VIEWPOINT

Will Medical Preprints Change Oncology Practice?

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Preprints are non–peer-reviewed manuscripts deposited to and permanently stored on a (preprint) server/website and are freely available.[1] They are time stamped by the preprint server on approval, assigned to a digital object identifier (doi), citable, discoverable, and indexed in many search engines (eg, Google Scholar, EuropePMC.org). Most preprint servers also regularly update the publication status of preprints, either through authors' notification or by searching indexing databases. The main purposes of posting preprints are claiming primary of the results, soliciting peer reviews, and informing the scientific community but not informing the public. The closest analogy of preprint is a meeting abstract, but meeting abstracts are usually subject to scientific/abstract review albeit less stringent than manuscripts that undergo journal review. In contrast, preprints are not reviewed by any assessors for scientific merits, which is its major limitation. Compared with meeting abstracts, preprints have the advantages of short turnaround time, flexible submission/publication time, much broader reach, dynamic feedback from a larger community (literally anyone on the internet), no costs to the authors (even travel and meeting registration expenses), and being immediately discoverable in search engines and indexing databases. Compared with peer-reviewed publications, preprints would not speed up the peer-review process and are harmful if used for treating patients without rigorous review or vetting.

Preprint servers were first started in physics, mathematics, and computer science decades ago (1991 for https://arxiv.org/). Preprints are very common in these fields and are their de facto publication route before submission to a journal. However, preprint servers for biology/biomedical sciences were not started until the 2010s, largely owing to hesitation from publishers and authors.[2] The leading biology preprint server is bioRxiv (pronounced *bio archive*), which is operated by Cold Spring Harbor Laboratory. After nearly 5 years of growth, bioRxiv alone received more than 2100 deposits in October 2018 and scored 1.1 million downloads for the same month.[2] Some of the biology, more precisely biomedicine, preprints involve medical and translational sciences, including https://www.preprints.org/. They have considerable clinical implication and ethical concerns. Therefore, bioRxiv launched a pilot program on the sections of clinical trials and epidemiology.

On conclusion of the 3.5-year–long experiment on preprints of clinical trials and epidemiology, Cold Spring Harbor Laboratory launched a new preprint server (medRxiv, pronounced *med archive*) solely dedicated to original manuscripts in health sciences on June 5, 2019, partnering with Yale University and the BMJ Publishing Group.[3] Given the success of bioRxiv and other biology preprint servers, we anticipate a similar success of medRxiv. Indeed, nearly 2.5 months after its launching, there were 206 preprints on medRxiv, all of which were discoverable in Google Scholar and EuropePMC.org. We believe the number of medical preprints will keep growing, likely exponentially. When cautiously interpreted, medical preprints may improve research transparency, reduce waste in research, and accelerate dissemination of medical research data,[4] while direct clinical use of medical preprints is considered harmful and unacceptable.[4-6] However, despite the very clear warning that "They [medical preprints] should not be relied on to guide clinical practice or health-related behavior"[5] on the website and preprints, some preprints will also leak to patients and raise the question on their validity and clinical usefulness.

Therefore, oncologists will soon have to discuss preprint papers with patients and colleagues. Some clinicians probably feel uncomfortable or less comfortable in dealing with medical preprints, while others will neglect them altogether for their ease of mind. Researchers too will face new challenges. Biomedical researchers are encouraged by funders to use preprints[1,7] and may have some disadvantages if not using preprints in grant application and reporting, but they are also concerned about plagiarism and limited publication options owing to journals' preclusion of preprints.

We believe that medical preprints will change oncology practice and research. The key is how to appropriately respond to the changes.

First, the limitations and risks of medical preprints should be thoroughly assessed, extensively discussed, and well understood by all involved parties.[4,5,7] As discussed before,[6] prepublication posting of medical preprints may help disseminate information faster but likely at the price of scientific rigor, care quality (potential medical error), and patients' well-being and their lives. Therefore, proper safeguard is required. This is particularly important for medical preprints on the diagnostics or interventions that are not yet rigorously peer reviewed or vetted by regulatory bodies such as the US Food and Drug Administration and the European Medicines Agency. The medical, publishing, research, and patient communities should all work together to mitigate the risks and maximize the potential benefits of medical preprints.

In our opinion, oncologists should be cautiously enthusiastic about the increasing adoption of medical preprints. We recommend a 2-step approach to the questions stemming from medical preprints that patients may bring up or clinicians may discover in literature search. The first step is to assess the remaining options in the standard of care for the patient,

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whose outcome dictates the next step. If there is any option in the standard of care, oncologists should tentatively discount the medical preprints. The reasons are that medical preprints are of little value in light of available options in standard of care and have uncertain patient outcomes and unfavorable medicolegal and financial consequences. It is not uncommon for oncologists to find themselves with no remaining options in the standard of care. For example, take a patient with late-stage lung cancer who had recurrent disease despite several rounds of targeted therapy and additional chemotherapy. In those situations, oncologists may, but are not obligated to, consider the new hope offered by medical preprints and assess the publication status, scientific rigor, and evidence level of the medical preprint. Oncologists may also use medical preprints to identify new/recent clinical trials for the patients who meet enrollment criteria. Such a practice will benefit both individual patients and the public. We strongly recommend an open, informative, and dynamic discussion with the patient about the preprint, focused on the potential risks and the non–peer-reviewed nature of preprints. Appropriate documentation on the discussion and conclusion is also needed.

Other health care stakeholders should also be involved in the discussion on the proper use of medical preprints. Health care institutions should discuss and establish formal policy on how to handle preprints. We also call for independent organizations to research, monitor, safeguard, and advocate on the quality and potential use of medical preprints, as Krumholz et al[4] recommended. Moreover, ethical and medicolegal experts should actively participate in the discussion and policy making. In addition, federal and state officials, patient advocates, and professional societies should weigh in on the safeguard and proper use of medical preprints. Finally, oncology researchers, reviewers, editors, and publishers should also study and discuss the risks and proper use of medical preprints, with a focus on the publication practice and patient protection.[1,4,7]

In summary, medical preprints in our view are going to change oncology practice. But they should first, do no harm. Such a principle is applicable to any emerging medical practice, device, and intervention.

ARTICLE INFORMATION

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