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Reporting Results of Research Involving Human Subjects: An Ethical Obligation

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Researchers have an ethical responsibility to report the results of research involving human subjects. Dissemination of results ensures that patient care is based on good science and that the field of medicine advances based on complete and accurate knowledge. However, current evidence suggests that publication is often neglected or substantially delayed, especially in the case of negative and inconclusive results. Researchers, editors and reviewers should value all high-quality research regardless of the conclusiveness of the results and ensure that all research involving human subjects is registered in a publicly accessible database.

Keywords: Ethics, Research; Results Reporting; Negative Results; Trial Registration

INTRODUCTION

There are many reasons why researchers choose to publish the results of their research but one of the most important is to contribute to the advancement of medicine and science. When research involves human subjects, sharing results is more than a personal choice, it is an ethical obligation (1). Publishing results ensures that patient care is based on good science and that the field of medicine advances according to accurate knowledge. It is also part of the commitment researchers make to research subjects. According to prominent bioethicists, the risks of clinical research are only justified if society gains knowledge, which is only possible when results are shared (2).

Although these principles are widely accepted, a substantial amount of human research continues to go unreported and unpublished. This article explores researchers' ethical obligation to report the results of research involving human subjects and discusses current challenges and solutions.

INTERNATIONAL POLICY

An important starting point for this discussion is a brief review of the Declaration of Helsinki. The Declaration of Helsinki is a set of international ethical principles regarding the conduct of human research. It was initially published in 1964 and has been amended 7 times, the most recent revision occurring in 2013 (3). It is a cornerstone document in the field of human research ethics and has been referred to as "the most widely accepted guidance worldwide on medical research involving human participants"(4). Many medical journals, including the Journal of Korean Medical Science, refer to the Declaration in their requirements for publication (5, 6).

The Declaration includes a section on the ethical requirement of registering, publishing and disseminating research results (1). The section addresses two main requirements: 1) That research involving human subjects must be registered in a publicly accessible database and 2) That there is an ethical obligation regarding publication and dissemination of research results. The Declaration specifically states that, "Researchers, authors, sponsors, editors and publishers all have ethical obligations with regard to the publication and dissemination of the results of research" (1). It goes on to clarify that negative, inconclusive and positive results all must be published or made publicly available (1).

CURRENT SITUATION

Publication

Although publication of research results is a widely accepted component of ethical research, in actual practice it is often neglected or substantially delayed (7). For example, one study found that only 46% of US NIH-funded trials were published in a peer-reviewed, MEDLINE-indexed journal within 30 months of completion (8). A similar finding was discovered of vaccine trials conducted in multiple countries. Manzoli et al. (9) found that "the proportion of trials published 12, 24, 36, and 48 months af-

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ter completion was 12%, 29%, 53%, and 73%, respectively" (9). Similarly, a study at a university in Germany found that only half of the studies approved by the ethics committee at the institution resulted in subsequent publication (10). Non-publication of results wastes resources and denies the field of medicine the opportunity to learn from the outcomes.

Negative and inconclusive results

One particular area of challenge is publication of negative and inconclusive results. Multiple studies have found that trials with negative results are published significantly less often and significantly less quickly than trials with positive results (11, 12). This type of publication bias can have a direct effect on patient care. An analysis in the field of psychiatry compared published literature against US FDA reviews of research involving antidepressant agents. Based on the published literature it appeared that 94% of studies were positive but the FDA analysis indicated that only 51% were positive (13). This discrepancy was because most of the negative results were not published or were published in a way that conveyed a positive outcome. The authors of the analysis concluded that the actual efficacy of the antidepressant drug class is less than would be expected based on published literature alone (13).

Higher publication of positive results is a global issue. For example, one study conducted at a hospital in Spain followed the publication outcomes of all drug-evaluating clinical trials approved by the ethics committee of the institution. The study found that trials with positive results were published significantly more often and significantly more quickly than trials with negative results (11). Additionally, a study that included manuscripts from multiple countries, including the Republic of Korea, found that the number of articles reporting positive results increased by over 20% during the years of 1990 through 2007 and that corresponding authors in Asian countries reported more positive results than those in the US and Europe (14).

The higher publication of positive results is a responsibility not only to researchers or authors but also to editors and reviewers. Some editors and reviewers devalue negative results or inconclusive findings and automatically reject the manuscript. Since human subject studies frequently produce negative or inconclusive results, the negative attitude of some editors and reviewers may be a barrier to publication. Editors should review negative results to determine if they are sound. Negative results due to bias or fault are not acceptable. The ICMJE recommends that editors make editorial decisions based on factors such as the manuscript's overall quality and relevance to the journal, and not on the conclusiveness of the results (15). The International Committee of Medical Journal Editors (ICMJE) reminds editors that negative and inconclusive results can make an important contribution to science and that findings that are not statistically significant may provide important data for a subsequent meta-analysis (15).

Trial registration

Clinical trial registration is another mechanism for publicly sharing information about research. The Declaration of Helsinki and the ICMJE both require registration of clinical trials in a publicly accessible database before patient enrollment (1, 16). This means that all journals that follow ICMJE guidance, including JKMS, only publish manuscripts on trials that were properly registered. Clinical trial registration is important because it improves transparency, helps to reduce research duplication, contributes to the scientific evidence base and circumvents the issues of publication bias and selective reporting (17). Studies suggest that data in registries may also be more complete than what is published in medical literature. For example, the US registry [clinicaltrials.gov] requires results reporting and one study found that the results in the registry, especially serious adverse events, were more complete than the results in published articles (18). However, the strength of registries depends on researchers' submission of timely and accurate data and evidence suggests that concerning gaps still exist (19).

SOLUTIONS FOR RESEARCHERS IN KOREA

Researchers in Korea should remain committed to publishing the results of all human research they conduct. JKMS is an ideal choice for publishing because it is committed to publishing high-quality research regardless if the results are positive, negative, or inconclusive. Other journals also provide good publication options for manuscripts that may otherwise be hard to publish. For example, several journals have launched sections focused on publishing negative results and a few journals exclusively publish negative or inconclusive results (20-23). This is not only a sound decision from an ethical and scientific standpoint, but may also benefit both the author and the publisher. One of the aforementioned studies determined that even though positive results were published more often and more quickly than negative results, the impact factor between the two groups was not significantly different (11).

Researchers in Korea should also abide by all trial registration requirements that govern the research they conduct. The online registration system for clinical trials conducted in the Republic of Korea is the Clinical Research Information Service (CRIS). CRIS is a primary register of the WHO International Clinical Trials Registry Platform (ICTRP) and was established at the Korea Centers for Disease Control and Prevention (KCDC) with support from the Ministry of Health and Welfare (MOHW) (24). The registry currently requires trial registration but does not require detailed results reporting. However, the reporting requirements may be updated in the future based on the WHO's current evaluation of ICTRP's policy on results reporting (25).

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CONCLUSION

All individuals involved in conducting or publishing human research have an ethical obligation to disseminate results regardless of the conclusiveness. To meet this commitment, researchers should register their trials in a publicly accessible database and disseminate their findings through publication or other public mechanisms. Editors and reviewers should make editorial decisions based on manuscripts' overall quality and relevance to the journal and not the conclusiveness of the results. Editors should also only publish papers regarding clinical trials that were properly registered.

Disseminating research results ensures that the field of medicine advances based on accurate knowledge. This paper aimed to inform, review current gaps, and discuss solutions regarding this ethical obligation.

DISCLOSURE

All of the authors have no conflicts of interest to disclose.

AUTHOR CONTRIBUTION

Study concept and design: Alley AB. Writing: Alley AB, Hong ST. Revision: Seo JW, Hong ST.

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