

Reporting the findings of clinical trials: a discussion paper

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Background

When researchers embark on a clinical trial, they make a commitment to conduct the trial and to report the findings in accordance with basic ethical principles. This includes preserving the accuracy of the results and making both positive and negative results publicly available.¹ However, a significant proportion of health-care research remains unpublished and, even when it is published, some researchers do not make all of their results available.² Selective reporting, regardless of the reason for it, leads to an incomplete and potentially biased view of a trial and its results.³

The consequences of publication bias and selective reporting have gained the attention of health-care consumers, the media and politicians. All have recognized the impact that undisclosed results can have on the ability of patients, practitioners and policy-makers to make well-informed decisions about health care. Concern over the underreporting of adverse events, in particular, has increased the demand for more transparent processes for registering clinical trials and reporting their findings. In recent years, trial registration has become increasingly widely accepted and implemented. There are now well-established mechanisms to register trials, assign unique identifiers and make this information publicly available. WHO's International Clinical Trials Registry Platform Search Portal helps bring the data from these registers together, making it much easier to search for the existence of a trial

(available at: <http://www.who.int/trialsearch>).

The value of registration goes far beyond the administrative benefits of having a complete collection of all trials. Trial registers may facilitate recruitment into clinical trials by raising awareness of their existence among potential participants and health-care practitioners. They may also lead to more ethical and successful research by avoiding the unintentional duplication of research already under way elsewhere. From the perspective of this paper, however, the greatest benefit of trial registration is enhanced transparency; that is, making it clear which trials are being conducted so that people can anticipate their results.

The next step to informed decision-making is to make the findings of clinical trials available, since it is knowledge of the findings, rather than of the existence of a trial, that is likely to have the greatest impact on people trying to choose between alternative interventions. The arrival and growth of electronic publishing and the Internet as dissemination tools without page or length restrictions has greatly expanded the ability of people to make findings available and accessible in full. The recognition of the need for reliable evidence to improve health care and to facilitate the synthesis of the results of research into systematic reviews has fuelled the demand for access to the findings of all research, as have the needs of the numerous other stakeholders in clinical research.

A proposed position

The position proposed by the members of the WHO Registry Platform Working Group on the Reporting of Findings of Clinical Trials is that "the findings of all clinical trials must be made publicly available". This paper discusses the principles underlying this position. Our goal is to contribute to the ongoing debate and to foster the collaboration that is necessary to ensure that the findings of clinical trials do not remain hidden from the people who need access to them.

What is a finding?

The language used to discuss the reporting of clinical trials usually focuses on "results" – often taken to mean the numerical results of an analysis for a specific outcome. For example, a summary estimate such as a relative risk. However, the reader or user of research also needs background information that will allow them to correctly interpret the results for specific outcomes. The type and amount of information required will depend on the nature of the audience and how it will use the information received but will have four key elements:

1. Methodological context

The user needs to know what the original plans for the trial were and how it was actually conducted. Some of the original plans will be available if the trial was registered, but more complete

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information should be in the full trial protocol. The actual conduct of the trial might, however, differ from that planned. Such differences may be valid but should be traceable, preferably via a clinical trial registry. The methodological context for a trial might also include information on the primary question that the researchers set out to answer; the hypothesis they were seeking to test; the methods they used to allocate or select participants for the interventions; whether any blinding or masking was done; and a description of the statistical methods planned and used, including a justification of the sample size.

2. Population context

The user needs to consider to whom the results of the trial can be applied. They need to know the characteristics of the population it was initially intended to recruit, as well as the characteristics of the population who were recruited. In reporting their findings, the researchers should therefore refer to the original inclusion and exclusion criteria and provide information on the population that actually took part, describing the extent to which participants left the trial early (with reasons for doing so) and whether interventions were delivered as planned.

3. A result for each outcome

A clinical trial will usually consider several outcomes, each of which might be measured in multiple ways or at multiple time points, and there might be more than one way to analyse each of these measures. The findings should contain the results for every outcome measure and analysis specified in the register entry for the trial, and set out in the protocol or statistical analysis plan. If any of these results are not reported, a reason should be provided for their absence. Any findings from analyses that were not pre-specified should be clearly identified as such.

4. Interpretation

The most contentious aspect of reporting the findings of a clinical trial may be whether the report should include the researchers' opinions and conclusions. It is in this section of a report where the objectivity of the research is confronted by the subjectivity of authors who "use their power as owners of their writing to emphasize one point of view more than another".⁴ Alternatively, linguistic spin is considered by some to be essential to scientific communication, being the opportunity for scientists to speculate and formulate new hypotheses.⁵ Distinguishing opinions and conclusions from advocacy or promotion can be difficult, and it may be preferable to leave the users of the findings to draw their own conclusions and form their own opinions of what the findings of a trial mean for them and their decision-making.

Public availability

Clinical trial results should be available to everyone, regardless of where they live. If the results are not made available within a reasonable period, the reasons for delay and a date by which the findings will be available should be submitted to the relevant clinical trials registry. It should be the responsibility of researchers to produce their findings in a format that can be accessed by potential users, and it should be the responsibility of the user to seek these results. The Internet could provide the main means by which this shared responsibility can be satisfied. Access also needs to be considered in terms of the end user's ability to both view and understand the information obtained.

Historically, access to the results of a trial has usually been achieved through publication in a peer-reviewed journal. This traditional publication model has its limitations, particularly

in an environment where the end users of research information now include health-care policy-makers, consumers, regulators and legislators who want rapid access to high quality information in a "user-friendly" format. In future, researchers may be legally required to make their findings publicly available within a specific timeframe (assuming any legislation created does not have escape clauses built in). In the United States of America, such legislation is already in place (available at: <http://www.fda.gov/oc/initiatives/HR3580.pdf>). This may compromise the ability of researchers to publish trial findings in a peer-reviewed journal. Although some journal editors have acknowledged the changing climate around results registration and reporting (available at: http://www.icmje.org/clin_trial07.pdf), they may have a conflict of interest in that they will probably want the key (and potentially most exciting) messages from a trial to appear first, and perhaps exclusively, in their publication.

Conclusion

People making decisions about health care need access to knowledge derived from the findings of clinical trial research. Following on from WHO's position that all clinical trials must be registered,⁶ it is proposed that the findings of all clinical trials must be made publicly available. This report is the start of a consultation process on how this goal of transparency can be achieved, with the intention that greater accessibility to the findings of all clinical trials will lead to improvements in health and health care. To contribute to the first phase of the consultation, please visit: <http://www.who.int/ictrp/results/consultation> ■

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