# $Results\ simulation\ study\ DelayedGSD$

October 26, 2023

# 1 Rejection rate

# 1.1 2 stages

Power by 1	method		(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	by metho	d (colum	ns) and	d sc	enario (ro	ws):		(nominal level $2.5\%$ )
scenario	n.sim	missing	binding	fixC	ar	method 1	method 2	method 3	
2	10000	TRUE	TRUE	FALSE	10	2.42%	2.39%	2.37%	
4	10000	TRUE	TRUE	FALSE	5	2.40%	2.40%	2.35%	
6	10000	TRUE	TRUE	TRUE	10	2.24%	2.22%	2.37%	
8	10000	TRUE	TRUE	TRUE	5	2.32%	2.31%	2.35%	
10	10000	TRUE	FALSE	TRUE	10	2.45%	2.47%	2.57%	
12	10000	TRUE	FALSE	TRUE	5	2.63%	2.64%	2.66%	
14	10000	TRUE	FALSE	FALSE	10	2.53%	2.53%	2.57%	
16	10000	TRUE	FALSE	FALSE	5	2.68%	2.68%	2.66%	
18	10000	FALSE	TRUE	FALSE	5	2.46%	2.46%	2.45%	

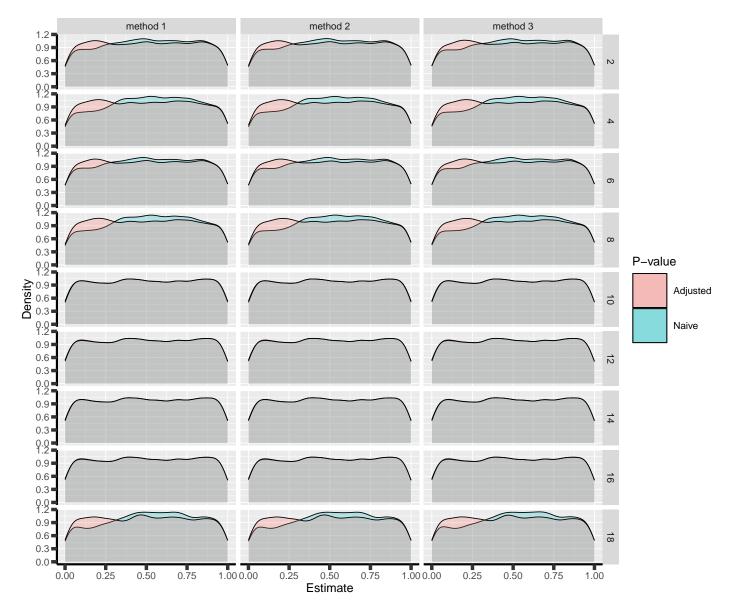


Figure 1: Naive and adjusted p-value distribution over all simulations under the null. Each row correspond to a different scenario

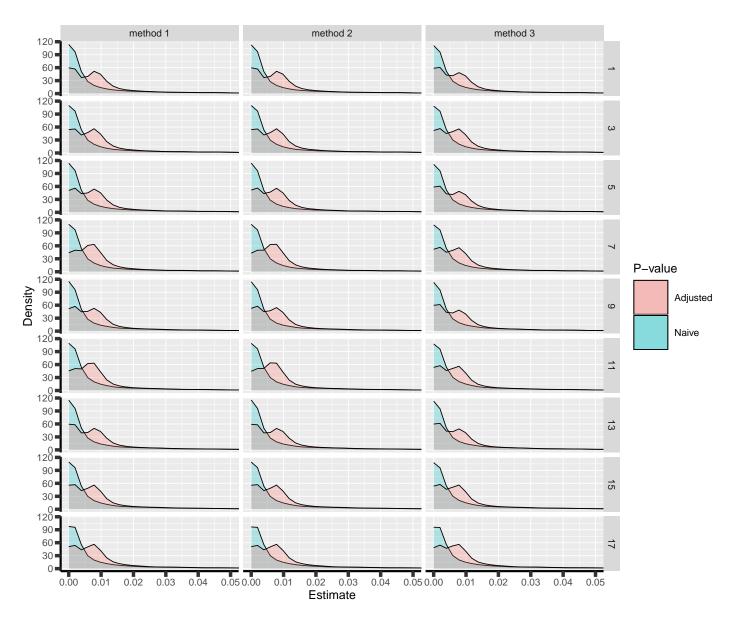


Figure 2: Naive and adjusted p-value distribution over all simulations under the alternative. Each row correspond to a different scenario

#### 1.2 3 stages

18 10000

**FALSE** 

TRUE FALSE 5

Power by method (columns) and scenario (rows): (nominal level 80%) scenario n.sim missing binding fixC ar method 1 method 2 method 3 1 10000 TRUE FALSE 10 TRUE 80.87% 80.79% 80.14% 9921 3 TRUE TRUE FALSE 5 80.57% 80.56% 80.08% 5 10000 TRUE TRUE TRUE 10 79.84% 80.05% 80.14% 7 9921 TRUE TRUE 5 79.98% 80.08% TRUE 80.08% 9 10000 TRUE FALSE TRUE 10 79.58% 79.94% 80.06% 11 10000 FALSE 79.92% 79.96% TRUE TRUE 80.15% 13 10000 TRUE FALSE FALSE 10 80.52% 80.44% 80.06% 15 10000 TRUE FALSE FALSE 5 80.44% 80.42% 79.96% 17 10000 **FALSE** TRUE FALSE 5 80.23% 80.21% 79.80% Type 1 error by method (columns) and scenario (rows): (nominal level 2.5%) scenario n.sim missing binding fixC ar method 1 method 2 method 3 2 10000 TRUE FALSE 10 2.48% TRUE 2.50% 2.38% 4 10000 2.43% 2.40% TRUE TRUE FALSE 5 2.42% 6 10000 TRUE 10 TRUE TRUE 2.31% 2.33% 2.38% 8 10000 TRUE TRUE TRUE 5 2.37% 2.36% 2.40% 10 10000 FALSE TRUE 10 2.44% 2.42% 2.52% TRUE 12 10000 TRUE TRUE FALSE 2.48% 2.48% 2.54% 14 10000 TRUE FALSE FALSE 10 2.54% 2.53% 2.52% 16 10000 FALSE FALSE 5 2.54% TRUE 2.61% 2.61%

2.57%

2.57%

2.48%

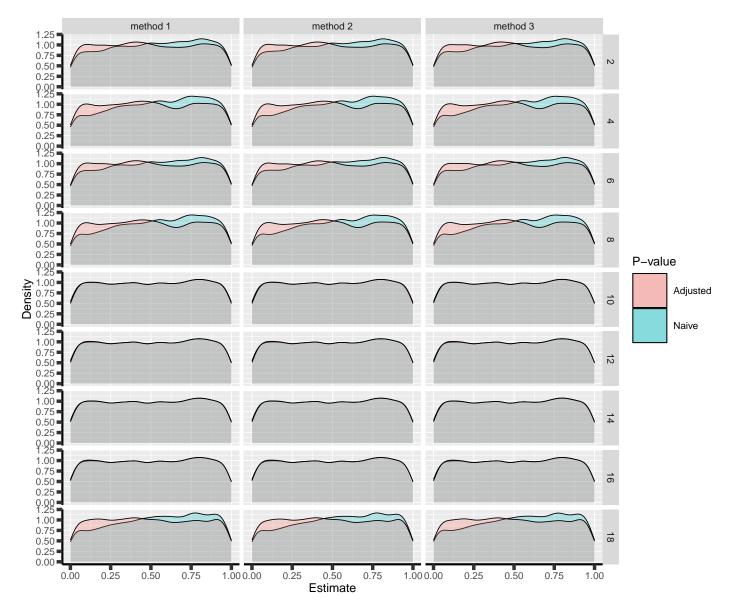


Figure 3: Naive and adjusted p-value distribution over all simulations under the null. Each row correspond to a different scenario

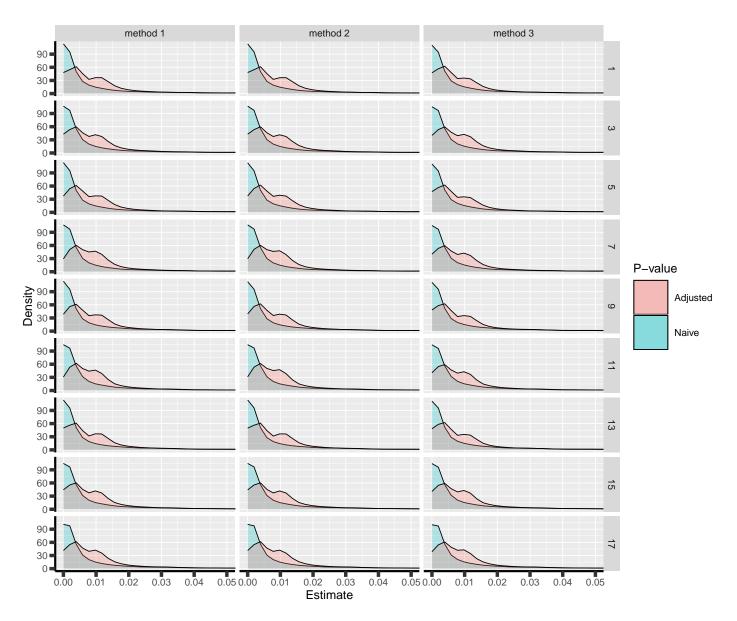


Figure 4: Naive and adjusted p-value distribution over all simulations under the alternative. Each row correspond to a different scenario

# 2 Conclusion of the trial

# **2.1 2** stages

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

#### • Method 1

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

# Method 2:

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

#### Method 3:

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

### Relative frequency of stopping for with a threshold below 1.96:

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

# **2.2 3** stages

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

### • Method 1

	N	missing	hypo	binding	fixC	ar	dec1.eff	dec1.fut	dec2.eff	dec2.fut	final.eff	final.fut
1:	10000	TRUE	power	TRUE	FALSE	10	19.91%	2.95%	29.31%	5.36%	31.65%	10.82%
2:	10000	TRUE	typeI	TRUE	FALSE	10	0.38%	46.24%	0.67%	35.38%	1.45%	15.88%
3:	9921	TRUE	power	TRUE	FALSE	5	18.33%	2.79%	28.75%	5.42%	33.48%	11.22%
4:	10000	TRUE	typeI	TRUE	FALSE	5	0.36%	44.03%	0.59%	36.50%	1.47%	17.05%
5:	10000	TRUE	power	TRUE	TRUE	10	19.39%	3.47%	28.80%	5.87%	31.65%	10.82%
6:	10000	TRUE	typeI	TRUE	TRUE	10	0.30%	46.32%	0.56%	35.49%	1.45%	15.88%
7:	9921	TRUE	power	TRUE	TRUE	5	18.07%	3.05%	28.42%	5.75%	33.48%	11.22%
8:	10000	TRUE	typeI	TRUE	TRUE	5	0.34%	44.05%	0.56%	36.53%	1.47%	17.05%
9:	10000	TRUE	power	FALSE	TRUE	10	20.80%	3.52%	27.86%	5.59%	30.92%	11.31%
10:	10000	TRUE	typeI	FALSE	TRUE	10	0.31%	0.10%	0.51%	0.63%	1.62%	96.83%
11:	10000	TRUE	power	FALSE	TRUE	5	19.31%	3.03%	28.11%	5.68%	32.50%	11.37%
12:	10000	TRUE	typeI	FALSE	TRUE	5	0.31%	0.04%	0.52%	0.10%	1.65%	97.38%
13:	10000	TRUE	power	FALSE	FALSE	10	21.28%	3.04%	28.32%	5.13%	30.92%	11.31%
14:	10000	TRUE	typeI	FALSE	FALSE	10	0.35%	0.06%	0.57%	0.57%	1.62%	96.83%
15:	10000	TRUE	power	FALSE	FALSE	5	19.50%	2.84%	28.44%	5.35%	32.50%	11.37%
16:	10000	TRUE	typeI	FALSE	FALSE	5	0.35%	0	0.61%	0.01%	1.65%	97.38%
17:	10000	FALSE	power	TRUE	FALSE	5	17.63%	2.93%	28.90%	5.11%	33.70%	11.73%
18:	10000	FALSE	typeI	TRUE	FALSE	5	0.48%	42.39%	0.71%	36.38%	1.38%	18.66%

### • Method 2

	N	missing	hypo	binding	fixC	ar	dec1.eff	dec1.fut	dec2.eff	dec2.fut	final.eff	final.fut
1:	10000	TRUE	power	TRUE	FALSE	10	19.94%	2.99%	29.32%	5.69%	31.53%	10.53%
2:	10000	TRUE	typeI	TRUE	FALSE	10	0.38%	46.48%	0.66%	35.66%	1.44%	15.38%
3:	9921	TRUE	power	TRUE	FALSE	5	18.34%	2.82%	28.81%	5.44%	33.40%	11.18%
4:	10000	TRUE	typeI	TRUE	FALSE	5	0.36%	44.08%	0.59%	36.47%	1.48%	17.02%
5:	10000	TRUE	power	TRUE	TRUE	10	19.17%	3.16%	28.74%	5.67%	32.14%	11.12%
6:	10000	TRUE	typeI	TRUE	TRUE	10	0.29%	44.63%	0.56%	36.01%	1.48%	17.03%
7:	9921	TRUE	power	TRUE	TRUE	5	17.92%	2.97%	28.25%	5.36%	33.91%	11.58%
8:	10000	TRUE	typeI	TRUE	TRUE	5	0.34%	43.09%	0.54%	36.68%	1.48%	17.87%
9:	10000	TRUE	power	FALSE	TRUE	10	20.72%	3.21%	27.71%	5.29%	31.51%	11.56%
10:	10000	TRUE	typeI	FALSE	TRUE	10	0.29%	0.10%	0.50%	0.49%	1.63%	96.99%
11:	10000	TRUE	power	FALSE	TRUE	5	19.19%	2.94%	28.01%	5.23%	32.95%	11.68%
12:	10000	TRUE	typeI	FALSE	TRUE	5	0.31%	0.04%	0.50%	0.09%	1.67%	97.39%
13:	10000	TRUE	power	FALSE	FALSE	10	21.30%	3.09%	28.33%	5.27%	30.81%	11.20%
14:	10000	TRUE	typeI	FALSE	FALSE	10	0.35%	0.06%	0.57%	0.58%	1.61%	96.83%
15:	10000	TRUE	power	FALSE	FALSE	5	19.51%	2.84%	28.44%	5.39%	32.47%	11.35%

16: 100	OO TRUE typeI	FALSE FALSE	5	0.35%	0	0.61%	0.01%	1.65%	97.38%
17: 100	00 FALSE power	TRUE FALSE	5	17.68%	2.94%	28.89%	5.17%	33.64%	11.68%
18: 100	00 FALSE typeI	TRUE FALSE	5	0.48%	42.46%	0.71%	36.41%	1.38%	18.56%

# • Method 3

	N	missing	hypo	binding	fixC	ar	${\tt dec1.eff}$	${\tt dec1.fut}$	dec2.eff	${\tt dec2.fut}$	${\tt final.eff}$	final.fut
1:	10000	TRUE	power	TRUE	FALSE	10	21.49%	3.26%	29.79%	5.96%	28.86%	10.64%
2:	10000	TRUE	typeI	TRUE	FALSE	10	0.32%	44.14%	0.60%	35.96%	1.46%	17.52%
3:	9921	TRUE	power	TRUE	FALSE	5	18.55%	3.10%	28.93%	5.47%	32.61%	11.34%
4:	10000	TRUE	typeI	TRUE	FALSE	5	0.37%	43.25%	0.56%	36.60%	1.47%	17.75%
5:	10000	TRUE	power	TRUE	TRUE	10	21.49%	3.26%	29.79%	5.96%	28.86%	10.64%
6:	10000	TRUE	typeI	TRUE	TRUE	10	0.32%	44.14%	0.60%	35.96%	1.46%	17.52%
7:	9921	TRUE	power	TRUE	TRUE	5	18.55%	3.10%	28.93%	5.47%	32.61%	11.34%
8:	10000	TRUE	typeI	TRUE	TRUE	5	0.37%	43.25%	0.56%	36.60%	1.47%	17.75%
9:	10000	TRUE	power	FALSE	TRUE	10	22.78%	3.32%	28.92%	5.74%	28.36%	10.88%
10:	10000	TRUE	typeI	FALSE	TRUE	10	0.33%	0.14%	0.65%	0.81%	1.54%	96.53%
11:	10000	TRUE	power	FALSE	TRUE	5	19.70%	3.12%	28.62%	5.49%	31.64%	11.43%
12:	10000	TRUE	typeI	FALSE	TRUE	5	0.32%	0.06%	0.59%	0.13%	1.63%	97.27%
13:	10000	TRUE	power	FALSE	FALSE	10	22.78%	3.32%	28.92%	5.74%	28.36%	10.88%
14:	10000	TRUE	typeI	FALSE	FALSE	10	0.33%	0.14%	0.65%	0.81%	1.54%	96.53%
15:	10000	TRUE	power	FALSE	FALSE	5	19.70%	3.12%	28.62%	5.49%	31.64%	11.43%
16:	10000	TRUE	typeI	FALSE	FALSE	5	0.32%	0.06%	0.59%	0.13%	1.63%	97.27%
17:	10000	FALSE	power	TRUE	FALSE	5	18.08%	3.12%	29.02%	5.26%	32.70%	11.82%
18:	10000	FALSE	typeI	TRUE	FALSE	5	0.41%	41.65%	0.68%	36.42%	1.39%	19.45%

Relative frequency of stopping for with a threshold below 1.96:

	scenario	missing	method	binding	fixC	ar	hypo	N	rejection	rejectionBelow196
1:	1	TRUE	1	TRUE	FALSE	10	power	10000	80.87%	1.03%
2:	1	TRUE	2	TRUE	FALSE	10	power	10000	80.79%	0.96%
3:	2	TRUE	1	TRUE	FALSE	10	typeI	10000	2.50%	0.19%
4:	2	TRUE	2	TRUE	FALSE	10	typeI	10000	2.48%	0.17%
5:	3	TRUE	1	TRUE	FALSE	5	power	9921	80.57%	0.58%
6:	3	TRUE	2	TRUE	FALSE	5	power	9921	80.56%	0.58%
7:	4	TRUE	1	TRUE	FALSE	5	typeI	10000	2.42%	0.05%
8:	4	TRUE	2	TRUE	FALSE	5	typeI	10000	2.43%	0.05%
9:	13	TRUE	1	FALSE	FALSE	10	power	10000	80.52%	0.94%
10:	13	TRUE	2	FALSE	FALSE	10	power	10000	80.44%	0.92%
11:	14	TRUE	1	FALSE	FALSE	10	typeI	10000	2.54%	0.10%
12:	14	TRUE	2	FALSE	FALSE	10	typeI	10000	2.53%	0.10%
13:	15	TRUE	1	FALSE	FALSE	5	power	10000	80.44%	0.52%
14:	15	TRUE	2	FALSE	FALSE	5	power	10000	80.42%	0.50%
15:	16	TRUE	1	FALSE	FALSE	5	typeI	10000	2.61%	0.13%
16:	16	TRUE	2	FALSE	FALSE	5	typeI	10000	2.61%	0.13%
17:	17	FALSE	1	TRUE	FALSE	5	power	10000	80.23%	0.52%
18:	17	FALSE	2	TRUE	FALSE	5	power	10000	80.21%	0.51%
19:	18	FALSE	1	TRUE	FALSE	5	typeI	10000	2.57%	0.18%
20:	18	FALSE	2	TRUE	FALSE	5	typeI	10000	2.57%	0.18%

### 3 Bias (True effect: 0.6 under the alternative)

#### 3.1 2 stages

Bias per estimator and method<sup>1</sup>:

```
hypo missing binding fixC ar biasMLE1 biasMLE2 biasMLE3 biasMUE1 biasMUE2 biasMUE3
                    TRUE FALSE 10 0.01345 0.01315 0.01468 0.00598 0.00566 -0.00286
1: power
            TRUE
2: typeI
                    TRUE FALSE 10 -0.01794 -0.01784 -0.01856 -0.00453 -0.00448 -0.00513
            TRUE
3: power
            TRUE
                    TRUE FALSE
                              5 0.02257 0.02255 0.02358 0.01044 0.01047 0.00364
4: typeI
            TRUE
                    TRUE FALSE
                               5 -0.03034 -0.03031 -0.03065 -0.01186 -0.01182 -0.01244
5: power
            TRUE
                    TRUE
                          TRUE 10
                                  0.01345 0.01403
                                                   0.01468 -0.01482 -0.01515 -0.00286
                          TRUE 10 -0.01794 -0.01871 -0.01856 -0.00553 -0.00619 -0.00513
6: typeI
            TRUE
                    TRUE
7: power
            TRUE
                    TRUE
                          TRUE
                               5
                                  0.02257
                                           0.02309
                                                    0.02358 -0.01511 -0.01521
                               5 -0.03034 -0.03085 -0.03065 -0.01249 -0.01307 -0.01244
8: typeI
            TRUE
                    TRUE
                          TRUE
9: power
            TRUE
                   FALSE
                          TRUE 10
                                  0.02897
10: typeI
            TRUE
                   FALSE
                          TRUE 10
                                   0.00019 0.00019 0.00051 -0.00087 -0.00079
                                                                               0.00073
11: power
            TRUE
                   FALSE
                          TRUE
                                   0.02366 0.02402
                                                    0.02438
                                                             0.01667 0.01524
                                                                               0.03653
12: typeI
            TRUE
                   FALSE
                          TRUE
                               5
                                  0.00091 0.00085 0.00101
                                                             0.00033 0.00027
                                                                               0.00086
13: power
            TRUE
                   FALSE FALSE 10
                                   0.01433 0.01416
                                                    0.01529
                                                             0.03552
                                                                     0.03589
                                                                               0.02897
14: typeI
            TRUE
                   FALSE FALSE 10
                                   0.00019 0.00019
                                                    0.00051 -0.00020 -0.00021
                                                                               0.00073
15: power
            TRUE
                   FALSE FALSE
                                   0.02366
                                           0.02365
                                                    0.02438
                                                             0.04186
                                                                     0.04202
                                                                               0.03653
16: typeI
            TRUE
                   FALSE FALSE
                                5
                                   0.00091
                                           0.00091
                                                    0.00101
                                                             0.00087
                                                                     0.00087
                                                                               0.00086
17: power
           FALSE
                    TRUE FALSE
                               5
                                  0.02284 0.02277
                                                    0.02381
                                                            0.01197 0.01196
                                                                               0.00412
18: typeI
           FALSE
                    TRUE FALSE
                               5 -0.02952 -0.02945 -0.02992 -0.01111 -0.01106 -0.01172
```

#### Median bias <sup>2</sup> per estimator and method:

	hypo	missing	binding	fixC	ar	${\tt mbiasMLE1}$	${\tt mbiasMLE2}$	${\tt mbiasMLE3}$	${\tt mbias MUE1}$	${\tt mbias MUE2}$	mbiasMUE3
1:	power	TRUE	TRUE	FALSE	10	0.0261	0.0260	0.0301	-0.00240	-0.00250	-0.00545
2:	typeI	TRUE	TRUE	FALSE	10	-0.0173	-0.0170	-0.0202	0.00100	0.00075	-0.00015
3:	power	TRUE	TRUE	FALSE	5	0.0405	0.0405	0.0432	-0.00345	-0.00335	-0.00545
4:	typeI	TRUE	TRUE	FALSE	5	-0.0330	-0.0329	-0.0345	0.00055	0.00055	0.00065
5:	power	TRUE	TRUE	TRUE	10	0.0261	0.0265	0.0301	-0.01110	-0.01050	-0.00545
6:	typeI	TRUE	TRUE	TRUE	10	-0.0173	-0.0197	-0.0202	0.00100	-0.00065	-0.00015
7:	power	TRUE	TRUE	TRUE	5	0.0405	0.0407	0.0432	-0.00865	-0.00755	-0.00545
8:	typeI	TRUE	TRUE	TRUE	5	-0.0330	-0.0346	-0.0345	0.00055	0.00075	0.00065
9:	power	TRUE	FALSE	TRUE	10	0.0326	0.0332	0.0327	0.02719	0.02475	0.02804
10:	typeI	TRUE	FALSE	TRUE	10	-0.0009	-0.0009	-0.0009	-0.00190	-0.00185	-0.00025
11:	power	TRUE	FALSE	TRUE	5	0.0462	0.0459	0.0489	0.02568	0.02469	0.02799
12:	typeI	TRUE	FALSE	TRUE	5	-0.0009	-0.0010	-0.0009	-0.00130	-0.00140	-0.00015
13:	power	TRUE	FALSE	FALSE	10	0.0326	0.0324	0.0327	0.03094	0.03184	0.02804
14:	typeI	TRUE	FALSE	FALSE	10	-0.0009	-0.0009	-0.0009	-0.00150	-0.00140	-0.00025
15:	power	TRUE	FALSE	FALSE	5	0.0462	0.0464	0.0489	0.02832	0.02865	0.02799

<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

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

# 3.2 3 stages

Bias per estimator and method<sup>3</sup>:

	hypo	${\tt missing}$	binding	fixC	ar	biasMLE1	biasMLE2	biasMLE3	biasMUE1	biasMUE2	biasMUE3
1:	power	TRUE	TRUE	FALSE	10	0.0228	0.0226	0.0248	0.01623	0.01605	0.0063
2:	typeI	TRUE	TRUE	FALSE	10	-0.0340	-0.0338	-0.0340	-0.01485	-0.01470	-0.0161
3:	power	TRUE	TRUE	FALSE	5	0.0345	0.0345	0.0357	0.02047	0.02041	0.0121
4:	typeI	TRUE	TRUE	FALSE	5	-0.0522	-0.0522	-0.0527	-0.02540	-0.02533	-0.0258
5:	power	TRUE	TRUE	TRUE	10	0.0228	0.0234	0.0248	-0.00558	-0.00569	0.0063
6:	typeI	TRUE	TRUE	TRUE	10	-0.0340	-0.0341	-0.0340	-0.01603	-0.01691	-0.0161
7:	power	TRUE	TRUE	TRUE	5	0.0345	0.0348	0.0357	-0.00620	-0.00639	0.0121
8:	typeI	TRUE	TRUE	TRUE	5	-0.0522	-0.0527	-0.0527	-0.02588	-0.02642	-0.0258
9:	power	TRUE	FALSE	TRUE	10	0.0223	0.0230	0.0246	0.03980	0.03755	0.0524
10:	typeI	TRUE	FALSE	TRUE	10	0.0011	0.0010	0.0014	-0.00021	-0.00038	0.0016
11:	power	TRUE	FALSE	TRUE	5	0.0343	0.0348	0.0351	0.03931	0.03719	0.0579
12:	typeI	TRUE	FALSE	TRUE	5	0.0017	0.0016	0.0019	0.00065	0.00066	0.0014
13:	power	TRUE	FALSE	FALSE	10	0.0223	0.0222	0.0246	0.05767	0.05820	0.0524
14:	typeI	TRUE	FALSE	FALSE	10	0.0011	0.0011	0.0014	0.00058	0.00057	0.0016
15:	power	TRUE	FALSE	FALSE	5	0.0343	0.0343	0.0351	0.06492	0.06503	0.0579
16:	typeI	TRUE	FALSE	FALSE	5	0.0017	0.0017	0.0019	0.00170	0.00170	0.0014
17:	power	FALSE	TRUE	FALSE	5	0.0346	0.0346	0.0360	0.02204	0.02206	0.0139
18:	typeI	FALSE	TRUE	FALSE	5	-0.0491	-0.0491	-0.0492	-0.02218	-0.02221	-0.0228

# Median bias $^4$ per estimator and method:

	hypo	missing	${\tt binding}$	fixC	ar	${\tt mbiasMLE1}$	${\tt mbiasMLE2}$	${\tt mbiasMLE3}$	mbiasMUE1	${\tt mbiasMUE2}$	mbiasMUE3
1:	power	TRUE	TRUE	FALSE	10	0.0359	0.0358	0.0374	-0.0037	-0.0040	-0.0095
2:	typeI	TRUE	TRUE	FALSE	10	-0.0367	-0.0365	-0.0380	0.0104	0.0100	0.0089
3:	power	TRUE	TRUE	FALSE	5	0.0551	0.0551	0.0565	-0.0045	-0.0043	-0.0087
4:	typeI	TRUE	TRUE	FALSE	5	-0.0556	-0.0557	-0.0574	0.0088	0.0088	0.0089
5:	power	TRUE	TRUE	TRUE	10	0.0359	0.0355	0.0374	-0.0166	-0.0172	-0.0095
6:	typeI	TRUE	TRUE	TRUE	10	-0.0367	-0.0379	-0.0380	0.0099	0.0090	0.0088
7:	power	TRUE	TRUE	TRUE	5	0.0551	0.0547	0.0565	-0.0167	-0.0168	-0.0087
8:	typeI	TRUE	TRUE	TRUE	5	-0.0556	-0.0569	-0.0574	0.0087	0.0088	0.0089
9:	power	TRUE	FALSE	TRUE	10	0.0321	0.0326	0.0358	0.0286	0.0250	0.0366
10:	typeI	TRUE	FALSE	TRUE	10	-0.0056	-0.0060	-0.0056	-0.0073	-0.0077	-0.0053
11:	power	TRUE	FALSE	TRUE	5	0.0498	0.0494	0.0502	0.0297	0.0259	0.0347
12:	typeI	TRUE	FALSE	TRUE	5	-0.0061	-0.0061	-0.0061	-0.0069	-0.0067	-0.0060
13:	power	TRUE	FALSE	FALSE	10	0.0321	0.0322	0.0358	0.0367	0.0376	0.0366
14:	typeI	TRUE	FALSE	FALSE	10	-0.0056	-0.0056	-0.0056	-0.0068	-0.0066	-0.0054
15:	power	TRUE	FALSE	FALSE	5	0.0498	0.0498	0.0502	0.0397	0.0398	0.0349
16:	typeI	TRUE	FALSE	FALSE	5	-0.0061	-0.0061	-0.0061	-0.0063	-0.0064	-0.0061
17:	power	FALSE	TRUE	FALSE	5	0.0573	0.0576	0.0595	0.0073	0.0074	0.0016

 $<sup>^3</sup>$ e.g. biasMLE1 mixed model estimator (treatment effect), method 1 (boundaries)

 $<sup>^4</sup>$ Relative frequency at which the estimate is greater than the truth minus 0.5

18: typeI FALSE TRUE FALSE 5 -0.0529 -0.0528 -0.0540 0.0097 0.0093 0.0100

# 4 Distribution of the estimates

# **4.1 2** stages

Distribution of the estimates:

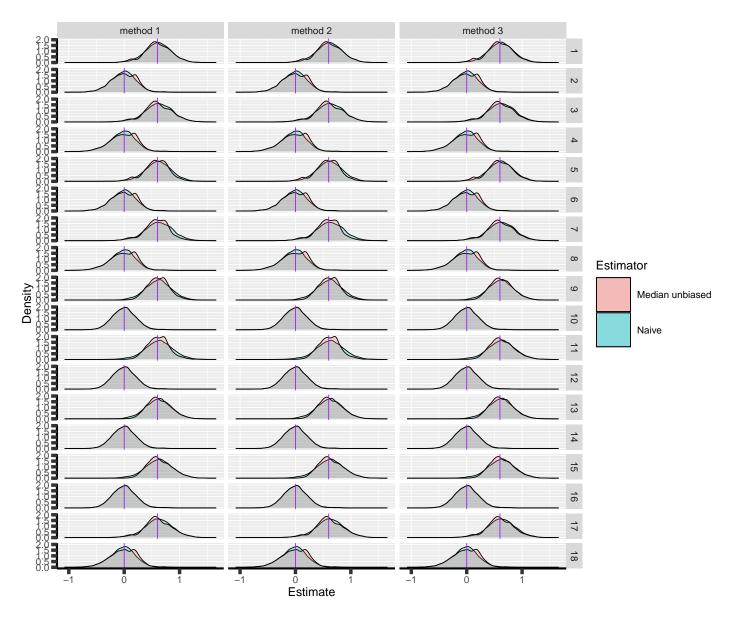


Figure 5: Naive and Median unbiased estimate distribution over all simulations. Each row correspond to a different scenario

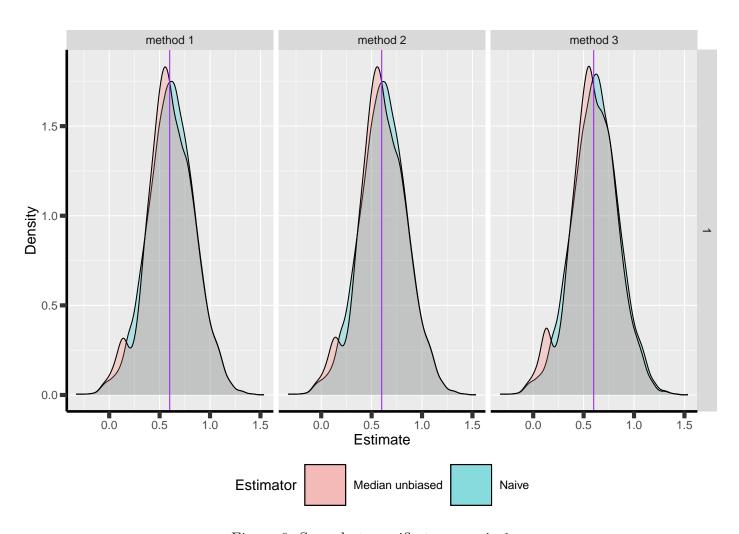


Figure 6: Same but specific to scenario 1

Distribution of the median unbiased estimate conditional to the stage:

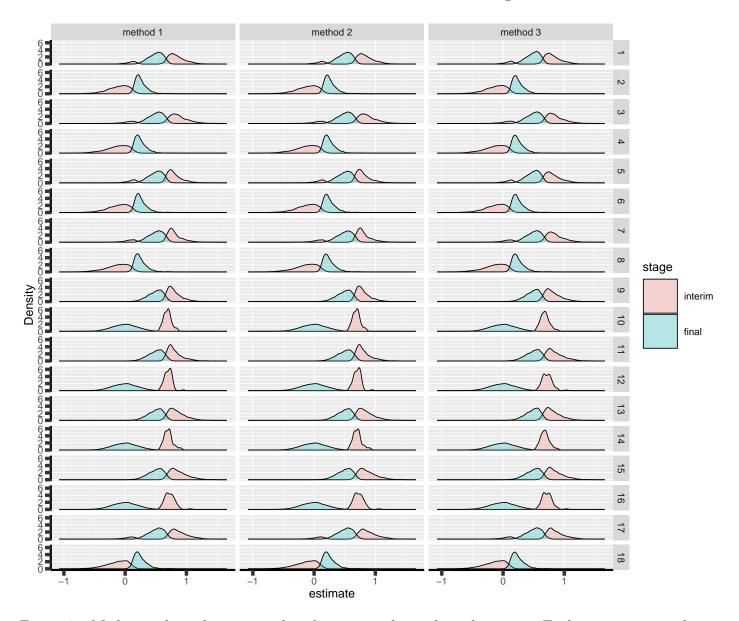


Figure 7: Median unbiased estimate distribution conditional to the stage. Each row correspond to a different scenario.

# **4.2 3** stages

Distribution of the estimates:

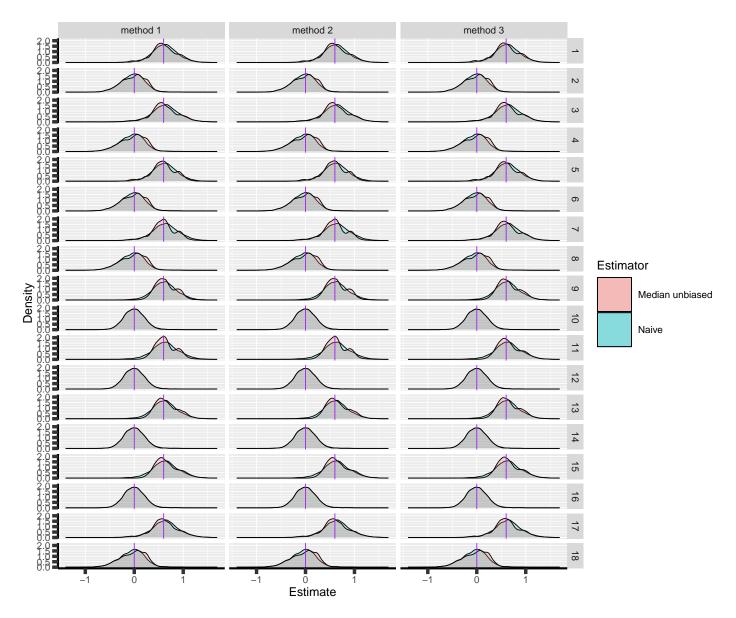


Figure 8: Naive and Median unbiased estimate distribution over all simulations. Each row correspond to a different scenario

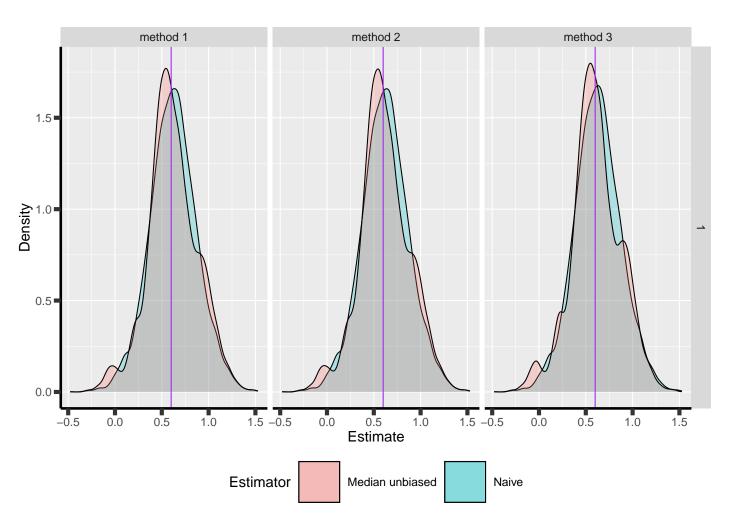


Figure 9: Same but specific to scenario 1

Distribution of the median unbiased estimate conditional to the stage:

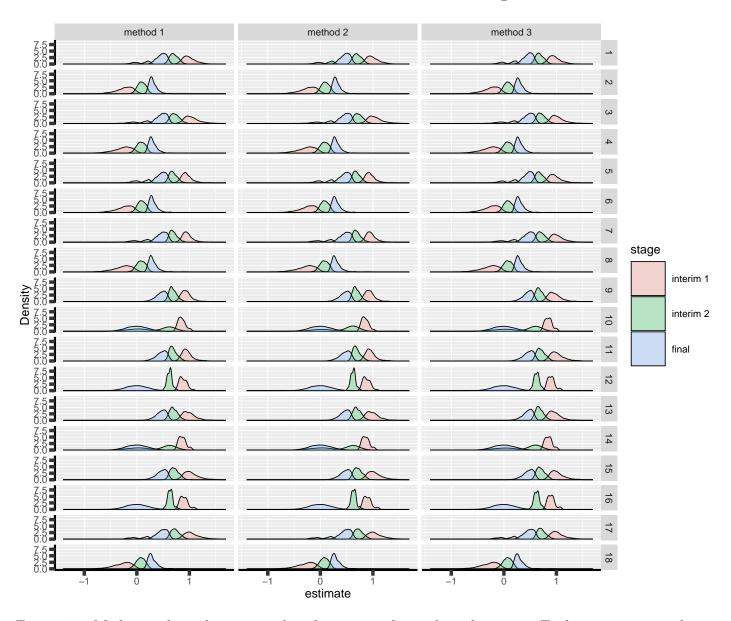


Figure 10: Median unbiased estimate distribution conditional to the stage. Each row correspond to a different scenario.

# 5 Special cases

# **5.1** 2 stages

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

		scenario	1	2	3	4	5	6	7	8		
reason	method											
decreasing information	1		0	0	1	1	0	0	1	1		
	2		0	0	1	1	0	0	1	1		
	3		0	0	1	1	0	0	1	1		
efficacy	1		3739	81	3573	74	3739	81	3573	74		
	2		3744	81	3576	74	3718	79	3545	71		
	3		4165	108	3721	82	4165	108	3721	82		
futility	1		632	7111	599	6932	632	7111	599	6932		
	2		659	7161	600	6938	574	6940	562	6828		
	3		545	6844	563	6828	545	6844	563	6828		
Imax reached	1		1	1	0	0	1	1	0	0		
	2		1	1	0	0	1	1	0	0		
	3		1	1	0	0	1	1	0	0		
no boundary crossed	1		5628	2807	5828	2994	5628	2807	5828	2994		
	2		5596	2757	5824	2988	5707	2980	5893	3101		
	3		5289	3047	5716	3090	5289	3047	5716	3090		
stop for futility at interim	1		0	0	0	0	0	0	0	0		
	2		0	0	0	0	0	0	0	0		
	3		11	1	2	0	11	1	2	0		
			0	10	11	10	10	1.1	1 =	16	17	10
	method	scenario	9	10	11	12	13	14	15	16	17	18
reason			3849	01	3680	76	3849	01	3680	76	3396	74
efficacy	1		3829		3661		3850		3683			74 74
	2				3831		4238		3831		3400	80
f.,+:1:+	3		4238	7122		6945		7122		6945	3528	
futility	1			6975		6838		7164		6950		6748 6755
	3			6890		6842		6890		6842		6642
no houndary around					5750							
no boundary crossed	1											
	2				5798 5626							
gton for futility at interior												
stop for futility at interim			0	0	0	0	0	0	0	0	0	0
	2		0	0	0	0	0	0	0	0	0	0
	3		8	0	0	0	8	0	0	0	1	0

**5.2 3** stages

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

	- , -	-		ĺ							
		scenario	1	2	3	4	5	6	7	8	
reason	method										
decreasing information	1		0	0	0	1	0	0	0	1	
	2		0	0	0	1	0	0	0	1	
	3		0	0	0	1	0	0	0	1	
efficacy	1		4871	107	4668	100	4871	107	4668	100	
	2		4873	107	4674	100	4846	105	4636	98	
	3		5264	136	4787	105	5264	136	4787	105	
futility	1		854	8147	818	8048	854	8147	818	8048	
	2		890	8198	824	8050	805	8034	772	7967	
	3		761	7951	774	7973	761	7951	774	7973	
Imax reached	1		28	13	0	0	28	13	0	0	
	2		31	13	0	0	23	10	0	0	
	3		25	15	0	0	25	15	0	0	
no boundary crossed	1		11961	7071	12260	7413	11961	7071	12260	7413	
	2		11913	6996	12244	7406	12093	7359	12361	7592	
	3		11475	7452	12133	7560	11475	7452	12133	7560	
stop for futility at interim	1		0	0	0	0	0	0	0	0	
	2		0	0	0	0	0	0	0	0	
	3		28	2	1	0	28	2	1	0	
		scenario	9	10	11	12	13	14	15	16	17
reason	method	Scenar 10	9	10	11	12	13	14	15	10	11
decreasing information	1		0	0	1	0	0	0	1	0	0
decreasing information	2		0	0	1	0	0	0	1	0	0
	3		0	0	1	0	0	0	1	0	0
efficacy	1		4912	112	4794		4912	112	4794	97	4643
ellicacy	2		4890	109	4771	94	4914	112	4797	97	4648
	3		5311	149	4921	110	5311	149	4921	110	4780
futility	1			12703		12404		12703		12404	814
Tuttitty	2			12441		12253		12774		12416	820
	3			12311		12273		12311		12273	768
Imax reached	1		24		0	0	24		0	0	0
imax reached	2		18		0	0	25	43	0	0	0
	3		24		0	0	25 24		0	_	0
no houndary areased			24 11791		12153		24 11791		12153	7464	
no boundary crossed	1				12153						12487
	2		11914				11762		12147		12470
	_		11314		12025		11314		12025		12332
stop for futility at interim	1		0	0	0	0	0	0	0	0	0

# 6 Reversal probability

# **6.1** 2 stages

Percentage of time we observe a reversal:

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

# **6.2** 3 stages

Percentage of time we observe a reversal:

	N	hypo	missing	ar	binding	fixC	${\tt fu2eff\_1}$	${\tt fu2eff\_2}$	${\tt fu2eff\_3}$	${\tt eff2fu\_1}$	${\tt eff2fu\_2}$	eff2fu_3
1:	10000	power	TRUE	10	TRUE	FALSE	0.68%	0.69%	0	0.39%	0.41%	1.55%
2:	10000	typeI	TRUE	10	TRUE	FALSE	0.12%	0.11%	0	0.14%	0.14%	0.44%
3:	9921	power	TRUE	5	TRUE	FALSE	0.13%	0.14%	0	0.10%	0.10%	0.78%
4:	10000	typeI	TRUE	5	TRUE	FALSE	0	0	0	0.05%	0.05%	0.12%
5:	10000	power	TRUE	10	TRUE	TRUE	0.36%	0.32%	0	1.10%	1.06%	1.55%
6:	10000	typeI	TRUE	10	TRUE	TRUE	0.04%	0.03%	0	0.25%	0.23%	0.44%
7:	9921	power	TRUE	5	TRUE	TRUE	0.01%	0.01%	0	0.56%	0.56%	0.78%
8:	10000	typeI	TRUE	5	TRUE	TRUE	0	0	0	0.10%	0.10%	0.12%
9:	10000	power	TRUE	10	FALSE	TRUE	0.36%	0.32%	0	1.00%	0.94%	1.60%
10:	10000	typeI	TRUE	10	FALSE	TRUE	0	0	0	0.30%	0.30%	0.51%
11:	10000	power	TRUE	5	FALSE	TRUE	0.02%	0.02%	0	0.54%	0.53%	0.89%
12:	10000	typeI	TRUE	5	FALSE	TRUE	0	0	0	0.14%	0.13%	0.19%
13:	10000	power	TRUE	10	FALSE	FALSE	0.68%	0.69%	0	0.38%	0.39%	1.60%
14:	10000	typeI	TRUE	10	FALSE	FALSE	0	0	0	0.20%	0.20%	0.51%
15:	10000	power	TRUE	5	FALSE	FALSE	0.11%	0.10%	0	0.11%	0.12%	0.89%
16:	10000	typeI	TRUE	5	FALSE	FALSE	0	0	0	0.01%	0.01%	0.19%
17:	10000	power	FALSE	5	TRUE	FALSE	0.15%	0.14%	0	0.05%	0.05%	0.70%
18:	10000	typeI	FALSE	5	TRUE	FALSE	0.06%	0.06%	0	0.03%	0.03%	0.17%

# 7 Logical consistency of p-values/CIs

# 7.1 Mismatch p-value / boundaries

#### 7.1.1 2 stages

When concluding for futility:

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

When concluding for efficacy:

	hypo	missing	ar	binding	fixC	${\tt method}$	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:	tvpeT	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:	tvpeI	FALSE	5	TRUE	FALSE	0	0	0

#### 7.1.2 3 stages

### When concluding for futility:

	hypo	missing	ar	binding	fixC	${\tt method}$	1	${\tt method}\ 2$	method 3
1:	power	TRUE	10	TRUE	FALSE		0	0.05%	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	0.05%	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	0.01%
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	0.05%
16:	typeI	TRUE	5	FALSE	FALSE		0	0	0.01%
17:	power	FALSE	5	TRUE	FALSE		0	0	0
18:	typeI	FALSE	5	TRUE	FALSE		0	0	0

#### Largest mismatch:

#### [1] 0.02499569043

# When concluding for efficacy:

	hypo	missing	ar	binding	fixC	${\tt method}$	1	${\tt method}$	2	method 3	3
1:	power	TRUE	10	TRUE	FALSE		0		0	C	)
2:	typeI	TRUE	10	TRUE	FALSE		0		0	C	)
3:	power	TRUE	5	TRUE	FALSE		0		0	C	)
4:	typeI	TRUE	5	TRUE	FALSE		0		0	C	)
5:	power	TRUE	10	TRUE	TRUE		0		0	C	)
6:	typeI	TRUE	10	TRUE	TRUE		0		0	C	)
7:	power	TRUE	5	TRUE	TRUE		0		0	0.01%	<b>'</b>
8:	typeI	TRUE	5	TRUE	TRUE		0		0	C	)
9:	power	TRUE	10	FALSE	TRUE		0		0	C	)
10:	typeI	TRUE	10	FALSE	TRUE		0		0	C	)
11:	power	TRUE	5	FALSE	TRUE		0		0	C	)
12:	typeI	TRUE	5	FALSE	TRUE		0		0	C	)
13:	power	TRUE	10	FALSE	FALSE		0	0.01	1%	0.01%	<b>%</b>
14:	typeI	TRUE	10	FALSE	FALSE		0		0	C	)
15:	power	TRUE	5	FALSE	FALSE		0		0	C	)

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	0.40%

Largest mismatch:

[1] 0.02500297183

# 7.2 Mismatch confidence intervals / boundaries

### **7.2.1** 2 stages

When concluding for futility:

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

When concluding for efficacy:

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

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

#### **7.2.2** 3 stages

When concluding for futility:

	hypo	missing	ar	binding	fixC		me	thod 1		method 2		method 3
1:	power	TRUE	10	TRUE	FALSE			0		C	0	(NA: 0.60%)
2:	typeI	TRUE	10	TRUE	FALSE			0		C	0	(NA: 0.02%)
3:	power	TRUE	5	TRUE	FALSE			0		C	0.05%	(NA: 0.10%)
4:	typeI	TRUE	5	TRUE	FALSE			0		C	)	0
5:	power	TRUE	10	TRUE	TRUE	0	(NA:	0.30%)	C	(NA: 0.45%)	0	(NA: 0.60%)
6:	typeI	TRUE	10	TRUE	TRUE	0	(NA:	0.02%)	C	(NA: 0.02%)	0	(NA: 0.02%)
7:	power	TRUE	5	TRUE	TRUE	0	(NA:	0.05%)	0.05%	(NA: 0.05%)	0	(NA: 0.10%)
8:	typeI	TRUE	5	TRUE	TRUE			0		C	)	0
9:	power	TRUE	10	FALSE	TRUE	0	(NA: 4	4.32%)	0	(NA: 42.22%)	0	(NA: 45.19%)
10:	typeI	TRUE	10	FALSE	TRUE	0	(NA:	0.31%)	C	(NA: 0.33%)	0	(NA: 0.52%)
11:	power	TRUE	5	FALSE	TRUE	0.09%	(NA: 4	3.38%)	0	(NA: 41.16%)	0	(NA: 42.96%)
12:	typeI	TRUE	5	FALSE	TRUE	0	(NA:	0.14%)	O	(NA: 0.13%)	0.01%	(NA: 0.19%)
13:	power	TRUE	10	FALSE	FALSE	0	(NA: 4	1.63%)	0	(NA: 42.43%)	0	(NA: 45.19%)
14:	typeI	TRUE	10	FALSE	FALSE	0	(NA:	0.21%)	O	(NA: 0.23%)	0	(NA: 0.52%)
15:	power	TRUE	5	FALSE	FALSE	0.09%	(NA: 4	1.87%)	0.09%	(NA: 42.03%)	0	(NA: 42.96%)
16:	typeI	TRUE	5	FALSE	FALSE	0	(NA:	0.01%)	O	(NA: 0.01%)	0	(NA: 0.19%)
17:	power	FALSE	5	TRUE	FALSE			0		C	0	(NA: 0.20%)
18:	typeI	FALSE	5	TRUE	FALSE			0		C	)	0

#### Largest mismatch:

#### [1] 0.002466353937

### When concluding for efficacy:

	hypo	${\tt missing}$	ar	binding	fixC		me	ethod 1		me	ethod 2		me	ethod 3
1:	power	TRUE	10	TRUE	FALSE	0	(NA:	0.04%)	0	(NA:	0.04%)			0
2:	typeI	TRUE	10	TRUE	FALSE			0			0			0
3:	power	TRUE	5	TRUE	FALSE	0	(NA:	0.01%)	0	(NA:	0.03%)	0	(NA:	0.01%)
4:	typeI	TRUE	5	TRUE	FALSE			0			0.41%			0
5:	power	TRUE	10	TRUE	TRUE	0	(NA:	0.04%)	0	(NA:	0.02%)			0
6:	typeI	TRUE	10	TRUE	TRUE			0			0			0
7:	power	TRUE	5	TRUE	TRUE	0	(NA:	0.01%)	0	(NA:	0.03%)	0	(NA:	0.01%)
8:	typeI	TRUE	5	TRUE	TRUE			0			0			0
9:	power	TRUE	10	FALSE	TRUE	0.01%	(NA:	0.01%)	0	(NA:	0.01%)	0.01%	(NA:	0.01%)
10:	typeI	TRUE	10	FALSE	TRUE			0			0			0
11:	power	TRUE	5	FALSE	TRUE	0	(NA:	0.01%)	0	(NA:	0.01%)	0	(NA:	0.01%)

```
12: typeI
           TRUE 5 FALSE TRUE
13: power
           TRUE 10 FALSE FALSE 0.01% (NA: 0.01%) 0.01% (NA: 0.01%) 0.01% (NA: 0.01%)
14: typeI
           TRUE 10
                   FALSE FALSE
                                                             0
15: power
         TRUE 5 FALSE FALSE
                                  O (NA: 0.01%) O (NA: 0.01%) O.01% (NA: 0.01%)
16: typeI
         TRUE 5 FALSE FALSE
                                                             0
17: power
                   TRUE FALSE
                                                  O (NA: 0.01%) 0.01% (NA: 0.01%)
          FALSE 5
                                  O (NA: 0.01%)
18: typeI
          FALSE 5
                     TRUE FALSE
                                          0.39%
                                                             0
```

[1] -0.005759153782

### 7.3 Range of p-values

#### **7.3.1** 2 stages

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

### **7.3.2** 3 stages

	missing	binding	fixC	ar	hypo	method 1	method 2	method 3
1:	TRUE	TRUE	FALSE	10	power	[0;0.9547]	[0;0.9547]	[0;0.9547]
2:	TRUE	TRUE	FALSE	10	typeI	[2e-04;0.9999]	[2e-04;0.9999]	[4e-04;0.9999]
3:	TRUE	TRUE	FALSE	5	power	[0;0.9954]	[0;0.9954]	[0;0.9954]
4:	TRUE	TRUE	FALSE	5	typeI	[1e-04;1]	[1e-04;1]	[1e-04;1]
5:	TRUE	TRUE	TRUE	10	power	[0;0.9547]	[0;0.9547]	[0;0.9547]
6:	TRUE	TRUE	TRUE	10	typeI	[6e-04;0.9999]	[6e-04;0.9999]	[4e-04;0.9999]
7:	TRUE	TRUE	TRUE	5	power	[0;0.9954]	[0;0.9954]	[0;0.9954]
8:	TRUE	TRUE	TRUE	5	typeI	[5e-04;1]	[5e-04;1]	[1e-04;1]
9:	TRUE	FALSE	TRUE	10	power	[0;1]	[0;1]	[0;1]
10:	TRUE	FALSE	TRUE	10	typeI	[6e-04;1]	[6e-04;1]	[3e-04;1]
11:	TRUE	FALSE	TRUE	5	power	[0;1]	[0;1]	[0;1]
12:	TRUE	FALSE	TRUE	5	typeI	[6e-04;1]	[6e-04;1]	[1e-04;1]
13:	TRUE	FALSE	FALSE	10	power	[0;1]	[0;1]	[0;1]
14:	TRUE	FALSE	FALSE	10	typeI	[2e-04;1]	[2e-04;1]	[3e-04;1]
15:	TRUE	FALSE	FALSE	5	power	[0;1]	[0;1]	[0;1]
16:	TRUE	FALSE	FALSE	5	typeI	[1e-04;1]	[1e-04;1]	[1e-04;1]
17:	FALSE	TRUE	FALSE	5	power	[0;0.9812]	[0;0.9812]	[0;0.9812]
18:	FALSE	TRUE	FALSE	5	typeI	[4e-04;1]	[4e-04;1]	[4e-04;1]

### 8 Coverage

#### 8.1 2 stages

```
hypo missing ar binding fixC
                                             method 1
                                                                 method 2
                                                                                    method 3
 1: power
            FALSE
                        TRUE FALSE 94.79% (NA: 0.02%) 94.79% (NA: 0.02%) 95.31% (NA: 0.02%)
                       FALSE FALSE 95.86% (NA: 5.72%) 95.86% (NA: 5.76%) 95.97% (NA: 5.48%)
2: power
             TRUE
             TRUE
                             TRUE 97.77% (NA: 6.16%) 97.76% (NA: 5.86%) 95.97% (NA: 5.48%)
3: power
                  5
                       FALSE
4: power
             TRUE
                        TRUE FALSE
                                                94.73%
                                                                   94.73%
             TRUE 5
                        TRUE TRUE
                                                96.28%
                                                                   96.32%
5: power
                                                                                      95.13%
6: power
             TRUE 10
                       FALSE FALSE 95.90% (NA: 5.95%) 95.89% (NA: 6.11%) 96.07% (NA: 5.30%)
                              TRUE 97.38% (NA: 6.59%) 97.45% (NA: 6.06%) 96.07% (NA: 5.30%)
7: power
             TRUE 10
8: power
             TRUE 10
                        TRUE FALSE 94.84% (NA: 0.02%) 94.82% (NA: 0.02%) 95.34% (NA: 0.02%)
                              TRUE 96.26% (NA: 0.02%) 96.31% (NA: 0.02%) 95.34% (NA: 0.02%)
9: power
             TRUE 10
10: typeI
            FALSE
                        TRUE FALSE 95.13% (NA: 0.15%) 95.13% (NA: 0.15%) 95.14% (NA: 0.17%)
                       FALSE FALSE 94.87% (NA: 0.01%) 94.87% (NA: 0.01%) 94.96% (NA: 0.09%)
11: typeI
             TRUE
                             TRUE 94.92% (NA: 0.06%) 94.91% (NA: 0.06%) 94.96% (NA: 0.09%)
12: typeI
             TRUE
13: typeI
             TRUE 5
                        TRUE FALSE 94.81% (NA: 0.14%) 94.81% (NA: 0.14%) 94.86% (NA: 0.14%)
             TRUE
                             TRUE 94.89% (NA: 0.14%) 94.90% (NA: 0.12%) 94.86% (NA: 0.14%)
14: typeI
                  5
             TRUE 10
                       FALSE FALSE 95.01% (NA: 0.12%) 95.01% (NA: 0.12%) 95.29% (NA: 0.33%)
15: typeI
             TRUE 10
                              TRUE 95.09% (NA: 0.20%) 95.07% (NA: 0.19%) 95.29% (NA: 0.33%)
16: typeI
                       FALSE
17: typeI
             TRUE 10
                        TRUE FALSE 95.16% (NA: 0.09%) 95.19% (NA: 0.10%) 95.20% (NA: 0.13%)
18: typeI
             TRUE 10
                             TRUE 95.34% (NA: 0.09%) 95.36% (NA: 0.07%) 95.20% (NA: 0.13%)
```

#### Average width of the confidence intervals

	hypo	missing	ar	${\tt binding}$	fixC	${\tt method}\ 1$	${\tt method}\ 2$	method 3
1:	power	FALSE	5	TRUE	FALSE	1.0517	1.0517	1.053
2:	power	TRUE	5	FALSE	FALSE	1.0355	1.0355	1.036
3:	power	TRUE	5	FALSE	TRUE	1.0410	1.0414	1.036
4:	power	TRUE	5	TRUE	FALSE	1.0512	1.0512	1.052
5:	power	TRUE	5	TRUE	TRUE	1.0573	1.0571	1.052
6:	power	TRUE	10	FALSE	FALSE	1.0465	1.0463	1.046
7:	power	TRUE	10	FALSE	TRUE	1.0531	1.0541	1.046
8:	power	TRUE	10	TRUE	FALSE	1.0623	1.0625	1.061
9:	power	TRUE	10	TRUE	TRUE	1.0700	1.0697	1.061
10:	typeI	FALSE	5	TRUE	FALSE	1.0427	1.0427	1.046
11:	typeI	TRUE	5	FALSE	FALSE	0.9995	0.9994	1.012
12:	typeI	TRUE	5	FALSE	TRUE	0.9994	0.9995	1.012
13:	typeI	TRUE	5	TRUE	FALSE	1.0412	1.0411	1.045
14:	typeI	TRUE	5	TRUE	TRUE	1.0413	1.0420	1.045
15:	typeI	TRUE	10	FALSE	FALSE	0.9927	0.9926	1.040
16:	typeI	TRUE	10	FALSE	TRUE	0.9926	0.9935	1.040
17:	typeI	TRUE	10	TRUE	FALSE	1.0456	1.0450	1.056
18:	typeI	TRUE	10	TRUE	TRUE	1.0457	1.0475	1.056

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

	hypo	missing	ar	binding	fixC	method 1	method 2	method 3
1:	power	FALSE	5	TRUE	FALSE	1.0553	1.0553	1.056
2:	power	TRUE	5	FALSE	FALSE	1.0476	1.0476	1.049
3:	power	TRUE	5	FALSE	TRUE	1.0530	1.0529	1.049
4:	power	TRUE	5	TRUE	FALSE	1.0555	1.0556	1.056
5:	power	TRUE	5	TRUE	TRUE	1.0608	1.0605	1.056
6:	power	TRUE	10	FALSE	FALSE	1.0534	1.0533	1.053
7:	power	TRUE	10	FALSE	TRUE	1.0601	1.0605	1.053
8:	power	TRUE	10	TRUE	FALSE	1.0640	1.0643	1.062
9:	power	TRUE	10	TRUE	TRUE	1.0710	1.0706	1.062
10:	typeI	FALSE	5	TRUE	FALSE	1.0489	1.0488	1.053
11:	typeI	TRUE	5	FALSE	FALSE	0.9994	0.9994	1.013
12:	typeI	TRUE	5	FALSE	TRUE	0.9995	0.9996	1.013
13:	typeI	TRUE	5	TRUE	FALSE	1.0478	1.0478	1.052
14:	typeI	TRUE	5	TRUE	TRUE	1.0479	1.0487	1.052
15:	typeI	TRUE	10	FALSE	FALSE	0.9928	0.9926	1.041
16:	typeI	TRUE	10	FALSE	TRUE	0.9928	0.9937	1.041
17:	typeI	TRUE	10	TRUE	FALSE	1.0492	1.0486	1.060
18:	typeI	TRUE	10	TRUE	TRUE	1.0493	1.0511	1.060

#### **8.2 3** stages

```
hypo missing ar binding fixC
                                             method 1
                                                                 method 2
                                                                                    method 3
 1: power
                  5
            FALSE
                        TRUE FALSE 94.91% (NA: 0.01%) 94.91% (NA: 0.01%) 95.52% (NA: 0.01%)
                       FALSE FALSE 96.43% (NA: 8.21%) 96.46% (NA: 8.25%) 96.25% (NA: 7.78%)
2: power
             TRUE
                             TRUE 98.42% (NA: 8.73%) 98.43% (NA: 8.19%) 96.26% (NA: 7.78%)
3: power
             TRUE
                  5
                       FALSE
4: power
             TRUE
                        TRUE FALSE 95.36% (NA: 0.02%) 95.33% (NA: 0.03%) 95.90% (NA: 0.03%)
                             TRUE 97.20% (NA: 0.02%) 97.21% (NA: 0.03%) 95.90% (NA: 0.03%)
5: power
             TRUE 5
             TRUE 10
                       FALSE FALSE 96.08% (NA: 8.13%) 96.08% (NA: 8.32%) 95.68% (NA: 7.49%)
6: power
7: power
             TRUE 10
                              TRUE 98.03% (NA: 9.06%) 98.06% (NA: 8.48%) 95.68% (NA: 7.49%)
             TRUE 10
                        TRUE FALSE 95.30% (NA: 0.03%) 95.28% (NA: 0.03%) 95.67% (NA: 0.05%)
8: power
9: power
             TRUE 10
                              TRUE 96.81% (NA: 0.04%) 96.75% (NA: 0.05%) 95.67% (NA: 0.05%)
                        TRUE FALSE 95.14% (NA: 0.10%) 95.12% (NA: 0.11%) 95.21% (NA: 0.11%)
10: typeI
            FALSE 5
                       FALSE FALSE 94.97% (NA: 0.03%) 95.00% (NA: 0.03%) 95.10% (NA: 0.21%)
11: typeI
             TRUE
                  5
                             TRUE 95.09% (NA: 0.16%) 95.10% (NA: 0.15%) 95.11% (NA: 0.21%)
12: typeI
             TRUE
                  5
             TRUE 5
                        TRUE FALSE 95.08% (NA: 0.08%) 95.08% (NA: 0.08%) 95.10% (NA: 0.08%)
13: typeI
14: typeI
             TRUE
                        TRUE
                             TRUE 95.13% (NA: 0.08%) 95.14% (NA: 0.07%) 95.10% (NA: 0.08%)
                  5
                       FALSE FALSE 95.05% (NA: 0.20%) 95.11% (NA: 0.22%) 95.41% (NA: 0.51%)
15: typeI
             TRUE 10
16: typeI
             TRUE 10
                              TRUE 95.15% (NA: 0.30%) 95.21% (NA: 0.32%) 95.43% (NA: 0.51%)
                       FALSE
17: typeI
             TRUE 10
                        TRUE FALSE 94.89% (NA: 0.16%) 94.91% (NA: 0.16%) 95.01% (NA: 0.22%)
18: typeI
             TRUE 10
                              TRUE 95.08% (NA: 0.18%) 95.06% (NA: 0.16%) 95.01% (NA: 0.22%)
```

#### Average width of the confidence intervals

	hypo	${\tt missing}$	ar	${\tt binding}$	fixC	method 1	method 2	method 3
1:	power	FALSE	5	TRUE	FALSE	1.0729	1.0729	1.073
2:	power	TRUE	5	FALSE	FALSE	1.0547	1.0548	1.055
3:	power	TRUE	5	FALSE	TRUE	1.0588	1.0588	1.055
4:	power	TRUE	5	TRUE	FALSE	1.0723	1.0724	1.072
5:	power	TRUE	5	TRUE	TRUE	1.0765	1.0760	1.073
6:	power	TRUE	10	FALSE	FALSE	1.0794	1.0793	1.079
7:	power	TRUE	10	FALSE	TRUE	1.0860	1.0865	1.079
8:	power	TRUE	10	TRUE	FALSE	1.0984	1.0984	1.097
9:	power	TRUE	10	TRUE	TRUE	1.1052	1.1040	1.097
10:	typeI	FALSE	5	TRUE	FALSE	1.0752	1.0751	1.079
11:	typeI	TRUE	5	FALSE	FALSE	0.9957	0.9956	1.012
12:	typeI	TRUE	5	FALSE	TRUE	0.9954	0.9955	1.012
13:	typeI	TRUE	5	TRUE	FALSE	1.0718	1.0718	1.076
14:	typeI	TRUE	5	TRUE	TRUE	1.0719	1.0724	1.076
15:	typeI	TRUE	10	FALSE	FALSE	0.9873	0.9881	1.053
16:	typeI	TRUE	10	FALSE	TRUE	0.9870	0.9875	1.053
17:	typeI	TRUE	10	TRUE	FALSE	1.0976	1.0972	1.109
18:	typeI	TRUE	10	TRUE	TRUE	1.0977	1.0983	1.109

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

	hypo	missing	ar	binding	fixC	method 1	method 2	method 3
1:	power	FALSE	5	TRUE	FALSE	1.0752	1.0753	1.075
2:	power	TRUE	5	FALSE	FALSE	1.0654	1.0654	1.066
3:	power	TRUE	5	FALSE	TRUE	1.0685	1.0682	1.066
4:	power	TRUE	5	TRUE	FALSE	1.0755	1.0756	1.076
5:	power	TRUE	5	TRUE	TRUE	1.0782	1.0776	1.076
6:	power	TRUE	10	FALSE	FALSE	1.0846	1.0844	1.085
7:	power	TRUE	10	FALSE	TRUE	1.0907	1.0905	1.085
8:	power	TRUE	10	TRUE	FALSE	1.0985	1.0985	1.097
9:	power	TRUE	10	TRUE	TRUE	1.1039	1.1027	1.097
10:	typeI	FALSE	5	TRUE	FALSE	1.0820	1.0818	1.086
11:	typeI	TRUE	5	FALSE	FALSE	0.9955	0.9954	1.013
12:	typeI	TRUE	5	FALSE	TRUE	0.9955	0.9956	1.013
13:	typeI	TRUE	5	TRUE	FALSE	1.0792	1.0792	1.084
14:	typeI	TRUE	5	TRUE	TRUE	1.0793	1.0797	1.084
15:	typeI	TRUE	10	FALSE	FALSE	0.9873	0.9882	1.054
16:	typeI	TRUE	10	FALSE	TRUE	0.9873	0.9878	1.054
17:	typeI	TRUE	10	TRUE	FALSE	1.1025	1.1021	1.115
18:	typeI	TRUE	10	TRUE	TRUE	1.1026	1.1030	1.115

# 9 Percentage of missing values (2 stages)

At the first interim

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

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

	${\tt method}$	missing	ar	hypo	fixC	${\tt binding}$	N	<pre>pc.all</pre>	${\tt pc.missing3}$	pc.missing23
1:	1	TRUE	5	power	FALSE	TRUE	10000	79.52	9.591	10.888
2:	1	TRUE	5	typeI	FALSE	TRUE	10000	79.52	9.591	10.888
3:	1	TRUE	5	power	TRUE	TRUE	10000	79.52	9.591	10.888
4:	1	TRUE	5	typeI	TRUE	TRUE	10000	79.52	9.591	10.888
5:	1	TRUE	5	power	TRUE	FALSE	10000	79.64	9.442	10.914
6:	1	TRUE	5	typeI	TRUE	FALSE	10000	79.64	9.442	10.914
7:	1	TRUE	5	power	FALSE	FALSE	10000	79.64	9.442	10.914
8:	1	TRUE	5	typeI	FALSE	FALSE	10000	79.64	9.442	10.914
9:	1	FALSE	5	power	FALSE	TRUE	10000	87.79	6.090	6.121
10:	1	FALSE	5	typeI	FALSE	TRUE	10000	87.79	6.090	6.121
11:	1	TRUE	10	power	FALSE	TRUE	10000	71.60	13.354	15.049
12:	1	TRUE	10	typeI	FALSE	TRUE	10000	71.60	13.354	15.049
13:	1	TRUE	10	power	TRUE	TRUE	10000	71.60	13.354	15.049
14:	1	TRUE	10	typeI	TRUE	TRUE	10000	71.60	13.354	15.049
15:	1	TRUE	10	power	TRUE	FALSE	10000	71.80	13.162	15.042
16:	1	TRUE	10	typeI	TRUE	FALSE	10000	71.80	13.162	15.042
17:	1	TRUE	10	power	FALSE	FALSE	10000	71.80	13.162	15.042
18:	1	TRUE	10	typeI	FALSE	FALSE	10000	71.80	13.162	15.042

# 10 Information

### 10.1 2 stages

Percentage of information for method  $1^5$ :

```
scenario missing binding fixC ar interim decision final
                    TRUE FALSE 10
                                    54.64
                                             75.34 102.70
       1
            TRUE
       2
            TRUE
                    TRUE FALSE 10
                                    54.64
                                             74.98 102.37
       3
                                             64.04 102.74
            TRUE
                    TRUE FALSE 5
                                    53.27
       4
            TRUE
                    TRUE FALSE 5
                                    53.27
                                             63.58 102.37
      13
            TRUE
                   FALSE FALSE 10
                                    54.50
                                             74.96 102.54
                   FALSE FALSE 10
                                    54.50
                                             75.17 103.13
      14
            TRUE
      15
            TRUE
                   FALSE FALSE 5
                                    53.16
                                             63.72 102.63
                   FALSE FALSE 5
                                    53.16
                                             64.61 103.13
      16
            TRUE
           FALSE
      17
                    TRUE FALSE 5
                                    52.07
                                             63.77 99.97
                    TRUE FALSE 5
      18
           FALSE
                                    52.07
                                             63.22 99.63
```

Similar results for other methods.

#### 10.2 3 stages

Percentage of information for method  $1^6$ :

scenario	missing	binding	fixC	ar	$\verb"interim1"$	decision1	${\tt interim2}$	${\tt decision2}$	final3
1	TRUE	TRUE	FALSE	10	38.86	59.57	64.51	85.16	102.36
2	TRUE	TRUE	FALSE	10	38.86	59.16	64.31	84.25	102.24
3	TRUE	TRUE	FALSE	5	37.56	48.40	63.18	73.86	102.46
4	TRUE	TRUE	FALSE	5	37.56	48.00	62.95	73.10	102.23
13	TRUE	FALSE	FALSE	10	38.82	59.12	64.30	84.50	102.19
14	TRUE	FALSE	FALSE	10	38.82	60.66	64.58	90.57	103.04
15	TRUE	FALSE	FALSE	5	37.54	48.15	62.99	73.43	102.29
16	TRUE	FALSE	FALSE	5	37.54	50.04	63.24	74.77	103.11
17	FALSE	TRUE	FALSE	5	36.91	48.66	61.76	73.28	99.66
18	FALSE	TRUE	FALSE	5	36.91	48.19	61.53	72.56	99.38

 $<sup>^5</sup>$ average over the reached stages

<sup>&</sup>lt;sup>6</sup>average over the reached stages