.995
		Pseudo likelihood	6.74	0.0987	0.996
		IPW2 prop. score	6.80	0.0988	0.998
		DR prop. score	6.46	0.0988	0.998
	5000	Binomial MLE	-1.15	0.0141	1
		Fitted logistic	-1.16	0.0141	0.999
		Pseudo likelihood	-1.16	0.0141	0.999
		IPW2 prop. score	-1.16	0.0141	0.999
		DR prop. score	-1.17	0.0141	0.999
0–0.32	100	Binomial MLE	-6.95	0.0678	1
		Fitted logistic	2.57	0.0748	1.214
		Pseudo likelihood	2.07	0.0745	1.205
		IPW2 prop. score	2.08	0.0745	1.206
		DR prop. score	2.61	0.0747	1.211
	5000	Binomial MLE	-1.51	0.0089	1
		Fitted logistic	-0.50	0.0100	1.253
		Pseudo likelihood	-0.48	0.0100	1.252
		IPW2 prop. score	-0.48	0.0100	1.252
		DR prop. score	-0.48	0.0100	1.251
0.68–1	100	Binomial MLE	-5.31	0.0669	1
		Fitted logistic	5.06	0.0721	1.162
		Pseudo likelihood	5.04	0.0719	1.156
		IPW2 prop. score	5.11	0.0719	1.158
		DR prop. score	5.14	0.0723	1.169
	5000	Binomial MLE	-1.12	0.0093	1
		Fitted logistic	-0.15	0.0101	1.192
		Pseudo likelihood	-0.13	0.0102	1.195
		IPW2 prop. score	-0.13	0.0102	1.195
		DR prop. score	-0.14	0.0102	1.194



Web Table 16: Additive binomial versus approximate methods, with 15% treatment effect and 0.15% age effect.

Risk range	n	Method	Bias (%)	Standard deviation	Relative MSE
0.39–0.61	100	Binomial MLE	0.33	0.0977	1
		Fitted logistic	0.06	0.0973	0.993
		Pseudo likelihood	0.08	0.0974	0.994
		IPW2 prop. score	0.05	0.0974	0.995
		DR prop. score	-0.06	0.0975	0.997
	5000	Binomial MLE	0.20	0.0140	1
		Fitted logistic	0.20	0.0140	1.000
		Pseudo likelihood	0.20	0.0140	1.000
		IPW2 prop. score	0.20	0.0140	1.000
		DR prop. score	0.20	0.0140	1.000
0-0.22	100	Binomial MLE	-3.58	0.0616	1
		Fitted logistic	-1.89	0.0611	0.977
		Pseudo likelihood	-2.05	0.0610	0.976
		IPW2 prop. score	-2.05	0.0610	0.977
		DR prop. score	-1.74	0.0613	0.983
	5000	Binomial MLE	-0.18	0.0085	1
		Fitted logistic	-0.04	0.0085	1.014
		Pseudo likelihood	-0.04	0.0085	1.014
		IPW2 prop. score	-0.04	0.0085	1.014
		DR prop. score	-0.04	0.0085	1.014
0.78-1	100	Binomial MLE	-2.29	0.0589	1
		Fitted logistic	-0.76	0.0580	0.968
		Pseudo likelihood	-0.89	0.0580	0.969
		IPW2 prop. score	-0.93	0.0581	0.970
		DR prop. score	-1.27	0.0584	0.982
	5000	Binomial MLE	0.02	0.0086	1
		Fitted logistic	0.12	0.0087	1.020
		Pseudo likelihood	0.11	0.0087	1.020
		IPW2 prop. score	0.11	0.0087	1.020
		DR prop. score	0.12	0.0087	1.021

Web Table 17: Additive binomial versus approximate methods, with 15% treatment effect and 0.3% age effect.

Risk range	n	Method	Bias (%)	Standard deviation	Relative MSE
0.36-0.64	100	Binomial MLE	1.34	0.1073	1
		Fitted logistic	1.14	0.1070	0.994
		Pseudo likelihood	1.15	0.1070	0.995
		IPW2 prop. score	1.10	0.1070	0.994
		DR prop. score	1.11	0.1069	0.993
	5000	Binomial MLE	0.34	0.0136	1
		Fitted logistic	0.34	0.0136	1.000
		Pseudo likelihood	0.34	0.0136	1.000
		IPW2 prop. score	0.34	0.0136	1.000
		DR prop. score	0.34	0.0136	1.000
0-0.29	100	Binomial MLE	-2.13	0.0688	1
		Fitted logistic	0.41	0.0684	0.985
		Pseudo likelihood	0.28	0.0683	0.983
		IPW2 prop. score	0.30	0.0684	0.987
		DR prop. score	0.57	0.0686	0.992
	5000	Binomial MLE	-0.43	0.0095	1
		Fitted logistic	-0.33	0.0096	1.027
		Pseudo likelihood	-0.33	0.0096	1.027
		IPW2 prop. score	-0.33	0.0096	1.027
		DR prop. score	-0.33	0.0096	1.027
0.72-1	100	Binomial MLE	-1.46	0.0683	1
		Fitted logistic	0.27	0.0682	0.997
		Pseudo likelihood	0.13	0.0682	0.997
		IPW2 prop. score	0.18	0.0682	0.997
		DR prop. score	0.06	0.0684	1.004
	5000	Binomial MLE	-0.31	0.0094	1
		Fitted logistic	-0.13	0.0096	1.048
		Pseudo likelihood	-0.13	0.0096	1.048
		IPW2 prop. score	-0.13	0.0096	1.048
		DR prop. score	-0.13	0.0096	1.048

Web Table 18: Additive binomial versus approximate methods, with 15% treatment effect and 0.6% age effect.

Risk range	n	Method	Bias (%)	Standard deviation	Relative MSE
0.29-0.71	100	Binomial MLE	-1.79	0.1038	1
		Fitted logistic	-1.92	0.1036	0.996
		Pseudo likelihood	-1.87	0.1036	0.997
		IPW2 prop. score	-1.86	0.1035	0.995
		DR prop. score	-1.78	0.1035	0.996
	5000	Binomial MLE	-0.05	0.0144	1
		Fitted logistic	-0.05	0.0144	1.000
		Pseudo likelihood	-0.05	0.0144	1.000
		IPW2 prop. score	-0.05	0.0144	1.000
		DR prop. score	-0.05	0.0144	1.000
0-0.42	100	Binomial MLE	-5.62	0.0799	1
		Fitted logistic	-2.14	0.0808	1.012
		Pseudo likelihood	-2.20	0.0807	1.009
		IPW2 prop. score	-2.21	0.0807	1.011
		DR prop. score	-2.15	0.0809	1.015
	5000	Binomial MLE	-0.14	0.0104	1
		Fitted logistic	0.09	0.0109	1.099
		Pseudo likelihood	0.09	0.0109	1.097
		IPW2 prop. score	0.09	0.0109	1.096
		DR prop. score	0.09	0.0109	1.096
0.58-1	100	Binomial MLE	-5.91	0.0806	1
		Fitted logistic	-2.22	0.0819	1.021
		Pseudo likelihood	-2.31	0.0820	1.024
		IPW2 prop. score	-2.41	0.0821	1.026
		DR prop. score	-2.51	0.0821	1.028
	5000	Binomial MLE	-0.61	0.0105	1
		Fitted logistic	-0.30	0.0109	1.081
		Pseudo likelihood	-0.30	0.0109	1.081
		IPW2 prop. score	-0.30	0.0109	1.081
		DR prop. score	-0.30	0.0109	1.081

## Web Appendix B

The supplementary materials include a zipped folder `R code.zip` that contains source code to implement the proposed method in R. These materials can be used to reproduce the results presented in Section 3.3 of the paper. The zipped folder contains the following files:

- `README.txt` — documentation for the main routine `addbin`.
- `addbin.r` — source code for fitting an additive binomial model. Note that the R package `combinat` must be loaded prior to running the `addbin` function.
- `addpois.r` — source code for fitting an additive Poisson model, which is used by `addbin.r`.
- `utilities.r` — source code for some additional functions used by the main routines.
- `ASSENT3.dat` — data from the ASSENT-3 trial.
- `ASSENT3.r` — reads in data from the ASSENT-3 trial. Running this code will produce datasets `assent3`, which is the original data (with age shifted such that 23 years old = 0), and `assent3.sample`, which is a bootstrapped sample taken with replacement from the original data. The R working directory must be set to the location of `ASSENT3.dat` for this to run as-is.
- `Example 1.r` — example code for running the analyses from Section 3.3.