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Nonrandomized studies are not always found even when selection criteria for health systems intervention reviews include them: a methodological study

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Abstract

Objective: Systematic reviews within the Cochrane Effective Practice and Organisation of Care Group (EPOC) can include both randomized and nonrandomized study designs. We explored how many EPOC reviews consider and identify nonrandomized studies, and whether the proportion of nonrandomized studies identified is linked to the review topic.

Study Design and Setting: We recorded the study designs considered in 65 EPOC reviews. For reviews that considered nonrandomized studies, we calculated the proportion of identified studies that were nonrandomized and explored whether there were differences in the proportion of nonrandomized studies according to the review topic.

Results: Fifty-one (78.5%) reviews considered nonrandomized studies. Forty-six of these reviews found nonrandomized studies, but the proportion varied a great deal (median, 33%; interquartile range, 25−50%). Reviews of health care delivery interventions had lower proportions of nonrandomized studies than those of financial and governance interventions.

Conclusion: Most EPOC reviews consider nonrandomized studies, but the degree to which they find them varies. As nonrandomized studies are believed to be at higher risk of bias and their inclusion entails a considerable effort, review authors should consider whether the benefits justify the inclusion of these designs. Research should explore whether it is more useful to consider nonrandomized studies in reviews of some intervention types than others.

Keywords: Nonrandomized studies; Systematic review; Methodology; The Cochrane Collaboration; Health systems; Trials

1. Background

Systematic reviews that evaluate the effects of health care interventions are regarded as key tools for evidence-informed decision making. But as decision-makers' exposure to systematic reviews increases, they may also become frustrated with the large numbers of reviews that conclude that evidence is lacking. This apparent lack of evidence may reflect the review authors' preference for randomized trials and their dismissal of nonrandomized studies that may include important information. It has been suggested that although randomized trials may be lacking, nonrandomized studies are frequently available [1], particularly in fields such as public health and the organization of health care delivery [2], and that the inclusion of nonrandomized studies in reviews of effectiveness should therefore be considered [2].

In a recent systematic review [3] published by the Cochrane Effective Practice and Organisation of Care Group (EPOC), we evaluated the effectiveness of lay health worker programs for maternal and child health and considered only

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What is new?

- Most Cochrane Effective Practice and Organisation of Care Group (EPOC) systematic reviews of health systems interventions consider nonrandomized studies.
- The degree to which EPOC reviews find nonrandomized studies varies greatly, and this variation appears to be linked to the topic of the intervention.
- As nonrandomized studies are believed to be at higher risk of bias and their inclusion entails a considerable extra effort, review authors should consider whether the benefits justify the inclusion of these designs.
- Research should explore whether it is more useful to consider nonrandomized studies in reviews of some intervention types than others.

randomized trials. However, for some of the topics covered by the review, we found few trials from low- and middle-income countries, potentially limiting the applicability of our review for these settings. We therefore decided to carry out a second review focusing specifically on the use of lay health worker programs for immunization uptake, in which we also considered nonrandomized controlled trials, interrupted time series, and controlled before−after designs [4].

This expansion of our inclusion criteria resulted in the inclusion of nine randomized trials, but only one controlled before−after study [5] and one interrupted time-series study [6]. The controlled before−after study did not include sufficient data to easily assess outcomes. For the interrupted time-series study, the results were similar overall to those found in the randomized trials. We concluded that these additional studies had a higher risk of bias than the randomized trials, according to EPOC's risk of bias tool [7], and did not change the results of the original Cochrane review of randomized trials.

This was a disappointing result given the amount of time and effort that this process had involved and the expectations that we had regarding the number of nonrandomized studies we were likely to find, and this led us to question the experiences of other EPOC authors working on the reviews of health systems questions.

2. Objectives

In this study, we aimed to explore the following:

- How many EPOC reviews of health systems interventions consider nonrandomized studies?
- How many nonrandomized studies they find?
- Whether there is a connection between the proportion of nonrandomized studies found and review topic?

3. Methods

In addition to randomized trials, the EPOC Review Group accepts nonrandomized controlled trials, interrupted time series, and controlled before−after designs (See Table 1). We examined all EPOC reviews published in March 2010, recording which study designs were accepted by each review's inclusion criteria. For reviews that considered nonrandomized studies, we calculated the proportion of included studies that were nonrandomized.

We then categorized the EPOC reviews according to the topic and explored whether there were differences across topics in the proportion of nonrandomized studies that the reviews had included. We categorized the reviews using the taxonomy adopted by the Health Systems Evidence database [8,9]. This taxonomy distinguishes between interventions associated with

- governance arrangements (political, economic, and administrative authority in the management of health systems, e.g., regulation of provider practice),
- financial arrangements (funding and incentive systems as well as financing, e.g., user fees),
- delivery arrangements (human resources for health and service delivery, e.g., the use of lay health worker programs to deliver services), and
- implementation strategies to support the use of interventions (e.g., continuing education meetings for providers).

To assess whether there were any differences in the numbers of nonrandomized studies identified across review types (governance, financial, delivery, or implementation), we used analysis of variance (ANOVA), adjusted for multiple comparisons with the Tukey−Kramer method. In addition, we carried out a sensitivity analysis using the nonparametric Kruskal−Wallis test.

4. Results

Fifty-one (78.5%) of EPOC's 65 reviews considered nonrandomized studies in their inclusion criteria. Of these reviews, five (10%) did not identify any studies at all, whereas 46 (90%) found at least one study, either randomized or nonrandomized.

Among these 46 reviews, the proportion of studies that were nonrandomized varied a great deal (median, 33%; interquartile range, 25−50%). When applying the Health Systems Evidence typology, we identified differences in the proportion of nonrandomized studies according to the intervention type (Table 2). Reviews evaluating interventions focused on delivery arrangements were significantly less likely to identify nonrandomized studies than those evaluating interventions focused on financial or governance arrangements [nonparametric (Kruskal−Wallis; $P = 0.0058$) and parametric (ANOVA; $P = 0.0010$) tests]. The reviews of implementation strategies did not appear to have a significantly