Understanding variation in n-of-1 trials

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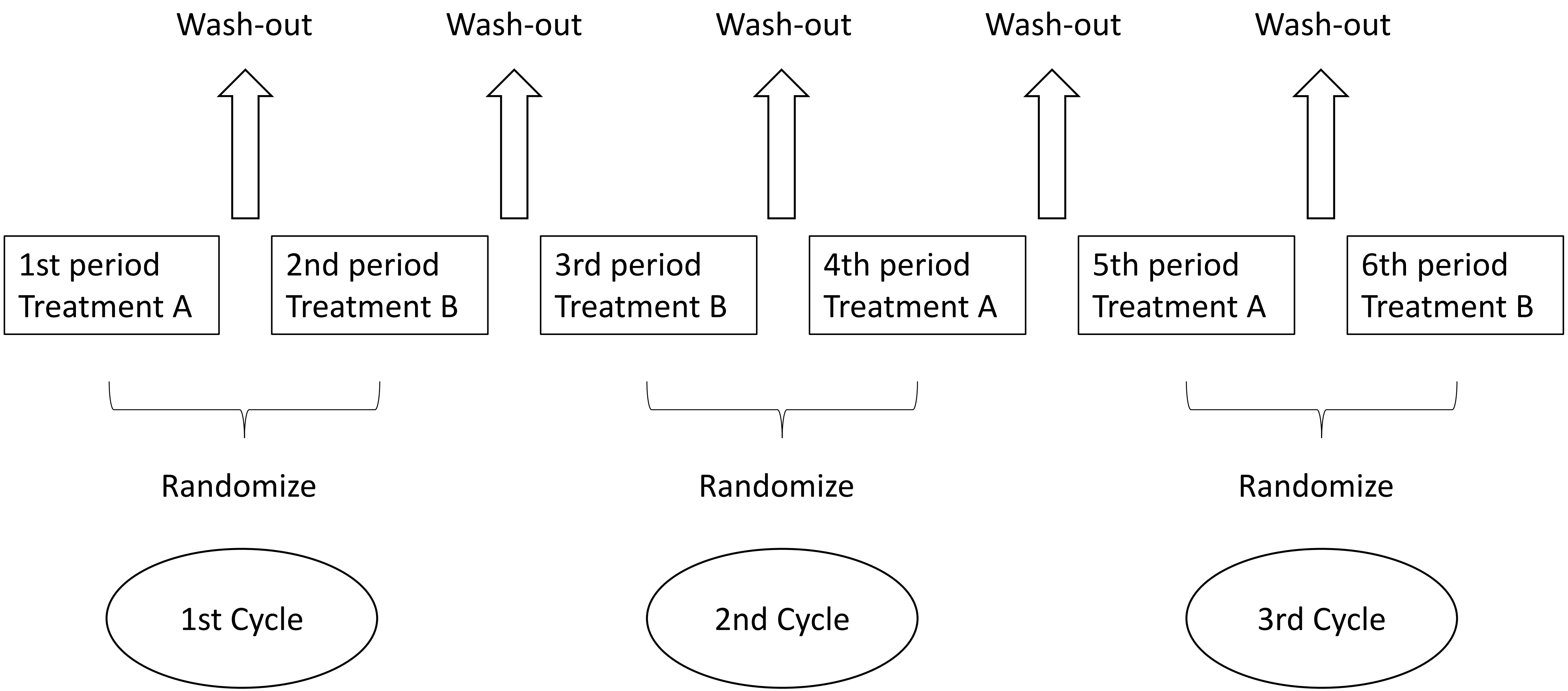
Introduction

- N-of-1 trials are performed on a single individual with the purpose of estimating individual treatment effects.
- Series of n-of-1 trials can be used to estimate an overall treatment effect as well as individual treatment effects.
- Distinct individual treatment effects arise as a consequence of a treatment by patient interaction.
- N-of-1 trials are undertaken in small populations when there is expectation a priori of a treatment by patient interaction.

Running the trial



Collecting the data

	Patient	Cycle	Period	Treatment	Outcome
1	1	1	1	1	136.40874
2	1	1	2	0	107.01942
3	2	1	1	0	88.61943
4	2	1	2	1	114.26834
5	2	2	3	1	113.23962
6	2	2	4	0	84.84709
7	2	3	5	1	113.21207
8	2	3	6	0	83.76118
9	3	1	1	0	91.18322
10	3	1	2	1	112.25541
11	3	2	3	0	94.48259
12	3	2	4	1	113.36506

Collecting the data

	Patient	Cycle	Period	Treatment	Outcome
1	1	1	1-2	1-0	29.38932
2	2	1	2-1	1-0	25.64891
3	2	2	3-4	1-0	28.39253
4	2	3	5-6	1-0	29.45090
5	3	1	2-1	1-0	21.07219
6	3	2	4-3	1-0	18.88247
7	4	1	2-1	1-0	18.41385
8	4	2	3-4	1-0	13.11547
9	5	1	2-1	1-0	15.27196
10	5	2	3-4	1-0	18.59932
11	6	1	2-1	1-0	27.25901

Methods

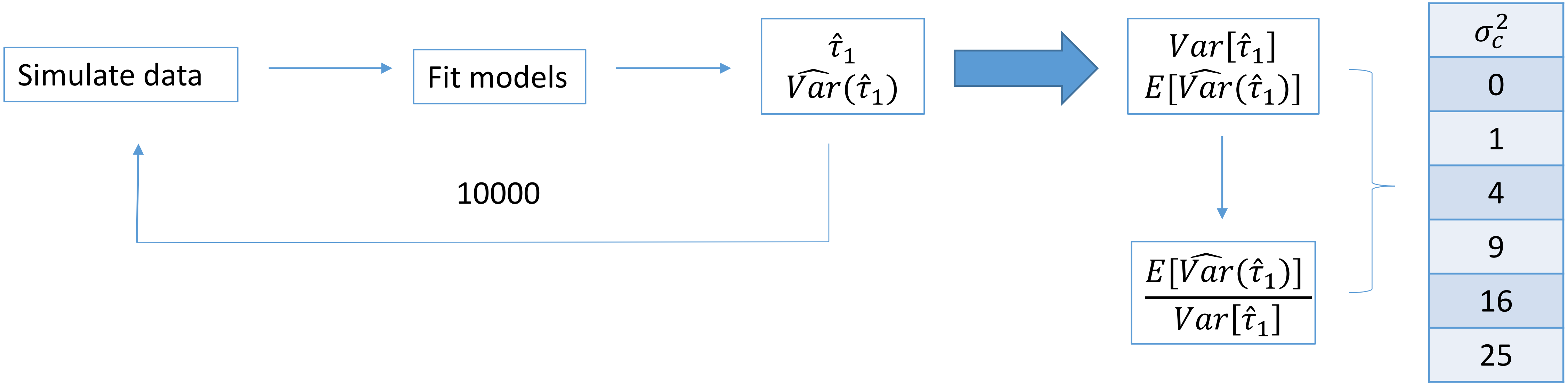
$$y_{ij[k]} = 100 + \tau_{[k]} + b_i + c_{i[k]} + e_{ij}$$

$$i = 1, \ldots, 30 \qquad j = 1, \ldots n_i \qquad k = 0,1$$

$$b_i \sim N(0,25) \qquad c_{i[k]} \sim N(0, \sigma_c^2) \qquad e_{ij} \sim N(0,9)$$

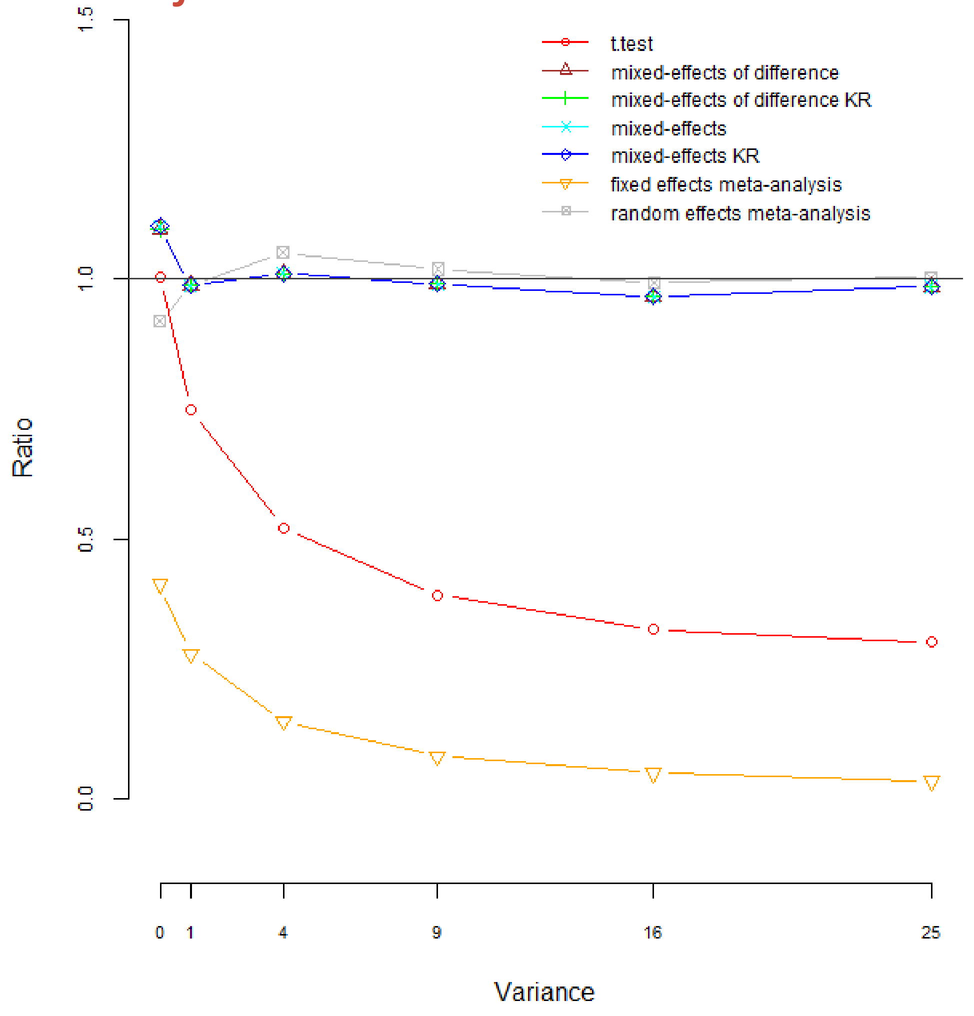
$$\tau_0 = 0 \qquad \tau_1 = 20$$

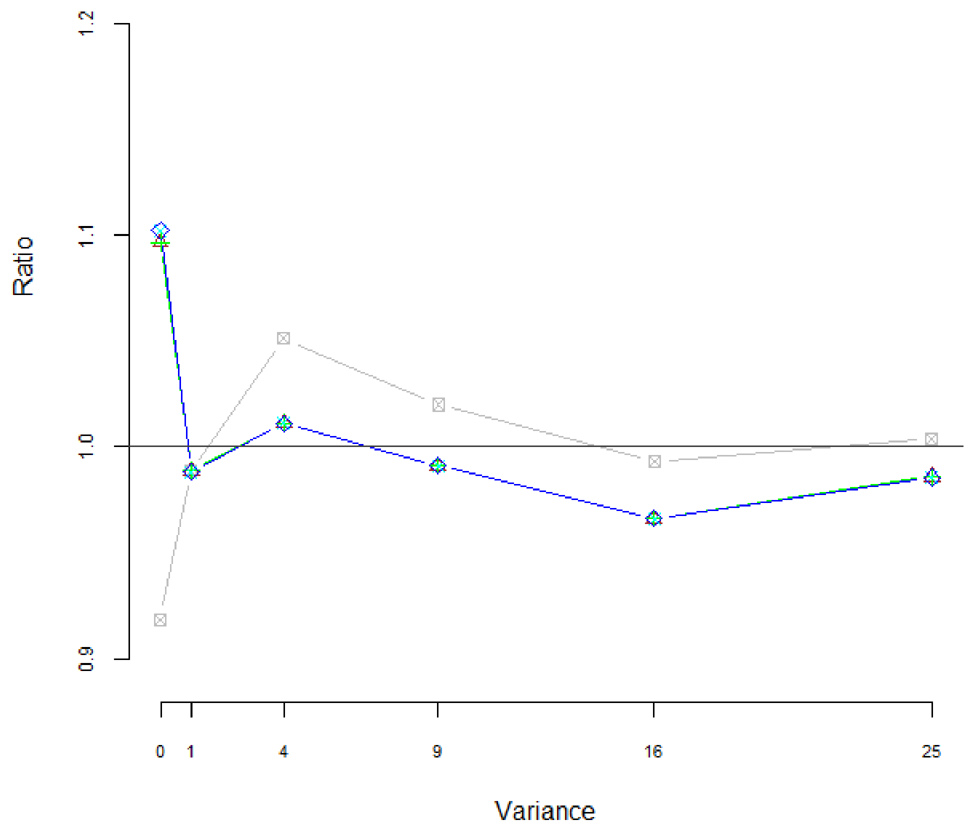
$$\max(n_1, \ldots, n_{30}) = 8 \qquad \min(n_1, \ldots, n_{30}) = 4$$



4 cycles balanced n-of-1 trials

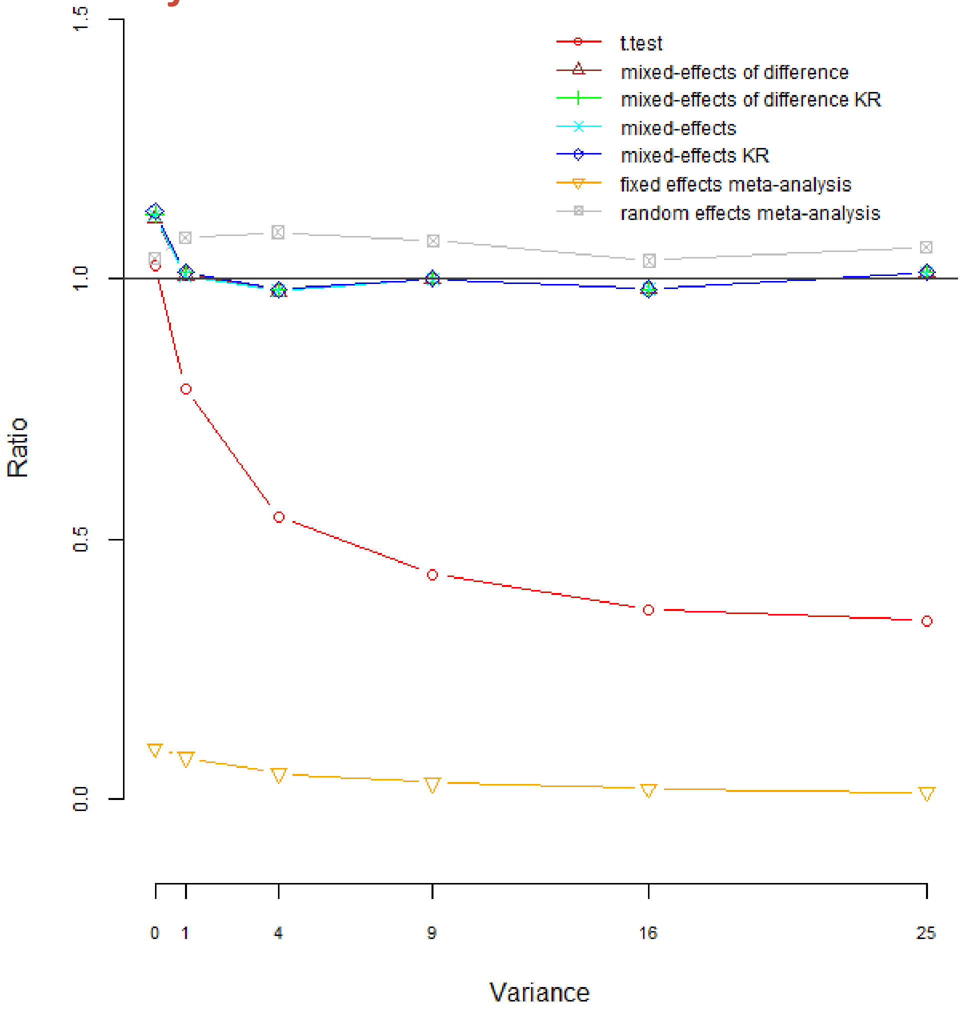
30 subjects

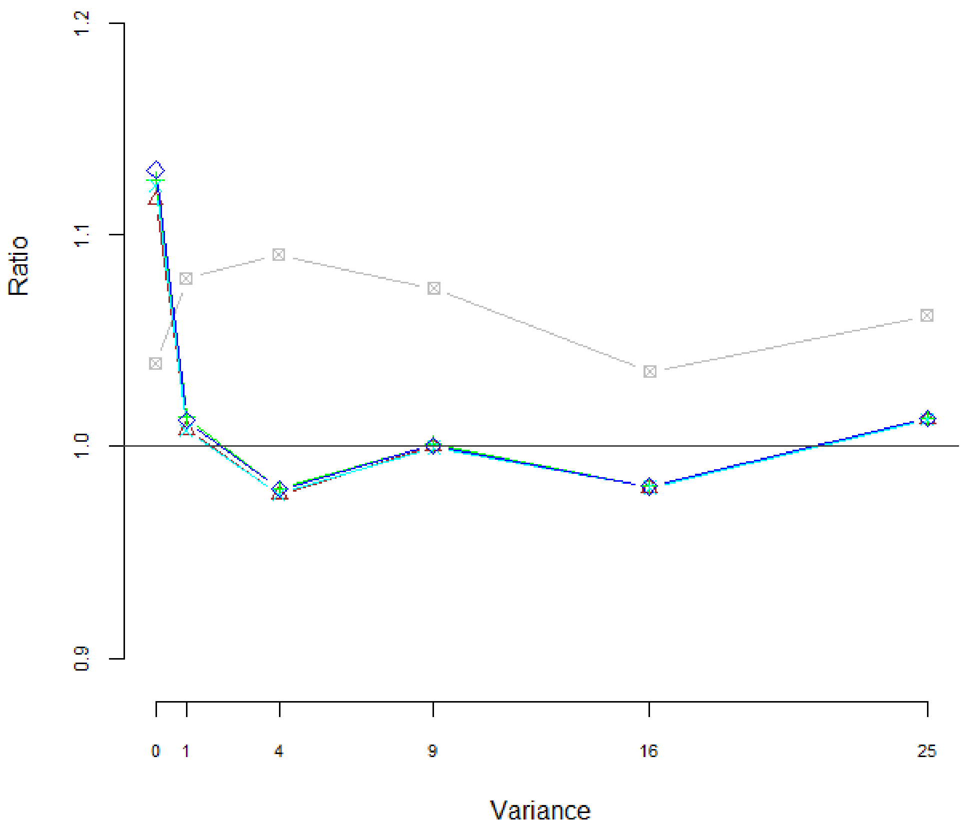




2 to 4 cycles unbalanced n-of-1 trials

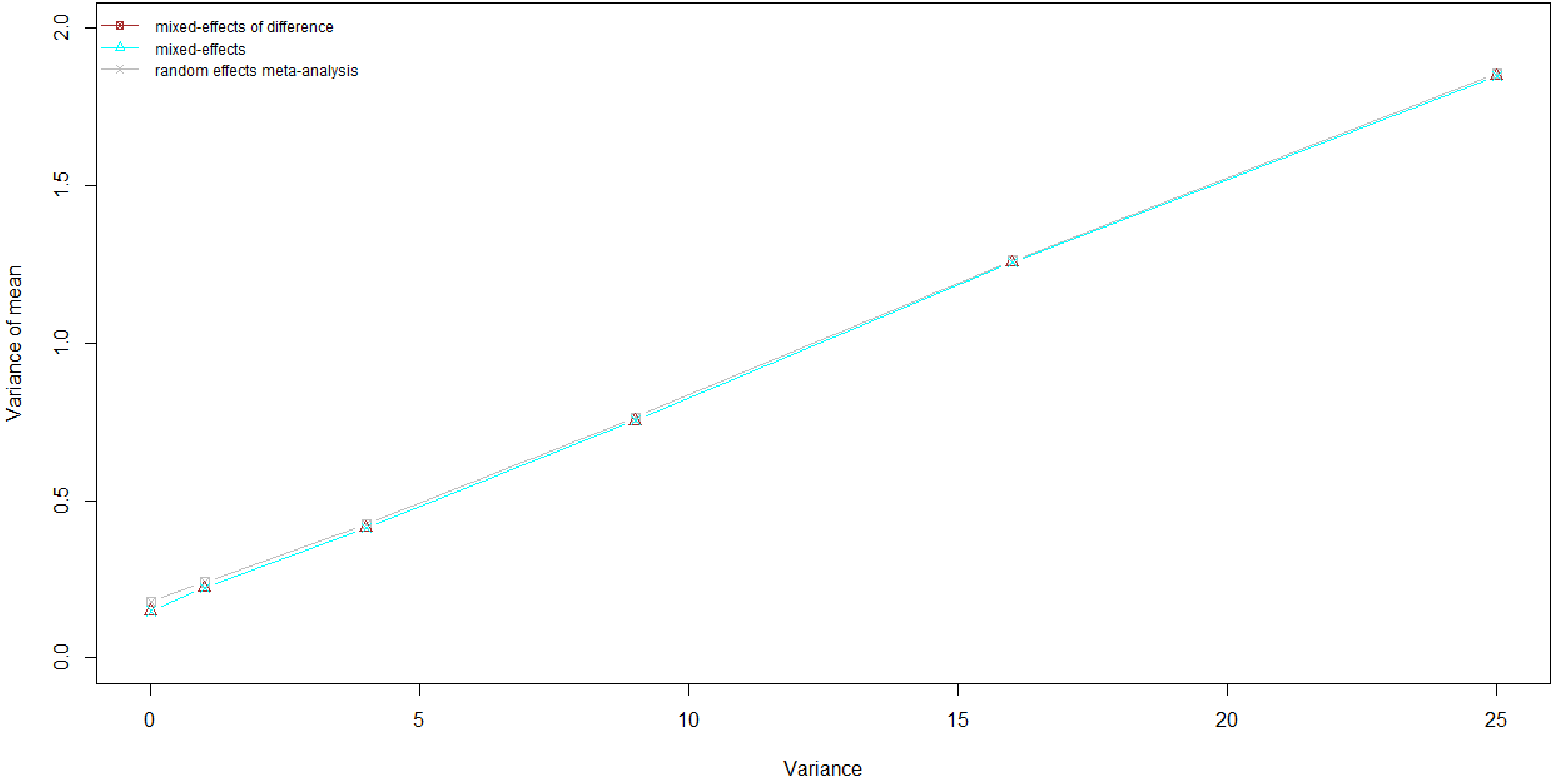
30 subjects





4 cycles balanced n-of-1 trials

30 subjects



2 to 4 cycles unbalanced n-of-1 trials

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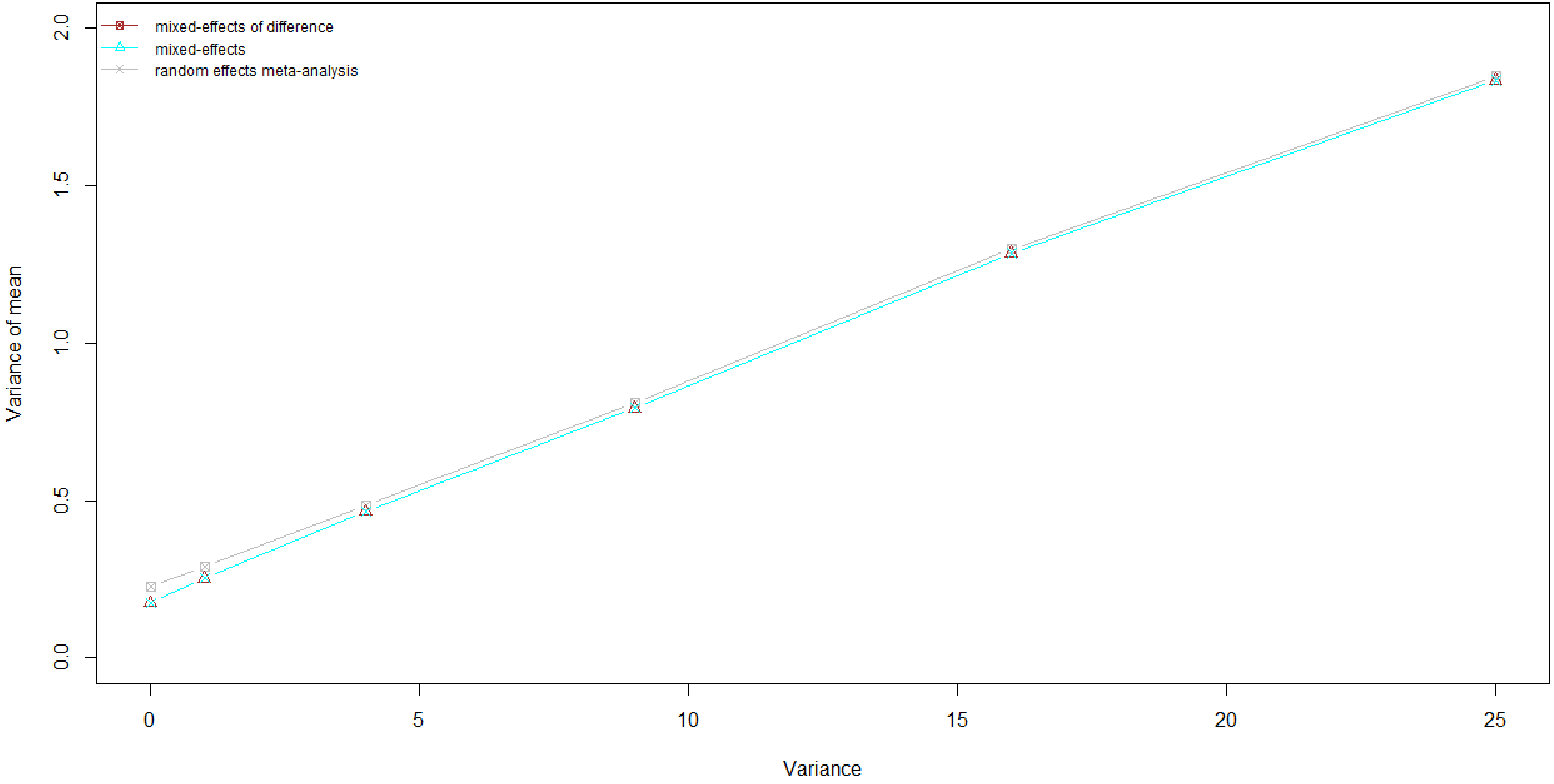

Conclusions

When the treatment by patient interaction is significant:

- The t-test and fixed effects meta-analysis underestimate the variance of the overall treatment effect estimate.
- The t-test does not permit the estimation of distinct individual treatment effects.
- Both the full mixed-effects model and the mixed-effects model of difference produce unbiased or near unbiased estimates of the variance of the overall treatment effect estimate.

References

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Thanks for your attention