Results simulation study DelayedGSD

October 10, 2023

1 Rejection rate

1.1 2 stages

Power by method (columns) and scenario (rows): (nominal level 80%)

scenario	n.sim	missing	binding	fixC	ar	method 1	method 2	method 3
1	10000	TRUE	TRUE	FALSE	10	81.00%	80.93%	80.43%
3	10000	TRUE	TRUE	FALSE	5	80.53%	80.53%	80.14%
5	10000	TRUE	TRUE	TRUE	10	80.15%	80.35%	80.43%
7	10000	TRUE	TRUE	TRUE	5	80.08%	80.20%	80.14%
9	10000	TRUE	FALSE	TRUE	10	79.86%	80.12%	80.26%
11	10000	TRUE	FALSE	TRUE	5	79.93%	80.04%	80.06%
13	10000	TRUE	FALSE	FALSE	10	80.50%	80.44%	80.26%
15	10000	TRUE	FALSE	FALSE	5	80.37%	80.36%	80.06%
17	10000	FALSE	TRUE	FALSE	5	80.31%	80.30%	79.92%

Type 1 error by method (columns) and scenario (rows): (nominal level 2.5%)

scenario	n.sim	missing	binding	fixC	ar	method 1	method 2	method 3
2	10000	TRUE	TRUE	FALSE	10	2.42%	2.39%	2.37%
4	10000	TRUE	TRUE	FALSE	5	2.40%	2.40%	2.35%
6	10000	TRUE	TRUE	TRUE	10	2.24%	2.22%	2.37%
8	10000	TRUE	TRUE	TRUE	5	2.32%	2.31%	2.35%
10	10000	TRUE	FALSE	TRUE	10	2.45%	2.47%	2.57%
12	10000	TRUE	FALSE	TRUE	5	2.63%	2.64%	2.66%
14	10000	TRUE	FALSE	FALSE	10	2.53%	2.53%	2.57%
16	10000	TRUE	FALSE	FALSE	5	2.68%	2.68%	2.66%
18	10000	FALSE	TRUE	FALSE	5	2.46%	2.46%	2.45%

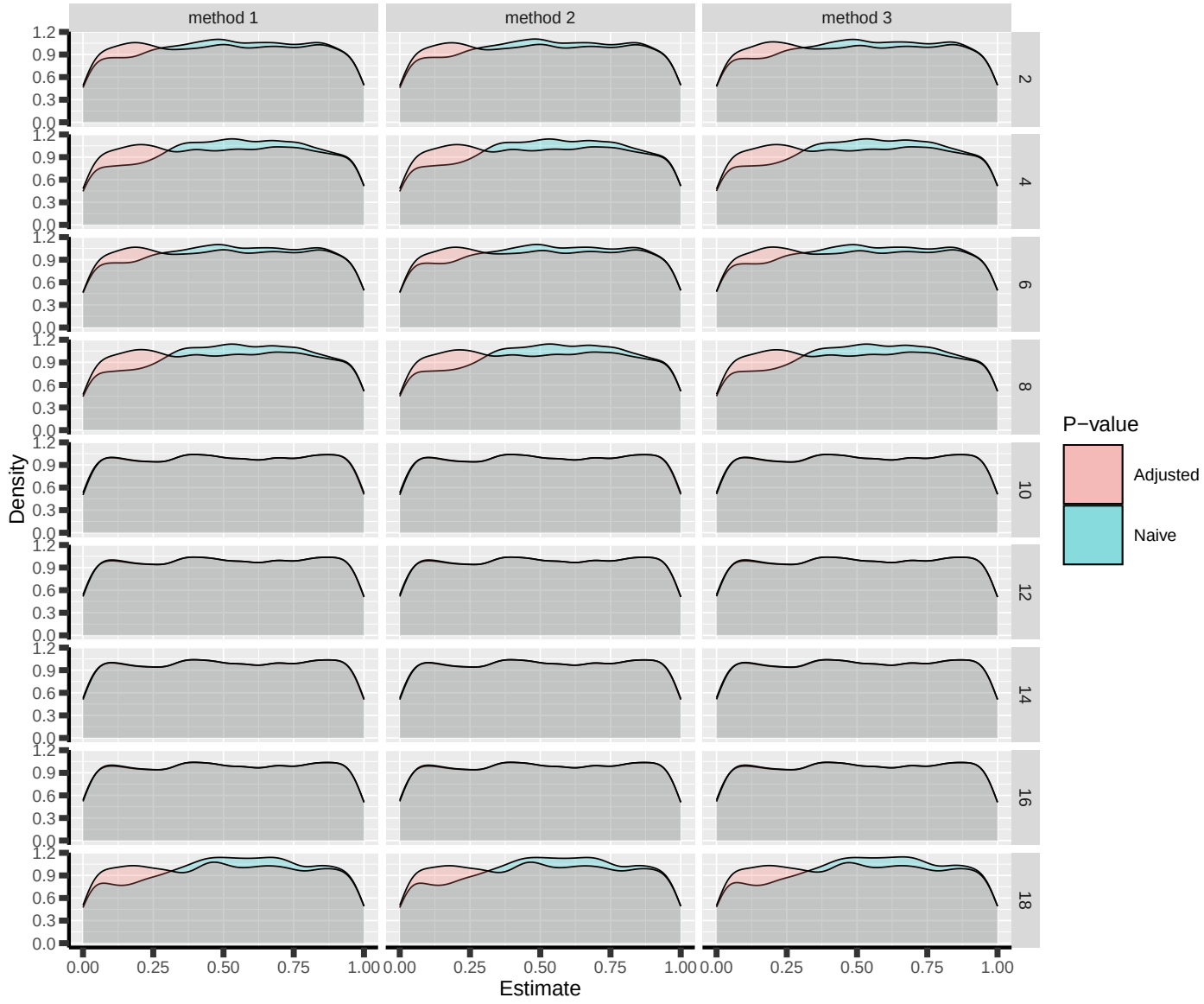

Figure 1: Naive and adjusted p-value distribution over all simulations under the null. Each row correspond to a different scenario

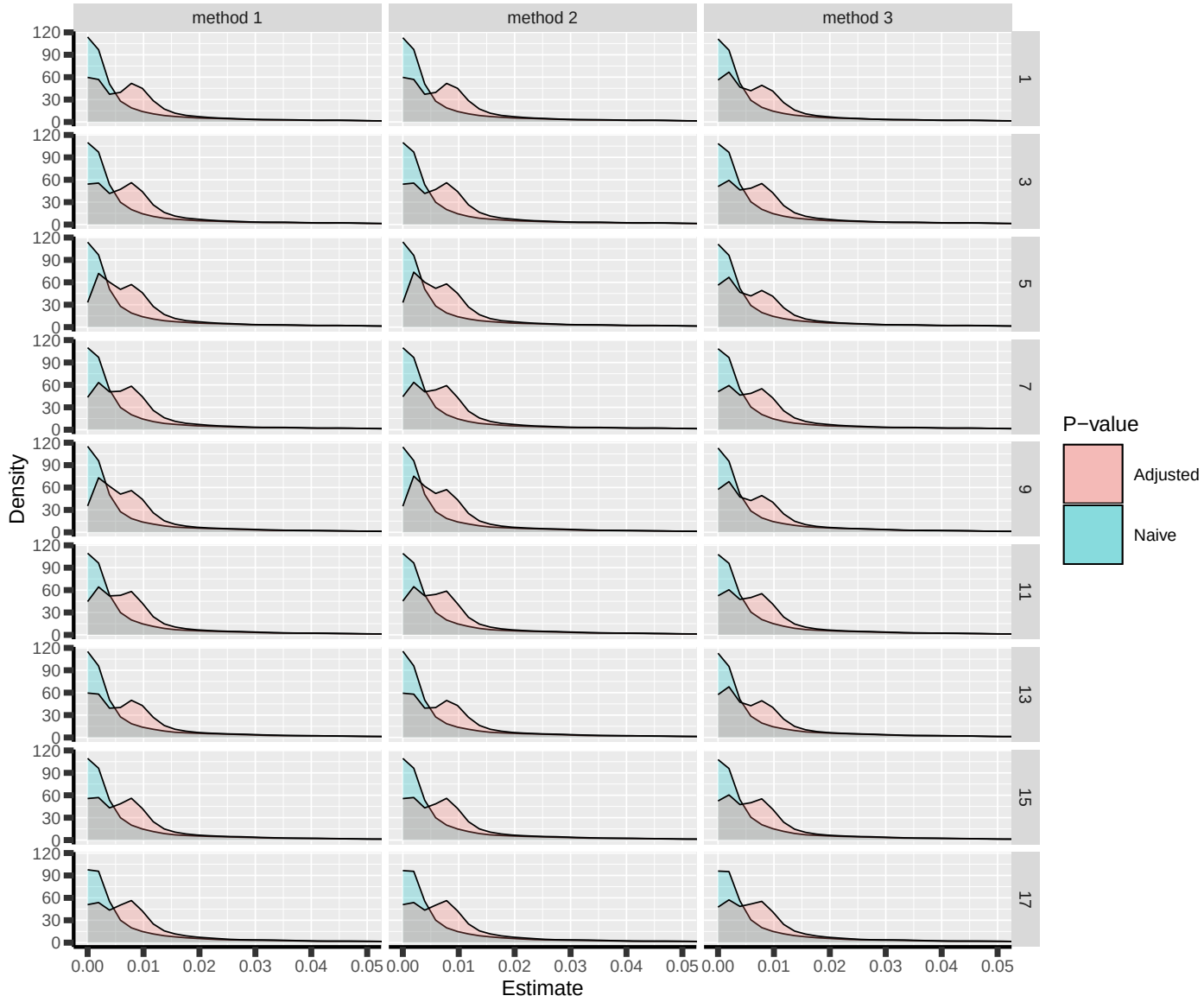

Figure 2: Naive and adjusted p-value distribution over all simulations under the alternative. Each row correspond to a different scenario

1.2 3 stages

Power by method (columns) and scenario (rows): (nominal level 80%)

scenario	n.sim	missing	binding	fixC	ar	method 1	method 2	method 3
1	1868	TRUE	TRUE	FALSE	10	75.32%	75.32%	75.00%
5	1934	TRUE	TRUE	TRUE	10	75.18%	76.01%	76.11%
7	245	TRUE	TRUE	TRUE	5	75.51%	75.92%	75.92%
9	2500	TRUE	FALSE	TRUE	10	74.80%	75.32%	75.00%
11	2500	TRUE	FALSE	TRUE	5	74.76%	75.44%	74.68%
13	2500	TRUE	FALSE	FALSE	10	75.28%	75.40%	75.36%
15	2500	TRUE	FALSE	FALSE	5	75.12%	75.24%	75.12%

Type 1 error by method (columns) and scenario (rows): (nominal level 2.5%)

scenario	n.sim	missing	binding	fixC	ar	method 1	method 2	method 3
2	2481	TRUE	TRUE	FALSE	10	2.94%	2.94%	2.70%
4	1127	TRUE	TRUE	FALSE	5	3.11%	3.11%	3.11%
6	2432	TRUE	TRUE	TRUE	10	1.89%	2.14%	2.01%
8	1042	TRUE	TRUE	TRUE	5	1.73%	1.92%	1.82%
10	2500	TRUE	FALSE	TRUE	10	2.36%	2.40%	2.32%
12	2500	TRUE	FALSE	TRUE	5	2.36%	2.28%	2.28%
14	2483	TRUE	FALSE	FALSE	10	3.02%	3.10%	3.10%
16	2500	TRUE	FALSE	FALSE	5	3.16%	3.12%	3.04%

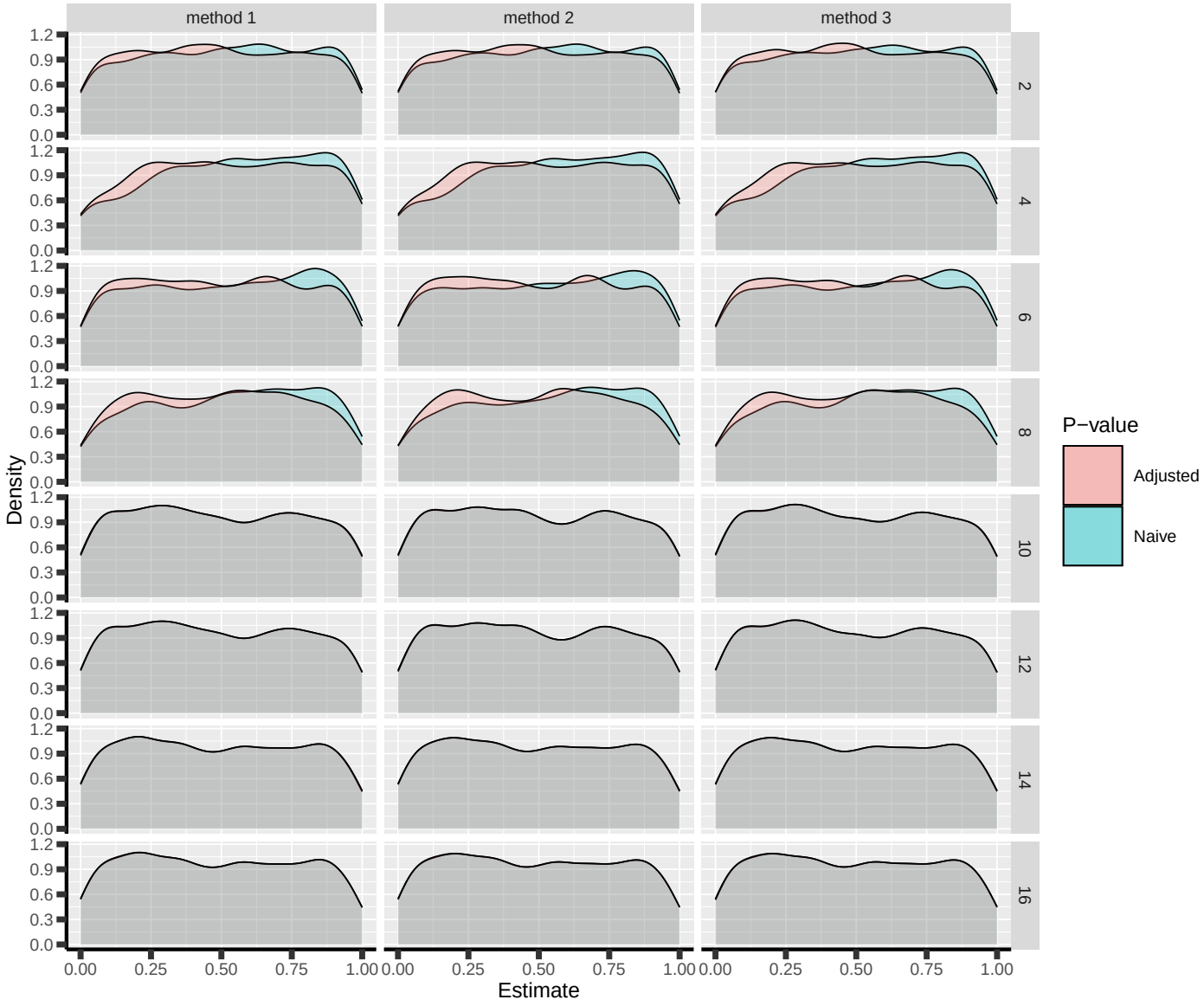

Figure 3: Naive and adjusted p-value distribution over all simulations under the null. Each row correspond to a different scenario

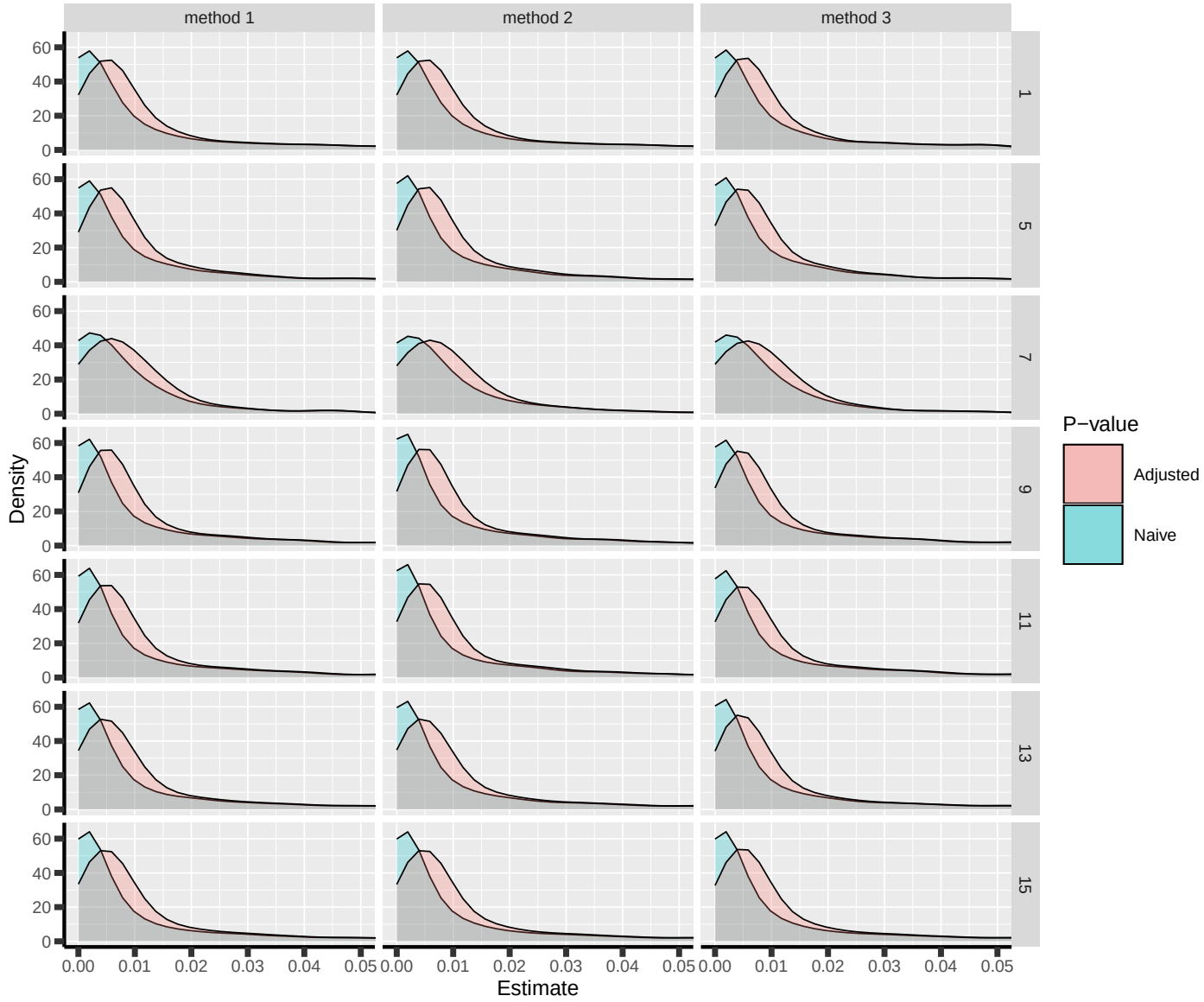

Figure 4: Naive and adjusted p-value distribution over all simulations under the alternative. Each row correspond to a different scenario

2 Conclusion of the trial

2.1 2 stages

Relative frequency of stopping for efficacy/futility at decision/final

- Method 1

	N	missing	hypo	binding	fixC	ar	decision.eff	decision.fut	final.eff	final.fut
1:	10000	TRUE	power	TRUE	FALSE	10	37.79%	5.93%	43.21%	13.07%
2:	10000	TRUE	typeI	TRUE	FALSE	10	0.80%	71.13%	1.62%	26.45%
3:	10000	TRUE	power	TRUE	FALSE	5	35.74%	5.98%	44.79%	13.49%
4:	10000	TRUE	typeI	TRUE	FALSE	5	0.74%	69.32%	1.66%	28.28%
5:	10000	TRUE	power	TRUE	TRUE	10	36.94%	6.78%	43.21%	13.07%
6:	10000	TRUE	typeI	TRUE	TRUE	10	0.62%	71.31%	1.62%	26.45%
7:	10000	TRUE	power	TRUE	TRUE	5	35.29%	6.43%	44.79%	13.49%
8:	10000	TRUE	typeI	TRUE	TRUE	5	0.66%	69.40%	1.66%	28.28%
9:	10000	TRUE	power	FALSE	TRUE	10	38.05%	6.57%	41.81%	13.57%
10:	10000	TRUE	typeI	FALSE	TRUE	10	0.61%	0.20%	1.84%	97.35%
11:	10000	TRUE	power	FALSE	TRUE	5	36.35%	6.15%	43.58%	13.92%
12:	10000	TRUE	typeI	FALSE	TRUE	5	0.70%	0.06%	1.93%	97.31%
13:	10000	TRUE	power	FALSE	FALSE	10	38.69%	5.93%	41.81%	13.57%
14:	10000	TRUE	typeI	FALSE	FALSE	10	0.69%	0.12%	1.84%	97.35%
15:	10000	TRUE	power	FALSE	FALSE	5	36.79%	5.71%	43.58%	13.92%
16:	10000	TRUE	typeI	FALSE	FALSE	5	0.75%	0.01%	1.93%	97.31%
17:	10000	FALSE	power	TRUE	FALSE	5	33.98%	5.33%	46.33%	14.36%
18:	10000	FALSE	typeI	TRUE	FALSE	5	0.74%	67.48%	1.72%	30.06%

Method 2:

	N	missing	hypo	binding	fixC	ar	decision.eff	decision.fut	final.eff	final.fut
1:	10000	TRUE	power	TRUE	FALSE	10	37.85%	6.19%	43.08%	12.88%
2:	10000	TRUE	typeI	TRUE	FALSE	10	0.79%	71.64%	1.60%	25.97%
3:	10000	TRUE	power	TRUE	FALSE	5	35.77%	5.99%	44.76%	13.48%
4:	10000	TRUE	typeI	TRUE	FALSE	5	0.74%	69.38%	1.66%	28.22%
5:	10000	TRUE	power	TRUE	TRUE	10	36.69%	6.24%	43.66%	13.41%
6:	10000	TRUE	typeI	TRUE	TRUE	10	0.59%	69.61%	1.63%	28.17%
7:	10000	TRUE	power	TRUE	TRUE	5	35.02%	6.05%	45.18%	13.75%
8:	10000	TRUE	typeI	TRUE	TRUE	5	0.63%	68.36%	1.68%	29.33%
9:	10000	TRUE	power	FALSE	TRUE	10	37.85%	6.04%	42.27%	13.84%
10:	10000	TRUE	typeI	FALSE	TRUE	10	0.61%	0.19%	1.86%	97.34%
11:	10000	TRUE	power	FALSE	TRUE	5	36.18%	5.84%	43.86%	14.12%
12:	10000	TRUE	typeI	FALSE	TRUE	5	0.69%	0.06%	1.95%	97.30%
13:	10000	TRUE	power	FALSE	FALSE	10	38.70%	6.09%	41.74%	13.47%
14:	10000	TRUE	typeI	FALSE	FALSE	10	0.69%	0.12%	1.84%	97.35%
15:	10000	TRUE	power	FALSE	FALSE	5	36.82%	5.75%	43.54%	13.89%
16:	10000	TRUE	typeI	FALSE	FALSE	5	0.75%	0.01%	1.93%	97.31%
17:	10000	FALSE	power	TRUE	FALSE	5	34.03%	5.36%	46.27%	14.34%
18:	10000	FALSE	typeI	TRUE	FALSE	5	0.74%	67.55%	1.72%	29.99%

Method 3:

	N	missing	hypo	binding	fixC	ar	decision.eff	decision.fut	final.eff	final.fut
1:	10000	TRUE	power	TRUE	FALSE	10	40.58%	6.53%	39.85%	13.04%
2:	10000	TRUE	typeI	TRUE	FALSE	10	0.74%	68.79%	1.63%	28.84%
3:	10000	TRUE	power	TRUE	FALSE	5	36.54%	6.30%	43.60%	13.56%
4:	10000	TRUE	typeI	TRUE	FALSE	5	0.69%	68.41%	1.66%	29.24%
5:	10000	TRUE	power	TRUE	TRUE	10	40.58%	6.53%	39.85%	13.04%
6:	10000	TRUE	typeI	TRUE	TRUE	10	0.74%	68.79%	1.63%	28.84%
7:	10000	TRUE	power	TRUE	TRUE	5	36.54%	6.30%	43.60%	13.56%
8:	10000	TRUE	typeI	TRUE	TRUE	5	0.69%	68.41%	1.66%	29.24%
9:	10000	TRUE	power	FALSE	TRUE	10	41.34%	6.20%	38.92%	13.54%
10:	10000	TRUE	typeI	FALSE	TRUE	10	0.77%	0.33%	1.80%	97.10%
11:	10000	TRUE	power	FALSE	TRUE	5	37.71%	6.03%	42.35%	13.91%
12:	10000	TRUE	typeI	FALSE	TRUE	5	0.73%	0.09%	1.93%	97.25%
13:	10000	TRUE	power	FALSE	FALSE	10	41.34%	6.20%	38.92%	13.54%
14:	10000	TRUE	typeI	FALSE	FALSE	10	0.77%	0.33%	1.80%	97.10%
15:	10000	TRUE	power	FALSE	FALSE	5	37.71%	6.03%	42.35%	13.91%
16:	10000	TRUE	typeI	FALSE	FALSE	5	0.73%	0.09%	1.93%	97.25%
17:	10000	FALSE	power	TRUE	FALSE	5	34.65%	5.59%	45.27%	14.49%
18:	10000	FALSE	typeI	TRUE	FALSE	5	0.68%	66.54%	1.77%	31.01%

Relative frequency of stopping for with a threshold below 1.96:

	scenario	missing	method	binding	fixC	ar	hypo	N	rejection	rejectionBelow196
1:	1	TRUE	1	TRUE	FALSE	10	power	10000	81.00%	0.85%
2:	1	TRUE	2	TRUE	FALSE	10	power	10000	80.93%	0.84%
3:	2	TRUE	1	TRUE	FALSE	10	typeI	10000	2.42%	0.18%
4:	2	TRUE	2	TRUE	FALSE	10	typeI	10000	2.39%	0.17%
5:	3	TRUE	1	TRUE	FALSE	5	power	10000	80.53%	0.45%
6:	3	TRUE	2	TRUE	FALSE	5	power	10000	80.53%	0.45%
7:	4	TRUE	1	TRUE	FALSE	5	typeI	10000	2.40%	0.08%
8:	4	TRUE	2	TRUE	FALSE	5	typeI	10000	2.40%	0.08%
9:	13	TRUE	1	FALSE	FALSE	10	power	10000	80.50%	0.64%
10:	13	TRUE	2	FALSE	FALSE	10	power	10000	80.44%	0.64%
11:	14	TRUE	1	FALSE	FALSE	10	typeI	10000	2.53%	0.08%
12:	14	TRUE	2	FALSE	FALSE	10	typeI	10000	2.53%	0.08%
13:	15	TRUE	1	FALSE	FALSE	5	power	10000	80.37%	0.44%
14:	15	TRUE	2	FALSE	FALSE	5	power	10000	80.36%	0.44%
15:	16	TRUE	1	FALSE	FALSE	5	typeI	10000	2.68%	0.05%
16:	16	TRUE	2	FALSE	FALSE	5	typeI	10000	2.68%	0.05%
17:	17	FALSE	1	TRUE	FALSE	5	power	10000	80.31%	0.42%
18:	17	FALSE	2	TRUE	FALSE	5	power	10000	80.30%	0.43%
19:	18	FALSE	1	TRUE	FALSE	5	typeI	10000	2.46%	0.08%
20:	18	FALSE	2	TRUE	FALSE	5	typeI	10000	2.46%	0.08%

2.2 3 stages

Relative frequency of stopping for efficacy/futility at decision/final

- Method 1

	N	missing	hypo	binding	fixC	ar	dec1.eff	dec1.fut	dec2.eff	dec2.fut	final.eff	final.fut
1:	1868	TRUE	power	TRUE	FALSE	10	8.73%	1.93%	19.86%	3.37%	46.73%	19.38%
2:	2481	TRUE	typeI	TRUE	FALSE	10	0.32%	26.64%	0.60%	35.95%	2.02%	34.46%
3:	1127	TRUE	typeI	TRUE	FALSE	5	0.44%	30.26%	0.27%	36.11%	2.40%	30.52%
4:	1934	TRUE	power	TRUE	TRUE	10	9.31%	1.71%	19.65%	3.67%	46.23%	19.44%
5:	2432	TRUE	typeI	TRUE	TRUE	10	0.08%	25.82%	0.16%	36.06%	1.64%	36.23%
6:	245	TRUE	power	TRUE	TRUE	5	14.29%	2.04%	13.47%	6.12%	47.76%	16.33%
7:	1042	TRUE	typeI	TRUE	TRUE	5	0.19%	27.45%	0	37.04%	1.54%	33.78%
8:	2500	TRUE	power	FALSE	TRUE	10	9.84%	1.88%	21.20%	3.60%	43.76%	19.72%
9:	2500	TRUE	typeI	FALSE	TRUE	10	0.20%	0.04%	0.44%	0.12%	1.72%	97.48%
10:	2500	TRUE	power	FALSE	TRUE	5	10.32%	1.80%	21.04%	3.32%	43.40%	20.12%
11:	2500	TRUE	typeI	FALSE	TRUE	5	0.08%	0.04%	0.52%	0	1.76%	97.60%
12:	2500	TRUE	power	FALSE	FALSE	10	9.36%	1.48%	20.68%	3.56%	45.24%	19.68%
13:	2483	TRUE	typeI	FALSE	FALSE	10	0.36%	0.12%	0.20%	0.04%	2.46%	96.82%
14:	2500	TRUE	power	FALSE	FALSE	5	9.92%	1.80%	20.64%	3.56%	44.56%	19.52%
15:	2500	TRUE	typeI	FALSE	FALSE	5	0.44%	0	0.40%	0	2.32%	96.84%

- Method 2

	N	missing	hypo	binding	fixC	ar	dec1.eff	dec1.fut	dec2.eff	dec2.fut	final.eff	final.fut
1:	1868	TRUE	power	TRUE	FALSE	10	8.73%	1.93%	19.86%	3.37%	46.73%	19.38%
2:	2481	TRUE	typeI	TRUE	FALSE	10	0.32%	26.68%	0.60%	35.99%	2.02%	34.38%
3:	1127	TRUE	typeI	TRUE	FALSE	5	0.44%	30.35%	0.27%	36.02%	2.40%	30.52%
4:	1934	TRUE	power	TRUE	TRUE	10	9.46%	1.60%	20.42%	3.41%	46.12%	18.98%
5:	2432	TRUE	typeI	TRUE	TRUE	10	0.12%	24.96%	0.16%	35.44%	1.85%	37.46%
6:	245	TRUE	power	TRUE	TRUE	5	13.88%	2.04%	13.06%	6.53%	48.98%	15.51%
7:	1042	TRUE	typeI	TRUE	TRUE	5	0.19%	26.97%	0.10%	37.04%	1.63%	34.07%
8:	2500	TRUE	power	FALSE	TRUE	10	9.92%	1.76%	21.44%	3.40%	43.96%	19.52%
9:	2500	TRUE	typeI	FALSE	TRUE	10	0.24%	0.04%	0.44%	0.08%	1.72%	97.48%
10:	2500	TRUE	power	FALSE	TRUE	5	10.36%	2.00%	21.32%	3.04%	43.76%	19.52%
11:	2500	TRUE	typeI	FALSE	TRUE	5	0.08%	0.08%	0.52%	0	1.68%	97.64%
12:	2500	TRUE	power	FALSE	FALSE	10	9.36%	1.48%	20.72%	3.44%	45.32%	19.68%
13:	2483	TRUE	typeI	FALSE	FALSE	10	0.36%	0.12%	0.20%	0	2.54%	96.78%
14:	2500	TRUE	power	FALSE	FALSE	5	9.92%	1.80%	20.40%	3.28%	44.92%	19.68%
15:	2500	TRUE	typeI	FALSE	FALSE	5	0.44%	0	0.32%	0	2.36%	96.88%

- Method 3

	N	missing	hypo	binding	fixC	ar	dec1.eff	dec1.fut	dec2.eff	dec2.fut	final.eff	final.fut
1:	1868	TRUE	power	TRUE	FALSE	10	8.94%	2.19%	20.77%	3.43%	45.29%	19.38%
2:	2481	TRUE	typeI	TRUE	FALSE	10	0.24%	25.39%	0.48%	35.99%	1.98%	35.91%
3:	1127	TRUE	typeI	TRUE	FALSE	5	0.35%	30.08%	0.27%	35.67%	2.48%	31.14%
4:	1934	TRUE	power	TRUE	TRUE	10	9.82%	1.55%	21.15%	3.46%	45.14%	18.87%
5:	2432	TRUE	typeI	TRUE	TRUE	10	0.08%	24.71%	0.21%	35.57%	1.73%	37.71%
6:	245	TRUE	power	TRUE	TRUE	5	14.69%	2.04%	13.88%	6.12%	47.35%	15.92%
7:	1042	TRUE	typeI	TRUE	TRUE	5	0.19%	27.06%	0	37.04%	1.63%	34.07%
8:	2500	TRUE	power	FALSE	TRUE	10	10.40%	1.80%	21.80%	3.32%	42.80%	19.88%
9:	2500	TRUE	typeI	FALSE	TRUE	10	0.20%	0.04%	0.44%	0.16%	1.68%	97.48%
10:	2500	TRUE	power	FALSE	TRUE	5	10.64%	1.80%	21.04%	3.36%	43.00%	20.16%
11:	2500	TRUE	typeI	FALSE	TRUE	5	0.12%	0.04%	0.48%	0	1.68%	97.68%
12:	2500	TRUE	power	FALSE	FALSE	10	10.36%	1.68%	21.36%	3.48%	43.64%	19.48%
13:	2483	TRUE	typeI	FALSE	FALSE	10	0.32%	0.16%	0.20%	0.04%	2.58%	96.70%
14:	2500	TRUE	power	FALSE	FALSE	5	9.96%	1.84%	20.68%	3.20%	44.48%	19.84%
15:	2500	TRUE	typeI	FALSE	FALSE	5	0.44%	0.04%	0.32%	0.04%	2.28%	96.88%

Relative frequency of stopping for with a threshold below 1.96:

	scenario	missing	method	binding	fixC	ar	hypo	N	rejection	rejectionBelow196
1:	1	TRUE	1	TRUE	FALSE	10	power	1868	75.32%	0.64%
2:	1	TRUE	2	TRUE	FALSE	10	power	1868	75.32%	0.64%
3:	2	TRUE	1	TRUE	FALSE	10	typeI	2481	2.94%	0.24%
4:	2	TRUE	2	TRUE	FALSE	10	typeI	2481	2.94%	0.24%
5:	4	TRUE	1	TRUE	FALSE	5	typeI	1127	3.11%	0.09%
6:	4	TRUE	2	TRUE	FALSE	5	typeI	1127	3.11%	0.09%
7:	13	TRUE	1	FALSE	FALSE	10	power	2500	75.28%	0.36%
8:	13	TRUE	2	FALSE	FALSE	10	power	2500	75.40%	0.32%
9:	14	TRUE	1	FALSE	FALSE	10	typeI	2483	3.02%	0.04%
10:	14	TRUE	2	FALSE	FALSE	10	typeI	2483	3.10%	0.04%
11:	15	TRUE	1	FALSE	FALSE	5	power	2500	75.12%	0.16%
12:	15	TRUE	2	FALSE	FALSE	5	power	2500	75.24%	0.16%
13:	16	TRUE	1	FALSE	FALSE	5	typeI	2500	3.16%	0.08%
14:	16	TRUE	2	FALSE	FALSE	5	typeI	2500	3.12%	0.08%

3 Bias (True effect: 0.6 under the alternative)

3.1 2 stages

Bias per estimator and method[1]:

	hypo	missing	binding	fixC	ar	biasMLE1	biasMLE2	biasMLE3	biasMUE1	biasMUE2	biasMUE3
1:	power	TRUE	TRUE	FALSE	10	0.01345	0.01315	0.01468	0.00598	0.00566	0.00221
2:	typeI	TRUE	TRUE	FALSE	10	-0.01794	-0.01784	-0.01856	-0.00453	-0.00448	-0.00510
3:	power	TRUE	TRUE	FALSE	5	0.02257	0.02255	0.02358	0.01045	0.01048	0.00870
4:	typeI	TRUE	TRUE	FALSE	5	-0.03034	-0.03031	-0.03065	-0.01190	-0.01185	-0.01243
5:	power	TRUE	TRUE	TRUE	10	0.01345	0.01403	0.01468	0.00110	0.00169	0.00221
6:	typeI	TRUE	TRUE	TRUE	10	-0.01794	-0.01871	-0.01856	-0.00542	-0.00609	-0.00510
7:	power	TRUE	TRUE	TRUE	5	0.02257	0.02309	0.02358	0.00788	0.00827	0.00870
8:	typeI	TRUE	TRUE	TRUE	5	-0.03034	-0.03085	-0.03065	-0.01230	-0.01288	-0.01243
9:	power	TRUE	FALSE	TRUE	10	0.01433	0.01490	0.01529	0.03456	0.03325	0.03453
10:	typeI	TRUE	FALSE	TRUE	10	0.00019	0.00019	0.00051	-0.00076	-0.00068	0.00077
11:	power	TRUE	FALSE	TRUE	5	0.02366	0.02402	0.02438	0.04130	0.04038	0.04201
12:	typeI	TRUE	FALSE	TRUE	5	0.00091	0.00085	0.00101	0.00052	0.00047	0.00091
13:	power	TRUE	FALSE	FALSE	10	0.01433	0.01416	0.01529	0.03552	0.03589	0.03453
14:	typeI	TRUE	FALSE	FALSE	10	0.00019	0.00019	0.00051	-0.00020	-0.00021	0.00077
15:	power	TRUE	FALSE	FALSE	5	0.02366	0.02365	0.02438	0.04186	0.04202	0.04201
16:	typeI	TRUE	FALSE	FALSE	5	0.00091	0.00091	0.00101	0.00087	0.00087	0.00091
17:	power	FALSE	TRUE	FALSE	5	0.02284	0.02277	0.02381	0.01197	0.01196	0.01001
18:	typeI	FALSE	TRUE	FALSE	5	-0.02952	-0.02945	-0.02992	-0.01111	-0.01106	-0.01168

Median bias [2] per estimator and method:

	hypo	missing	binding	fixC	ar	mbiasMLE1	mbiasMLE2	mbiasMLE3	mbiasMUE1	mbiasMUE2	mbiasMUE3
1:	power	TRUE	TRUE	FALSE	10	0.0261	0.0260	0.0301	-0.00240	-0.00250	-0.00535
2:	typeI	TRUE	TRUE	FALSE	10	-0.0173	-0.0170	-0.0202	0.00100	0.00075	-0.00015
3:	power	TRUE	TRUE	FALSE	5	0.0405	0.0405	0.0432	-0.00340	-0.00330	-0.00530
4:	typeI	TRUE	TRUE	FALSE	5	-0.0330	-0.0329	-0.0345	0.00055	0.00055	0.00065
5:	power	TRUE	TRUE	TRUE	10	0.0261	0.0265	0.0301	-0.01050	-0.01010	-0.00535
6:	typeI	TRUE	TRUE	TRUE	10	-0.0173	-0.0197	-0.0202	0.00100	-0.00065	-0.00015
7:	power	TRUE	TRUE	TRUE	5	0.0405	0.0407	0.0432	-0.00770	-0.00650	-0.00530
8:	typeI	TRUE	TRUE	TRUE	5	-0.0330	-0.0346	-0.0345	0.00055	0.00075	0.00065
9:	power	TRUE	FALSE	TRUE	10	0.0326	0.0332	0.0327	0.02772	0.02517	0.02868
10:	typeI	TRUE	FALSE	TRUE	10	-0.0009	-0.0009	-0.0009	-0.00190	-0.00185	-0.00025
11:	power	TRUE	FALSE	TRUE	5	0.0462	0.0459	0.0489	0.02621	0.02512	0.02820
12:	typeI	TRUE	FALSE	TRUE	5	-0.0009	-0.0010	-0.0009	-0.00130	-0.00140	-0.00015
13:	power	TRUE	FALSE	FALSE	10	0.0326	0.0324	0.0327	0.03094	0.03184	0.02868
14:	typeI	TRUE	FALSE	FALSE	10	-0.0009	-0.0009	-0.0009	-0.00150	-0.00140	-0.00025
15:	power	TRUE	FALSE	FALSE	5	0.0462	0.0464	0.0489	0.02832	0.02865	0.02820

[1] e.g. `biasMLE1` mixed model estimator (treatment effect), method 1 (boundaries)

[2] Relative frequency at which the estimate is greater than the truth minus 0.5

```
16: typeI    TRUE   FALSE FALSE  5   -0.0009   -0.0009   -0.0009  -0.00105  -0.00105  -0.00015
17: power   FALSE    TRUE FALSE  5    0.0383    0.0383    0.0400  -0.00265  -0.00255  -0.00485
18: typeI   FALSE    TRUE FALSE  5   -0.0329   -0.0327   -0.0353   0.00420   0.00420   0.00330
```

3.2 3 stages

Bias per estimator and method[3]:

	hypo	missing	binding	fixC	ar	biasMLE1	biasMLE2	biasMLE3	biasMUE1	biasMUE2	biasMUE3
1:	power	TRUE	TRUE	FALSE	10	0.0191	0.0191	0.0201	0.0181	0.0179	0.0133
2:	typeI	TRUE	TRUE	FALSE	10	-0.0278	-0.0276	-0.0263	-0.0233	-0.0230	-0.0245
3:	typeI	TRUE	TRUE	FALSE	5	-0.0688	-0.0690	-0.0693	-0.0528	-0.0531	-0.0541
4:	power	TRUE	TRUE	TRUE	10	0.0197	0.0202	0.0217	0.0187	0.0211	0.0200
5:	typeI	TRUE	TRUE	TRUE	10	-0.0341	-0.0336	-0.0340	-0.0252	-0.0240	-0.0253
6:	power	TRUE	TRUE	TRUE	5	0.0167	0.0148	0.0177	0.0354	0.0190	0.0157
7:	typeI	TRUE	TRUE	TRUE	5	-0.0547	-0.0539	-0.0542	-0.0342	-0.0350	-0.0361
8:	power	TRUE	FALSE	TRUE	10	0.0251	0.0254	0.0262	0.0561	0.0553	0.0523
9:	typeI	TRUE	FALSE	TRUE	10	0.0085	0.0081	0.0085	0.0100	0.0096	0.0101
10:	power	TRUE	FALSE	TRUE	5	0.0377	0.0377	0.0374	0.0569	0.0570	0.0547
11:	typeI	TRUE	FALSE	TRUE	5	0.0087	0.0085	0.0088	0.0092	0.0091	0.0092
12:	power	TRUE	FALSE	FALSE	10	0.0266	0.0268	0.0296	0.0539	0.0538	0.0536
13:	typeI	TRUE	FALSE	FALSE	10	0.0111	0.0106	0.0106	0.0130	0.0124	0.0130
14:	power	TRUE	FALSE	FALSE	5	0.0416	0.0419	0.0428	0.0605	0.0593	0.0584
15:	typeI	TRUE	FALSE	FALSE	5	0.0126	0.0122	0.0125	0.0137	0.0132	0.0134

Median bias [4] per estimator and method:

	hypo	missing	binding	fixC	ar	mbiasMLE1	mbiasMLE2	mbiasMLE3	mbiasMUE1	mbiasMUE2	mbiasMUE3
1:	power	TRUE	TRUE	FALSE	10	0.034	0.034	0.038	0.0134	0.0134	0.0054
2:	typeI	TRUE	TRUE	FALSE	10	-0.022	-0.022	-0.020	0.0147	0.0151	0.0139
3:	typeI	TRUE	TRUE	FALSE	5	-0.072	-0.072	-0.075	-0.0138	-0.0129	-0.0138
4:	power	TRUE	TRUE	TRUE	10	0.028	0.029	0.029	0.0031	0.0041	0.0057
5:	typeI	TRUE	TRUE	TRUE	10	-0.029	-0.033	-0.032	0.0086	0.0095	0.0074
6:	power	TRUE	TRUE	TRUE	5	-0.018	-0.014	-0.018	-0.0347	-0.0347	-0.0429
7:	typeI	TRUE	TRUE	TRUE	5	-0.054	-0.047	-0.057	-0.0106	-0.0106	-0.0134
8:	power	TRUE	FALSE	TRUE	10	0.039	0.038	0.040	0.0520	0.0576	0.0484
9:	typeI	TRUE	FALSE	TRUE	10	0.022	0.023	0.020	0.0228	0.0232	0.0220
10:	power	TRUE	FALSE	TRUE	5	0.048	0.050	0.046	0.0372	0.0428	0.0352
11:	typeI	TRUE	FALSE	TRUE	5	0.023	0.023	0.021	0.0228	0.0236	0.0212
12:	power	TRUE	FALSE	FALSE	10	0.034	0.030	0.036	0.0460	0.0444	0.0408
13:	typeI	TRUE	FALSE	FALSE	10	0.018	0.015	0.015	0.0171	0.0151	0.0159
14:	power	TRUE	FALSE	FALSE	5	0.044	0.040	0.042	0.0452	0.0392	0.0384
15:	typeI	TRUE	FALSE	FALSE	5	0.018	0.015	0.015	0.0180	0.0152	0.0156

[3] e.g. `biasMLE1` mixed model estimator (treatment effect), method 1 (boundaries)

[4] Relative frequency at which the estimate is greater than the truth minus 0.5

4 Distribution of the estimates

4.1 2 stages

Distribution of the estimates:

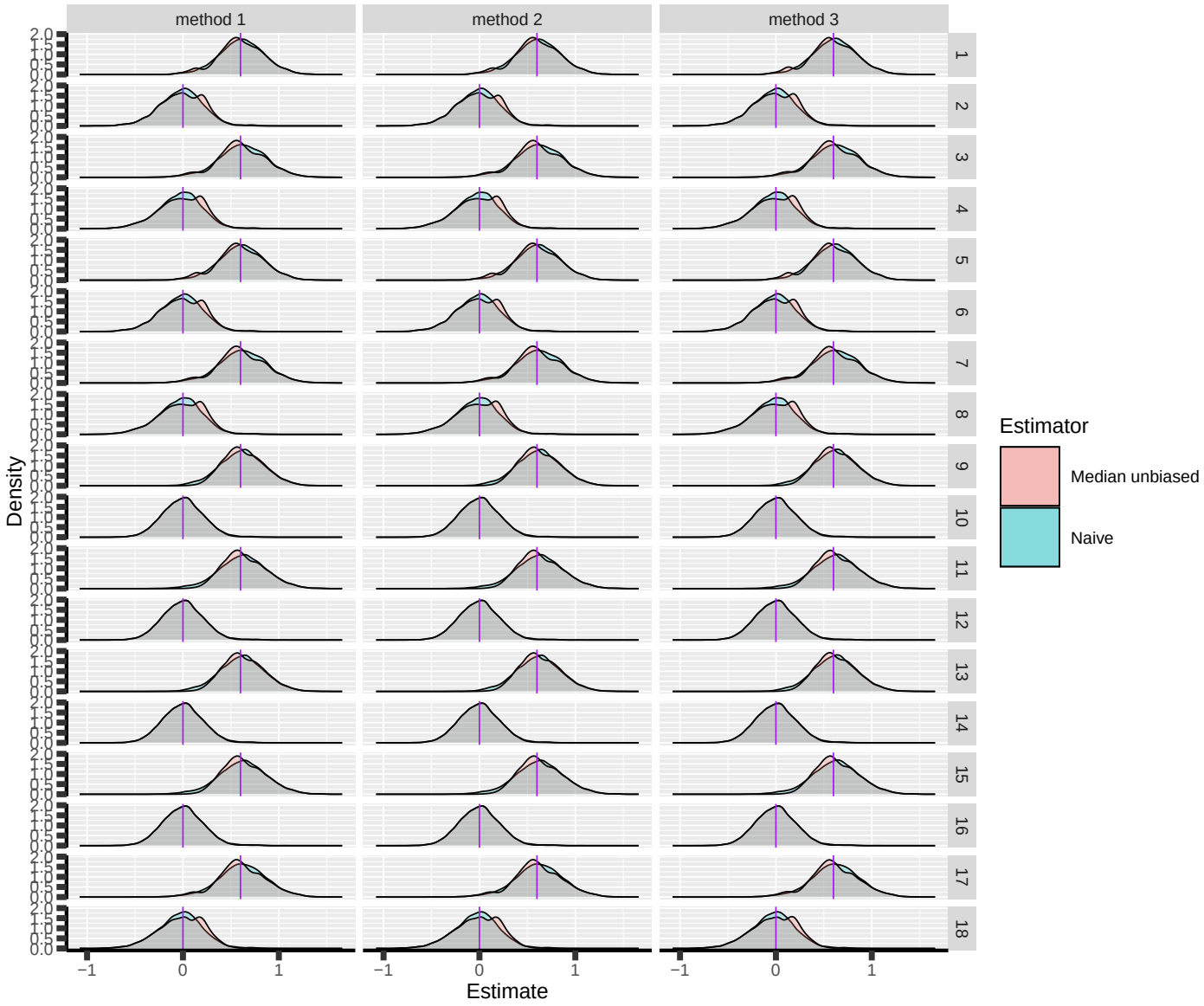

Figure 5: Naive and Median unbiased estimate distribution over all simulations. Each row correspond to a different scenario

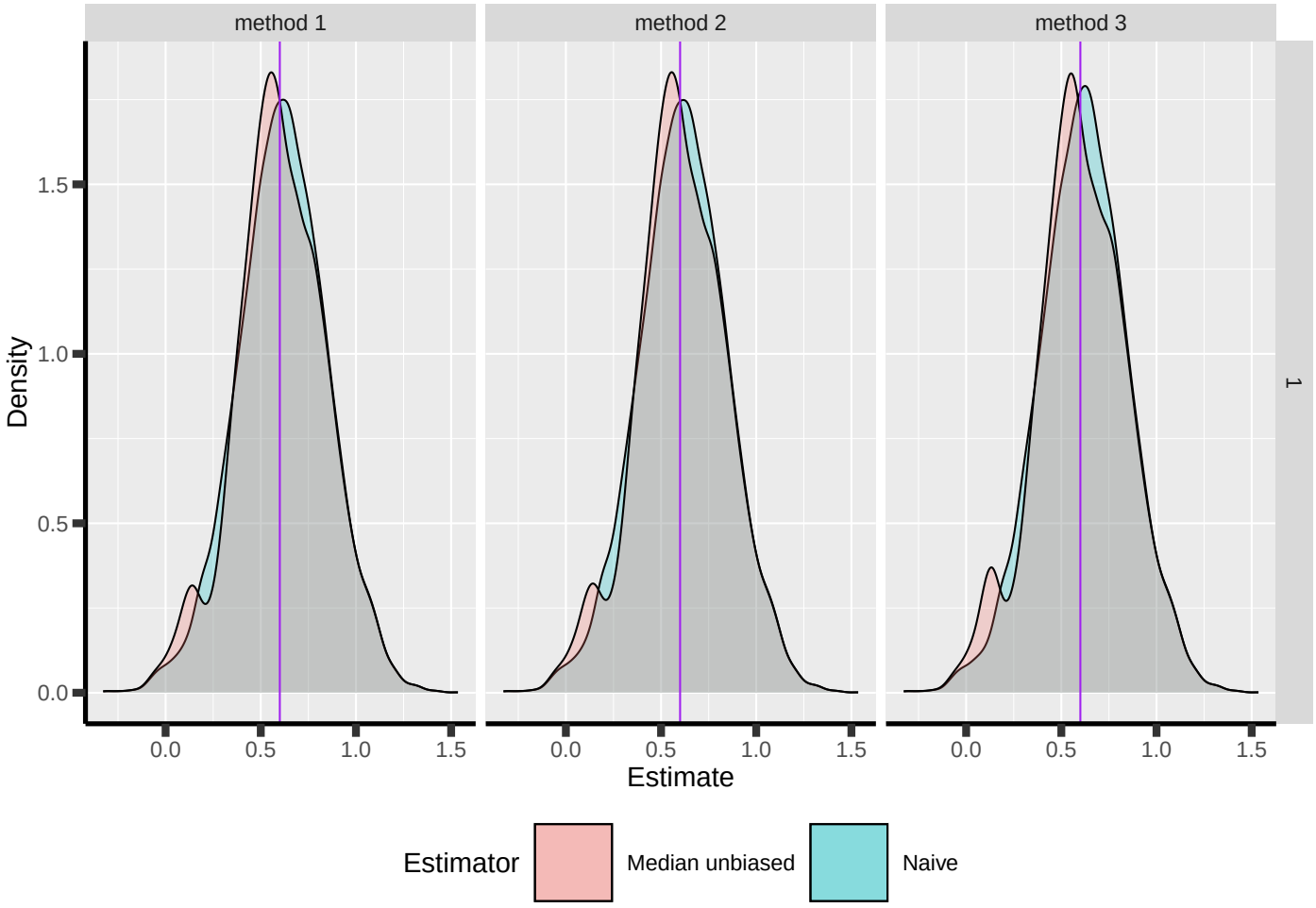

Figure 6: Same but specific to scenario 1

Distribution of the median unbiased estimate conditional to the stage:

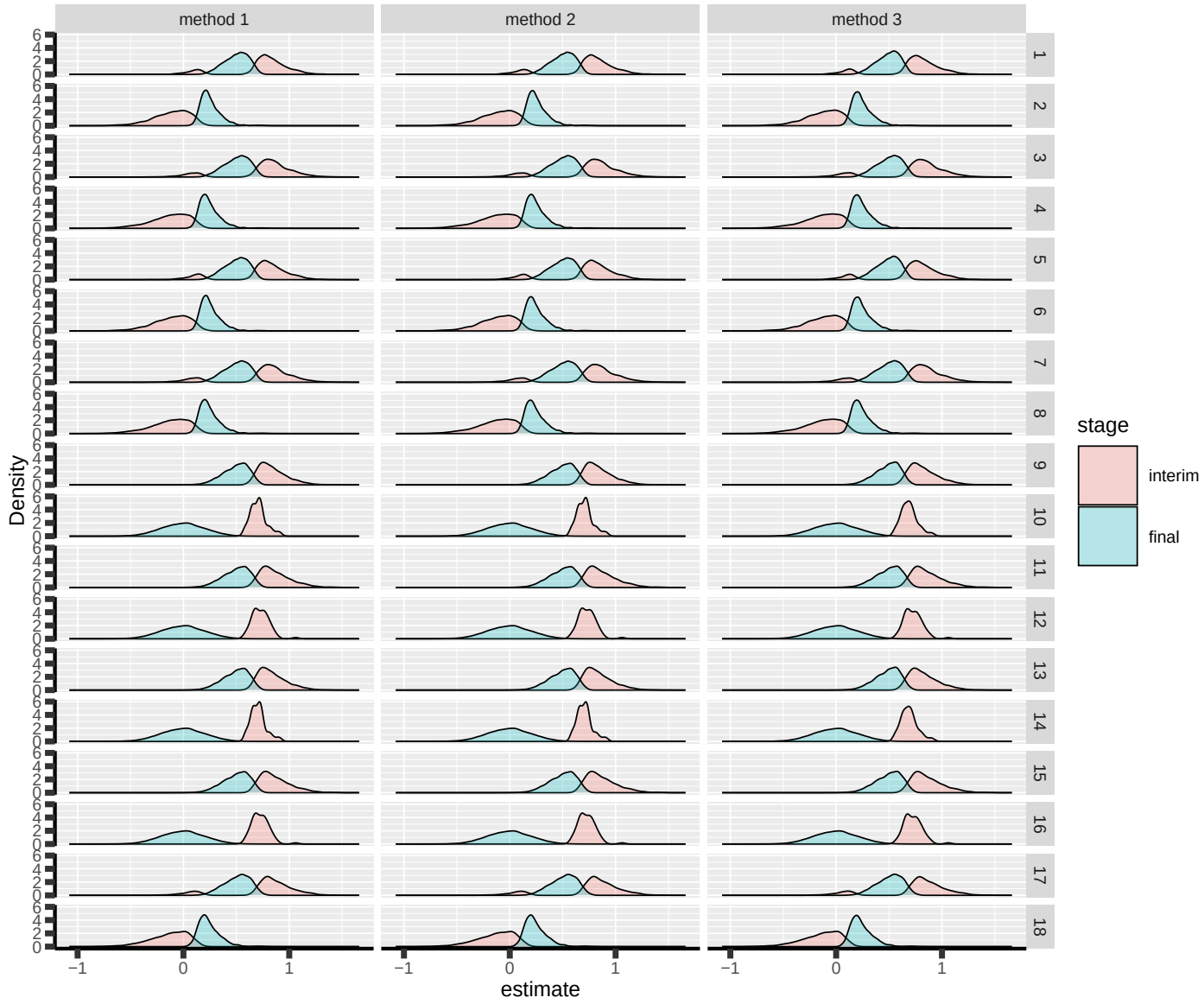

Figure 7: Median unbiased estimate distribution conditional to the stage. Each row correspond to a different scenario.

4.2 3 stages

Distribution of the estimates:

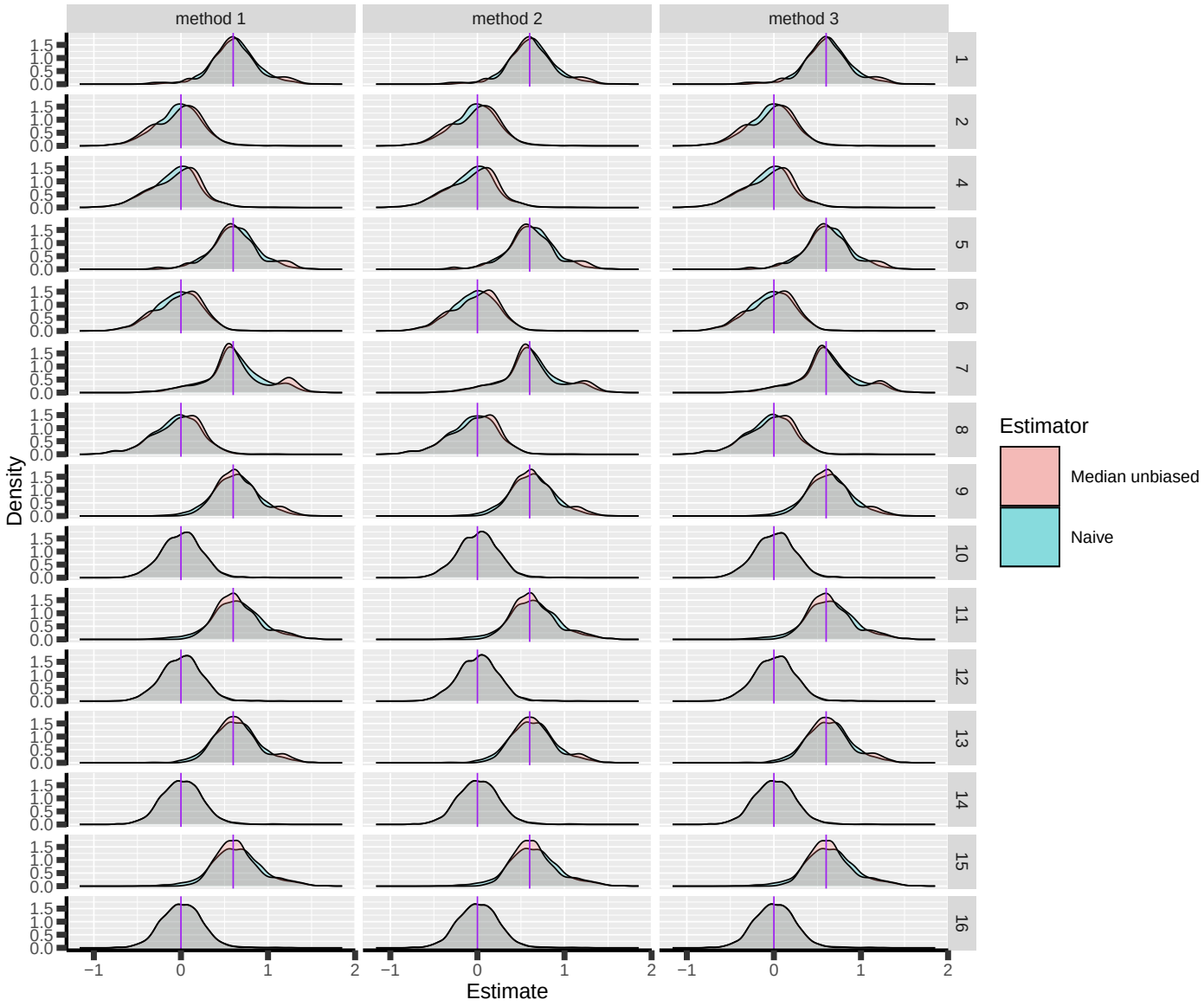

Figure 8: Naive and Median unbiased estimate distribution over all simulations. Each row correspond to a different scenario

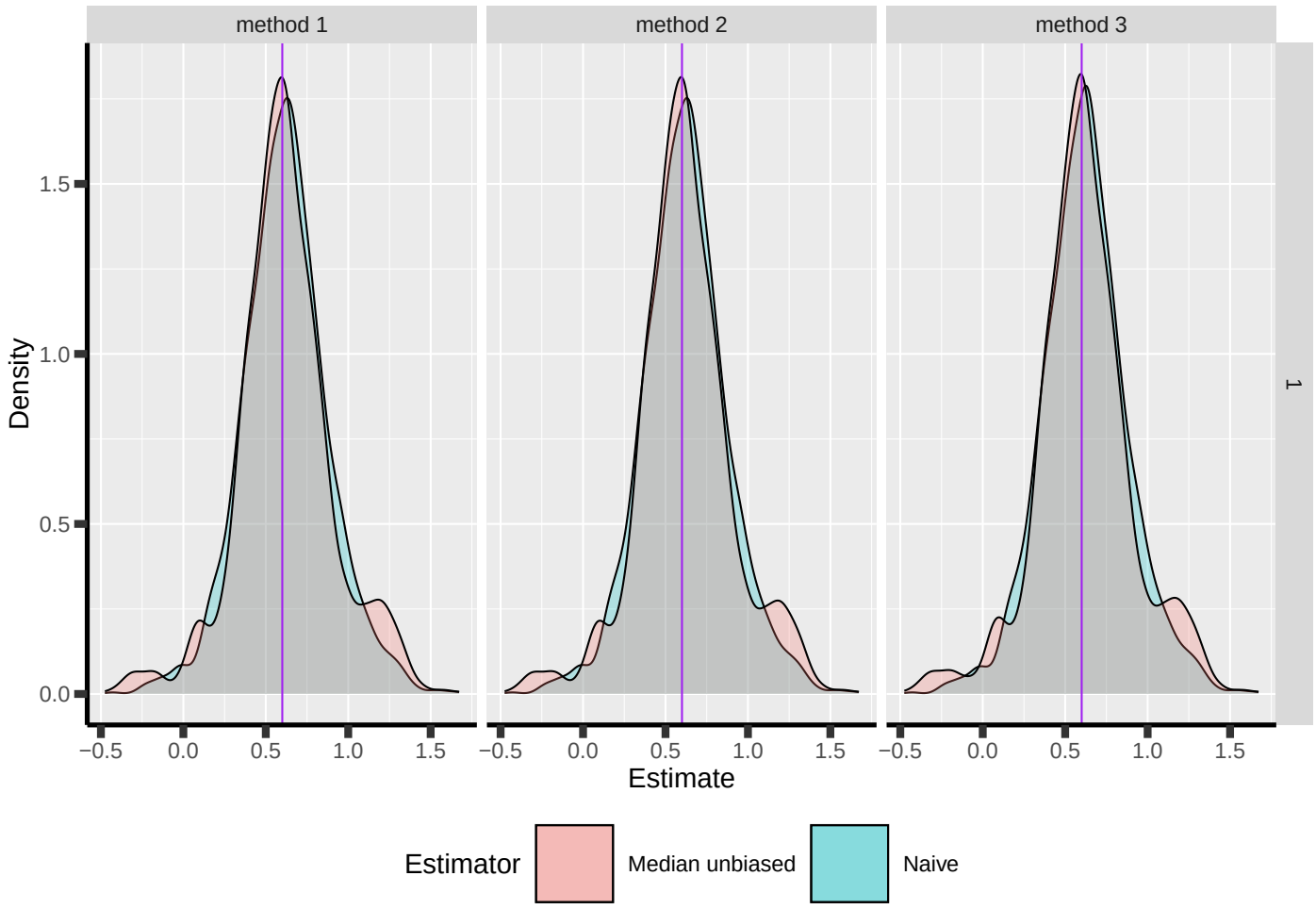

Figure 9: Same but specific to scenario 1

Distribution of the median unbiased estimate conditional to the stage:

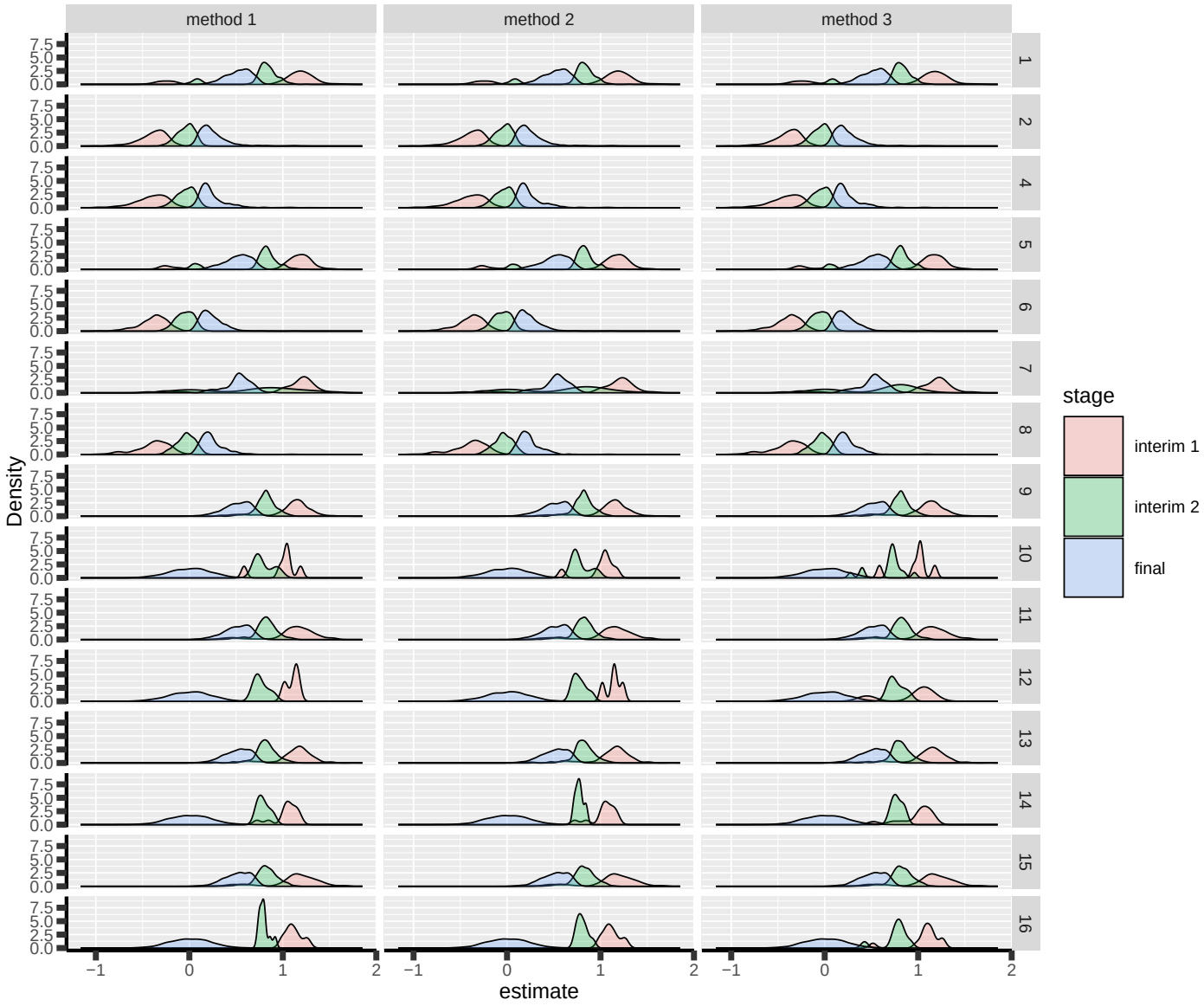

Figure 10: Median unbiased estimate distribution conditional to the stage. Each row correspond to a different scenario.

5 Special cases

5.1 2 stages

Reason for stopping (efficacy, futility, Imax reached), continuing the trial (decreasing information, no boundary crossed), or concluding (stop for futility at interim):

	scenario	1	2	3	4	5	6	7	8
reason	method								
decreasing information	1	0	0	1	1	0	0	1	1
	2	0	0	1	1	0	0	1	1
	3	0	0	1	1	0	0	1	1
efficacy	1	3739	81	3573	74	3739	81	3573	74
	2	3744	81	3576	74	3718	79	3545	71
	3	4165	108	3721	82	4165	108	3721	82
futility	1	632	7111	599	6932	632	7111	599	6932
	2	659	7161	600	6938	574	6940	562	6828
	3	545	6844	563	6828	545	6844	563	6828
Imax reached	1	1	1	0	0	1	1	0	0
	2	1	1	0	0	1	1	0	0
	3	1	1	0	0	1	1	0	0
no boundary crossed	1	5628	2807	5828	2994	5628	2807	5828	2994
	2	5596	2757	5824	2988	5707	2980	5893	3101
	3	5289	3047	5716	3090	5289	3047	5716	3090
stop for futility at interim	1	0	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0	0
	3	11	1	2	0	11	1	2	0

	scenario	9	10	11	12	13	14	15	16	17	18
reason	method										
efficacy	1	3849	81	3680	76	3849	81	3680	76	3396	74
	2	3829	80	3661	75	3850	81	3683	76	3400	74
	3	4238	110	3831	82	4238	110	3831	82	3528	80
futility	1	613	7122	570	6945	613	7122	570	6945	535	6748
	2	560	6975	541	6838	629	7164	574	6950	539	6755
	3	516	6890	543	6842	516	6890	543	6842	496	6642
no boundary crossed	1	5538	2797	5750	2979	5538	2797	5750	2979	6069	3178
	2	5611	2945	5798	3087	5521	2755	5743	2974	6061	3171
	3	5246	3000	5626	3076	5246	3000	5626	3076	5976	3278
stop for futility at interim	1	0	0	0	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0	0	0	0
	3	8	0	0	0	8	0	0	0	1	0

5.2 3 stages

Reason for stopping (efficacy, futility, Imax reached), continuing the trial (decreasing information, no boundary crossed), or concluding (stop for futility at interim):

	scenario	1	2	4	5	6	7	8
reason	method							
efficacy	1	529	20	9	566	10	69	5
	2	529	20	9	584	12	67	7
	3	566	22	9	609	12	71	5
futility	1	104	1556	747	98	1501	19	669
	2	104	1558	747	91	1464	20	663
	3	94	1519	739	87	1461	19	665
no boundary crossed	1	2904	2717	1152	2991	2723	362	1122
	2	2904	2714	1151	2979	2778	364	1131
	3	2868	2785	1163	2952	2788	359	1130
stop for futility at interim	1	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0
	3	2	1	0	0	0	0	0

	scenario	9	10	11	12	13	14	15	16
reason	method								
efficacy	1	782	20	794	16	749	18	764	21
	2	792	20	798	17	750	17	758	19
	3	814	21	802	16	804	18	770	21
futility	1	131	2200	118	2242	128	2248	134	2282
	2	121	2148	120	2242	125	2243	127	2278
	3	119	2110	119	2216	118	2181	122	2257
no boundary crossed	1	3794	2774	3785	2739	3852	2688	3809	2686
	2	3795	2825	3773	2737	3854	2694	3822	2692
	3	3762	2863	3768	2764	3777	2755	3813	2710

6 Reversal probability

6.1 2 stages

Percentage of time we observe a reversal:

	N	hypo	missing	ar	binding	fixC	fu2eff_1	fu2eff_2	fu2eff_3	eff2fu_1	eff2fu_2	eff2fu_3
1:	10000	power	TRUE	10	TRUE	FALSE	0.57%	0.61%	0	0.17%	0.20%	1.07%
2:	10000	typeI	TRUE	10	TRUE	FALSE	0.10%	0.09%	0	0.11%	0.11%	0.34%
3:	10000	power	TRUE	5	TRUE	FALSE	0.08%	0.08%	0	0.07%	0.07%	0.67%
4:	10000	typeI	TRUE	5	TRUE	FALSE	0.02%	0.02%	0	0.02%	0.02%	0.13%
5:	10000	power	TRUE	10	TRUE	TRUE	0.22%	0.16%	0	0.67%	0.65%	1.07%
6:	10000	typeI	TRUE	10	TRUE	TRUE	0.02%	0.01%	0	0.21%	0.21%	0.34%
7:	10000	power	TRUE	5	TRUE	TRUE	0.02%	0.02%	0	0.46%	0.45%	0.67%
8:	10000	typeI	TRUE	5	TRUE	TRUE	0	0	0	0.08%	0.08%	0.13%
9:	10000	power	TRUE	10	FALSE	TRUE	0.14%	0.11%	0	0.58%	0.55%	1.04%
10:	10000	typeI	TRUE	10	FALSE	TRUE	0	0	0	0.20%	0.19%	0.33%
11:	10000	power	TRUE	5	FALSE	TRUE	0.01%	0.01%	0	0.46%	0.44%	0.60%
12:	10000	typeI	TRUE	5	FALSE	TRUE	0	0	0	0.06%	0.06%	0.09%
13:	10000	power	TRUE	10	FALSE	FALSE	0.41%	0.42%	0	0.21%	0.22%	1.04%
14:	10000	typeI	TRUE	10	FALSE	FALSE	0	0	0	0.12%	0.12%	0.33%
15:	10000	power	TRUE	5	FALSE	FALSE	0.03%	0.03%	0	0.04%	0.04%	0.60%
16:	10000	typeI	TRUE	5	FALSE	FALSE	0	0	0	0.01%	0.01%	0.09%
17:	10000	power	FALSE	5	TRUE	FALSE	0.06%	0.07%	0	0.04%	0.04%	0.63%
18:	10000	typeI	FALSE	5	TRUE	FALSE	0.01%	0.01%	0	0.01%	0.01%	0.12%

6.2 3 stages

Percentage of time we observe a reversal:

	N	hypo	missing	ar	binding	fixC	fu2eff_1	fu2eff_2	fu2eff_3	eff2fu_1	eff2fu_2	eff2fu_3
1:	1868	power	TRUE	10	TRUE	FALSE	0.32%	0.32%	0	0.05%	0.05%	0.59%
2:	2481	typeI	TRUE	10	TRUE	FALSE	0.20%	0.20%	0	0.08%	0.08%	0.16%
3:	1127	typeI	TRUE	5	TRUE	FALSE	0	0	0	0.09%	0.09%	0.18%
4:	1934	power	TRUE	10	TRUE	TRUE	0	0	0	0.31%	0.31%	0.52%
5:	2432	typeI	TRUE	10	TRUE	TRUE	0	0	0	0.16%	0.21%	0.21%
6:	245	power	TRUE	5	TRUE	TRUE	0	0	0	0.41%	0.41%	0.41%
7:	1042	typeI	TRUE	5	TRUE	TRUE	0	0	0	0.29%	0.38%	0.29%
8:	2500	power	TRUE	10	FALSE	TRUE	0.04%	0	0	0.28%	0.32%	0.36%
9:	2500	typeI	TRUE	10	FALSE	TRUE	0	0	0	0.16%	0.12%	0.20%
10:	2500	power	TRUE	5	FALSE	TRUE	0	0	0	0.40%	0.24%	0.40%
11:	2500	typeI	TRUE	5	FALSE	TRUE	0	0	0	0.04%	0.08%	0.04%
12:	2500	power	TRUE	10	FALSE	FALSE	0.12%	0.12%	0	0.04%	0.04%	0.44%
13:	2483	typeI	TRUE	10	FALSE	FALSE	0	0	0	0.16%	0.12%	0.20%
14:	2500	power	TRUE	5	FALSE	FALSE	0	0	0	0	0	0.16%
15:	2500	typeI	TRUE	5	FALSE	FALSE	0	0	0	0	0	0.08%

7 Logical consistency of p-values/CIs

7.1 Mismatch p-value / boundaries

7.1.1 2 stages

When concluding for futility:

	hypo	missing	ar	binding	fixC	method 1	method 2	method 3
1:	power	TRUE	10	TRUE	FALSE	0	0	0
2:	typeI	TRUE	10	TRUE	FALSE	0	0	0
3:	power	TRUE	5	TRUE	FALSE	0	0	0
4:	typeI	TRUE	5	TRUE	FALSE	0	0	0
5:	power	TRUE	10	TRUE	TRUE	0	0	0
6:	typeI	TRUE	10	TRUE	TRUE	0	0	0
7:	power	TRUE	5	TRUE	TRUE	0	0	0
8:	typeI	TRUE	5	TRUE	TRUE	0	0	0
9:	power	TRUE	10	FALSE	TRUE	0	0	0
10:	typeI	TRUE	10	FALSE	TRUE	0	0	0
11:	power	TRUE	5	FALSE	TRUE	0	0	0
12:	typeI	TRUE	5	FALSE	TRUE	0	0	0
13:	power	TRUE	10	FALSE	FALSE	0	0	0
14:	typeI	TRUE	10	FALSE	FALSE	0	0	0
15:	power	TRUE	5	FALSE	FALSE	0	0	0
16:	typeI	TRUE	5	FALSE	FALSE	0	0	0
17:	power	FALSE	5	TRUE	FALSE	0	0	0
18:	typeI	FALSE	5	TRUE	FALSE	0	0	0

When concluding for efficacy:

	hypo	missing	ar	binding	fixC	method 1	method 2	method 3
1:	power	TRUE	10	TRUE	FALSE	0	0	0
2:	typeI	TRUE	10	TRUE	FALSE	0	0	0
3:	power	TRUE	5	TRUE	FALSE	0	0	0
4:	typeI	TRUE	5	TRUE	FALSE	0	0	0
5:	power	TRUE	10	TRUE	TRUE	0	0	0
6:	typeI	TRUE	10	TRUE	TRUE	0	0	0
7:	power	TRUE	5	TRUE	TRUE	0	0	0
8:	typeI	TRUE	5	TRUE	TRUE	0	0	0
9:	power	TRUE	10	FALSE	TRUE	0	0	0
10:	typeI	TRUE	10	FALSE	TRUE	0	0	0
11:	power	TRUE	5	FALSE	TRUE	0	0	0
12:	typeI	TRUE	5	FALSE	TRUE	0	0	0
13:	power	TRUE	10	FALSE	FALSE	0	0	0
14:	typeI	TRUE	10	FALSE	FALSE	0	0	0

```
15: power    TRUE  5   FALSE FALSE        0        0        0
16: typeI    TRUE  5   FALSE FALSE        0        0        0
17: power   FALSE  5    TRUE FALSE        0        0        0
18: typeI   FALSE  5    TRUE FALSE        0        0        0
```

7.1.2 3 stages

When concluding for futility:

	hypo	missing	ar	binding	fixC	method 1	method 2	method 3
1:	power	TRUE	10	TRUE	FALSE	0	0	0
2:	typeI	TRUE	10	TRUE	FALSE	0	0	0
3:	typeI	TRUE	5	TRUE	FALSE	0	0	0
4:	power	TRUE	10	TRUE	TRUE	0	0	0
5:	typeI	TRUE	10	TRUE	TRUE	0	0	0
6:	power	TRUE	5	TRUE	TRUE	0	0	0
7:	typeI	TRUE	5	TRUE	TRUE	0	0	0
8:	power	TRUE	10	FALSE	TRUE	0	0.16%	0
9:	typeI	TRUE	10	FALSE	TRUE	0	0	0
10:	power	TRUE	5	FALSE	TRUE	0	0	0
11:	typeI	TRUE	5	FALSE	TRUE	0	0	0
12:	power	TRUE	10	FALSE	FALSE	0	0	0
13:	typeI	TRUE	10	FALSE	FALSE	0	0	0
14:	power	TRUE	5	FALSE	FALSE	0	0	0
15:	typeI	TRUE	5	FALSE	FALSE	0	0	0

When concluding for efficacy:

	hypo	missing	ar	binding	fixC	method 1	method 2	method 3
1:	power	TRUE	10	TRUE	FALSE	0	0	0
2:	typeI	TRUE	10	TRUE	FALSE	0	0	0
3:	typeI	TRUE	5	TRUE	FALSE	0	0	0
4:	power	TRUE	10	TRUE	TRUE	0	0	0
5:	typeI	TRUE	10	TRUE	TRUE	0	0	0
6:	power	TRUE	5	TRUE	TRUE	0	0	0
7:	typeI	TRUE	5	TRUE	TRUE	0	0	0
8:	power	TRUE	10	FALSE	TRUE	0	0	0
9:	typeI	TRUE	10	FALSE	TRUE	0	0	0
10:	power	TRUE	5	FALSE	TRUE	0	0	0
11:	typeI	TRUE	5	FALSE	TRUE	0	0	0
12:	power	TRUE	10	FALSE	FALSE	0	0.05%	0
13:	typeI	TRUE	10	FALSE	FALSE	0	0	0
14:	power	TRUE	5	FALSE	FALSE	0	0.05%	0
15:	typeI	TRUE	5	FALSE	FALSE	0	0	0

7.2 Mismatch confidence intervals / boundaries

7.2.1 2 stages

When concluding for futility:

	hypo	missing	ar	binding	fixC	method 1	method 2	method 3
1:	power	TRUE	10	TRUE	FALSE	0	0	0 (NA: 0.05%)
2:	typeI	TRUE	10	TRUE	FALSE	0	0	0
3:	power	TRUE	5	TRUE	FALSE	0	0	0
4:	typeI	TRUE	5	TRUE	FALSE	0	0	0
5:	power	TRUE	10	TRUE	TRUE	0	0	0 (NA: 0.05%)
6:	typeI	TRUE	10	TRUE	TRUE	0	0	0
7:	power	TRUE	5	TRUE	TRUE	0	0	0
8:	typeI	TRUE	5	TRUE	TRUE	0	0	0
9:	power	TRUE	10	FALSE	TRUE	0 (NA: 32.62%)	0 (NA: 30.38%)	0 (NA: 31.41%)
10:	typeI	TRUE	10	FALSE	TRUE	0 (NA: 0.21%)	0 (NA: 0.19%)	0 (NA: 0.34%)
11:	power	TRUE	5	FALSE	TRUE	0 (NA: 30.64%)	0 (NA: 29.26%)	0 (NA: 30.24%)
12:	typeI	TRUE	5	FALSE	TRUE	0 (NA: 0.06%)	0 (NA: 0.06%)	0 (NA: 0.09%)
13:	power	TRUE	10	FALSE	FALSE	0 (NA: 30.41%)	0 (NA: 31.13%)	0 (NA: 31.41%)
14:	typeI	TRUE	10	FALSE	FALSE	0 (NA: 0.12%)	0 (NA: 0.12%)	0 (NA: 0.34%)
15:	power	TRUE	5	FALSE	FALSE	0 (NA: 29.09%)	0 (NA: 29.28%)	0 (NA: 30.24%)
16:	typeI	TRUE	5	FALSE	FALSE	0 (NA: 0.01%)	0 (NA: 0.01%)	0 (NA: 0.09%)
17:	power	FALSE	5	TRUE	FALSE	0	0	0
18:	typeI	FALSE	5	TRUE	FALSE	0	0	0

When concluding for efficacy:

	hypo	missing	ar	binding	fixC	method 1	method 2	method 3
1:	power	TRUE	10	TRUE	FALSE	0 (NA: 0.02%)	0 (NA: 0.02%)	0 (NA: 0.01%)
2:	typeI	TRUE	10	TRUE	FALSE	0	0	0
3:	power	TRUE	5	TRUE	FALSE	0	0	0
4:	typeI	TRUE	5	TRUE	FALSE	0	0	0
5:	power	TRUE	10	TRUE	TRUE	0 (NA: 0.02%)	0 (NA: 0.02%)	0 (NA: 0.01%)
6:	typeI	TRUE	10	TRUE	TRUE	0	0	0
7:	power	TRUE	5	TRUE	TRUE	0	0	0
8:	typeI	TRUE	5	TRUE	TRUE	0	0	0
9:	power	TRUE	10	FALSE	TRUE	0 (NA: 0.03%)	0 (NA: 0.02%)	0 (NA: 0.01%)
10:	typeI	TRUE	10	FALSE	TRUE	0	0	0
11:	power	TRUE	5	FALSE	TRUE	0 (NA: 0.01%)	0 (NA: 0.02%)	0 (NA: 0.02%)
12:	typeI	TRUE	5	FALSE	TRUE	0	0	0
13:	power	TRUE	10	FALSE	FALSE	0 (NA: 0.02%)	0 (NA: 0.02%)	0 (NA: 0.01%)
14:	typeI	TRUE	10	FALSE	FALSE	0	0	0
15:	power	TRUE	5	FALSE	FALSE	0 (NA: 0.01%)	0 (NA: 0.01%)	0 (NA: 0.02%)
16:	typeI	TRUE	5	FALSE	FALSE	0	0	0

```
17: power   FALSE  5    TRUE FALSE 0 (NA: 0.02%) 0 (NA: 0.02%) 0 (NA: 0.03%)
18: typeI   FALSE  5    TRUE FALSE             0             0             0
```

7.2.2 3 stages

When concluding for futility:

```
     hypo missing ar binding  fixC           method 1       method 2           method 3
 1: power    TRUE 10    TRUE FALSE                  0              0                  0
 2: typeI    TRUE 10    TRUE FALSE                  0              0                  0
 3: typeI    TRUE  5    TRUE FALSE                  0              0                  0
 4: power    TRUE 10    TRUE  TRUE                  0              0                  0
 5: typeI    TRUE 10    TRUE  TRUE                  0              0                  0
 6: power    TRUE  5    TRUE  TRUE                  0              0                  0
 7: typeI    TRUE  5    TRUE  TRUE                  0              0                  0
 8: power    TRUE 10   FALSE  TRUE 0.20% (NA: 21.43%) 0 (NA: 20.42%) 1.97% (NA: 18.88%)
 9: typeI    TRUE 10   FALSE  TRUE      0 (NA: 0.12%)  0 (NA: 0.08%)  0.16% (NA: 0.04%)
10: power    TRUE  5   FALSE  TRUE     0 (NA: 19.65%) 0 (NA: 20.36%) 2.51% (NA: 18.33%)
11: typeI    TRUE  5   FALSE  TRUE      0 (NA: 0.04%)  0 (NA: 0.04%)              0.04%
12: power    TRUE 10   FALSE FALSE     0 (NA: 20.39%) 0 (NA: 20.00%) 2.99% (NA: 18.51%)
13: typeI    TRUE 10   FALSE FALSE      0 (NA: 0.17%)  0 (NA: 0.12%)  0.04% (NA: 0.17%)
14: power    TRUE  5   FALSE FALSE     0 (NA: 21.54%) 0 (NA: 20.52%) 0.80% (NA: 19.61%)
15: typeI    TRUE  5   FALSE FALSE                  0              0              0.08%
```

When concluding for efficacy:

```
     hypo missing ar binding  fixC method 1 method 2 method 3
 1: power    TRUE 10    TRUE FALSE        0        0        0
 2: typeI    TRUE 10    TRUE FALSE        0        0        0
 3: typeI    TRUE  5    TRUE FALSE        0        0        0
 4: power    TRUE 10    TRUE  TRUE        0        0        0
 5: typeI    TRUE 10    TRUE  TRUE        0        0        0
 6: power    TRUE  5    TRUE  TRUE        0        0        0
 7: typeI    TRUE  5    TRUE  TRUE        0        0        0
 8: power    TRUE 10   FALSE  TRUE        0        0        0
 9: typeI    TRUE 10   FALSE  TRUE        0        0        0
10: power    TRUE  5   FALSE  TRUE        0        0        0
11: typeI    TRUE  5   FALSE  TRUE        0        0        0
12: power    TRUE 10   FALSE FALSE        0        0        0
13: typeI    TRUE 10   FALSE FALSE        0        0        0
14: power    TRUE  5   FALSE FALSE        0        0        0
15: typeI    TRUE  5   FALSE FALSE        0        0        0
```

7.3 Range of p-values

7.3.1 2 stages

	missing	binding	fixC	ar	hypo	method 1	method 2	method 3
1:	TRUE	TRUE	FALSE	10	power	[0;0.9147]	[0;0.9147]	[0;0.9147]
2:	TRUE	TRUE	FALSE	10	typeI	[1e-04;0.9999]	[1e-04;0.9999]	[1e-04;0.9999]
3:	TRUE	TRUE	FALSE	5	power	[0;0.9015]	[0;0.9015]	[0;0.9015]
4:	TRUE	TRUE	FALSE	5	typeI	[1e-04;0.9998]	[1e-04;0.9998]	[1e-04;0.9998]
5:	TRUE	TRUE	TRUE	10	power	[7e-04;0.9147]	[7e-04;0.9147]	[0;0.9147]
6:	TRUE	TRUE	TRUE	10	typeI	[0.0016;0.9999]	[0.0016;0.9999]	[1e-04;0.9999]
7:	TRUE	TRUE	TRUE	5	power	[1e-04;0.9015]	[1e-04;0.9015]	[0;0.9015]
8:	TRUE	TRUE	TRUE	5	typeI	[5e-04;0.9998]	[5e-04;0.9998]	[1e-04;0.9998]
9:	TRUE	FALSE	TRUE	10	power	[8e-04;1]	[8e-04;1]	[0;1]
10:	TRUE	FALSE	TRUE	10	typeI	[0.0015;1]	[0.0015;1]	[5e-04;1]
11:	TRUE	FALSE	TRUE	5	power	[1e-04;1]	[1e-04;1]	[0;1]
12:	TRUE	FALSE	TRUE	5	typeI	[6e-04;1]	[5e-04;1]	[2e-04;1]
13:	TRUE	FALSE	FALSE	10	power	[0;1]	[0;1]	[0;1]
14:	TRUE	FALSE	FALSE	10	typeI	[1e-04;1]	[1e-04;1]	[5e-04;1]
15:	TRUE	FALSE	FALSE	5	power	[0;1]	[0;1]	[0;1]
16:	TRUE	FALSE	FALSE	5	typeI	[0;1]	[0;1]	[2e-04;1]
17:	FALSE	TRUE	FALSE	5	power	[0;0.9642]	[0;0.9642]	[0;0.9642]
18:	FALSE	TRUE	FALSE	5	typeI	[0;1]	[0;1]	[3e-04;1]

7.3.2 3 stages

	missing	binding	fixC	ar	hypo	method 1	method 2	method 3
1:	TRUE	TRUE	FALSE	10	power	[0;0.9417]	[0;0.9417]	[0;0.9426]
2:	TRUE	TRUE	FALSE	10	typeI	[1e-04;0.9998]	[1e-04;0.9998]	[4e-04;0.9998]
3:	TRUE	TRUE	FALSE	5	typeI	[1e-04;0.9998]	[1e-04;0.9998]	[3e-04;0.9998]
4:	TRUE	TRUE	TRUE	10	power	[3e-04;0.9071]	[3e-04;0.8993]	[1e-04;0.9091]
5:	TRUE	TRUE	TRUE	10	typeI	[0.0013;0.9995]	[0.0014;0.9995]	[0.0012;0.9995]
6:	TRUE	TRUE	TRUE	5	power	[1e-04;0.8871]	[1e-04;0.8987]	[0;0.8873]
7:	TRUE	TRUE	TRUE	5	typeI	[9e-04;0.9975]	[9e-04;0.9979]	[9e-04;0.9975]
8:	TRUE	FALSE	TRUE	10	power	[3e-04;1]	[2e-04;1]	[0;1]
9:	TRUE	FALSE	TRUE	10	typeI	[8e-04;1]	[8e-04;1]	[7e-04;1]
10:	TRUE	FALSE	TRUE	5	power	[1e-04;1]	[0;1]	[0;1]
11:	TRUE	FALSE	TRUE	5	typeI	[0.0012;1]	[0.0012;1]	[0.0012;1]
12:	TRUE	FALSE	FALSE	10	power	[0;1]	[0;1]	[0;1]
13:	TRUE	FALSE	FALSE	10	typeI	[7e-04;1]	[7e-04;1]	[8e-04;1]
14:	TRUE	FALSE	FALSE	5	power	[0;1]	[0;1]	[0;1]
15:	TRUE	FALSE	FALSE	5	typeI	[1e-04;0.9999]	[1e-04;0.9998]	[1e-04;0.9999]

8 Coverage

8.1 2 stages

	hypo	missing	ar	binding	fixC	method 1	method 2	method 3
1:	power	FALSE	5	TRUE	FALSE	94.79000	94.79000	94.92000
2:	power	TRUE	5	FALSE	FALSE	95.86382	95.86207	95.66505
3:	power	TRUE	5	FALSE	TRUE	96.30458	96.26486	95.66505
4:	power	TRUE	5	TRUE	FALSE	94.74000	94.74000	94.87000
5:	power	TRUE	5	TRUE	TRUE	95.08000	95.08000	94.87000
6:	power	TRUE	10	FALSE	FALSE	95.98172	96.04941	95.75968
7:	power	TRUE	10	FALSE	TRUE	96.79139	96.75297	95.75968
8:	power	TRUE	10	TRUE	FALSE	94.84000	94.82000	95.12000
9:	power	TRUE	10	TRUE	TRUE	95.73000	95.65000	95.12000
10:	typeI	FALSE	5	TRUE	FALSE	95.14000	95.14000	95.15000
11:	typeI	TRUE	5	FALSE	FALSE	94.86949	94.86949	95.39954
12:	typeI	TRUE	5	FALSE	TRUE	94.91695	94.90745	95.39954
13:	typeI	TRUE	5	TRUE	FALSE	94.82000	94.82000	94.87000
14:	typeI	TRUE	5	TRUE	TRUE	94.90000	94.91000	94.87000
15:	typeI	TRUE	10	FALSE	FALSE	95.01402	95.01402	96.04407
16:	typeI	TRUE	10	FALSE	TRUE	95.09116	95.07162	96.04407
17:	typeI	TRUE	10	TRUE	FALSE	95.16000	95.19000	95.21000
18:	typeI	TRUE	10	TRUE	TRUE	95.34000	95.36000	95.21000

Average width of the confidence intervals

	hypo	missing	ar	binding	fixC	method 1	method 2	method 3
1:	power	FALSE	5	TRUE	FALSE	1.0517981	1.0518066	1.053592
2:	power	TRUE	5	FALSE	FALSE	1.0355785	1.0355525	1.030753
3:	power	TRUE	5	FALSE	TRUE	1.0410966	1.0414270	1.030753
4:	power	TRUE	5	TRUE	FALSE	1.0513207	1.0513607	1.052634
5:	power	TRUE	5	TRUE	TRUE	1.0570088	1.0563598	1.052629
6:	power	TRUE	10	FALSE	FALSE	1.0469276	1.0468858	1.039428
7:	power	TRUE	10	FALSE	TRUE	1.0634581	1.0625586	1.039438
8:	power	TRUE	10	TRUE	FALSE	1.0624494	1.0626858	1.062576
9:	power	TRUE	10	TRUE	TRUE	1.0765867	1.0753692	1.062555
10:	typeI	FALSE	5	TRUE	FALSE	1.0431774	1.0431218	1.046821
11:	typeI	TRUE	5	FALSE	FALSE	0.9997886	0.9998440	1.018905
12:	typeI	TRUE	5	FALSE	TRUE	0.9996979	0.9996859	1.018905
13:	typeI	TRUE	5	TRUE	FALSE	1.0416221	1.0415882	1.045180
14:	typeI	TRUE	5	TRUE	TRUE	1.0416986	1.0423673	1.045180
15:	typeI	TRUE	10	FALSE	FALSE	1.0182710	1.0227130	1.049875
16:	typeI	TRUE	10	FALSE	TRUE	1.0183637	1.0101640	1.049882
17:	typeI	TRUE	10	TRUE	FALSE	1.0459447	1.0453954	1.056218
18:	typeI	TRUE	10	TRUE	TRUE	1.0461003	1.0478314	1.056215

Average ratio between the length of the MUE CIs vs. the ML CIs

	hypo	missing	ar	binding	fixC	method 1	method 2	method 3
1:	power	FALSE	5	TRUE	FALSE	1.0554164	1.0554324	1.057018
2:	power	TRUE	5	FALSE	FALSE	1.0477000	1.0477317	1.043003
3:	power	TRUE	5	FALSE	TRUE	1.0532445	1.0529897	1.043003
4:	power	TRUE	5	TRUE	FALSE	1.0556658	1.0557135	1.056796
5:	power	TRUE	5	TRUE	TRUE	1.0607293	1.0599867	1.056792
6:	power	TRUE	10	FALSE	FALSE	1.0539283	1.0540501	1.045799
7:	power	TRUE	10	FALSE	TRUE	1.0695786	1.0683330	1.045809
8:	power	TRUE	10	TRUE	FALSE	1.0641965	1.0644562	1.064036
9:	power	TRUE	10	TRUE	TRUE	1.0773006	1.0760174	1.064016
10:	typeI	FALSE	5	TRUE	FALSE	1.0496649	1.0496083	1.053799
11:	typeI	TRUE	5	FALSE	FALSE	0.9997633	0.9998237	1.019473
12:	typeI	TRUE	5	FALSE	TRUE	0.9998075	0.9997468	1.019473
13:	typeI	TRUE	5	TRUE	FALSE	1.0486330	1.0486034	1.052752
14:	typeI	TRUE	5	TRUE	TRUE	1.0487063	1.0493717	1.052752
15:	typeI	TRUE	10	FALSE	FALSE	1.0194380	1.0240187	1.051009
16:	typeI	TRUE	10	FALSE	TRUE	1.0196328	1.0111242	1.051015
17:	typeI	TRUE	10	TRUE	FALSE	1.0497075	1.0491459	1.060913
18:	typeI	TRUE	10	TRUE	TRUE	1.0498579	1.0516113	1.060910

9 Percentage of missing values

At the first interim

- `pc.all` percentage of observations with full data (with respect to all observations, i.e. patients with baseline measurement)
- `pc.missing3` percentage of observations missing the final outcome but with intermediate outcome value and baseline.
- `pc.missing23` percentage of observations with only baseline value

Here only for method 1 - values are very similar between different methods:

	method	missing	ar	hypo	fixC	binding	N	pc.all	pc.missing3	pc.missing23
1:	1	TRUE	5	power	FALSE	TRUE	10000	79.52088	9.591086	10.888036
2:	1	TRUE	5	typeI	FALSE	TRUE	10000	79.52088	9.591086	10.888036
3:	1	TRUE	5	power	TRUE	TRUE	10000	79.52088	9.591086	10.888036
4:	1	TRUE	5	typeI	TRUE	TRUE	10000	79.52088	9.591086	10.888036
5:	1	TRUE	5	power	TRUE	FALSE	10000	79.64470	9.441772	10.913523
6:	1	TRUE	5	typeI	TRUE	FALSE	10000	79.64470	9.441772	10.913523
7:	1	TRUE	5	power	FALSE	FALSE	10000	79.64470	9.441772	10.913523
8:	1	TRUE	5	typeI	FALSE	FALSE	10000	79.64470	9.441772	10.913523
9:	1	FALSE	5	power	FALSE	TRUE	10000	87.78863	6.090240	6.121126
10:	1	FALSE	5	typeI	FALSE	TRUE	10000	87.78863	6.090240	6.121126
11:	1	TRUE	10	power	FALSE	TRUE	10000	71.59741	13.353880	15.048710
12:	1	TRUE	10	typeI	FALSE	TRUE	10000	71.59741	13.353880	15.048710
13:	1	TRUE	10	power	TRUE	TRUE	10000	71.59741	13.353880	15.048710
14:	1	TRUE	10	typeI	TRUE	TRUE	10000	71.59741	13.353880	15.048710
15:	1	TRUE	10	power	TRUE	FALSE	10000	71.79650	13.161615	15.041889
16:	1	TRUE	10	typeI	TRUE	FALSE	10000	71.79650	13.161615	15.041889
17:	1	TRUE	10	power	FALSE	FALSE	10000	71.79650	13.161615	15.041889
18:	1	TRUE	10	typeI	FALSE	FALSE	10000	71.79650	13.161615	15.041889

10 Information

Percentage of information for method 1[5]:

scenario	missing	binding	fixC	ar	interim	decision	final
1	TRUE	TRUE	FALSE	10	54.63712	75.34460	102.69691
2	TRUE	TRUE	FALSE	10	54.63712	74.98217	102.36588
3	TRUE	TRUE	FALSE	5	53.26864	64.03618	102.73604
4	TRUE	TRUE	FALSE	5	53.26864	63.58436	102.37416
5	TRUE	TRUE	TRUE	10	54.63712	75.34460	102.69691
6	TRUE	TRUE	TRUE	10	54.63712	74.98217	102.36588
7	TRUE	TRUE	TRUE	5	53.26864	64.03618	102.73604
8	TRUE	TRUE	TRUE	5	53.26864	63.58436	102.37416
9	TRUE	FALSE	TRUE	10	54.50012	74.96442	102.53821
10	TRUE	FALSE	TRUE	10	54.50012	75.17490	103.12700
11	TRUE	FALSE	TRUE	5	53.15854	63.71662	102.62539
12	TRUE	FALSE	TRUE	5	53.15854	64.60960	103.12516
13	TRUE	FALSE	FALSE	10	54.50012	74.96442	102.53821
14	TRUE	FALSE	FALSE	10	54.50012	75.17490	103.12700
15	TRUE	FALSE	FALSE	5	53.15854	63.71662	102.62539
16	TRUE	FALSE	FALSE	5	53.15854	64.60960	103.12516
17	FALSE	TRUE	FALSE	5	52.06840	63.77019	99.96969
18	FALSE	TRUE	FALSE	5	52.06840	63.21929	99.62860

Similar results for other methods.

[5] average over the reached stages