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A reanalysis of cluster randomized trials showed interrupted time-series studies were valuable in health system evaluation

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Abstract

Objectives: There is often substantial uncertainty about the impacts of health system and policy interventions. Despite that, randomized controlled trials (RCTs) are uncommon in this field, partly because experiments can be difficult to carry out. An alternative method for impact evaluation is the interrupted time-series (ITS) design. Little is known, however, about how results from the two methods compare. Our aim was to explore whether ITS studies yield results that differ from those of randomized trials.

Study Design and Setting: We conducted single-arm ITS analyses (segmented regression) based on data from the intervention arm of cluster randomized trials (C-RCTs), that is, discarding control arm data. Secondarily, we included the control group data in the analyses, by subtracting control group data points from intervention group data points, thereby constructing a time series representing the difference between the intervention and control groups. We compared the results from the single-arm and controlled ITS analyses with results based on conventional aggregated analyses of trial data.

Results: The findings were largely concordant, yielding effect estimates with overlapping 95% confidence intervals (CI) across different analytical methods. However, our analyses revealed the importance of a concurrent control group and of taking baseline and follow-up trends into account in the analysis of C-RCTs.

Conclusion: The ITS design is valuable for evaluation of health systems interventions, both when RCTs are not feasible and in the analysis and interpretation of data from C-RCTs. © 2015 The Authors. Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/3.0/).

Keywords: Evaluation methods; Randomized trials; Interrupted time-series; Quasi-experimental design; Impact evaluations; Health services research

1. Introduction

The randomized controlled trial (RCT) is widely regarded as the gold standard research design for measuring the impacts of interventions, and RCTs dominate effectiveness research in clinical medicine.

The field of health system and policy evaluation is very different: randomized trials are seldom carried out, despite substantial uncertainty about the impacts of health system interventions on the costs and outcomes of care. This is

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What is new?

- Our findings support the position that concurrent control groups are important, but the single-arm interrupted time-series design, in which the preintervention period serves as control, yielded findings that were usually concordant with the randomized controlled trials (RCTs).
- If data from RCTs are analyzed without taking baseline and follow-up trends into account, our results indicate that the findings may sometimes be misleading.
- Those who commission or conduct impact evaluations of health system interventions should routinely use graphical displays of longitudinal data and time-series analysis methods when evaluating intervention effects, whether randomization is feasible or not.

due in part to practical difficulties encountered when conducting randomized trials of health system interventions, such as nationwide reforms (eg, introducing user fee exemptions for pregnant women and children). Therefore, other study designs are often used in this field. The simplest pre–post design uses single observations before and after an intervention to evaluate whether a change occurs. However, because factors other than the intervention (eg, secular trends) may cause an observed change (or lack of change), this is considered a weak method [1,2]. An extension of this approach is the single-arm interrupted time-series (ITS) design, where multiple measurements are carried out before and after an intervention, which can control for preintervention and postintervention trends [3–5]. The ITS method is widely recommended for impact evaluation of system and policy changes and has been promoted as "a particularly strong quasi-experimental alternative to randomized designs when the latter are not feasible" [6].

It is widely recognized that different study designs differ in internal validity and various study designs are sometimes placed in a hierarchy [7]. In these hierarchies, randomized trials are typically rated above nonrandomized studies, including ITS studies. Most systematic reviews published through the Cochrane Collaboration only include randomized trials. Among the exceptions are systematic reviews from the "Effective Practice and Organisation of Care" review group, which often include nonrandomized studies (including ITS studies) [8]. Findings from ITS studies are, however, generally considered to have a higher risk of bias than findings from RCTs [9]. This is based on the logical argument that only randomization is able to control for confounders that are not known or measured, whereas other study designs can only control for confounders that are known and measured [10]. Studies have investigated the effectiveness of randomization in limiting selection bias (and thus ensuring comparable groups in effectiveness evaluations), but this work has mainly focused on clinical trials and less on health system and policy interventions [11]. Also, previous research comparing the results from randomized trials with those from other study designs has often lumped together many different types of nonrandomized studies. This may be inappropriate because all nonrandomized study designs are not equally prone to bias.

An overview of existing reviews addressed the issue of whether RCTs provide the same effect size and variance as nonrandomized studies of similar policies [12]. The authors reported that in many cases, the effect sizes from RCTs differed from nonrandomized studies. Consequently, they concluded that "policy evaluations should adopt randomized designs whenever possible." However, ITS analyses were not considered separately in that report.

There are few empirical data from which to draw firm conclusions regarding the relative merits of different study designs for effectiveness evaluations. Debates on this topic are largely based on theoretical arguments. This is particularly the case for ITS because little has been done to compare findings from ITSs and RCTs in a systematic way.

In practice, randomized experiments of system interventions are almost invariably cluster randomized trials (C-RCTs) that randomize groups rather than individuals (eg, clinics, hospitals, communities). We recently conducted a reanalysis of one C-RCT and found that estimates from ITS analyses of the intervention arm only (single-arm ITS), and incorporating both the intervention and control groups (controlled ITS), were concordant with the C-RCT result [13]. Additional comparisons of the same sort would help to determine whether those findings can be generalized.

The aim of this article was to further explore whether ITSs yield results that differ from those of cluster randomized controlled trials (C-RCTs) and to identify possible explanatory factors for such differences. Our primary objective was to compare each trial result with the effect estimate based on the single-arm ITS (ie, only intervention group data, discarding the control group). In addition, we conducted ITS analyses incorporating data from both arms of each trial.

2. Methods

The full study protocol is found in the Appendix at www.jclinepi.com.

2.1. Search for trials

We searched for C-RCTs of health system interventions where data were available for a series of time points before and after the interventions were implemented. The amount of data had to be sufficient to allow for meaningful ITS

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