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Editorial

Clinical Trial Registration in the Eastern Mediterranean Region

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Clinical trials offer immensely to the evidence cart through the introduction of improved therapeutic regimens and better patient care. Registration of clinical trials ensures free accessibility of trial related information to the public and conforms to international standards. Clinical trial registration is an ethical, scientific and moral responsibility, as well as an obligation upon all investigators and sponsors. Clinical trial registries have not been established in several countries especially in the Eastern Mediterranean Region. The aim of this editorial is to highlight the status of clinical trial registration and regulations to provide new evidence on the issue targeting researchers to register their studies.

Evidence-based medicine (EBM) is increasingly being incorporated into healthcare system by healthcare professionals and policymakers to implement the most effective treatment options based on documented evidence.[1,2] In the EBM pyramid, meta-analyses of randomized controlled trials constitute the highest level of evidence. The results of several clinical trials are often not being published, particularly those with negative or equivocal results. Some studies have reported publication bias of clinical trial results favoring the investigational product that funded the research.[3,4] This publication bias can adversely affect the available evidence and can lead to deluding conclusions when pooling the results of several clinical trials.

In addition to the publication bias, scientific misconduct in clinical research has been published in the media and in medical literature.[5,6] Consequently, the number of participants enrolling onto trials is on the descent, and the results of these trials are affected, while the release of potential new drugs into the market is hindered. All trial related information should be made available to all subjects participating in the clinical trials and they should also be notified of the current status of the trials that they have enrolled onto and whether their participation has made any significant contribution to medical science.

To address these issues, the collaborative enterprise of governmental agencies, journal editors, World Health Organization (WHO), International Conference on Harmonization and Cochrane collaboration led to the development of clinical trial registries for increased transparency of clinical trials data.[7] In response to the 58th World Health Assembly resolution, WHO International Clinical Trial Registry Platform (ICTRP) was established in 2006. WHO-ICTRP is "a voluntary platform to link clinical trial registers in order to ensure a single point of access and the unambiguous identification of trials with a view of enhancing access to information by patients, families, patient groups and others."[7]

Clinical Trial Registry (CTR) provides an internationally-concurred set of details about the design, conduct and implementation of the clinical trials. The details are published on a publicly-accessible website managed by a non-profit organization and conform with international standards set by WHO-ICTRP and International Committee on Medical Journal Editors (ICMJE).[7] This system allows any individual to track any trial throughout its lifecycle from protocol to the dissemination of results. All types of clinical trials; interventional, observational, randomized or non-randomized trials should be registered before the initiation of patient enrolment.[8]

CTR facilitates the dissemination of clinical trial information to healthcare providers, researchers, patients and the public. Transparency established through CTR would restore public trust in clinical research and increase the possibility of patients to identify trials for participation and in turn increase subject recruitment into ongoing trials, at the same time, the concern about unethical use of participants in trials will be kept in check.[8,9] CTR allows journal editors and reviewers to understand the context of study results and increases the publication of trials with negative or inconclusive results. In 2004, the member journals of ICMJE set up a policy to publish only registered clinical trials, thus ensuring that trial results are not lost or abandoned.[8-10] CTR assists researchers to identify areas in healthcare that entail further research. Unintentional duplication of clinical trials can be avoided and the system also encourages collaboration between investigators involved in similar research.[7,10] Potential problems in the research identified during the process of registration would improve the quality of trials.[7]

Ethically, CTR offers the patients participating in trials a web portal for all the study related information, but this information may possibly be used by pharmaceutical companies as an advertisement for trial recruitment.[11] Clinical trial sponsors debate that CTR could result in technical delays and free access of their research plans competitors which would obliterate their competitive edge.

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However, trial registration information disclosed should not breach confidentiality.[11]

Since the initiation of CTRs, several types of registries have been established; public/non-public registries, international/national registries, and registries for new trials/completed trials/both; as well as CTRs run by non-profit/for-profit organizations. This has resulted in multiple entries of a single clinical trial and has thus diminished the credibility of the registries.[7] To overcome this, the WHO-ICTRP provides a unique trial registration number for every trial, the 'Universal Trial Number.'[7]

Although the ICH-GCP Guidelines do not mention the point about clinical trial registration, the 2008 version of the Declaration of Helsinki states that, "Every clinical trial must be registered in a publicly accessible database before recruitment of the first subject."[12] The success of a CTR depends on the collaborative efforts by the pharmaceutical industry, academic institutions, ethics committees and medical journal editors.

There is a tremendous increase in the number of clinical trials conducted in the Eastern Mediterranean region. The Middle East is predicted to be one of the leading regions for clinical research outsourcing due to the availability of essential infrastructure for the conduct of clinical trials, access to required patients and financial benefits. Though many countries in the world have created CTR at the national level to serve as primary registries in the WHO Registry Network,[8] CTRs are yet to be fully established in most of the countries in the region. The Iranian Registry for Clinical Trials is the primary registry that is linked to the WHO-ICTRP and a few other countries in the region such as Jordan, Syrian Arab Republic, and the United Arab Emirates have formulated laws governing the conduct of clinical trials.[13,14] The regulatory, legal, ethical, funding and other requirements for the conduct of clinical trials vary between countries and therefore trials carried out in a particular region should comply with the requirements of each country.[7] Recommendations have been put forward for the WHO-EMRO to establish a regional CTR, to bridge the small clinical trial registries in countries of the region and the WHO-ICTRP.[13,15]

In conclusion, clinical trial registration enables free access of trial related information, confirms that a trial conforms with the accepted international standards and is mandatory for publication of trial results. Establishment of CTRs in the region would encourage prospective registration of clinical trials and research by investigators, facilitate research governance, and promote evidence-based medicine practice, as well as assist policy-makers to regulate the process.

References

1. Thomas V. "Think research" in everyday clinical practice: fostering research culture in health care settings. Oman Med J 2011 Mar;26(2):75-76.
2. Al-Riyami A. Health researchers and policy makers: a need to strengthen relationship. Oman Med J 2010 Oct;25(4):251-252.
3. Bhandari M, Busse JW, Jackowski D, et al. Association between industry funding and statistically significant proindustry findings in medical and surgical randomized trials. Can Med Assoc J 2004;170:477-480.
4. Ridker PM, Torres J. Reported outcomes in major cardiovascular clinical trials funded by for-profit and not-for-profit organizations: 2000-2005. JAMA 2006 May;295(19):2270-2274.
5. Graham DJ. COX-2 inhibitors, other NSAIDs, and cardiovascular risk: the seduction of common sense. JAMA 2006 Oct;296(11):1651-1656.
6. Steinman MA, Bero LA, Chren MM, Landefeld CS. Narrative review: the promotion of gabapentin: an analysis of internal industry documents. Ann Intern Med 2006 Aug;145(4):294-291.
7. World Health Organization. International Clinical Trial Registry Platform. (www.who.int/ictrp, Accessed June 25 2012).
8. De Angelis C, Drazen JM, Frizelle FA, Haug C, Hoey J, Horton R, et al; International Committee of Medical Journal Editors. Clinical trial registration: a statement from the International Committee of Medical Journal Editors. Lancet 2004 Sep;164(9418):911-912.
9. Irwin RS. Clinical trial registration promotes patient protection and benefit, advances the trust of everyone, and is required. Chest 2007 Mar;111(1):619-641.
10. Sim I, Chan AW, Gülmezoglu AM, Evans T, Pang T. Clinical trial registration: transparency is the watchword. Lancet 2006 May;167(9521):1611-1611.
11. Johan PE, Marjorie A. Reviewing Clinical Trials: A Guide for the Ethics Committee. Available from: URL: http://www.pfizer.com/files/research/research_clinical_trials/ethics_committee_guide.pdf
12. Krleza-Jerić K, Lemmens T. 7th revision of the Declaration of Helsinki: good news for the transparency of clinical trials. Croat Med J 2009 Apr;50(2):105-110.
13. Fathalla MF. Registration of clinical trials–a regional perspective. East Mediterr Health J 2012 Jan;18(1):4-6.
14. Al-Gasseer N, Shideed O. Clinical trial registration in the Eastern Mediterranean region: a luxury or a necessity? East Mediterr Health J 2012 Feb;18(2):108-111.
15. World Health Organization Eastern Mediterranean Regional Office. Clinic trials. 2012. Available from: URL: http://www.emro.who.int/pdf/rpc/about-clinic-trials/clinic-trials.pdf. (Accessed June 26 2012).