Critical appraisal criteria for randomized crossover trials

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Background:
Critical appraisal criteria for randomized parallel trials do not fit well for randomized crossover trials. The CONSORT statement (updated 2010) does not cover crossover trials. The Cochrane Handbook (version 5.1.0) includes risk of bias assessment criteria for cross-over trials in its March 2011 update.

Aims:
We defined explicit criteria for defining high-quality evidence (level 1 evidence) derived from randomized crossover trials.

Methods:
Criteria were derived from critical appraisal criteria used for randomized trials in DynaMed and risk of bias criteria for cross-over trials in the Cochrane Handbook version 5.1.0 (section 16.4.3). The criteria were shared with DynaMed editors and with the International Society for Evidence-based Health Care listserv for feedback.

Results:
Our derived criteria for high-quality evidence for a clinical conclusion from a randomized crossover trial include:

Criteria for any randomized trial (parallel or crossover):
1. Clinical outcome (also called patient-oriented outcomes)
2. Population, intervention, comparison, and outcome in the study is representative of expected clinical practice
3. Random allocation method (i.e. not assigned by date of birth, day of presentation, “every other”)
4. Blinding of all persons (patient, treating clinician, outcome assessor) if possible
5. Follow-up (endpoint assessment) of at least 80% of study entrants AND adequate such that losses to follow-up could not materially change the results
6. Accounting for dropouts (even if not included in analysis)
7. Confidence intervals do not include both presence and absence of clinically meaningful differences

Additional criteria for randomized crossover trials:
1. Trial conducted in patients with condition not expected to change spontaneously during course of trial
2. Random allocation method for order of assignment
3. Washout period between interventions long enough to avoid carryover effects between interventions
4. Adequate duration of intervention and assessment period to represent outcome being measured
5. Analysis of paired data
6. Analysis not suggesting period effects (i.e. effect resulting for order of intervention), or period effects if present not materially changing results

Average pain response in patients with fibromyalgia receiving low-dose naltrexone vs. placebo in randomized crossover trial

source: Arthritis Rheum 2013 Feb;65(2):529

Limits:
These criteria do not address additional factors which may complicate randomized trial assessment including crossover trials with more than two interventions being compared, cluster-randomized trials, and trials with early termination.

Conclusions:
Formalizing criteria for critical appraisal of randomized crossover trials will improve consistency of evidence analysis for systematic reviewers and guideline developers.