# Results simulation study DelayedGSD

February 21, 2023

### 1 Rejection rate

Power by method (columns) and scenario (rows): (nominal level											
scenario	N	missing	binding	fixC	ar	method 1	method 2	method 3			
1	10000	TRUE	TRUE	FALSE	10	81.00	80.79	80.45			
3	10000	TRUE	TRUE	FALSE	5	80.60	80.45	80.21			
5	10000	TRUE	TRUE	TRUE	10	79.81	80.41	80.39			
7	10000	TRUE	TRUE	TRUE	5	80.00	80.46	80.08			
9	10000	TRUE	FALSE	TRUE	10	80.50	80.85	80.91			
11	10000	TRUE	FALSE	TRUE	5	80.73	80.82	80.75			
13	10000	TRUE	FALSE	FALSE	10	80.67	80.60	80.65			
15	10000	TRUE	FALSE	FALSE	5	80.65	80.64	80.46			
17	10000	FALSE	TRUE	FALSE	5	80.31	80.28	79.93			

⚠ slightly too high power for some scenario

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

scenario	N	missing	binding	fixC	ar	method 1	method 2	method 3
2	10000	TRUE	TRUE	FALSE	10	2.46	2.53	2.40
4	10000	TRUE	TRUE	FALSE	5	2.42	2.41	2.40
6	10000	TRUE	TRUE	TRUE	10	2.25	2.25	2.45
8	10000	TRUE	TRUE	TRUE	5	2.42	2.39	2.50
10	10000	TRUE	FALSE	TRUE	10	2.16	2.18	2.31
12	10000	TRUE	FALSE	TRUE	5	2.36	2.35	2.38
14	10000	TRUE	FALSE	FALSE	10	2.44	2.44	2.58
16	10000	TRUE	FALSE	FALSE	5	2.51	2.50	2.58
18	10000	FALSE	TRUE	FALSE	5	2.46	2.44	2.45

Type 1 error slightly below nominal level when fixC is TRUE (as expected?)

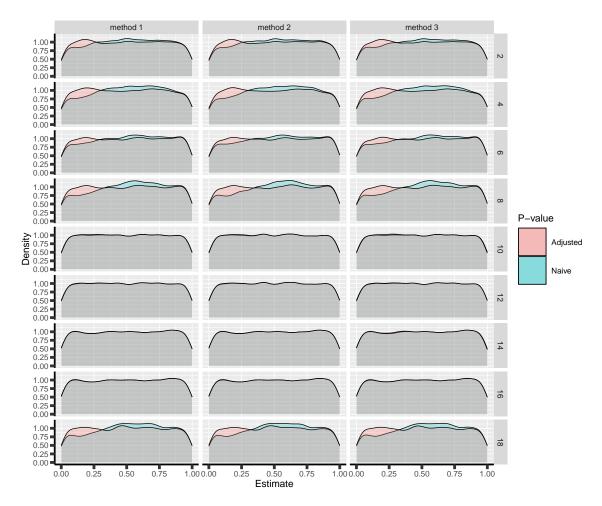


Figure 1: Naive and adjusted p-value distribution over all simulations under the null. Each row correspond to a different scenario

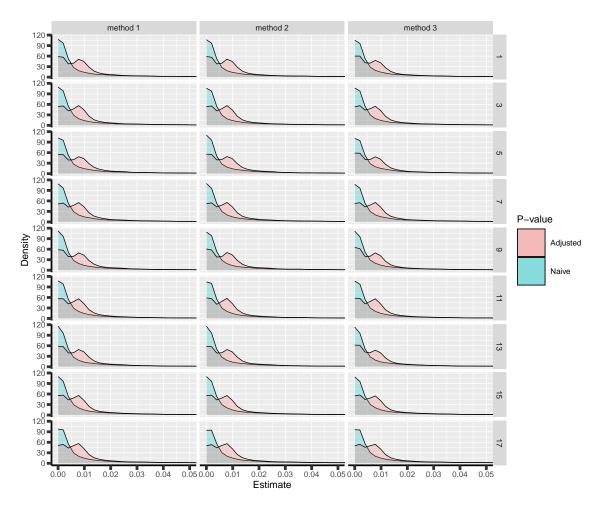


Figure 2: Naive and adjusted p-value distribution over all simulations under the alternative. Each row correspond to a different scenario

## 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	37.82	6.05	43.18	13.0
2:	10000	TRUE	typeI	TRUE	FALSE	10	0.79	70.85	1.67	26.7
3:	10000	TRUE	power	TRUE	FALSE	5	35.60	6.02	45.00	13.4
4:	10000	TRUE	typeI	TRUE	FALSE	5	0.68	69.21	1.74	28.4
5:	10000	TRUE	power	TRUE	TRUE	10	36.45	6.53	43.36	13.7
6:	10000	TRUE	typeI	TRUE	TRUE	10	0.64	71.29	1.61	26.5
7:	10000	TRUE	power	TRUE	TRUE	5	34.68	5.86	45.32	14.1
8:	10000	TRUE	typeI	TRUE	TRUE	5	0.72	69.11	1.70	28.5
9:	10000	TRUE	power	FALSE	TRUE	10	37.57	6.63	42.93	12.9
10:	10000	TRUE	typeI	FALSE	TRUE	10	0.57	0.28	1.59	97.6
11:	10000	TRUE	power	FALSE	TRUE	5	36.02	6.28	44.71	13.0
12:	10000	TRUE	typeI	FALSE	TRUE	5	0.73	0.09	1.63	97.5
13:	10000	TRUE	power	FALSE	FALSE	10	38.32	5.87	42.35	13.5
14:	10000	TRUE	typeI	FALSE	FALSE	10	0.69	0.09	1.75	97.5
15:	10000	TRUE	power	FALSE	FALSE	5	36.75	5.70	43.90	13.6
16:	10000	TRUE	typeI	FALSE	FALSE	5	0.67	0.00	1.84	97.5
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	37.66	6.22	43.13	13.0
2:	10000	TRUE	typeI	TRUE	FALSE	10	0.85	71.18	1.68	26.3
3:	10000	TRUE	power	TRUE	FALSE	5	35.55	6.10	44.90	13.5
4:	10000	TRUE	typeI	TRUE	FALSE	5	0.67	69.05	1.74	28.5
5:	10000	TRUE	power	TRUE	TRUE	10	36.82	5.94	43.59	13.6
6:	10000	TRUE	typeI	TRUE	TRUE	10	0.63	70.02	1.62	27.7
7:	10000	TRUE	power	TRUE	TRUE	5	35.06	5.63	45.40	13.9
8:	10000	TRUE	typeI	TRUE	TRUE	5	0.71	68.46	1.68	29.1
9:	10000	TRUE	power	FALSE	TRUE	10	37.76	6.21	43.09	12.9
10:	10000	TRUE	typeI	FALSE	TRUE	10	0.56	0.26	1.62	97.6
11:	10000	TRUE	power	FALSE	TRUE	5	36.07	6.10	44.75	13.1
12:	10000	TRUE	typeI	FALSE	TRUE	5	0.72	0.07	1.63	97.6
13:	10000	TRUE	power	FALSE	FALSE	10	38.33	6.11	42.27	13.3
14:	10000	TRUE	typeI	FALSE	FALSE	10	0.69	0.09	1.75	97.5
15:	10000	TRUE	power	FALSE	FALSE	5	36.78	5.72	43.86	13.6
16:	10000	TRUE	typeI	FALSE	FALSE	5	0.66	0.01	1.84	97.5
17:	10000	FALSE	power	TRUE	FALSE	5	33.68	5.17	46.60	14.5
18:	10000	FALSE	typeI	TRUE	FALSE	5	0.72	67.42	1.72	30.1

#### Method 3:

	N	missing	hypo	binding	fixC	ar	decision.eff	decision.fut	final.eff	final.fut
1:	10000	TRUE	power	TRUE	FALSE	10	40.44	6.54	40.01	13.0
2:	10000	TRUE	typeI	TRUE	FALSE	10	0.74	68.77	1.66	28.8
3:	10000	TRUE	power	TRUE	FALSE	5	36.49	6.42	43.72	13.4
4:	10000	TRUE	typeI	TRUE	FALSE	5	0.68	68.37	1.72	29.2
5:	10000	TRUE	power	TRUE	TRUE	10	39.85	5.83	40.54	13.8
6:	10000	TRUE	typeI	TRUE	TRUE	10	0.73	68.89	1.72	28.7
7:	10000	TRUE	power	TRUE	TRUE	5	35.70	5.81	44.38	14.1
8:	10000	TRUE	typeI	TRUE	TRUE	5	0.78	68.26	1.72	29.2
9:	10000	TRUE	power	FALSE	TRUE	10	41.03	6.39	39.88	12.7
10:	10000	TRUE	typeI	FALSE	TRUE	10	0.72	0.38	1.59	97.3
11:	10000	TRUE	power	FALSE	TRUE	5	37.08	6.14	43.67	13.1
12:	10000	TRUE	typeI	FALSE	TRUE	5	0.74	0.14	1.64	97.5
13:	10000	TRUE	power	FALSE	FALSE	10	41.47	6.05	39.18	13.3
14:	10000	TRUE	typeI	FALSE	FALSE	10	0.81	0.31	1.77	97.1
15:	10000	TRUE	power	FALSE	FALSE	5	37.37	5.86	43.09	13.7
16:	10000	TRUE	typeI	FALSE	FALSE	5	0.75	0.08	1.83	97.3
17:	10000	FALSE	power	TRUE	FALSE	5	34.66	5.58	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 method<sup>1</sup>:

```
biasMLE1
     hypo missing binding fixC ar
                                               biasMLE2
                                                          biasMLE3
                                                                    biasMUE1
                                                                              biasMUE2 biasMUE3
 1: power
             TRUE
                     TRUE FALSE 10
                                     0.012970
                                               0.013058
                                                          0.014139
                                                                    0.005472
                                                                              0.005564
                                                                                         0.00216
 2: typeI
             TRUE
                     TRUE FALSE 10 -0.018416 -0.018430 -0.018509 -0.004261 -0.004326 -0.00464
 3: power
             TRUE
                     TRUE FALSE
                                 5
                                    0.022430
                                               0.022231
                                                          0.023386
                                                                   0.010079
                                                                              0.010156
                                                                                         0.00864
 4: typeI
                     TRUE FALSE
                                  5 -0.030419 -0.030822 -0.030577 -0.011757 -0.012140 -0.01213
             TRUE
                                    0.011558 0.012119
                                                          0.012968
                                                                   0.001017
                                                                             0.001972 0.00212
 5: power
             TRUE
                     TRUE
                           TRUE 10
 6: typeI
             TRUE
                     TRUE
                           TRUE 10 -0.022074 -0.022256 -0.022266 -0.008120 -0.008149 -0.00830
7: power
             TRUE
                     TRUE
                           TRUE
                                    0.021638 0.022029
                                                          0.022692 0.008407
                                                                             0.008660
                                                                                         0.00842
                           TRUE
                                  5 -0.033857 -0.034379 -0.034138 -0.014560 -0.014719 -0.01503
 8: typeI
             TRUE
                     TRUE
 9: power
             TRUE
                    FALSE
                           TRUE 10
                                     0.015026
                                               0.015050
                                                          0.016312
                                                                    0.000405
                                                                              0.000655
                                                                                         0.00121
10: typeI
             TRUE
                    FALSE
                           TRUE 10
                                     0.000543
                                               0.000547
                                                          0.000883
                                                                    0.001271
                                                                              0.001309
                                                                                         0.00208
11: power
             TRUE
                    FALSE
                           TRUE
                                     0.024204
                                               0.024192
                                                                    0.006976
                                 5
                                                          0.025190
                                                                              0.006478
                                                                                         0.00759
                           TRUE
12: typeI
             TRUE
                    FALSE
                                 5
                                     0.001472
                                               0.001451
                                                          0.001545
                                                                    0.001680
                                                                              0.001708
                                                                                         0.00172
             TRUE
                    FALSE FALSE 10
                                     0.014415
                                                                    0.003384
13: power
                                               0.014146
                                                          0.015747
                                                                              0.002971
                                                                                         0.00239
                    FALSE FALSE 10
14: typeI
             TRUE
                                     0.000139
                                               0.000139
                                                          0.000555
                                                                    0.000611
                                                                              0.000628
                                                                                         0.00181
                    FALSE FALSE
                                     0.023380
                                                                    0.008843
15: power
             TRUE
                                  5
                                               0.023344
                                                          0.024346
                                                                              0.008827
                                                                                         0.00767
16: typeI
                                  5
                                     0.000602
                                               0.000602
             TRUE
                    FALSE FALSE
                                                          0.000949
                                                                    0.000637
                                                                               0.000599
                                                                                         0.00125
                                  5
                                     0.022836
                                               0.022825
                                                          0.023807
17: power
            FALSE
                     TRUE FALSE
                                                                    0.011971
                                                                              0.012078
                                                                                         0.01031
18: typeI
            FALSE
                     TRUE FALSE
                                  5 -0.029516 -0.029722 -0.029915 -0.011048 -0.011395 -0.01144
```

#### Median bias <sup>2</sup> 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	0.0250	0.0240	0.0266	-0.0023	-0.0017	-0.0062
typeI	TRUE	TRUE	FALSE	10	-0.0193	-0.0198	-0.0223	0.0002	-0.0013	0.0001
power	TRUE	TRUE	FALSE	5	0.0387	0.0382	0.0406	-0.0030	-0.0016	-0.0026
typeI	TRUE	TRUE	FALSE	5	-0.0346	-0.0339	-0.0361	0.0000	-0.0002	0.0001
power	TRUE	TRUE	TRUE	10	0.0164	0.0188	0.0179	-0.0132	-0.0126	-0.0101
typeI	TRUE	TRUE	TRUE	10	-0.0327	-0.0314	-0.0347	-0.0113	-0.0079	-0.0099
power	TRUE	TRUE	TRUE	5	0.0356	0.0369	0.0361	-0.0106	-0.0114	-0.0082
typeI	TRUE	TRUE	TRUE	5	-0.0473	-0.0492	-0.0493	-0.0105	-0.0081	-0.0105
power	TRUE	FALSE	TRUE	10	0.0328	0.0301	0.0345	-0.0089	-0.0106	-0.0055
typeI	TRUE	FALSE	TRUE	10	0.0007	-0.0019	0.0007	0.0024	-0.0005	0.0034
power	TRUE	FALSE	TRUE	5	0.0479	0.0459	0.0499	-0.0049	-0.0048	-0.0034
typeI	TRUE	FALSE	TRUE	5	0.0009	-0.0017	0.0009	0.0012	-0.0012	0.0020
power	TRUE	FALSE	FALSE	10	0.0326	0.0324	0.0339	-0.0033	-0.0036	-0.0004
typeI	TRUE	FALSE	FALSE	10	-0.0039	-0.0039	-0.0037	-0.0031	-0.0030	-0.0011
power	TRUE	FALSE	FALSE	5	0.0442	0.0442	0.0465	-0.0010	-0.0010	-0.0037
typeI	TRUE	FALSE	FALSE	5	-0.0039	-0.0039	-0.0039	-0.0039	-0.0039	-0.0028
power	FALSE	TRUE	FALSE	5	0.0383	0.0378	0.0400	-0.0026	-0.0008	-0.0046
typeI	FALSE	TRUE	FALSE	5	-0.0329	-0.0336	-0.0353	0.0044	0.0031	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         0.0250           typeI         TRUE         TRUE         FALSE         10         -0.0193           power         TRUE         TRUE         FALSE         5         0.0387           typeI         TRUE         TRUE         FALSE         5         -0.0346           power         TRUE         TRUE         TRUE         10         0.0164           typeI         TRUE         TRUE         TRUE         10         -0.0327           power         TRUE         TRUE         TRUE         5         -0.0473           power         TRUE         FALSE         TRUE         10         0.0328           typeI         TRUE         FALSE         TRUE         10         0.0027           power         TRUE         FALSE         TRUE         5         0.0479           typeI         TRUE         FALSE         TRUE         5         0.0009           power         TRUE         FALSE         FALSE         10         -0.0039           power         TRUE         FALSE         5         0.0442           typeI         TRUE         FALSE	power         TRUE         TRUE         FALSE         10         0.0250         0.0240           typeI         TRUE         TRUE         FALSE         10         -0.0193         -0.0198           power         TRUE         TRUE         FALSE         5         0.0387         0.0382           typeI         TRUE         TRUE         FALSE         5         -0.0346         -0.0339           power         TRUE         TRUE         TRUE         10         0.0164         0.0188           typeI         TRUE         TRUE         TRUE         10         -0.0327         -0.0314           power         TRUE         TRUE         TRUE         5         0.0356         0.0369           typeI         TRUE         TRUE         TRUE         5         -0.0473         -0.0492           power         TRUE         FALSE         TRUE         10         0.0328         0.0301           typeI         TRUE         FALSE         TRUE         5         0.0479         0.0459           typeI         TRUE         FALSE         TRUE         5         0.0009         -0.0017           power         TRUE         FALSE         FALSE <td>power         TRUE         TRUE         FALSE         10         0.0250         0.0240         0.0266           typeI         TRUE         TRUE         FALSE         10         -0.0193         -0.0198         -0.0223           power         TRUE         TRUE         FALSE         5         0.0387         0.0382         0.0406           typeI         TRUE         TRUE         FALSE         5         -0.0346         -0.0339         -0.0361           power         TRUE         TRUE         TRUE         10         0.0164         0.0188         0.0179           typeI         TRUE         TRUE         TRUE         10         -0.0327         -0.0314         -0.0347           power         TRUE         TRUE         TRUE         5         0.0356         0.0369         0.0361           typeI         TRUE         TRUE         5         -0.0473         -0.0492         -0.0493           power         TRUE         FALSE         TRUE         10         0.0328         0.0301         0.0345           typeI         TRUE         FALSE         TRUE         5         0.0479         0.0459         0.0499           typeI         TRUE</td> <td>power         TRUE         TRUE         FALSE         10         0.0250         0.0240         0.0266         -0.0023           typeI         TRUE         TRUE         FALSE         10         -0.0193         -0.0198         -0.0223         0.0002           power         TRUE         TRUE         FALSE         5         0.0387         0.0382         0.0406         -0.0030           typeI         TRUE         TRUE         FALSE         5         -0.0346         -0.0339         -0.0361         0.0000           power         TRUE         TRUE         TRUE         10         0.0164         0.0188         0.0179         -0.0132           typeI         TRUE         TRUE         TRUE         10         -0.0327         -0.0314         -0.0347         -0.0113           power         TRUE         TRUE         TRUE         5         0.0356         0.0369         0.0361         -0.0106           typeI         TRUE         FALSE         TRUE         10         0.0328         0.0301         0.0345         -0.0089           typeI         TRUE         FALSE         TRUE         5         0.0479         0.0459         0.0499         -0.0049</td> <td>typeI         TRUE         TRUE FALSE         10         -0.0193         -0.0198         -0.0223         0.0002         -0.0013           power         TRUE         TRUE FALSE         5         0.0387         0.0382         0.0406         -0.0030         -0.0016           typeI         TRUE         TRUE FALSE         5         -0.0346         -0.0339         -0.0361         0.0000         -0.0002           power         TRUE         TRUE TRUE         10         0.0164         0.0188         0.0179         -0.0132         -0.0126           typeI         TRUE         TRUE TRUE         10         -0.0327         -0.0314         -0.0347         -0.0113         -0.0079           power         TRUE         TRUE TRUE         5         0.0356         0.0369         0.0361         -0.0106         -0.0114           typeI         TRUE         TRUE TRUE         5         -0.0473         -0.0492         -0.0493         -0.0105         -0.0081           power         TRUE FALSE TRUE         10         0.0027         -0.0019         0.0007         0.0024         -0.0089         -0.0106           typeI         TRUE FALSE TRUE 5         0.00479         0.0459         0.0499         -0.0049</td>	power         TRUE         TRUE         FALSE         10         0.0250         0.0240         0.0266           typeI         TRUE         TRUE         FALSE         10         -0.0193         -0.0198         -0.0223           power         TRUE         TRUE         FALSE         5         0.0387         0.0382         0.0406           typeI         TRUE         TRUE         FALSE         5         -0.0346         -0.0339         -0.0361           power         TRUE         TRUE         TRUE         10         0.0164         0.0188         0.0179           typeI         TRUE         TRUE         TRUE         10         -0.0327         -0.0314         -0.0347           power         TRUE         TRUE         TRUE         5         0.0356         0.0369         0.0361           typeI         TRUE         TRUE         5         -0.0473         -0.0492         -0.0493           power         TRUE         FALSE         TRUE         10         0.0328         0.0301         0.0345           typeI         TRUE         FALSE         TRUE         5         0.0479         0.0459         0.0499           typeI         TRUE	power         TRUE         TRUE         FALSE         10         0.0250         0.0240         0.0266         -0.0023           typeI         TRUE         TRUE         FALSE         10         -0.0193         -0.0198         -0.0223         0.0002           power         TRUE         TRUE         FALSE         5         0.0387         0.0382         0.0406         -0.0030           typeI         TRUE         TRUE         FALSE         5         -0.0346         -0.0339         -0.0361         0.0000           power         TRUE         TRUE         TRUE         10         0.0164         0.0188         0.0179         -0.0132           typeI         TRUE         TRUE         TRUE         10         -0.0327         -0.0314         -0.0347         -0.0113           power         TRUE         TRUE         TRUE         5         0.0356         0.0369         0.0361         -0.0106           typeI         TRUE         FALSE         TRUE         10         0.0328         0.0301         0.0345         -0.0089           typeI         TRUE         FALSE         TRUE         5         0.0479         0.0459         0.0499         -0.0049	typeI         TRUE         TRUE FALSE         10         -0.0193         -0.0198         -0.0223         0.0002         -0.0013           power         TRUE         TRUE FALSE         5         0.0387         0.0382         0.0406         -0.0030         -0.0016           typeI         TRUE         TRUE FALSE         5         -0.0346         -0.0339         -0.0361         0.0000         -0.0002           power         TRUE         TRUE TRUE         10         0.0164         0.0188         0.0179         -0.0132         -0.0126           typeI         TRUE         TRUE TRUE         10         -0.0327         -0.0314         -0.0347         -0.0113         -0.0079           power         TRUE         TRUE TRUE         5         0.0356         0.0369         0.0361         -0.0106         -0.0114           typeI         TRUE         TRUE TRUE         5         -0.0473         -0.0492         -0.0493         -0.0105         -0.0081           power         TRUE FALSE TRUE         10         0.0027         -0.0019         0.0007         0.0024         -0.0089         -0.0106           typeI         TRUE FALSE TRUE 5         0.00479         0.0459         0.0499         -0.0049

<sup>&</sup>lt;sup>1</sup>e.g. biasMLE1 mixed model estimator (treatment effect), method 1 (boundaries)

<sup>&</sup>lt;sup>2</sup>Relative frequency at which the estimate is greater than the truth minus 0.5

## 4 Distribution of the estimates

Distribution of the estimates:

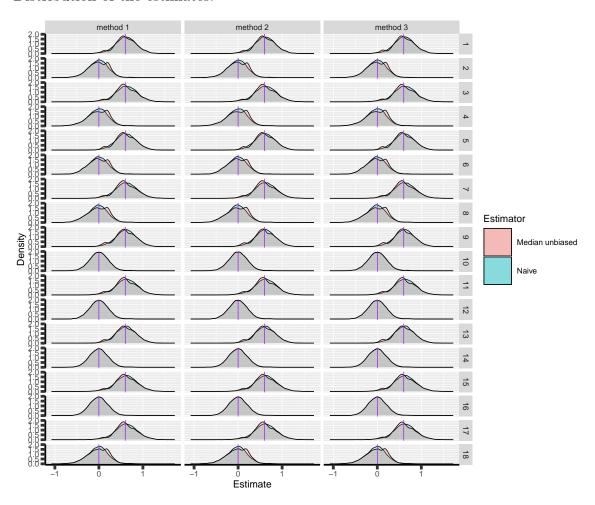


Figure 3: Naive and Median unbiased estimate distribution over all simulations. Each row correspond to a different scenario

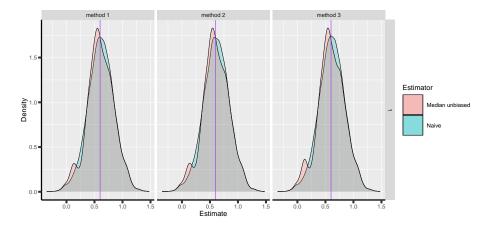


Figure 4: Same but specific to scenario 1

Distribution of the median unbiased estimate conditional to the stage:

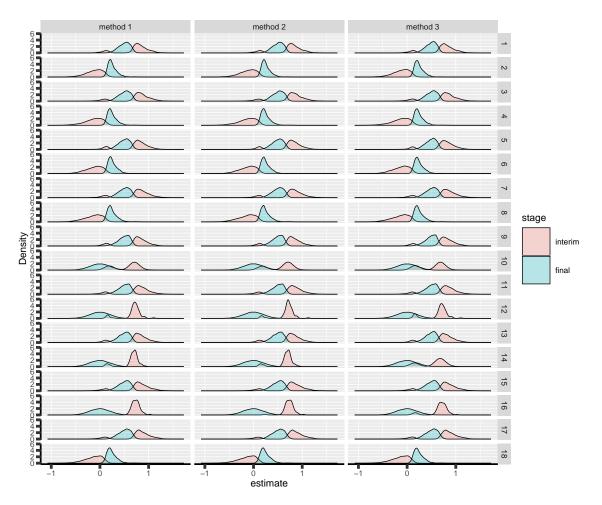


Figure 5: Median unbiased estimate distribution conditional to the stage. Each row correspond to a different scenario.

# 5 Special cases

Reason for stopping (first 4) or continuing the trial (last):

		scenario	1	2	3	4	5	6	7	8
reason	method									
decreasing information	1		0	0	1	1	0	0	0	0
	2		0	0	1	1	0	0	0	0
	3		0	0	1	1	0	0	0	0
efficacy	1		3740		3559	67	3696	82	3502	82
	2		3729	82	3554	68	3732	82	3546	83
	3		4137	107	3712	83	4071	110	3632	92
futility	1		646	7086	603	6922	600	7109	552	6901
	2		658	7120	611	6904	542	6981	523	6834
	3		560	6843	579	6822	495	6850	519	6812
Imax reached	1		1	1	0	0	2	2	0	0
	2		1	1	0	0	2	2	0	0
	3		1	1	0	0	2	2	0	0
no boundary crossed	1		5613	2836	5838	3011	5702	2807	5946	3017
	2		5612	2797	5835	3028	5724	2935	5931	3083
	3		5302	3049	5709	3095	5432	3038	5849	3096
		scenario	9	10	11	12	13	14	15	16
reason	method	scenario	9	10	11	12	13	14	15	16
reason decreasing information		scenario	9	10	11	12	13	14	15 0	16 0
		scenario								
	1	scenario	0	0	1	0	0	0	0	0
	1 2	scenario	0	0 0	1	0 0	0	0 0	0	0
decreasing information	1 2 3	scenario	0 0	0 0 0 84	1 1 1	0 0 0 82	0 0	0 0 0 78	0 0	0 0
decreasing information	1 2 3 1	scenario	0 0 0 3805	0 0 0 84 81	1 1 1 3634	0 0 0 82 79	0 0 0 3815	0 0 0 78 78	0 0 0 3674	0 0 0 67
decreasing information	1 2 3 1 2	scenario	0 0 0 3805 3824 4206	0 0 0 84 81	1 1 1 3634 3646 3761	0 0 0 82 79	0 0 0 3815 3816 4238	0 0 0 78 78	0 0 0 3674 3677 3788	0 0 0 67 67
decreasing information efficacy	1 2 3 1 2 3	scenario	0 0 0 3805 3824 4206 614	0 0 0 84 81 109	1 1 3634 3646 3761 596	0 0 0 82 79 88	0 0 0 3815 3816 4238 604	0 0 0 78 78 112	0 0 0 3674 3677 3788 571	0 0 0 67 67 83
decreasing information efficacy	1 2 3 1 2 3 1	scenario	0 0 0 3805 3824 4206 614 572	0 0 0 84 81 109 7130	1 1 3634 3646 3761 596 571	0 0 0 82 79 88 6957	0 0 0 3815 3816 4238 604 628	0 0 0 78 78 112 7126	0 0 0 3674 3677 3788 571 573	0 0 0 67 67 83 6920
decreasing information efficacy	1 2 3 1 2 3 1 2	scenario	0 0 0 3805 3824 4206 614 572	0 0 0 84 81 109 7130 7044	1 1 3634 3646 3761 596 571	0 0 0 82 79 88 6957 6907	0 0 0 3815 3816 4238 604 628	0 0 78 78 112 7126 7180	0 0 0 3674 3677 3788 571 573	0 0 0 67 67 83 6920
decreasing information efficacy futility	1 2 3 1 2 3 1 2 3	scenario	0 0 3805 3824 4206 614 572 535	0 0 0 84 81 109 7130 7044 6914	1 1 3634 3646 3761 596 571 561	0 0 0 82 79 88 6957 6907 6867	0 0 0 3815 3816 4238 604 628 514	0 0 78 78 112 7126 7180 6870	0 0 0 3674 3677 3788 571 573 535	0 0 0 67 67 83 6920 6925 6837
decreasing information efficacy futility	1 2 3 1 2 3 1 2 3 1 2 3	scenario	0 0 3805 3824 4206 614 572 535	0 0 84 81 109 7130 7044 6914	1 1 3634 3646 3761 596 571 561	0 0 82 79 88 6957 6907 6867 0	0 0 3815 3816 4238 604 628 514 0	0 0 78 78 112 7126 7180 6870 0	0 0 0 3674 3677 3788 571 573 535 0	0 0 67 67 83 6920 6925 6837 0
decreasing information efficacy futility	1 2 3 1 2 3 1 2 3 1 2 3	scenario	0 0 3805 3824 4206 614 572 535 1 1	0 0 84 81 109 7130 7044 6914 1	1 1 3634 3646 3761 596 571 561 0 0	0 0 82 79 88 6957 6907 6867 0 0	0 0 0 3815 3816 4238 604 628 514 0 0	0 0 78 78 112 7126 7180 6870 0 0	0 0 3674 3677 3788 571 573 535 0	0 0 67 67 83 6920 6925 6837 0 0
decreasing information efficacy futility Imax reached	1 2 3 1 2 3 1 2 3 1 2 3 1 2 3	scenario	0 0 3805 3824 4206 614 572 535 1 1 1	0 0 84 81 109 7130 7044 6914 1 1 2785	1 1 3634 3646 3761 596 571 561 0 0 5770	0 0 0 82 79 88 6957 6907 6867 0 0	0 0 3815 3816 4238 604 628 514 0 0 0	0 0 78 78 112 7126 7180 6870 0 0 2796	0 0 3674 3677 3788 571 573 535 0 0	0 0 67 67 83 6920 6925 6837 0 0 3013
decreasing information efficacy futility Imax reached	1 2 3 1 2 3 1 2 3 1 2 3 1 2 3	scenario	0 0 3805 3824 4206 614 572 535 1 1 5580 5603	0 0 84 81 109 7130 7044 6914 1 1 2785 2874	1 1 3634 3646 3761 596 571 561 0 0 5770 5783	0 0 82 79 88 6957 6907 6867 0 0 2961 3014	0 0 0 3815 3816 4238 604 628 514 0 0 5581 5556	0 0 78 78 112 7126 7180 6870 0 0 2796 2742	0 0 0 3674 3677 3788 571 573 535 0 0 5755	0 0 67 67 83 6920 6925 6837 0 0 3013 3008

# 6 Reversal probability

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	FALSE	5	TRUE	FALSE	0.06	0.07	0.01	0.04	0.04	0.63
2:	10000	power	TRUE	5	FALSE	FALSE	0.04	0.04	0.00	0.03	0.03	0.51
3:	10000	power	TRUE	5	FALSE	TRUE	0.04	0.03	0.03	0.36	0.42	0.56
4:	10000	power	TRUE	5	TRUE	FALSE	0.06	0.08	0.02	0.05	0.07	0.65
5:	10000	power	TRUE	5	TRUE	TRUE	0.02	0.02	0.01	0.36	0.42	0.63
6:	10000	power	TRUE	10	FALSE	FALSE	0.35	0.38	0.05	0.18	0.21	0.96
7:	10000	power	TRUE	10	FALSE	TRUE	0.15	0.13	0.10	0.63	0.61	1.13
8:	10000	power	TRUE	10	TRUE	FALSE	0.57	0.57	0.13	0.15	0.20	1.06
9:	10000	power	TRUE	10	TRUE	TRUE	0.17	0.16	0.11	0.70	0.68	0.99
10:	10000	typeI	FALSE	5	TRUE	FALSE	0.01	0.03	0.00	0.01	0.03	0.12
11:	10000	typeI	TRUE	5	FALSE	FALSE	0.00	0.00	0.00	0.00	0.01	0.08
12:	10000	typeI	TRUE	5	FALSE	TRUE	0.00	0.00	0.00	0.09	0.07	0.14
13:	10000	typeI	TRUE	5	TRUE	FALSE	0.02	0.02	0.00	0.01	0.03	0.15
14:	10000	typeI	TRUE	5	TRUE	TRUE	0.00	0.00	0.00	0.10	0.12	0.14
15:	10000	typeI	TRUE	10	FALSE	FALSE	0.00	0.00	0.00	0.09	0.09	0.31
16:	10000	typeI	TRUE	10	FALSE	TRUE	0.00	0.00	0.00	0.27	0.25	0.37
17:	10000	typeI	TRUE	10	TRUE	FALSE	0.11	0.11	0.03	0.09	0.08	0.36
18:	10000	typeI	TRUE	10	TRUE	TRUE	0.02	0.00	0.00	0.22	0.21	0.39

#### 7 Frequency mismatch p-value / boundaries

#### When concluding for futility:

```
hypo missing ar binding fixC
                                    method 1
                                                method 2
                                                           method 3
 1: power
           FALSE 5
                       TRUE FALSE 0.00000000 0.00000000 0.74738416
2: power
            TRUE 5
                      FALSE FALSE 0.41343669 0.41322314 0.56294780
3: power
            TRUE 5
                      FALSE TRUE 1.34924754 0.93847758 0.57142857
4: power
            TRUE 5
                       TRUE FALSE 0.00000000 0.00000000 0.55583628
5: power
            TRUE 5
                       TRUE TRUE 2.55000000 1.84237462 0.65261044
 6: power
            TRUE 10
                      FALSE FALSE 2.43145370 2.47422680 1.34366925
7: power
            TRUE 10
                      FALSE TRUE 3.33333333 3.39425587 0.68098481
8: power
            TRUE 10
                       TRUE FALSE 0.00000000 0.00000000 1.07416880
9: power
            TRUE 10
                       TRUE TRUE 3.91282813 3.77743747 1.22386537
10: typeI
           FALSE 5
                       TRUE FALSE 0.00000000 0.00000000 0.02050231
                      FALSE FALSE 0.03077239 0.03076923 0.06158900
11: typeI
            TRUE 5
                       FALSE TRUE 0.07169193 0.06144393 0.02048760
12: typeI
            TRUE 5
                       TRUE FALSE 0.00000000 0.00000000 0.02049180
13: typeI
            TRUE 5
                       TRUE TRUE 0.14347202 0.12293822 0.02051282
14: typeI
            TRUE 5
15: typeI
            TRUE 10
                       FALSE FALSE 0.14350144 0.14350144 0.10264833
16: typeI
            TRUE 10
                      FALSE TRUE 0.20441537 0.16356573 0.05118231
            TRUE 10
                       TRUE FALSE 0.00000000 0.00000000 0.01024590
17: typeI
18: typeI
            TRUE 10
                       TRUE TRUE 0.26598465 0.25575448 0.09226038
```

#### When concluding for efficacy:

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

### 8 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

	${\tt method}$	missing	ar	hypo	fixC	binding	N	pc.all	<pre>pc.missing3</pre>	pc.missing23
1:	1	TRUE	5	power	FALSE	TRUE	10000	79.53472	9.562374	10.902910
2:	1	TRUE	5	typeI	FALSE	TRUE	10000	79.53472	9.562374	10.902910
3:	1	TRUE	5	power	TRUE	TRUE	10000	79.44022	9.531225	11.028558
4:	1	TRUE	5	typeI	TRUE	TRUE	10000	79.44022	9.531225	11.028558
5:	1	TRUE	5	power	TRUE	FALSE	10000	79.71917	9.427430	10.853396
6:	1	TRUE	5	typeI	TRUE	FALSE	10000	79.71917	9.427430	10.853396
7:	1	TRUE	5	power	FALSE	FALSE	10000	79.64196	9.449136	10.908902
8:	1	TRUE	5	typeI	FALSE	FALSE	10000	79.64196	9.449136	10.908902
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	71.60971	13.327969	15.062319
12:	1	TRUE	10	typeI	FALSE	TRUE	10000	71.60971	13.327969	15.062319
13:	1	TRUE	10	power	TRUE	TRUE	10000	71.52189	13.282615	15.195496
14:	1	TRUE	10	typeI	TRUE	TRUE	10000	71.52189	13.282615	15.195496
15:	1	TRUE	10	power	TRUE	FALSE	10000	71.85935	13.144488	14.996166
16:	1	TRUE	10	typeI	TRUE	FALSE	10000	71.85935	13.144488	14.996166
17:	1	TRUE	10	power	FALSE	FALSE	10000	71.79364	13.168843	15.037522
18:	1	TRUE	10	typeI	FALSE	FALSE	10000	71.79364	13.168843	15.037522

#### 9 Information

Percentage of information for method  $1^3$ :

```
scenario missing binding fixC ar interim decision
                                                        final
           TRUE
                    TRUE FALSE 10 54.63862 63.33698 102.69943
       1
      2
           TRUE
                    TRUE FALSE 10 54.63862 68.96135 102.32310
      3
                    TRUE FALSE 5 53.27109 57.38550 102.74966
           TRUE
      4
                    TRUE FALSE 5 53.27109 60.22345 102.34459
           TRUE
      5
           TRUE
                    TRUE
                         TRUE 10 54.54008 63.10923 102.78945
                          TRUE 10 54.54008 68.95137 102.12003
      6
           TRUE
                    TRUE
      7
           TRUE
                    TRUE
                          TRUE
                               5 53.17744 57.18426 102.80673
                          TRUE 5 53.17744 60.12266 102.22328
      8
           TRUE
                    TRUE
      9
           TRUE
                   FALSE
                          TRUE 10 54.51044 63.16647 102.56935
                   FALSE
                         TRUE 10 54.51044 54.66970 103.09893
      10
           TRUE
                          TRUE
                                5 53.17317 57.27740 102.61166
      11
           TRUE
                   FALSE
                                5 53.17317 53.24797 103.10060
      12
           TRUE
                   FALSE
                         TRUE
                   FALSE FALSE 10 54.49750 63.16580 102.56590
      13
           TRUE
           TRUE
                   FALSE FALSE 10 54.49750 54.64468 103.12067
     14
                   FALSE FALSE 5 53.15611 57.29003 102.60917
           TRUE
     15
                   FALSE FALSE 5 53.15611 53.21806 103.12463
      16
           TRUE
     17
           FALSE
                    TRUE FALSE 5 52.06840 56.28978 99.96969
                    TRUE FALSE 5 52.06840 59.42197 99.62860
      18
           FALSE
```

Similar results for other methods.

<sup>&</sup>lt;sup>3</sup>average over the reached stages