PERSPECTIVES PERSPECTIVES

The challenge of preprints for public health

O desafio dos preprints para a saúde pública

El desafío de los preprints para la salud pública

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doi: 10.1590/0102-311XEN168222

Preprints are "a form of a scholarly article which is not peer-reviewed yet but made available either as paper format or electronic copy" ¹. After an early attempt by the U.S. National Institutes of Health in the early 1960s, this format really took hold in the early 1990s, first as an email server at Los Alamos National Laboratory, which later became a web service known as arXiv ¹. In the following years, the number of both preprint servers and total preprints submitted to web services increased considerably, however, preprints are still a small fraction (6.4%) of the total output of scientific publication ¹.

Despite disagreements over whether this form of publication is actually beneficial or not, its advantages and problems present a high degree of convergence among advocates and detractors. On the one hand, preprint is beneficial because it is a quicker way to disseminate scientific content with open access to everyone; on the other hand, the lack of adequate vetting, especially for peer reviews, increases the risk of disseminating bad science and can lead to several problems ². The dissent lies in considering to what extent possible risks overcome possible benefits (or vice versa).

The argument about this rapid dissemination has strong supporting evidence. A study on preprint publication showed that preprint are published on average 14 months earlier than peer-reviewed journal articles ¹. This is expected considering that the time-intensive process of peer reviews and revising manuscripts is totally bypassed. However, in this strength lies its very fragility: how to assure that this shorter process will not compromise the quality of the publication?

ASAPbio (Accelerating Science and Publication in Biology) ³ is a group of biology researchers that promotes preprint publication and has produced a number of studies that attempt to allay concerns about its quality, claiming, for example, that published articles previously submitted to a preprint server did not show relevant changes for its publication ⁴. Authors from this group have argued that the current approaches to evaluate research and researchers hold back a more widespread adoption of the preprint methodology ⁵, which would explain its relatively small participation on the general panorama of scientific publication.

Despite claims to the contrary, however, there are examples of poor studies published as preprints, which caused undesirable consequences in public health. Two methodologically flawed studies about a protective effect of tobacco smoking against COVID-19 (one of which has an author with known connections with the tobacco industry), for example, increased the commercialization of tobacco products in France and Iran ⁶ and a virology study that erroneously stated that the SARS-COV-2 virus had "HIV insertions" fueled conspiracy theories about the former virus being a bioweapon,

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which lingered on even after the preprint was removed from the server due to its egregious errors 7. Studies have found that much of the public discussion and even policy was indeed driven by what was published in preprints rather than in scientific journals 7,8,9,10, thus, quality issues are a major cause of concern.

On the other hand, similar errors have been observed within traditional publishing; the publication of a poor quality paper with undisclosed conflicts of interest in one of the most prestigious medical journals, *The Lancet*, which became the trigger for the contemporary wave of anti-vaccine activism, is a major, and regretful, example. Understanding to what extent this problem is likely to occur with or without gatekeeping mechanisms is necessary.

Preprint advocates countered that the effect of poor science disseminated via preprints would be lessened by media reporting that explicitly indicated that those studies did not undergo any peer review and, thus, required more criticism and reserve before being considered essential sources for a public debate. It was probably the case of South African media 8, but in Brazil, a study found that less than 40% of preprint-based reports on mass media clearly showed their provisional character 11.

A hypothesized advantage for preprints – namely open to wider discussion, as opposed to the limited criticism offered by editors and peer reviewers – does not seem to exist in real life. Most preprints do not elicit any comment, even considering a sharp increase in COVID-19-related articles (17.5% and 12.3% on *bioRxiv* and *medRxiv*, respectively, versus 3.2% and 1.4% for non-COVID-19-related material on both servers). Moreover, to date, comments were limited to one per article ¹² and very few preprints showed any change since they were submitted to a server. Very few existed in more than two versions ⁹. Much of the aforementioned problems resulted from scientific publishing, especially on biomedical sciences, which was overloaded with the COVID-19 pandemic ^{13,14}.

The analysis of published articles about COVID-19, although they were proportionately small in comparison with the overall number of published articles, was considerably higher (0.097) than that of comparable publications on other world health emergency viral epidemics (from 0.023 to 0.024). This difference is even more concerning when considering that the time window of publications on other cases, such as Ebola or SARS, was considerably larger ¹⁵. Similar rates of retractions were observed in preprint servers and journals, but for the former most retractions were related to ethical issues, which might have been noticed by editors and reviewers ¹⁶. Still in the context of the pandemic, the proportion of preprints that were published in journals was far below than what was observed by Xie et al. ¹ in a general context. The publication rate was only 5.7%, even allowing for a somewhat extended period of observation ¹⁷.

The quality issues of preprints have been acknowledged even by its advocates and the major servers have adopted several measures to give some assurance to their users. Both *arXiv* and *bioRxiv* have advisory boards and rules for submission: the latter, for instance, checks for plagiarism and materials with offensive and/or non-scientific content that might pose health risks ^{1,18} and added a warning about the preliminary nature of preprints, especially those about the pandemic ¹⁹. Other repositories have enhanced their screening on articles related to the pandemic and *bioRxiv* no longer accept articles about COVID-19 treatments based only on computational work ¹. Efforts to curate preprint materials have been proving to be effective regarding later acceptance for publication. Preprints included in the Centers for Disease Control and Prevention (CDC) COVID-19 Science Update had a much higher publication rate – almost two thirds if sufficient time allowed ²⁰. However, does not adopting such measures bring preprint servers closer to the traditional publishing model? According to Maslove ¹⁸ (p. 444), "to some extent, these measures are euphemisms for editorial boards and peer-review processes, raising the question of whether preprint servers differ from traditional journals in kind, or simply by degree".

Accelerating the production of knowledge and expanding the scope of criticism over it are worthy goals, however, such goals must be pondered with possible risks of prematurely disseminating uncertain or even wrong information. As some sociologists of scientific knowledge accurately suggested, the timing of politics and the timing of science are to great extent different ^{21,22}. The pressure to produce results in the face of a major public health challenge – such as the COVID-19 pandemic – is understandable, but allowing such pressure to compromise the very research outcomes society depends on to make proper decisions is counterproductive, to say the least. The implications of bringing out (relatively) unvetted materials are quite different for fields such as high-energy physics, in which the first successful preprint server arose, and those that directly affect the health of popula-

tions. During the last years, immense efforts to implement controls to avoid the publication of flawed clinical trials, for example, have emerged. Is it worth to sacrifice the necessary time to rigorously evaluate those in order to gain a few months in terms of publication?

Finally, cooperation between different research groups is the norm in contemporary science. Over the last years, networks of researchers tackling specific issues have been established worldwide. Information flows within such networks already exist regardless of the preprints, thus, the extent that those would add to such interactions is debatable.

Despite the criticisms, preprints are a reality in contemporary scientific publishing and can play a positive role in the production and dissemination of knowledge, as long as adequate care is taken to prevent bad or dangerous works to negatively affect the general public. The possibility of more widespread criticism of articles is a worthy goal and should be incentivized. This issue is linked to a wider discussion about peer review in scientific publishing, which requires its own debate.

Contributors

K. R. Camargo Jr. contributed to the study conception, writing, and review. C. M. Coeli contributed to the study conception and review. Both authors approved the final version to be published.

Additional informations

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Acknowledgments

The authors thank the Brazilian National Research Council (CNPq; C.M.C.: 303295/2019-8 and K.R.C.Jr.: 306228/2021-1), the Carlos Chagas Filho Rio de Janeiro State Research Foundation (FAPERJ; C.M.C.: E-26/200.003/2019 and K.R.C.Jr.: E-26/202.893/2018), and the Rio de Janeiro State University (UERJ; Programa Prociência).

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