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Is there really any benefit to stratified randomisation in practice?

A simulation study with continuous outcome...

Pavankumar Bhagat | 09JUNE2025 |PSI 2025 Conference - London, UK

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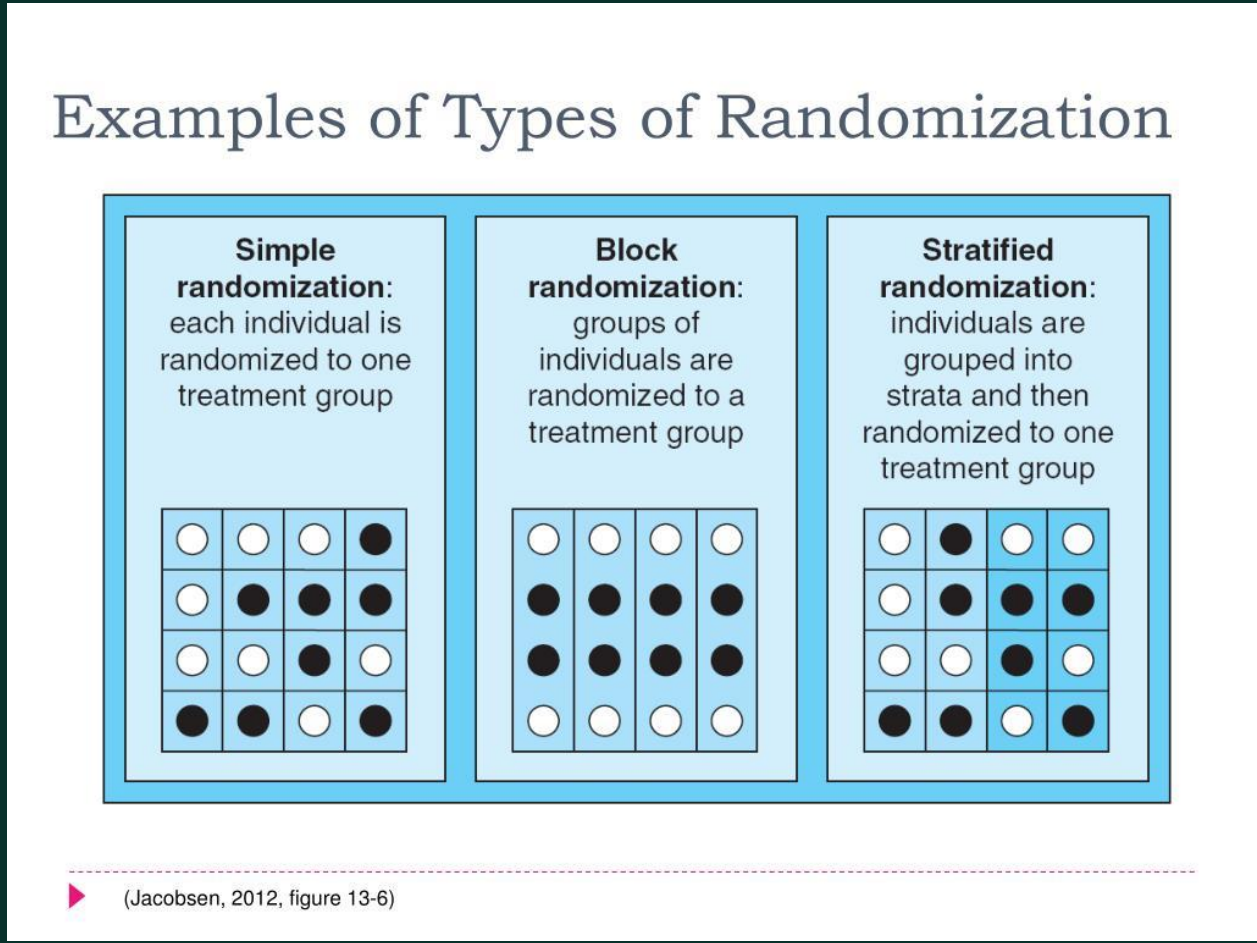
Disclaimer

- The following slides include statements and approaches that represent my personal perspective and may not necessarily reflect the official positions or recommendations of Boehringer Ingelheim.
- It is important to acknowledge that the subject matter allows for a variety of valid approaches, and the methods I present are not intended to be extensive.
- Where applicable, I have indicated the locations of official sources. The primary focus of this presentation, however, is a description of my past and current research.

Motivation

- RCTs stands as gold standard in modern clinical trial design
- Reduces selection and assignment bias
- Improves internal validity
- Stratified randomisation reduces random imbalance between treatment groups
- it's unlikely to find imbalances in clinical factors for a randomized large group
- Is stratified randomisation better than simple practically?



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Simulation Study - Continuous outcome

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Simulation study – ADEMP structure

Aim :

Power benefit while using stratified randomisation versus simple (ANCOVA)

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Power benefit while using stratified randomisation versus simple (ANCOVA)

Data Generating Mechanism:

1. Under different sample sizes
2. Different strength of association between covariates and outcome
3. With different effects of treatment

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Performance Measures:

Power, empirical standard error, type I error rate, bias, and coverage.

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Simulation study – Design and Assumptions

- Design overview: Two-arm, parallel design RCT with 1:1 allocation
- Treatment variable (X1) was generated randomly from a uniform distribution
- Baseline variable (B1) randomly generated from a normal distribution.
- Threshold was created based on the stratum sizes and baseline variable (B1)
- Stratification factor variable(B_stratify) generated with 2 levels
- Treatment variable(X2) was generated using block randomisation and strata.
- Missing Data: assumed to be complete.
- Significance Level (α) = 0.05, outcome variable (Y1/Y2) follows normal distribution.

Simulation inputs and execution - Pseudocode

```r
# Define the parameters
sample_sizes <- c(50, 250, 500, 1000)
stratum_sizes_list <- 0.5 #Equal allocation
its <- 100000
alpha <- 0.05
theta <-c(0.6, 1)
baseline_effects_to_test <- list(log(1.2), log(2), log(9))
```

Sample Sizes: 50, 250, 500, 1000

Strength of association between outcome and covariate: weak: log(1.2), moderate: log(2), strong: log(9)

Stratum Proportions: equal (1:1) : 0.5

Iterations: 100,000 simulated datasets.

R-packages: blockrand , dplyr, tidyr , ggplot2

True treatment effect set to 0.6 (for power) , 0 (for Type I error).

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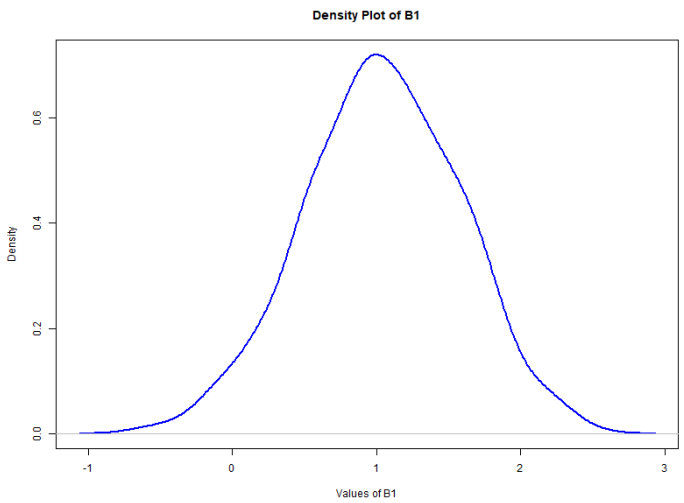
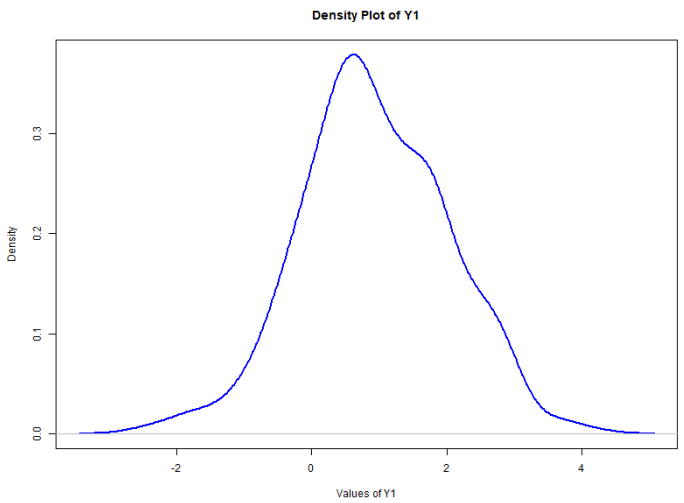
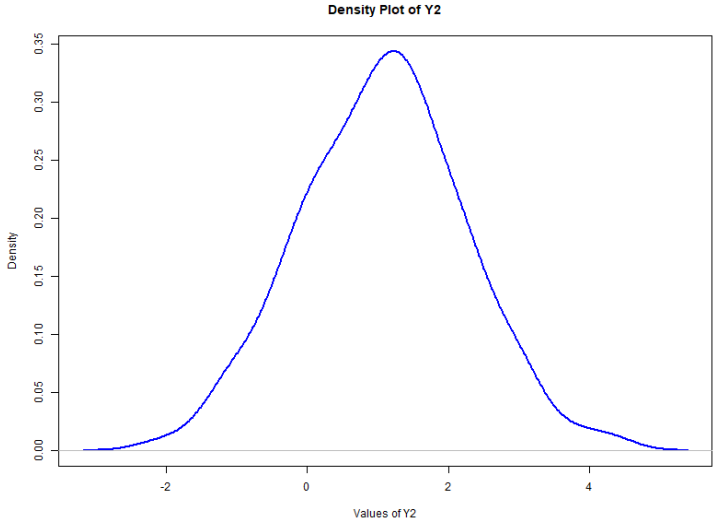
Analysis







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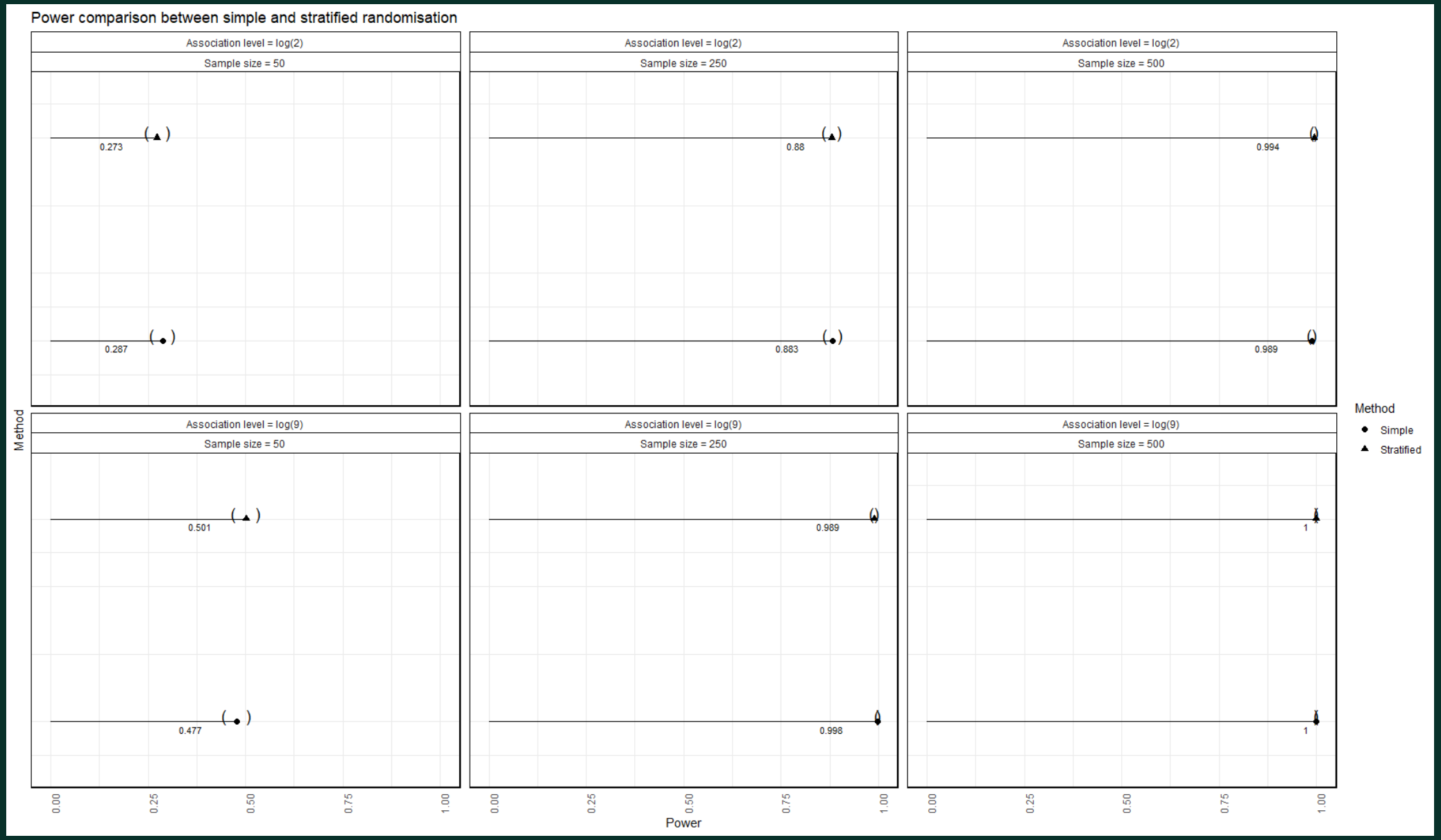
Results - Power



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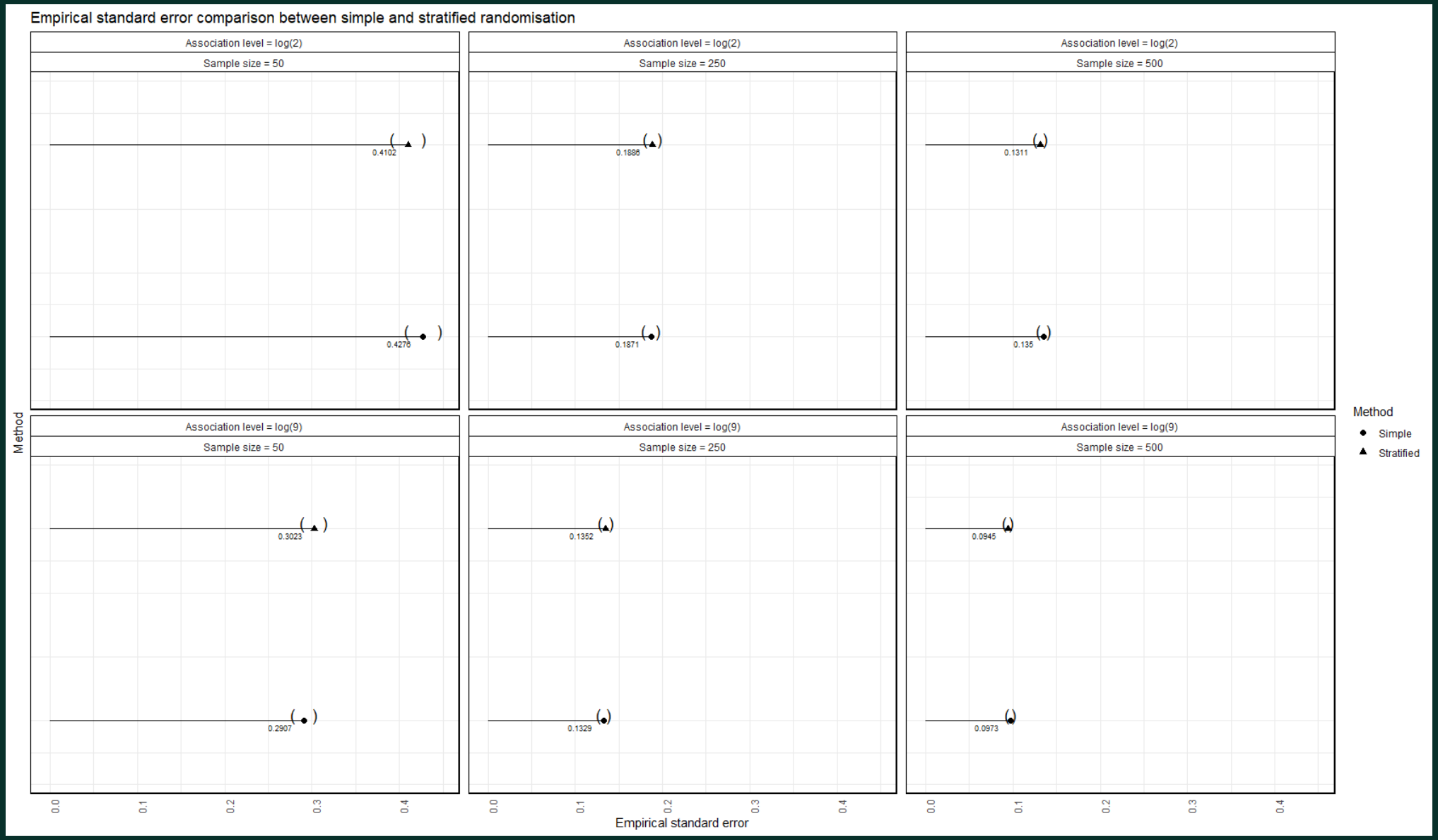
Results - Empirical standard error



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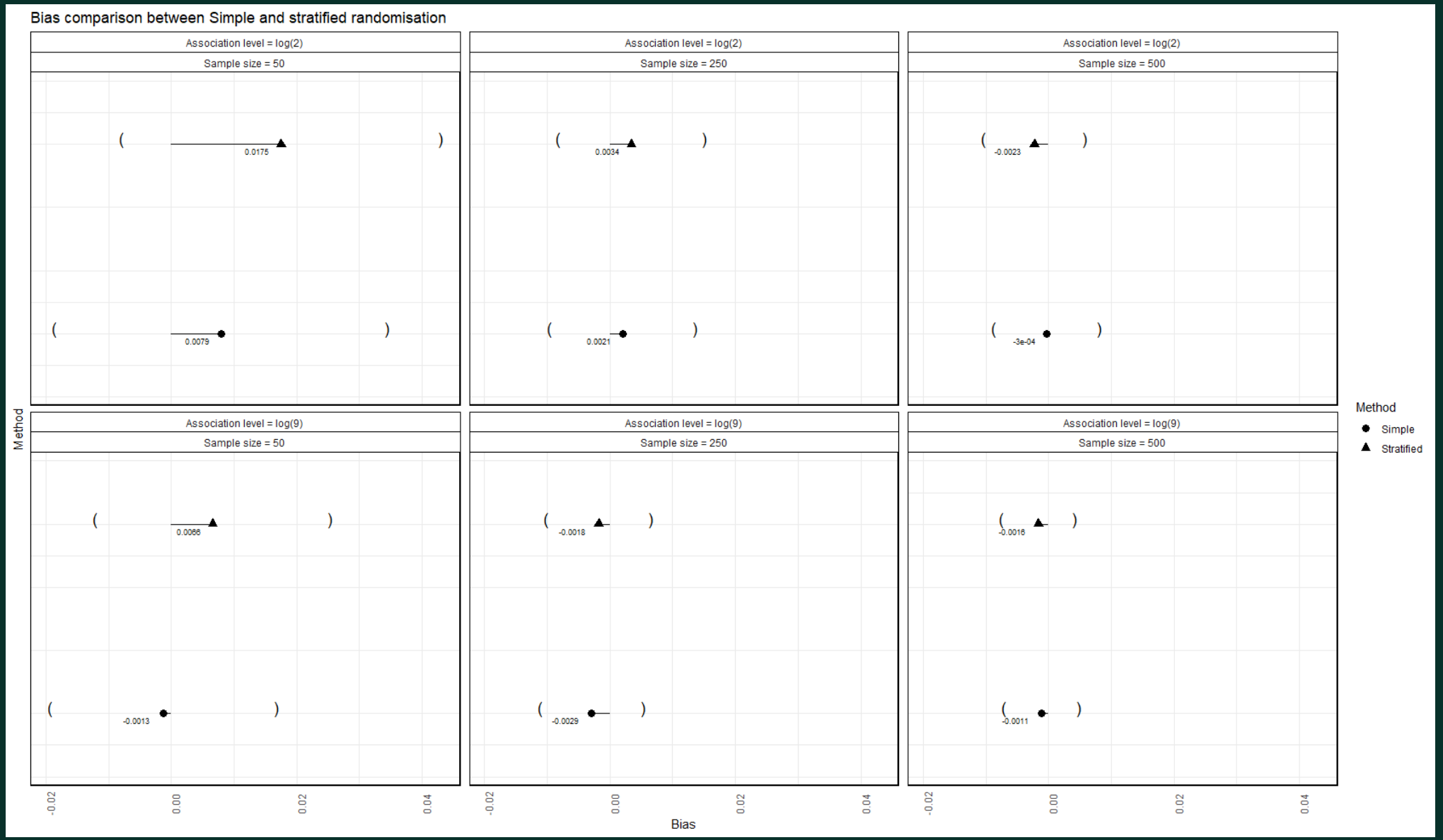
Results - Bias



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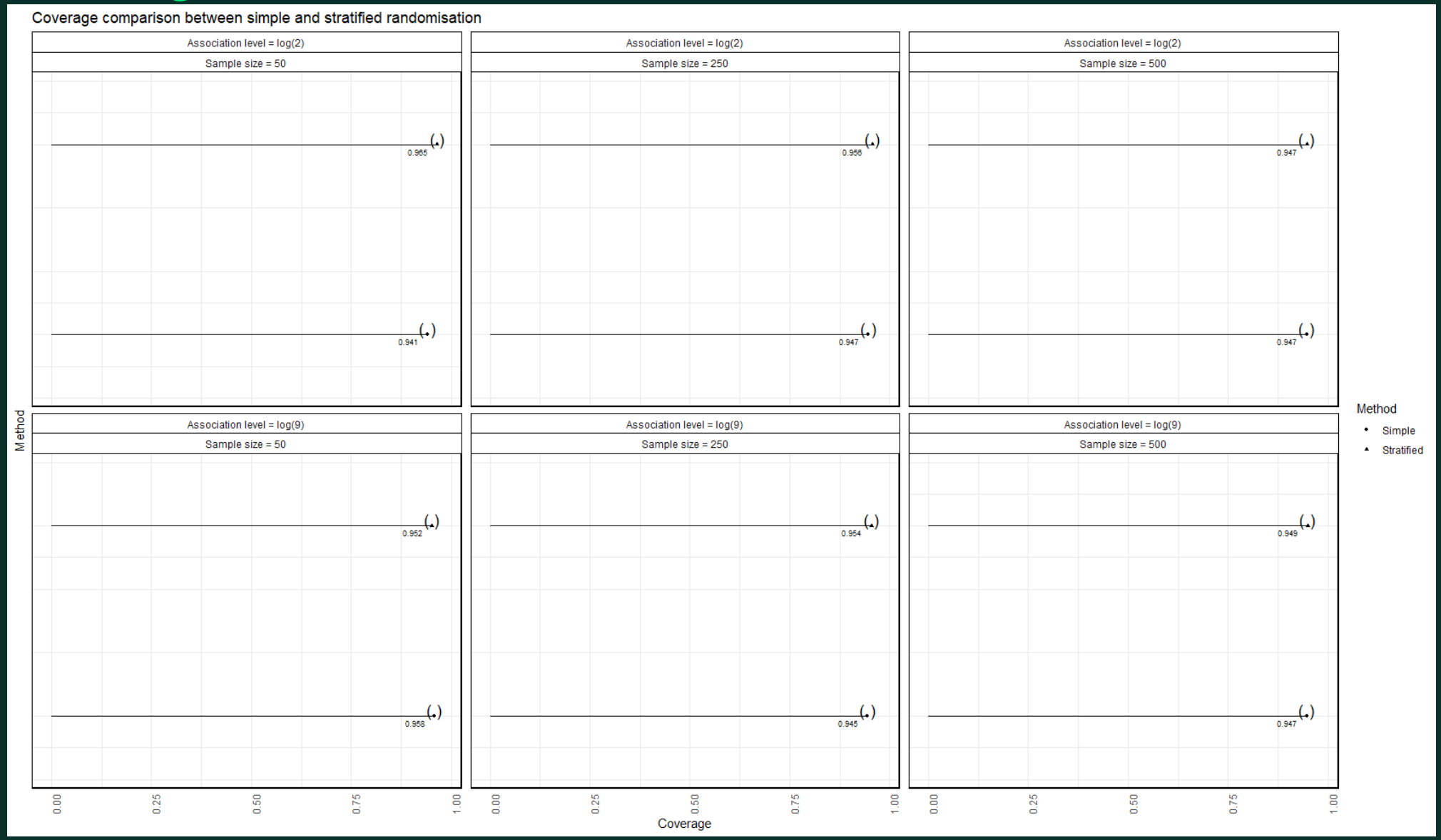
Results - Coverage



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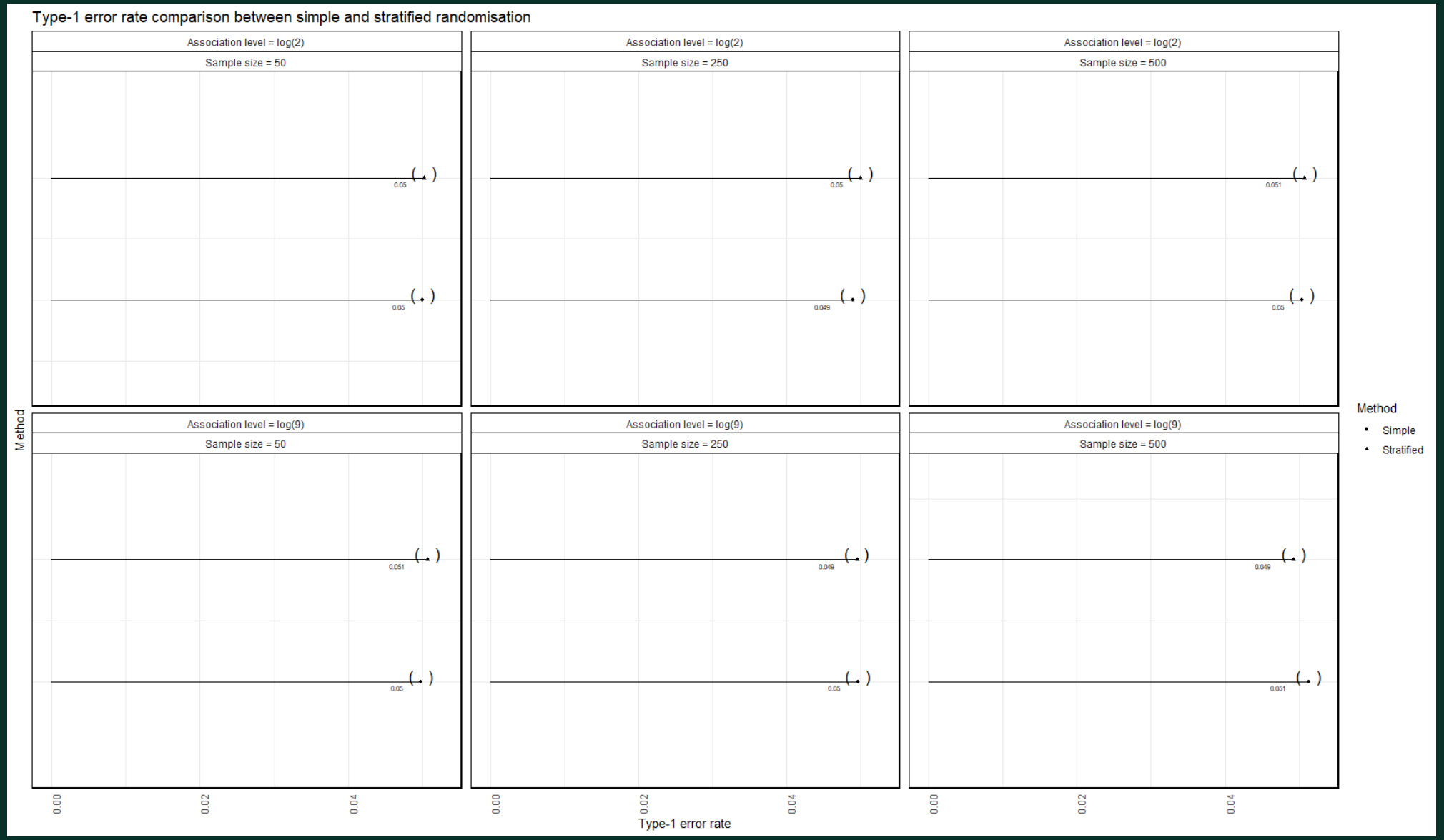
Results - Type 1- error



Conclusions

Summary:

- No meaningful benefit of stratified randomisation over simple randomisation with covariate adjustment - especially in large trials.
- Stratified randomisation demonstrates theoretical advantages in balance; however, the complexity may not translate to improved performance in all settings.

Future Directions:

- Exploration of benefits with different outcomes(binary/time to event)
- Further research on optimal stratification factors and different stratum sizes.

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Acknowledgements and References

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- 1. Kahan, B. C., & Morris, T. P. (2012). Reporting and analysis of trials using stratified randomisation in leading medical journals: Review and reanalysis.
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- 4. Morris, T. P., & White, I. R. (2019). Using simulation studies to evaluate statistical methods.

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Thank You for your attention ☺

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