Debates Article

Registration of Clinical Trials: Is it Really Needed?

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Abstract

Background and Aims: Withholding findings of clinical trials for publication or presentation to the regulatory authorities is a major concern. We aimed to address the importance of clinical trial registration and whether it is needed or not. **Discussion:** For ethical conduct of clinical trial, registration is an important but debatable issue due to proprietary interest of the pharmaceutical industry. Over the years, investigating agencies uncovered several instances of misconduct during the clinical trial. The International committee of medical journal editors requires registration of trial methodology, but does not require registration of trial results; however, the U.S. Food and Drug Administration Amendments does require researchers to register results. **Conclusion:** Prospective registration of clinical trial is mandatory for more transparent research and sustaining the validity of evidence based practice and availability of reliable data. Clinical trials registration has the potential to contribute substantially to improve clinical trial transparency and reducing publication bias and selective reporting.

Keywords: Clinical trials, Ethics, Healthcare, Registration, Research

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Background and Aims

Clinical trials play an important role for the development of health information and research for public health care. The guiding principles of clinical research are based on maximum benefit and minimal risk to the patients enrolled in a study. Furthermore, protection of patient interest and confidentiality are essential to prevent unethical conduct of clinical trials. Difficulty in the enrollment of suitable candidates might create situations for scientific misconduct integrity, which should be overcome through proper monitoring and trial audit. The International committee of medical journal editors (ICMJE) requires registration of trial methodology, but does not require registration of trial results, however, the U.S. Food and Drug Administration Amendments Act of 2007 does require researchers to register results. Clinical trials, register or not to register?, it is not the rule of "All or None." Herein, we aim to address the importance of registration of clinical trial and whether it is needed or not.

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Discussion

Why pharmaceutical companies hesitate to register clinical trials?

Transparency of clinical trial is an utmost important issue to be solved at different levels starting from academic institutions, pharmaceutical industry, ethical boards, data monitoring team and legislative committees. For ethical conduct of clinical trial, registration is an important, but debatable issue particularly for the pharmaceutical industries. Most of the pharmaceutical companies hesitate to register their clinical trial because of the (a) fear of intellectual property being plagiarized, (b) loss of market value of investigational medical product, (c) reluctance to release sensitive information earlier to the general public, (d) compromise of the profit due to availability of information to the competitors. Though, these concerns prevail in the industry, compliance to international standards is also mandatory for filing a copyright or a patent.

How to overcome misconduct in clinical trial?

Though, correct reporting of study or trial findings is the most important ethical obligation for conducting a

research study involving humans. Over the past decade, several instances of misconduct during the clinical trial have been uncovered by investigating agencies.[1] The investigating agencies found that both sponsors as well as trial investigators were involved in the misconducts. Failing to obtain approval from research ethics committees, inclusion of trial participants without obtaining informed consent and data fabrication are some of the common misconducts observed during the audit of clinical trials.[2] Investigations have also revealed that some sponsors retain negative findings of the trial to be published or presented to the regulatory authorities.[3] Willyard[4] reported such misconduct to be more common in trials conducted in the developing nations.

On the other hand, investigation of National Institutes of Health funded research in the US claimed minimal instances of fraud and misconduct. Another retrospective review of audit reports on Cancer and Leukemia Group B in Washington revealed only two cases of misconduct among 691 institutional audits and showed good protocol compliance.[5] Schmidt *et al*.[6] observed a single instance of misconduct out of the total 234 on-site audits performed in Europe and South Africa.

Sometimes it is difficult to enroll suitable patients in a trial which might create situations to compromise the scientific integrity through fabrication, falsification, or plagiarism.[7] Nearly 60% of the disintegration is done through the way of falsifying the data followed by fabrication and plagiarism.[7] Such situations might be overcome through proper monitoring and audit of a clinical trial according to good clinical practice guidelines. The audit should be done by various monitoring boards in different academic institutions and pharmaceutical industries. Nonetheless, some companies guarantee to stick to the recommendations and registry guidelines. To substantially minimize the instances of misconducts in research studies, the clinical trial should be registered prospectively before starting the recruitment process. Therefore, presenting major protocol information regarding the clinical trial in the public domain can potentially prevent at least some of the misconducts.

Up to what extent regulations interplay with clinical trials?

Transparency in research and dissemination of relevant information to the public domain is pre-requisite for the conduction of clinical trials in industrial research. Recently, World Health Organization (WHO) has implemented new regulations for the disclosure of the research data. The data should be supplemented by a comprehensive review of the literature. It promotes more transparent research, helps to maintain the validity of evidence based medicine and availability of reliable data for the meta-analysis. Therefore, the implementation of these regulations is intended to safe guard the integrity of clinical research.

According to the revised Declaration of Helsinki "every clinical trial must be registered in a public accessible database before recruitment of first subject".[8] The ICMJE also advocated for registration of all clinical trials. Therefore, from 1st July 2005 onwards ICMJE consider only those clinical trials for publication which have been registered before the start of patient recruitment.[9] Similarly, the editors of PLoS Medicine and PLoS Clinical Trials accept only those clinical trials for evaluation that have been registered before patient enrollment. The WHO International Clinical Trials Registry Platform also advocated the registration of all clinical trials performed either on patients or healthy volunteers. It is also recommended that the complete trial details supplied during registration should be disclosed at public domain for the sake of transparency. To satisfy the trial registration criteria, a set of 20 mandatory data items (pre-requisite information) should be provided by the clinical trial applicant.[10] These data items constitute key information regarding the type of study, inclusion and exclusion criteria, name and description of interventions, primary and secondary outcomes, sponsors, contact persons and other relevant data which are crucial for overall understanding of the trial by public domain.

Conclusion

The above debate (or report) attempts to address clinical trails registration has the potential to contribute substantially to improving clinical trial transparency and reducing publication bias and selective reporting. Therefore, for obtaining reliable and accurate data for various health care interventions (drugs, diagnostics or therapeutic) registration of clinical trials is of paramount importance and makes the research more transparent. The utmost priority of a researcher should be to serve the mankind rather than the benefit to the commercial industries or academic institutions.

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