

Editorial

Registration of clinical trials

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In an editorial published in the second issue of the fifth volume of the *Nursing Practice Today*, an issue was raised about an inconsistency between the registration information and the final report of a clinical trial published in the first issue of the fifth volume of the Journal. The publication entitled, *“The effect of self-management education on the quality of life and severity of the disease in patients with severe psoriasis: a non-randomized clinical trial”*. This trial had been registered in the Iranian Registry of Clinical Trials as a “randomized clinical trial”, while the title of its final report shows that it was “a non-randomized clinical trial”.

In the draft of that publication, there were ambiguities in the randomization of participants to the arms of the trial. Given the critical importance of randomization in clinical trials, the reviewers of the Journal asked the authors to clarify the ambiguities and clearly explain the randomization procedure. Then, based on the explanations and clarifications provided by the authors, the Editor of the Journal recommended the authors to revise the draft as a non-randomized clinical trial. However, despite the importance of congruence between the registration information and the final report of a trial, the authors provided no explanation about the inconsistency between the randomization techniques reported in the registration information and the final report of that study (1, 2). Thus, the present Editorial was written about the

importance of clinical trial registration and its applications.

Around one thousand years ago, the famous Iranian physician, Ibn-e Sina (known as Avicenna in the west; 980–1037), wrote an article entitled the *“Determination of temperaments of simple drugs through experiment”*. That article—published as the second section of the second volume of his influential book, *“The Canon of Medicine”*—is considered as the first formal introduction of clinical trial. In that article, Ibn-e Sina introduced seven main requirements for drug experiments, the seventh of which holds that any judgment about the effects and the strengths of drugs should be made based on the results of studies on humans (3).

Currently, clinical trials are considered as the most reliable method of producing evidence for clinical practice (4) and a key strategy for the advancement of medical sciences. However, there have always been concerns over the credibility of the results of clinical trials. Therefore, several standard guidelines have been developed for registering, conducting, and reporting clinical trials (5, 6).

Studies show that the positive results of some clinical trials are frequently published in different formats, while their negative results are not published at all or are published with delay. Such selective outcome reporting has caused strong biases in using or not using a drug or a treatment protocol and has brought about destructive effects on human

beings. Consequently, in 2004, the International Committee of Medical Journal Editors decided to publish only those trials which had been registered in formal registries before sampling onset (6). The aim of this policy shift was to oblige researchers to clearly and completely report all positive and negative results of their clinical trials and thereby, to prevent any kind of reporting biases and any misuses of the results (7–10). One month later, the health ministers who had participated in the annual meeting of the World Health Organization required this organization to develop a centralized network of authentic primary clinical trial registries in order to facilitate and organize the registration and the retrieval of clinical trials through a single platform. Accordingly, the International Clinical Trials Registry Platform was set up at the following address, www.who.int/ictcp. In its meeting in South Korea in October 2008, the World Medical Association also added the Principle 19 to the Declaration of Helsinki which holds that the registration of a clinical trial before its onset is mandatory (6, 11). Following these movements, the Iranian Registry of Clinical Trials (retrievable at www.irct.ir) was set up and connected to the International Clinical Trials Registry Platform in December 2008 as the ninth clinical trial registry center approved by the World Health Organization. After that, in December 2009, the Research Administration of the Iranian Ministry of Health and Medical Education required all Iranian research journals of medical sciences to consider only those clinical trials for publication which had been registered in the Iranian Registry of Clinical Trials (9, 10). The Iranian Society of Medical Science Journal Editors also strongly supported this requirement and encouraged researchers to register their clinical trials in this national registry and provide the registration number of their trials in the final reports of their works (10, 12).

Some of the main reasons for the essentiality of registering clinical trials are as the following:

- Registration provides governments, academic institutions, and research centers with reliable information related to clinical trials and enables them to make wiser decisions about funding new researches instead of repetitive works. This will save limited research budget for new studies, particularly in developing countries.
- Registration helps the editors and the reviewers of journals more accurately evaluate completed clinical trials and provide them with information about similar publications and uncompleted works. Moreover, it provides them with the opportunity of comparing the final reports of clinical trials with their registration information in order to judge about the accuracy of the reports.
- Registration provides a valuable source of information for the public. People who are willing to participate in clinical trials can access registration information and decide whether to apply for participation in trials of their interest.
- Registration requires researchers to more strictly adhere to the principles of research ethics and helps protect patient rights.
- Registration promotes the credibility of the generated results (13–16).

Despite the importance of registration and the great emphasis on its application, studies on published clinical trials show inconsistencies between the registration information and the final reports of clinical trials respecting their designs, methodologies, and results. For instance, a systematic review reported the high prevalence of inconsistencies between the primary plans and the reported results (14). In the final reports of clinical trials, researchers need to report any inconsistencies between the registration information and the final reports and provide clear explanations about the reasons for such inconsistencies (4). Moreover, editors

and reviewers of journals need to take registration information of clinical trials into account when considering their final reports for publication. The author guidelines of journals should also be revised to provide researchers and authors with detailed information about the principles and the processes of clinical trial registration as well as with standard guidelines and checklists for reporting clinical trials and other types of studies (15, 16).

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References:

1. MacPherson H, Altman DG, Hammerschlag R, Youping L, Taixiang W, White A, et al. Revised Standards for reporting interventions in clinical trials of acupuncture (STRICTA): Extending the CONSORT Statement. *Acupuncture and Related Therapies*. 2015;3(4):35-46.
2. Sajadi MM, Mansouri D, Sajadi M-RM. Ibn Sina and the clinical trial. *Annals of internal medicine*. 2009; 150(9):640-3.
3. Friedman LM, Furberg C, DeMets DL, Reboussin D, Granger CB. *Fundamentals of clinical trials*. Springer; 2015.
4. Pandis N, Chung B, Scherer RW, Elbourne D, Altman DG. CONSORT 2010 statement: extension checklist for reporting within person randomised trials. *Bmj*. 2017;j357: 2835.
5. Altman DG, Moher D, Schulz KF. Harms of outcome switching in reports of randomised trials: CONSORT perspective. *BMJ: British Medical Journal (Online)*. 2017;356.
6. Editors ICoMJ. *Clinical trials registration*. 2014.
7. Eldridge SM, Chan CL, Campbell MJ, Bond CM, Hopewell S, Thabane L, et al. CONSORT 2010 statement: extension to randomised pilot and feasibility trials. *Pilot and feasibility studies*. 2016;2(1):64.
8. Viergever RF, Li K. Trends in global clinical trial registration: an analysis of numbers of registered clinical trials in different parts of the world from 2004 to 2013. *BMJ Open*. 2015;5(9):8932.
9. Feizabadi M, Fahimnia F, Mosavi Jarrahi A, Naghshineh N, Tofighi S. Iranian clinical trials: An analysis of registered trials in International Clinical Trial Registry Platform (ICTRP). *Journal of evidence-based medicine*. 2017; 10(2):91-6.
10. Vasei M, Ghanei M. Iranian registry of clinical trials: a four-year steady progress. *Archives of Iranian medicine*. 2013; 16(11):671.
11. *Clinical Trials*. International Committee of Medical Journal Editors; 2018 [updated 2018; cited 2018]; Available from: <http://www.icmje.org/recommendations/browse/publishing-and-editorial-issues/clinical-trial-registration.html>.
12. Solaymani-Dodaran M, Khalili D, Hosseini H, Najafi L, Kamali K, Ranjbar P, et al. Iranian Registry of Clinical Trials two years on and the timing of registrations. *Journal of evidence-based medicine*. 2011;4(3):168-71.
13. Mayo-Wilson E, Heyward J, Keyes A, Reynolds J, White S, Atri N, et al. Clinical trial registration and reporting: a survey of academic organizations in the United States. *Bmc Med*. 2018; 16(1):60.
14. Jones CW, Keil LG, Holland WC, Caughey MC, Platts-Mills TF. Comparison of registered and published outcomes in randomized controlled trials: a systematic review. *Bmc Med*. 2015;13(1):282.
15. Rikos D, Dardiotis E, Tsvigoulis G, Zintzaras E, Hadjigeorgiou GM. Reporting quality of randomized-controlled trials in multiple sclerosis from 2000 to 2015, based on CONSORT statement. *Multiple sclerosis and related disorders*. 2016; 9:135-9.
16. Gray R, Badnapurkar A, Hassanein E, Thomas D, Barguir L, Baker C, et al. Registration of randomized controlled trials in nursing journals. *Research Integrity and Peer Review*. 2017; 2(1):8.