Considering Trial Registries as a Platform for Timely Access to Study Results

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Oncology is one of the most active fields in medical research. Timely publication of research findings is critical for informed decision-making in research, policy, and clinical practice. Liu et al.1 reviewed the reporting of findings from completed or terminated oncology trials registered on ClinicalTrials.gov from 2007 to 2017. Allowing for a minimum of 24 months for publication of results after trial completion, the authors searched for trial results published in journals and posted on the trials registry in 2019. They found that of 12,240 registered oncology trials, only 60.7% (n = 7,425) reported results within a median follow-up of 80 months. Of these 7,425 trials, more than two-thirds (n = 2,807) were posted only on ClinicalTrials.gov without any traceable journal publication. Publication within 24 months increased via both channels during the studied decade, increasing to 39.1% in 2017. In line with previous research from various fields,2 the article by Liu et al.1 stresses the gap between trial conduct and results reporting, which is especially pronounced for trials that are small, with terminated status, or with no effect or adverse outcomes.

A number of factors may affect this finding, including the tendency of journals to accept manuscripts in favor of experimental treatments and with strong conclusions.3 The inability of investigators to publish complete trial results, even if patient outcomes are not affected or are unfavorable, is a critical waste of resources that may lead to duplicate work and distortion of the perceived association between a treatment and the examined health outcomes. In addition, this practice may encourage investigators to spin results to increase their chances for publication.4 To counteract this potential source of publication bias with possibly harmful implications for patients and public resources, Liu et al.1 suggest that trial registries can serve as an urgently needed platform that makes data from these nonpublishable studies accessible. Trial registries are an open-access portal and can be used to disseminate research findings to a wide audience. However, some challenges need to be overcome first for registries to become a primary means for posting data results.

First, although ClinicalTrials.gov is the largest and most well-known clinical trial registry in the world, many other international and national registries exist, but they do not have the same functionality as ClinicalTrials.gov and do not provide a comparable infrastructure for posting study results. Several registries are linked to each other by the registration number of a trial, but not all studies have an entry on ClinicalTrials.gov, and each registry record has to be manually updated by the study investigators.

Second, in the article by Liu et al.,1 the number of studies registered served as the denominator to ascertain whether study results were available, assuming that, generally, all clinical trials had been registered. This assumption is reasonable for oncology trials given that the policy on mandatory clinical trial registration of the International Committee of Medical Journal Editors was implemented in 2005. A search in trial registries should identify all randomized clinical trials. The assumption of complete coverage of clinical trials in registries may not apply to all medical fields. Depending on the context, prospective trial registration ranged from excellent (100% of studies, based on grant monitoring5) to worrying for nonregulated health care interventions.6

Third, in addition to the resulting bias from lack of publication, selective reporting of outcomes is another complex issue. A lack of consistent reporting of safety and quality-of-life data is a recurrent theme in many systematic reviews. Most oncology trials define at protocol stage how they will measure outcomes, but safety, symptoms, and quality of life are not always listed in the study registries.

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Safety outcomes and patient-reported outcomes are not always listed in the study registries. Often, registries contain only a selected version of the protocol, which leads to frequent inconsistencies in outcomes when compared with the original study protocol and journal publications, even for primary outcomes. To prevent selective outcome reporting (ie, changing the importance of outcomes, outcome measurement instruments, time points, or combination of end points, or simply omitting outcomes), a thorough cross-check between study protocol and registry would need to be mandated at the time of registration, which would form the basis for the later publication of results in the registry. In addition, journals could counteract selective reporting by having editors check the completeness of results against both study protocols and trial registrations and, in case any discrepancies are identified, by informing the registries. At the same time, representation of inconsistent definitions of common outcomes, such as adverse events and quality of life, could be standardized to facilitate comparability between trials and combination of results by meta-analyses.

In the meantime, encouraging the use of data-sharing agreements, including study reports and individual patient data, is an approach to increasing the transparency of the results of investigated medicines or interventions. This approach may help reduce monetary or intellectual biases.

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REFERENCES