Registration of Clinical Trials: How Developing Countries Could Prepare for the Upcoming Storm

The interest in using and conducting clinical trials in developing world is rising promptly. Knowing the importance of this kind of research in generating therapeutic evidence, many clinical researchers in developing countries including Iran are getting involved in performing clinical trials. Authors performed a quick search in ISI Web of Knowledge database (May 2008) which shows interesting results. The number of Iranian clinical trials indexed in the database rose exponentially from 2 in 1997 to 80 in 2006 and 122 in 2007. This is the tip of the iceberg, because many of them are published in local Persian or English language journals which are not indexed in international databases. Increasing number of ongoing clinical trials emphasizes the need for mechanisms to keep eye on their quality, transparency, and ethical considerations.

The worldwide registration movement

The members of the International Committee of Medical Journal Editors (ICMJE) stated in a joint report that “We will consider a trial which starts recruiting on or after July 1, 2005 for publication only if it has been registered before the enrolment of the first patient”.1 This policy was adopted by many other journals and some national policy making bodies, which led to a rapid increase in the number of registered trials in available registry databases like ClinicalTrials.gov with more than 200 new trial registrations weekly in 2007.2 Trying to harmonize the standards of trial registration and reporting and coordinate the international efforts for registering clinical trials, the World Health Organization initiated the International Clinical Trials Registration Platform (ICTRP). The ICMJE have participated in WHO ICTRP project and have supported it.3 The ICTRP search portal—launched at May 2007—enables the users to search for trials registered in majority of trial registries worldwide (http://www.who.int/trialsearch/). Through these efforts trial registration transformed from an exception to a rule.

Why trials should be registered?

There are many reasons for a comprehensive, publicly available registration of clinical trials4:

First, a searchable publicly accessible trial registry database will assist governmental, academic, and private funding bodies to make more informed decisions in sponsoring new trials to reduce unnecessary duplication of work. This advantage is especially meaningful for developing countries where the resources are constrained and information is locked in the organizations due to the lack of scientific networks and media.

Second, registration makes it more difficult to censor the undesirable findings by the researchers or funding companies. Selective reporting of positive findings and underreporting of negative adverse events are widespread problems, particularly in industry-supported trials. Empirical evidence has shown that more than 20% of measured outcomes in clinical trials were incompletely reported, mainly due to non-significance.5 Inadequacy of monitoring and quality control mechanisms might exaggerate this problem. This tendency to selectively reporting the significant findings and subsequent publication of their containing studies is called “publication bias”. Because of its direct impact on skewed clinical judgment and health outcomes, attention has been drawn to its incidence, and the ways to overcoming it. Permanent registration of information of ongoing trials is an effective solution. Existence of updating trial registries assists systematic reviewers become informed of ongoing trials, which also reduces the occurrence of publication bias in systematic reviews.

Third, a registry helps peer reviewers and editors in the assessment of existing completed trials, to be aware of published works in a given topic, as well as ongoing efforts.

Fourth, it is a useful source for community. The patients who are interested in participation in a trial could easily locate them appropriately. In addition, it is a good way to thank the participants who risked joining the clinical trials. They deserve to
know that the information revealed by these trials is a part of public evidence. This warrants the need for trial registries in local languages to be understandable by the community.

Developing countries experience

ICTRP accepted the clinical trial registries of India (www.ctri.in), China (www.chictr.org), and Sri Lanka (www.slctr.lk) as its primary registries, of which only the Chinese registry displays the information in trial’s native language too. Many features of them are under development, and the number of registered trials within them is gradually increasing.

The Ibero-American Cochrane Network has set up the Latin American Ongoing Clinical Trials Register (LATINREC). This trial register supposed to play an active role in locating ongoing trials, contacting government entities, research centers, universities, companies, funding bodies, known trialists, and researchers possibly involved in clinical trials in Latin America found through searching periodically on bibliographic databases.

Most above mentioned registers stated the insufficiency of durable financial supports, and technical database problems as the most challenging barriers (presentations in the 2nd Registers Working Group Meeting, WHO Headquarters, Geneva, November 30, 2007).

Clinical trial registry of Tehran University of Medical Sciences (TUMS)

In early 2007 the Vice Chancellor for Research of Tehran University of Medical Sciences approved the establishment of a Clinical Trial Center with the following aims:

- To organize the registration of clinical trials in accordance with international standards;
- To increase the public tendency of contribution in clinical trials;
- To promote the education of investigators in designing, performing, and, analyzing clinical trials;
- To control the quality and the conformity of methodological, ethical, and financial principles in clinical trials;
- To link the organizations, investigators, and patients together to facilitate performing clinical trials; and
- To signify the priorities in health care system and guiding investigators to those topics.

A clinical registry database was developed to offer a free publicly accessible bilingual (Persian and English) access to information of registered clinical trials, provide a searchable database for various users (clinicians, researchers, health decision makers, and patients), monitor the accuracy of registered data, and regularly update the registered data.

The database has been developed to be in line with the gradually finalizing WHO ICTRP standards. In early 2008 the database passed the final pilot tests and launched in February 2008; and now is accessible through: http://rctregistry.tums.ac.ir/. It is not limited to the TUMS trials, and is open for all interested researchers from the region. Trials could be submitted in English or Persian, but all information will be translated to the counterpart language, and the researchers are able to review the accuracy of translation on demand. The flowchart of the registration process is shown in Figure 1.

To assure the accuracy and quality of submitted information an important pre-requirement of trial registration is submission of an approval letter signed by the responsible body of supporting institution/university approving the legitimacy of the submitted contents. The letter must contain the name and contacts of the responsible person signed and the official reference number/date for future quotations. The registry accepts the copy or picture of the letter. We believe that this strategy will promote the legitimacy of reporting trial information, and participation of funding bodies in quality control of clinical trials.

The way forward

Registration of clinical trials in a local, quality-assured databases in native and English languages is an emerging need of developing countries. Archives of Iranian Medicine has adopted a policy of requiring clinical trial registration since January 2008. The Journal editors hope that this will promote the integrity of the research in this field. The Journal accepts many international registries as well as TUMS registry (see the Instruction for Authors), to promote the first Iranian and (to the best of our knowledge) regional clinical trials registry.

Reza Yousefi-Nooraie MD*, Kamran Yazdani MD MPH**, Arash Etemadi MD PhD**
*Clinical Trials Center, Tehran University of Medical Sciences, Tehran, Iran, **Department of Epidemiology and Biostatistics, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran.
Figure 1. The flowchart of trial registration process in the clinical trials registry database of the Tehran University of Medical Sciences.

References