National and multinational prospective trial registers

Clinical trials are an essential source of scientific evidence on the safety and effectiveness of health interventions. Prospectively registering information about a trial before enrolling participants, tracking changes to that information via a publicly accessible audit trail, and reporting results on completion of the trial helps protect against reporting biases and over-optimistic conclusions about treatment benefits. Open-access registries should decrease wasteful duplication of research, promote more efficient allocation of research funds, and ensure trial information is disseminated and incorporated into the appropriate body of evidence for clinical, funding, and ethical decision-making.

The increased commitment to prospective trial registration and the establishment of trial registers has the potential to increase the number of duplicate registrations (panel). It has been argued that if duplicate trial registration is left unchecked, the integrity of trial registries may be compromised, which would falsely over-inflate the number of trials and confuse users. Limiting the number of registries has been proposed as a possible mechanism to prevent duplicate trial registration. Despite these concerns, there are several compelling reasons why both national and multinational registers are important.

National registers are ideally placed to promote, identify, and track clinical trials in a specific country. Such registers can fully integrate into local ethics and regulatory processes, which thus ensures complete and comprehensive registration of all trials in their region of influence. Such decentralised trial registration is essential to achieve a comprehensive global register of all clinical trials. A philosophical reason underpinning the need for national registers is that most national registers have been developed within specific political frameworks and policy makers value them as a source of national pride. It may therefore not be politically expedient to dismiss these registers or undermine their legitimacy.

Multinational registers can be especially important in resource-poor settings where individual countries do not have the necessary resources to establish national registers. Such registers serve the needs of several neighbouring countries, usually with similar disease burdens. By sharing technical and operational resources, costs to individual countries can be reduced and promotion of registration can be streamlined across countries (eg, by working with established regulatory or inter-government organisations, such as WHO/AFRO in Africa or the Pan American Health Organisation in Latin America).

There is an urgent need, particularly in resource-poor countries, to improve the ability of researchers to do high-quality clinical trials. National and multinational registers are able to identify and meet the needs of these researchers, by ensuring that information on various aspects of study design is collected and checked on registration. At an operational level, national and multinational registers can customise the registration process to suit the needs of their particular users (eg, displaying information in the local language).

It is essential that WHO’s International Clinical Trial Registry Platform continues to work closely with governments and multinational bodies that have the necessary

---

Panel: Duplicate trial registration across different registers

**What is meant by duplicate trial registration?**
Duplicate trial registration occurs when same trial is registered more than once in different registers.

**What is meant by intentional duplicate registration?**
Duplicate trial registration might be intentional if specific national requirements compel trialists to register in more than one register. For example, in multinational trial, it might be ethics requirement that trial be registered in each country’s national register. Intentional duplicate registration can also occur when different versions of same trial are done in different parts of world or different jurisdictions. Each version is then registered with specific national or multinational register where trial is being done. For example, trial might aim to compare three different interventions (treatments A and B, and placebo) in India and thus is registered as such on Clinical Trials Registry—India. If same trial is then done in Australia but for some logistical reason treatment B is not included, this version might be registered with the Australian New Zealand Clinical Trials Registry. It is debatable whether or not variations in protocol are seen as different versions of same trial. If such variations in protocol are seen as different versions of same trial, registration of these different versions in different registries could be considered as intentional duplication.

Duplicate trial registration might also occur intentionally when smaller registers routinely submit trial information to larger umbrella registers. This form of intentional duplicate registration is transparent because trials are closely cross-referenced.

**What is meant by unintentional duplicate registration?**
Unintentional duplicate registration is more complicated and less easy to monitor. Poor communication among members of research team about who is responsible for registering trial and registration status of trial might result in it being unintentionally registered more than once on different registers.
Comment

capacity and resources to develop prospective trial registers which fulfil the Platform’s operational requirements and standards from the outset. We propose that WHO consider awarding interim Primary Register status to qualifying registers, while Primary Register status is worked towards. All newly emerging national or multinational registers capable of meeting the requirements of a WHO Primary Registry could be given time-dependent interim status as a Primary Register, before receiving full status. If stipulated criteria were not met within a specified time, the register would be encouraged to partner with a pre-existing relevant Primary Register. This system would allow registers, particularly those in resource-poor settings, to develop capacity and to promote and expand clinical trial registration in their region, while working toward full status.

Open sharing of trial information between registers would meet the needs of national and multinational registers, while minimising duplicate registration. Common standards for data collection and open transfer of data between registries would facilitate appropriate cross-referencing of identification numbers, and thus simultaneously populate local registers and identify any duplicate entries. The adoption of a Universal Trial Reference Number by WHO’s International Clinical Trial Registry Platform is a way to reduce duplicate registration by providing each trial with a unique identifier, regardless of where the trial is registered. Results of the pilot process of the Universal Trial Reference Number are awaited, and will be necessary before it can be presented as the solution to duplicate trial registration. In the absence of reliable data, we propose that the true extent of duplicate trial registration should be investigated systematically, together with the possible confusion and increased workload thought to accompany it. The outcomes of such a study would facilitate evidence-based solutions to this issue.

WHO’s International Clinical Trial Registry Platform, the International Committee of Medical Journal Editors, and many other stakeholders have made tremendous progress in establishing guidelines and principles for prospective trial registration. The increasing emergence of national and multinational registries presents challenges, but more importantly provides opportunities to increase the promotion, coverage, and monitoring of trial registration throughout the world. There is a collective need to co-operate, while recognising and supporting the needs of individual countries and regions.

*Liesl Grobler, Nandi Siegfried, Lisa Askie, Lotty Hooft, Prathap Tharyan, Gerd Antes
Institute of Infectious Disease and Molecular Medicine, University of Cape Town, Cape Town 7925, South Africa (LG); South African Cochrane Centre and HIV/AIDS, TB and Malaria Clinical Trials Registry, Medical Research Council of South Africa, Tygerberg, South Africa (LG, NS); Australian New Zealand Clinical Trials Registry, NHMRC Clinical Trials Centre, University of Sydney, NSW, Australia (LA); Netherlands Trial Register, Dutch Cochrane Centre, Academic Medical Centre, Amsterdam, Netherlands (LH); South Asian Cochrane Network & Centre, Prof BV Moses & ICMR Advanced Centre for Research & Training in Evidence Informed Health Care, Christian Medical College, Vellore, Tamil Nadu, India (PT); and German Cochrane Centre, Institute for Medical Biometry and Medical Informatics, University of Freiburg, Freiburg, Germany (GA)
liesl.grobler@uct.ac.za

Until March, 2008, LG managed the HIV/AIDS, TB and Malaria (ATM) Clinical Trial Registry, funded by the European and Developing Country Clinical Trial Partnership and based at the South African Cochrane Centre. NS is co-director of the South African Cochrane Centre and is responsible for the oversight and management of the ATM Clinical Trials Registry. LA is manager of the Australian New Zealand Clinical Trials Registry and member of the WHO Registry Network. LH is manager of the Netherlands Trial Register and member of the WHO Registry Network. PT is Director of the South Asian Cochrane Network & Centre, member of the Steering and Technical Advisory Groups of the Clinical Trials Registry-India, and past member of the Scientific Advisory Group of the WHO International Clinical Trials Registry Platform. GA is Director of the German Cochrane Centre and coordinator of the German Clinical Trials Register.

3 Chalmers I. Underreporting research is scientific misconduct. JAMA 1990; 263: 1405–08.