Different methods of allocation to groups in randomized trials are associated with different levels of bias. A meta-epidemiological study

Abstract

Objective: Insecure hiding of the treatment allocation in randomized trials is associated with bias. It is less certain how much bias is associated with different methods of treatment allocation.

Study Design and Setting: Meta-epidemiological study of 389 randomized trials from 19 systematic reviews and 65 meta-analyses with differing methods of treatment allocation. Pooled ratios of odds ratios (RORs) and 95% confidence intervals (95% CI) were calculated from trials with different methods of treatment allocation. An ROR less than one shows exaggeration of treatment effect.

Results: There is no evidence that the use of sealed envelopes with enhancement was different from central randomization (ROR 1.02, 95% CI: 0.85e1.23). Sealed envelopes without enhancement were associated with an exaggeration of the estimate of effect (ROR 0.87, 95% CI: 0.76e1.00). Where allocation concealment for double-blind trials was unclear, the ROR is 0.86 (95% CI: 0.78e0.96) and if not hidden, the ROR is 0.89 (95% CI: 0.70e1.15).

Conclusion: Sealed envelopes with some form of enhancement (opaque, sequentially numbered, and so forth) may give adequate concealment. Description of a study as "double blind" does not imply a lack of bias when concealment of allocation is unclear.

Peter Herbison, Jean Hay-Smith and William J. Gillespie. Journal of Clinical Epidemiology, 64 (2011) 1070-1075.