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Should Lack of Ethical Committee's Approval of Human Research Lead to Rejection of Resulting Manuscripts?

Context

Compliance with ethical principles in clinical research is a vital aspect of scientific publication.[1] It is particularly important because the published data may directly affect human health.[2] There have been some concerns about the extent of adherence to ethical principles that lead to increased scrutiny of publication ethics, policies, and practices in various regions and disciplines.[3,4] These infringements involve knowledge and behavior of authors, competence and complacency of editors, and adequacy of regulatory provisions.

Recently, the Ibnosina Journal of Medicine and Biomedical Sciences received few clinical research manuscripts that seemed, on their face value, exciting and have contributing valuable knowledge to their subject. Surprisingly, these submissions had no mention of formal ethical approval despite involving human subjects. On further inquiry, it was readily revealed that no ethical review was undertaken. The authors furnished different arguments for such ethical oversight including ignorance about the need for such approvals or lack of Institutional Review Boards (IRBs) in their setting. We were particularly alarmed that some of these authors hold high qualifications from established universities and were employed in academic positions in their institutions. Unfortunately, they failed to recognize the mandatory nature of the formal prior ethical review of human research.[1,2] Hence, in this viewpoint, we consider the core principles of good practice in scientific publishing, emphasize ethics as a core value in research, and highlight ethical pitfalls by authors, editors, and institutions.

Publication: An ethical imperative

Publication of clinical research is both a monitor of the researcher's ethics and an audit of the local and regional ethics committees that approved it.[5] Peer-reviewed biomedical journals are expected to publish accurate and vital information. In the process, numerous ethical issues may arise from within both the editorial and research communities. The general ethical issues include what constitutes authorship, fair and serious peer-review processes, avoidance of duplicate or repetitive publication, and declaration of potential conflict of interest.[6] Issues of authorship include multiple authorship, misconduct among coauthors, guest and honorary authorship, the order of authorship, and credit for those not qualifying for authorship. Peer reviews attempt to ensure that what is published is valid.[7] Ethical issues of peer reviews include confidentiality of the manuscript, potential editor and reviewer bias, and conflict of interest on the part of the reviewer. Duplicate or repetitive publication, in which the same information is reported two or more times, can damage a journal's reputation for publishing new and vital information and can waste its resources. Conflict of interest, in which financial and personal considerations may affect the investigator's judgment, can severely damage the integrity of the author and the journal.[7]

Why ethical approval is required for research publications?

Opinions may differ about what is ethically allowable in clinical and benchtop medical researches. Ethical permission and ethical monitoring of medical research are subject to a hierarchy of pyramidal controls, starting in the hospital and ending with the local, institutional, or regional ethical committees. Such committees function with varying degrees of efficiency and quality of output, and with differing viewpoints on many ethical issues.[8] Most academic journals that publish studies involving human participants require evidence that the research has been approved by a human research ethics committee commonly known as IRBs. Journals continue to receive submissions from authors who have failed to obtain such approval.[9] The IRB is an independent body constituted of medical, scientific, and nonscientific members, whose responsibility is to ensure the protection of the rights, safety, and well-being of human subjects involved in clinical research. IRBs do their role by, among other things, reviewing, approving, and providing continuing review of the research protocol and amendments and the methods and materials to be used in obtaining and documenting informed consent of the research subjects in accordance with the International Conference on Harmonization (ICH) Harmonized Tripartite Guideline.[2] Four justifications for requiring ethical approval before publication include the following: first, IRB approval adds legitimacy to the research; second, the process of obtaining IRB approval can improve the quality of an intervention being investigated; third, obtaining IRB approval can help mitigate harm; and lastly, obtaining IRB approval demonstrates respect for persons.[9]

Pitfalls and solutions for authors and editors

The growing emphasis on the importance of publishing scientific findings in the academic world has led to increasing discovery of potentially significant publications in which scientific and ethical rigor may be questioned. This has hindered research progress but also eroded public trust in all scientific advances. Due to the increasing concern and the complexity of research misconduct, the Committee on Publication Ethics (COPE) was established in 1997 to manage cases with ethical implications.[10] COPE is a professional body providing a discussion forum and advice for scientific editors; it aims to find practical ways to

deal with the publishing issues and to develop good practice. It is essential to customize and outline the best practice in the ethics of scientific publishing. These strategies of COPE are valuable for all those involved in clinical research. Scholarly trustworthiness should be actively encouraged in all medical and scientific courses of study and should be used to inform publication ethics and prevent misconduct. It is with that in mind these guidelines have been produced.[11] COPE publishes cases referred to it with its verdict and advice to the editors on its website. For this editorial, we present the summary of selected real-life instances published by COPE under the subheading "ethical oversight questionable/unethical research."[11] They all demonstrate the inappropriateness and potential risk to human subjects posed by research being conducted without prior ethical approval. The examples presented here give a wide range of scenarios from utter ignorance of the regulation, lack of rules, and lack of structure to making false assumptions [Box 1]. Many more ethical issues are available on the COPE website and are worth a careful consideration by those with an interest and they can be used for educational sessions to stimulate discussion around the subject.

Ethical compliance is a responsibility for all

The advancement of medical science and practice relies on research that must eventually involve human subjects. Therefore, obtaining ethical approval should be a moral reflex for researchers. Unfortunately, this is not the case with too many researchers bypassing the ethics approval procedure, or perhaps unaware of its fundamental importance. Research expectedly involves risks taken by the research participants and uses health-care funds from public, private, or charitable sources in the process. These mandate the research endeavor to aim at attaining the highest degree of respect for the sacrifices made by others for science.[12] Some researchers may confuse scientific clearance or even worse administrative approval with ethical approval. For a study to be ethically sound, it

Box 1: Summary of four examples of real cases published by Committee On Publication Ethics on "Ethical oversight and questionable or unethical research"*

Case summary	COPE's verdict and advice
A. No ethics approval or informed consent? A thesis by a student was submitted by his guide. An editor found the research unethical and asked for confirmation of IRB approval. He received a verbal commitment that prior approval had been granted and that the approval letter will follow. However, the editor found that the approval was obtained post-research and the patients were not aware that they had been randomized into two groups. The author aimed to prove that omission of an expensive drug could lead to no change in results. The author based his hypothesis on a paper that was since withdrawn. Several articles are indicating the contrary	Verdict: The editorial team has a moral responsibility to take further action (as patients may be put at risk) Advice: The editor should write to the EC to determine if approval had been obtained and whether it was obtained retrospectively. If the EC may not be in a position to take any action, authors' institution should be contacted. The institution should be presented with the facts and then allowed to investigate the matter themselves. Authors should be informed by editors about all intentions to communicate. [COPE case number: 7-2 (year 2007)]
B. "Research" without EC approval Eighteen patients and ten controls had various measurements taken after being given an oral glucose load. Participants also had routine blood sampling and were put on a defined diet for 3 days. The authors did not consider it necessary to obtain IRB approval, but all participants signed a consent form recording their agreement to take part and to have the results published. The journal deemed the research scientifically meaningless. The editors think that IRB approval should have been obtained. The authors disagree	Context: Some groups do fall between organization's setup to approve research, and it is difficult for them to know who to approach for ethical approval. The main problem is the incoherence of the structures particularly, where the IRB system is less comprehensive. Occasionally, editors receive papers from countries with no research ethical review system Advice: Editors should only publish research that would meet the standards of an IRB in a developed country. They should not assume that the IRB approval process had been carried out to the same level as in developed countries. The editor should report his/her concerns to that national regulatory body after informing the authors. [COPE case number: 3-12 (year 2003)]
C. No ethical committee approval of a study Two different techniques for patients in the ICU were described. There was no IRB approval. The editors asked if approval was obtained. Authors did not apply for IRB approval "as it was a comparison of two existing methods, none of them experimental. All patients had an indication for the technique, and the technique was introduced in their ICUs before the beginning of the study period." "Every other patient who received the technique during the study period was assigned to different techniques." There was no informed consent	Verdict: The described project was clearly research and not a service audit. It appeared, in fact, to be a prospective randomized trial and so it should have been registered and ethical approval should have been obtained. Retrospective approval would not be appropriate. In addition, all participants should have given their informed consent. The lack of consent suggests a breach of the Helsinki declaration Advice: The editor should contact the author's institution and inform them of the situation and ask them to investigate. [COPE case number: 10-28 (year 2010)]
D. Low-risk study with no ethical committee approval A manuscript was submitted that describes a social media advocacy campaign that was run by an international NGO for the purpose of eliciting public support for new law in a low-middle income country	Advice: The editor should obtain retrospective ethical approval for the study. It is up to the editor, and it is his/her judgment call; if the editor is happy with the current position, and common sense tells him/her that the study is sound, then he/she should publish. Follow-up is available on the website. [COPE case number: 16-06 (year 2016)]

*Full details are available under the reference of the given case numbers on the COPE website available from: https://www.publicationethics.org (Last accessed on Jun 15, 2018). IRB: Institutional Review Board, COPE: Committee on Publication Ethics, ICU: Intensive Care Unit, NGO: Nongovernmental organization, EC: Ethical committee

must be scientifically sound. This is only one of the activities carried out during protocol review. The researcher has the responsibility of systematically consulting with IRB for advice and consequent approvals or ethical waivers. Journal editors and reviewers have the duty to evaluate the ethical soundness of manuscripts submitted for review systematically. Capacity building in research ethics and institutional support for IRBs to speed up protocol review could reduce the incentive of researching human subjects without ethical approvals. It is hypocritical and idle to continue to expect optimal reviews on time and of good quality, from IRBs functioning purely on altruistic grounds. Building capacity for researchers in research ethics, institutional reforms, and support for IRBs appear not to have received the attention they truly deserve.[12] In developing countries, IRBs may be seen as luxury rather than necessity components of institutions. IRB members may be called upon to join based on personal interest with no protected time to undertake the necessary review work. Lack of administrative support may make difficult for researchers to submit applications and burden IRB members with unnecessary administrative tasks.

Finally, it is essential that academicians make their utmost effort to maintain the integrity of scientific research and uphold its ethical standards. Authors, editors, journals, and institutions have to work together to this end. Authors must adhere to the spirit and letter of the international research ethics guidelines and journal instructions, while editors should play a gatekeeper role to protect research participants, uphold scientific integrity, and maintain public trust in the experimental process and profession. Medical journals should inspect ethical review more critically. Names of IRB bodies granting the approvals as well as reference code numbers (rather than accepting a generic statement) should be incorporated in the manuscript. Institutions should enforce the provisions for ethical approvals for all kinds of research by putting in place rules and regulations and clear pathways spanning the full range of research work from student projects to pharma-sponsored studies.

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Conflicts of interest

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Compliance with ethical principles

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