Commentary

The Ottawa Statement. *International registration of protocol information and results from human trials of health related interventions*

Zbys Fedorowicz, *BDS, LDS RCS (Eng),*
Amani A. Al-Hajeri, *MD.*

The impact of recent events,[1] with the selective reporting of the results of clinical trials has led to an erosion of public and academic confidence in the publication of clinical trials, and which has motivated renewed calls for increased control of trial registration.[2] The publication of these systematic reviews on the effects of selective serotonin reuptake inhibitors for childhood depression[3] appears to have galvanized individual stakeholders into action. Not least of all their highly publicized sequelae have emphasized the dangers of incomplete disclosure of trial results, heightened the significance of trial registration, and recognized the increased urgency for a globally acceptable method of trial registration. Significantly, there has been a positive response from leading journal editors,[4] the International Committee of Medical Journal Editors (ICMJE),[5] medical associations[6] and industry[7] in perhaps recognizing the contribution that would be made to social good if the totality of research, some of which remains 'buried', was made available to the global community.

An open meeting in Ottawa on the 4th of October 2004 hosted by the Canadian Institutes of Health, and a follow up meeting at the Cochrane Colloquium in Ottawa assembled a group of individuals interested in fostering international consensus on trial registration. The vision held by the contributors was to develop a protocol that may shape the transition to a new paradigm of health research based on transparency, full disclosure, and collaboration. The results of these and subsequent consultations led to the development of the Ottawa Statement, which has as its main aim the establishment of internationally recognized principles for the registration of clinical trials. The full statement is available at http://ottawagroup.ohri.ca/staement.html, but here we highlight the rationale and some of its key principles.

Rationale for registration of clinical trials. 1) Ethical. Respect the investigator-participant covenant to contribute to biomedical knowledge by making trial methods and results public. Provide global open access to information. Reduce unnecessary duplication of invested research resources through awareness of existing trials. Assure accountability with regard to global standards for ethical research. Enable monitoring of adherence to ethical principles and process. 2) Scientific. Increase the reliability and availability of evidence upon which healthcare decisions are based. Improve trial participation. Increase opportunities for collaboration. Ensure transparency of trial design and methods. Provide open review of protocols to improve trial quality, and the refining of the methods of trial conduct. Provide means for identification and prevention of biased under or over-reporting of research. Accelerate knowledge creation.

Outline of the Ottawa Statement (Part 1). Key principles. a) Registering all types of trials. "Protocol information and results from all trials related to health or healthcare regardless of topic, design, outcomes, or market status of interventions examined should be registered and publicly available." b) Timing of public release of protocol information. "The public should have cost-free access to the Unique ID, minimum protocol items, and consent forms prior to the participant enrollment. Registered amendments should be made publicly available as they occur." c) Registering unpublished results. "At a minimum, results for outcomes and analyses specified in the protocol (as approved by the institutional review boards/ independent ethics committees), as well as data on harms, should be registered regardless of whether or not they are published."

Summary of the principles. Sponsors, principal investigators, journals, and ethics committees all have certain responsibilities to ensure comprehensive registration of trials. The mandatory registration of all trials will have 3 components: a) Obtaining an internationally unique identification number (Unique ID), b) Registering the original protocol along with subsequent amendments, and c) Registering the trial results.

The Ottawa group currently consists of over 80 individuals, representing a number of research organizations and individuals from 5 continents, with an interest in ensuring that health research is based on transparency, full disclosure and collaboration, who will continue to consult broadly regarding the most effective and practical ways to enact these principles in a coordinated fashion worldwide. Additional initiatives are being driven by the World Health Organization, which has assembled a group to guide the development of global trial registration and has used an earlier draft of the statement to shape its plans. The Cochrane Collaboration has also endorsed this statement, and through its network[8] is encouraging further dissemination of the principles of the Ottawa Statement. The members of the Ottawa group are encouraging other stakeholders to do the same and to thereby contribute to public discussion of this important issue.

Summary points. Registration and early public release of accurate information regarding all trials is necessary to fulfill an ethical obligation to participants. Although, protection of commercial and other interests is important, the social contract with participants should take precedence. All trial results should be registered and publicly available, along with sufficient protocol information to enable critical assessment of their validity.

Implications for clinical trials in the region. There are a number of questions that need to be asked if we are to ensure that clinical trials conducted in the region comprehensively address this issue. Should there be a registry established in the region? Who should be responsible for maintaining it? What mechanisms are available for regional editors to come to an agreement regarding mandatory registration of all clinical trials conducted in the region? What could be the role of WHO, Eastern Mediterranean Regional Office, Eastern Mediterranean Association of Medical Editors, and the regional entity of the Cochrane Collaboration, in this initiative?

Received 3rd July 2005. Accepted for publication in final form 11th September 2005.

From the Bahrain Branch of the UK Cochrane Center (Fedorowics) and from the Bahrain Medical Bulletin (Al-Hajeri), Awali, Bahrain. Address correspondence and reprint requests to: Dr. Zbys Fedorowicz, Director, The Bahrain Branch of the UK Cochrane Center, Box 25438, Awali, Bahrain. E-mail: zbysfedo@batelco.com.bh

References

1. Dyer O. Glaxo Smith Kline faces US lawsuit over concealment of trial results. ***BMJ*** 2004; 328: 1395.
2. De Angelis C, Drazen JM, Frizelle FA, Haug C, Hoey J, Horton R, et al. Clinical trial registration: a statement from the International Committee of Medical Journal Editors. ***Lancet*** 2004; 364: 911-912.
3. Whittington CJ, Kendall T, Fonagy P, Cottrell D, Cotgrove A, Boddington E. Selective serotonin reuptake inhibitors in childhood depression: systematic review of published versus unpublished data. ***Lancet*** 2004; 363: 1341-1345.
4. Abbasi K. Compulsory registration of clinical trials. ***BMJ*** 2005; 32: 637-638.
5. De Angelis C, Drazen JM, Frizelle FA, Haug C, Hoey J, Horton R, et al. Is this clinical trial fully registered? A statement from the International Committee of Medical Journal Editors. ***CMAJ*** 2005; 172: 1700-1702.
6. American Medical Association. Influence of funding source on outcome, validity, and reliability of pharmaceutical research. 2004. [cited 2005 March 30]. Available from: URL: http://www.ama-assn.org/ama/pub/category/14314.html
7. Dyer O. Glaxo Smith Kline to set up comprehensive online clinical trials register. ***BMJ*** 2004; 329: 590-591.
8. The Cochrane Collaboration. Available from: URL: http://www.cochrane.org