Invited Article

Contemporary Understanding of Ethics in Clinical Research and Publication in India

https://doi.org/10.47210/bjohns.2022.v30i2.823

Nitya Goddanti,[1] D Dwarakanatha Reddy,[1] L Sudarshan Reddy[1]

ABSTRACT

Ethics, in principle, is what distinguishes the acceptable from unacceptable. The role of ethics in biomedical research and publication has a new found growing importance in the recent times. Its initial role was merely in safeguarding the participant's interests. The role of ethics in biomedical research has now expanded by encompassing not only the safety and integrity of subjects, but also in curbing the unlawful practices in the publication of the study material. Violation of the rules laid by the various regulatory bodies is now considered an offence. This article aims to give a crisp and concise picture of the role of ethics, various misconducts and its repercussions, in clinical study and publication in today's time.

Keywords

Ethics; Clinical Research; Publication; Misconduct

The term 'Ethics' is defined as norms of conduct that distinguish between acceptable and unacceptable behaviour. Various factors like integrity, moral values, honesty and conscience contribute to Ethics. Clinical research on the other hand encompasses research to improve human health extending from "basic research" that may apply to "preclinical understanding" to "clinical research". Clinical research is the cornerstone to evidence based medicine. Research is however a laborious and time consuming process that needs continuous vigilance and follow up. To document the study findings and publishing them for extended awareness among peers eventually helps in improving the health care delivery system. Ethics plays a very important role in both conducting a clinical study and its publication. Ethics in clinical research focuses on identifying and implementing the acceptable conditions for exposure of participants to risks and burdens for the benefit of the society.[1] Ethics in clinical research saw the light of the day only after instances of inhuman practices with participants were reported. The first international code that laid ethical principles for clinical research was the Nuremberg Code. Subsequently, the World Health Organisation (WHO) formulated guidelines under Declaration of Helsinki in 1964. The Indian Council for Medical Research (ICMR), in the year 2000, formulated the 'Ethical Guidelines for Biomedical Research on Human Subjects', later revised in the year 2006.[2] These guidelines have elaborated the three basic ethical principles: respect for person, beneficence and justice by inducting twelve general principles, as described below.

Ethical violations in conducting medical research always promote unethical scientific publications.[1]

Principles for Clinical Research

A clinical study or research involves several coordinated stages. Devising an appropriate research question is of paramount importance. To question the legitimacy, need and the benefit to the society of the research question lays a road map for a quality study. Most common reasons

1 - Department of ENT, Government ENT Hospital, Koti, Hyderabad, Telangana, India

Corresponding author:
Dr Nitya Goddanti
email: nityag24@gmail.com

for a study failure are badly defined research question and objectives, unrealistic timescales, inappropriate and inefficient execution and inadequate monitoring.[3] A *Scientific review* of a clinical study evaluates if the research question and objectives are sound and valid. *Ethical review* is to monitor the safety and welfare of the participants. *Regulatory review* aids in understanding if the research methods are appropriate.

Planning a study

Planning a clinical study is the most pivotal part of its framework. Improper planning leads to ill defined objectives which results in difficult data analysis, data interpretation and inability to implement data interpretation in new programme or policy making. The various steps are described in (Fig. 1). Formulating appropriate objectives, determining the right study design, preparing the analysis outline and estimating sample size are quintessential to planning a clinical study.

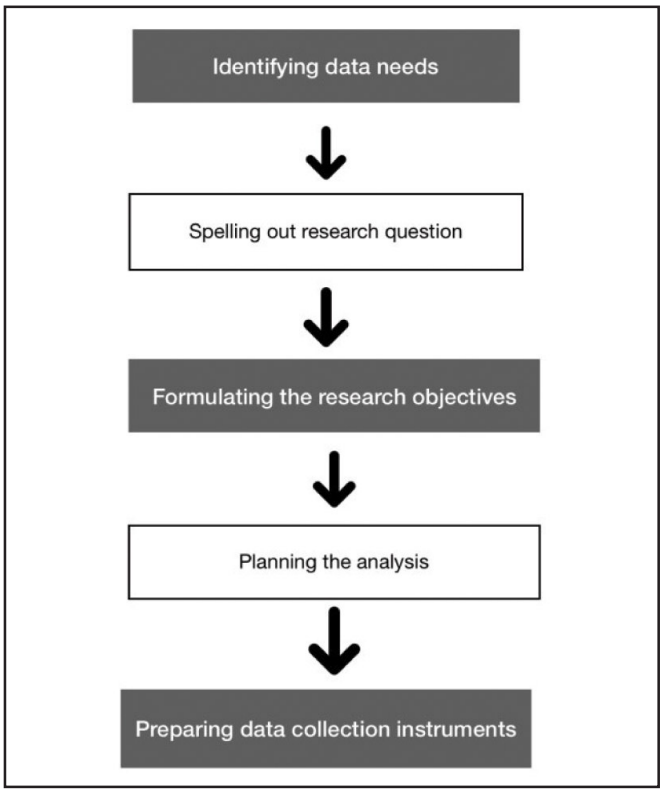

Fig. 1. Showing the principle steps of clinical study planning

Register

A robust, transparent, simple and well-established regulatory system is important to ensure safety and quality of a clinical research study. In the past few years, it has been made mandatory from 2019 to register every clinical trial with the Clinical Trials Registry of India.

Ethics committee approval

The Institutional Ethics Committee (IEC) comprises the following

1. Chairperson (outside the institution)
2. Two persons from basic medical science area
3. Two clinicians from other institutions
4. One legal expert or retired judge
5. One social scientist
6. One philosopher
7. One lay person from the community
8. Member secretary - from the same institution

The basic responsibility of the IEC is to ensure the timely safeguarding of ethical aspects of participants like dignity, safety and rights. It also evaluates the study for its community benefit and mechanism for provision of safety and support to the participants.[3] The IEC clearance for a study design is must before implementation. Timely supervision and scrutiny to rule out any violations is a must. Participant consent and safety cannot be negotiated in any clinical research.

Participant selection

An ideal study population must be 'representative', of 'adequate size' and of 'acceptable cost'. Various selection criteria must be met with to be a part of the study sample which are classified as inclusion and exclusion criteria (Table I).The general population subject to clinical and demographic criteria gives us a 'Target population'. Target population when subjected to geographical and temporal characteristics, gives us the 'Accessible population'. When exclusion criteria are implemented on the accessible population, it gives us the final 'Study sample'. A well

documented informed consent includes the following: a detailed description of the study, the potential risks and benefits, assurance of confidentiality and freedom to withdraw at any point; all of which are vital.

Table I: Various inclusion and exclusion criteria for sample selection

INCLUSION CRITERIA (Specifying populations relevant to research question and study)	**Demographic characteristics**	**Based on age and sex particulars**
	Clinical characteristics	**Based on specific clinical conditions**
	Geographic characteristics	**Participants belonging to a particular region**
	Temporal characteristics	**Participants appearing in a specific time frame**
EXCLUSION CRITERIA (Subset of population will not be studied because of)	**Loss to follow up**	**Those who are likely to move out of the study**
	Interfere with quality of data	**Participants indulging in other modalities that might interfere with the study**
	High risk individuals	**Those having adverse comorbid conditions**

Data collection

Adequate and valid data is one the pillars of a clinical research. Different tools can be used to collect data like review of records, questionnaires and interviews. Data collection has a very high chance of inviting 'bias'. Two cornerstones of data collection are 'reliability' and 'accuracy'. Trained staff must be employed for data collection without succumbing to bias towards participants.

Data analysis and conclusion

Collected data needs to structured according to the variables that are studied. The main use of data analysis is to interpret the validity of our findings. As it is not possible to conduct a study on the entire population, a study sample is selected. Any intervention and conclusions drawn in a study is only applicable to the study sample. Thus, to know if the results drawn are significant and can be projected to the entire population, data analysis is a must. Fabricating the data to alter the results to meet one's own demands is an offence.

Ethics pertaining to study participants

The basic essence of ethics in a clinical study can be broadly classified as 1) Respect for subjects 2) Beneficence to the subject and to society eventually 3) Non-maleficence to human or animal subjects 4) Justice with equal opportunity to all participants. ICMR has expanded these four basic principles into 12 general principles which are as follows[4] :

I. *Principle of Essentiality* whereby after due consideration of all alternatives in the light of existing knowledge, the use of human participants is considered to be essential for the proposed research. This should be duly vetted by an ethics committee (EC) independent of the proposed research.

II. *Principle of voluntariness* whereby respect for the right of the participant to agree or not to agree

to participate in research, or to withdraw from research at any time, is paramount. The informed consent process ensures that participants' rights are safeguarded.

III. *Principle of non-exploitation* whereby research participants are equitably selected so that the benefits and burdens of the research are distributed fairly and without arbitrariness or discrimination. Sufficient safeguards to protect vulnerable groups should be ensured.

IV. *Principle of social responsibility* whereby the research is planned and conducted so as to avoid creation or deepening of social and historic divisions or in any way disturb social harmony in community relationships.

V. *Principle of ensuring privacy and confidentiality* whereby to maintain privacy of the potential participant, her/his identity and records are kept confidential and access is limited to only those authorised. However, under certain circumstances (suicidal ideation, homicidal tendency, HIV positive status, when required by court of law etc.) privacy of the information can be breached in consultation with the EC for valid scientific or legal reasons as the right to life of an individual supersedes the right to privacy of the research participant.

VI. *Principle of risk minimisation* whereby due care is taken by all stakeholders at all stages of the research to ensure that the risks are minimised and appropriate care and compensation is given if any harm occurs.

VII. *Principle of professional competence* whereby the research is planned, conducted, evaluated and monitored throughout by persons who are competent and have the appropriate and relevant qualification, experience and/or training.

VIII. *Principle of maximisation* of benefit whereby due care is taken to design and conduct the research in such a way as to directly or indirectly maximise the benefits to the research participants and/or to the society.

IX. *Principle of institutional arrangements* whereby institutions where the research is being conducted, have policies for appropriate research governance and take the responsibility to facilitate research by providing required infrastructure, manpower, funds and training opportunities.

X. *Principle of transparency and accountability* whereby the research plan and outcomes emanating from the research are brought into the public domain through registries, reports and scientific and other publications while safeguarding the right to privacy of the participants. Stakeholders involved in research should disclose any existing conflict of interest and manage it appropriately. The research should be conducted in a fair, honest, impartial and transparent manner to guarantee accountability. Related records, data and notes should be retained for the required period for possible external scrutiny/ audit.

XI. *Principle of totality of responsibility* whereby all stakeholders involved in research are responsible for their actions. The professional, social and moral responsibilities compliant with ethical guidelines and related regulations are binding on all stakeholders directly or indirectly.

XII. *Principle of environmental protection* whereby researchers are accountable for ensuring protection of the environment and resources at all stages of the research, in compliance with existing guidelines and regulation.

Principles of scientific publication and publication ethics

There is no use of a clinical research if it does not have a reach. Publishing one's research is a way of enlightening the fellow readers. Publishing a study for personal interests leads to unethical practices.

The Committee on Publication Ethics (COPE) is an international forum for editors and publishers of journals that provide the "code of conduct" and "best practise guidelines" that define publication ethics and advises

editors on how to handle cases of research and publication misconduct.[5,6]

Publication ethics are as pivotal as ethics pertaining to clinical research. Any publication ethical misconduct will harm the readers and is unjust to everyone participating in the planning and implementation of the study. COPE has formulated the guidelines for publication and houses the authority to punish those violating the guidelines.

Breach of confidentiality

This primarily includes data confidentiality which refrains you from sharing the data with anyone from other institutions without the permission of the parent institute. Violation of this amounts to serious ethical misconduct.

Data manipulation

Fabrication and falsification are extremely serious forms of research misconduct. Fabrication refers to conclusions drawn from the data that are not generated by the clinical study. Whereas, falsification is when conclusions drawn are generated by manipulating the data. These misconducts can be easily deciphered by taking a look at the statistical analysis of a study. Editors and reviewers can always ask for the worksheets if a suspicion arises, even after publication. This calls for foolproof worksheets with detailed data analysis and the need to save them for a sizeable period even after publication.

Plagiarism

The use of previously published work by another author in one's own manuscript without consent, credit or acknowledgment and fraudulently passing it as one's own work is referred to as plagiarism. This is the most common and serious form of misconduct in manuscript writing. Plagiarism can be either clear plagiarism, wherein word-for-word copying of large parts of another manuscript is done, and minor, wherein only short phrases are used with slight alteration from another publication. *Self-plagiarism*, also known as, recycling is the term used to describe when an author uses the same text in multiple papers without citation of prior work. Plagiarism can be avoided by writing the manuscript in one's own words and avoiding "copy-paste". Citing the references accurately and running the manuscript through anti-plagiarism softwares is warranted.

Authorship criteria

1. International Committee of Medical Journal Editors (ICJME) states, "All persons designated as authors should qualify for authorship, and all those who qualify should be listed." The mandatory criteria for author accreditation are: Substantial contribution to the conduct of study including its conception and design, data acquisition, statistical analysis and interpretation.[7]
2. Drafting or revising the article for intellectual content.
3. Approval of the final version.
4. Agreement to be accountable for all aspects of the clinical study and publication.

Various misconducts pertaining to authorship are *Ghost authorship* (contribute to study substantially but are not given authorship), *Gift authorship* (merely due to the affiliation of the author to an institute where the study was conducted), *Guest authorship* (given to those whose name as a coauthor improves the chances of acceptance of manuscript).

Conflict of interest

Conflicts of interest, also called as competing interests, are defined as financial, personal, social or other interests that directly or indirectly influence the conduct of the author with respect to the particular manuscript. Failure to disclose such interests severely jeopardise the outcomes reported. ICMJE has decided a form to disclose any such conflicts of interests that has to acknowledged by every co-author. Once disclosed, it is up to the reader to gauge the reliability of the study and the influence of such interests on the author.

Redundant publications

Unlike in plagiarism where large portions of phrases are duplicated from another publication, redundant or duplicate or 'salami' publications refer to studies where identical

data, hypothesis, images etc., are repeated with minor changes like changing the title, authorship order etc.. Publications in regional languages are usually used for such misconduct. Simultaneous submission of the article to two separate journals is also considered an ethical offence.

Conclusion

The field of medicine is ever evolving with dynamic changes in disease patterns. This requires the professionals to be alert and aware. Clinical research is the tool to understand the changing trends in disease pattern and treatment protocols. It is by default conducted keeping in mind the 'greater good' or the benefit of the larger society. A good clinical research must either give a new perspective to the disease profile or shed light on novel treatment methods. This comes with the responsibility of conducting the study ethically and by abiding by the rules. Like every human activity, clinical research also has the scope for corruption. The importance of ethics in research and publication have gained a greater importance in the recent times. So much so that, any violation amounts to an offence as it can meddle with safety of study participants, or affect the judgment of those who consume the study. This article was aimed to give a current, lucid and precise idea about various potential misconducts which a researcher may wilfully or ignorantly commit.

References

1. Sanmukhani J, Tripathi CB. Ethics in clinical research: the Indian perspective. Indian J Pharm Sci. 2011 Mar;73(2):125-30. doi: 10.4103/0250-474x.91564
2. Das KK, Vallabha T, Ray J, Murthy PS. Conflict of interest-serious issue on publication ethics for Indian medical journals. JNMA J Nepal Med Assoc. 2013;52:357-60
3. [Last accessed on 2022 Nov 22]. Available from: http://www.nie.gov.in/icmr_sph/BCBR.html
4. [Last accessed on 2022 Nov 22]. Available from:https://main.icmr.nic.in/sites/default/files/guidelines/ICMR_Ethical_Guidelines_2017.pdf
5. [Last accessed on 2022 Nov 22]. Available from: http://www.publlicationethics.org
6. Wager E. The Committee on Publication Ethics (COPE): Objectives and achievements 1997-2012 Presse Med. 2012;41(9 Pt 1):861-6
7. [Last accessed on 2022 Nov 22]. Available from: http://www.icmje.org/recommendations/browse/roles-and-responsibilities/defining-the-role-of-authors-and-contributors.html.