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Article

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Editorial policy regarding the citation of preprints in the British Journal of Pharmacology (BJP)

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1. Current BJP policy

Since 2017, BJP has had a policy regarding preprints that focused on only one issue and was covered by the statements below in our Instructions to Authors:

"BJP accepts articles previously published on preprint servers.

Authors may also post the submitted version of a manuscript to a preprint server at any time. Authors are requested to update any pre-publication versions with a link to the final published article."

This statement clearly demonstrates that BJP is strongly supportive of preprint options for authors with no prejudice against publication following review and acceptance. Moreover, the statement highlights the Journal's commitment to Open Science.

However, during the COVID-19 pandemic BJP, as many other journals, has experienced a large number of article submissions focussed upon the pandemic; specifically, submissions focussed on understanding the molecular pathways of infection, disease progression and ultimately therapeutics. In many of these submissions the rationale for the studies and the explanation and discussion of findings were accompanied by references to unreviewed preprint articles that supported the authors' ideas and interpretations. Prior to 2020, BJP published very few manuscripts citing preprint material and thus, the Journal had no stated position on this issue. But by the end of November 2020, 12 published papers cited preprints in that year.

In the past there has been discussion regarding the issues surrounding preprint citation, with arguments for and against (e.g. Crotty, 2018). In addition, current guidelines from the Committee on Publication Ethics (COPE) guidelines briefly cover this issue and state support for preprint citation, but also leave the options on this with each individual journal (COPE, 2018).

This guidance was published in 2018 (pre-pandemic) and our understanding is that COPE is currently reviewing their preprint policy; a review that will inevitably be illuminated and informed by the publishing experience during the pandemic. We look forward to learning of the outcome of these discussions.

However, because of the increasing number of articles submitted to BJP over the past year and that cite preprint material, the Editor-In-Chief and senior editors with the full Editorial Board of BJP have undertaken a review of the issues and our discipline- relevant data to set policy on the issue of preprint citation for the Journal.

Background

The preprint approach that we understand today was devised by Paul Ginsparg, a theoretical physicist who, in 1991, created the community-funded hep-th@xxx.lanl.gov preprint server, now known as arXiv. Intended to democratize the 'preprint' concept, the repository provided a mechanism that resolved the limitations of making available information via restricted email distribution lists. The purpose was to stimulate ***open*** engagement with anyone, anywhere, to evaluate new research, to improve the study and manuscript pre-publication, and to develop future research directions. Reflecting the success of this laudable mission, today arXiv hosts nearly two million preprints and has a coverage extending to other disciplines including computer science, quantitative finance, statistics, electrical engineering and economics.

We in the biomedical science world have wanted to replicate this altruistic approach to sharing and engagement, and newer repositories have been created, such as bioRxiv and medRxiv. These resources have been instrumental in enabling the rapid dissemination of new biomedical research, particularly lauded as an important vehicle for discoveries in research areas, advancing very pressing issues such as public health emergencies (Yozwiak et al, 2015; Brierley, 2021). However, as we have reflected previously- in the context of the challenges in developing a 'one-size-fits-all' approach to making available biomedical research data (George et al., 2017; George et al., 2019) - there are discipline-specific issues relating to preprinting in biomedical research that must be acknowledged. As Ginsparg himself recognised presciently: "*In the biomedical and life sciences, for example, adoption of preprint servers may be impeded by a long-standing tradition of regarding only refereed journal publication as a legitimate intellectual priority claim, together with concerns about public-health implications of the distribution of potentially misleading unrefereed results*." (Ginsparg, 2011).

The note of caution expressed by Ginsparg was realised, to devastating effect, by the exceptional circumstances around the COVID-19 pandemic. In a bid to support the urgency of communicating scientific discovery, to enable development of approaches to combat a disease that has now infected more than 160 million people and killed almost 3.4 million people worldwide, preprint servers have endeavoured to accelerate the process for acceptance and posting novel research. While the motivations are sound, the high profile failure of processes relating to COVID-19 research has exposed the consequences of ignoring Ginsberg's warning. Three such examples include the withdrawal of a bioRxiv preprint suggesting that SARS-CoV-2 had been engineered from HIV (Oransky and Marcus, 2020), and an influential preprint regarding the use of the anti-parasitic drug ivermectin. The latter, which informed government policy on treating severely ill COVID-19 patients in Latin America, was based on a fabricated dataset (Orford, 2020; Davey et al., 2020). Finally, a preprint, lauded by UK government ministers, suggesting the use of Vitamin D in treating COVID-19 patients, was retracted following post-publication comments that shone a spotlight on the sub-standard experimental protocol and a rather shocking trial design (Oransky, 2021). The third story also highlights a concern regarding longer-term consequences of using content hosted on preprint servers as a platform for subsequent study. Although the preprint was removed from the server within 28 days of being posted, 96 clinical trials on the use of Vitamin D have been registered and are in progress (Clinical Trials, 2020). Some of these studies have confirmed a lack of efficacy of Vitamin D (for example, Murai et al., (2021)).

In response to these issues, bioRxiv now features a disclaimer that preprints hosted on this server "…..are preliminary reports that have not been peer reviewed. They should not be regarded as conclusive, guide clinical practice/health-related behavior, or be reported in news media as established information". Similarly, medRxiv states that "…..articles on medRxiv have not been finalized by authors, might contain errors and report information ..not yet accepted or endorsed in any way by the scientific or medical community…". However, despite these disclaimers, and aware of the potential spread of misinformation stemming from those preprints that report flawed science, these repositories have taken other steps to boost confidence in the legitimacy of the preprint material they host. These include, for instance, an expansion of the team of scientists available to review material prior to acceptance for posting and a blanket rejection of all articles using computational methods to propose potential treatments without any prospective experiments testing efficacy (Kwon, 2020). These interventions blur further the boundary between preprints and peer-reviewed publication and make it important to consider what exactly a 'preprint' has become, and what purpose does it serve in today's canon of

scientific publishing platforms.

The above discussion highlights the negative aspects of preprints, but it is important to be balanced in our considerations and to note that, during the COVID-19 pandemic, the availability of preprints has been viewed as a key factor in the break-neck speed with which the biomedical research community has shared research on insights regarding the biology and clinical features of the infection, resulting in the rapid and timely delivery of much needed therapeutic options (https://www.nature.com/articles/d41586-020-03564-y). An excellent example is the Randomised Evaluation of COVID-19 Therapy (RECOVERY) trial which showed the benefit of the simple and low-cost utility of dexamethasone that has saved many lives globally. The RECOVERY trial was published as a preprint on June 22nd 2020 (Horby el al., 2020) and as a peer-reviewed article published as an epub in the New England Journal of Medicine on July 17th 2020 (RECOVERY collaborative group, 2021). Whilst it is highly likely that the preprint publication and sharing of the results saved lives during the short time between preprint posting and full publication, the data were made available to regulatory authorities and clinicians prior to full publication.

2. Preprinting: beyond enabling rapid scientific communication

Using data from bioRxiv, Figure 1 shows the rapid rise in the numbers of preprints and the increase in the number of citations of those preprints over time. The COVID-19 pandemic fuelled acceleration of citations in 2020 of all preprints on the server (Figure 1A). Those preprints badged as being focused on ‘pharmacology’- or ‘pharmaceutical sciences’-focused (Figure 1B, respectively) reflect the appetite of the biomedical research community to engage with preprinting as a citable unit of new research. Indeed, as of March 2021, 11,979 preprints on COVID-19-related biomedical research have been uploaded to bioRxiv and medRxiv servers and they had received 70,421 citations (average 5.8 per preprint). Central to the background to this editorial is the question of how do peer-reviewed journals mitigate the perils posed by a burgeoning culture of citing preprints?

It is also clear that the purpose of preprints is changing. In addition to the primary aims of preprinting - to make freely available to other researchers at the earliest opportunity novel findings and to enable transparent evaluation - preprints now have a broader reach. Some of these repurposings are beneficial; they enable due attribution of claims of research priority; they provide a means of making available methods and other findings that avoid the duplication of effort or wasting of resources. More recently, preprints are now encouraged by funders as a

useful intermediate stage, offering a means to provide evidence of productivity as preliminary data for the evaluation of applications for funding while the work in question navigates sometimes protracted cycles of revision along the way to eventual publication (UKRI, 2021).

However, there is a growing sense of (mis)use of preprinting for purposes that deviate from the aims as originally conceived. Preprinting is sometimes used to generate publicity and 'over -claim', to discourage competition and, in an era of increasingly metric-driven signifiers of 'success', their inclusion in reference lists can be used to distort algorithm-driven metrics of citation (e.g. GoogleScholar) (Crotty, 2018; Greenberg, 2009). Some authors also believe that the availability of their preprint confers advantages in navigating journals' editorial triage processes and biases decisions towards securing external peer review of a manuscript.

3. Pharmacology, the BJP, preprinting and citation

The number of preprints focusing on pharmacological- or pharmaceutical science is comparatively small (Figure 1B). Indeed, analysis of bioRxiv- and medRxiv data reveal that of all the COVID-19-related preprints posted to these servers in 2019-20 (11,979 in total) only 69 (0.6%) were categorized as pharmacology research. However, these 69 preprints have received a substantial number of citations (437; average 6.3 per preprint). When combined with the increasing number of pharmacology-focused papers that cite preprints (Figure 2), there is an upward trajectory for both the numbers of preprints posted onto servers and the citation of those preprints across the wider pharmacology landscape. This evidence cannot be ignored.

Insights into the patterns of submissions to the BJP suggest that our authors remain lukewarm towards the benefits of preprinting. Since the launch of Authorea – the BJP's publishers own preprint service - 28% of authors submitting papers to the BJP have chosen to preprint their papers on this platform (just 5% of manuscripts were already available as preprints). The citation of preprints in papers published in the BJP is also low; in 2020, out of the 403 articles published in the BJP there were just 17 citations of preprints (average 0.04 citations per BJP paper; 53% of these were to COVID-19-related articles).

However, given the possibility that the number of preprints might exceed the number of peer-reviewed publications year-on-year, it is timely to consider mechanisms that ensure the reliability of the data published in preprints and how the quality and integrity of scientific reporting of pharmacology research are preserved. Enabling the citation of preprints brings with it the responsibility to discriminate the validity of early research findings from those with flawed content.

4. Do all preprints end up as published papers?

Figure 3 shows the assumption that manuscripts posted on preprint servers will eventually be published in a peer reviewed journal is incorrect. Since 2016, the proportion of preprints that become fully published papers has not exceeded 71%. Some possible explanations for this have been offered (Lin, 2020), and other factors complicate the interpretation of the 'preprint versus published' disparity. For instance, many more papers are now being submitted to preprint servers than in the past, and tracking the eventual outcome of a preprint is becoming more difficult (especially since the title of the published article may differ from the title of the preprint). Also, for the reasons discussed above, researchers might be obliged to preprint at an earlier stage with the consequence that it takes considerably longer for a published paper to emerge following revision through the peer review process. Some researchers consider preprint servers as the natural home for making available "difficult to publish" work that has intrinsic value to the research community (i.e., methods, protocols, comparisons between experimental approaches and negative results).

While these factors offer some mitigation, the reason that many papers sit unpublished on preprint servers is likely to be simple: the science does not survive the scrutiny of the peer review process. This archive of citable, incompletely formed, non-peer-reviewed 'second tier' web content adds to a cacophonous (mis)information overload and is of real concern. There is already evidence of the ease through which the citation of flawed science is perpetuated in the scientific literature (Piller, 2021) and current mechanisms for preventing this are not adequate (Tijdink et al., 2020).

5. Surveying the BJP editorial board on citing preprint

In consideration of the issues described in this editorial, the Editor-In-Chief and the Senior Editorial team of the BJP felt it important to clarify how the BJP would handle the citation of preprints. The BJP does not, at present, have a policy on the citation of preprints and 'Instructions to Authors' relates solely to a statement that "the *availability* of a manuscript on a preprint server is not a disqualifier for submission to the BJP". To address this point, at the BJP's Editorial Board meeting in December 2020, with a follow-up survey distributed in February 2021, we asked the BJP's Editorial Board about their views on preprinting in general and, more specifically, how the journal should develop its policy on the citation of preprints (Figure 4). The results of the survey are shown in Figure 5. The number of discussion points that can be drawn from the responses are too many to consider in this editorial; readers can evaluate for themselves the data presented in Figure 5. However, we take the opportunity to

distil some key points below.

Although the many merits of preprints were recognised, important concerns were voiced. The majority view was that preprints cover a gamut of work of highly variable quality, credibility and value and should be considered as incomplete ‘works-in-progress' (one respondent offered the alternative term ‘tentative publication’). There was also concern that preprinting offers the outlet for straight-to-web research content with the express purpose of creating citable items, while evading robust peer review.

The most benevolent interpretation of the responses received was that preprints were the equivalent of unpublished observations (unvetted and unvalidated) akin to conference presentations (with the added benefit of digital archiving/accessibility of figures and data) or content made available on institutional webpages, social media or blogs. While these fora have their uses, none of these would be considered as the final version of record for the research in question and the responses affirmed that the original published article should be the item of citation and therefore trump all other options for reference.

The stand-out point from the survey was the strong feeling amongst the Editorial Board of BJP that preprints are ‘non-legacy’ documents and that the Journal should not allow the citation of preprints (31% respondents (22/70) scored ‘zero’ when asked whether the BJP should allow the citation of preprints; see Q8, Figure 5).

5. Conclusion: the BJP will not allow the formal citation of preprints.

The Editorial Board of the BJP support the principles of preprinting. However, given the potential risks associated with allowing the citation of preprints, it is our collective view, supported by feedback received from the Journal’s international Editorial Board, that BJP should take all reasonable steps to avoid perpetuating these risks. This feedback is particularly noteworthy, as it comes from a truly diverse population of experienced and senior biomedical researchers representing 22 different countries from across the globe, of whom ~30% are female. At present, it is not possible to implement a satisfactory editorial process to permit the citation of preprints that would be aligned fully with the Journal’s remit to publish high quality, transparent and reproducible pharmacological research. Of note, BJP policy does not allow ‘data not shown’ and encourages authors to disclose all relevant data in their manuscripts. ***For these reasons, the BJP will not allow the citation of preprints in the reference section of papers accepted for publication in the journal.***

Whilst it would be technically feasible to refer to a preprint using a hyperlink in the main text (and not appearing in the main reference list at the end of an article), ensuring the validity of

each cited preprint would, in effect, require some degree of peer review in addition to peer review of the paper. This places unacceptable demands on time and consistency of the editorial process and we do not consider this to be a workable solution. However, should an outstanding study submitted to the BJP depend critically on previous work that existed only as a preprint hosted on an established preprint server, we reserve the right to allow the paper accepted for publication to refer to the preprint in question in a non-citable format (i.e. hyperlink).

We are aware that the issue of preprint citation is under discussion at COPE and that the British Pharmacological Society is establishing a working group to review this issue more broadly across its publications. Thus the stated editorial position will be reviewed and if solutions to the problems highlighted above emerge, we will revisit our policy. Our decision to not allow the formal citation of preprints does not affect our current policy on handling submissions and we encourage the submission of manuscripts that have been posted to preprint servers for consideration for publication.

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