5.7 Rain dance: the role of randomization in clinical trials

https://www.youtube.com/watch?v=fnVy-zkEmvk

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Abstract

Randomized clinical trials are the gold standard for testing efficacy of treatment interventions. However, although randomization protects against deliberately biased samples, it does not guarantee random imbalances will not occur. Methods of intentional allocation that can overcome such deficiency of randomization have been developed, but are less frequently applied than randomization. Initially, we introduce a fictitious case example to revise and discuss the reasons of researchers' resistance to intentionally allocate instead of simply randomizing. We then introduce a real case example to evaluate the performance of an intentional protocol for allocation based on compositional data balance. A real case of allocation of 50 patients in two arms was compared with an optimal allocation of global instead of sequential arrivals. Performance was measured by a weighted average of Aitchison distances, between arms, of prognostic factors. To compare the intentional allocation with simple random allocation, 50,000 arrival orderings of 50 patients were simulated. To each one of the orders, both kinds of allocations into two arms were considered. Intentional allocation performed as well as optimal allocation in the case considered. In addition, out of the 50,000 simulated orders, 61% of them performed better with intentional allocation than random allocation. Hence, we conclude that intentional allocation should be encouraged in the design of future interventional clinical trials as a way to prevent unbalanced samples. Our sequential method is a viable alternative to overcome technical difficulties for study designs that require sequential inclusion of patients as it does not require prior knowledge about the total sample composition.