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Should all clinical trials of oral health be registered?

Randomised controlled trials (RCTs) and their meta-analyses are considered the gold standard to making informed decisions about which treatment is best. In fact, meta-analyses combine the findings of several RCTs and may overcome the limitations of individual trials. However, because of the vast amount of unpublished results of RCTs, the conclusions of a systematic review can be misleading¹. Waste in biomedical research is caused by reporting bias, including publication bias and selective outcome reporting². In fact, investigators and sponsors tend not to make public the results of RCTs or specific outcomes or analyses because of the direction, magnitude or statistical significance of the results³. Negative results are less likely to be reported and therefore systematic reviews are skewed toward the positive⁴.

Prospective registration of clinical trials represents the best solution to reporting bias⁵. Trial registration does not ensure that all trial results will be published but is a key factor in reducing reporting bias⁶. Indeed, peer reviewers, readers or meta-analysts can compare reports of published results with the registered trial record: they can find the unpublished RCTs in public registries and hence assess publication bias; they can also detect the poor reporting of outcomes that can be omitted or changed^{7,8}. Thus, investigators should prospectively register their trials in a public registry⁹. The International Committee of Medical Journal Editors (ICMJE) has made registration a requirement for publication in their journals since September 2005¹⁰.

However, oral health research appears to be lagging behind other biomedical fields in trial registration. In fact, only 23% of a sample of 317 RCTs published in oral health journals in 2013 was registered in a public registry, regardless of the editorial policy on registration described on the journal website¹¹. In six previous studies, the mean proportion of regis-

tered trials in general or specialty medicine was 46% (range 20% to 72%)¹².

The proportion of registered trials being low in the field of oral health is probably not an individual fault but is attributable to the whole research system¹³. We propose two complementary approaches to improve trial registration: (i) investigators being informed of the importance of registration; and (ii) editors of all oral health-related journals requiring authors to register their trials.

Trial registration should proceed as follows. The largest trial registry is ClinicalTrials.gov, run by the US National Library of Medicine at the National Institutes of Health¹⁴. The other registries are the primary registries in the World Health Organization (WHO) Registry Network that meet the requirements of the ICMJE. Trials accepted by a registry are assigned a unique trial identifying number, which should be reported in the published report. The registration must be prospective, that is, before the enrolment of the first participant. Researchers should register any trial design, including split-mouth RCTs, which are relatively frequent in oral health research. In a meta-epidemiological study, split-mouth trials contributed half of the evidence in meta-analyses of oral health research¹⁵. Registration of these trials is particularly important because ClinicalTrials.gov, the most prominent registry, does not currently allow for capturing the split-mouth design (only 'single-group', 'parallel', 'cross-over' or 'factorial' study designs are proposed). Investigators should be informed that clinical trial registration is quick, easy, and free of charge. The amount of effort required to register a trial is negligible compared to that required to obtain funding, ethical approval, conduct the trial, and analyse and report its findings.

Transparency in oral health research is the responsibility of researchers as well as journal edi-

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tors¹⁶. Therefore, editors of all oral health journals should now require trial registration and include the reporting of a trial identification number in their author guidelines. In February 2014, we contacted the editors of all oral health journals publishing RCT reports to ask if trial registration was required or recommended and if so, how this editorial policy was implemented. An email reminder was sent after 10 days. Of the 78 journals contacted, we received 46 (59%) answers; 10 editors (22%) declared requiring trial registration and 7 (15%) recommended it. For these journals, trial registration was checked at the administrative processing stage, right after manuscript submission or by the editors or associate editors. Many editors (39%) declared that they did not have an editorial policy on trial registration; 7 answered that they planned to address this issue in their editorial policy in the near future. In another survey of biomedical journals editors, in 2011, 253 of 692 (37%) editors responded: 50% declared that trial registration was required and 18% checked submitted papers against registered records¹⁷.

Some editors may be reluctant to adopt trial registration because it requires additional work or they might lose manuscripts. However, if oral health journals required a trial registration number on manuscript submission but did not check the number, peer reviewers could assess non-registration, and the burden for journal editors would be minor. Moreover, editors could initially allow for a transition period during which unregistered trials would not be rejected, and the new policy would apply to trials that recruited participants after a defined date. Finally, the creation of an International Committee of Editors for Oral Health Journals may help with adopting prospective registration for all clinical trials. Such committees exist for other medical fields; recently, the International Society of Physiotherapy Journal Editors recommended that all physiotherapy journals require mandatory prospective registration of clinical trials¹⁸.

■ References

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