

Guest Editorial

Maximising the effectiveness of trial registries in resource-constrained settings

Disparity in the information recorded on the methodology of and results from controlled trials has been recognised for some time. Clinical trial registries are databases in which key administrative and scientific information about planned, ongoing, and completed trials is stored. To ensure disclosure of relevant trial information and standardisation of trial information, the World Health Organisation (WHO) created a 20-item minimum dataset for prospective trial registration. Following on from this, in 2005, the International Committee of Medical Journal Editors (ICJME) released a statement mandating that, for a trial to be published in a participating journal, it must be registered prospectively in a WHO-recognised primary registry (e.g., the Australian New Zealand Clinical Trials Registry [ANZCTR]).^[1] In response to this declaration, the Pan-African Clinical Trials Registry (PACTR) was established to actively promote prospective clinical trial registration on all diseases throughout the African continent.^[2]

People enrolling in clinical trials expect their contributions to be used to improve health care for everyone. Reporting bias, over-optimism about treatment efficacy, or any other form of selective reporting creates an incomplete view of a trial and its results.^{[3][4][5]} Open and free access to information about ongoing and completed trials can promote greater trust and public confidence in clinical research in any setting. In registering a trial, researchers commit to reporting any findings in accordance with basic ethical principles. Coupling registration with the capacity to track changes to trial design over the research period through a publicly accessible audit trail reduces selective reporting of trial results. Transparent trial registration could also lead to a decrease in wasteful duplication of research, promotion of international research collaboration, and more efficient and effective allocation of research funds.^[6]

The benefits of clinical trial registration can be felt by a wide audience, including policy makers, health professionals, clinical trial funders, development agencies, researchers, and the lay public. Registries can assist in meeting the ethical obligations of clinical trials to their participants by allowing the lay public access to information about clinical trials being conducted in their communities, and health professionals can take advantage of information on trials in progress when advising patients about participation in trials. Searching registry databases can help to identify "gaps" in the evidence in an area, and in doing so focus research objectives and activities. The regulatory aspects of a registry enable policy makers to track clinical trial activity in their country, region, or area covered by the registry, giving them a clearer idea of how clinical-trial activity is serving the health needs of the population. Those providing financial backing for trials can use the information available (on where and what research is being conducted, and by whom) to inform decision-making on how best to allocate their funds. Considering Africa as an example, numerous development agencies have dedicated funding for the advancement of clinical trial activity and capabilities across the continent: the information contained in registries can assist funders in understanding the clinical trial activity and capacity in Africa, which informs funders of where needs are unmet, or in which direction clinical trial activity should proceed.

A national registry is developed within a specific political framework and policy-making environment that is valued by the country hosting the registry. As such, a national registry can be a source of national pride,^[7] and will ideally function effectively within the bureaucracy of each locality in a way that a multi-national registry cannot. National registers are able to integrate fully into the ethics and regulatory processes of the country, which ensures complete and comprehensive registration of all trials in that region.^{[7][8]} Thus, decentralised trial registration through national

registers is ideal for promoting, identifying, and tracking clinical trials in a specific country. However, in resource-constrained countries, or in regions lacking the resources to establish national registers, multi-national registers (such as the PACTR) can simultaneously serve the needs of several neighbouring countries that, more often than not, have similar disease burdens.[7] Resource-sharing, which is intrinsic to multi-national registries, can minimise costs to individual countries, and will ideally encourage information sharing.

Despite the benefits of trial registration, applications to the PACTR have been fewer than expected. Since the PACTR opened in late July 2007, and went live (online) in February 2008, there have been only 22 applications to the registry. Active promotion of prospective registration is clearly required to increase the visibility of the PACTR across the continent. India shares similar healthcare obstacles to many African countries, such as a shortage of healthcare resources and poor health outcomes. However, in contrast to African countries, the incidence of trial conduct and associated registration is rising. The increase in trial registration in India is attributed in part to the strengthening of legislative frameworks (the FDA Revitalization Act) and in part to the creation of networks between ethics committees, regulatory authorities, medical journal editors, and clinical trial registries that served to promote communication between those involved, increasing the efficiency of clinical trial regulation, as well as enabling the oversight process.[9][10] To ensure oversight and increase trial registration in Africa, it is imperative that similar frameworks are introduced and networks established. Trial registration, as a means of centralising and standardising information to curb the possibility of participant exploitation, can assist those responsible for the regulatory environment. The PACTR is well-placed to lead the integration of ethics, regulation, and registration across Africa.

Clinical trial registration does not replace the need for legislation, and should not function as an ethics watch-group, but a registry can promote ethical compliance and encourage such compliance and regulation through links forged between all stakeholders. Whether national or multi-national, a registry, as a means of networking and transparency, allows for information sharing that can decrease duplication of research, and thus squandering of resources. In situations where national registries cannot be supported due to resource constraints, multi-national registries can serve the purpose of information sharing, thereby increasing networking and assistance with oversight of regulations. Sustaining such endeavours will ensure consistency in the information available, thus enabling the maintenance and tracking of a complete history of clinical trials which facilitates a longitudinal understanding of trial activity in resource-constrained countries. Crucially, trial registries and registration will also encourage scientific collaboration to further research efforts, and reduce the economic burden of research in resource-constrained settings.

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PACTR is a multi-national registry based at the South African Cochrane Centre that was developed in partnership with the Cochrane Infectious Disease Group (based in the UK) and the Cochrane HIV/AIDS Review Groups (based in South Africa and the USA). It is funded by the European and Developing Countries Clinical Trial Partnership (EDCTP). The PACTR is aligned with the EDCTP mission to "accelerate the development of new or improved drugs, vaccines and microbicides against HIV/AIDS, malaria and tuberculosis" in sub-Saharan Africa.[11]

Appendix added 5th October 2009

The Pan African Clinical Trials Registry (PACTR) is delighted to announce their endorsement by the WHO as a primary registry. As a primary registry, PACTR will feed data into the global WHO's International Clinical Trials Registry Platform (ICTRP) search portal, facilitating African representation in the global picture of planned, ongoing, and completed clinical trials.

Davina Gheri, head of the WHO's ICTRP, says the approval of PACTR as a primary registry is a significant milestone in the quest for transparency. "Our hope is that the PACTR will make it easier to capture information about trials involving people in the region. We look forward to filling the gap in our knowledge about clinical trials in Africa."

"We are delighted to be able to offer access to a WHO primary register to all trialists in Africa! We hope the PACTR will become the first choice for African trial registration," says Nandi Siegfried, co-director at the South African Cochrane Centre.

References

1. Uniform Requirements for Manuscripts Submitted to Biomedical Journals: Writing and Editing for Biomedical Publication. <http://www.icmje.org> (last accessed 6 July 2009).
2. Pan African Clinical Trials registry. <http://www.atmregistry.org/ATMWeb/appmanager/atm/atmregistry> (last accessed 6 July 2009).
3. Chan AW, Hrobjartsson A, Haahr MT, et al. Empirical evidence for selective reporting of outcomes in randomized trials: comparison of protocols to published articles. *JAMA* 2004;291:2457–2465.
4. Dickersin K, Min YI. Publication bias: the problem that won't go away. *Ann N Y Acad Sci* 1993;703:135–146.
5. Chalmers I. Underreporting research is scientific misconduct. *JAMA* 1990;263:1405–1408.
6. Dickersin K, Rennie D. Registering clinical trials. *JAMA* 2003;290:516–523.
7. Grobler L, Siegfried N, Askie L, et al. National and multinational prospective trial registers. *Lancet* 2008;372:1201–1202.
8. Tharyan P. Ethics committees and clinical trials registration in India: opportunities, obligations, challenges and solutions. *Indian J Med Ethics* 2007;4:168–189.
9. Drazen JM, Morrissey S, Curfman GD. Open clinical trials. *N Engl J Med* 2007;357:1756–1757.
10. Tharyan, P. Prospective Registration of Clinical Trials in India: Strategies, Achievements & Challenges. *J Evid Based Med* 2009;2:19–29.
11. European and Developing Countries Clinical Trial Partnership: Mission.