

Should You Register Your Study as a Clinical Trial?

Governments and international organizations have been working steadily to make clinical trial information more transparent and widely available and to standardize registries and processes of registering. I'd like to briefly discuss which studies should be registered, the reasons why registration is important, and some remaining issues of debate.

A *clinical trials registry* is a publicly available, sanctioned site for registering a clinical trial. The most widely used registry is ClinicalTrials.gov (access <https://clinicaltrials.gov>), which is maintained by the U.S. National Library of Medicine. Registration requirements vary by country, but in 2005 the International Committee of Medical Journal Editors (ICMJE) began mandating that all ICMJE member journals require registration of clinical trials as a condition of consideration for publication (access http://www.icmje.org/recommendations/archives/2005_urm.pdf). National Institutes of Health (NIH)-funded trials require registration at ClinicalTrials.gov, and the ICMJE provides a listing of additional registries accepted by ICMJE (access <http://www.icmje.org/about-icmje/faqs/clinical-trials-registration>).

Importantly, many more studies now qualify for registry since the NIH (2014) broadened its definition of a clinical trial to: "A research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of those interventions on health-related biomedical or behavioral outcomes" (para. 4). This highly inclusive definition does not require random allocation to study conditions, the use of a control group, or the estimation of a required sample size sufficient to avoid a Type II error. Hence, within this definition, many pilot studies, feasibility studies, and studies that use a pretest-posttest design without a control or comparison group should be registered. The World Health Organization's (2019) definition of clinical trials is used by the ICMJE and is as broad and inclusive as the NIH definition.

There are scientific, ethical, and clinical reasons why registration is important. Registration helps eliminate

publication biases, as the results of only 50% of trials are ever published (Jones, 2013). One review found that trial results, especially serious adverse events, are more completely reported at ClinicalTrials.gov than in the published article (Riveros et al., 2013). Clinicians and public policymakers require complete and accurate information regarding the efficacy and adverse effects of interventions.

Requirements regarding prospective registration of trials can mitigate suppression of outcomes that do not support efficacy or changing hypotheses based on results obtained. A systematic review of 22 analyses for selective outcome reporting found that 40% to 62% of studies had at least one primary outcome changed, added, or omitted from protocol to publication (Dwan, Gamble, Williamson, & Kirkham, 2013). Another study of 21 trials published in *The BMJ* found that 27% (89/333) of outcomes prespecified in the protocol were not reported in the manuscript, and 11% (31/275) of reported outcomes were not prespecified (Weston et al., 2016). Scientists who perform meta-analyses and other systematic reviews can only provide accurate summaries of findings when positive and negative results are accessible. Providing the questions to be studied and the key aspects of the study methodology in the registry can inform other researchers of ongoing work and methods being used and possibly prevent some duplication of efforts. From an ethical point of view, registries support international scientific cooperation, provide global access to cutting-edge research, increase a patient's ability to learn of new experimental studies accepting participants, and provide opportunities to evaluate adherence to scientific and ethical standards.

Several reports of prospective and retrospective registration have shown that many clinical trials are never registered or are registered after participants have been enrolled (Harriman & Patel, 2016; Huser & Cimino, 2013; Scott, Rucklidge, & Mulder, 2015). A review of randomized controlled trials published in three nursing journals between 2011 and 2016 found that 58% were not registered

and only 8% met criteria for timely registration (Gray et al., 2017). Trials not registered before enrolling participants are by definition less transparent and decrease confidence that amendments to the protocol, hypotheses, and outcomes have been adequately reported.

Registration of a study provides no determination of quality or even that a rigorous clinical trial design has been used. In addition to issues of quality, a remaining concern is the broad nature of what is included as a clinical trial. Although the relatively new definition of a clinical trial was not intended to expand the scope of the category of clinical trials, the definition does not specifically require randomization or a control group. Studies that are one-group comparisons from pre- to posttest qualify as clinical trials if the principal investigator can answer “yes” to these four questions (NIH, 2018, para. 3):

1. Does the study involve human participants?
2. Are the participants prospectively assigned to an intervention?
3. Is the study designed to evaluate the effect of the intervention on the participants?
4. Is the effect being evaluated a health-related biomedical or behavioral outcome?

Small feasibility studies and pilot studies may meet the criteria for registration under the NIH definition of a clinical trial. These studies are often used primarily to demonstrate to proposal reviewers that methods planned for a large clinical trial are rigorous and feasible, but they also often include some measurement of the effects of an intervention. These studies are often not adequately powered and do not use randomization and other control strategies to protect internal validity. If the primary purpose of these studies is to sort out methods, the need for registration is unclear. Including these preliminary studies in translational work and systematic reviews could distort conclusions.

In our list of author submission guidelines, *Research in Gerontological Nursing (RGN)* states that we follow ICMJE guidelines. At this point, we report all submitted registrations and require registration of all intervention studies with randomization to study conditions that are not classified as pilot or feasibility studies. We will continue to evaluate this policy as the momentum of current discussions is favoring expanded requirements for registering trials and reporting results of clinical trials. The ICMJE (2016) suggests that if researchers are uncertain whether their study meets the definition for a clinical trial, they should err on the side of registration. We encourage all authors submitting intervention studies to *RGN* to report positive

and negative findings as well as any adverse events. Transparent reporting of research benefits clinicians, scientists, patients, and public policymakers.

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