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FROM THE EDITOR

MICHAEL G. BAKER, PHD



First Word

You and I as medical communicators are fortunate to be living in a time that reasonably can be characterized as a medical renaissance period. Meaningful, rapid advances in research, preventive, and treatment-oriented medicine are in evidence not just in our professional but also our personal lives. Witness the emergence of not one but multiple COVID-19 vaccines that have been developed and approved in a strikingly short period of time relative to how long previous vaccines have taken to go from virus identification and characterization to vaccine candidate development to shots in arms. With recently embraced messenger RNA technology, as just one example of contemporary research-based medical advancement, have we vanquished the typical 10+ year timeframe to develop a safe and effective vaccine? Multiply this concept across tens of thousands of areas of medical advancement and you grasp the magnitude of our progress.

Simply put, we have the privilege of contributing to and reporting on the fruits of this renaissance. Our role as medical communicators is to inform, educate, and contribute to the scientific body of knowledge during this period of rapid and prolific advancements. Although the opportunity is exciting and a privilege, the sheer volume of information to which we are exposed, need to absorb, and operationalize is daunting. Regulations governing the development of diagnostics, devices, and therapeutics are evolving rapidly in the United States and around the world, thousands of medical journal articles are published each day in English alone, and medical practice standards are changing at an unprecedented rate.

Thus, the skills required to be a medical communicator are substantial—not only scientific and linguistic, but also interpersonal, with a capacity for prioritizing and juggling multiple projects, adapting to change, and adhering to tight deadlines. It is a rare individual who can thrive as a modern day medical communicator. Whether working in regulatory writing, scientific publications, health communication, continuing education, or promotional writing, we face the ongoing challenge of getting our messages to our often information-overwhelmed and time-constrained audiences quickly, clearly, and meaningfully.

So, I ask, what does the *AMWA Journal* do to help you thrive as a medical communicator? We will continue to provide opportunities to learn from and connect with peers, practical tools to do your job, and insights into ethical concepts, regulatory issues, scientific matters, and other topics. Key upcoming goals are to provide improved access to our content via an enhanced digital presence, emphasize the value of our diversity across a range of indicators, and further connect with our medical communication counterparts around the world. Theme issues, new regular columns, and forward-looking topics on medical communication also are in the works. In coming issues, you will hear further from me on our progress in these areas.

As the proud tradition of the *AMWA Journal* continues with a new Editor and my sincere appreciation to Jim Cozzarin and the Editors before him, the top-notch editorial team and I welcome your contributions, insights, and, yes, constructive criticism. Serving our audience with a spirit of information-sharing, collaboration, and mutual support will continue to be guiding principles of the *AMWA Journal*.

Yours in medical communication excellence,
—Michael

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INTRODUCTION

Maintenance of Quality in Publications During Public Health Emergencies

Timely release of data in the form of peer-reviewed publications is crucial in medical research and necessary for productive scientific discourse. However, during public health crises such as a pandemic, the need to communicate science rapidly can lead to abbreviated vetting and substantially increase the risk of compromised quality and accuracy in data analysis and reporting. Indeed, the pressing requirement for speed in tackling a pandemic and the necessary collaboration between academia, industry, and regulatory agencies on an international level creates a significant dilemma: the need to rapidly release data on PubMed Central and other resources, such as the World Health Organization's databases, while upholding the quality of the communication and the data. Maintenance of integrity and accuracy in scientific publications via a thorough vetting process prior to public release requires time and implementation of quality-control measures. Medical communicators have an important role to play in this process.

By way of their speed, some publication modalities, such as preprints, may seem particularly attractive when quick release of information and rapid scientific discourse is desired. However, because such preliminary scientific reports are generally not subject to thorough peer review, there is an inevitable increase in the concomitant risk of lower quality and lack of precision. Thus, full disclosure of whether a publication has been peer-reviewed and transparency about the quality-control process are absolutely required.

In this Joint Position Statement (JPS) from AMWA, EMWA, and ISMPP, we provide suggestions and a structured framework, including a number of practical recommendations that can be implemented to help maintain quality and avoid damaging public trust in scientific and medical communication. The practical recommendations in the current JPS are intended to support quality-control processes in both the acute phase of intense reactions during the course of a public health emergency as well as the longer-term evergreen need to maintain quality in medical publications. The persistent call for rapid sharing of scientific advances against a firm background of insistence on high quality enables acceleration of medical innovation. Safeguards are presented as a clear and concise checklist that can be used by journalists, authors, and medical communicators in the preparation and review of manuscripts before submission.

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AMWA-EMWA-ISMPPP Joint Position Statement on Medical Publications, Preprints, and Peer Review

1. BACKGROUND

In medical publications, just as in research and development, quality depends on the expertise and integrity of researchers/authors as well as qualified peer reviewers and journal editors. However, the laborious and time-consuming process of the traditional peer review¹ can be compromised by the pressure to publish quickly—particularly during a health crisis, when timely distribution of credible medical information can make a substantial difference.² Recent examples of negative consequences are two articles on COVID-19 that were hastily published in high-profile medical journals and subsequently retracted.^{3,4}

Traditional peer review, although not perfect, remains the most frequently used process for vetting scientific publications.

However, it has become more common for manuscripts to be released without prior review, which raises new concerns.

The potential value of rapid publication should be weighed against the potential harm of inadequate validation of the final output. There is a danger that lowering the threshold of publication oversight sets a precedent that cannot be easily reversed, potentially eroding standards and public trust in medical science.²

We have joined in a multi-party consortium among three eminent professional organizations for medical communication professionals—AMWA, EMWA, and ISMPP—to advocate for the adoption of standards by all stakeholders to better ensure the integrity of published scientific and medical information. Thus, the following Joint Position Statement has been

developed to provide practical and implementable suggestions to uphold data integrity and quality, and the transparency of medical publications.

Note: We use the term “medical writer” to represent the spectrum of professionals who prepare documents either for submission to regulatory authorities or for publication in peer-reviewed journals.⁵

2. COMMUNICATION OF RESEARCH: ISSUES AND SUGGESTED SOLUTIONS

2.1. Preprints

Preprints are preliminary scientific reports that are made publicly available online for anyone to read, comment on, and discuss before they have been peer reviewed. Some preprint servers scrutinize submissions for scope and for basic quality standards before making them publicly available.⁶⁻⁸ Once the preprint is posted, most reputable preprint servers assign a unique digital object identifier (DOI) to aid traceability. Authors can revise preprints according to readers’ comments and post iterative versions. Preprints are often not indexed on mainstream bibliographic services, although Europe PMC now indexes preprints,⁹ and there are standalone tools for searching named preprint servers to improve discoverability.¹⁰

Preprints have been rapidly adopted by physicians and scientists, their obvious benefits being the immediate availability to their peers and the public, avoiding lengthy peer-review processes prior to release, and the option of readers to leave comments. However, there are issues associated with preprints that ideally should be addressed by standards jointly developed by a convened body of all stakeholders.

Issues with preprints:

- While preprints enable rapid release and discussion of data, many are never revised, and only about a third to a half are ever fully published.^{11,12}
- “Once the toothpaste is out of the tube, it cannot (easily) be stuffed back in.”¹³ Provocative or poor quality research results could be reported by the media, or posted and discussed on social media, with little regard to the preliminary nature of the findings.^{14,15} No amount of retrospective “tagging” will have much effect. Misinformation or deliberately misleading or sloppy science can be freely circulated, cited, and believed ad infinitum, regardless of whether it is ultimately debunked and retracted.

Our suggested solutions:

- Preprints should not be used as references in any medical publication unless these are cited in the manner of a personal communication, that is, as an in-text reference (using

the preprint link, DOI, or both) rather than as bibliographic references. It should be clearly disclosed that the source is a preprint.

- Clearly distinguishing preprints from peer-reviewed articles might help to reduce the tendency of readers to view the work as fully vetted.^{14,15} This should be done by
 - Watermarking the article, as is done, for example, by medRxiv and bioRxiv, with the information that it has *not* been peer reviewed.
 - Placing a clearly-worded disclosure in the body of the article highlighting that the findings have not been formally peer reviewed.
- Pre-publication vetting:
 - Pre-publication checks by server hosts. MedRxiv performs a basic screening process for plagiarism, non-scientific content, and material that might pose a health risk, including material that might compromise existing public health measures.⁷ However, these checks should be more extensive and consistent across server hosts, and a comprehensive checklist should be used (Appendix I).
 - Encouraging authors to ensure that preprints that have been subsequently fully published be marked as such on the preprint server and linked via DOI to the fully published article.

2.2. Post-publication peer review

In post-publication peer review, an article is published in its original form, then subjected to informal (as with preprints) as well as invited peer review. For instance, with the model used by the F1000 publishing platform,¹⁶ articles are posted online after passing pre-publication checks and after an article processing charge (APC) is paid. When posted, articles are assigned a DOI and opened to comments from registered users. Expert peer reviewers are invited to review in the usual way. All comments, peer review reports, and article revisions are available with the article, and once the article receives two favorable peer review reports, the final, peer-reviewed version is indexed in external bibliographic databases and becomes fully discoverable. The benefits of this model are similar to those of preprints – rapid access for readers and the option for readers to comment.

Issues with post-publication peer review:

- The issues with post-publication peer review are basically identical to those of preprints, but it should be noted that the requirement for an APC would potentially discourage casual or low-quality submissions. Articles are clearly marked as “under peer review,” and the progress of that review is accessible to readers.

- As with preprints, articles undergoing post-publication peer review should not be used as references in any medical publication until the peer review process is completed and the article is approved for publication. If the article is cited, we suggest the citation be made in the same manner suggested for preprints.
- Issues associated with traditional peer review also apply and are addressed in Section 2.3, below.

Our suggested solutions:

- Our suggested solutions include those proposed for preprints; however, we suggest that the publication be indexed by mainstream bibliographic databases (if applicable) once it has been fully peer reviewed, as is done on the F1000 platform.

2.3. Traditional peer review

Traditional peer review occurs after a submitted article is accepted for consideration by a journal, then passed to expert peer reviewers. The reviewers' comments are sent to the authors to use in revising their article, or else the article is rejected after review. For rejected articles, authors can start the process again with another journal. If an article is revised to the peer reviewers' satisfaction, the article is published and assigned a DOI, after which the article is indexed in mainstream bibliographic databases. Peer review reports and revisions may or may not be available with the final article, depending on the peer review model the journal uses. The benefit of traditional peer review is that information is released to the readers only after there has been quality control applied by subject matter experts.

Issues with traditional peer review

- Lengthy review process, which may impede the timely release of valuable information – particularly in a pandemic or public health crisis
- Inadequate time for high-quality peer review
- Inconsistency among reviewers
- Difficulty in “recruiting” qualified reviewers, given time commitment, particularly in times of health crises when the most appropriate reviewers are likely to have a high clinical workload

Our suggested solutions:

- Authors:
 - Submit rejection comments to second-choice journals, with itemized rebuttals and updates to the manuscript (portable peer review).^{17,18}
 - Be more accepting of editor referrals to cascade journals.¹⁹
- Journal editors:
 - Accept, request, or require portable peer review as

described above, thereby reducing the need for additional review cycles.

- Consider commercial back-end services that expedite peer review (eg, ResearchSquare [<https://www.researchsquare.com/>], as used by the BMC journals and others).
- Form a rapid response team of reviewers, with appropriate expertise, who can provide peer review with a quick turnaround time.
- Publishers:
 - Standardize formatting requirements to expedite resubmission.²⁰
 - Offer fast-track options for potentially practice-changing work.
 - Consider incentives for reviewers.²¹

3. SUGGESTED SOLUTIONS FOR ALL FORMATS

3.1. Quality control

- Make use of existing publication guidelines^{22–24} and available checklists²⁵ to ensure high-quality publication development.
- Include Clinical Trial Protocols and Statistical Analysis Plans (SAPs) as supplementary material.
- Ask all authors to sign an author form confirming that they had full access to the relevant data reported in their article, and accept responsibility for submitting the article for publication. Furthermore, the contributor statement should name the authors (at least 2) who have accessed and verified the underlying data, as suggested in the revised *Lancet* publication guidelines.²⁶
- Journals should clearly explain the initial quality review that editors perform on newly submitted manuscripts.

3.2. Training in peer review

- Authors, peer reviewers, and editors should be adequately trained in the nature and technical aspects of peer review.
- Guidelines should be used, such as those created by the Committee on Publication Ethics (COPE),²⁵ along with the reviewers' checklist in Appendix I.
- Medical journalists and the public should be educated on how preprints and pre-publications differ from peer-reviewed literature.

4. THE ROLE OF PROFESSIONAL MEDICAL WRITERS AND SCIENTIFIC COMMUNICATORS IN EXPEDITING THE PUBLICATION PROCESS

- Evidence suggests that the use of professional medical writers enhances publication quality and speed,^{27–33} and such assistance has been associated with a reduced risk for retractions due to misconduct.³⁴ If a qualified medical writer is

part of the team, they should be involved in the process as early as possible.⁵ The medical writer should have access to the clinical study report (if available), source data, and related documents, including statistical outputs and patient narratives, to the extent that data-protection regulations allow.

- Professional medical writers should have an active role in ensuring the high quality of publications, including their development, editing, and referencing,^{22,24,35} and the use of appropriate publication checklists.³⁶ Medical writers and statisticians should be actively involved in peer review, during which the medical writer will critically assess the quality of the manuscript according to common appraisal criteria, thereby augmenting the traditional subject-matter-expert review (Appendix I).
- Medical writers could also be involved in pre-publication vetting, act as trainers, or both (see Section 3.2).

As professional medical writers and communicators, we have identified areas that could benefit from increased quality assurance. We have suggested some processes that we believe would better ensure effective oversight of scientific and medical publications, whether in the context of a health emergency or not. To maintain confidence in published science, each involved party (including the reader) must take responsibility for exercising their best judgment and selecting information from sources with good publishing practices that are rigorous and transparent.

5. ACKNOWLEDGMENTS

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6. APPENDICES

Appendix I: Reviewers' checklist

7. REFERENCES

1. Rennie D, Flanagan A. Three decades of peer review congresses. *JAMA - J Am Med Assoc.* 2018;319(4):350-353. doi:10.1001/jama.2017.20606
2. Palayew A, Norgaard O, Safreed-Harmon K, Andersen TH, Rasmussen LN, Lazarus JV. Pandemic publishing poses a new COVID-19 challenge. *Nat Hum Behav.* 2020;4(7):666-669. doi:10.1038/s41562-020-0911-0
3. Mehra MR, Desai SS, Ruschitzka F, Patel AN. RETRACTED: Hydroxychloroquine or chloroquine with or without a macrolide for treatment of COVID-19: a multinational registry analysis. *Lancet.* 2020;0(0). doi:10.1016/S0140-6736(20)31180-6
4. Mehra MR, Desai SS, Kuy S, Henry TD, Patel AN. Cardiovascular disease, drug therapy, and mortality in Covid-19. *N Engl J Med.* 2020;382(25):e102. doi:10.1056/NEJMoa2007621
5. AMWA-EMWA-ISMPP joint position statement on the role of professional medical writers. 2017. Accessed November 27, 2017. <http://journal.emwa.org/writing-better/amwa-emwa-ismpp-joint-position-statement-on-the-role-of-professional-medical-writers>
6. bioRxiv. Advancing the sharing of research results for the life sciences. bioRxiv. Accessed September 21, 2020. <https://www.biorxiv.org/about-biorxiv>
7. medRxiv. Submit your article to bioRxiv, an online archive and distribution service for preprints in the life sciences. medRxiv. Accessed September 21, 2020. <https://www.biorxiv.org/submit-a-manuscript>
8. Preprints.org. Preprints.org: How it works. preprints.org. Accessed September 21, 2020. https://www.preprints.org/how_it_works#screen
9. Levchenko M. Preprints in Europe PMC: Reducing friction for discoverability. Europe PMC. Accessed September 21, 2020. <http://blog.europepmc.org/2018/07/preprints.html>
10. Iwema CL, LaDue J, Zack A, Chattopadhyay A. search.bioPreprint: A discovery tool for cutting edge, preprint biomedical research articles [version 2; referees: 2 approved]. *F1000Research.* 2016;5. doi:10.12688/F1000RESEARCH.8798.2
11. Abdill RJ, Blekhan R. Tracking the popularity and outcomes of all bioRxiv preprints. *Elife.* 2019;8. doi:10.7554/eLife.45133
12. Fraser N, Momeni F, Mayr P, Peters I. The relationship between bioRxiv preprints, citations and altmetrics. *Quant Sci Stud.* April 2020:1-21. doi:10.1162/qss_a_00043
13. Gertel A. The data economy | Rush to publication – What do we have to lose? *Med Writ.* 2020;29(2). Accessed September 21, 2020. <https://journal.emwa.org/the-data-economy/rush-to-publication-what-do-we-have-to-lose>
14. Maslove DM. Medical preprints – a debate worth having. *JAMA - J Am Med Assoc.* 2018;319(5):443-444. doi:10.1001/jama.2017.17566
15. Penfold NC, Polka JK. Technical and social issues influencing the adoption of preprints in the life sciences. Shafee T, ed. *PLOS Genet.* 2020;16(4):e1008565. doi:10.1371/journal.pgen.1008565
16. F1000Research. About F1000Research | How it works | Beyond a research journal. F1000Research. Accessed September 21, 2020. <https://f1000research.com/about>
17. Wiley. Catheterization and cardiovascular interventions. Author Guidelines. Wiley. Accessed September 21, 2020. <https://onlinelibrary.wiley.com/page/journal/1522726x/homepage/forauthors.html>
18. Bell GP, Kvajo M. Tackling waste in publishing through portable peer review. *BMC Biol.* 2018;16(1):146. doi:10.1186/s12915-018-0619-z
19. Taylor & Francis. Article transfers - Author services. Taylor & Francis. Accessed September 21, 2020. <https://authorservices.taylorandfrancis.com/peer-review/transfers>
20. Wiley. Free format submission. Wiley. Accessed September 21, 2020. <https://authorservices.wiley.com/author-resources/Journal-Authors/Prepare/free-format-submission.html>
21. Tennant JP, Ross-Hellauer T. The limitations to our understanding of peer review. *Res Integr Peer Rev.* 2020;5(1):6. doi:10.1186/s41073-020-00092-1
22. Battisti WP, Wager E, Baltzer L, et al. Good publication practice for communicating company-sponsored medical research: GPP3. *Ann Intern Med.* 2015;163(6):461-464. doi:10.7326/M15-0288

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REVIEWERS' CHECKLIST

This checklist is intended to be used by journals. However, it can also guide authors and medical writers in their review of manuscripts before submission.

The checks should be performed by a suitably qualified team, preferably consisting of editors, subject matter experts (ie, peer reviewers; not required for preprints), medical writers, statisticians, and trained researchers. The review team should comprise at least two reviewers.

Not every reviewer is required to complete all fields, but all items need to be checked by at least one accountable reviewer.

Item	Medical Writer Reviewer	Clinical Reviewer	Biostatistical Reviewer	Peer Reviewer A	Peer Reviewer B
Source documents (if available and required by journal)					
Clinical Study Protocol					
Redacted Clinical Study Report Synopsis					
Statistical Analysis Plan					
Tables/Listings/Graphs					
Attestations					
Data sharing statement (ICMJE template)					
Author contribution form ^a					
Signed author forms confirming that the authors had full access to the data reported in the article and accept responsibility for submitting the article ^b					
Author confirmation that verified data were used to develop the manuscript					
Conflict of interest statement (ICMJE template recommended)					
List of sources of funding for the study and any supporting activities					
Suggested Checks for Preprint Editorial Review					
Manuscript contains no offensive or nonscientific content					
No material is plagiarized					
Basics of the statistical methods are sound (eg, adequacy of analysis population, adequate handling of missing data)					
End points and inclusion/exclusion criteria are in alignment with the study registration on a publicly available registry (eg, ClinicalTrials.gov), provided this is required. For primary reports of clinical trials, all end points are mentioned in the results section.					
Content is consistent and clear across each section of the manuscript (eg, information in abstract matches results, hypothesis posed in introduction is addressed in discussion)					
Discussion points and conclusions are supported by the reported data					
Adherence to guidelines (eg, CONSORT, STROBE, PRISMA, SPIRIT, CARE) Specify guideline(s): _____					
No ethical concerns					
Additional Checks for Peer Review					
Further statistical considerations: - adequacy of sample size calculation (eg, adequate comparator) - adequacy of statistical methods - check for random errors - sources of bias addressed					
Methodological quality ^c - confounding influences (eg, concomitant treatments) - inadequate disclosure of information - misinterpretation					
Study design ^b - adequacy and relevance of endpoints - adequacy of inclusion/exclusion criteria - blinding - adequacy of follow-up period - adequacy of reporting complications - adequacy of data presentation					

^aShould include a question if medical writing support was used.

^bMay be merged with author contribution form.

^cAdapted from MEDDEV 2.7/1; alternatively, other criteria can be used to appraise the manuscript (eg, <https://libguides.napier.ac.uk/litrev/critapp>).

Additional columns and signature lines can be added as needed.

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23. ICMJE. Recommendations for the conduct, reporting, editing, and publication of scholarly work in medical journals. ICMJE. 2019. Accessed September 21, 2020. <http://www.icmje.org/recommendations>
24. Matcham J, Julious S, Pyke S, et al. Proposed best practice for statisticians in the reporting and publication of pharmaceutical industry-sponsored clinical trials. *Pharm Stat*. 10(1):70-73. doi:10.1002/pst.417
25. Ethical guidelines for peer reviewers (English) | COPE: Committee on publication ethics. doi:10.24318/cope.2019.1.9
26. The editors of the Lancet Group. Learning from a retraction. *Lancet*. 2020;396(10257):1056. doi:10.1016/S0140-6736(20)31958-9
27. Jacobs A. Adherence to the CONSORT guideline in papers written by professional medical writers. *Med Writ*. 2010;19(3):196-200.
28. Gattrell WT, Hopewell S, Young K, et al. Professional medical writing support and the quality of randomised controlled trial reporting: a cross-sectional study. *BMJ Open*. 2016;6(2):e010329. doi:10.1136/bmjopen-2015-010329
29. Bailey M. Science editing and its effect on manuscript acceptance time. *J Am Med Writ Assoc*. 2011;26:147-152.
30. Hamilton CW, Gertel A, Jacobs A, Marchington J, Weaver S, Woolley K. Mythbusting medical writing: Goodbye ghosts, hello help. *Account Res*. 2016;23(3):178-194. doi:10.1080/08989621.2015.1088788
31. Woolley KL, Ely JA, Woolley MJ, et al. Declaration of medical writing assistance in international, peer-reviewed publications and effect of pharmaceutical sponsorship. *Fifth Int Congr Peer Rev Biomed Publ Chicago*. 2006;296(8):932-934. doi:10.1001/jama.296.8.932-b
32. Breugelmans R, Barron JP. The role of in-house medical communications centers in medical institutions in nonnative English-speaking countries. *Chest*. 2008;134(4):883-885. doi:10.1378/chest.08-1068
33. Manring MMM, Panzo JA, Mayerson JL. A framework for improving resident research participation and scholarly output. *J Surg Educ*. 2014;71(1):8-13. doi:10.1016/j.jsurg.2013.07.011
34. Woolley KL, Lew RA, Stretton S, et al. Lack of involvement of medical writers and the pharmaceutical industry in publications retracted for misconduct: a systematic, controlled, retrospective study. *Curr Med Res Opin*. 2011;27(6):1175-1182. doi:10.1185/03007995.2011.573546
35. Chipperfield L, Citrome L, Clark J, et al. Authors' submission toolkit: a practical guide to getting your research published. *Curr Med Res Opin*. 2010;26(8):1967-1982. doi:10.1185/03007995.2010.499344
36. The EQUATOR network | Enhancing the QUALity and transparency of health research. Accessed September 21, 2020. <https://www.equator-network.org>

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A Brief History of the COVID-19 Pandemic and Current Efforts to Combat It

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ABSTRACT

The coronavirus disease 2019 (COVID-19) pandemic has necessitated that medical writers adapt their work practices quickly to assist with the preparation of documentation related to COVID-19 research and clinical trials, as well as to assess the impact of the pandemic on other clinical trials. Complexities and challenges medical writers have faced include the growing scientific knowledge of the virus, the burgeoning global footprint of the pandemic, and the evolving regulatory landscape on both COVID-19 and non-COVID-19 clinical trials.

INTRODUCTION

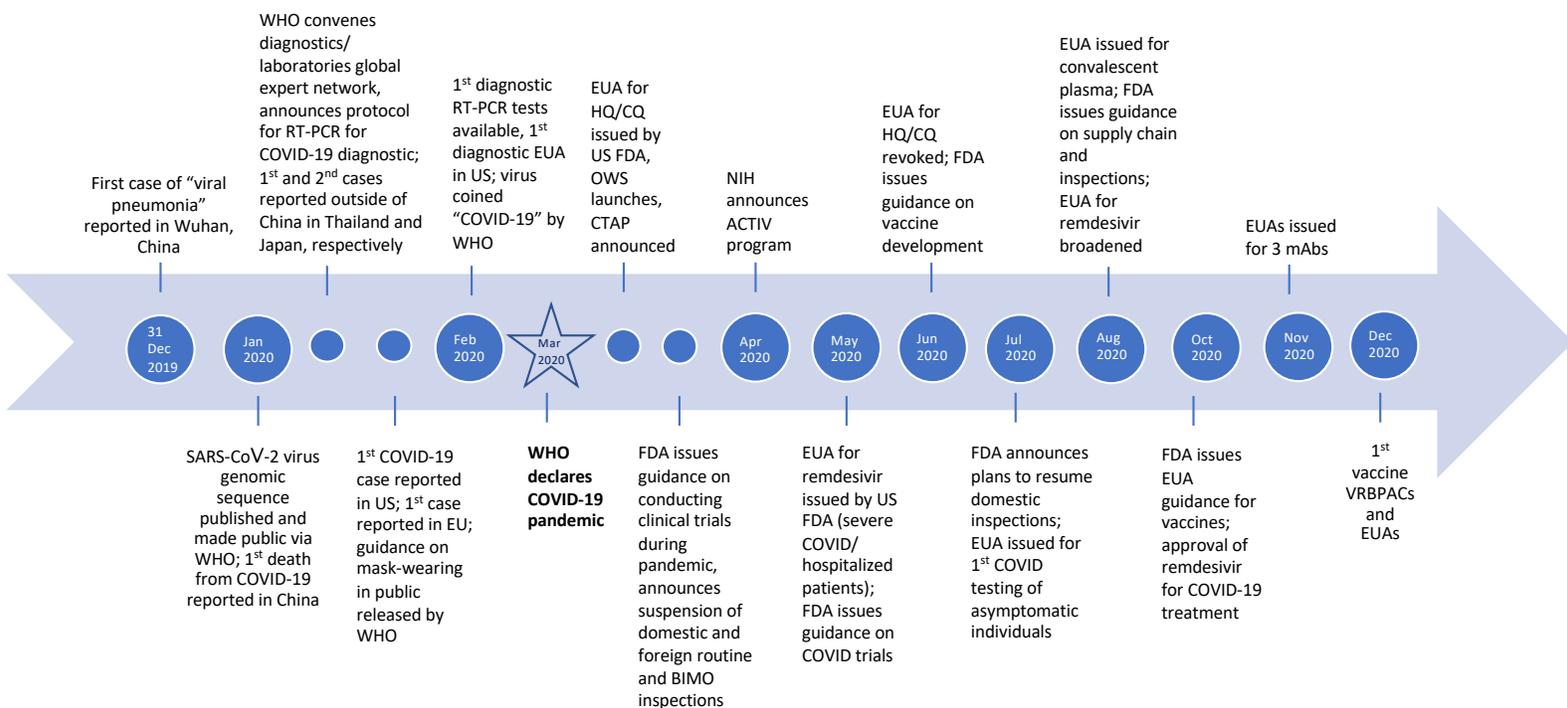
When cases of a novel coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), surfaced in the Hubei province of China in December 2019, leading to the outbreak of a complex respiratory illness (later coined coronavirus disease 2019 [COVID-19]), the world watched to see what would happen next. Many were cautiously optimistic that the virus would remain endemic to the region of the outbreak, as Middle East respiratory syndrome (MERS) had in 2012,¹ or, at worst, that it could be contained as the severe acute respiratory syndrome (SARS) epidemic had been in 2003.² The challenge of trying to contain the novel coronavirus was complicated by a lack of clarity on exactly how it was transmitted³; it was not until January 19, 2020, that the World Health Organization (WHO) announced that there was evidence of human-to-human transmission of the virus.⁴

This article provides a brief overview of the COVID-19 pandemic time course, the regulatory actions taken to allow for unprecedented rapid development of diagnostic and therapeutic products in the United States for COVID-19, and the impact of the pandemic on medical writers in the biotech and pharmaceutical industry.

Arrival of COVID-19 in the United States and Initial Impact on Biotech and Pharmaceutical Companies

A recent retrospective analysis of SARS-CoV-2-reactive antibodies in archived blood donation samples, spanning 9 states from the East to West coasts, indicates that COVID-19 may have been widely introduced into the United States as early as mid-December 2019.⁵ Despite the first cases of COVID-19 being observed in the United States and Europe on January 19 and 24, 2020, respectively (Figure),^{4,6} operations for biotech and pharmaceutical companies in the United States continued as normal into February. On February 26 and 27, a large conference was hosted by a biotech company in Boston, Massachusetts, which was later deemed a “superspreader” event,⁷ with approximately 100 diagnosed cases after the event ultimately being associated by genomic analysis with up to 330,000 subsequent cases. Following this event, biotech and pharmaceutical companies across the United States, particularly those in states experiencing a surge in cases, began enacting business continuity plans per local and state guidelines, including sheltering in place to the extent possible. Meanwhile, a shortage of personal protective equipment led many companies to donate their current laboratory supplies to local health care centers in surge states in early spring.⁸ For those employees who did have to go on site at their companies to perform experiments, a lack of COVID-19 testing supplies contributed to uncertainty for how to continue critical research while minimizing the risk for virus spread.

With guidelines on safe business operation being issued at the state level, it was not immediately clear how planned research and development (R&D) activities would be impacted or for how long. To address local social distancing requirements, some companies had to prioritize laboratory research for COVID-19 and for certain conditions with unmet need.⁹ It was also not immediately clear to what extent biotech and pharmaceutical companies, and the venture capital firms that finance their R&D activities, would invest in developing treat-



Abbreviations: ACTIV, Accelerating COVID-19 Therapeutic Interventions and Vaccines; BIMO, Biomedical Research Monitoring; COVID-19, novel coronavirus 2019; CQ, chloroquine; CTAP, Coronavirus Treatment Acceleration Program; EU, European Union; EUA, Emergency Use Authorization; FDA, Food and Drug Administration; HQ, hydroxychloroquine; mAb, monoclonal antibody; NIH, National Institutes of Health; OWS, Operation Warp Speed; RT, reverse transcription polymerase chain reaction; SARS-CoV-2, virus that causes coronavirus 2019 disease; US, United States; VRBPAC, Vaccines and Related Biological Products Advisory Committee; WHO, World Health Organization.

Figure. Timeline of key events associated with the COVID-19 pandemic. Sources: WHO,^{3,4,10} GenBank,¹¹ FDA.^{15,18-22,24,33,47-49}

ments for a novel virus that might not persist in the long term, based on evolving information on SARS-CoV-2 as well as prior SARS/MERS experience. These factors represented an initial threat to an industry that is largely dependent upon the continuous advancement of research.

Declaration of a Pandemic, the US Food and Drug Administration Response, and the Shift to Real-Time Drug Development

Pursuant to a rise in the number, severity, and location of cases, a pandemic was formally declared on March 11, 2020, by WHO.¹⁰ The Director of WHO urged countries worldwide to change the course of the pandemic and to “First, prepare and be ready. Second, detect, protect and treat. Third, reduce transmission. Fourth, innovate and learn.”

As more became known publicly about the clinical course of the virus, many global biotech and pharmaceutical companies sprang into action to see if existing technology or assets could contribute to a cure or a treatment for COVID-19 or its sequelae. These companies included those already developing vaccines, those developing therapeutics who entered vaccine development *de novo*, those repurposing existing antiviral

and other drugs, and those developing new drugs. Several companies partnered with other biotech companies or academic institutions to optimize efficiency. The sequence of the virus was first made public in early January 2020,^{4,11} and by late January, the US Food and Drug Administration (FDA) announced that it was “actively leveraging the vast breadth of the FDA’s expertise” and had “begun employing the full range of our public health authorities to facilitate the development and availability of investigational medical products to help address this urgent public health situation.”¹² On January 31, 2020, the US Department of Health and Human Services declared that COVID-19 constituted a US public health emergency and that an Emergency Use Authorization (EUA) was needed to mitigate the threat of COVID-19. This action enabled the FDA, in consultation with the National Institutes of Health and Centers for Disease Control and Prevention (CDC), to authorize the emergency use of unapproved medical products (Table 1).^{13,14}

With so many companies advancing new COVID-19 pipeline assets, many of the biotech and pharmaceutical employees who were initially impacted by the halt of other clinical trials eventually were reassigned to COVID-19-related work.⁹

Table 1. Global and United States COVID-19 Preventive and Therapeutic Initiatives

Initiative Owner(s)	Initiative	Purpose
Various governments, scientists, businesses, civil societies, philanthropists, and global health organizations	The ACT Accelerator	Global collaboration to accelerate the development, production, and equitable access to COVID-19 tests, treatments, and vaccines. ^{38,39,a}
WHO + global experts	R&D Blueprint	A global strategy and preparedness plan to fast-track the availability of effective tests, vaccines, and medicines that can be used to save lives and avert large-scale crises. Global Research Roadmap released in March 2020. ^{40,41}
WHO	Solidarity II international clinical trial ^{25,b} COVID-19 technical guidance: The Unity Studies: Early Investigation Protocols	Global collaboration led by WHO that promotes the implementation of serological surveys of SARS-CoV-2. Promotes standardized epidemiological, molecular, and serological methods to facilitate international comparisons so that both countries and the global community can collectively address knowledge gaps and inform an evidence-based COVID-19 response. ⁴²
US DHHS	OWS	Partnership among components of the DHHS, including the CDC, NIH, BARDA, and DoD with private firms and other federal agencies. Coordinates existing DHHS-wide efforts, including the NIH's ACTIV partnership, NIH's RADx initiative, and work by BARDA. Vaccine candidates from 3 companies are part of this initiative. ⁴³
FNIH	ACTIV	Public-private partnership to speed COVID-19 vaccine and treatment options. ⁴⁴
US DHHS, NIH	COVPN	Merged 4 existing NIAID-funded clinical trials networks: the HIV Vaccine Trials Network, HIV Prevention Trials Network, Infectious Diseases Clinical Research Consortium, and AIDS Clinical Trials Group. ⁴⁵
US DHHS, FDA	CTAP	Special emergency program for possible COVID-19 therapies. ⁴⁶ Provides FDA subject matter expertise for ACTIV initiatives, including for clinical trial design/conduct and regulatory standards.

ACT, Access to COVID-19 Tools; ACTIV, Accelerating COVID-19 Therapeutic Interventions and Vaccines; AIDS, acquired immunodeficiency syndrome; BARDA, Biomedical Advanced Research and Development Authority; COVPN, COVID-19 Prevention Trials Network; CTAP, Coronavirus Treatment Acceleration Program; DHHS, Department of Health and Human Services; DoD, Department of Defense; FNIH, Foundation of the National Institutes of Health; HIV, human immunodeficiency virus; NIAID, National Institute of Allergy and Infectious Diseases; NIH, National Institutes of Health; OWS, Operation Warp Speed; RADx, Rapid Acceleration of Diagnostics.

^a COVAX is the vaccines pillar of the ACT Accelerator. More information on the nonvaccine pillars of the ACT Accelerator is available at <https://www.who.int/initiatives/act-accelerator>. On December 31, 2020, the first vaccine received emergency use validation from WHO.³⁹

^b The results of the Solidarity I adaptive treatment trial became available October 15, 2020, and concluded that the 4 treatments studied (remdesivir, hydroxychloroquine, lopinavir/ritonavir, and interferon) had little or no effect compared with standard of care on overall mortality, initiation of ventilation, and duration of hospital stay in hospitalized patients. Additional agents to be evaluated per WHO.

As the author experienced, and based on personal communication of the author with industry colleagues, medical writers set to work alongside researchers on manuscripts for COVID-19 research, many times resulting in unprecedented rapid review and release of results in journals ahead of peer review to allow for real-time dissemination. Regulatory medical writers collaborated with cross-functional colleagues on investigational new drug (IND) application and EUA documentation to enable clinical evaluation of diagnostic, therapeutic, and preventive products; others participated in conversations with contract research organizations (CRO) and sites, balancing

operational feasibility and cost while implementing evolving regulatory guidance, to determine if certain non-COVID-19 trials would be able to continue during the pandemic.

Although medical writers have connected with colleagues remotely via various electronic media for a long time, many recently have had to cope with a new shift in their workload and priorities. In addition, medical writers have had to change how and how often they communicate during the writing process to meet the demand of real-time drug development, oftentimes working in coauthoring environments or live meetings rather than iteratively.

Diagnostics and Medical Equipment for COVID-19 Under EUA

In early February 2020, the first EUA for a reverse transcription polymerase chain reaction COVID-19 diagnostic was issued for use at CDC laboratories.¹⁵ Emergency use authorizations were also subsequently issued for equipment needed to protect health care workers and treat patients with COVID-19 as well as for additional diagnostics at non-CDC laboratories that would reduce the time to and accuracy of results, including home testing kits most recently.^{13,16}

The issuance of FDA guidance on diagnostic testing in May 2020¹⁶ enabled the subsequent availability of additional testing options (for example, rapid antigen testing).

Upon availability of such testing options, medical writers began incorporating COVID-19 testing strategies into study protocols and amendments, with built-in flexibility in language to allow for regional differences in testing availability or adoption of CDC recommendations—a critical step toward the restart of early-phase trials, which often have an in-residence component at the Phase 1 unit.

Preventive and Therapeutic Products, Including Vaccines, for COVID-19 Under EUA

The writing of clinical trial protocols for COVID-19 studies began in the context of the burgeoning geographic footprint of the pandemic, with health care centers in some regions too overwhelmed by critically ill patients to contribute to research while simultaneously in dire need of experimental treatments, leading to an added layer of volatility in an already dynamic process. Accordingly, regulatory advice on the conduct of such studies developed over time. Medical writers worked in concert with their cross-functional partners, regulators, and other stakeholders to overcome these challenges and produce protocols for evaluation of a novel virus and to interpret and convey the results of those studies in record time.

The first EUA for a COVID-19 therapeutic was granted in March 2020 for antimalarial agents hydroxychloroquine and chloroquine (Table 2).¹³ The FDA issued several guidance documents in May 2020 toward expediting development of COVID-19 products,¹⁷ including information on the process for initiating discussions with the FDA (pre-IND)¹⁸ and study design recommendations, including patient selection, endpoints, and analyses.^{19,20} Guidelines on vaccine development were issued the following month and updated in October and most recently in February of 2021 to outline the vaccine EUA process.^{21,22} Subsequent EUAs were granted for 9 additional products, including an antiviral in May, convalescent plasma in August, monoclonal antibody regimens in November, and the first vaccines in December 2020 (Table 2).^{13,23} Monitoring of previously issued EUAs continues and, in some cases, has

led to the withdrawal of the EUA, such as that which occurred for hydroxychloroquine and chloroquine upon analysis of conflicting data (including results from a randomized, controlled trial) that brought into question the benefit-risk profile of this regimen for treatment of COVID-19.^{13,24,25} The EUA issued for antiviral remdesivir in May led to approval of the drug as the first treatment for COVID-19 under the Coronavirus Treatment Acceleration Program (see Table 1) in October 2020.

As of January 2021, a search on the US National Library of Medicine's Clinicaltrials.gov (search terms of COVID-19 and SARS-CoV-2, with a recruitment status of not yet recruiting, recruiting, enrolling by invitation, active, or not recruiting) returns results for over 3,500 COVID-19 clinical trials that are ongoing or in start-up.²⁶

Clinical Trials During the COVID-19 Pandemic

Between approximately March and May 2020, thousands of clinical trials (or around 80% of non-COVID-19 trials) reported a disruption,²⁷⁻³⁰ with the majority of these being early-phase trials that had not yet started enrolling patients.^{27,29} The most affected therapeutic areas included those enrolling participants with advanced or life-threatening conditions such as cardiovascular disease or oncology—indeed, the very patients who are most at risk for COVID-19³¹—who often have few other treatment options; the typical intravenous administration route of oncologic treatments, which require patients to go to the clinical site for infusions, has led to additional logistical hurdles.^{29,32} Disruptions were reported as delay or suspension in enrollment, delay in study start-up activities or initiation of certain sites, delay in dosing, termination of enrollment at specific sites, early trial termination, and delay in trial completion or availability of data.^{26,29} In many cases, clinical trials that were nearly or already fully enrolled in patient populations with life-threatening conditions continued with modifications to address the uncertainties and challenges of conducting clinical trials in an already burdened health care system.²⁹

In March 2020, the FDA issued guidance on the conduct of clinical trials during the COVID-19 pandemic, with the goal of ensuring “the safety of trial participants, maintaining compliance with good clinical practice and minimizing risks to trial integrity.”³³ The guidance has been updated on a regular basis and covers key topics, such as:

- Electronic and other remote informed consent options
- Alternative formats for visits (eg, phone contact, virtual visit, alternative locations, local laboratory or imaging centers, home nursing)
- Alternative formats for clinical outcome assessments (ie, patient-reported outcomes, clinician-reported outcomes, and observer-reported outcomes), including protection of data privacy

Table 2. COVID-19 Therapeutics and Biological Products Approved Under EUA

Date of First EUA Issuance (Reissuance, if Applicable)	Approved Product Under EUA	Therapy Type	Authorized Use
March 29, 2021	Janssen COVID-19 vaccine	Recombinant, replication-incompetent human Ad26 vectored vaccine encoding a stabilized variant of the SARS-CoV-2 S protein	For the prevention of COVID-19 for individuals ≥ 18 years old
December 18, 2020 (Reissued February 25, 2021)	Moderna COVID-19 vaccine	mRNA vaccine	For the prevention of COVID-19 for individuals ≥ 18 years old
December 11, 2020 (Reissued February 25, 2021)	Pfizer-BioNTech COVID-19 vaccine	mRNA vaccine	For the prevention of COVID-19 for individuals ≥ 16 years old
February 09, 2021 (Reissued February 25, 2021)	Bamlanivimab and etesevimab	Antibodies	For the treatment of mild-to-moderate COVID-19 in adult and pediatric patients with positive results of direct SARS-CoV-2 viral testing who are ≥ 12 years old, weigh at least 40 kg, and are at high risk for progressing to severe COVID-19 and/or hospitalization
November 21, 2020 (Reissued February 25, 2021)	Casirivimab and imdevimab	Antibodies	For the treatment of mild-to-moderate COVID-19 in adults and pediatric patients (≥ 12 years old weighing ≥ 40 kg) with positive results of direct SARS-CoV-2 viral testing and who are at high risk for progressing to severe COVID-19 and/or hospitalization
November 19, 2020	Baricitinib in combination with remdesivir	Antibody + antiviral	For emergency use by health care providers for the treatment of suspected or laboratory-confirmed COVID-19 in hospitalized adults and pediatric patients ≥ 2 years of age requiring supplemental oxygen, invasive mechanical ventilation, or ECMO
August 23, 2020 (Reissued March 09, 2021)	COVID-19 convalescent plasma	Convalescent plasma	For the treatment of hospitalized patients with COVID-19
August 13, 2020	Sodium chloride and sodium citrate renal replacement and regional solution for anticoagulation of the extracorporeal circuit	Replacement solution for CRRT	To be used as a replacement solution only in adult patients treated with CRRT, and for whom regional citrate anticoagulation is appropriate, in a critical care setting
May 8, 2020	Propofol 2%	Sedative	To maintain sedation via continuous infusion in patients >16 years old with suspected or confirmed COVID-19 who require mechanical ventilation in an ICU setting
May 1, 2020 (Reissued October 22, 2020) ^a	Remdesivir for certain hospitalized patients with COVID-19	Antiviral	For emergency use by licensed health care providers for the treatment of suspected or laboratory-confirmed COVID-19 in hospitalized pediatric patients weighing 3.5 kg to <40 kg or hospitalized pediatric patients <12 years old weighing at least 3.5 kg
April 30, 2020	Potassium-free and 2, 3, and 4 mmol/L potassium solution for hemodialysis/hemofiltration	Replacement solution for CRRT	To provide CRRT to treat patients in an acute care environment during the COVID-19 pandemic

Source: FDA 2021.¹³

Ad26, adenovirus serotype 26; CRRT, continuous renal replacement therapy; ECMO, extracorporeal membrane oxygenation; ICU, intensive care unit; mRNA, messenger RNA.

^aThe original EUA for remdesivir issued May 1, 2020, was for the treatment of suspected or laboratory-confirmed COVID-19 in adult and pediatric patients hospitalized with severe disease. The EUA was expanded to include adult and pediatric patients with COVID-19 irrespective of severity on August 28, 2020. Remdesivir was the first treatment to receive approval under Coronavirus Treatment Acceleration Program on October 22, 2020, for use in adults and pediatric patients with COVID-19 who are ≥ 12 years old and weigh ≥ 40 kg requiring hospitalization; the EUA was reissued to allow for continued access to a subset of hospitalized pediatric patients with suspected or laboratory-confirmed COVID-19 who weigh 3.5 kg to <40 kg or who are <12 years old and weigh at least 3.5 kg.

- Supply chain considerations, such as direct-to-patient shipping, administration by a home nurse, and disposal of the investigational product
- Remote site monitoring considerations, including prioritization of monitoring activities in the circumstance of clinical trial site closures, infectious disease control restrictions, or local travel constraints
- Serious adverse event (SAE) reporting, including reporting of cases of COVID-19 on non-COVID-19 clinical trials and cross-reporting of SAEs in the case of multiple INDs

A key takeaway of the guidance is to ensure collection of information on when and how any mitigations were implemented in a clinical trial to facilitate subsequent reporting on the impact of COVID-19 on the trial objectives.

In addition, the biotech and pharmaceutical industry has contributed to the discussion of clinical trial mitigations necessitated by COVID-19. TransCelerate Biopharma, a collection of member biotech and pharmaceutical companies working to standardize key clinical trial activities, released a number of COVID-19–related initiatives, including a data-sharing platform called DataCelerate for COVID-19 research, tools for risk-based monitoring and protocol deviation management, and a clinical study report template for outlining details on COVID-19–related clinical trial impact.^{34,35} With information changing regularly because of the dynamic nature of the pandemic and its regionally varied effects, and with ongoing updates from global health agencies, however, it is clear that any such tool will be a work in progress rather than a static guideline and that medical writers will need to stay informed on any updates over time.

It is unclear as of yet what impact these mitigations have had on the overall continuation of non-COVID-19 clinical trials during the pandemic. The success of the mitigations will need to be analyzed and reported on at an individual study level, depending on the company's assessment of what measures were needed at the time the pandemic affected the trial, with any publications based on the trial footnoted accordingly with this context. Based on regional variation on how the measures could be implemented, it is also possible that some mitigations will be successful in some regions but not others or that some mitigations were successful overall, whereas other planned mitigations were unsuccessful because of local circumstances. It is clear that properly contextualizing and reporting out the results of any such mitigations will be a time-consuming effort that requires complete source documentation and follow-up on details with CRO and site partners.

Looking Forward

For medical writers, the pandemic has provided both opportunities, such as the opportunity to work on the surge of COVID-

19–related clinical study protocols and manuscripts, and challenges, such as the interruption of some non-COVID-19 studies or research and the need to work with urgency to produce communication for various purposes.

As we pass the 1-year mark from when the first cases of COVID-19 were reported, with the recent approval of vaccines, some aspects of the medical writing profession and the industry in general may start to return to normal. Time will tell how biotech and pharmaceutical companies, which are reliant on raising capital for operational costs, will fare with the delay of important milestone reporting that helps raise those funds. Trials of preventive and therapeutic products for COVID-19 will continue, including those in nonhospitalized settings³⁶ and in different age groups and populations; sequelae of COVID-19 will also require treatment. Viral mutations and their implications on available treatments and vaccines will require monitoring,³⁷ and new waves of lockdowns may cause continued clinical trial enrollment and execution challenges as certain regions with increased case counts return to lockdown. It remains to be determined how some of the efficiencies gained during the pandemic will be applied as learning for future processes in a sustainable way.

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References

1. Middle East respiratory syndrome coronavirus (MERS-CoV). World Health Organization. Published March 11, 2019. Accessed December 6, 2020. [https://www.who.int/news-room/fact-sheets/detail/middle-east-respiratory-syndrome-coronavirus-\(mers-cov\)](https://www.who.int/news-room/fact-sheets/detail/middle-east-respiratory-syndrome-coronavirus-(mers-cov))
2. Severe acute respiratory syndrome (SARS). World Health Organization. Published 2020. Accessed December 6, 2020. https://www.who.int/health-topics/severe-acute-respiratory-syndrome#tab=tab_1
3. Emergencies preparedness, response. Novel Coronavirus – China. World Health Organization. Published January 12, 2020. Accessed December 6, 2020. <https://www.who.int/emergencies/disease-outbreak-news/item/2020-DON229>
4. Timeline of WHO's response to COVID-19. World Health Organization. Accessed January 31, 2021. <https://www.who.int/emergencies/diseases/novel-coronavirus-2019/interactive-timeline#event-22>
5. Basavaraju SV, Patton ME, Grimm K, et al. Serologic testing of US blood donations to identify severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)–reactive antibodies: December 2019–January 2020. *Clin Infect Dis*. Published online November 30, 2020. doi:10.1093/cid/ciaa1785
6. Holshue ML, DeBolt C, Lindquist S, et al.; for the Washington State 2019-nCoV Case Investigation Team. First case of 2019 novel coronavirus in the United States. *N Engl J Med*. 2020;382(10):929-936.
7. Lemieux J, Siddle KJ, Shaw BM, et al. Phylogenetic analysis of SARS-CoV-2 in Boston highlights the impact of superspreading events. *Science*. 2021;371(6529):eabe3261.
8. Cordeiro J. The impact of the Massachusetts Life Sciences Emergency SupplyHub. MassBio. Published March 25, 2020. Accessed January 31, 2021. <https://www.massbio.org/news/recent-news/the-impact-of-the-massachusetts-life-sciences-supplyhub/>

9. Kwon D. How the pharma industry pulled off the pivot to COVID-19. *The Scientist*. Published July 13, 2020. Accessed January 31, 2021. <https://www.the-scientist.com/bio-business/how-the-pharma-industry-pulled-off-the-pivot-to-covid-19-67719>
10. WHO Director-General's opening remarks at the media briefing on COVID-19 - 11 March 2020. World Health Organization. Published March 11, 2020. Accessed December 6, 2020. <https://www.who.int/director-general/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19---11-march-2020>
11. Severe acute respiratory syndrome coronavirus 2 isolate Wuhan-Hu-1, complete genome. GenBank: MN908947.1, MN908947.2, MN908947.3. National Center for Biotechnology Information. Accessed December 6, 2020. <https://www.ncbi.nlm.nih.gov/nucleotide/MN908947>
12. FDA announces key actions to advance development of novel coronavirus medical countermeasures. US Food and Drug Administration. Published January 27, 2020. Accessed December 6, 2020. <https://www.fda.gov/news-events/press-announcements/fda-announces-key-actions-advance-development-novel-coronavirus-medical-countermeasures>
13. Emergency use authorization. US Food and Drug Administration. Published December 11, 2020. Accessed January 2, 2021. <https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization>
14. Emergency use authorization of medical products and related authorities: guidance for industry and other stakeholders. US Food and Drug Administration. Published January 2017. Accessed December 6, 2020. <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/emergency-use-authorization-medical-products-and-related-authorities>
15. FDA takes significant step in coronavirus response efforts, issues emergency use authorization for the first 2019 novel coronavirus diagnostic: critical milestone reached in response to this outbreak. US Food and Drug Administration. Published February 4, 2020. Accessed December 6, 2020. <https://www.fda.gov/news-events/press-announcements/fda-takes-significant-step-coronavirus-response-efforts-issues-emergency-use-authorization-first>
16. Policy for coronavirus disease-2019 tests during the public health emergency (revised): immediately in effect guidance for clinical laboratories, commercial manufacturers, and Food and Drug Administration staff. US Food and Drug Administration. Published May 2020. Accessed December 6, 2020. <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/policy-coronavirus-disease-2019-tests-during-public-health-emergency-revised>
17. Coronavirus (COVID-19) update: FDA takes new actions to accelerate development of novel prevention, treatment options for COVID-19. US Food and Drug Administration. Published May 11, 2020. Accessed December 12, 2020. <https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-takes-new-actions-accelerate-development-novel-prevention-treatment>
18. COVID-19 public health emergency: general considerations for pre-IND meeting requests for COVID-19 related drugs and biological products: guidance for industry and investigators. US Food and Drug Administration. Published May 2020. Accessed December 12, 2020. <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/covid-19-public-health-emergency-general-considerations-pre-ind-meeting-requests-covid-19-related>
19. COVID-19: developing drugs and biological products for treatment or prevention: guidance for industry. US Food and Drug Administration. Published May 2020. Accessed Dec 12, 2020. <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/covid-19-developing-drugs-and-biological-products-treatment-or-prevention>
20. Statistical considerations for clinical trials during the COVID-19 public health emergency: guidance for industry. US Food and Drug Administration. Published June 2020. Accessed December 12, 2020. <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/statistical-considerations-clinical-trials-during-covid-19-public-health-emergency-guidance-industry>
21. Development and licensure of vaccines to prevent COVID-19: guidance for industry. US Food and Drug Administration. Published June 2020. Accessed December 13, 2020. <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/development-and-licensure-vaccines-prevent-covid-19>
22. Emergency use authorization for vaccines to prevent COVID-19: guidance for industry. US Food and Drug Administration. Published February 22, 2021. Accessed April 19, 2021. <https://www.fda.gov/media/142749/download>
23. Pfizer-BioNTech COVID 19 vaccine. US Food and Drug Administration. Published December 11, 2020. Accessed January 31, 2021. <https://www.fda.gov/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/pfizer-biontech-covid-19-vaccine>
24. Frequently asked questions on the revocation of the emergency use authorization for hydroxychloroquine sulfate and chloroquine phosphate. US Food and Drug Administration. Published June 19, 2020. Accessed December 6, 2020. <https://www.fda.gov/media/138946/download>
25. "Solidarity" clinical trial for COVID-19 treatments. World Health Organization. Published 2020. Accessed December 6, 2020. <https://www.who.int/emergencies/diseases/novel-coronavirus-2019/global-research-on-novel-coronavirus-2019-ncov/solidarity-clinical-trial-for-covid-19-treatments>
26. Clinicaltrials.gov. <https://www.clinicaltrials.gov>. Accessed January 2, 2021.
27. Fidler B. A guide to clinical trials disrupted by the coronavirus pandemic. BioPharma Dive. Published May 15, 2020. Accessed December 6, 2020. <https://www.biopharmadive.com/news/coronavirus-clinical-trial-disruption-biotech-pharma/574609/>
28. Rees V. Impact of COVID-19 on clinical trials continuing, say researchers. *European Pharmaceutical Review*. Published September 11, 2020. Accessed January 2, 2021. <https://www.europeanpharmaceuticalreview.com/news/128134/impact-of-covid-19-on-clinical-trials-continuing-say-researchers/>
29. van Dorn A. COVID-19 and readjusting clinical trials. *Lancet*. 2020;396(10250):523-524.
30. Asaad M, Habibullah NK, Butler CE. The impact of COVID-19 on clinical trials. *Ann Surg*. 2020;272(3):e222-e223.
31. Certain medical conditions and risk for severe COVID-19 illness. Centers for Disease Control and Prevention. Published December 29, 2020. Accessed January 2, 2021. <https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical-conditions.html>
32. Common questions about the COVID-19 outbreak. American Cancer Society. Published December 21, 2020. Accessed January 2, 2021. <https://www.cancer.org/latest-news/common-questions-about-the-new-coronavirus-outbreak.html>
33. Coronavirus (COVID-19) update: FDA issues guidance for conducting clinical trials. US Food and Drug Administration. Published March 18, 2020. Accessed December 6, 2020. <https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-issues-guidance-conducting-clinical-trials>
34. COVID-19. TransCelerate Biopharma, Inc. Accessed December 13, 2020. <https://www.transceleratebiopharmainc.com/covid-19/>
35. Clinical Content & Reuse Solutions. Clinical Template Suite (CTS); Template, Resources, and Use Guidance: 2020 CSR Updates. CSR considerations for studies disrupted by the COVID-19 pandemic. TransCelerate Biopharma, Inc. Accessed December 13, 2020. <https://www.transceleratebiopharmainc.com/assets/clinical-content-reuse-solutions/>
36. Assessing COVID-19-related symptoms in outpatient adult and adolescent subjects in clinical trials of drugs and biological products for COVID-19 prevention or treatment: guidance for industry. US Food and Drug Administration. Published September 2020. Accessed December 13, 2020. <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/assessing-covid-19-related-symptoms-outpatient-adult-and-adolescent-subjects-clinical-trials-drugs>
37. Interim: implications of the emerging SARS-CoV-2 variant VOC 202012/01. Centers for Disease Control and Prevention. Published

- December 29, 2020. Accessed April 19, 2021. <https://stacks.cdc.gov/view/cdc/99303>
38. Global equitable access to COVID-19 vaccines estimated to generate economic benefits of at least US\$ 153 billion in 2020–21, and US\$ 466 billion by 2025, in 10 major economies, according to new report by the Eurasia Group. World Health Organization. Published December 3, 2020. Accessed December 6, 2020. <https://www.who.int/news/item/03-12-2020-global-access-to-covid-19-vaccines-estimated-to-generate-economic-benefits-of-at-least-153-billion-in-2020-21>
 39. WHO issues its first emergency use validation for a COVID-19 vaccine and emphasizes need for equitable global access. World Health Organization. Published December 31, 2020. Accessed January 2, 2021. <https://www.who.int/news/item/31-12-2020-who-issues-its-first-emergency-use-validation-for-a-covid-19-vaccine-and-emphasizes-need-for-equitable-global-access>
 40. R&D Blueprint and COVID-19. World Health Organization. Published 2020. Accessed December 13, 2020. <https://www.who.int/teams/blueprint/covid-19>
 41. A coordinated global research roadmap. World Health Organization. Published March 12, 2020. Accessed December 13, 2020. <https://www.who.int/publications/m/item/a-coordinated-global-research-roadmap>
 42. Coronavirus disease (COVID-19) technical guidance: The Unity Studies: early investigation protocols. World Health Organization. Published 2020. Accessed December 13, 2020. <https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/early-investigations>
 43. Fact Sheet: Explaining Operation Warp Speed. US Department of Health and Human Services. Published November 30, 2020. Accessed December 6, 2020. <https://health.mo.gov/living/healthcondiseases/communicable/novel-coronavirus-lpha/pdf/fact-sheet-operation-warp-speed.pdf>
 44. NIH to launch public-private partnership to speed COVID-19 vaccine and treatment options. National Institutes of Health. Published April 17, 2020. Accessed December 6, 2020. <https://www.nih.gov/news-events/news-releases/nih-launch-public-private-partnership-speed-covid-19-vaccine-treatment-options>
 45. NIH launches clinical trials network to test COVID-19 vaccines and other prevention tools. National Institutes of Health. Published July 8, 2020. Accessed December 6, 2020. <https://www.nih.gov/news-events/news-releases/nih-launches-clinical-trials-network-test-covid-19-vaccines-other-prevention-tools>
 46. Coronavirus Treatment Acceleration Program (CTAP). US Food and Drug Administration. Published November 17, 2020. Accessed December 6, 2020. <https://www.fda.gov/drugs/coronavirus-covid-19-drugs/coronavirus-treatment-acceleration-program-ctap>
 47. Coronavirus disease 2019 (COVID-19). US Food and Drug Administration. Published December 11, 2020. Accessed December 13, 2020. <https://www.fda.gov/emergency-preparedness-and-response/counterterrorism-and-emerging-threats/coronavirus-disease-2019-covid-19>
 48. Manufacturing, supply chain, and drug and biological product inspections during COVID-19 public health emergency - questions and answers: guidance for industry. US Food and Drug Administration. Published August 2020. Accessed December 13, 2020. <https://www.fda.gov/media/141312/download>
 49. Coronavirus (COVID-19) update: FDA authorizes first diagnostic test for screening of people without known or suspected COVID-19 infection. US Food and Drug Administration. Published July 24, 2020. Accessed December 13, 2020. <https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-authorizes-first-diagnostic-test-screening-people-without-known-or>

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Intersections of Severe Acute Respiratory Syndrome Coronavirus 2, Coronavirus Disease 2019, and the Cardiovascular System

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ABSTRACT

Coronavirus disease 2019 (COVID-19), caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has far-reaching impacts on human health. First identified as a disease of the respiratory system, COVID-19 also causes gastrointestinal, renal, neurological, and/or cardiovascular symptoms. This article elucidates biological relationships between COVID-19 and the cardiovascular system. It postulates molecular and physiological mechanisms behind COVID-19-related cardiovascular ailments and examines intersections among the cardiovascular system, SARS-CoV-2, COVID-19, and certain medications. New scientific information on COVID-19 and the cardiovascular system accumulates weekly. In recognition of such rapidity, this paper offers a framework in which the reader will be able to place the growing and evolving field of knowledge.

EFFECTS OF SEVERE ACUTE RESPIRATORY SYNDROME CORONAVIRUS 2 INFECTION ON THE CARDIOVASCULAR SYSTEM

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infects cells through an interaction between the virus's spike (S) protein and angiotensin-converting enzyme (ACE) 2 in host cells.¹⁻⁵ Within the cardiovascular system, ACE2 is reportedly located on heart muscle cells,⁶⁻¹¹ endothelial cells (ECs) that line the interior of blood vessels and regulate blood clotting and blood pressure,^{12,13} pericytes that surround and aid ECs,⁶⁻⁸ and arterial smooth muscle cells (SMCs) that control vascular diameter and thereby blood pressure and flow.^{7,12,13} SARS-CoV-2 infection of these cells hinders their health-promoting work.

Cardiovascular health is also threatened when SARS-CoV-2 invades noncardiac areas and triggers immune responses. To fight the “intruder,” local white blood cells activate, recruit other white blood cells, and produce pro-inflammatory chemicals, which increases inflammation. Interestingly, a source of these chemicals may be direct SARS-CoV-2 infection of macrophages—a type of white blood cell that expresses ACE2.¹⁴ As

the immune system battles the virus, the affected body organ may (temporarily) malfunction. These malfunctions and the pro-inflammatory chemicals released into the blood may elicit negative effects on blood vessels and the heart.¹⁵

Cardiovascular conditions induced by these direct and indirect effects of SARS-CoV-2 infection include myocarditis (inflamed heart tissue), blood pressure irregularities, abnormal blood clot (thrombus) formation, hypoxia, arteriosclerotic heart disease (ASHD), myocardial infarctions (MIs; heart attacks), arrhythmias, and heart failure (Figure 1).¹⁶⁻²⁹ If left unchecked or if severe enough, these ailments could be fatal.

Myocarditis

Myocarditis compromises contractility of the heart muscle. As a result, the heart compensates in order to insure proper delivery of blood (and O₂) to the body. Compensation occurs by one of at least 2 methods: (1) thickening of the heart muscle layer (hypertrophy), and (2) heart rate elevation (tachycardia). Both choices could progressively worsen the heart's already precarious condition.

Blood Pressure Irregularities

Some patients with coronavirus disease 2019 (COVID-19) present with hypertension.¹⁹ The causal link between this elevated blood pressure and SARS-CoV-2 may be ACE2. Besides being the binding target of SARS-CoV-2's S protein, ACE2 is part of the renin-angiotensin system (RAS) pathway (Figure 2). The RAS pathway controls SMC contraction and relaxation and thereby influences blood pressure. SMC contraction narrows vessels' diameter (vasoconstriction) and raises blood pressure. SMC relaxation widens vessels' diameter (vasodilation) and lowers blood pressure. SMC contraction and relaxation are controlled by the RAS pathway's angiotensin II and angiotensin (1-7), respectively. ACE1 converts relatively inactive angiotensin I into angiotensin II, a highly active vasoconstrictor. ACE2 converts angiotensin II into angiotensin (1-7), a vasodilator (Figure 2).³⁰ ACE2 levels likely decline in SARS-CoV-2-infected

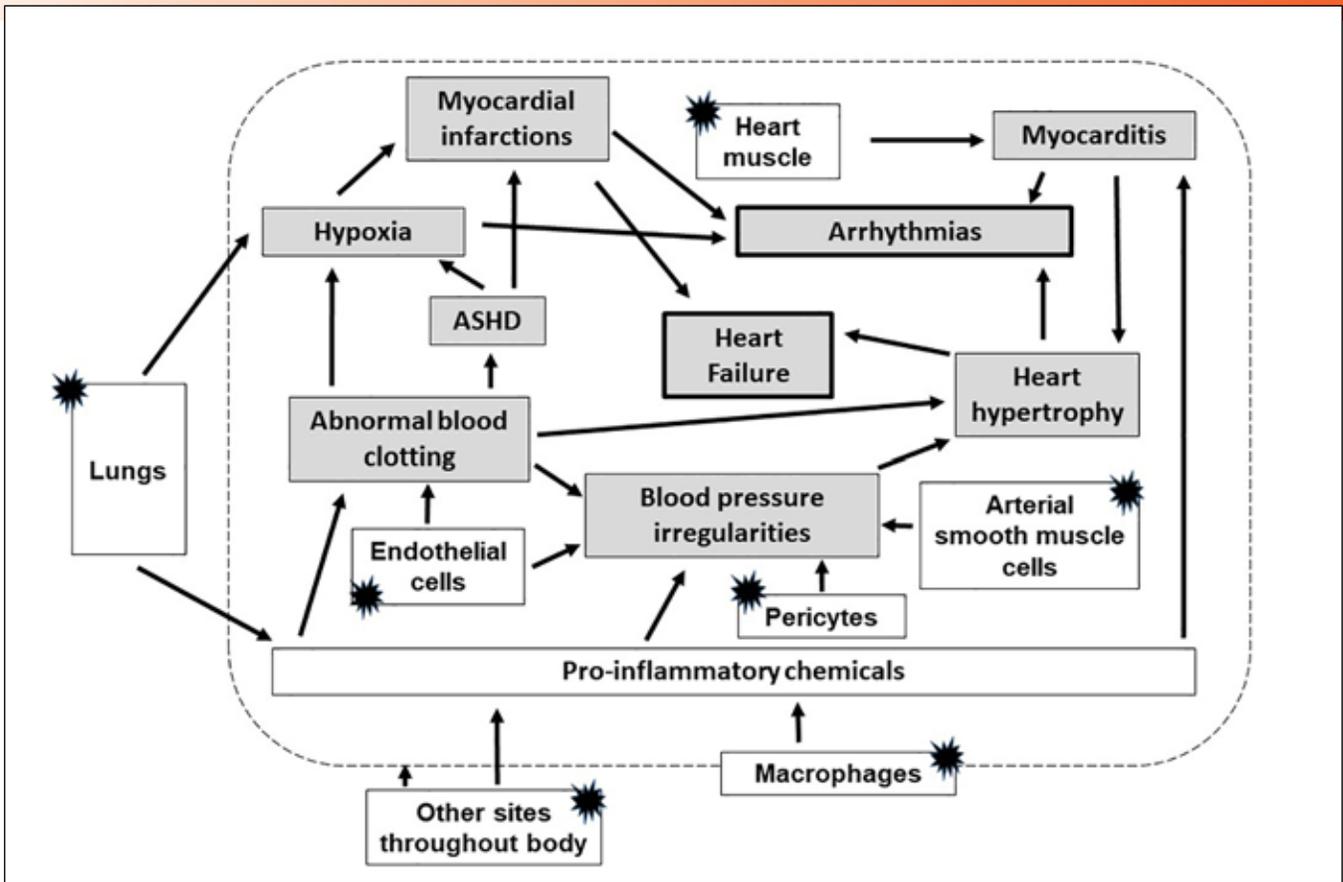


Figure 1. Confirmed and plausible mechanisms by which severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection causes cardiovascular symptoms. Several cell types and organs (indicated by the spiked star symbol) are reported targets for SARS-CoV-2 infection. Some of these host cells are part of the cardiovascular system, macrophages may lie within or outside of the cardiovascular system, and other sites lie outside of the cardiovascular system. (The cardiovascular system is defined by the thin-dashed enclosure.) Infections initiate a variety of cardiovascular symptoms (shaded boxes) that, if prolonged and severe enough, cause arrhythmias and heart failure (shaded boxes with thick outline). Viral infection of other organs may also affect the cardiovascular system in ways not specified here. Related schematics can be found in Guzik et al.¹⁷ and Atri et al.¹⁶ ASHD, arteriosclerotic heart disease.

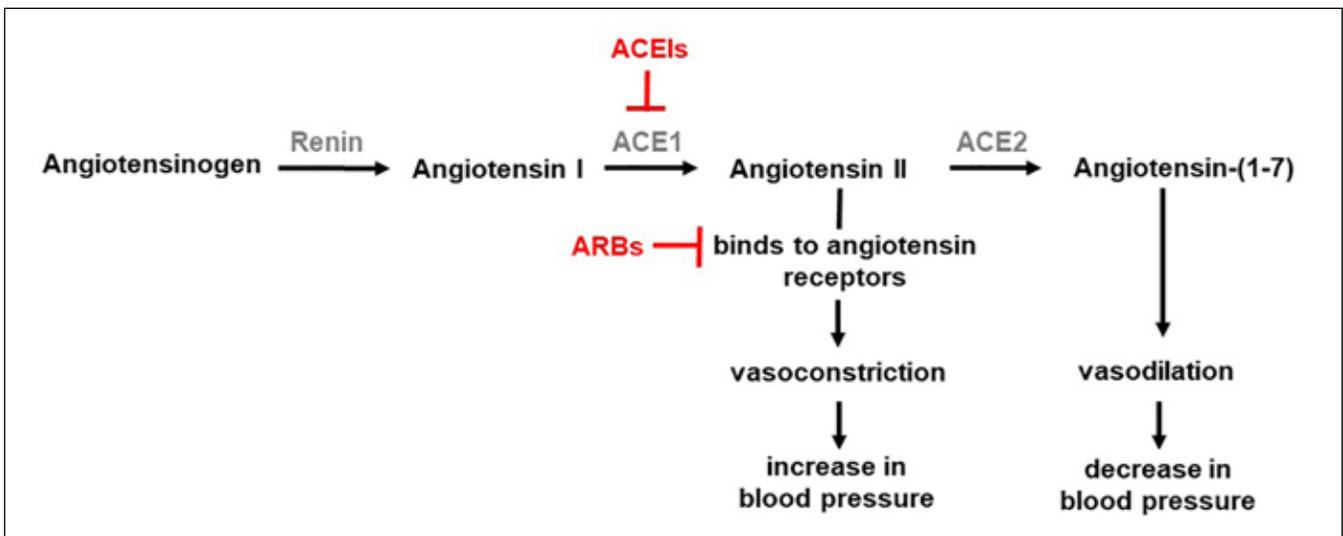


Figure 2. The renin-angiotensin system (RAS) pathway and sites of angiotensin-converting enzyme (ACE) inhibitor (ACEI) and angiotensin receptor blocker (ARB) inhibition. In the RAS pathway, renin (produced by the kidneys) converts angiotensinogen (produced by the liver) into angiotensin I. Angiotensin I is modified into angiotensin II, an active vasoconstrictor, by ACE1. ACE2 (the target for SARS-CoV-2 infection) produces the vasodilator angiotensin (1-7) from angiotensin II. The ACEI and ARB high-blood-pressure medications work by preventing vasoconstriction. They inhibit ACE1 and binding of angiotensin II to its receptors, respectively.

cells.³¹⁻³³ Without ACE2, levels of angiotensin (1-7) would decrease, and angiotensin II levels would likely increase. These events would tip the scales toward vasoconstriction and elevated blood pressure. This mechanistic explanation for hypertension, although plausible, needs to be strengthened with additional research.

Another explanation for hypertension development in patients with COVID-19 lies in direct viral infection of ECs and perhaps pericytes. Both of these cell types impact blood vessel diameter (Figure 1).³⁴⁻³⁶ A deficit of vasodilation or a prevalence of vasoconstriction likely causes hypertension.

Some patients with COVID-19 develop low blood pressure (hypotension) rather than high blood pressure.²² Hypotension is a symptom of acute respiratory distress syndrome (ARDS),³⁷ so it is likely the result of SARS-CoV-2 infection of lung cells.

Thrombi Formation and Hypoxia

Another blood-related condition found in some patients with COVID-19 is the presence of thrombi.²³⁻²⁵ These abnormal blood clots form in arteries or veins. Interference of arterial blood flow jeopardizes delivery of O₂ and nutrients to areas downstream of the blockage, whereas impedance of blood flow through a vein may cause swelling in the body upstream of the clot.

Besides blood-flow alteration, thrombi pose an additional risk to patients: pieces may break off the clot, travel through the bloodstream, and lodge in another blood vessel. These traveling clots (emboli) endanger other organs. When an embolus in a large systemic artery flows to a narrower artery within an organ, it may get stuck, hinder blood flow, and deprive downstream organs—or areas within an organ—of O₂.

Emboli in veins pose a significant risk to the lungs. Such emboli could migrate through the right heart chambers, lodge in the lungs' narrow arterial branches, and impede blood flow to the pulmonary capillaries. Complications of pulmonary emboli include right ventricular hypertrophy, swelling (edema), and low O₂ levels in the blood (hypoxia) (Figure 1).

Right ventricular hypertrophy and edema are indirect effects of a pulmonary embolism. To force blood past the pulmonary embolism, the heart's right ventricle hypertrophies in an attempt to strengthen its pumping power. At best, this adjustment is a temporary fix. Persistence of the embolism increases blood pressure in the right side of heart, and by extension, in the body's veins. This elevated vascular pressure induces edema. Gravity causes the swelling to be most prominent in the lower limbs.

Such edema also occurs in the lungs. This fluid buildup impedes the diffusion of O₂ from the lungs' alveoli to the blood in the pulmonary capillaries. It also reduces alveolar ventilation (O₂ entry into the alveoli), as fluid-filled sacs fail to remain

open. Diminished blood flow to alveoli on account of pulmonary emboli may also prevent the blood from picking up adequate O₂. Collectively, these emboli-initiated events cause hypoxia.

Two culprits induce thrombi formation: injured ECs and pro-inflammatory chemicals (Figure 1). ECs may be damaged by direct SARS-CoV-2 infection.³⁸ Such damaged cells activate platelets and make them more "sticky"; thus, they adhere to the vessel wall and to each other. Clotting factors in the blood set off a chain reaction that culminates in the modification of fibrinogen to fibrin. Fibrin threads attach to the mass of platelets to form the clot. If ECs are undamaged, a clot may still form: pro-inflammatory chemicals may activate platelets and clotting factors (Figure 1).³⁹

Preexisting hypertension, ASHD, arrhythmias, MIs, and heart failure seem to increase the severity of COVID-19 symptoms in patients.

ASHD, MIs, and Arrhythmias

Thrombi may form in the coronary arteries of some patients with COVID-19, a condition known as ASHD.²⁶⁻²⁸ Coronary arteries carry O₂-rich blood to the heart tissue. Such O₂ helps fuel the heart's vital blood-pumping actions. Partial or complete blockage of these coronary vessels is life-threatening. Whether through blocked delivery or through hypoxia, insufficient O₂ causes heart muscle cells to malfunction and die. The likelihood of MIs increases (Figure 1). MIs in a small number of patients with COVID-19 have been reported.²⁶⁻²⁸

Arrhythmias have also been reported in some patients with COVID-19.^{16,18,29} In the general population, these altered heart rhythms are caused by ASHD, MIs, myocarditis, and heart hypertrophy. Therefore, these cardiovascular conditions are the current "suspects" for reported arrhythmias in COVID-19-related cases.^{16,18,29}

Heart Failure

Persistence of these aforementioned cardiovascular problems gradually weakens the heart, compromises its pumping ability and effectiveness, and can lead to heart failure (Figure 1). The heart becomes progressively more incapable of delivering O₂- and nutrient-rich blood to the body. Preexisting heart failure appears to increase the likelihood of death from the disease in patients with COVID-19.⁴⁰

MEDICATIONS AND HEALTH (COVID-19 AND CARDIOVASCULAR) RISKS

COVID-19 impacts the cardiovascular system, but the inverse may also be true. Percentages of patients with COVID-19 and cardiovascular conditions are not higher than the prevalence of these conditions in the general population.^{18-20,40-46} Therefore, these cardiovascular illnesses do not appear to increase one's risk of developing COVID-19. However, preexisting hypertension,^{18-20,40,41} ASHD,^{18,19,40,41} arrhythmias,^{19,20,41} MIs,²⁰ and heart failure^{19,20,41} seem to increase the severity of COVID-19 symptoms in patients. This observation led scientists to examine whether certain cardiovascularly related medications alter patients' risk of SARS-CoV-2 infection and/or COVID-19 severity. (It is worth noting that classifications of "severity" vary among studies. Distinctions include normal vs high protein [troponin] concentrations in the blood, nonsevere vs severe disease, nonhospitalized patients vs hospitalized patients, non-intensive care unit [ICU] patients vs ICU patients, and survivors vs nonsurvivors.^{17,29})

ACE Inhibitors and Angiotensin Receptor Blockers

Some antihypertensive medications are the focus of such research. Many Americans (13% to nearly 50%, depending on definitions and the data source) have hypertension.^{42,45,46} This percentage increases as one ages.⁴⁵ To lower high blood pressure, physicians may prescribe ACE inhibitors (ACEIs) and/or angiotensin receptor blockers (ARBs). These medications minimize production of angiotensin II and block angiotensin II's interaction with receptors, respectively (Figure 2), thereby preventing the vasoconstriction that elevates blood pressure (Figure 2).

However, certain ACEIs and ARBs likely increase levels and activity of ACE2 throughout the body.⁴⁷⁻⁴⁹ Because ACE2 is the receptor for SARS-CoV-2 binding, it is important to ascertain whether ACEIs and ARBs alter patients' risk of contracting SARS-CoV-2 and/or developing COVID-19. Mackey et al⁵⁰ provide regular updates on newly published research articles pertaining to this topic. Articles sampled from this compilation show wide variability in the study design.^{44,50-54} Differences include variations in comparison groups, ethnic groups, statistical analyses, sample sizes, dates of studies (before or after widespread COVID-19 testing), lengths of time on ACEIs or ARBs, attention levels paid to confounding health issues, and definitions of "severe COVID-19." Some articles are retrospective observational studies. Such studies are subjective to selection bias; for example, a cohort of hypertensive patients tested for COVID-19 leaves out hypertensive patients who did not get tested because they were asymptomatic. Identification of patients prescribed ACEIs or ARBs also assumes that the patients take these medications as prescribed, which may not be the case.

Nevertheless, most studies come to the same conclusion: use of ACEIs or ARBs *does not* increase one's risk of SARS-CoV-2 infection or development of severe COVID-19.^{55,56} Currently, the Centers for Disease Control and Prevention (CDC) and other cardiovascular health organizations advise patients to continue their ACEI or ARB prescriptions, unless advised otherwise by a physician.^{57,58} Clinical trials concerning ACEIs, ARBs, and COVID-19 are ongoing.⁵⁹

Interestingly, the ACEI- and ARB-induced increase in ACE2 expression levels may be advantageous to patients.^{52,54} It may counteract virally induced reduction of ACE2 levels and thereby preserve the production of angiotensin (1-7), which lowers elevated blood pressure, promotes structural health of blood vessels and ECs, protects against cardiac hypertrophy, and may enhance blood cell production.^{60,61}

COVID-19 Treatments and Cardiac Health Risks

Some medications—lopinavir/ritonavir, hydroxychloroquine (HCQ), favipiravir, remdesivir, and tocilizumab—were originally developed for other uses but demonstrate various levels of efficacy in treating patients with COVID-19. Lopinavir/ritonavir and HCQ reportedly disrupt SARS-CoV-2's entry into host cells.⁶² Favipiravir and remdesivir likely prevent the replication of the virus's genome.⁶² Tocilizumab reduces inflammation by limiting the effectiveness of pro-inflammatory chemicals.⁶² Last year, a multinational study of more than 10,000 patients examined the effects of some of these drugs on the mortality of patients with COVID-19.⁶³ The tests using HCQ (low doses) and lopinavir/ritonavir were halted prematurely, as no improvements were seen.⁶⁴ Currently, the National Institutes of Health (NIH) recommends against their use as a treatment for COVID-19.^{65,66}

These drugs have been linked to cardiovascular side effects. Lopinavir/ritonavir, HCQ, favipiravir and remdesivir may cause arrhythmias.^{29,67-69} Lopinavir/ritonavir may trigger MIs.⁷⁰ Furthermore, lopinavir/ritonavir and tocilizumab may compromise the effectiveness of cardiovascular medications.^{29,71} These cardiovascular risks are inferred primarily from a small number of studies with a small number of subjects without COVID-19. A more robust examination of these drugs' cardiovascular effects in patients with COVID-19 has begun in several clinical trials funded by the NIH.²⁹

CONCLUSION

Approximately 1.5 years have passed since SARS-CoV-2 and COVID-19 were identified.^{1,72,73} In this time, much scientific understanding of SARS-CoV-2 infection patterns and COVID-19 comorbidities has been acquired. Improved treatment procedures enhance patients' prognoses, and awareness of drug side effects likely reduces health complications. This article

illuminates the landscape of SARS-CoV-2 and COVID-19 in relationship with the cardiovascular system and provides a biological foundation to support readers as they engage with the burgeoning quantity of scientific studies on this topic. Indeed, the necessity of continued research remains. Some current information is conjecture, drawn from studies on the first severe acute respiratory syndrome coronavirus or in patients without COVID-19. Other knowledge is based on only a few small studies and needs stronger support. Longitudinal studies are necessary to determine the long-term effects of SARS-CoV-2 and COVID-19 on human health. Regardless, the approval of effective SARS-CoV-2 vaccines,^{74,75} enhancements to patient care, and funded clinical trials provide hope for a future in which SARS-CoV-2 infection rates decline, patient mortality decreases, and life without social-distancing restrictions resumes.

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References

- Zhou P, Yang XL, Wang XG, et al. A pneumonia outbreak associated with a new coronavirus of probable bat origin. *Nature*. 2020;579(7798):270-273. doi:10.1038/s41586-020-2012-7
- Shang J, Ye G, Shi K, et al. Structural basis of receptor recognition by SARS-CoV-2. *Nature*. 2020;581(7807):221-224. doi:10.1038/s41586-020-2179-y
- Yan R, Zhang Y, Li Y, Xia L, Guo Y, Zhou Q. Structural basis for the recognition of SARS-CoV-2 by full-length human ACE2. *Science*. 2020;367(6485):1444-1448. doi:10.1126/science.abb2762
- Hoffmann M, Kleine-Weber H, Schroeder S, et al. SARS-CoV-2 cell entry depends on ACE2 and TMPRSS2 and is blocked by a clinically proven protease inhibitor. *Cell*. 2020;181(2):271-280, e8. doi:10.1016/j.cell.2020.02.052
- Wang Q, Zhang Y, Wu L, et al. Structural and functional basis of SARS-CoV-2 entry by using human ACE2. *Cell*. 2020;181(4):894-904, e9. doi:10.1016/j.cell.2020.03.045
- Chen L, Li X, Chen M, Feng Y, Xiong C. The ACE2 expression in human heart indicates new potential mechanism of heart injury among patients infected with SARS-CoV-2. *Cardiovasc Res*. 2020;116(6):1097-1100. doi:10.1093/cvr/cvaa078
- Nicin L, Abplanalp WT, Mellentin H, et al. Cell type-specific expression of the putative SARS-CoV-2 receptor ACE2 in human hearts. *Eur Heart J*. 2020;41(19):1804-1806. doi:10.1093/eurheartj/ehaa311
- Litvinuková M, Talavera-López C, Maatz H, et al. Cells of the adult human heart. *Nature*. 2020;588(7838):466-472. doi:10.1038/s41586-020-2797-4
- Gallagher PE, Ferrario CM, Tallant EA. Regulation of ACE2 in cardiac myocytes and fibroblasts. *Am J Physiol-Heart Circ Physiol*. 2008;295(6):H2373-H2379. doi:10.1152/ajpheart.00426.2008
- Pérez-Bermejo JA, Kang S, Rockwood SJ, et al. SARS-CoV-2 infection of human iPSC-derived cardiac cells predicts novel cytopathic features in hearts of COVID-19 patients. *Sci Transl Med*. Published online March 15, 2021. doi:10.1126/scitranslmed.abb7872
- Hikmet F, Méar L, Edvinsson Å, Micic P, Uhlén M, Lindskog C. The protein expression profile of ACE2 in human tissues. *Mol Syst Biol*. 2020;16(7):e9610. doi:10.15252/msb.20209610
- Hamming I, Timens W, Bulthuis MLC, Lely AT, Navis GJ, van Goor H. Tissue distribution of ACE2 protein, the functional receptor for SARS coronavirus. A first step in understanding SARS pathogenesis. *J Pathol*. 2004;203(2):631-637. doi:10.1002/path.1570
- Bertram S, Heurich A, Lavender H, et al. Influenza and SARS-coronavirus activating proteases TMPRSS2 and HAT are expressed at multiple sites in human respiratory and gastrointestinal tracts. *PLoS One*. 2012;7(4):e35876. doi:10.1371/journal.pone.0035876
- Zheng J, Wang Y, Li K, Meyerholz DK, Allamargot C, Perlman S. Severe acute respiratory syndrome coronavirus 2-induced immune activation and death of monocyte-derived human macrophages and dendritic cells. *J Infect Dis*. 2021;223:785-795. doi:10.1093/infdis/jiaa753
- Akhmerov A, Marbán E. COVID-19 and the heart. *Circ Res*. 2020;126(10):1443-1455. doi:10.1161/CIRCRESAHA.120.317055
- Atri D, Siddiqi HK, Lang JP, Nauffal V, Morrow DA, Bohula EA. COVID-19 for the cardiologist: basic virology, epidemiology, cardiac manifestations, and potential therapeutic strategies. *JACC Basic Transl Sci*. 2020;5(5):518-536. doi:10.1016/j.jacbs.2020.04.002
- Guzik TJ, Mohiddin SA, Dimarco A, et al. COVID-19 and the cardiovascular system: implications for risk assessment, diagnosis, and treatment options. *Cardiovasc Res*. 2020;116(10):1666-1687. doi:10.1093/cvr/cvaa106
- Wang D, Hu B, Hu C, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. *JAMA*. 2020;323(11):1061-1069. doi:10.1001/jama.2020.1585
- Lala A, Johnson KW, Januzzi JL, et al. Prevalence and impact of myocardial injury in patients hospitalized with COVID-19 infection. *J Am Coll Cardiol*. 2020;76(5):533-546. doi:10.1016/j.jacc.2020.06.007
- Casas-Rojo JM, Antón-Santos JM, Millán-Núñez-Cortés J, et al. Clinical characteristics of patients hospitalized with COVID-19 in Spain: results from the SEMI-COVID-19 registry. *Rev Clínica Esp Engl Ed*. 2020;220(8):480-494. doi:10.1016/j.rceng.2020.07.003
- Inciardi RM, Lupi L, Zaccone G, et al. Cardiac involvement in a patient with coronavirus disease 2019 (COVID-19). *JAMA Cardiol*. 2020;5(7):819-824. doi:10.1001/jamacardio.2020.1096
- Robinson FA, Mihealsick Ryan P, Wagener BM, et al. Role of angiotensin-converting enzyme 2 and pericytes in cardiac complications of COVID-19 infection. *Am J Physiol-Heart Circ Physiol*. 2020;319(5):H1059-H1068. doi:10.1152/ajpheart.00681.2020
- Long H, Nie L, Xiang X, et al. D-dimer and prothrombin time are the significant indicators of severe COVID-19 and poor prognosis. *BioMed Res Int*. 2020;2020:1-10. doi:10.1155/2020/6159720
- Chan NC, Weitz JI. COVID-19 coagulopathy, thrombosis, and bleeding. *Blood*. 2020;136(4):381-383. doi:10.1182/blood.2020007335
- Al-Samkari H, Karp Leaf RS, Dzik WH, et al. COVID-19 and coagulation: bleeding and thrombotic manifestations of SARS-CoV-2 infection. *Blood*. 2020;136(4):489-500. doi:10.1182/blood.2020006520
- Tedeschi D, Rizzi A, Biscaglia S, Tumscitz C. Acute myocardial infarction and large coronary thrombosis in a patient with COVID-19. *Catheter Cardiovasc Interv*. 2021;97(2):272-277. doi:10.1002/ccd.29179
- Guagliumi G, Sonzogno A, Pescetelli I, Pellegrini D, Finn AV. Microthrombi and ST-segment-elevation myocardial infarction in COVID-19. *Circulation*. 2020;142(8):804-809. doi:10.1161/CIRCULATIONAHA.120.049294
- Stafanini GG, Montorfano M, Trabattoni D, et al. ST-elevation myocardial infarction in patients with COVID-19. *Circulation*. 2020;141(25):2113-2116. doi:10.1161/CIRCULATIONAHA.120.047525
- Driggin E, Madhavan MV, Bikdeli B, et al. Cardiovascular considerations for patients, health care workers, and health systems during the COVID-19 pandemic. *J Am Coll Cardiol*. 2020;75(18):2352-2371. doi:10.1016/j.jacc.2020.03.031
- Crackower MA, Sarao R, Oudit GY, et al. Angiotensin-converting enzyme 2 is an essential regulator of heart function. *Nature*. 2002;417(6891):822-828. doi:10.1038/nature00786

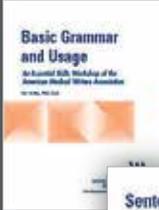
31. Kuba K, Imai Y, Rao S, et al. A crucial role of angiotensin converting enzyme 2 (ACE2) in SARS coronavirus-induced lung injury. *Nat Med*. 2005;11(8):875-879. doi:10.1038/nm1267
32. Wang H, Yang P, Liu K, et al. SARS coronavirus entry into host cells through a novel clathrin- and caveolae-independent endocytic pathway. *Cell Res*. 2008;18(2):290-301. doi:10.1038/cr.2008.15
33. Gheblawi M, Wang K, Viveiros A, et al. Angiotensin-converting enzyme 2: SARS-CoV-2 receptor and regulator of the renin-angiotensin system. *Circ Res*. 2020;126(10):1456-1474. doi:10.1161/CIRCRESAHA.120.317015
34. Armulik A, Genové G, Betsholtz C. Pericytes: developmental, physiological, and pathological perspectives, problems, and promises. *Dev Cell*. 2011;21(2):193-215. doi:10.1016/j.devcel.2011.07.001
35. Lee LL, Chintalgattu V. Pericytes in the heart. In: Birbrair A, ed. *Pericyte Biology in Different Organs. Adv Exp Med Biol*. Springer; 2019:187-210. doi:10.1007/978-3-030-11093-2_11
36. Hashitani H, Mitsui R. Role of pericytes in the initiation and propagation of spontaneous activity in the microvasculature. In: Hashitani H, Lang RJ, eds. *Smooth Muscle Spontaneous Activity: Physiological and Pathological Modulation. Adv Exp Med Biol*. Springer; 2019:329-356. doi:10.1007/978-981-13-5895-1_14
37. ARDS - symptoms and causes. Mayo Clinic. Accessed January 10, 2021. <https://www.mayoclinic.org/diseases-conditions/ards/symptoms-causes/syc-20355576>
38. Zhang J, Tecson KM, McCullough PA. Endothelial dysfunction contributes to COVID-19-associated vascular inflammation and coagulopathy. *Rev Cardiovasc Med*. 2020;21(3):315-319. doi:10.31083/j.rcm.2020.03.126
39. Jose RJ, Manuel A. COVID-19 cytokine storm: the interplay between inflammation and coagulation. *Lancet Respir Med*. 2020;8(6):e46-e47. doi:10.1016/S2213-2600(20)30216-2
40. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet*. 2020;395(10229):1054-1062. doi:10.1016/S0140-6736(20)30566-3
41. Gold JAW, Wong KK, Szablewski CM, et al. Characteristics and clinical outcomes of adult patients hospitalized with COVID-19—Georgia, March 2020. *MMWR Morb Mortal Wkly Rep*. 2020;69. doi:10.15585/mmwr.mm6918e1
42. Raised blood pressure (SBP \geq 140 OR DBP \geq 90) (age-standardized estimate). The Global Health Observatory. Published 2021. Accessed January 9, 2021. [https://www.who.int/data/gho/data/indicators/indicator-details/GHO/raised-blood-pressure-\(sbp=140-or-dbp=90\)-\(age-standardized-estimate\)](https://www.who.int/data/gho/data/indicators/indicator-details/GHO/raised-blood-pressure-(sbp=140-or-dbp=90)-(age-standardized-estimate))
43. Centers for Disease Control and Prevention. Heart disease facts. Centers for Disease Control and Prevention. Published September 8, 2020. Accessed January 9, 2021. <https://www.cdc.gov/heartdisease/facts.htm>
44. Bean DM, Kraljevic Z, Searle T, et al. Angiotensin-converting enzyme inhibitors and angiotensin II receptor blockers are not associated with severe COVID-19 infection in a multi-site UK acute hospital trust. *Eur J Heart Fail*. 2020;22(6):967-974. doi:10.1002/ehf.1924
45. Fryar CD, Ostchega Y, Hales CM, Zhang G, Kruszon-Moran D. Hypertension prevalence and control among adults: United States, 2015–2016. cdc.gov. Published October 2017. Accessed April 8, 2021. <https://www.cdc.gov/nchs/products/databriefs/db289.htm>
46. American Heart Association News. Is high blood pressure inevitable? Here's how to keep it in check. www.heart.org. Published May 18, 2020. Accessed January 9, 2021. <https://www.heart.org/en/news/2020/05/18/is-high-blood-pressure-inevitable-heres-how-to-keep-it-in-check>
47. Vaduganathan M, Vardeny O, Michel T, McMurray JVV, Pfeffer MA, Solomon SD. Renin-angiotensin-aldosterone system inhibitors in patients with COVID-19. *N Engl J Med*. 2020;382:1653-1659. doi:10.1056/NEJMs2005760
48. Ferrario CM, Jessup J, Chappell MC, et al. Effect of angiotensin-converting enzyme inhibition and angiotensin II receptor blockers on cardiac angiotensin-converting enzyme 2. *Circulation*. 2005;111(20):2605-2610. doi:10.1161/CIRCULATIONAHA.104.510461
49. Igase M, Strawn WB, Gallagher PE, Geary RL, Ferrario CM. Angiotensin II AT1 receptors regulate ACE2 and angiotensin-(1-7) expression in the aorta of spontaneously hypertensive rats. *Am J Physiol-Heart Circ Physiol*. 2005;289(3):H1013-H1019. doi:10.1152/ajpheart.00068.2005
50. Mackey K, King VJ, Gurley S, et al. Risks and impact of angiotensin-converting enzyme inhibitors or angiotensin-receptor blockers on SARS-CoV-2 infection in adults. *Ann Intern Med*. 2020;173(3):195-203. doi:10.7326/M20-1515
51. Dublin S, Walker R, Floyd JS, et al. Renin-angiotensin-aldosterone system inhibitors and COVID-19 infection or hospitalization: a cohort study. *Am J Hypertens*. Published online October 13, 2020. doi:10.1093/ajh/hpaa168
52. Palazzuoli A, Mancone M, Ferrari GM, et al. Antecedent administration of angiotensin-converting-enzyme inhibitors or angiotensin II receptor antagonists and survival after hospitalization for COVID-19 syndrome. *J Am Heart Assoc*. 2020;9(22):e017364. doi:10.1161/JAHA.120.017364
53. Xu J, Huang C, Fan G, et al. Use of angiotensin-converting enzyme inhibitors and angiotensin II receptor blockers in context of COVID-19 outbreak: a retrospective analysis. *Front Med*. 2020;14(5):601-612. doi:10.1007/s11684-020-0800-y
54. Zhang P, Zhu L, Cai J, et al. Association of inpatient use of angiotensin-converting enzyme inhibitors and angiotensin II receptor blockers with mortality among patients with hypertension hospitalized with COVID-19. *Circ Res*. 2020;126(12):1671-1681. doi:10.1161/CIRCRESAHA.120.317134
55. Reynolds HR, Adhikari S, Pulgarin C, et al. Renin-angiotensin-aldosterone system inhibitors and risk of COVID-19. *N Engl J Med*. 2020;382(25):2441-2448. doi:10.1056/NEJMoa2008975
56. Fernández-Ruiz I. RAAS inhibitors do not increase the risk of COVID-19. *Nat Rev Cardiol*. 2020;17(7):383-383. doi:10.1038/s41569-020-0401-0
57. Centers for Disease Control and Prevention. COVID-19 and your health: people with certain medical conditions. Centers for Disease Control and Prevention. Published February 11, 2020. Accessed January 2, 2021. <https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical-conditions.html>
58. Patients taking ACE-i and ARBs who contract COVID-19 should continue treatment, unless otherwise advised by their physician. American Heart Association. Published March 17, 2020. Accessed January 2, 2021. <https://newsroom.heart.org/news/patients-taking-ace-i-and-arbs-who-contract-covid-19-should-continue-treatment-unless-otherwise-advised-by-their-physician>
59. Search of: COVID-19, ACE, ARB. ClinicalTrials.gov. Published 2021. Accessed January 11, 2021. https://clinicaltrials.gov/ct2/results?cond=Covid19&term=ACE%2C+ARB&type=&rslt=&recrs=a&recrs=f&recrs=d&age_v=&gndr=&intr=&titles=&outc=&spons=&lead=&id=&cntry=&state=&city=&dist=&locn=&rsub=&strd_s=&strd_e=&prcd_s=&prcd_e=&sfpd_s=&sfpd_e=&rfrpd_s=&rfrpd_e=&lupd_s=&lupd_e=&sort=
60. Santos RA. Angiotensin-(1-7). *Hypertension*. 2014;63(6):1138-1147. doi:10.1161/HYPERTENSIONAHA.113.01274
61. Iusuf D, Henning RH, van Gilst WH, Roks AJM. Angiotensin-(1-7): pharmacological properties and pharmacotherapeutic perspectives. *Eur J Pharmacol*. 2008;585(2-3):303-312. doi:10.1016/j.ejphar.2008.02.090
62. Vijayvargiya P, Garrigos ZE, Almeida NEC, Gurram PR, Stevens RW, Razonable RR. Treatment considerations for COVID-19. *MAYO Clin Proc*. 2020;95(7):1454-1466.
63. WHO Solidarity Trial Consortium. Repurposed antiviral drugs for COVID-19—interim WHO Solidarity trial results. *N Engl J Med*. 2021;384(6):497-511. doi:10.1056/NEJMoa2023184
64. WHO discontinues hydroxychloroquine and lopinavir/ritonavir treatment arms for COVID-19. World Health Organization. Published July 4, 2020. Accessed April 7, 2021. <https://www.who.int/news/item/04-07-2020-who-discontinues-hydroxychloroquine-and-lopinavir-ritonavir-treatment-arms-for-covid-19>

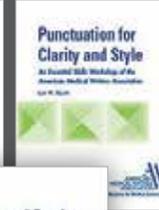
65. Chloroquine or hydroxychloroquine with or without azithromycin. COVID-19 Treatment Guidelines. Published October 9, 2020. Accessed October 31, 2020. <https://www.covid19treatmentguidelines.nih.gov/antiviral-therapy/chloroquine-or-hydroxychloroquine-with-or-without-azithromycin/>
66. Lopinavir/ritonavir and other HIV protease inhibitors. COVID-19 treatment guidelines. National Institutes of Health. Published February 11, 2021. Accessed April 7, 2021. <https://www.covid19treatmentguidelines.nih.gov/antiviral-therapy/lopinavir-ritonavir-and-other-hiv-protease-inhibitors/>
67. Naksuk N, Lazar S, Peeraphatdit TB. Cardiac safety of off-label COVID-19 drug therapy: a review and proposed monitoring protocol. *Eur Heart J Acute Cardiovasc Care*. 2020;9(3):215-221. doi:10.1177/2048872620922784
68. Hooks M, Bart B, Vardeny O, Westanmo A, Adabag S. Effects of hydroxychloroquine treatment on QT interval. *Heart Rhythm*. 2020;17(11):1930-1935. doi:10.1016/j.hrthm.2020.06.029
69. Costedoat-Chalumeau N, Hulot JS, Amoura Z, et al. Heart conduction disorders related to antimalarials toxicity: an analysis of electrocardiograms in 85 patients treated with hydroxychloroquine for connective tissue diseases. *Rheumatology*. 2007;46(5):808-810. doi:10.1093/rheumatology/kel402
70. Bavinger C, Bendavid E, Niehaus K, et al. Risk of cardiovascular disease from antiretroviral therapy for HIV: a systematic review. Landay A, ed. *PLoS One*. 2013;8(3):e59551. doi:10.1371/journal.pone.0059551
71. Kaletra tablets and oral solution. AbbVie. Accessed January 9, 2021. <https://www.rxabbvie.com/pdf/kaletratabpi.pdf>
72. Zhu N, Zhang D, Wang W, et al. A novel coronavirus from patients with pneumonia in China, 2019. *N Engl J Med*. 2020;382(8):727-733. doi:10.1056/NEJMoa2001017
73. Naming the coronavirus disease (COVID-19) and the virus that causes it. World Health Organization. Accessed September 10, 2020. [https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/naming-the-coronavirus-disease-\(covid-2019\)-and-the-virus-that-causes-it](https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/naming-the-coronavirus-disease-(covid-2019)-and-the-virus-that-causes-it)
74. Office of the Commissioner. Pfizer-BioNTech COVID-19 vaccine. US Food and Drug Administration. Published online January 5, 2021. Accessed January 11, 2021. <https://www.fda.gov/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/pfizer-biontech-covid-19-vaccine>
75. Office of the Commissioner. Moderna COVID-19 vaccine. US Food and Drug Administration. Published online January 6, 2021. Accessed January 11, 2021. <https://www.fda.gov/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/moderna-covid-19-vaccine>

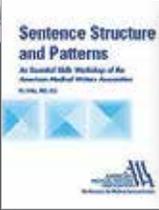
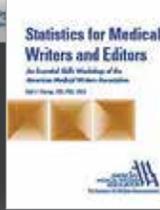


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Little-Known Tips for Using Microsoft Word for Clear Writing

Monisha Arya, MD¹; Sheeva Azma, MS² / ¹Independent Medical Writer & Editor, Arya Communications, Houston, TX; ²Independent Science Writer & Editor, Fancy Comma, LLC, Oklahoma City, OK

Introduction

With over 1.2 billion users,¹ Microsoft Word is arguably the most commonly used word processing and editing software throughout the world.

Medical writers use Microsoft Word daily for a variety of tasks, including manuscript preparation, proofing of patient-facing public health documents, medical presentations, and more. They are proficient with basic functionalities of Word, but they may not be aware of more advanced features.

Here, we provide our best tips for producing better writing using Microsoft Word. These tips apply both to the current version of Word included in Microsoft Office 365 and the standalone version currently available, called Microsoft Word 2019, which is part of Microsoft Office 2019.

Monisha's Tip: Use Advanced Proofing Features of Microsoft Word

Clear and impactful medical writing requires education and experience in medicine or health, writing skills and talent, attention to detail, and passion. Microsoft Word's little-known proofing features can be another key to producing great copy. Microsoft Word's hidden proofing features take a bit of time to find, but they are well worth the effort.

It was many years into my medical writing career that I learned about Microsoft Word's advanced proofing features. That is because these features are "hidden" and are not enabled by default.

Did you know that Microsoft Word can alert you to jargon, simpler language, and passive voice? This Microsoft Word proofing review will make suggestions for you to accept or ignore. Keep in mind the style guide for your target publication or for your target audience. For example, sometimes passive voice may be acceptable in medical and scientific writing; if the proofing review suggests you have used passive voice, consider whether it is appropriate and accept or reject Microsoft Word's suggestion.

I run a complete proofing check on all of my writing products. Here is how to get started:

Monisha's Little-Known Tips to Uncover Hidden Proofing Features in Microsoft Word

Open a blank document in Microsoft Word.

1. Go to File and select "Options" at the very bottom of the menu.
2. Under Word Options, select "Proofing" (Figure 1).
3. Go the section entitled, "When correcting spelling and grammar in Word."
4. Ensure that all boxes are checked.
5. For Writing Style, select the drop-down option for "Grammar & Refinements" (This may also be listed as "Grammar & More"; in Word 2010, it is listed as "Grammar and Style").
6. Click on "Settings..." (Here is where a lot of the proofing features live!) (Figure 2 on next page).

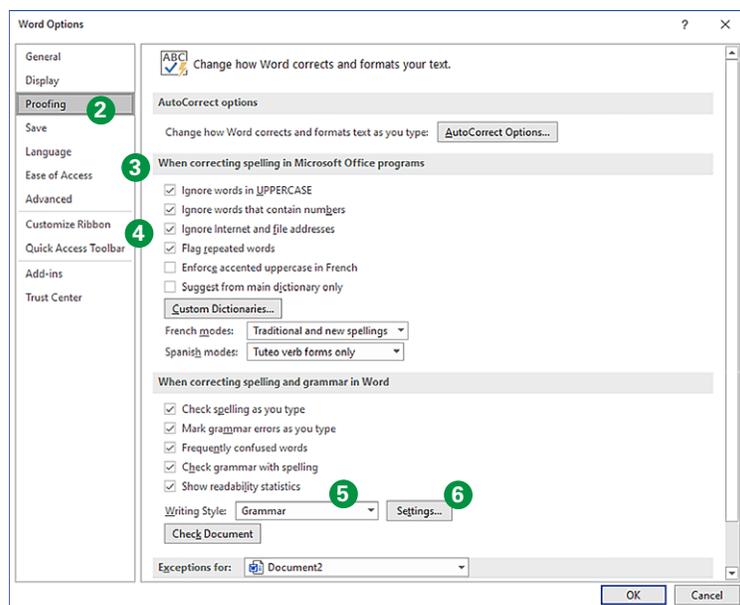


Figure 1. Microsoft Word's proofing options.

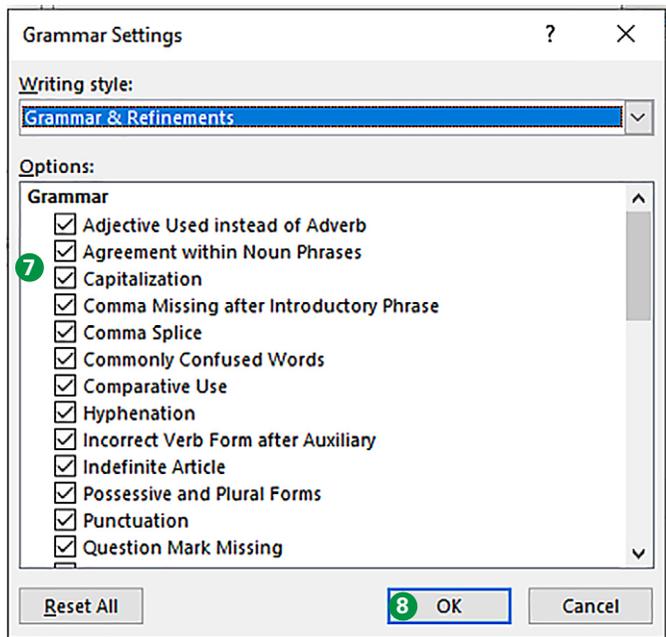


Figure 2. Microsoft Word’s “Grammar and Refinements” menu bar contains all of the little-known proofing features of the popular software.

7. There are over 100 (!) features listed! *I select ALL of them.*

Remember that the style guide of your target publication or audience can help guide which “suggested” changes you should accept after Microsoft Word performs the review.

8. Click “OK” to save changes.

9. Click “Check Document” (Figure 3) to allow Microsoft Word to do a new review (This may also be listed as “Recheck Document.”).

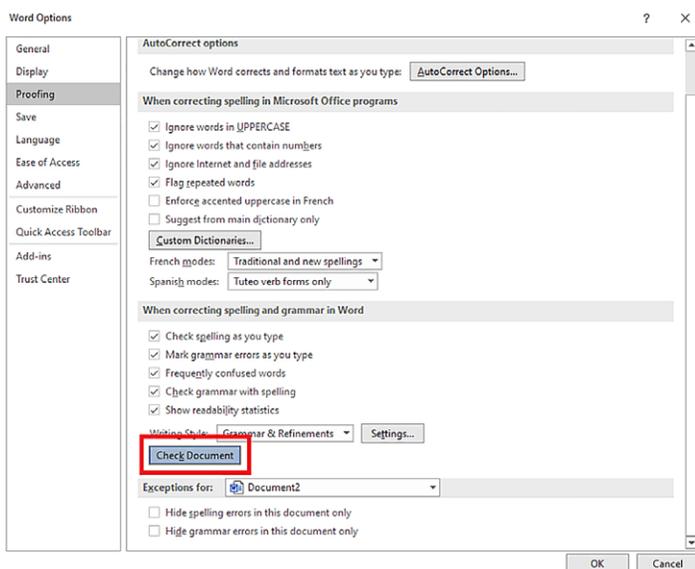


Figure 3. Once you select your desired proofing options, remember to click “Check Document” to apply them to your file.

After clicking on “Check Document,” another dialog box may appear asking you if you wish to reset the Microsoft Word spelling and grammar checker and apply the new settings. You will need to click “Yes” here.

There is another way to get to the Proofing features in Microsoft Word. You may also see the Editor icon in the Review panel of your version of Microsoft Word (Figure 4). You can click on this button, and then click “Settings.” Then, follow the steps above starting at number 6.

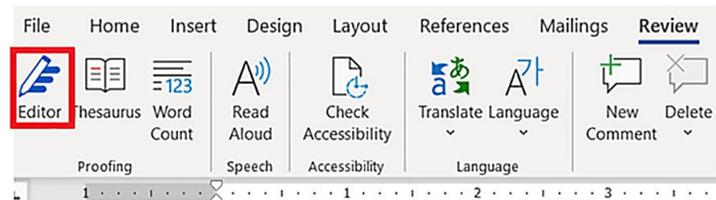


Figure 4. Clicking the “Editor” button in the Review tab of Microsoft Word’s menu bar is an easy way to access these little-known proofing options.

Of course, the Microsoft Word proofing feature is not perfect, and will not find all elements that you could (or should) refine to make your writing clearer and impactful. The proofing feature also sometimes recommends changes that you should not make in the context of your document. I have found that the proofing feature still misses some grammar or syntax mistakes. Using the feature is a start, and you may need to make additional refinements to add a human element to proofing.

Sheeva’s Tip: Use Microsoft Word’s “Read Aloud” Feature

I am always learning new things, even after using Microsoft Word and other Office suite products for over 2 decades. Recently, I learned that Microsoft Office 2019 has a “Read Aloud” function which will read your Word file out loud. This can be useful in editing if you perhaps need to do a quick pass to catch errors in the text as it is being read aloud. With the Read Aloud function, you can sit back as Microsoft reads through the document.

Our brains use different cognitive processes to read text from a page compared with listening to text being read out loud. A study out of the University of Perugia in Italy suggests that actively listening to text being read out loud may lead to more “intense and deeper information processing,” according to a report by the British Broadcasting Corporation.²

Sheeva’s Tip to Reveal the Read Aloud Feature in Microsoft Word

The Read Aloud function of Microsoft Word 2019 can be found in the Review tab (Figure 5).

When you click the Read Aloud button, a sidebar pops up with controls shown in Figure 6.

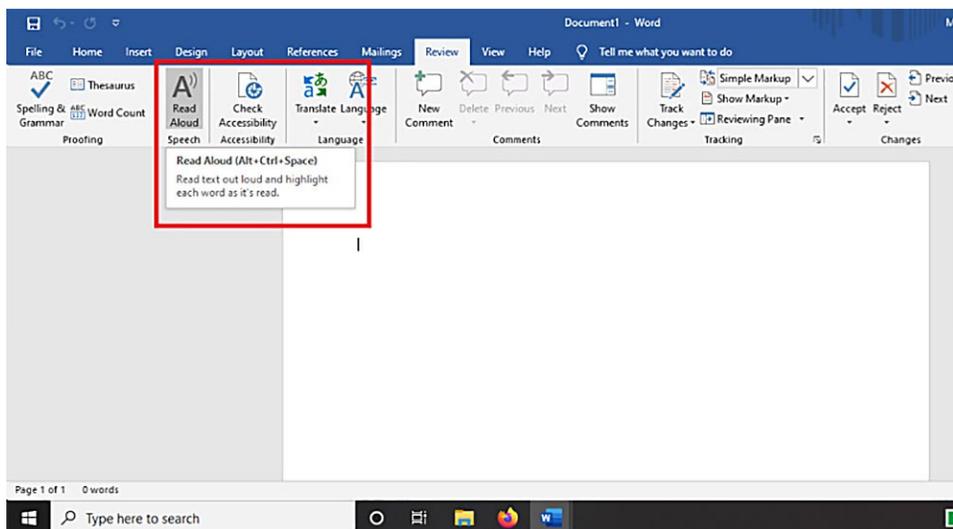


Figure 5. The “Review” tab contains the Read Aloud option in Microsoft Word.



Figure 6. Microsoft Word’s Read Aloud function button controls. From left to right, they are Back, Play/Pause, Forward, Settings, and Exit.

The settings icon allows you to select from different reading voices and change reading speed. If you are, like me, using the American English version of Microsoft Word, you can choose from several reading voices, including 2 male voices (Microsoft David and Microsoft Mark) and a female voice (Microsoft Zira).

Microsoft Word’s Read Aloud feature can be useful to quickly review a document for errors. When you catch an error, you can pause Read Aloud, make the changes, move your cursor back to where you want to start reading, and use the controls to restart Read Aloud.

There are a couple of disadvantages to the Read Aloud function. One downside of the Read Aloud function is that, if you try to type or make edits to the document while it is being read, you risk accidentally deleting text as the cursor tracks the text being read. You must first exit or pause Read Aloud mode before making any changes to the document.

Another downside of using Read Aloud is that it does not work seamlessly with the Track Changes feature in Word. When there are tracked changes in your document, the Read Aloud function simply reads the text that is on the page, whether it has been modified (deleted using Track Changes) or not. So, it is best to use a final copy of your text that does not have tracked changes in order to achieve the best results with Read Aloud.

We hope that learning about these little-known tools will help you optimize your use of Microsoft Word and help you write more clearly.

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References

1. Callaham J. There are now 1.2 billion Office users and 60 million Office 365 commercial customers. Windows Central website. Published 2016. Accessed January 1, 2021. <https://www.windowscentral.com/there-are-now-12-billion-office-users-60-million-office-365-commercial-customers>
2. Hardach S. Why you should read this out loud. BBC website. Published 2020. Accessed January 1, 2021. <https://www.bbc.com/future/article/20200917-the-surprising-power-of-reading-aloud>

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Phyllis Minick

Q What are the pros and cons of different types of medical writing (ie, pharmaceutical/biotech, regulatory, managed-care industry, the publishing industry, public relations, lay press, public health, nonprofits, and hospital/university)?

A My 20 years as a full-time writer/editor at a research facility attached to a hospital included the preparation of texts for journal publication, talks for meetings, editing of books, and management of 13 annual reports. This wide range of experiences led to not only subsequent employment at a pharmaceutical company but also access to contacts as a freelancer for clients in 6 countries. Obvious advantages of the full-time situation, of course, are steady salary, benefits (insurance, etc.), and retirement plan, all based on that of a university medical school. Less obvious is the personal growth in skills and opportunities, for example, company-paid membership in the American Medical Writers Association (AMWA)! The only real disadvantage was time constraints, such as limits on vacation time.

Afterward, when a new Director of the institution replaced me and much of the former staff, my subsequent job was as freelance writer for a commercial pharmaceutical company. Advantageously, the hourly pay was about 1½ times higher than before. Sometimes I could work from home, and because the company freelancers were a team, I could choose amounts of time off. The disadvantage that surprised me was resentment from my full-time colleagues that I could come and go at will.

Finally, I became a roving freelancer. I am still amazed that post docs from early in my full-time research-institution career had advanced to become department heads, particularly in China and Japan, and requested editorial services at my choice of cost/hour. However, that situation included the disadvantage of a lag in time of payment, sometimes weeks or months after completion of a project, because the clients preferred to lump costs together.

This saga would not be complete without citing the advantageous gift of AMWA membership, which provided professional contacts and teaching opportunities that did and still do underlie my career.

— Phyllis Minick

Although I have worked for all of the above industries, I will focus here on the area of my most extensive experience: pharmaceutical/biotech companies. All of these companies need medical communication professionals. Many people think that the industry is all about regulatory affairs; it is not. Regulatory affairs work is its own thing, often quite apart from other areas of the industry. For example, departments aside from regulatory affairs that generate work for writers and editors in a pharma/biotech company may include the following

- Advertising
- Animal sciences
- Biological sciences
- Clinical research
- Corporate communication (public relations)
- Corporate or product development
- Human resources
- Marketing communication
- Medical affairs/medical services
- Medical communication
- Pharmacology
- Professional training and education (for non-MD health care professionals)
- Sales training and communication
- Website management

Thus, one could say that medical communication in pharma/biotech includes virtually every aspect of communication, a wide variety of target audiences, and all media. As an employee and later a freelancer, I have worked for all of these departments.

For years, I contracted directly with the companies, but today, most companies (the larger ones, at least) prefer to hire outside agencies to handle their writing/editing/communication needs. For regulatory affairs and clinical research projects and reports, a contract research organization is used; for most other communication projects, agencies for MedCom, continuing medical education, advertising, or sales training are hired.

As a freelancer, some advantages of contracting directly with a company include more intimate contact with the players; the ability to call an expert in the company any time you need to, generally a higher rate, and a feeling of being

more immediately connected with the entire process, whether it be medical affairs, marketing, or regulatory affairs. When contracting with an outside agency, you are one step removed; you generally are paid a bit less because one must consider the agency's need for profit/markup, and you sometimes get paid late (some agencies even ask the freelancer to wait until they have been paid before paying the freelancer). Moreover, depending on the agency, they may be rather paranoid about allowing you to speak directly with the pharma/biotech client, ie, worried that the company might want to hire you directly. So, usually you must sign a "noncompete" agreement in addition to the nondisclosure agreement, and sometimes negotiations over the reasonableness of such contracts can become complicated.

Regardless of whether you contract with a pharma/biotech company directly or through one of their agencies, there are many advantages to working in this industry, a few of which include

- A chance to work on a wide range of projects and/or therapeutic areas
- A plethora of work because of the vast number of such companies and agencies
- The opportunity to work with intelligent people and teams
- The joy of being able to work on projects that are genuinely interesting and fun (usually when working in MedCom, Marketing, Sales Training)
- Interesting travel opportunities paid by the company
- Helpful education and training
- Generally a higher hourly rate than paid by other industries

There are, of course, also some disadvantages as well. Below are some that are mostly related to regulatory affairs (although some of these can be seen as advantages if you enjoy studying and learning):

- You must study and understand well the industry as a whole, including the process of proving new drugs, devices, or biologicals.
- You need to be comfortably familiar with Food and Drug Administration regulations and guidelines in general as well as those relating to the production of specific types of reports and clinical summaries.
- You should understand thoroughly the structure and contents of an NDA submission (ie, the Common Technical Document), even if you are writing only a specific segment or section of such submission.
- You may end up with a team (in-house or in-agency) filled with tension and fear because their bonuses and raises depend on achieving milestones and deadlines demanding enough to increase your stress level, to say nothing of the horrendous stress level of the associates with whom

you end up working. (In this regard, the agencies do have more burden, because they contract with the companies for extremely high dollars and are liable for errors and omissions for which a freelance writer in pharma/biotech should never accept liability.)

- You could be working with an inept Project Manager and thus find yourself receiving a "data dump" that takes hours to dissect and organize, leading to "scope creep" that requires you to fill the role of Project Manager, which function should pay more; thus, you may have to renegotiate your fees (I charge $\geq 30\%$ more for project management and organization than for writing.)
- You could find yourself in the uncomfortable position of having to tell the company or agency employees that their "ask" would violate ethics as well as regulations. This could be about a particular "spin" the client wants you to create from clinical study results (eg, in a Clinical Study Report or a journal article), claims a marketing group wishes to make in collateral materials for sales representatives and/or health care professionals, hiding or omitting data that are unflattering to the company, and other questionable practices.

Overall, the pluses outweigh the minuses; otherwise, I might have dedicated most of my career to working for nonprofits.

— Cathryn D. Evans

All types of medical writing have pros and cons. Although you should choose the type of medical writing you do, your background, experience, and writing skill are usually more important than your preferences. For example, regulatory writing pays more than other types of medical writing and is in high demand. But with my journalism degrees and my freelance experience in health care content marketing and health journalism, I'm not qualified to do regulatory writing.

Likewise, many freelancers with clinical or scientific degrees and experience wouldn't do well at what's usually considered the more glamorous side of medical writing: public relations, content marketing, most work for patients and the public, and marketing-oriented work for health care professionals. You need very strong writing skills for this type of work.

If you work with the right clients like I do, the pay for this type of work is very good but not usually as high as most other types of medical writing. The deadlines are usually much more reasonable than in other types of medical writing, and there are very few meetings or team-based work, which I like.

There's a lot more freelance work in what I call clinical and scientific medical writing (pharmaceutical/biotech, regulatory, etc.) than the type of work I do. That's good news because most medical writers have clinical or scientific backgrounds.

Learn more about different types of medical writing before deciding what might be right for you. Talk to other freelancers

about what they like and don't like about their work. Look for courses, tutorials, and other opportunities to try types of medical writing that seem interesting to you.

— Lori De Milto

Q Have you offered daily rates to your clients? If so, what are the situations in which daily rates have worked best for you?

A I have never offered daily rates to my clients and would never do this. As freelancers, we need to have time for the inevitable revisions that come in when we aren't expecting them and rush projects for good clients. If we agree to spend a full day doing work for one client, then we either can't serve our other clients or we have to work too much to be productive.

Also, under the Internal Revenue Service standard for independent contractors, "the payer has the right to control or direct only the result of the work, not what will be done and how it will be done." A daily rate could violate this standard. It is also very likely to be a problem in any legislation that might be passed, such as the PRO Act.

In my freelance business, most days, I do work for 2 or 3 clients. Although I occasionally spend all or most of one day or a few days on work for one client, I would never commit myself to doing this by offering a daily rate. A project rate is a much better way to bill clients. It gives clients the cost of the job for budgeting purposes and gives us the flexibility to do the job when it works best for us as long as we meet the deadline.

— Lori De Milto

I have offered daily rates for projects requiring travel, eg, my hourly rate times 8.0 hours per day, including flying/travel time,

regardless of how many hours are actually "worked" that day. If the client wants more than 8-10 hours of work in a single day, I charge my hourly rate for the hours above that. (I do not charge the time for going out to dinner with the group, unless it is a working dinner.) Otherwise, for most projects I simply charge hourly, although for some clients I will produce something for a fixed fee.

— Cathryn D. Evans

I don't think it's good idea to offer clients daily rates because it ties your value to your time, and there's a finite amount of money any client will pay for an hour of your time. Worse yet, the thinking behind a daily rate is that the client's giving you a full day of work, so your day rate should be discounted from your accumulated hourly rate for a day of work.

First of all, the client isn't doing you any favors because tying you up for a day keeps you from being able to juggle the other clients and assignments you have. Second, suggesting you give a client a break for a full day of work implies you don't otherwise have a full day of work on your plate, because if you did, you'd make more money doing that work instead. Whether you really have a full day of work on your plate or not, your client should believe you do and pay you accordingly.

That said, I do use a "daily rate" in my estimates for attending in-person advisory board meetings. Remember when they used to be a thing? My "daily rate" in those circumstances is actually a bit higher than what the client might pay as a cumulative hourly rate. They're taking me away from juggling everything else on my plate, and sometimes, those days can be pretty long. The client is paying for my undivided attention, whether I'm actually in the meeting or traveling across the country to get to the meeting and get home. This also helps ensure that clients only take me out of the office when they really need me.

— Brian Bass



General Principles of Word Usage

Choose the right word for accuracy and clarity.
www.amwa.org/online_learning



AMWA EDUCATION
 Write better. Write now.

.death*

Morgan Katz, DO / Resident Physician, Abington–Jefferson Health

“.death is the easiest note to write,” they told me.

It’s the same for every patient.

They have no pulse, no spontaneous movement.

No breath sounds auscultated. No sign of life.

But the phone call, that’s the hardest part.

How? When? Why? Was it painful?

Am I allowed to say I’m sorry?

Because I really am sorry.

I’m sorry you dropped your dad off,

And didn’t know it was goodbye.

Do we really do no harm?

Blood sticks and drips, central lines hurt.

But maybe dying alone is easier,

They don’t see you at the unimaginable end.

They don’t see your heart kill your kidney,

Gram-negative rods infect your blood.

But I see you. I watch your labs and check your chart.

I dread actually looking at you suffer.

I turn my eyes away from your agonal breath,

But I sit a little longer and hold your hand.

Hoping if I stay for a few more minutes,

You won’t have to do it alone.

.death—will it ever get easier?

Will I ever not feel my throat tighten and tears come when I talk to your family?

But maybe I want the doctor to cry,

Instead of typing .death without adding a single word.

**“.death” is an expandable dot phrase. Dot phrases are used in electronic medical records for a frequently used note or phrase.*

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Three Exercises to Identify Ideal Clients You Can Nurture Into Long-Term Relationships

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Introduction

Freelance medical writers and editors who have long-term relationships with their ideal clients enjoy many benefits.¹ Among them are increased productivity and efficiency, financial stability, and peace of mind. When the expertise, services, availability, and interests of the freelancer match the needs and goals of a new client, the relationship often clicks and the project proceeds smoothly. In such cases, the characteristics of the freelancer and the client likely match in 4 categories: type and topic of project, required time frame, business agreements, and personal compatibility (Figure 1). Ideally, the expertise and interests of the freelancer should match the needs of the client, and the freelancer has sufficient availability to perform the services within the client's requested time frame. The business agreements and fees are

fair to both parties, and the freelancer and the client have good rapport.

Marketing, including advertising and social media, is a common way to acquire clients that desire and need your services,^{2,3} but “a” client isn’t necessarily an “ideal” client. The trick is to find the clients that will be ideal for you. The following 3 exercises will help you build your business by identifying clients that may be ideal for you. For clarification, the term “suitable clients” refers to clients that match many of your preferred characteristics, whereas “preferred clients” match most of your preferred characteristics and avoid most of the negative attributes. “Ideal clients” match all your preferred characteristics and avoid all the negative attributes. Once you have begun working with them, you can nurture them into long-term relationships by using the suggestions outlined in our article “16 Tips for Nurturing Clients Into Long-Term Relationships.”¹

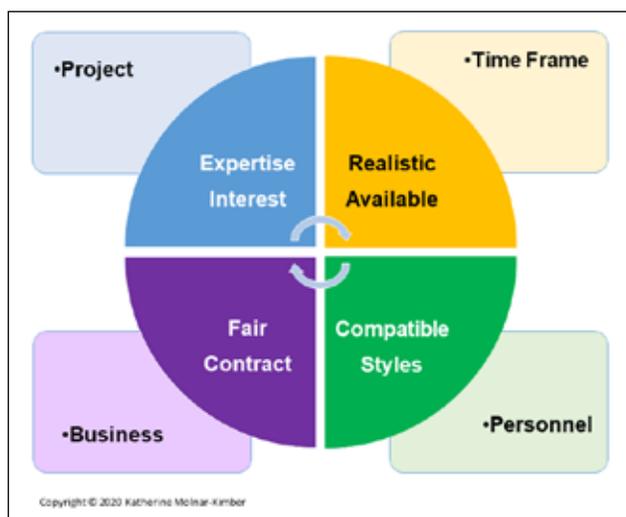


Figure 1. The 4 main aspects of freelancer–client relationships usually align in collaborative, productive business deals, which can be nurtured into long-term freelancer–client relationships.

Exercise 1. Assess Your Strengths, Preferences, and Interests

Exercise 1 focuses on recognizing your strengths and preferences with respect to the types of deliverables, writing styles, subject areas, and project responsibilities. It will also help identify your desired areas for expanding your current range of services. Examples of many deliverables, writing styles, subject areas, and medical writing and project management responsibilities are listed in Table 1. Consider selecting and/or expanding the niches to suit your situation in the Exercise 1 worksheet to consolidate the strengths of your freelance services and goals. Freelancers who know their strengths and preferences have a better chance of getting the work they like and want to do and have a better chance of finding potential clients who need the services they provide.

Table 1. Examples of Medical Writing Deliverables, Writing Styles, Subject Areas, and Project Management Responsibilities

Areas of Strength and Experience	Examples
Deliverables	<ul style="list-style-type: none"> • Regulatory documents • Manuscripts for peer-reviewed journals • Abstracts, posters, podium presentations • Grants • Slide decks • Newsletters • Promotional materials (eg, white papers, websites, branded presentations, video scripts) • Educational materials for health care professionals (eg, CME, guidelines) • Needs assessments for CME • Training materials for sales representatives • Educational materials for patients or the general public (eg, lay summaries, narratives, health news)
Writing Styles	<ul style="list-style-type: none"> • Prescriptive (eg, regulatory documents) • Scientific (eg, manuscripts, video abstracts, educational materials) • Promotional (eg, websites, branded slide decks) • Plain language (eg, patient/caregiver materials)
Subject Areas	<ul style="list-style-type: none"> • Therapeutic areas • Rare diseases • Pharmaceuticals • Devices • Pharmacoeconomics • Managed care • Modalities (eg, biologics, gene therapy)
Project Responsibilities	<ul style="list-style-type: none"> • Writing clear concise content • Annotating references • Formatting references and documents • Project management • Tables and figures • Collaboration with scientific graphic designers • Incorporating revisions and compiling feedback from multiple stakeholders

CME, continuing medical education.

Exercise 1 Worksheet. Assess Your Strengths, Preferences, and Interests to Match to Your Ideal Clients

Area	Degree of Experience			Areas of Interest
	High	Moderate	Low	
Deliverables				
Writing Styles				
Subject Areas				
Project Responsibilities				

Use the examples in Table 1, and your own ideas, to list the areas in which you have experience and interest.

Exercise 2. Identify Suitable Client Types and Preferable Characteristics

Table 2 lists many types of clients that hire freelancers. Exercise 2 focuses on identifying the types of clients with whom you want to work: those who complement your strengths, benefit from your expertise, and match your working style and interests. On the Exercise 2A worksheet, identify clients that need your expertise and abilities, whether that is in a particular type of deliverable, writing style, or subject area. In general, go with

what you know because it is more time-consuming and challenging to produce your best work when you also have to learn as you go. This exercise will also help you identify the specific preferred client characteristics. To spur thinking about the characteristics of your ideal client, we have listed several in Table 3. Consider compiling your own list of ideal characteristics, too. Using the Exercise 2B worksheet, compile a list of 10 potential clients that hire freelancers and would belong to the very strong-match category you identified in Exercise 2A.

Table 2. Examples of Types of Clients That Hire Medical Writers

Types of Clients
<ul style="list-style-type: none"> • Pharmaceutical companies • Biotech companies • Hospitals • Academia • Publishers • Professional societies • Medical communication companies • Medical education companies • Medical advertising agencies • Public relations agencies

Exercise 2A Worksheet. Identify Suitable Client Types and Preferable Characteristics

Very Strong Match	Strong Match	Match

Use the examples in Table 2, and your own ideas, to list the types of clients that match your strengths, preferences, and interests

Table 3. Examples of Client Characteristics Preferred by Freelancers

Preferred Client Characteristics
<ul style="list-style-type: none"> • Recognizing and valuing your expertise • Compensating you accordingly • Paying your invoices on time • Offering projects in your preferred writing style(s), formats, and topics • Providing manageable timelines • Offering contracts that protect both you and the client and allow you to work with your preferred software and hardware on your preferred schedule • Being professional and pleasant

Exercise 2B Worksheet. Assemble a List of Names of Companies With Appropriate Department(s) That Strongly Match Your Interests, Expertise, and Preferred Working Style

Very Strong Match	Contact(s)	Comments

Compile lists of actual client names that fit the very-strong-match category and identify ways to meet representatives.

Consider ways to meet their representatives, such as through professional organizations or LinkedIn. As one strategy to expand your client base, consider marketing your skills for specific deliverables and therapeutic areas to these identified potential clients with preferred or ideal characteristics. There is nothing better than doing work you love for clients you love.

Exercise 3. Identify the Aspects of Projects and Freelancer–Client Relationships You Prefer to Avoid or to Negotiate

In Exercise 1, you identified your preferred types of deliverables, writing styles, subject areas, and project responsibilities. In Exercise 2, you identified the types of clients with whom you want to work, your specific preferred client characteristics, and 5 to 10 clients that match these attributes. Knowing what you do not like is just as important for helping you find and work with ideal clients: hence, Exercise 3.

Challenges can arise in any freelancer–client relationship, and knowledge about which you prefer to avoid or renegotiate can help relieve stress. Table 4 lists some challenging aspects of projects and freelancer–client relationships many freelancers may want to avoid and potential strategies that may help you address or prevent these issues. Consider creating your own list of client attributes you would like to avoid by combining your own ideas with the attributes in Table 4 on the Exercise 3 worksheet. Knowing the aspects of projects and freelancer–client relationships you prefer to avoid, clarify, or negotiate will give you the time and energy to find and work with ideal clients on the projects you love.

Exercise 3 Worksheet. Identify the Aspects of Projects and Freelancer–Client Relationships You Want to Avoid

I Want To Avoid or Negotiate . . .
1.
2.
3.
4.
5.

Use the examples in Table 4, and your own ideas, to list the aspects of projects and freelancer–client relationships you want to avoid or negotiate, so you have more time to find and work with ideal clients.

Summary

Nurturing long-term relationships with ideal clients can help freelancers increase productivity, efficiency, financial stability, and peace of mind. Every prospective client presents an opportunity to explore working relationships and the fit of the freelancer’s services with the expected deliverables. When freelancers are clear about the types of work they like and can do well, their available bandwidth in the requested time frame, and the characteristics of their ideal clients or working relationships, freelancers can more quickly assess whether to proceed with the potentially ideal client. Thus, freelancers can focus their marketing efforts on attracting clients aligned with their expertise and interests. The 3 exercises recommended

Table 4. Examples of Less Desirable Client Characteristics and Potential Strategies to Handle Challenging Situations

Aspects of Projects and Freelancer–Client Relationships to Consider Whether to Avoid	Strategies to Handle Challenging Situations
<ul style="list-style-type: none"> • Chronically tight timelines 	<ul style="list-style-type: none"> • Clarify expectation of scientific depth, goals, audience, and length of deliverable. • Offer a realistic timeline. • Turn down the project.
<ul style="list-style-type: none"> • Chronic project scope creep without compensation 	<ul style="list-style-type: none"> • Write detailed specifications for the project. • For major scope creep, ask for increased compensation. • For repeat clients with this attribute, consider a quote that includes the relevant percentage of scope creep for that client.
<ul style="list-style-type: none"> • Lack of boundaries (eg, emails/phone calls at night or on weekends or holidays) 	<ul style="list-style-type: none"> • Clarify times when you'll check emails.
<ul style="list-style-type: none"> • Lack of consideration (eg, scheduling teleconferences or videoconferences without first asking for your availability) 	<ul style="list-style-type: none"> • If unavailable, then state it. Usually, the client will reschedule the call as needed. • If you know about an upcoming meeting to be scheduled, provide available dates and times proactively. • Provide dates for other commitments (meetings and vacation) ahead of time.
Potential Contract Issues	Strategies to Handle Challenging Situations
<ul style="list-style-type: none"> • Restriction of trade with any and all of company's clients at all their departments and all locations 	<ul style="list-style-type: none"> • Request revision of restriction of trade to the departments and locations of agency's clients for which you actually work or interact with under the agency's supervision. Most companies will agree. • Request that knowledge of their clients be sent on a need-to-know basis.
<ul style="list-style-type: none"> • Contracts that severely limit your ability to work in broad topics with other clients (ie, restrictive of trade in modality or broad therapeutic area such as oncology) 	<ul style="list-style-type: none"> • Negotiate a restriction for a narrower field (eg, PD1 inhibitors in non-small-cell lung cancer). • Offer to accept restriction in exchange for retainer fee.
<ul style="list-style-type: none"> • Contract provides many subjective descriptions before payment, but no definitive milestones (eg, submission to journal) 	<ul style="list-style-type: none"> • Request 20%-30% deposit before beginning project. • In the transfer of copyright clause in the contract, add the phrase "after payment of all invoices." Most companies will accept the change.
<ul style="list-style-type: none"> • No obligation to protect confidentiality of freelancer's confidential information (eg, EIN, bank account information) 	<ul style="list-style-type: none"> • Request revision and most companies will agree as they already do it.
<ul style="list-style-type: none"> • Project specifications do not yet include the responsible party and the procedure for obtaining published articles behind a paywall (implied freelancer's responsibility) 	<ul style="list-style-type: none"> • Ask for clarification, most companies will clarify the responsible party and procedure in their contract or statement of work.

EIN, Employer Identification Number; PD1, programmed cell death 1.

in this article will enable you to assess your strengths, preferences, and interests; identify suitable client types and their preferable characteristics; and identify the aspects of projects and freelancer–client relationships to avoid or negotiate. By doing so, you will be well on your way toward finding the clients that are right for you.

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References

1. Molnar-Kimber K, Drake T, Bass B, Cooper N. 16 Tips for nurturing clients into long-term relationships. *AMWA J.* 2020;35(4):186-189.
2. DeMillo L. *The Mighty Marketer: Your Guide to Making More Money as a Freelance Medical Writer.* Booklocker.com, Inc; 2015.
3. Bly RW. *Bob Bly's Guide to Freelance Writing Success: How to Make \$100,000 a Year as a Freelance Writer and Have the Time of Your Life Doing It.* Filbert Publishing; 2016.

Considerations for Developing Ethical Biomedical Grant Proposals for the National Institutes Of Health

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Introduction

Highly trained medical writers are typically familiar with case studies of scientific misconduct, defined as data fabrication, data falsification, and plagiarism.¹ However, less than 2% of researchers are thought to engage in scientific misconduct.² In recognition that avoiding scientific misconduct is only a small part of research ethics, the National Institutes of Health (NIH) released the following statement in 2009: “[R]esponsible conduct of research is defined as the practice of scientific investigation with integrity. It involves the awareness and application of established professional norms and ethical principles in the performance of all activities related to scientific research.”³ This guiding principle can be used to shape every aspect of our work when developing grant proposals.

The ethical codes from the American Grant Writers’ Association⁴ and the Grant Professionals Association⁵ highlight key ethical issues for grant writers, including avoiding conflicts of interest, following confidentiality guidelines, avoiding plagiarism, and accurately representing the prior work and future capabilities of the funding recipient. They also describe the importance of not allowing payment to be contingent on grant success.

This article addresses additional areas in which we commonly see room for improvement for the medical writer regarding research ethics, with a focus on NIH proposals. The NIH supports the work of over 300,000 biomedical scientists through competitive research funding amounting to \$41.7 billion in 2020,⁶ making the NIH the largest public funder of research worldwide. The NIH received 54,903 research grant proposals in 2019,⁷ many of which were written or edited by professional medical writers.

In the last half decade, the NIH has taken concrete action to improve the responsible conduct of research. In late 2015, the NIH released a major change to the application instructions and review criteria for research projects, called “Implementing Rigor and Transparency in NIH & AHRQ Research Grant Applications,”⁸ which was updated in 2018.⁹

In 2020, the NIH also released an updated Policy for Data Management and Sharing (DMS),¹⁰ which builds upon existing requirements for disseminating research results to the public. These policy statements cover a range of ethical issues in biomedical research, which will be discussed in the next sections. The portions of these policy statements that focus on clinical research design and dissemination of human subjects’ research data will not be covered here, as those topics are beyond the scope of this article.

Given that one of the medical writer’s responsibilities is to ensure that the text is compliant with the funder’s policies, the new NIH policy statements represent important areas in which the medical writer can make a positive impact on ethical conduct in the grant development process.

Research Plan: Enhancing Rigor and Reproducibility

The reviewers will assess 4 elements of rigor.^{8,9,11} Below are descriptions of those elements and recommendations to consider.

1. Rigor of the prior research. When justifying the research aims, typically in the Significance section, applicants may be tempted to focus solely on their work and to emphasize only the positive. However, such a narrow focus can give reviewers a biased impression of the state of the field. Therefore, applicants are encouraged to write a more balanced narrative describing the strengths and weaknesses of prior work in light of the whole field and acknowledging competing viewpoints.

Table 1. Considerations for Describing Rigor of the Prior Research

✓ Does the Significance section refer to work performed by other research groups?
✓ Does the Significance section critically appraise the technical and/or intellectual rigor of prior work by the applicant and by others?
✓ Does the Significance section address whether the prior work led to consensus or controversy?

2. Rigor of the proposed work. When describing the current research plans in the Approach section, applicants must justify their experiments in light of the weaknesses in prior work. This justification could be as obvious as clarifying the research milestone that made the present work possible, or it could be more complicated, especially if the proposed work attempts to overcome a controversy. Asserting the rigor of the proposed work also means providing enough detail on the experimental plans and statistical analysis for reviewers to have confidence that the research team can navigate experimental subtleties to arrive at meaningful answers. Consensus guidelines for reporting research results, such as ARRIVE (Animal Research: Reporting of In Vivo Experiments), can clarify how much detail to include in the study design.^{12,13}

Table 2. Considerations for Describing Rigor of the Proposed Work

✓ Does the Approach section explain how the current research plans fill any knowledge gaps left by prior work?
✓ Does the Approach section provide sufficient methodological detail to demonstrate that the applicants know the pitfalls in their field and how to avoid them?
✓ Does the Approach section provide a statistical analysis plan, including a power analysis when appropriate?

3. Biological variables. To enhance reproducibility, applicants are expected to justify the experimental design and analysis choices in light of the relevant biological variables that may impact the interpretation of results. The NIH uses a broad definition of biological variables, including intrinsic factors (eg, sex, weight, age, and genetic background) and extrinsic factors (eg, food source and housing conditions for animal studies).¹⁴ In particular, for work with human subjects or vertebrate animals, reviewers will evaluate whether the proposal adequately considers sex as a biological variable, and strong justification is required for experiments using only one sex.^{15,16}

Table 3. Considerations for Accounting for Biological Variables

✓ Does the Approach section consider sex as a biological variable in the design and analysis of work with human subjects or vertebrate animals?
✓ Does the Approach section consider additional biological variables, especially those recognized as important in prior research in the field?
✓ Are any proposed analyses based on relevant biological variables sufficiently powered to generate meaningful results?

4. Authentication. Research performed with reagents that are unreliable or mislabeled can lack reproducibility. Thus, applicants must briefly describe the plan for validating key biological and chemical resources, such as cell lines, antibodies, specialty chemicals, and transgenic animals.¹⁷ The goal is

to describe the methods used to validate reagents, including validation performed by commercial sources.

Table 4. Considerations for Describing Authentication of Reagents and Key Resources

✓ Is there a separate Authentication Plan for Key Biological and/or Chemical Resources?
✓ Does the Authentication Plan contain information about reagents and resources and not preliminary data or methods?
✓ Does the Authentication Plan sufficiently detail how and at what frequency key resources will be authenticated?

Data Management and Sharing Plan: Storing and Disseminating Biomedical Research Data

Because science advances through building on past findings, sharing data is a best practice that positively benefits applicants, their fields, and funding agencies. Additionally, because the NIH uses public funds, there is an additional ethical duty to share research findings with the public.

The current NIH Data Sharing Policy¹⁸ went into effect in 2003 and remains in effect until January 2023. Under the 2003 policy, all investigator-initiated applications seeking >\$500,000 in direct costs per year, or as specified in the individual Funding Opportunity Announcement (FOA), are required to include a plan for the sharing of final research data or a justification for why data sharing is not possible (eg, privacy concerns, third-party agreements, and national security issues). This policy was extended in 2014 by the Genomic Data Sharing policy, which establishes expectations for the broad and responsible sharing of genomic research data.¹⁹ Beginning in 2023, all NIH applications must include a DMS Plan and adhere to the updated NIH policy¹⁰ and supplemental information,^{15,20,21} including abiding by FAIR (Findable, Accessible, Interoperable, and Reusable) data principles.²² Because the 2023 policy includes all of the elements of the 2003 policy and expands upon several key concepts, we will focus on the ethical considerations for writing a DMS Plan that complies with the newer guidance.

DMS plans will be evaluated for compliance in the following areas²⁰:

1. Data type, common data standards, and repository selection. Applicants are expected to describe what types of data and accompanying metadata will be preserved and shared and what common data standards will be applied to the shared data and metadata, if applicable. Decisions on what to preserve and share should be based on justifiable ethical, legal, and technical considerations. Applicants are strongly encouraged to use existing data repositories, especially those that follow FAIR principles. The NIH does not always require deposition into an NIH-supported repository, so it can be appropriate to consider third-party repositories.

Table 5. Considerations for Describing Data Types, Common Data Standards, and Repository Selection

✓ Does the DMS Plan briefly summarize the types of data and associated metadata to be preserved and shared?
✓ Does the DMS Plan indicate what common data standards will be applied to the data and metadata? If no applicable common data standards exist, is that noted in the Plan?
✓ Does the DMS Plan identify appropriate NIH-supported or third-party data repository archive(s)?
✓ Does the DMS Plan indicate if the selected archive(s) is limited to certain data types? If required by the FOA, does the DMS Plan affirm the use of a designated NIH-supported repository?

2. Timelines and plans for data preservation, access, and sharing. Data and metadata should be preserved, at a minimum, in accordance with all applicable guidance (eg, data repository policies, specific award requirements, and journal policies). Final research data and metadata should be accessible no later than the time of publication or the end of the performance period, whichever is earlier, unless there are justifiable exceptions explained in the DMS Plan.

Table 6. Considerations for Describing Data Preservation, Access, and Sharing

✓ Does the DMS Plan conform to FAIR principles for the identification, access, and reuse of shared data and metadata? Does the DMS Plan indicate how shared data and metadata will be findable and identifiable?
✓ Does the DMS Plan affirm an acceptable timeline for sharing data and metadata?
✓ If specialized tools are needed to access or manipulate shared scientific data and metadata to support reuse or replication, will these tools be available as long as the data are shared? How can these tools be accessed?

3. Limitations on access, reuse, and distribution. Certain types of data and metadata may be confidential, sensitive, or proprietary. The NIH expects data and associated metadata to be shared to the maximum extent allowable. Any limitations or controls on their access, reuse, and distribution must be justified on ethical, policy-based, or legal grounds.

Table 7. Considerations for Describing Limitations on Access, Reuse, and Distribution

✓ If the data and/or metadata are confidential, sensitive, or proprietary, has a reasonable justification for exclusion from sharing been provided in the DMS Plan?
✓ Are there any restrictions on how data can be accessed, reused, or distributed, for example, only with explicit approval?
✓ If there are no limitations, has that been indicated?

In addition to the above considerations, the NIH will also expect a statement on how the DMS Plan will be managed and monitored and by whom.

Conclusions

Recent world events have underscored the ethical justification to ensure biomedical research is conducted in a rigorous manner and that the fruits of research are shared with the larger scientific community and the public. For example, the coronavirus disease 2019 (COVID-19) pandemic has demonstrated what the scientific community can quickly achieve when rigorous methods are applied and when high-quality data are disseminated widely and rapidly. We have focused on a subset of ethical considerations to guide the development of biomedical research grant applications for the NIH; however, the underlying ethical ethos of ensuring scientific rigor and the timely sharing of scientific data can guide the development of proposals for all funding agencies.

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References

1. Smith R. Research misconduct: the poisoning of the well. *J Roy Soc Med.* May 2006;99(5):232-237. doi: 10.1258/jrsm.99.5.232
2. Fanelli D. How many scientists fabricate and falsify research? A systematic review and meta-analysis of survey data. *PLOS ONE.* 2009;4(5):e5738. doi: 10.1371/journal.pone.0005738
3. NOT-OD-10-019 - Update on the requirement for instruction in the responsible conduct of research. National Institutes of Health website. Published 2009. Accessed March 15, 2021. <https://grants.nih.gov/grants/guide/notice-files/not-od-10-019.html>
4. AGWA professional standards and code of ethics. American Grant Writers' Association website. Published 2016. Accessed March 15, 2021. <http://www.agwa.us/ethics>
5. Code of ethics. Grant Professionals Association website. Published 2011. Accessed March 15, 2021. <https://grantprofessionals.org/page/ethics>
6. Budget. National Institutes of Health website. Published 2020. Accessed March 15, 2021. <https://www.nih.gov/about-nih/what-we-do/budget>
7. Extramural investments in research: FY 2019 by the numbers. Open Mike blog. National Institutes of Health website. Published 2020. Accessed March 15, 2021. <https://nexus.od.nih.gov/all/2020/05/05/extramural-investments-in-research-fy-2019-by-the-numbers/>
8. NOT-OD-16-011 - Implementing rigor and transparency in NIH & AHRQ research grant applications. National Institutes of Health website. Published 2015. Accessed March 15, 2021. <https://grants.nih.gov/grants/guide/notice-files/NOT-OD-16-011.html>
9. NOT-OD-18-228 - NIH & AHRQ announce upcoming updates to application instructions and review criteria for research grant applications. National Institutes of Health website. Published 2018. Accessed March 15, 2021. <https://grants.nih.gov/grants/guide/notice-files/NOT-OD-18-228.html>
10. NOT-OD-21-013 - Final NIH policy for data management and sharing. National Institutes of Health website. Published 2020. Accessed March 15, 2021. <https://grants.nih.gov/grants/guide/notice-files/NOT-OD-21-013.html>
11. NIH enhancing reproducibility guidelines. National Institutes of Health website. Accessed March 15, 2021. <https://grants.nih.gov/reproducibility/documents/grant-guideline.pdf>

12. Percie du Sert N, Hurst V, Ahluwalia A, et al. The ARRIVE guidelines 2.0: updated guidelines for reporting animal research. *PLOS Biology*. 2020;18(7):e3000410. doi: 10.1371/journal.pbio.3000410
13. Reporting guidelines. Equator Network website. Accessed March 15, 2021. <https://www.equator-network.org/reporting-guidelines/>
14. Consideration of relevant biological variables in NIH grant applications. Open Mike blog. National Institutes of Health website. Published 2016. Accessed March 15, 2021. <https://nexus.od.nih.gov/all/2016/01/29/consideration-of-relevant-biological-variables-in-nih-grant-applications/>
15. Arnegard ME, Whitten LA, Hunter C, Clayton JA. Sex as a biological variable: a 5-year progress report and call to action. *J Womens Health*. 2020;29(6):858-864. doi: 10.1089/jwh.2019.8247
16. NOT-OD-15-102 - Consideration of sex as a biological variable in NIH-funded research. National Institutes of Health website. Published 2015. Accessed March 15, 2021. <https://grants.nih.gov/grants/guide/notice-files/NOT-OD-15-102.html>
17. NOT-OD-17-068 - Reminder: authentication of key biological and/or chemical resources. National Institutes of Health website. Published 2017. Accessed March 15, 2021. <https://grants.nih.gov/grants/guide/notice-files/NOT-OD-17-068.html>
18. NOT-OD-03-032 - Final NIH statement on sharing research data. National Institutes of Health website. Published 2003. Accessed March 15, 2021. <https://grants.nih.gov/grants/guide/notice-files/not-od-03-032.html>
19. NOT-OD-14-124 - NIH genomic data sharing policy. National Institutes of Health website. Published 2014. Accessed March 15, 2021. <https://grants.nih.gov/grants/guide/notice-files/NOT-OD-14-124.html>
20. NOT-OD-21-014 - Supplemental information to the NIH policy for data management and sharing: elements of an NIH data management and sharing plan. National Institutes of Health website. Published 2020. Accessed March 15, 2021. <https://grants.nih.gov/grants/guide/notice-files/NOT-OD-21-014.html>
21. NOT-OD-21-016 - Supplemental information to the NIH policy for data management and sharing: selecting a repository for data resulting from NIH-supported research. National Institutes of Health website. Published 2020. Accessed March 15, 2021. <https://grants.nih.gov/grants/guide/notice-files/NOT-OD-21-016.html>
22. Wilkinson MD, Dumontier M, Aalbersberg IJ, et al. The FAIR Guiding Principles for scientific data management and stewardship. *Sci Data*. 2016;3:160018. doi: 10.1038/sdata.2016.18



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FROM THE PRESIDENT

Spring Forward



Gail V. Flores, PhD / 2020–2021 AMWA President

As I write this article, we are 1 month into spring. This season is traditionally known as a time of regrowth and renewal, when the flowers start to bloom and the birds begin to chirp—and baby animals enter the world, perhaps with some hesitation, yet also with optimism. This spring in the United States, many of us are feeling a parallel with the season, as to a certain degree, we are emerging from the COVID-19 pandemic with both hesitation and optimism. However, we are not returning to the pre-2020 world; rather, we are learning to adapt as we create our new normal.

I wish we had a crystal ball to show us what the world will look like in October. Because we don't, AMWA leadership recently made the call to hold the 2021 AMWA Medical Writing & Communication Conference virtually. This decision was driven by data, both from public health experts and from our members. The results of a recent member survey indicated that an overwhelming percentage of members would be unable or unwilling to travel in October, for reasons ranging from employer restrictions to personal issues to uncertainty about how the pandemic will continue to unfold. Now that the decision had been made, we can shift our focus from concern about the ability to put on a safe, excellent, in-person conference to implementation of an amazing virtual event.

The first month of spring was quite busy for AMWA! In mid-March, the US House of Representatives passed the Protecting the Right to Organize Act, legislation that would negatively affect the livelihood of freelance medical communicators. We quickly issued a press release stating that AMWA strongly opposes this act, reaffirming our position from 2020 regarding such legislation. Special thanks to Lori De Milto for reaching out to us directly and providing critical information and sources to help shape our response.

Less than 2 weeks later, an article criticizing current oncologic clinical trial design was published in *JAMA Oncology*; among several arguments, a negative, if not insulting, light was cast on the role and intent of medical writers in the manuscript development process. Swiftly, AMWA engaged with the European Medical Writers Association (EMWA) and International Society for Medical Publication Professionals (ISMPP) to submit a letter to the Editor of *JAMA Oncology*

contesting the authors' remarks about medical writers, refuting the statement that medical writers introduce "spin" (studies have been conducted and no such evidence exists) and noting that medical writer involvement actually improves compliance with reporting guidelines and provides more complete reporting of trial results, a greater rate of publication over time, and a lower risk of publication retraction due to misconduct. I would like to thank my AMWA Board of Directors colleagues R. Michelle Sauer Gehring and Brian Bass for their support in information gathering, resource provision, and generating many emails and calls regarding this matter. I am also very thankful to my co-authors and collaborators on the letter, Thomas M. Schindler and Jacqueline M. Marchington.

In addition to reacting to these 2 emergencies, AMWA also has much to celebrate this spring! On March 22, we announced that Michael G. Baker, PhD, has been named Editor-in-Chief of *AMWA Journal*. He has hit the ground running, and we are all excited to watch the journal continue to evolve under his leadership. In addition, on April 1, our AMWA-EMWA-ISMPP joint position statement on medical publication, preprints, and peer review as well as a checklist were published in *Current Research and Medical Opinion*. Since publication, the statement has received positive press and feedback on social media.

A highlight of the AMWA year is recognition of those who excel in medical communication. Be sure to read the articles about the worthy recipients of the highest AMWA awards, the John P. McGovern, Walter C. Alvarez, and Harold Swanberg Awards, in this issue. It is such a joy to welcome Stacy L. Christiansen, Harriet A. Washington, and Lori L. Alexander to our circle of award recipients.

There is a saying that "Life isn't about waiting for the storm to pass; it's about learning to dance in the rain." As we emerge from our period of waiting for the storm to pass, I hope we can learn how to dance in the rain. In this new normal, let's continue to work hard, advocate for our profession, engage with each other, and lift each other up virtually, and put on the best virtual conference ever. Let's spring forward!

Yours in AMWA,
Gail

Harold Swanberg Distinguished Service Award

Elise Eller / 2020–2021 Director–At–Large and Chair and Board Liaison, Member Awards Committee

The Harold Swanberg Distinguished Service Award, named in honor of one of the founders of AMWA, is presented to an active AMWA member who has made distinguished contributions to medical communication or rendered unusual and distinguished services to the medical profession.

This year's Swanberg recipient is **Lori L. Alexander, MTPW, ELS, MWC**. Lori has made distinguished contributions to the medical communication profession for more than 30 years, most recently in the area of education of medical communicators.

Lori is an advocate for professional development and lifelong learning. Lori's work history in medical communication has spanned a variety of settings, providing experience in different types of medical communication. Her work has involved editing, writing, project management, and development of educational resources for health care professionals and the lay public.

Lori's contributions to the field of medical communication span service both within and outside of AMWA. Highlights of Lori's service to AMWA include serving as editor of the *AMWA Journal*, chairing the Annual Conference Programming Committee (twice) and the Education Committee, serving on several working groups and task forces, serving as AMWA President and on the AMWA Board of Directors, and, most recently, serving as AMWA Director of Education. In these roles, Lori has explored and determined members' educational needs and preferences, helped AMWA create educational activities and resources to fit those needs, developed processes that ensure the consistent high quality of AMWA's educational products, and thought and acted strategically to help AMWA achieve its goals. It is because of Lori that AMWA has a content strategy for developing educational offerings online and at the annual Medical Writing & Communication Conference. It is also because of Lori that AMWA is now offering new workshops and the new Knowledge Builders in the AMWA catalog.

Lori also helped establish and develop a Medical Writing and Editing Certificate Program, which focuses on regulatory writing, journal publications, continuing education, and grant writing, for the University of California San Diego Extension. Until her retirement, Lori continued to serve as the consulting director and lead faculty to provide strategic direction for the program.

Lori's long-standing service demonstrates her passion for promoting excellence in medical communication. AMWA is proud to recognize Lori as the recipient of the 2021 Harold Swanberg Distinguished Service Award.

Sadly for the AMWA community and all who knew her, Lori passed away on June 4, 2021. We will miss Lori's energy and sense of humor, and our thoughts go out to Lori's wife, Deb Whippen, and to her family and friends.



2021 John P. McGovern Award Recipient: Stacy L. Christiansen, MA

Gail V. Flores, PhD / 2020–2021 AMWA President

The John P. McGovern Award is named in honor of John P. McGovern and is presented to a member or nonmember of the American Medical Writers Association (AMWA) to recognize a preeminent contribution to any of the various modes of medical communication. The McGovern Award is presented during the annual AMWA Medical Writing & Communication Conference.

I am pleased to announce this year's John P. McGovern Award recipient: **Stacy L. Christiansen, MA**. Ms Christiansen's contribution to the field of medical communication is crystal clear to so many members of AMWA, as she is the managing editor of the *Journal of the American Medical Association (JAMA)* and chair of the *American Medical Association (AMA) Manual of Style* committee. In the words of her colleagues who nominated her, "Ms Christiansen's numerous, important contributions to multiple modes of medical communication embody all that the John P. McGovern Award represents—leadership, excellence in medical writing and editing, and benevolent mentoring of editors, manuscript editors, authors, and writers."

Ms Christiansen received a Bachelor of Arts and Master of Arts in English language and literature from Northern Illinois University. She has worked for *JAMA* since 1998 and has worked as the managing editor since 2013. Many AMWA members also know her through her active membership and engagement in the Council of Science Editors (CSE); Ms Christiansen serves as a faculty member for the CSE Short Course for Manuscript Editors. She has taught in the University of Chicago Medical Writing and Editing Program.

As Managing Editor of *JAMA*, Ms Christiansen regularly communicates with *JAMA* authors and representatives of international professional societies and agencies from around the world to provide advice about communicating research results and medical information and often resolves complicated editorial and policy issues with authors. Her colleagues cite her recent challenge of navigating more than 10,000 coronavirus disease 2019 (COVID-19)–related submissions to the journal, for which she subsequently led efficient

and excellent editing and publication of more than 300 COVID-19–related articles to inform clinicians, policy makers, and the public.

The *AMA Manual of Style* was first published in 1962.¹ As Chair of the *AMA Manual of Style* committee, Ms

Christiansen was responsible for leading the major revision and publication of the 11th edition, published in 2020. She continues to guide the committee to address ongoing issues in medical writing and editing, as well as changes in usage that parallel the constantly changing ways we communicate. For example, during 2020, she led efforts to modify guidance for the reporting of race and ethnicity in medical publications and developed usage nomenclature for terms related to the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and COVID-19.

The McGovern Award recipient is not required to be a member of AMWA. However, not only is Ms Christiansen an active member, but she has also presented at many conferences, written articles for *AMWA Journal*, and regularly connects with AMWA members on Twitter—as the resident tweeter for the *AMA Manual of Style*. On behalf of our entire organization, it is a joy to congratulate Ms Christiansen on this prestigious award!

Author declaration and disclosures: *The author notes no commercial associations that may pose a conflict of interest in relation to this article.*

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Reference

1. American Medical Association. *AMA Manual of Style: a guide for authors and editors*. Brief history of the *AMA Manual of Style*. Accessed April 25, 2021. <https://www.amamanualofstyle.com/page/AMAhistory>



2021 Walter C. Alvarez Award Recipient: Harriet Washington

Sarah Dobney, MPH / AMWA Annual Conference Chair, Galion, OH

The Walter C. Alvarez Award, named in honor of an early medical communicator, is presented to an individual who is the epitome of excellence in communicating health care developments and concepts to the public. This year's Alvarez Award winner is Ms Harriet Washington.

Harriet A. Washington is a science writer, editor, and ethicist who is the author of *Carte Blanche: The Erosion of Informed Consent in Medical Research* (2021, Columbia Global Reports) and *A Terrible Thing to Waste: Environmental Racism and Its Assault on the American Mind*. She has been Writing Fellow in Bioethics at Harvard Medical School, the 2015-2016 Miriam Shearing Fellow at the University of Nevada's Black Mountain Institute, a Research Fellow in Medical Ethics at Harvard Medical School, Visiting Fellow at the Harvard TH Chan School of Public Health, a visiting scholar at DePaul University College of Law, and a senior research scholar at the National Center for Bioethics at Tuskegee University. She has also held fellowships at Stanford University and teaches bioethics at Columbia University, where she delivered the 2020 commencement speech to Columbia's School of Public Health graduates, and won the 2020 Mailman School of Public Health's Public Health Leadership Award, as well as the 2020-2021 Kenneth and Mamie Clark Distinguished Lecture Award. In 2016, she was elected a Fellow of the New York Academy of Medicine.

Her work helped provide the basis for the AMA apology to the nation's black physicians in 2008 and led to the banishment of the James Marion Sims statue from Central Park in 2018.

Ms Washington has written widely for popular and science publications and has been published in referenced books and journals such as *Nature*, *JAMA*, *The American Journal of Public Health*, *The New England Journal of Medicine*, the *Harvard Public Health Review*, *Isis*, and *The Journal of Law, Medicine, and Ethics*. She has been Editor of the *Harvard Journal of Minority Public Health*, has been a guest Editor of the *Journal of Law, Medicine and Ethics*, and is a reviewer for the *Journal of the American Association of Bioethics and the Humanities*. Her other books include *Infectious Madness: The Surprising Science of How We "Catch" Mental Illness*, *Deadly Monopolies: The Shocking Corporate Takeover of Life Itself*, and *Medical Apartheid: The Dark History of Experimentation from Colonial Times to the Present*, which won a National Book Critics Circle Award, the PEN/Oakland Award, and the American Library Association Black Caucus Nonfiction Award.

A film buff and lover of baroque music, Ms Washington has also worked as manager of a poison-control center and as a classical-music announcer for public radio station WXXI-FM in Rochester, New York, and she curates a medical-film series.

Author declaration and disclosures: *The author notes no commercial associations that may pose a conflict of interest in relation to this article.*

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VIRTUALLY AMAZING AMWA 2021

Sarah Dobney, MPH / AMWA Annual Conference Chair, Galion, OH

AMWA's 2021 Medical Writing & Communication Conference will be held virtually on October 27-29, 2021.

2020 delivered **disruption**, ignited **innovation**, and required **resilience** in our professional and personal lives. #AMWA2021 will shine a spotlight on the importance of medical communication, and the strength and commitment of the medical writing community, during these difficult yet amazing times.

In making the decision to go virtual, AMWA relied on public health guidance, federal and state-by-state event restrictions, and member survey feedback and concluded that is not feasible to plan and implement an in-person, large-scale, multiday conference for the AMWA community this fall.

We are redoubling our efforts to ensure that #AMWA2021 delivers the best content and experiences possible. Building on our success from last year's first virtual conference, we will be creating an online experience that meets attendees' professional development and networking needs. Join us for engaging education sessions with live chats; small-group, interactive roundtable discussions; insightful poster presentations, and inspiring plenary sessions. We will also celebrate the accomplishments of our colleagues and peers over the past year. Profiles of AMWA's award winners can be found in this issue.

#AMWA2021 Education Session Preview

- A Systematic Approach to Manuscript Editing
- Best Practices for Medical Writing with a Disclosure Mindset
- Bridging the Gap: Transitioning Into Regulatory Medical Writing
- Catapult Your Career Using LinkedIn
- Copyright 101: A Practical Guide to Properly Reusing and Sharing Journal Publications Information
- Data, Design, and Technology: Effective Infographic Strategies for Health Communication
- Describing Mental Disorders Using the Language of Neuroscience
- How to Master Scientific Publications: A Medical Writer's Bag of Tricks
- Launching and Building a Freelance Business: A Proven 10-Step Process
- Leveraging Accessibility Best Practices to Elevate Your Social Media and Health Communication Strategies
- Not a Ghost in the Machine: Building a Rich, Virtual Culture
- Sales Training and Beyond: Developing Educational Content Across the Pharma/Biotech Landscape
- Teaching the Next Generation of Regulatory Medical Writers
- The Case for Business Intelligence in Medical Writing
- WFH! WTF? What I've Learned From 32 Years of Working From Home That Might Just Help You Survive

And many more!

**Full program and registration information available at
www.amwa.org/conference.**

We look forward to seeing you online for #AMWA2021!

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