

**Strengths and Weaknesses of the Research Enterprise during the Pandemic**

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**Abstract**

The pandemic precipitated a surge of time-sensitive questions about the transmission, morbidity and mortality and treatment of COVID-19. Here, I reflect on the strengths and weaknesses of the research enterprise's response to these questions based on a review of publication volume, authorship and collaboration, the peer review process, and the accessibility, impact and quality of papers written about COVID-19. Although there is a dearth of bibliometric data on COVID-19 papers about neurology, in general, and neuro-ophthalmology, in particular, I broadly address COVID-19 papers from all disciplines, but provide focused commentary on papers about neurology and ophthalmology when able.

When the world's attention was first captured by COVID-19, clinicians, policymakers and society had innumerable questions and an urgent need for answers. There was a time-sensitive demand for fast-paced research to: reduce transmission, morbidity and mortality; improve diagnosis, treatment and prognostication; and determine public policy/health measures. Further, rapid dissemination of results could provide support for other research and reduce duplication of efforts. However, the importance of timeliness needed to be superseded by accuracy, objectivity and integrity of the publication process to avoid transmission of misinformation, confusion for both the scientific and public communities and unsubstantiated changes to public policy/health measures resulting in mistrust. Ideally, in the setting of a new crisis, the international scientific community should aim for papers to be based on big data and have transparent methodology, rapid distribution and broad availability with the opportunity for open data processing and analysis to easily assess for reproducibility and replicability.<sup>1</sup> It is also beneficial to have a large diverse author and reviewer pool to provide a multitude of perspectives, minimize bias and prevent inaccuracies.

Here, I reflect on the strengths and weaknesses of the research enterprise during the pandemic as pertains to publication volume, authorship and collaboration, peer review, accessibility, impact and quality (Table 1). As there is a dearth of bibliometric data on COVID-19 papers about neurology, in general, and neuro-ophthalmology, in particular, I broadly address COVID-19 papers from all disciplines, but provide focused commentary on papers about neurology and ophthalmology when able.

### **Publication Volume**

The number of COVID-19 papers indexed on PubMed escalated quickly: while there were 114 posted in January 2020, 695 were added in February and 2,029 were added in March.<sup>2</sup> These papers were published in 632 different journals (32% American, 22% British, 8% Chinese, 5% Dutch, 4% German, 5% other), 521 of which were indexed by the Journal of Citation Reports and had a median

impact factor of 5.099 (IQR 0.161-70.67). By late April, twelve weeks after the World Health Organization declared COVID-19 a public health emergency of international concern, there were 7,155 papers on COVID-19 indexed on PubMed.<sup>3</sup> The publication rate worldwide rose proportionately to the death rate and was significantly related to COVID-19 cases per capita, healthcare access and quality index, gross domestic product per capita and health spending per capita (all  $p < 0.0001$ ) and pre-COVID-19 H-index, global health security-index, physicians per 1000 inhabitants and nurses per 1000 inhabitants (all  $p < 0.05$ ).<sup>4,5</sup>

By the end of May, there were 92% more submissions to Elsevier's health and medicine journals compared with 2019 and 17,564 papers on COVID-19 were indexed on PubMed.<sup>6,7</sup> At the end of 2020, there were over 100,000 papers on COVID-19, comprising 8% of all records indexed on PubMed over the course of the year.<sup>7,8</sup> The majority of these papers were research (>80,000), followed by comments/editorials (~30,000). An August 2021 bibliometric analysis of the Scopus database (which includes both published papers and preprints) identified 210,863 papers related to COVID-19, 3.7% of papers indexed on Scopus from January 2020 to August 2021 (54% research articles).<sup>9</sup>

Compared to 2019, there was a 22% increase in new papers on ophthalmology indexed on PubMed between March and August 2020, but only 4% of the ophthalmology publications from January to August 2020 were related to COVID-19.<sup>10</sup> However, in a search of the Web of Science in February 2021, Kalra et al. identified 616 papers on ophthalmology and COVID-19 published in 63 sources (39% original articles, 30% letters, 22% editorials, 9% reviews and 1% corrections).<sup>11</sup> By October 2021, a PubMed search identified 5,400 papers using the search terms "COVID-19 and neurology" and 2,207 papers using the search terms "COVID-19 and ophthalmology."

### **Authorship & Collaboration**

In the first quarter of 2020, 10,756 authors contributed to a paper on COVID-19 that was indexed on PubMed (median of 1 paper/author (interquartile range (IQR) 1-31); 39% of first authors during this time period were from China, followed by the USA (17%), United Kingdom (10%), Italy (6%) and Singapore (3%).<sup>2</sup> By August 2021, 720,801 unique authors (3,862,276 total authors) contributed to a Scopus-indexed paper on COVID-19 (7% of all authors who had a paper on any topic indexed on Scopus from January 2020 to August 2021); 20% were from the USA followed by 10% from China, 7% from the United Kingdom, 6% from India and 4% from Spain.<sup>9</sup>

Unfortunately, reviews of the authorship of COVID-19 publications demonstrated notable gender disparity.<sup>12-14</sup> By the end of May 2020, there was a nearly 40% increase in manuscripts submitted to Elsevier's health and medicine journals compared with 2019 for male doctors, but only a nearly 30% increase for female doctors.<sup>7</sup> This gender gap was also evident in a comparison of first authorship in 2020 vs. 2019: women were first authors on 45% of papers from 2019, but only 38% of COVID-19 papers indexed on PubMed from February 2020 to January 2021.<sup>12</sup> The change was less notable, though still significant, for last authorship (31.9% vs. 30.5%), indicating junior women were impacted more than senior women. These differences can likely be attributed, in part, to shift in personal responsibilities during the pandemic, so they are hopefully temporary; nonetheless, further evaluation of means to improve gender publication parity is needed.

There were varied opinions on whether the number of authors for papers on COVID-19 represented a missed opportunity for collaboration, an impressive amount of collaboration, or an unnecessary proliferation of "collaborators".<sup>1,2,15</sup> Based on a review of the literature and preprint postings from December 2019 to April 2020, Homolak et al. reported they were disappointed to see that the number of authors/paper on articles about COVID-19 was similar to that for articles on other topics and those published December 2018 to April 2019 (median of 4 (IQR 5.25)) vs. 5 (IQR 5) vs. 5 (IQR 6)).<sup>1</sup>

Contrastingly, Diéguez-Campa et al. were impressed with the degree of collaboration on COVID-19 papers; they reported that the median link strength (representing the extent of author collaborations) for the 2,530 papers indexed on PubMed between January and March 2020 was 9 (IQR 0-194) and that there were 79 clusters of 4,724 linked authors during this time period ranging from 13-158 authors.<sup>2</sup> They further noted the average number of coauthors was 7.5 for the first author country of France followed by 6.8 for Singapore, 6.5 for China, 5.8 for Italy, 5.1 for India and 4.6 for the USA, though publications with the most authors were from the USA (55) and China (54). In a review of 6,694 papers on COVID-19 added to the Web of Science database prior to August 2020, Farooq et al. found the top authorship patterns were two authors (830 papers) followed by three (763 papers), four (718 papers) and one (712 papers), but there were 3,671 papers (55%) with five or more authors.<sup>16</sup> There were 1,817 papers with international collaboration, the most of which were between the USA and China (272). Finally, Papakis lamented the authorship proliferation seen in case reports on COVID-19, noting that in a comparison of authorship on 1,552 case reports on COVID-19 to 496 case reports on other infectious diseases indexed on Medline from February to August 2020, there were significantly more COVID-19 case reports with  $\geq 15$  authors (3.3% vs. 1.4%,  $p=0.03$ ).<sup>15</sup>

As of this writing, there is no published authorship data on papers about neurology and COVID-19, but 2,398 authors contributed to the 616 papers on ophthalmology and COVID-19 identified in Kalra et al.'s February 2021 search of the Web of Science; the average number of authors/paper was 3.9 and papers/author was 0.26.<sup>11</sup> These papers were predominantly written by authors in India (22%), followed by the USA (15%), the United Kingdom (10%), China (10%) and Italy (6%).<sup>11</sup> It is also worth noting that neurologists from 13 countries and 4 continents collaborated on a large international publication on the global incidence of neurological manifestations in hospitalized patients with COVID-19.<sup>17</sup>

## Peer Review

The peer review process was designed to maintain the integrity of the research enterprise through critical scrutiny to ensure publications are ethically sound, high quality, scientifically rigorous and nonbiased. Although many journals offered the option to fast-track articles before the pandemic, this had never been done on the same scale as in early 2020.<sup>3</sup> Of the 2,113 papers on COVID-19 indexed on Pubmed between January and April 2020 that included submission and acceptance dates, Palayew et al. found the median time from submission to acceptance was 6 days (IQR 12) and that 59% were accepted within 7 days and 93% within 30 days.<sup>3</sup> Contrastingly, other articles published in journals with COVID-19 publications during this timeframe had a median time from submission to acceptance of 84 days (IQR 103) and 3% were accepted within 7 days and 18% within 30 days. Papers published in these journals during the same period in 2019 had a median time from submission to acceptance of 93 days (IQR 100) and 2% were accepted within 7 days and 13% within 30 days. Homolak et al. found that of journals indexed on PubMed or Scopus with at least 15 published articles on COVID-19 from December 2019 to April 2020, the submission-to-publication time for papers on COVID-19 was an average of ten times faster than the submission-to-publication time from December 2018 to April 2019, a reduction that was not seen for papers on other topics.<sup>1</sup> Most papers on COVID-19 had a submission-to-publication time <1 week and some even had a submission-to-publication time <24 hours. Putman et al. also reported a significantly shorter average review time for papers on COVID-19 compared with those on other topics posted on bioRxiv, medRxiv or the National Center for Biotechnology Information section LitCovid from November 2019 to May 2020 (11 days vs. 106 days,  $p < 0.001$ ).<sup>18</sup>

While a quick review time allows for expedited dissemination of information, it prompts questions about the integrity of the review process and introduces the potential for reporting errors and bias. It is also worth noting that in contrast to the increased pace of the review process for papers on COVID-19, the review process for papers on topics other than COVID-19 was slower in the first six months of 2020 than it was in 2019.<sup>7</sup>

## Accessibility

To improve the speed and range of information dissemination, with the encouragement of the World Health Organization and the International Committee of Medical Journal Editors, researchers escalated use of preprint platforms, journals increased the frequency of ahead-of-print publication, many publishers made all COVID-19 content freely available via open-access and new databases were designed to organize papers on COVID-19.<sup>1,3,6,8,19</sup> Preprint posting allows scientific work to be viewed, commented on and cited prior to publication, and a pre-pandemic comparison of published papers with and without preprints demonstrated papers that were posted as preprints had more citations.<sup>6,20</sup> However, failure to appreciate and acknowledge the limitation of preprints due to lack of peer review could negatively impact morbidity and mortality, prognostication, other research and public policy, leading to confusion and mistrust of science.

New preprint platforms emerged early in the pandemic, and preprint posting surged.<sup>1</sup> Lever et al. reported that while journals like *CHEST*, *JAMA*, *Lancet*, *Journal of Medical Virology* and *Clinical Infectious Diseases* each published ~500 papers on COVID-19 in 2020, there were ~3,000 papers posted on both arXiv and bioRxiv and ~1,000 on medRxiv.<sup>8</sup> These numbers are particularly impressive given that bioRxiv had only 7,750 preprints from November 2013 to January 2017.<sup>20</sup> Of 5,061 papers posted on bioRxiv, medRxiv and Research Square from January to May 2020, only 6% were published as of August 2020; time from preprint posting to publication was 0-117 days (median 24).<sup>6</sup> This assessment of publication after preprint posting was performed over a short time period, but it is worth noting that 34% of preprints posted to bioRxiv from November 2013 to January 2017 were ultimately published.<sup>20</sup> Thus, it is unclear if the low publication rate of preprints on COVID-19 reflected low quality of science, saturation of the peer review process delaying publication or, less likely, lack of submission of preprints to journals for consideration of publication. However, by the end of 2020, almost a quarter of medRxiv's



preprints about COVID-19 were published.<sup>7</sup> At that point, more than two-thirds of papers posted on medRxiv (which launched in June 2019) were about COVID-19, and 10% of preprints posted to all databases over the course of the year were about COVID-19.<sup>7</sup>

In addition to increased use of preprint platforms, the accessibility of COVID-19 papers was enhanced via ahead-of-print publishing and creation of databases dedicated to COVID-19.<sup>1,3,8</sup> While <25% of papers on topics other than COVID-19 were published ahead-of-print, >50% of papers on COVID-19 were published ahead-of-print.<sup>1</sup> To process and organize the large volume of preprints and papers using machine learning, new curated databases were designed (e.g. LitCovid (US National Library of Medicine), Novel Coronavirus Research Compendium (Johns Hopkins Bloomberg School of Public Health), WHO COVID-19 Global Literature on Coronavirus Disease Database and CoronaCentral).<sup>3,8</sup>

## Impact

One of the early barriers to dissemination of knowledge about COVID-19 was the fact that the pandemic began in China and >50% of papers about COVID-19 written by authors from China were published in Chinese (8% of articles indexed on PubMed from January to March 2020), which made it challenging for clinicians and researchers outside of China to learn from these findings.<sup>1,2,5</sup> Despite this, 62% of the papers on COVID-19 that were cited during this time period were from China, and each paper had an average of 41 citations.<sup>2</sup>

More broadly, the 2,379 papers on COVID-19 with citation data that were indexed on PubMed from January to March 2020 accumulated 59,104 citations by June (an average of 23 citations/paper).<sup>2</sup> Additionally, preprints posted from January to May 2020 that were not published by August 2020 were cited 0-168 times (median 0 (IQR 0-1); mean 1.99) and the 283 published preprints were cited 0-170 times as preprints (median 1 (IQR 0-5); mean 6.29) and 0-3,757 times overall (median 9 (IQR 2-38);

mean 72.12).<sup>6</sup> Papers were cited more after publication than as preprints and published papers were cited more than unpublished preprints (both  $p < 0.001$ ).

While impact has historically been driven by long-term metrics like citation count, the more modern way to assess this is based on the amount of attention a paper receives in mainstream media, public policy documents, social and academic networks in addition to peer reviewed publications—the Altmetric score, a weighted score that accounts for volume, sources and authors.<sup>21</sup> The median Altmetric score for reviews on COVID-19 published prior to June 2020 (which was achieved over 3-9 months, depending on time of publication) was comparable to the median Altmetric score for a paper in *BMJ* after 2 years (17 vs. 16).<sup>19</sup> However, the mean number of Google Scholar citations for the reviews on COVID-19 was 82, which is substantially higher than the average 12-month citation score for health and medical science articles (25). In a review of the 250 papers on COVID-19 published from January to April 2020 with the highest Altmetric scores as of June 2020, Khatter et al. found that 66% were not research studies (40% of which were editorials), but that of the 84 research studies, the median Altmetric score was 2,015 (IQR 1,105-4,015.5) and the median journal impact factor was 12.8 (IQR 5-44.2).<sup>22</sup> In a comparison between the top 50 cited COVID-19 full-length original clinical investigations in June 2020 and similar historical control articles published in the same journal in 2019, Elgendy et al. found the median number of citations and Altmetric scores were markedly higher for papers about COVID-19 (207 vs. 10 and 611 vs. 20, respectively).<sup>23</sup>

As of October 1, 2021, a PubMed search using the terms “COVID-19” and “bibliometric” yielded 274 results, but there was little data on the impact of neuroscience papers. However, a scoping review of the top 15 cited articles on COVID-19 MRI and PET/CT research through April 2021 included 11 articles about imaging of the nervous system; these articles were cited 43-669 times, with the most citations for a case report from Japan published in *International Journal of Infectious Diseases* (impact

factor 3.6) in May 2020 about a comatose man with hyperintense lesions in the temporal lobe who had a negative nasopharyngeal SARS-CoV-2 PCR but a positive cerebrospinal fluid SARS-CoV-2 PCR (with cycle threshold of 36.44).<sup>24,25</sup>

The average number of citations/paper for the 616 articles on ophthalmology and COVID-19 identified in Kalra et al.'s aforementioned February 2021 search of the Web of Science was 4.019; the papers with the most citations were from China (940; average 16 citations/paper), followed by Singapore (455; average 25 citations/paper), India (266; average 2 citations/paper) and the USA (204; average 2 citations/paper).<sup>11</sup> The top 20 most cited papers each had 20-259 citations, with the most citations for a case series from China on ocular findings in patients with COVID-19 published in *JAMA Ophthalmology* (impact factor 7.4) in May 2020.<sup>11,26</sup>

## Quality

Unfortunately, despite the best of intentions, the research enterprise infrastructure is imperfect. At the 8<sup>th</sup> International Congress on Peer Review and Scientific Publication in 2017, attendees noted concerns about quality, limited data sharing and, most importantly, bias by authors (including use of spin to alter interpretation of results, failure to publish final results or financial conflicts of interest) or reviewers (such as decision-making based on consideration of an author's prestige, gender or nationality).<sup>27</sup>

Thus, the quantity of content, diverse authorship, speed of review, accessibility and attention for papers on COVID-19 is not indicative of quality or methodological rigor. The aforementioned systematic review of reviews demonstrated that there was no significant difference in Altmetric scores or citations for systematic and non-systematic reviews.<sup>19</sup> Further, 67% of systematic reviews did not register their protocol, 51% did not include critical appraisal and 36% did not refer to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. However, it is worth

noting that these flaws have also been cited in prepandemic systematic reviews.<sup>28</sup> Using AMSTAR-2, a tool to assess methodological quality of systematic reviews, the authors found that 97% of systematic reviews on COVID-19 had one or more critical flaws in methodology or reporting rendering their quality “low” or “critically low.”<sup>19</sup>

Similarly, in Khatter et al.’s review of the 84 research studies published from January to April 2020 with the highest Altmetric scores in June 2020, 55% had high or unclear risk of bias; there was no association between risk of bias and Altmetric scores ( $p=0.89$ ) or journal impact factor ( $p=0.91$ ).<sup>22</sup> In a comparison between the top 50 cited COVID-19 full-length original clinical investigations on June 24, 2020 and similar historical control articles published in the same journal in 2019, Elgendy et al. found the articles on COVID-19 were significantly more likely to be at increased risk of bias in several domains.<sup>23</sup> This was also seen in a study comparing research papers on COVID-19 to those on other topics published in *BMJ*, *Journal of the American Medical Association*, *The Lancet*, and *New England Journal of Medicine* between February and May 2020.<sup>29</sup> In a larger comparison study of 539 papers on COVID-19 to historical controls, Jung et al. similarly found the COVID-19 case series, case-control studies, cohort studies and diagnostic studies all had significantly lower methodological quality scores.<sup>30</sup>

In a review of abstracts for randomized-controlled trials about COVID-19 indexed on PubMed before November 2020, Wang et al. found reporting quality was significantly lower for articles from a single center ( $p=0.008$ ) in Asia ( $p=0.015$ ) by a smaller author group ( $p<0.001$ ) with a smaller sample size ( $p=0.002$ ) that had a shorter word count ( $p=0.006$ ) and unstructured format of the abstract ( $p=0.006$ ) and were published in a specialty journal ( $p=0.009$ ) with lower impact factor ( $p<0.001$ ).<sup>31</sup> On multivariate analysis, only shorter word count remained significantly related to quality. They further reported that 56% of the 27 abstracts with insignificant findings contained spin (a reporting strategy that can distort results and mislead readers by highlighting interventions that did not lead to a significant

difference in the primary outcome), 60% of which used >2 spin strategies; 1 abstract used 7 spin strategies. Spin was associated with Asia authorship ( $p=0.004$ ) and publication in lower impact ( $p=0.023$ ) specialty journals ( $p=0.005$ ) on univariate analysis, with only Asian authorship remaining a significant predictor of spin on multivariate analysis.

As of the end of September 2021, Retraction Watch had identified 143 papers about COVID-19 that were retracted/withdrawn and CoronaCentral had identified 150 articles that were withdrawn by the authors/journal.<sup>32,33</sup> For comparison, of all papers published from January 2020 to September 2021, Retraction Watch identified 1,333 retractions.<sup>32</sup> However, it is too early to compare retractions for papers on COVID-19 to those on other topics, as retractions usually take a few years, though retractions for COVID-19 papers have been faster than other retractions.<sup>32,34</sup> This is at least partly due to increased scrutiny, but it may also be a testament of the overall quality of papers on COVID-19.

## Conclusion

The COVID-19 pandemic precipitated an unprecedented appetite for scientific knowledge which researchers responded to via a surge in papers that has been referred to as the “infodemic,” “paperdemic,” “Corona-Minotaur” and “Covidization of the research enterprise.”<sup>2,6,9,35</sup> Papers were widely accessible and had a high impact, meeting the call for urgency. However, as Moher noted in the plenary address at the 8<sup>th</sup> International Congress on Peer Review and Scientific Publication in 2017: “What we have accomplished to date is still not optimal. This is not the best way to instill confidence in readers, provide value for money for funders, or ensure the public can trust the research record.”<sup>27</sup> Researchers, editors, reviewers and publishers must examine ways to improve accuracy and objectivity to avoid transmission of biased information or misinformation resulting in confusion and mistrust. Accordingly, the 9<sup>th</sup> International Congress on Peer Review and Scientific Publication call for abstracts includes the following topics of interest: 1) the effects of the pandemic on reporting quality,

dissemination, quality control, equity, peer review and editorial workflows among journals, publishers, funders, news media and social media; 2) the effects of the pandemic on dissemination of scientific information, misinformation and disinformation; and 3) the reporting of science, publishing, dissemination and access in emergency situations.<sup>36</sup>

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**Table 1:** Strengths and Weaknesses of the Research Enterprise during the Pandemic

Aspect of the Research Enterprise	Factors to Consider	Strengths	Weaknesses
Research/Manuscript Production Speed	<ul style="list-style-type: none"> <li>• Limited researcher time due to change in professional/personal responsibilities</li> <li>• Potential delays in review by Institutional Review Board</li> <li>• Decrease in research funding</li> </ul>	<ul style="list-style-type: none"> <li>• Large volume of papers produced quickly</li> <li>• Broad range of journals</li> </ul>	
Collaboration/Diversity of Authorship	<ul style="list-style-type: none"> <li>• Varying timeframes of surges in different locations</li> <li>• Limited researcher time due to change in professional/personal responsibilities</li> <li>• Minimal/no infrastructure early in the pandemic</li> </ul>	<ul style="list-style-type: none"> <li>• Multinational papers</li> <li>• Many examples of optimal collaboration</li> <li>• Consortia to coordinate efforts improved over time</li> </ul>	<ul style="list-style-type: none"> <li>• Gender disparity amongst first authors</li> <li>• Some missed opportunities for collaboration, particularly early in the pandemic</li> <li>• Authorship proliferation on case reports</li> </ul>
Submission to Publication Time	<ul style="list-style-type: none"> <li>• Limited reviewer pool</li> <li>• Potential delays in review pace due to professional/personal responsibilities</li> <li>• Saturated editorial/administrative processing team due to increased number of submissions</li> </ul>	<ul style="list-style-type: none"> <li>• Rapid dissemination of information</li> </ul>	<ul style="list-style-type: none"> <li>• Potential for diminished quality of peer review</li> <li>• Potential for bias</li> <li>• Potential for reporting errors</li> </ul>
Accessibility		<ul style="list-style-type: none"> <li>• Increased preprint posting accelerated speed and range of dissemination of information</li> <li>• New preprint platforms</li> <li>• Increased frequency of ahead-of-print publication</li> <li>• Some publishers made all COVID-19 content freely available via open-access</li> </ul>	

		<ul style="list-style-type: none"> <li>• New curated databases</li> </ul>	
Impact	<ul style="list-style-type: none"> <li>• Challenging to sort through and digest large volume of preprints/publications</li> <li>• Regional journals are not indexed</li> </ul>	<ul style="list-style-type: none"> <li>• High citation counts</li> <li>• High Altmetric scores</li> </ul>	<ul style="list-style-type: none"> <li>• Language barriers</li> </ul>
Accuracy/Quality	<ul style="list-style-type: none"> <li>• Limited reviewer pool</li> <li>• Saturated editorial/administrative processing team due to increased number of submissions</li> <li>• Desire to disseminate information quickly</li> </ul>		<ul style="list-style-type: none"> <li>• Lack of peer review prior to posting on preprint server</li> <li>• Potential for diminished quality of peer review for publications</li> <li>• Potential for reporting errors</li> <li>• Frequent use of spin</li> <li>• Bias</li> <li>• Inclusion of a given patient in multiple case reports/series makes it challenging to determine case prevalence</li> </ul>