Results simulation study DelayedGSD

August 10, 2023

1 Rejection rate

Power by r	nethod	l (column	s) and so	enario	(ro	ws):	(n	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 l	oy metho	d (colum	ns) and	d sc	cenario (ro	ws): (n	ominal 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

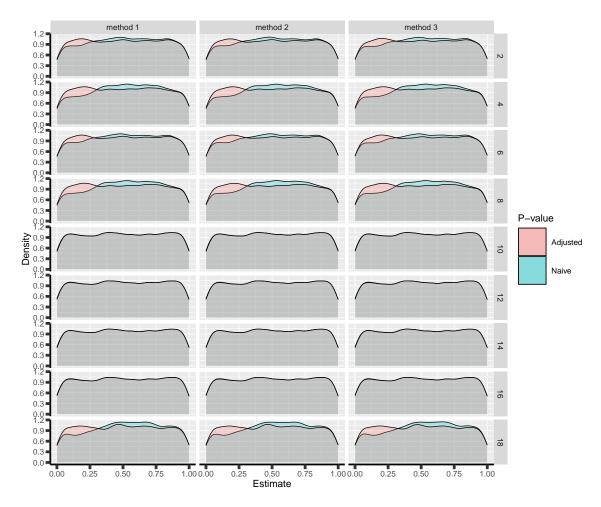


Figure 1: Naive and adjusted p-value distribution over all simulations under the null. Each row correspond to a different scenario

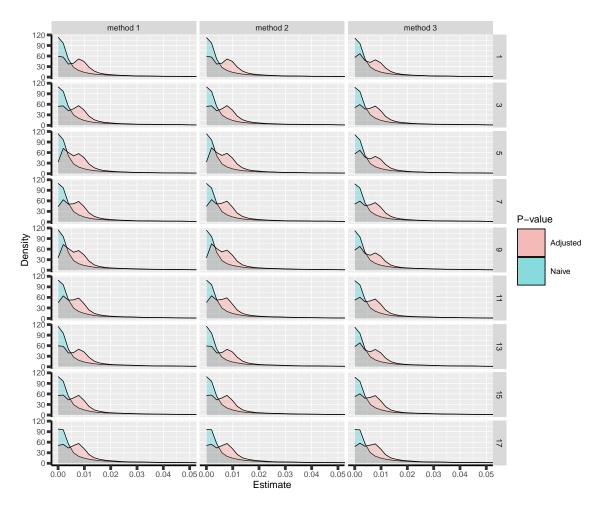


Figure 2: Naive and adjusted p-value distribution over all simulations under the alternative. Each row correspond to a different scenario

2 Conclusion of the trial

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

• Method 1

	N	${\tt missing}$	hypo	${\tt binding}$	fixC	ar	decision.eff	decision.fut	final.eff	final.fut
1:	10000	TRUE	power	TRUE	FALSE	10	37.79	5.93	43.21	13.1
2:	10000	TRUE	typeI	TRUE	FALSE	10	0.80	71.13	1.62	26.5
3:	10000	TRUE	power	TRUE	FALSE	5	35.74	5.98	44.79	13.5
4:	10000	TRUE	typeI	TRUE	FALSE	5	0.74	69.32	1.66	28.3
5:	10000	TRUE	power	TRUE	TRUE	10	36.94	6.78	43.21	13.1
6:	10000	TRUE	typeI	TRUE	TRUE	10	0.62	71.31	1.62	26.5
7:	10000	TRUE	power	TRUE	TRUE	5	35.29	6.43	44.79	13.5
8:	10000	TRUE	typeI	TRUE	TRUE	5	0.66	69.40	1.66	28.3
9:	10000	TRUE	power	FALSE	TRUE	10	38.05	6.57	41.81	13.6
10:	10000	TRUE	typeI	FALSE	TRUE	10	0.61	0.20	1.84	97.4
11:	10000	TRUE	power	FALSE	TRUE	5	36.35	6.15	43.58	13.9
12:	10000	TRUE	typeI	FALSE	TRUE	5	0.70	0.06	1.93	97.3
13:	10000	TRUE	power	FALSE	FALSE	10	38.69	5.93	41.81	13.6
14:	10000	TRUE	typeI	FALSE	FALSE	10	0.69	0.12	1.84	97.4
15:	10000	TRUE	power	FALSE	FALSE	5	36.79	5.71	43.58	13.9
16:	10000	TRUE	typeI	FALSE	FALSE	5	0.75	0.01	1.93	97.3
17:	10000	FALSE	power	TRUE	FALSE	5	33.98	5.33	46.33	14.4
18:	10000	FALSE	typeI	TRUE	FALSE	5	0.74	67.48	1.72	30.1

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	12.9
2:	10000	TRUE	typeI	TRUE	FALSE	10	0.79	71.64	1.60	26.0
3:	10000	TRUE	power	TRUE	FALSE	5	35.77	5.99	44.76	13.5
4:	10000	TRUE	typeI	TRUE	FALSE	5	0.74	69.38	1.66	28.2
5:	10000	TRUE	power	TRUE	TRUE	10	36.69	6.24	43.66	13.4
6:	10000	TRUE	typeI	TRUE	TRUE	10	0.59	69.61	1.63	28.2
7:	10000	TRUE	power	TRUE	TRUE	5	35.02	6.05	45.18	13.8
8:	10000	TRUE	typeI	TRUE	TRUE	5	0.63	68.36	1.68	29.3
9:	10000	TRUE	power	FALSE	TRUE	10	37.85	6.04	42.27	13.8
10:	10000	TRUE	typeI	FALSE	TRUE	10	0.61	0.19	1.86	97.3
11:	10000	TRUE	power	FALSE	TRUE	5	36.18	5.84	43.86	14.1
12:	10000	TRUE	typeI	FALSE	TRUE	5	0.69	0.06	1.95	97.3
13:	10000	TRUE	power	FALSE	FALSE	10	38.70	6.09	41.74	13.5
14:	10000	TRUE	typeI	FALSE	FALSE	10	0.69	0.12	1.84	97.4
15:	10000	TRUE	power	FALSE	FALSE	5	36.82	5.75	43.54	13.9
16:	10000	TRUE	typeI	FALSE	FALSE	5	0.75	0.01	1.93	97.3
17:	10000	FALSE	power	TRUE	FALSE	5	34.03	5.36	46.27	14.3
18:	10000	FALSE	typeI	TRUE	FALSE	5	0.74	67.55	1.72	30.0

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	13.0
2:	10000	TRUE	typeI	TRUE	FALSE	10	0.74	68.79	1.63	28.8
3:	10000	TRUE	power	TRUE	FALSE	5	36.54	6.30	43.60	13.6
4:	10000	TRUE	typeI	TRUE	FALSE	5	0.69	68.41	1.66	29.2
5:	10000	TRUE	power	TRUE	TRUE	10	40.58	6.53	39.85	13.0
6:	10000	TRUE	typeI	TRUE	TRUE	10	0.74	68.79	1.63	28.8
7:	10000	TRUE	power	TRUE	TRUE	5	36.54	6.30	43.60	13.6
8:	10000	TRUE	typeI	TRUE	TRUE	5	0.69	68.41	1.66	29.2
9:	10000	TRUE	power	FALSE	TRUE	10	41.34	6.20	38.92	13.5
10:	10000	TRUE	typeI	FALSE	TRUE	10	0.77	0.33	1.80	97.1
11:	10000	TRUE	power	FALSE	TRUE	5	37.71	6.03	42.35	13.9
12:	10000	TRUE	typeI	FALSE	TRUE	5	0.73	0.09	1.93	97.2
13:	10000	TRUE	power	FALSE	FALSE	10	41.34	6.20	38.92	13.5
14:	10000	TRUE	typeI	FALSE	FALSE	10	0.77	0.33	1.80	97.1
15:	10000	TRUE	power	FALSE	FALSE	5	37.71	6.03	42.35	13.9
16:	10000	TRUE	typeI	FALSE	FALSE	5	0.73	0.09	1.93	97.2
17:	10000	FALSE	power	TRUE	FALSE	5	34.65	5.59	45.27	14.5
18:	10000	FALSE	typeI	TRUE	FALSE	5	0.68	66.54	1.77	31.0

3 Bias (True effect: 0.6 under the alternative)

Bias per estimator and method¹:

```
biasMLE1
     hypo missing binding fixC ar
                                               biasMLE2
                                                          biasMLE3
                                                                    biasMUE1
                                                                               biasMUE2 biasMUE3
 1: power
             TRUE
                     TRUE FALSE 10
                                     0.013450
                                               0.013150
                                                          0.014680
                                                                    0.005983
                                                                               0.005659
                                                                                         0.00218
 2: typeI
             TRUE
                     TRUE FALSE 10 -0.017939 -0.017844 -0.018560 -0.004484 -0.004412 -0.00508
 3: power
             TRUE
                     TRUE FALSE
                                  5
                                     0.022570
                                               0.022551
                                                          0.023584
                                                                    0.010450
                                                                              0.010477
                                                                                         0.00870
 4: typeI
                     TRUE FALSE
                                  5 -0.030342 -0.030312 -0.030651 -0.011844 -0.011798 -0.01238
             TRUE
                                                          0.014680
                                                                   0.001094 0.001687
 5: power
             TRUE
                     TRUE
                           TRUE 10
                                    0.013450 0.014032
                                                                                         0.00217
 6: typeI
             TRUE
                     TRUE
                           TRUE 10 -0.017939 -0.018711 -0.018560 -0.005373 -0.006062 -0.00508
7: power
             TRUE
                     TRUE
                           TRUE
                                  5
                                     0.022570 0.023089
                                                          0.023584
                                                                    0.007878
                                                                              0.008275
                                                                                         0.00870
                           TRUE
                                  5 -0.030342 -0.030850 -0.030651 -0.012252 -0.012829 -0.01238
 8: typeI
             TRUE
                     TRUE
 9: power
             TRUE
                    FALSE
                           TRUE 10
                                     0.014326
                                               0.014903
                                                          0.015285
                                                                    0.037532
                                                                              0.035615
                                                                                         0.03135
10: typeI
             TRUE
                    FALSE
                           TRUE 10
                                     0.000186
                                               0.000192
                                                          0.000511
                                                                    0.000991
                                                                               0.000981
                                                                                         0.00263
11: power
             TRUE
                    FALSE
                           TRUE
                                     0.023657
                                               0.024021
                                                          0.024379
                                                                    0.042787
                                  5
                                                                               0.041614
                                                                                         0.04039
                           TRUE
                                     0.000912
12: typeI
             TRUE
                    FALSE
                                 5
                                               0.000853
                                                          0.001008
                                                                    0.001112
                                                                              0.001062
                                                                                         0.00136
             TRUE
                    FALSE FALSE 10
                                                          0.015285
                                                                    0.036631
13: power
                                     0.014326
                                               0.014160
                                                                              0.037167
                                                                                         0.03139
                    FALSE FALSE 10
                                     0.000186
14: typeI
             TRUE
                                               0.000186
                                                          0.000511
                                                                    0.000793
                                                                               0.000783
                                                                                         0.00264
                    FALSE FALSE
                                     0.023657
                                               0.023651
                                                          0.024379
15: power
             TRUE
                                  5
                                                                    0.041744
                                                                               0.041949
                                                                                         0.04040
16: typeI
                                  5
                                     0.000912
                                                          0.001008
             TRUE
                    FALSE FALSE
                                               0.000912
                                                                    0.000964
                                                                               0.000962
                                                                                         0.00137
                                  5
                                     0.022836
                                               0.022775
                                                          0.023807
17: power
            FALSE
                     TRUE FALSE
                                                                    0.011971
                                                                               0.011956
                                                                                         0.01001
18: typeI
            FALSE
                     TRUE FALSE
                                  5 -0.029516 -0.029448 -0.029915 -0.011048 -0.011005 -0.01162
```

Median bias ² per estimator and method:

		1								
hypo	missing	${\tt binding}$	fixC	ar	${\tt mbiasMLE1}$	${\tt mbiasMLE2}$	${\tt mbiasMLE3}$	${\tt mbias MUE1}$	${\tt mbias MUE2}$	mbiasMUE3
power	TRUE	TRUE	FALSE	10	0.0261	0.0260	0.0301	-0.0024	-0.0025	-0.0054
typeI	TRUE	TRUE	FALSE	10	-0.0173	-0.0170	-0.0202	0.0011	0.0009	-0.0001
power	TRUE	TRUE	FALSE	5	0.0405	0.0405	0.0432	-0.0034	-0.0033	-0.0053
typeI	TRUE	TRUE	FALSE	5	-0.0330	-0.0329	-0.0345	0.0007	0.0007	0.0008
power	TRUE	TRUE	TRUE	10	0.0261	0.0265	0.0301	-0.0105	-0.0101	-0.0054
typeI	TRUE	TRUE	TRUE	10	-0.0173	-0.0197	-0.0202	0.0011	-0.0006	-0.0001
power	TRUE	TRUE	TRUE	5	0.0405	0.0407	0.0432	-0.0077	-0.0065	-0.0053
typeI	TRUE	TRUE	TRUE	5	-0.0330	-0.0346	-0.0345	0.0007	0.0009	0.0008
power	TRUE	FALSE	TRUE	10	0.0326	0.0332	0.0327	0.0390	0.0345	0.0277
typeI	TRUE	FALSE	TRUE	10	-0.0009	-0.0009	-0.0009	-0.0008	-0.0008	0.0014
power	TRUE	FALSE	TRUE	5	0.0462	0.0459	0.0489	0.0338	0.0315	0.0294
typeI	TRUE	FALSE	TRUE	5	-0.0009	-0.0010	-0.0009	-0.0008	-0.0010	0.0003
power	TRUE	FALSE	FALSE	10	0.0326	0.0324	0.0327	0.0390	0.0403	0.0277
typeI	TRUE	FALSE	FALSE	10	-0.0009	-0.0009	-0.0009	-0.0008	-0.0008	0.0014
power	TRUE	FALSE	FALSE	5	0.0462	0.0464	0.0489	0.0337	0.0342	0.0294
typeI	TRUE	FALSE	FALSE	5	-0.0009	-0.0009	-0.0009	-0.0008	-0.0008	0.0003
power	FALSE	TRUE	FALSE	5	0.0383	0.0383	0.0400	-0.0026	-0.0025	-0.0047
typeI	FALSE	TRUE	FALSE	5	-0.0329	-0.0327	-0.0353	0.0044	0.0044	0.0035
	power typeI power	power TRUE typeI TRUE TRUE power TRUE typeI TRUE power TRUE	power TRUE TRUE typeI TRUE TRUE power TRUE TRUE typeI TRUE TRUE power TRUE TRUE typeI TRUE TRUE typeI TRUE TRUE power TRUE TRUE typeI TRUE TRUE typeI TRUE FALSE power TRUE FALSE typeI TRUE FALSE power TRUE FALSE	power TRUE TRUE FALSE typeI TRUE TRUE FALSE power TRUE TRUE FALSE typeI TRUE TRUE FALSE typeI TRUE TRUE TRUE FALSE power TRUE TRUE TRUE typeI TRUE TRUE TRUE power TRUE TRUE TRUE typeI TRUE TRUE TRUE typeI TRUE FALSE TRUE typeI TRUE FALSE TRUE typeI TRUE FALSE TRUE typeI TRUE FALSE TRUE power TRUE FALSE TRUE typeI TRUE FALSE TRUE typeI TRUE FALSE FALSE typeI TRUE FALSE FALSE typeI TRUE FALSE FALSE typeI TRUE FALSE FALSE power TRUE FALSE FALSE typeI TRUE FALSE FALSE typeI TRUE FALSE FALSE	power TRUE TRUE FALSE 10 typeI TRUE TRUE FALSE 10 power TRUE TRUE FALSE 5 typeI TRUE TRUE FALSE 5 power TRUE TRUE TRUE 10 typeI TRUE TRUE TRUE 10 power TRUE TRUE TRUE 5 typeI TRUE TRUE TRUE 5 typeI TRUE TRUE TRUE 5 power TRUE FALSE TRUE 10 typeI TRUE FALSE TRUE 10 power TRUE FALSE TRUE 5 typeI TRUE FALSE TRUE 5 typeI TRUE FALSE TRUE 5 typeI TRUE FALSE FALSE 10 power TRUE FALSE FALSE 10 power TRUE FALSE FALSE 5 typeI TRUE FALSE FALSE 5 typeI TRUE FALSE FALSE 5	power TRUE TRUE FALSE 10 0.0261 typeI TRUE TRUE FALSE 10 -0.0173 power TRUE TRUE FALSE 5 0.0405 typeI TRUE TRUE FALSE 5 -0.0330 power TRUE TRUE TRUE 10 0.0261 typeI TRUE TRUE TRUE 10 -0.0173 power TRUE TRUE TRUE 5 0.0405 typeI TRUE TRUE TRUE 5 -0.0330 power TRUE FALSE TRUE 10 -0.0326 typeI TRUE FALSE TRUE 10 -0.0009 power TRUE FALSE TRUE 5 -0.0009 power TRUE FALSE FALSE 10 -0.0009 power TRUE FALSE FALSE 5 0.0462 typeI TRUE FALSE FALSE 5 -0.0009 power TRUE FALSE FALSE 5 -0.0009 power TRUE FALSE FALSE 5 -0.0009	power TRUE TRUE FALSE 10 0.0261 0.0260 typeI TRUE TRUE FALSE 10 -0.0173 -0.0170 power TRUE TRUE FALSE 5 0.0405 0.0405 typeI TRUE TRUE FALSE 5 -0.0330 -0.0329 power TRUE TRUE TRUE 10 0.0261 0.0265 typeI TRUE TRUE TRUE 10 -0.0173 -0.0197 power TRUE TRUE TRUE 5 0.0405 0.0407 typeI TRUE TRUE TRUE 5 -0.0330 -0.0197 power TRUE FALSE TRUE 5 -0.0330 -0.0346 power TRUE FALSE TRUE 10 -0.0326 0.0332 typeI TRUE FALSE TRUE 5 -0.0009 -0.0010 power TRUE FALSE FALSE	power TRUE TRUE FALSE 10 0.0261 0.0260 0.0301 typeI TRUE TRUE FALSE 10 -0.0173 -0.0170 -0.0202 power TRUE TRUE FALSE 5 0.0405 0.0405 0.0432 typeI TRUE TRUE FALSE 5 -0.0330 -0.0329 -0.0345 power TRUE TRUE TRUE 10 0.0261 0.0265 0.0301 typeI TRUE TRUE TRUE 10 -0.0173 -0.0197 -0.0202 power TRUE TRUE TRUE 5 0.0405 0.0407 0.0432 typeI TRUE TRUE 5 -0.0330 -0.0346 -0.0345 power TRUE FALSE TRUE 10 -0.0326 0.0332 0.0327 typeI TRUE FALSE TRUE 5 -0.0009 -0.0009 -0.0009 power TRUE<	power TRUE TRUE FALSE 10 0.0261 0.0260 0.0301 -0.0024 typeI TRUE TRUE FALSE 10 -0.0173 -0.0170 -0.0202 0.0011 power TRUE TRUE FALSE 5 0.0405 0.0405 0.0432 -0.0034 typeI TRUE TRUE FALSE 5 -0.0330 -0.0329 -0.0345 0.0007 power TRUE TRUE TRUE 10 0.0261 0.0265 0.0301 -0.0105 typeI TRUE TRUE TRUE 10 -0.0173 -0.0197 -0.0202 0.0011 power TRUE TRUE TRUE 5 0.0405 0.0407 0.0432 -0.0077 typeI TRUE TRUE TRUE 5 -0.0330 -0.0346 -0.0345 0.0007 power TRUE FALSE TRUE 10 -0.0326 0.0332 0.0327 0.0390	typeI TRUE TRUE FALSE 10 -0.0173 -0.0170 -0.0202 0.0011 0.0009 power TRUE TRUE FALSE 5 0.0405 0.0405 0.0432 -0.0034 -0.0033 typeI TRUE TRUE FALSE 5 -0.0330 -0.0329 -0.0345 0.0007 0.0007 power TRUE TRUE TRUE 10 -0.0261 0.0265 0.0301 -0.0105 -0.0101 typeI TRUE TRUE TRUE 10 -0.0173 -0.0197 -0.0202 0.0011 -0.0006 power TRUE TRUE TRUE 5 0.0405 0.0407 0.0432 -0.0077 -0.0065 typeI TRUE TRUE TRUE 5 -0.0330 -0.0346 -0.0345 0.0007 0.0009 power TRUE FALSE TRUE 10 -0.0326 0.0332 0.0327 0.0390 0.0345 typeI TRUE FALSE TRUE 5 -0.0009 -0.0009 -0.0009 -0.0009

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

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

4 Distribution of the estimates

Distribution of the estimates:

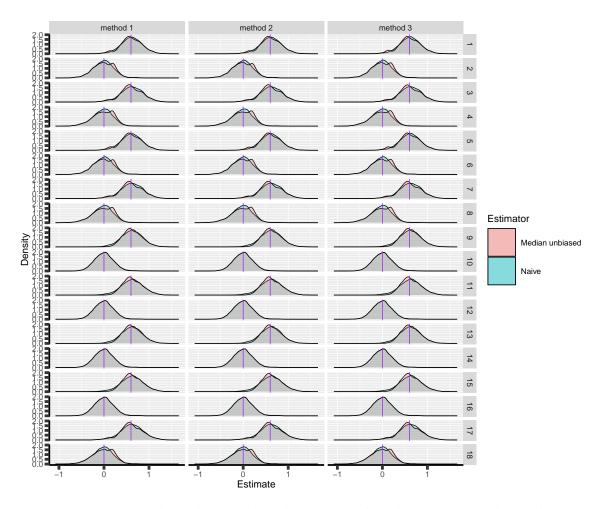


Figure 3: Naive and Median unbiased estimate distribution over all simulations. Each row correspond to a different scenario

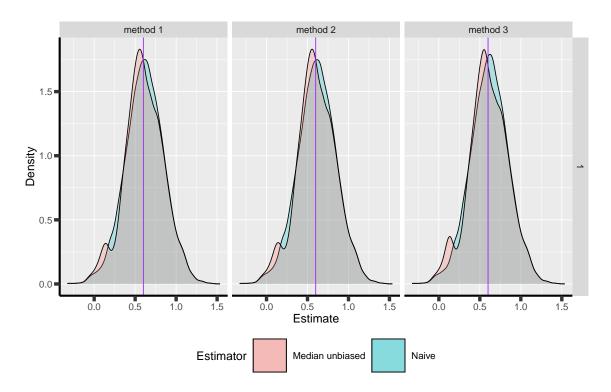


Figure 4: Same but specific to scenario 1

Distribution of the median unbiased estimate conditional to the stage:

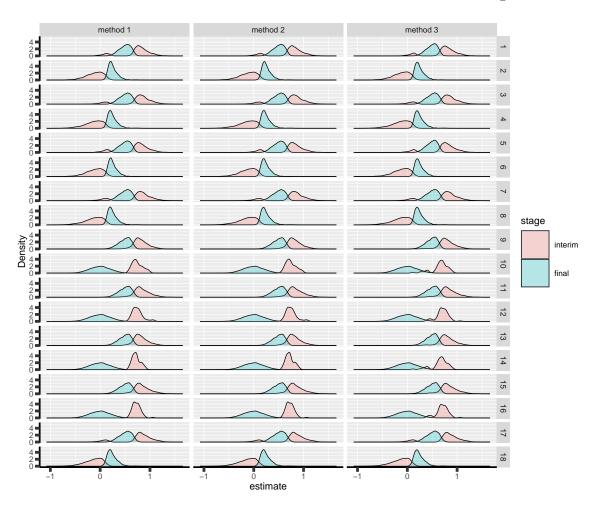


Figure 5: Median unbiased estimate distribution conditional to the stage. Each row correspond to a different scenario.

5 Special cases

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
reason	method										
efficacy	1		3849	81	3680	76	3849	81	3680	76	3396
	2		3829	80	3661	75	3850	81	3683	76	3400
	3		4238	110	3831	82	4238	110	3831	82	3528
futility	1		613	7122	570	6945	613	7122	570	6945	535 6
	2		560	6975	541	6838	629	7164	574	6950	539 6
	3		516	6890	543	6842	516	6890	543	6842	496 6
no boundary crossed	1		5538	2797	5750	2979	5538	2797	5750	2979	6069 3
	2		5611	2945	5798	3087	5521	2755	5743	2974	6061 3
	3		5246	3000	5626	3076	5246	3000	5626	3076	5976 3
stop for futility at interim	1		0	0	0	0	0	0	0	0	0
-	2		0	0	0	0	0	0	0	0	0
	3		8	0	0	0	8	0	0	0	1

6 Reversal probability

Percentage of time we observe a reversal:

	N	hypo	missing	ar	binding	fixC	$fu2eff_1$	${\tt fu2eff_2}$	${\tt fu2eff_3}$	${\tt eff2fu_1}$	${\tt eff2fu_2}$	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	0.00	0.00	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	0.00	0.00	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	0.00	0.00	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	0.00	0.00	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	0.00	0.00	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

7 Logical consistency of p-values/CIs

7.1 Mismatch p-value / boundaries

When concluding for futility:

	hypo	missing	ar	binding	fixC	${\tt method}$	1	${\tt method}$	2	${\tt method}$	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	${\tt method}$	2	${\tt method}$	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

7.2 Mismatch confidence intervals / boundaries

When concluding for futility:

```
hypo missing ar binding fixC method 1 method 2 method 3
             TRUE 10
                        TRUE FALSE
                                          0
                                                   0 0.0000000
 1: power
 2: typeI
             TRUE 10
                        TRUE FALSE
                                          0
                                                   0 0.0000000
3: power
             TRUE 5
                        TRUE FALSE
                                          0
                                                   0 0.0000000
4: typeI
             TRUE 5
                        TRUE FALSE
                                          0
                                                   0 0.0000000
5: power
             TRUE 10
                        TRUE
                             TRUE
                                          0
                                                   0 0.000000
6: typeI
             TRUE 10
                        TRUE TRUE
                                          0
                                                   0 0.0000000
7: power
             TRUE 5
                        TRUE TRUE
                                          0
                                                   0 0.0000000
8: typeI
            TRUE 5
                        TRUE
                             TRUE
                                          0
                                                   0 0.0000000
9: power
            TRUE 10
                       FALSE TRUE
                                          0
                                                   0 7.8484438
10: typeI
             TRUE 10
                       FALSE
                             TRUE
                                          0
                                                   0 0.1747533
11: power
             TRUE 5
                       FALSE TRUE
                                          0
                                                   0 4.1322314
12: typeI
             TRUE 5
                       FALSE TRUE
                                          0
                                                   0 0.0821946
13: power
             TRUE 10
                       FALSE FALSE
                                          0
                                                   0 7.8484438
14: typeI
             TRUE 10
                       FALSE FALSE
                                          0
                                                   0 0.1747533
15: power
             TRUE 5
                       FALSE FALSE
                                          0
                                                   0 4.1322314
16: typeI
             TRUE 5
                       FALSE FALSE
                                          0
                                                   0 0.0821946
17: power
           FALSE 5
                        TRUE FALSE
                                          0
                                                   0 0.0000000
18: typeI
           FALSE 5
                        TRUE FALSE
                                          0
                                                   0 0.0000000
```

This only occurs for non-binding futility rules and concluding futility, e.g.: $\#+END_{SRC}$ When concluding for efficacy:

	hypo	missing	ar	binding	fixC	${\tt method}$	1	${\tt method}$	2	${\tt method}$	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

7.3 Range of p-values

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

8 Coverage

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
                      TRUE FALSE 1.0513207 1.0513607 1.052634
4: power
           TRUE 5
5: power
                      TRUE TRUE 1.0570088 1.0563598 1.052629
           TRUE 5
```

```
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
                              TRUE 1.0765867 1.0753692 1.062555
 9: power
             TRUE 10
10: typeI
            FALSE 5
                        TRUE FALSE 1.0431774 1.0431218 1.046821
             TRUE 5
                       FALSE FALSE 0.9997886 0.9998440 1.018905
11: typeI
12: typeI
             TRUE
                              TRUE 0.9996979 0.9996859 1.018905
13: typeI
             TRUE 5
                        TRUE FALSE 1.0416221 1.0415882 1.045180
14: typeI
             TRUE 5
                              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
                        TRUE TRUE 1.0461003 1.0478314 1.056215
18: typeI
             TRUE 10
```

9 Percentage of missing values

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

- pc.all percentage of observations with full data
- 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

```
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
                    5 typeI FALSE
 2:
         1
              TRUE
                                      TRUE 10000 79.52088
                                                              9.591086
                                                                           10.888036
         1
 3:
              TRUE 5 power
                                      TRUE 10000 79.52088
                              TRUE
                                                              9.591086
                                                                           10.888036
         1
                                      TRUE 10000 79.52088
 4:
              TRUE 5 typeI
                              TRUE
                                                              9.591086
                                                                           10.888036
 5:
         1
              TRUE 5 power
                              TRUE
                                     FALSE 10000 79.64470
                                                              9.441772
                                                                           10.913523
         1
              TRUE 5 typeI
                                     FALSE 10000 79.64470
                                                              9.441772
 6:
                              TRUE
                                                                           10.913523
7:
         1
              TRUE 5 power FALSE
                                     FALSE 10000 79.64470
                                                              9.441772
                                                                           10.913523
         1
 8:
              TRUE 5 typeI FALSE
                                     FALSE 10000 79.64470
                                                              9.441772
                                                                           10.913523
         1
                                      TRUE 10000 87.78863
9:
             FALSE 5 power FALSE
                                                              6.090240
                                                                            6.121126
10:
         1
             FALSE 5 typeI FALSE
                                      TRUE 10000 87.78863
                                                              6.090240
                                                                            6.121126
         1
11:
              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
         1
14:
              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
         1
              TRUE 10 typeI
16:
                              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 1^3 :

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

Similar results for other methods.

³average over the reached stages