Results simulation study DelayedGSD

$March\ 22,\ 2023$

1 Rejection rate

Power by r	nethod	l (column	s) and so	enario	(ro	ws):	(r	nominal level 80%	(v)
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?)

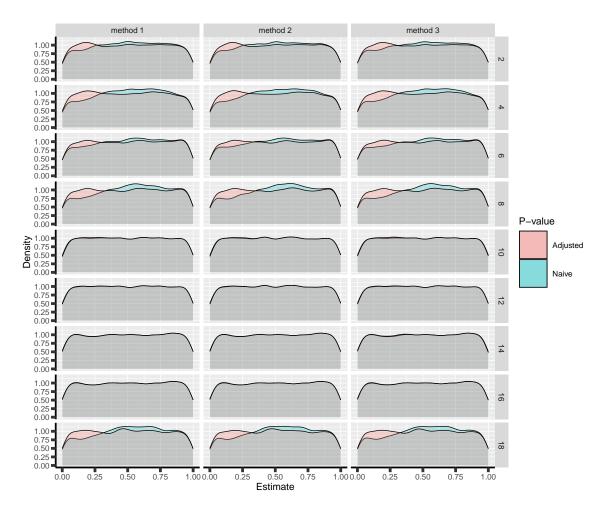


Figure 1: Naive and adjusted p-value distribution over all simulations under the null. Each row correspond to a different scenario

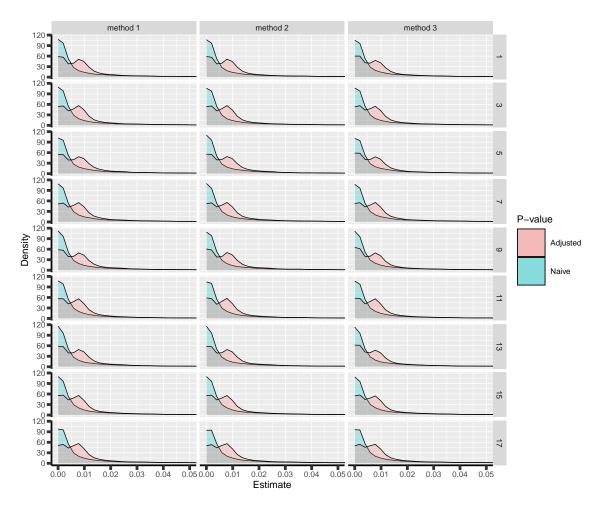


Figure 2: Naive and adjusted p-value distribution over all simulations under the alternative. Each row correspond to a different scenario

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 method¹:

```
biasMLE1
     hypo missing binding fixC ar
                                              biasMLE2
                                                        biasMLE3
                                                                   biasMUE1
                                                                             biasMUE2
                                                                                       biasMUE3
 1: power
             TRUE
                     TRUE FALSE 10
                                    0.012970
                                              0.013058
                                                         0.014139
                                                                   5.47e-03
                                                                             5.56e-03
                                                                                       0.001778
 2: typeI
             TRUE
                     TRUE FALSE 10 -0.018416 -0.018430 -0.018509 -4.26e-03 -4.33e-03 -0.004919
 3: power
             TRUE
                     TRUE FALSE
                                5
                                   0.022430 0.022231
                                                        0.023386 1.01e-02 1.02e-02
                                                                                      0.008425
 4: typeI
                     TRUE FALSE
                                 5 -0.030419 -0.030822 -0.030577 -1.18e-02 -1.21e-02 -0.012275
             TRUE
                                   0.011558 0.012119
                                                        0.012968 -1.55e-04 8.16e-04 0.001723
 5: power
             TRUE
                     TRUE
                           TRUE 10
 6: typeI
             TRUE
                     TRUE
                           TRUE 10 -0.022074 -0.022256 -0.022266 -9.04e-03 -9.08e-03 -0.008580
                                                        0.022692 7.84e-03 8.10e-03
7: power
             TRUE
                     TRUE
                           TRUE
                                   0.021638 0.022029
                           TRUE
                                 5 -0.033857 -0.034379 -0.034138 -1.50e-02 -1.51e-02 -0.015168
 8: typeI
             TRUE
                     TRUE
 9: power
             TRUE
                    FALSE
                           TRUE 10
                                    0.015026
                                              0.015050
                                                        0.016312 -7.62e-04 -4.88e-04
                                                                                       0.000843
10: typeI
             TRUE
                    FALSE
                           TRUE 10
                                    0.000543
                                              0.000547
                                                         0.000883 -6.54e-05 -1.08e-06
                                                                                       0.001751
11: power
             TRUE
                    FALSE
                           TRUE
                                    0.024204
                                              0.024192
                                                        0.025190
                                                                  6.44e-03 5.95e-03
                                5
                                                                                       0.007381
                           TRUE
12: typeI
             TRUE
                    FALSE
                                5
                                    0.001472
                                              0.001451
                                                         0.001545
                                                                   1.17e-03 1.21e-03
                                                                                       0.001552
             TRUE
                    FALSE FALSE 10
                                    0.014415
13: power
                                              0.014146
                                                        0.015747
                                                                   3.10e-03
                                                                            2.68e-03
                                                                                       0.002008
                    FALSE FALSE 10
14: typeI
             TRUE
                                    0.000139
                                              0.000139
                                                        0.000555 -1.53e-05 -2.18e-05
                                                                                       0.001472
                    FALSE FALSE
                                    0.023380
                                                                   8.80e-03 8.79e-03
15: power
             TRUE
                                5
                                              0.023344
                                                         0.024346
                                                                                       0.007463
16: typeI
                                    0.000602
                                              0.000602
                                                                            5.00e-04
             TRUE
                    FALSE FALSE
                                 5
                                                         0.000949
                                                                   5.40e-04
                                                                                       0.001079
                                 5
                                    0.022836
                                              0.022825
                                                         0.023807
                                                                   1.20e-02 1.21e-02
17: power
            FALSE
                     TRUE FALSE
                                                                                       0.010058
18: typeI
            FALSE
                     TRUE FALSE
                                5 -0.029516 -0.029722 -0.029915 -1.10e-02 -1.14e-02 -0.011615
```

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
1:	power	TRUE	TRUE	FALSE	10	0.0250	0.0240	0.0266	-0.0023	-0.0017	-0.0062
2:	typeI	TRUE	TRUE	FALSE	10	-0.0193	-0.0198	-0.0223	0.0002	-0.0013	0.0001
3:	power	TRUE	TRUE	FALSE	5	0.0387	0.0382	0.0406	-0.0030	-0.0016	-0.0026
4:	typeI	TRUE	TRUE	FALSE	5	-0.0346	-0.0339	-0.0361	0.0000	-0.0002	0.0001
5:	power	TRUE	TRUE	TRUE	10	0.0164	0.0188	0.0179	-0.0134	-0.0128	-0.0102
6:	typeI	TRUE	TRUE	TRUE	10	-0.0327	-0.0314	-0.0347	-0.0113	-0.0079	-0.0099
7:	power	TRUE	TRUE	TRUE	5	0.0356	0.0369	0.0361	-0.0106	-0.0115	-0.0082
8:	typeI	TRUE	TRUE	TRUE	5	-0.0473	-0.0492	-0.0493	-0.0105	-0.0081	-0.0105
9:	power	TRUE	FALSE	TRUE	10	0.0328	0.0301	0.0345	-0.0092	-0.0110	-0.0055
10:	typeI	TRUE	FALSE	TRUE	10	0.0007	-0.0019	0.0007	0.0008	-0.0018	0.0030
11:	power	TRUE	FALSE	TRUE	5	0.0479	0.0459	0.0499	-0.0049	-0.0049	-0.0034
12:	typeI	TRUE	FALSE	TRUE	5	0.0009	-0.0017	0.0009	0.0009	-0.0017	0.0013
13:	power	TRUE	FALSE	FALSE	10	0.0326	0.0324	0.0339	-0.0033	-0.0036	-0.0005
14:	typeI	TRUE	FALSE	FALSE	10	-0.0039	-0.0039	-0.0037	-0.0039	-0.0039	-0.0015
15:	power	TRUE	FALSE	FALSE	5	0.0442	0.0442	0.0465	-0.0010	-0.0010	-0.0038
16:	typeI	TRUE	FALSE	FALSE	5	-0.0039	-0.0039	-0.0039	-0.0039	-0.0039	-0.0031
17:	power	FALSE	TRUE	FALSE	5	0.0383	0.0378	0.0400	-0.0026	-0.0008	-0.0046
18:	typeI	FALSE	TRUE	FALSE	5	-0.0329	-0.0336	-0.0353	0.0044	0.0031	0.0035

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:

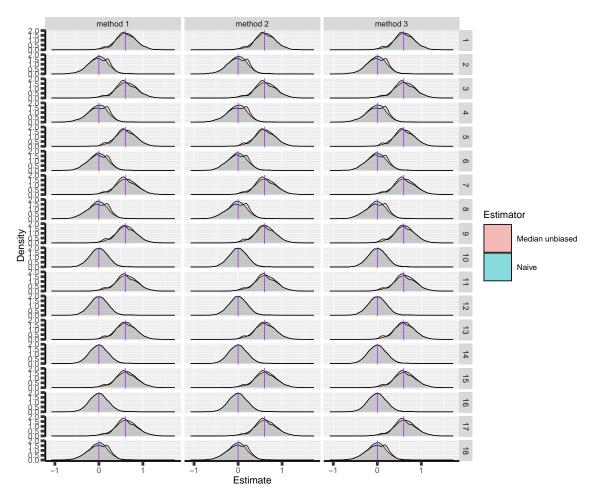


Figure 3: Naive and Median unbiased estimate distribution over all simulations. Each row correspond to a different scenario

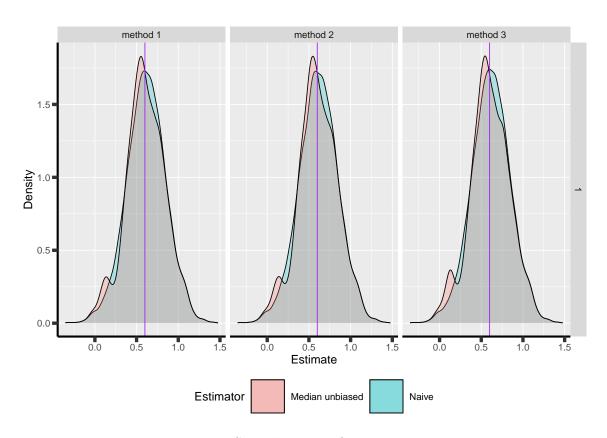


Figure 4: Same but specific to scenario 1

Distribution of the median unbiased estimate conditional to the stage:

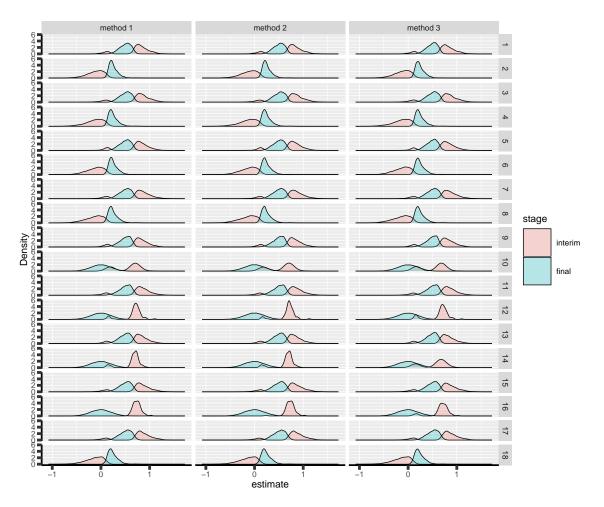


Figure 5: Median unbiased estimate distribution conditional to the stage. Each row correspond to a different scenario.

5 Special cases

Reason for stopping (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	77	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
		sconorio	۵	10	11	10	12	1/	15	16
roagon	mothod	scenario	9	10	11	12	13	14	15	16
reason	method	scenario								
reason decreasing information	1	scenario	0	0	1	0	0	0	0	0
	1 2	scenario	0	0	1	0	0	0	0	0
decreasing information	1 2 3	scenario	0 0	0 0	1 1 1	0 0	0 0	0 0	0 0	0 0
	1 2 3 1	scenario	0 0 0 3805	0 0 0 84	1 1 1 3634	0 0 0 82	0 0 0 3815	0 0 0 78	0 0 0 3674	0 0 0 67
decreasing information	1 2 3 1 2	scenario	0 0 0 3805 3824	0 0 0 84 81	1 1 1 3634 3646	0 0 0 82 79	0 0 0 3815 3816	0 0 0 78 78	0 0 0 3674 3677	0 0 0 67 67
decreasing information efficacy	1 2 3 1 2 3	scenario	0 0 0 3805 3824 4206	0 0 0 84 81 109	1 1 1 3634 3646 3761	0 0 0 82 79 88	0 0 0 3815 3816 4238	0 0 0 78 78 112	0 0 0 3674 3677 3788	0 0 0 67 67 83
decreasing information	1 2 3 1 2 3 1	scenario	0 0 0 3805 3824 4206 614	0 0 0 84 81 109 7130	1 1 3634 3646 3761 596	0 0 0 82 79 88 6957	0 0 0 3815 3816 4238 604	0 0 0 78 78 112 7126	0 0 0 3674 3677 3788 571	0 0 0 67 67 83 6920
decreasing information efficacy	1 2 3 1 2 3 1 2	scenario	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 6925
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	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	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 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 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	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 0 67 67 83 6920 6925 6837 0 0
decreasing information efficacy futility	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 5580	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 0 3815 3816 4238 604 628 514 0 0 0 5581	0 0 78 78 112 7126 7180 6870 0 0 2796	0 0 0 3674 3677 3788 571 573 535 0 0 0 5755	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 3674 3677 3788 571 573 535 0 0	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	${\tt fu2eff_2}$	${\tt fu2eff_3}$	${\tt eff2fu_1}$	${\tt eff2fu_2}$	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

7.1 p-value / boundaries

When concluding for futility:

	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

When concluding for efficacy:

	hypo	${\tt missing}$	ar	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:	tvpeI	TRUE	10	TRUE	TRUE		0		0		0

7.2 confidence intervals

When concluding for futility:

```
hypo missing ar binding fixC
                                    method 1
                                                method 2
                                                           method 3
            FALSE 5
                        TRUE FALSE 0.00000000 0.00000000 0.00000000
 1: power
                      FALSE FALSE 0.00000000 0.00000000 0.00000000
2: power
            TRUE 5
                      FALSE TRUE 0.05189414 0.05213764 0.05194805
3: power
            TRUE 5
                        TRUE FALSE 0.00000000 0.00000000 0.00000000
4: power
            TRUE 5
            TRUE 5
                        TRUE TRUE 0.00000000 0.00000000 0.00000000
5: power
6: power
            TRUE 10
                      FALSE FALSE 0.00000000 0.00000000 0.00000000
7: power
            TRUE 10
                      FALSE TRUE 0.05128205 0.05221932 0.05238345
            TRUE 10
                        TRUE FALSE 0.05263158 0.05205622 0.05115090
8: power
            TRUE 10
                        TRUE TRUE 0.00000000 0.00000000 0.00000000
9: power
                        TRUE FALSE 0.00000000 0.00000000 0.00000000
10: typeI
            FALSE 5
            TRUE 5
                      FALSE FALSE 0.00000000 0.00000000 0.00000000
11: typeI
                      FALSE TRUE 0.00000000 0.00000000 0.00000000
12: typeI
            TRUE 5
13: typeI
            TRUE 5
                        TRUE FALSE 0.01024800 0.01024695 0.01024590
14: typeI
            TRUE 5
                        TRUE TRUE 0.00000000 0.00000000 0.00000000
                      FALSE FALSE 0.00000000 0.00000000 0.00000000
15: typeI
            TRUE 10
            TRUE 10
                       FALSE TRUE 0.00000000 0.00000000 0.00000000
16: typeI
                        TRUE FALSE 0.00000000 0.00000000 0.00000000
17: typeI
            TRUE 10
                        TRUE TRUE 0.00000000 0.00000000 0.00000000
            TRUE 10
18: typeI
```

I think the issues arise du to special cases, e.g. decreasing information:

```
infoPC statistic p.value_ML p.value_MUE
    scenario method stage
                               type
1:
           1
                  1
                         1 decision 0.9551434 1.7322474 0.04182771
                                                                               1
2:
           1
                  2
                         1 decision 0.9559423 1.7322474 0.04182771
                                                                               1
3:
           1
                  3
                         1 decision 0.9538148 1.7322474 0.04182771
                                                                               1
                         1 decision 0.6270978 0.3678716 0.35654991
4:
           4
                  1
                                                                               1 decreasing in
                  2
                         1 decision 0.6276223 0.3678716 0.35654991
                                                                               1 decreasing in
5:
           4
6:
           4
                  3
                         1 decision 0.6262255 0.3678716 0.35654991
                                                                               1 decreasing in
                         1 decision 0.9267393 1.8635206 0.03139115
7:
           9
                  1
                                                                               1
8:
           9
                  2
                         1 decision 0.9219480 1.7901042 0.03692049
                                                                               1
                                                                               1
9:
           9
                  3
                         1 decision 0.9269087 1.8635206 0.03139115
                         1 decision 0.8045784 1.7609106 0.03937283
10:
          11
                  1
                                                                               1 decreasing in
                  2
                         1 decision 0.7881215 1.5699238 0.05846867
                                                                               1 decreasing in
11:
          11
                         1 decision 0.8047255 1.7609106 0.03937283
12:
          11
                  3
                                                                               1 decreasing in
```

When concluding for efficacy:

	hypo	missing	ar	binding	fixC	method	1	method	2	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 Coverage

	hypo	missing	ar	binding	fixC	method 1	method 2	method 3
1:	power	FALSE	5	TRUE	FALSE	94.79	94.82	94.92
2:	power	TRUE	5	FALSE	FALSE	93.60	93.61	93.93
3:	power	TRUE	5	FALSE	TRUE	94.21	94.22	94.28
4:	power	TRUE	5	TRUE	FALSE	94.76	94.59	94.89
5:	power	TRUE	5	TRUE	TRUE	95.44	95.38	95.22
6:	power	TRUE	10	FALSE	FALSE	93.38	93.36	94.14
7:	power	TRUE	10	FALSE	TRUE	94.24	94.15	94.53
8:	power	TRUE	10	TRUE	FALSE	94.75	94.73	94.98
9:	power	TRUE	10	TRUE	TRUE	95.97	95.91	95.46
10:	typeI	FALSE	5	TRUE	FALSE	95.14	95.20	95.15
11:	typeI	TRUE	5	FALSE	FALSE	95.01	95.02	95.57
12:	typeI	TRUE	5	FALSE	TRUE	95.07	95.08	95.74
13:	typeI	TRUE	5	TRUE	FALSE	94.71	94.78	94.73
14:	typeI	TRUE	5	TRUE	TRUE	95.06	95.24	94.98
15:	typeI	TRUE	10	FALSE	FALSE	95.08	95.08	96.19
16:	typeI	TRUE	10	FALSE	TRUE	95.27	95.25	96.48
17:	typeI	TRUE	10	TRUE	FALSE	94.87	94.82	94.93
18:	typeI	TRUE	10	TRUE	TRUE	95.33	95.29	95.13

Average width of the confidence intervals (ratio width(MUE) and width(ML))

```
hypo missing ar binding fixC method 1 method 2 method 3
 1: power
           FALSE
                  5
                        TRUE FALSE 1.0517981 1.0518767 1.053589
 2: power
             TRUE
                  5
                       FALSE FALSE 1.0430641 1.0430645 1.045294
3: power
             TRUE
                  5
                       FALSE TRUE 1.0490757 1.0494445 1.045526
4: power
             TRUE
                        TRUE FALSE 1.0516795 1.0515698 1.052909
                  5
5: power
             TRUE 5
                        TRUE
                             TRUE 1.0580807 1.0575936 1.054137
6: power
                       FALSE FALSE 1.0532980 1.0532804 1.055866
             TRUE 10
7: power
             TRUE 10
                             TRUE 1.0679703 1.0676474 1.056350
                       FALSE
8: power
             TRUE 10
                        TRUE FALSE 1.0625603 1.0625641 1.062728
9: power
                             TRUE 1.0774122 1.0766805 1.063708
             TRUE 10
10: typeI
            FALSE
                  5
                        TRUE FALSE 1.0431774 1.0434979 1.046821
             TRUE
                       FALSE FALSE 0.9994186 0.9994094 1.019993
11: typeI
                  5
12: typeI
             TRUE
                       FALSE TRUE 0.9994042 0.9994106 1.020071
                  5
13: typeI
             TRUE
                        TRUE FALSE 1.0417925 1.0419051 1.045259
                  5
14: typeI
             TRUE
                             TRUE 1.0424393 1.0429751 1.045768
                  5
15: typeI
             TRUE 10
                       FALSE FALSE 0.9946568 0.9949442 1.052180
16: typeI
             TRUE 10
                             TRUE 0.9951513 0.9954542 1.051935
                       FALSE
17: typeI
             TRUE 10
                        TRUE FALSE 1.0462148 1.0458686 1.056152
                        TRUE TRUE 1.0462813 1.0476594 1.056027
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 79.53472
                                                              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
                                                                           11.028558
                                                              9.531225
4:
         1
              TRUE
                    5 typeI
                              TRUE
                                      TRUE 10000 79.44022
                                                              9.531225
                                                                           11.028558
         1
              TRUE 5 power
                                     FALSE 10000 79.71917
 5:
                              TRUE
                                                              9.427430
                                                                           10.853396
                                     FALSE 10000 79.71917
 6:
         1
              TRUE 5 typeI
                             TRUE
                                                              9.427430
                                                                           10.853396
7:
         1
              TRUE 5 power FALSE
                                     FALSE 10000 79.64196
                                                              9.449136
                                                                           10.908902
         1
              TRUE 5 typeI FALSE
                                     FALSE 10000 79.64196
                                                              9.449136
                                                                           10.908902
8:
9:
         1
             FALSE 5 power FALSE
                                      TRUE 10000 87.78863
                                                              6.090240
                                                                            6.121126
         1
             FALSE 5 typeI FALSE
                                      TRUE 10000 87.78863
10:
                                                              6.090240
                                                                            6.121126
         1
              TRUE 10 power FALSE
                                      TRUE 10000 71.60971
                                                             13.327969
                                                                           15.062319
11:
         1
              TRUE 10 typeI FALSE
                                      TRUE 10000 71.60971
12:
                                                             13.327969
                                                                           15.062319
         1
              TRUE 10 power
                                      TRUE 10000 71.52189
13:
                              TRUE
                                                             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
                                                                           14.996166
                                                             13.144488
              TRUE 10 typeI
16:
         1
                             TRUE
                                     FALSE 10000 71.85935
                                                             13.144488
                                                                           14.996166
17:
         1
              TRUE 10 power FALSE
                                     FALSE 10000 71.79364
                                                             13.168843
                                                                           15.037522
              TRUE 10 typeI FALSE
                                     FALSE 10000 71.79364
18:
         1
                                                             13.168843
                                                                           15.037522
```

10 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
                   FALSE FALSE 10 54.49750 54.64468 103.12067
            TRUE
      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.

³average over the reached stages