Balance and Predictability in randomisation: A simulation study

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Background

The randomised controlled trial is considered the gold standard when evaluating interventions. Randomising participants can help guard against selection bias by producing random, unpredictable sequences. Sometimes however, methods may be used to create more balanced comparable groups at the expense of being a more predictable sequence.

These concepts are well known to be important in trials, but this work aims to:

1. Quantify the balance and predictability of sequences
2. Compare the balance and predictability of different randomisation methods for different study designs

Methods

Real clinical trials data was used to simulate datasets.

Each dataset was randomised using the specified randomisation methods for different study designs.

Code	Randomisation method
SIM	Simple randomisation
COM	Complete randomisation
STR	Stratified randomisation
SMN	Minimisation stratified by site (random factor of 80)
MIN 70	Minimisation (random factor 70)
MIN 80	Minimisation (random factor 80)
MIN 90	Minimisation (random factor 90)

Study Feature	Simulated Scenarios
Sample Size	50, 100, 200, 500, 1000, 1900
Number of centres	1, 5, 15, 30, 75, 115

All methods perform fairly well (wrt predictability) in a multicentre trial where randomisation is not restricted by site. Minimisation is more predictable when site is a minimisation variable.

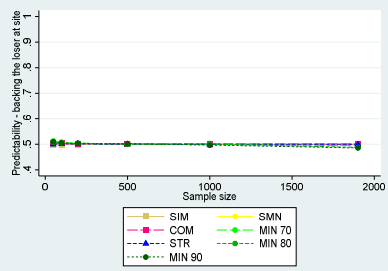
The metrics at a glance

The metrics aim to quantify different aspects of balance and predictability.

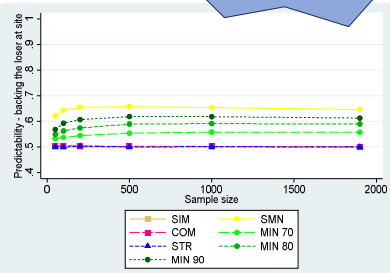
Metric	Details
Predictability	
Alternation	Proportion of correct guesses assuming the next allocation is the opposite of the previous.
Back the loser	Proportion of correct guesses assuming the next allocation is the group with the fewest current allocations.
Balance	Proportion of correct guesses assuming the next allocation would minimise imbalance.
Imbalance	
End of trial group size	The ratio of the group with the most allocations and the group with the fewest. Measures departure from perfect balance where perfect balance is 0.
Chronological group size	The ratio of the group with the most allocations and the group with the fewest. This is calculated after each allocation, and the worst value through recruitment taken.
End of trial characteristic imbalance	Based on a Chi-squared test, this measures departure from expected balance. Here lower than 0.05 is a departure from balance higher than expected by chance.
Chronological characteristic imbalance	Based on a Chi-squared test, this measures departure from expected balance. This is calculated after each allocation, and the worst value through recruitment taken.

Results

Predictability through backing the loser vs sample size:

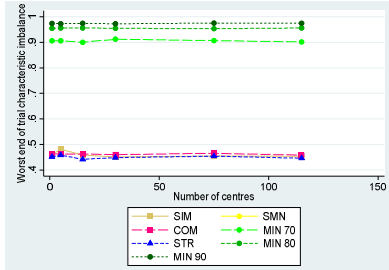


Randomisation variables: Age, surgery type & ER status

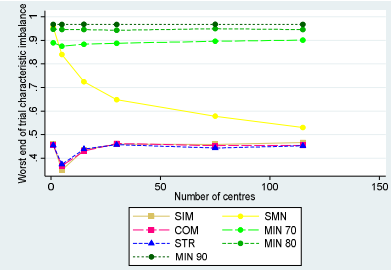


Randomisation variables: Age, surgery type, ER status & site

End of trial characteristic imbalance vs number of centres:



Randomisation variables: Age, surgery type & ER status



Randomisation variables: Age, surgery type, ER status & site

Discussion

Preliminary results show that features of the study design such as sample size and the number of recruiting centres and whether the randomisation is restricted by site can influence the performance of the method with respect to balance and predictability hence more thought should be given to which method will perform well given the design of the study.

To Come…

More Features: Full study also considers the distribution of recruitment across centres and the variables (number of strata) included in the randomisation.

More methods: Full study also includes block randomisation and stratified block randomisation. (for a variety of block sizes)

Code available: Programs to compute these metrics for your own study will be available to download

Minimisation creates more balanced sequences than other methods. For stratified minimisation, the more sites included the less balance achieved.

For more information on the research at Nottingham Clinical Trials Unit:

Keep up to date with this research:

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