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Sri Lanka clinical trials registry

The need for trial registration

Clinical trials advance scientific knowledge, and are indispensable in evaluating the potential benefits and harms of new interventions and treatments. All is however not rosy in the world of clinical trials. Every trial that is conducted does not get published. Of the one million or so randomised controlled trials done since the landmark trial of streptomycin in treatment of tuberculosis, it is estimated that only half have been reported [1], and of the presentations of clinical trials made at scientific meetings, only about half get published [1]. Selective non-publication mainly affects trials with 'negative' or inconclusive results; they are the Cinderellas of the clinical trials world. The authors don't want to report them, journal editors don't want to publish them, and if they are sponsored by the pharmaceutical industry, they want to hide them. But everybody loves a 'positive' trial; some are published twice, and others many times over [2].

Selective reporting is scientific misconduct, as it distorts the evidence available for clinical decision making [3]. If only 'positive' trials of an intervention were published, and 'negative' results concealed, the available evidence would show an overall benefit, whereas the reality may well be the opposite. Multiple publications of 'positive' trials can exaggerate the effects of an intervention in a meta-analysis. The potential for harm of selective publication is very real, as emphasised by several reports of drug 'mishaps', eg. class I anti-arrhythmics after myocardial infarction [4], selective serotonin reuptake inhibitors in childhood depression [5]. Selective publication also undermines the faith placed by trial volunteers in the scientific community; they participate in a trial, at risk of potential harm to themselves, in the belief that their participation would lead to better health care for their fellow men. The best way of repaying this trust is the ethical conduct and full reporting of trials [1,3].

Mandatory registration of all clinical trials, before trial commencement and recruitment of volunteers, can be the way to minimise the negative impact of selective trial publication. From being a nascent idea articulated by a few concerned people in the '70s and '80s [6,7], it has now come to stay. This is largely due to the efforts of the International Committee of Medical Journal Editors (ICMJE) who decreed that all clinical trials involving human subjects should be prospectively registered before they will be considered for publication in biomedical journals which follow their guidelines [3,8].

The WHO has strongly supported the call for mandatory trial registration. It has taken the lead in getting all interested parties together – researchers, clinicians, pharmaceutical industry and health care planners – by establishing the International Clinical Trials Registry Platform (ICTRP) and its allied Collaborating Register Network. The WHO considers 'registration of all interventional trials a scientific, ethical and moral responsibility' [9,10]. The

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ICTRP is envisaged to be a 'one-stop shop' for information on all trials conducted worldwide.

Prospective trial registration has many benefits for scientists, clinicians, health care planners and the public. It ensures free access to trial details in a public domain. Prior registration minimises the negative impact of unpublished trials. Dissemination of the results of all trials is important, as the scientific community needs to be aware of findings from previously conducted trials, and volunteers participating in trials need to be assured that their participation would lead to advancement of scientific knowledge and improvement of patient care. Awareness of planned or on-going trials among the research community helps to avoid duplication of trials, minimising wastage of research effort and funds. Prospective registration also facilitates multi-centre participation in clinical trials.

After a period of initial scepticism, the scientific community has welcomed the concept of trial registration. Several registries have now been developed at national, regional and international levels. Some are disease specific, and some are maintained by the pharmaceutical industry. Perhaps the most widely used are the International Standard Randomized Controlled Trial Number (ISRCTN) scheme managed by Current Controlled Trials Ltd (<http://www.controlled-trials.com/isrctn/>), and the registry maintained by the United States National Institutes of Health (<http://www.clinicaltrials.gov/>). The Collaborating Register Network of the WHO-ICTRP and the metaRegister of Clinical Trials (<http://www.controlled-trials.com/mrct/>) are focal points of access for multiple trial registries.

The ICMJE and the WHO have specified common criteria for a trial registry; it should be web-based, managed by a not-for-profit agency, and should ensure free access to researchers, clinicians, funding agencies and the public. All trials that study the effects of any health care intervention in human subjects need registration. A 'minimum data set' about the trial should be made available, including details of trial identity, trial design, interventions planned, outcomes to be studied, funding sources and contact information of investigators. Some authorities, such as the Ottawa Group, go beyond simple registration of trials, and are calling for even greater transparency, requesting full disclosure of trial protocols and results [11, 12]. Many journals have supported this move by accepting trial protocols for publication.

Establishing the Sri Lanka clinical trials registry

Recognising the need for a national body for trial registration, the Sri Lanka Medical Association (SLMA) and the *Ceylon Medical Journal* (CMJ) have jointly taken the initiative to establish the Sri Lanka Clinical Trials Registry (SLCTR). The CMJ has pledged to abide by the ICMJE recommendations, and will not accept for publication any articles describing the results of clinical trials that have not been registered with the SLCTR or other recognised clinical trials registry.

The SLCTR is an internet-based, not-for-profit registry, with free access to researchers, clinicians, and the public. It will facilitate trial registration by local researchers, and welcomes registration of trials conducted overseas. It has been designed to meet all the requirements specified by the WHO-ICTRP and the ICMJE. The SLCTR has been operational from November 2006, less than a year from the publication of a leading article in the CMJ exhorting the SLMA to 'take a pivotal role in establishing a national registry' [13]. Several trials have already been registered, and their details are freely accessible at the SLCTR website (<http://www.slctr.lk/>). The SLMA can be proud of the fact that the SLCTR is the first fully functioning Clinical Trials Registry in south Asia.

Looking forward

The SLCTR aims to join the WHO-ICTRP register network as a contributing primary register. More needs to be done to create awareness among the scientific community about the need for trial registration. The Ministry of Health strongly supports and endorses the activities of the SLCTR. The SLMA and the CMJ call upon all stakeholders – clinicians, researchers, health care planners, patients and the public – to help make this endeavour a continuing success story.

References

1. Dickersin K, Rennie D. Registering clinical trials. *Journal of the American Medical Association* 2003; **290**: 516-23.
2. Gotzsche PC. Multiple publication of reports of drug trials. *European Journal of Clinical Pharmacology* 1989; **36**: 429-32.
3. De Angelis CD, Drazen JM, Frizelle FA, et al. Clinical trials registration. A statement from the International Committee of Medical Journal Editors. *Journal of the American Medical Association* 2004; **292**: 1363-64.
4. Teo KK, Yusuf S, Furberg CD. Effects of prophylactic antiarrhythmic drug therapy in acute myocardial infarction: an overview of results from randomized controlled trials. *Journal of the American Medical Association* 1993; **270**: 1589-95.
5. Whittington CJ, Kendall T, Fonagy P, et al. Selective serotonin reuptake inhibitors in childhood depression: systematic review of published versus unpublished data. *Lancet* 2004; **363**: 1341-5.
6. Chalmers TC. Randomize the first patient! *New England Journal of Medicine* 1977; **296**: 107.
7. Simes RJ. Publication bias: the case for an international registry of clinical trials. *Journal of Clinical Oncology* 1986; **4**: 1529-41.
8. De Angelis CD, Drazen JM, Frizelle FA, et al. Is this clinical trial fully registered? A statement from the International Committee of Medical Journal Editors. *New England Journal of Medicine* 2005; **352**: 2436-8.
9. Humphreys G. Giving patients better access to trial information. *Bulletin of the World Health Organization* 2006; **84**: 429-31.
10. International Clinical Trials Registry Platform (ICTRP). Geneva: World Health Organization. (Accessed September 30, 2007, at <http://www.who.int/ictip/about/details/en/index.html>).
11. Krljeza-Jeric K, Chan A-W, Dickersin K, et al for the Ottawa Group. Principles for international registration of protocol information and results from human trials of health related interventions: Ottawa statement (part 1). *British Medical Journal* 2005; **330**: 956-8.
12. Krljeza-Jeric K. Clinical trial registration: The differing views of industry, the WHO, and the Ottawa Group. *PLoS Medicine* 2005; **2**: e378 (doi:10.1371/journal.pmed.0020378)
13. Goonaratna C. Mandatory registration of clinical trials. *Ceylon Medical Journal* 2005; **50**: 139-41.

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