Registering clinical trials is necessary for ethical, scientific and economic reasons

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For unbiased judgement of the effectiveness of medications or non-pharmaceutical therapies, controlled clinical trials are the most important elements in deciding whether an intervention does more good than harm. Often undervalued, but increasingly used under the concept of evidence-based medicine, trial results are of utmost importance as the basis of decision-making in health care. As controlled trials are one of the main sources of medical knowledge, it is essential that results of completed trials and information about ongoing ones are available to all those professionally involved in health research and health care as well as to patients.

Public access to trial information is essential from various perspectives. First of all, research is a cumulative process, the unbiased synthesis of which is particularly important in order to summarize existing knowledge about a specific problem. Systematic reviews need to have complete information about ongoing and completed trials: the widespread phenomenon of not publishing trials with negative or disappointing results can seriously distort perceptions of the effectiveness of medical interventions (*1*). Knowledge of unreported trials may help to reduce the detrimental effects of this publication bias.

Next, reliable information about trials is necessary to identify evidence gaps and thus indicate where further trials are needed. Planning of new trials has to be based on knowledge gained from previous ones, and information about similar trials is necessary to avoid duplication of effort and to ensure optimal use of resources. Prioritization of research programmes is dependent on complete knowledge of the evidence from trials.

Finally, it is particularly important for patients and doctors to be able to obtain support to find trials suitable for participation. Patients and consumers of health care need access to information about trial results to allow them to make an informed choice. Participants in clinical trials expect the results to be made fully available to future patients; this is stipulated in the contract when they agree to participate in a trial, with its associated risks of not receiving the optimal treatment or experiencing adverse events. Underreporting of trial results is thus unacceptable from an ethical point of view and should be overcome by publicly accessible registers (*2*).

In view of these convincing arguments which have been put forward for more than 30 years (*3*, *4*), it is surprising that no system has yet been developed that allows systematic access to information about past or current clinical trials. Various local as well as publicly accessible registers have been set up over the past decade. For example, the United States National Institutes of Health, through the National Library of Medicine (*5*) and the National Cancer Institute, have developed publicly available web sites that facilitate searching for clinical trials (*6*, *7*). In Europe, the European Science Foundation published a policy briefing that strongly recommends registration of controlled trials (*8*, *9*) and urged its members to introduce registration. However, all these registers are of limited use as they cover only specific geographical regions or medical specialties and are not mandatory. In contrast, existing comprehensive registers (usually restricted to drug development) maintained by regulatory drug development authorities in several countries do not allow access to the public but only to authorities and, in some cases, to ethics committees.

Very recently, WHO decided that all randomized controlled trials approved by its ethics review board will be assigned an International Standard Randomised Controlled Trial Number (*10*), under the global unique numbering system for randomized controlled trials developed by Current Controlled Trials Ltd as part of the Current Science Group in London (*11*). This step will substantially increase the visibility and accessibility of trials supported by WHO.

Strengthening the role of public trial registers is part of WHO's increased efforts to improve the use of research results in health care. Recently introduced knowledge management concepts express increasing concern that research results are not utilized efficiently in health care. Comprehensive, publicly accessible trial registration is a prerequisite to correct the situation and reduce the knowledge gap.

The increased support of prospective trial registration by WHO is of tremendous importance for local and national activities in various countries: it will facilitate the establishment of regional registers and compulsory registration by sponsors of trials. After many years and numerous failed attempts to organize this field, there is now hope of achieving more transparency by introducing complete, publicly accessible registration of clinical trials. With WHO taking a prominent role in this development, all those who have pursued this endeavour over the past years are encouraged to optimism that trial registration will become a reality. ■

1. Dickersin K, Rennie D. Registering clinical trials. *JAMA* 2003;290:516-23.
2. Antes G, Chalmers I. Under-reporting of clinical trials is unethical. *Lancet* 2003;361:978-9.
3. Simes RJ. Publication bias. The case for an international registry of clinical trials. *Journal of Clinical Oncology* 1985;4:1529-40.
4. Horton R, Smith R. Time to register randomised trials. *Lancet* 1999;354:1138-9.
5. McCray AT. Better access to information about clinical trials. *Annals of Internal Medicine* 2002;133:609-614.
6. http://www.cancer.gov/clinicaltrials
7. http://www.clinicaltrials.gov/
8. *Controlled clinical trials. European Science Foundation Policy Briefing 13.* Strasbourg: European Science Foundation; 2001. Available at: http://www.esf.org/publication/90/ESPB13.pdf
9. Tonks A. A clinical trials register for Europe. *BMJ* 2002;325:1314-5.
10. World Health Organization. *WHO leads drive for international coordination of clinical research.* Press release WHO/23, 2 April 2004.
11. http://www.controlled-trials.com/

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