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Clinical Trial Registry - India (CTR-I): A meaningful initiative. How to take it forward?

Volunteers agree to participate in clinical trials with a sense of selflessness and trust. They assume that information generated in the clinical trial that they participate in, will help in the advancement of medical knowledge, improvement in therapeutic options and making the healthcare systems better. However, for a variety of reasons, many trials and trial results remain out of bounds for other stakeholders in biomedical research, which include other researchers, research participants, patients, doctors, regulators and insurance companies. Investigators' and editors' inclination to publish only those trials that have proved the new intervention to be better than standard therapy is one of the reasons for several trials with so-called 'negative results' remaining unpublished. There have been instances where some pharmaceutical companies have at times chosen not to report certain observations made during clinical trials to the regulators for various considerations, including commercial ones. This tendency has caused a great deal of upheaval in the medical fraternity and patients' rights groups. Such non-revelation of information leads to marketing of the drug without these aspects being mentioned as a cautionary note.[6] The doctors, therefore, prescribe the drug without being aware of the complete picture. Although the drug may eventually get withdrawn when the side-effects become evident during the post-marketing phase; this generally happens only after several individuals have got exposed to or suffered from the drug's side-effects.

Concealing such information is ethically abhorrent. It underlines the need for taking steps to ensure that sponsors and investigators do not conceal the existence of trials and do not keep uncomfortable observations in a clinical trial under wraps. Arguments in favor of clinical trial registration are rooted in both bioethics and science.[6] By making trial methods and results public, the investigators can be seen to fulfill the pledge they make to research participants to contribute to medical knowledge. In the absence of a formal consensus on international norms and standards for reporting of study results, at present,[7] the initiative is limited to registration of clinical trials. Even this partial step has a great potential in providing global access to information, reducing unnecessary duplication of research efforts and wasteful squandering of resources, decreasing the potential for patient harm and enabling monitoring of the way research is conducted. It could enhance the reliability of evidence on which healthcare-related decisions are based. It could also assure the public that research is conducted in an ethical and transparent manner and for the benefit of mankind. The step could help boost public confidence in research activities and improve trial participation. As information regarding fellow researchers becomes available, opportunities for building collaborations and improving research designs could multiply.[6,8] Thus, trial registration would help raise the overall scientific and ethical quality of research.

In the absence of a law mandating such registration, the International Committee of Medical Journal Editors (ICMJE) took the first step towards ensuring greater transparency in reporting clinical trials.[9] The ICMJE averred that for a trial to be reported in the member journals, it should have been registered in an openly accessible registry. It prescribed certain criteria for a registry to be eligible and also described the certain minimum information regarding the trial that should be available.[9] Over the years, several other journals and the pharmaceutical industry have endorsed the ICMJE initiative[6,10-13] and this step has been successful in demonstrating a large increase in the number of clinical trial registrations.[14,15]

The National Institute of Medical Statistics (NIMS), Indian Council of Medical Research (ICMR) has set up a clinical trial registry called the Clinical Trial Registry- India (CTR-I) in 2007. This effort has been funded by the Department of Science and Technology (DST). The World Health Organization has provided financial and technical support for its establishment. The registration is voluntary and free of charge. The CTR-I encourages all clinical trials conducted in India to be prospectively registered before enrollment of trial participants is initiated. It also allows for registration of trials conducted in other countries in the region. Registration mandates disclosing details of 20 items deemed mandatory by the WHO International Clinical Trial Registry Platform (ICTRP) dataset. The CTR-I also requires disclosure of certain additional information such as clearance from ethics committees and regulatory agencies [Table 1]. The CTR-I meets the ICMJE requirements and is recognized as a primary register by the WHO for its International Clinical Trials Registry Platform (ICTRP). The CTR-I contributes data to the WHO search portal.

The Way Forward

Now that an easily accessible registry with a mandate to register clinical trials in India has been established, editors of Indian biomedical journals have decided to take this initiative forward. A Policy Statement is being formulated. The Indian biomedical journals and their editorial boards after having avowed to wholeheartedly support the initiative of trial registration should take steps that would strengthen the initiative and encourage investigators and sponsors to register their clinical trials. They should:
Collaborate with professional organizations and the Indian Council of Medical Research to inform researchers, members of the institutional ethics committees and other members of the scientific community regarding issues related to clinical trial registry and motivate them to register trials in CTR-I or other registries compatible with the WHO criteria.

Engage other editors of Indian biomedical journals and encourage them to join the initiative.

Appeal to other stakeholders including ethics committees, the pharmaceutical industry, governmental and non-governmental funding agencies to act in a manner that would encourage and motivate investigators to register their trials.

Possible Impact

In India, most clinical trials are sponsor-initiated and are supported by grants from the pharmaceutical industry. Many of these trials get reported in journals published abroad. It is possible that many multi-centric international clinical trials sponsored by multinational companies are already being registered with other registries, since the sponsors would like to publish the trials in reputed international journals that may be endorsing ICMJE guidelines. Hence, trials undertaken by the Indian pharmaceutical industry and those that are undertaken by postgraduate students as a part of their dissertation work would get registered with CTR-I. Many trials done as a part of dissertation work are carried out as preliminary studies without enough attention being paid to determination of adequate sample size, appropriate study design or other protocol-related issues. As many of these issues will be required to be decided apriori at the time of registration, these young scientists would be required to pay greater attention to these details resulting in better quality research being conducted in the country. Trial registration would generate information about Indian researchers and the kind of clinical trials conducted on Indian soil. As stated earlier, it might avoid waste of resources as funding agencies would become aware of research work that is already in progress. In addition, Indian researchers would be able to collaborate with other researchers doing similar work in the country. It is feared that for various reasons, many research studies in India are carried out without the requisite ethical clearance. If this intervention is used in collaboration with the ethics committees, it would ensure greater compliance with the requirement of ethics committee approval. This could lead to greater adherence to the principles of ethics in conduct of clinical trials.

There is a flip side to registration as well. Clinicians in India find it difficult to conduct clinical trials due to various factors; one of them being the proportion of time that they have to devote to patient care. They will be expected to commit additional time for complying with the requirements of registering clinical trials. However, considering the advantages of better scientific and ethical research, this would result in time well spent. There could be an impact on medical journals as well. Editors will have to face a situation where they would be required to desist publishing a well-designed well-conducted trial on an important health issue just because it has not been registered. Many researchers may loathe the idea of registering trials for the fear of bureaucratic hurdles and would rather choose to select a journal not insisting on trial registration. As a consequence, it is feared, that many small journals may find it difficult to sustain if fewer research articles are submitted to them. Although there may be some substance in these apprehensions, we do not feel that insisting on registration would have a significant adverse effect on Indian journals. In any case, the greater public good should take precedence.

It is possible that over the next few months a consensus might evolve regarding providing results of clinical trials in public domain. When this happens, individual patients and support groups will have access to individual trial results. They will have to appreciate that usually observations made in a single trial do not bring about a change in medical practice. In addition, the media will have to report these results responsibly and without sensationalization to ensure that patients do not clamor for unproven therapies and treating doctors are not forced to use an intervention that has not been convincingly proved to be safe and efficacious.

JPGM Commitment

Enhancing knowledge, improving preventive and curative strategies and finding better healthcare delivery systems are the basic aims of conducting clinical research. Registering clinical trials is not a panacea for all the ills related to selective reporting of data, concealing information generated during clinical trials or duplicate publications; it is nevertheless an important step that could help build and boost public confidence in the way clinical research is conducted by assuring greater transparency and allowing public scrutiny. We also hope that registering clinical trials will ensure that data from such trials will be reported with greater transparency and utmost honesty. JPGM endorses the initiative taken by the ICMR in
establishing CTR-I. JPGM would like to assure the public, in general, and the scientific community, in particular, that it would collaborate with other Indian biomedical journals and with other stakeholders in clinical research for taking steps that would encourage investigators to register their clinical trials.

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