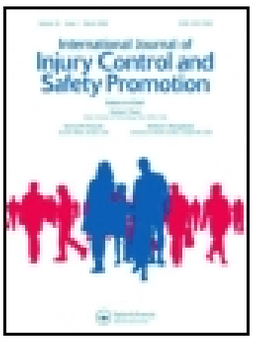

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ACCIDENTAL NOTE

Studying the effect of interventions in injury research: experimental design options

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1. Introduction

In order to understand the effect of an intervention to promote safety or to prevent traumatic injury, an experimental study design is preferred over an observational study design. An experimental design allows the investigator the opportunity to control not only the intervention type, intensity and duration, who receives it and who does not, but also other potential factors that may impact the effect of the intervention. The desire is to be able to claim that there is a causal relationship between the intervention and an outcome of interest, after controlling for other potential factors. In order to exercise any control, intervention studies must be prospective (Figure 1). Different types of prospective study designs for studying the effects of interventions have varying degrees of control over potential confounding factors. This Accidental Note reviews study designs that are used in the injury field to assess the effects of interventions, focusing on design and conduct considerations and how they affect the inferences that can be made about the effects of the intervention. We first present non-experimental study designs, sometimes referred to as 'quasi-experimental studies,' followed by true experimental study designs.

2. Non-experimental study designs

Non-experimental study designs are ones in which an intervention takes place, but there is no process of randomization, so that the investigator does not control the assignment. They may also have less control over potential confounders of the effect of the intervention.

2.1. Pre-post or before-after study designs

One of the most common study designs used in injury research is the 'before-after' study (Hauer, 1997). Instead of comparing subjects who receive the intervention to those who do not, one compares a subjects' before situation to their own situation after they got the intervention if done at the individual level (Figure 2). This study design is very commonly used, especially for interventions at the community level, such as changes in policy or laws, or environmental improvements. One compares the situation in the community during the time periods before the intervention, to the situation in the same community during the time periods after the intervention has been implemented. The major strength of this design is that individual (or community) characteristics are assumed to remain the same in the before and after periods and thus should not affect the estimate of the effect of the intervention. The major weakness of this design, is that one does not know if other individuals (or communities) that did not participate in the intervention would have also had a similar effect, since the 'before situation' is the comparison or counterfactual situation for the 'after situation.' Analytically, measures of the effect of the intervention are paired-data statistics such as the Wilcoxon signed-ranks test (see Bangdiwala, 2013) and the paired *t*-test for continuous outcomes, or McNemar's test if outcomes are binary.

For example, Pulugurtha and Chittoor Khader (2014) assess the effects of introducing a permitted phase, through the use of a flashing yellow arrow (FYA) signal for left-turning vehicles, in reducing crashes at intersections. They conducted a before-after comparison study in 18 intersections in the city of Charlotte, NC, USA. They compared the estimated number of left-turn crashes, had the FYA signal not been installed, to the actual number of left-turn crashes, to assess the direct effect of the intervention. The authors claim that their results show that the FYA signal helps reduce the left-turn crashes.

2.2. Comparative studies

A comparative study is one in which selected individuals (or communities) receive an intervention, and another independent set of individuals (or communities) do not, and these in turn serve as the control or counterfactual group (Figure 3). Since the comparison group is independent from the intervention group, one can use common measures of the effect of the intervention such as the Wilcoxon–Mann–Whitney test and the two-sample *t*-test for continuous outcomes, or common ratios of measures of effects (e.g. odds ratios,

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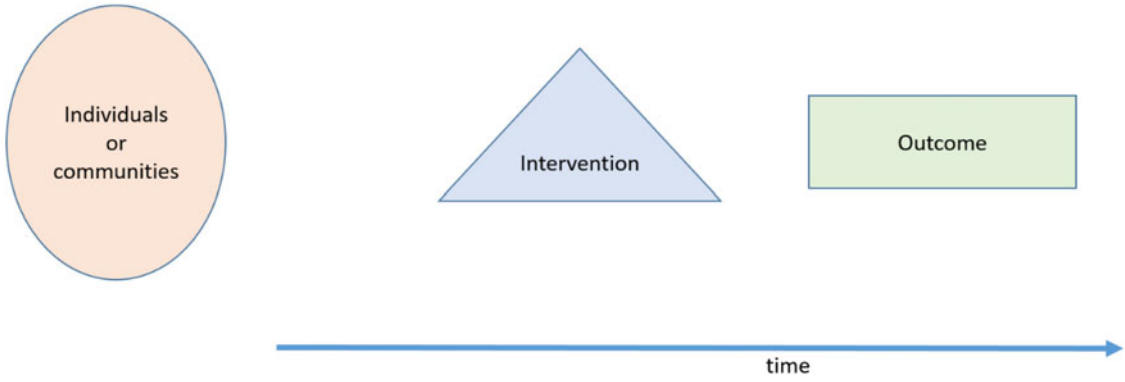

Figure 1. Schematic diagram of a prospective intervention study.

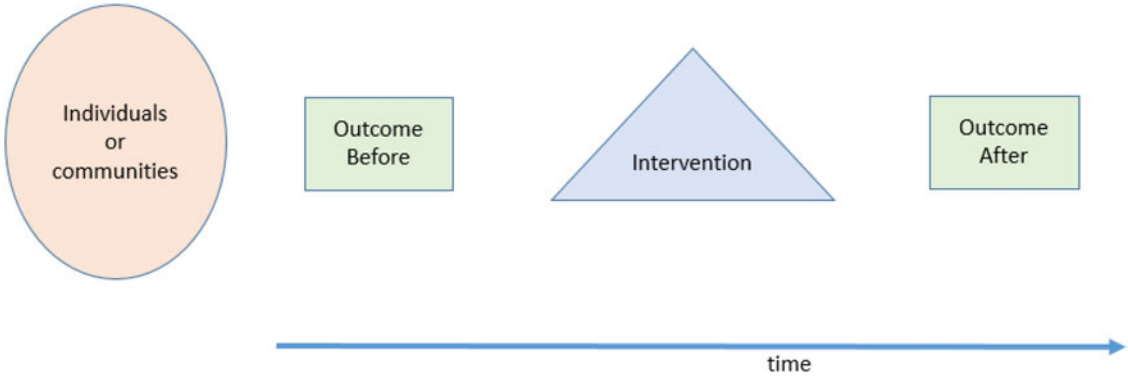

Figure 2. Schematic diagram of a 'before-after' intervention study.

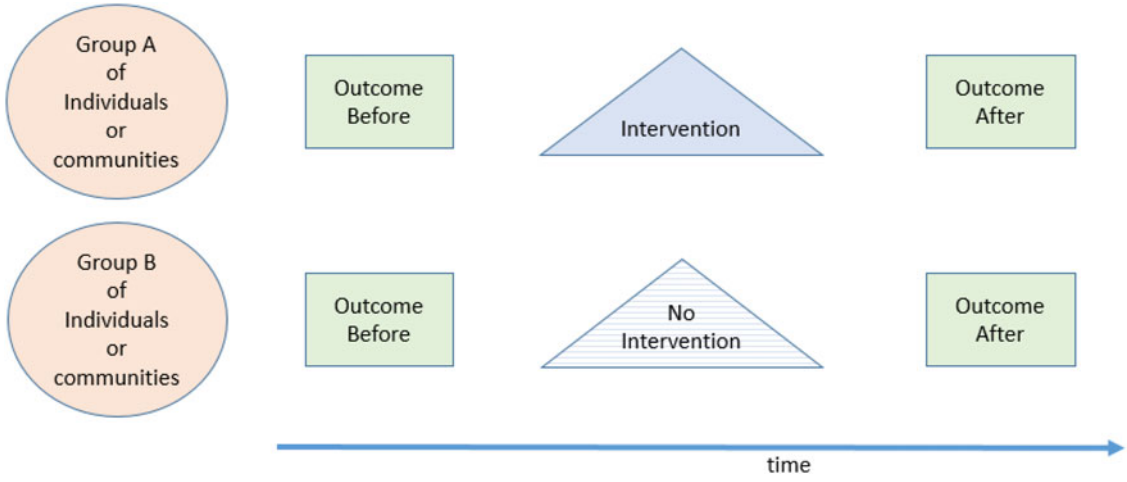

Figure 3. Schematic diagram of a two-group comparison (non-randomized) intervention study.

relative risks) if outcomes are binary or categorical. The major weakness of this study design is the potential bias from individuals or groups self-selecting themselves to receive or not the intervention.

For example, Rubio-Romero, Carrillo-Castrillo, and Gibb (2015) evaluated the impact of a subsidy policy that enabled construction companies in Andalusia (Spain) to acquire new scaffolds. Subsidies were granted to companies based on a public and competitive call. The rates of accidents involving falls in subsidized companies where compared to the rates in a random sample of companies selected from the social security census of companies. They used a difference in before–after rates between the intervention companies and the control companies, and claim that the improvement of scaffolds was effective in reducing rates of accidents of falls to a lower level.

2.3. Natural experiments

In a natural experiment, a set of individuals (or communities) from some population are naturally exposed to some factor, but not because of a planned intervention (Craig, Katikireddi, Leyland, & Popham, 2017). If there is no independent comparator, sometimes the before situation is used as the counterfactual, and it would be called a 'before-after

natural experiment.' If possible to find an independent comparison group that is similar to the group that received the intervention, it would be called a 'comparison natural experiment'. Analytically, measures of the effect of the intervention are similar to the before-after studies or to the comparison studies, depending on the counterfactual used. Since no self-selection occurs, that potential bias is not present. However, usually there is no information from the 'before' periods, and it is hard to find 'similar' comparison groups, so that finding a suitable counterfactual is a major weakness of this study design.

For example, in 2003, the US state of Oregon failed to agree on a budget, which resulted in the layoff of over one-third of the traffic police force. De Angelo and Hansen (2014) compared the injury and fatality rates in Oregon with rates in two neighbouring states before and after the layoff, in this natural experiment. They looked at the differences before and after in each state and the differences of these differences from the state of Oregon in what is called a 'difference in differences' comparative analysis. After accounting for other factors, the 'intervention' of less policing was associated with a 12%–14% increase in fatalities.

3. Experimental designs

True experimental designs are ones in which randomization is used to control who gets and who does not get the intervention. The process of randomization is key, as it permits valid assessments of the effect of the intervention using the standard two-sample tests already mentioned. The amount of control the investigator has on potential confounders is greater than in non-experimental designs.

3.1. Individual randomized experimental designs

The randomized controlled trial (RCT) is the accepted classic design to establish the causal relationship between an exposure (the intervention) and an outcome of interest (Figure 4). Selected individuals that meet strict inclusion and exclusion criteria (minimizing heterogeneity in control factors) are randomly assigned to intervention or control (avoiding self-selection bias and also balancing out potential confounders' effect on the intervention), a standardized protocol is followed (minimizing heterogeneity in other related factors), and the outcome is carefully defined and measured (minimizing ascertainment bias). It is usually not very common in the injury field, since often interventions are policies, laws, or infrastructure changes that cannot be implemented individually.

An example of a parallel design RCT is the study of Babul, Olsen, Janssen, McIntee, and Raina (2007) to test an intervention aimed at addressing the risk of injury in infants 2–12 months of age. Eligible parents ($n = 600$) were randomly assigned to one of three groups: (1) home visit plus safety kit; (2) safety kit alone; (3) control group. Outcomes were assessed at 2, 6 and 12 month after randomization. Unfortunately, neither of the interventions was associated with a reduction in parent-reported injuries among children in this 3-arm RCT.

Factorial RCT designs, where all levels of two or more intervention modalities are simultaneously varied and implemented in an experimental study, is described by Bangdiwala (2016), along with their advantages and limitations, and statistical analytic strategies. An r by c factorial design is essentially an rc-arm parallel RCT. They also are not commonly used in the injury field, but do allow the possibility of simultaneously testing multiple interventions. For example, Campbell et al. (2005) evaluated the effects of a home safety program and a home exercise program to reduce falls and injuries in older people with low vision in New Zealand. Participants were randomized to receive a home safety assessment and modification program delivered by an occupational therapist, an exercise program prescribed at home by a physiotherapist plus vitamin D supplementation, both interventions, or none – just social visits. They found fewer falls occurred in the group randomized to the home safety program but not in the exercise program. However, neither intervention was effective in reducing injuries from falls.

Crossover RCTs assign individuals to one of two interventions, and after a period of time, are 'crossed-over' to the other intervention (Figure 5). They are not very common in the injury field since they require that participants revert back to their baseline state at the end of the first study period, and that there are no carry-over effects into the second period of the experiment. Other temporal period effects must also be considered in the analyses. Outcomes must also occur in a relatively short amount of time. The potential benefit is for increased study power, since the same individuals provide estimates of the intervention effects more than once. A recent example is from Sczesny-Kaiser et al. (2019), who performed a crossover clinical trial comparing conventional physiotherapy (CPT) and hybrid assistive limb for body-weight supported treadmill training (HAL-BWSTT) to improve walking functions in spinal cord injury and chronic stroke patients. In a small sample of 18 patients, they used a randomized, crossover study design, but found no statistically significant effects.

3.2. Group (or cluster) randomized experimental designs

Interventions in the injury field are more commonly administered to groups rather than to individuals for practical and for ethical reasons (Figure 6). It is thus more common to have RCTs that randomize clusters or groups of individuals rather than individuals to intervention arms. Standard parallel designs of group RCTs are similar in design to individual RCTs, but have substantially different additional issues to handle. The unit of randomization in the cluster, but the unit of analysis is the individual members of clusters. The benefits of randomization in balancing out potential confounders is usually not reached in cluster RCTs. Since interventions are administered to groups, there is less control over who actually receives the intervention; and adherence to the intervention is more difficult to monitor in group settings. Furthermore, one must account for the 'group (or

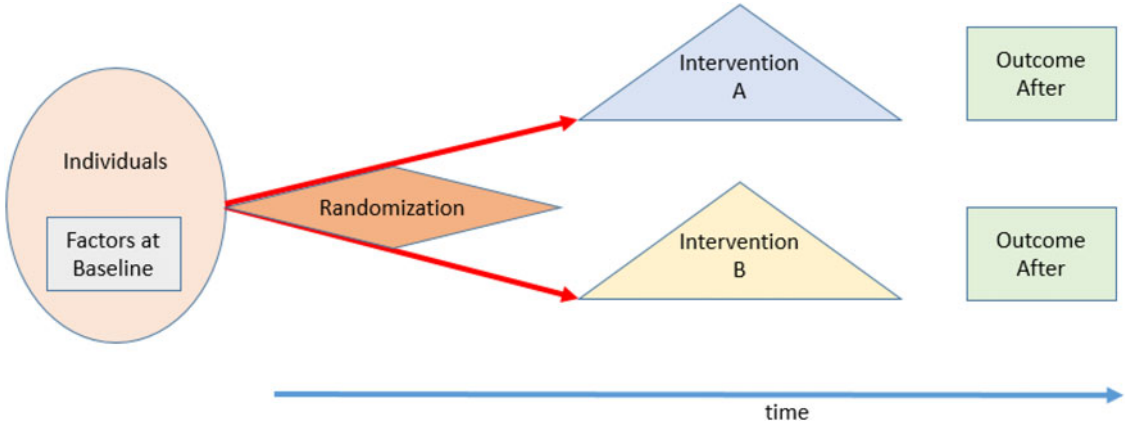

Figure 4. Schematic diagram of a two-arm, parallel-design, randomized controlled trial (RCT) intervention study.

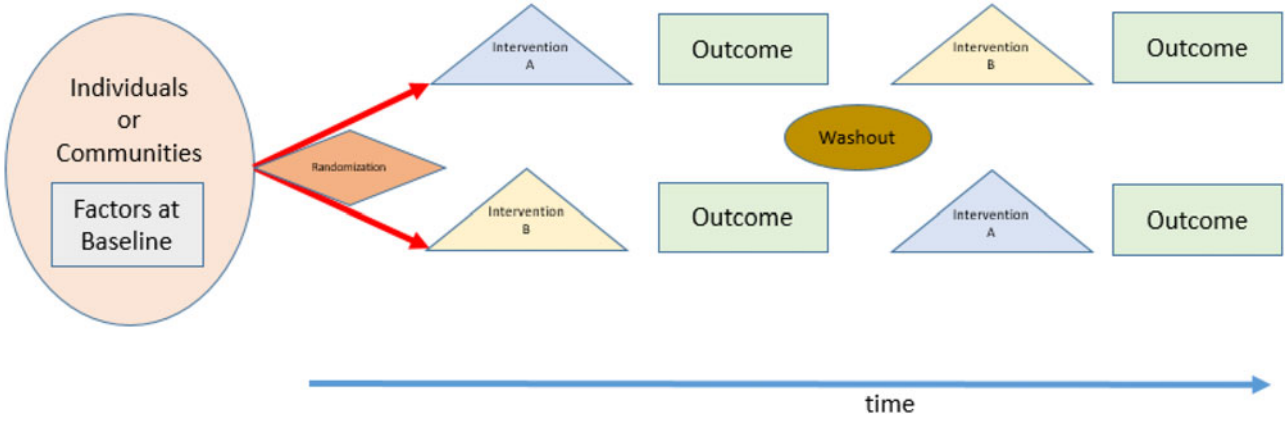

Figure 5. Schematic diagram of a two-period crossover randomized controlled trial (RCT) intervention study.

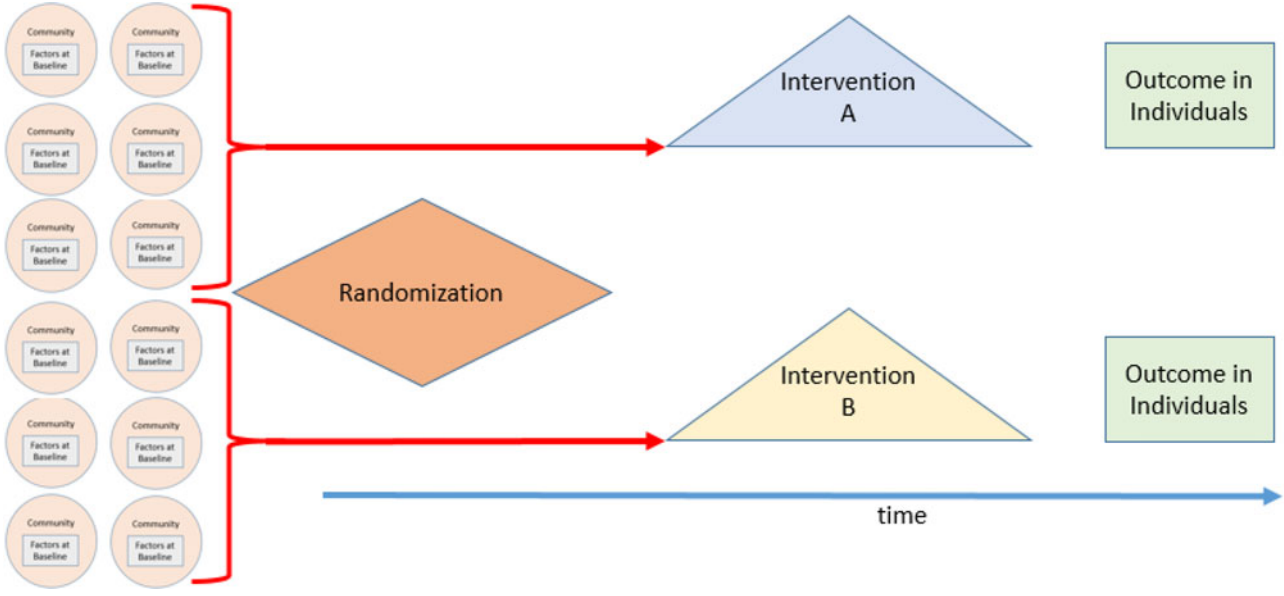

Figure 6. Schematic diagram of a cluster randomized controlled trial (RCT) intervention study, with 12 clusters.

cluster) effect,' which induces a correlation among the individuals within a group, quantified by the intraclass correlation coefficient (ICC). Group RCTs must take the ICC into consideration at the planning phase, in deciding total numbers of clusters and average number of members within a cluster. The ICC must also be taken into consideration at the analysis stage, usually using complex regression models such as generalized linear mixed models (GLMM) or generalized estimating equation (GEE) models.

An example of a cluster RCT is the study of Goodall, Pope, Coyle, and Neumayer (2013), which randomized 10 cohorts of army recruits undergoing the 80-day basic training at an Australian Army Recruit Training Center, to an intervention arm with structured balance and agility

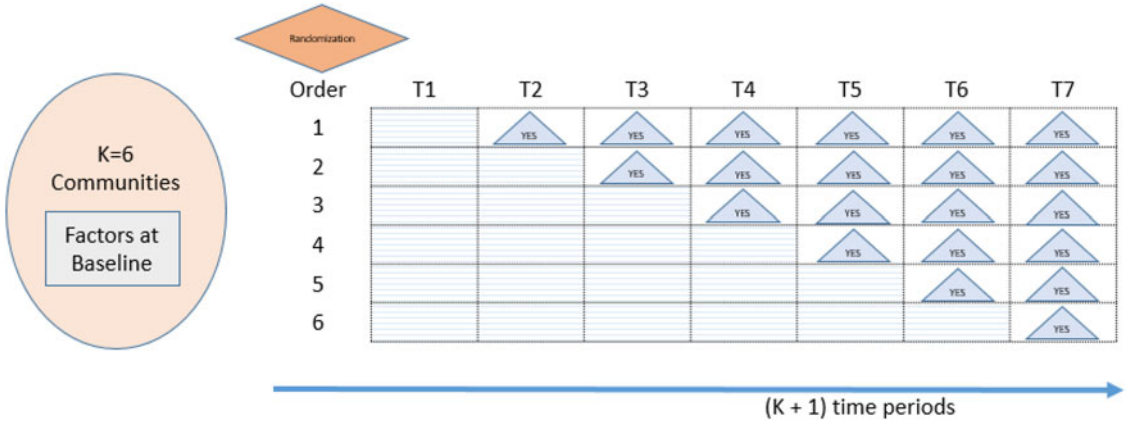

Figure 7. Schematic diagram of a stepped-wedge cluster randomized controlled trial (RCT) intervention study with K = 6 clusters/communities.

exercises added to the physical training program, or to the control intervention arm which involved the normal physical training program. A total of 867 individuals were randomized. The outcomes studied were lower limb, knee and ankle injuries during basic training. They concluded that the intervention, implemented as an addition to the basic physical training, was possibly harmful.

A less-common cluster randomized design is the crossover cluster randomized design. It has the same methodological issues as the individual crossover experimental design, in addition to the issues related to randomizing groups of individuals to the intervention arms. Furthermore, in cluster crossover studies, the individuals from a given cluster may or may not be different in the different periods. McDonall et al. (2019) conducted a cluster randomized, four-period crossover trial to test the efficacy of multimedia intervention for supporting patient recovery after total knee replacement surgery. Their primary outcome was patients' reported worst pain intensity on day 3 after the surgery. They randomized wards rather than patients for pragmatic resource allocation reasons, to periods of 12–16 weeks in which the intervention was administered or not, with a wash-out period of 2 weeks in between. Two wards were randomly assigned to different sequences of control (C) and intervention (I) periods, C–I–I–C and I–C–C–I. A third ward served as a control ward – C–C–C–C. They found that the intervention enhanced patients' involvement in their care and that pain intensity was reduced.

The 'stepped-wedge' study design is a cluster randomized experimental design in which $K > 2$ clusters (groups of individuals or communities) are randomized over varying time periods to receive the intervention. Once a cluster receives the intervention, it is not removed. This design is especially appropriate for environmental or policy interventions, which are not possible to be allocated to individuals but to groups of individuals, and which are difficult or impossible to reverse. The basic stepped-wedge design has an initial 'baseline control' period in which no cluster has received the intervention, and after periods of equal duration, one of the remaining clusters is randomly selected to receive the intervention. This leads to $K+1$ time periods, and to $(K)(K+1)/2$ observations of clusters under the intervention as well as $(K)(K+1)/2$ observations of clusters under the control (Figure 7). Note that the clustering and period effects must also be considered in the analyses.

Linder et al. (2019) evaluate the effectiveness of the Swedish national two-tier trauma team activation (TTA) criteria implemented starting in 2016 using a prospective stepped-wedge cohort study design in 5 centers. They used information from the Swedish trauma registry prior to and after stepwise introduction of the new TTA criteria. They found that the newly implemented Swedish TTA criteria resulted in an increased efficiency in use of resources and that patient safety was not compromised.

4. Concluding remarks

When assessing the effects of interventions, true experimental designs are preferred over quasi-experimental designs. Even when randomized experimental studies are conducted, they have varying degrees of control over potential confounding factors. Cluster based studies have less control over such factors than individual randomized studies. However, the choice of intervention study design is usually dictated by pragmatic and practical reasons, as well as by the types of interventions to be undertaken.

The Consolidated Standards of Reporting Trials (CONSORT) statement, initially published in 1996, was developed to improve the reporting of randomized controlled trials. It originally focused on what to report from individual parallel arms randomized controlled trials. It has been updated (Schulz, Altman, Moher, & CONSORT Group, 2010), and has also been expanded to cover how to report crossover trials (Dwan, Li, Altman, & Elbourne, 2019), cluster randomized studies (Campbell, Piaggio, Elbourne, Altman, & for the CONSORT Group, 2012), and stepped-wedge designs (Hemming et al., 2018). For proper reporting, it is imperative that one follow the CONSORT publication guidelines appropriate for the particular experimental design used.

Disclosure statement

No potential conflict of interest was reported by the authors.

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