



Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.



Medical Staff Responses to COVID-19 'Data': Have We Misplaced Our Skeptic's Eye?

The size and speed of the coronavirus disease 2019 (COVID-19) tsunami and associated public apprehension that slammed into health care systems worldwide blew in with it profound changes in how medical care is delivered inside and outside of hospitals.

Among the most notable of these deviations from traditional approaches is the way in which medical staffs across the world engaged with new "information" about COVID-19 derived from "alternative sources," which in some cases was not actually "informative," clarifying, or helpful. New treatment algorithms based on these new sources of "information" were adopted with breathtaking rapidity. Some are already a source of remorse for the introspective¹ physician. Sidelined, at least temporarily, was the deliberative and iterative approach. Where was our healthy professional skepticism that serves so well in normal times? It was seemingly replaced by a new priority: "Don't just stand there; do something." In Joseph Conrad's novel, *Nostromo: A Tale of the Seaboard* (1902), a character finds that a single death "filled his breast with a mournful and angry desire for action." The author observes, "Action is consolatory. It is the enemy of thought and the friend of flattering illusions."² But we must pause and ask, "to whom was the action consolatory?" The public? Perhaps, but also to those of us shouldering the burden of direct patient care. It is understandable then that we err on the side of action when faced, not with a single death, but with a mass of mortality.

What oracles have replaced the accumulated clinical trial evidence that in normal times buttress professional society guidelines? A witches' brew of press conferences,³ professional blogs, forwarded email chains, hospital websites, and manuscripts that are displayed on websites but sit unreviewed. Apparently, all practitioners are to be their own reviewer. All physicians are to be their own thresher.

It is a form of crowdsourced medical care but, not in the best sense of that term wherein the many contribute data to achieve insights.⁴

In these strange times, even the editorial and peer-review process has resulted in anomalies. Important but "preliminary" reports show up in journals weeks after being posted on the Internet, prolonging equipoise to those who seek clarity. Publications making broad declamations from small sample sizes⁵ or from observational methodologies arise like springtime mushrooms. One observational study of just 18 patients with cancer and COVID-19 found a high risk of mortality and injudiciously advocated for postponing elective cancer surgery and adjuvant chemotherapy in endemic areas.⁶ Most disappointing of all is the phenomenon of withdrawn publications that had been editorially assigned and peer-reviewed⁷⁻⁹ but with retrospectively obvious disqualifying gaffes. Alas, retraction is a late and weak remedy. As Jonathan Swift noted, more than 300 hundred years ago, "Falsehood flies, and the Truth comes limping after it; so that when Men come to be undeceiv'd, it is too late; the Jest is over, and the Tale has had its Effect."¹⁰

The COVID-19 response has also included a promiscuous pattern of biomarker test ordering, ranging from the humble erythrocyte sedimentation rate to the exotic measurements of interleukins sent off to reference labs. The driving forces behind this pattern of test ordering are varied but surely include early publications "associating" high levels of inflammation markers with poor outcomes in COVID-19¹¹ and a physiologic framework of "cytokine storm." But, for what purpose this promiscuity? To "confirm" a diagnosis that is suspected by a medical history and already confirmed by chest imaging or molecular studies of COVID-19 RNA? Perhaps occasionally but not routinely. Do we really need a platform of lab tests to tell us when the patient is getting better or worse? We have visual inspection, vital signs, ventilator settings, and oxygen saturation levels for that. Where is the study to say that monitoring inflammatory markers is both predictive and actionable?

More worrisome and more dangerous are the well-meaning therapeutic interventions that were added empirically

Funding: None.

Conflicts of Interest: None.

Authorship: The author is solely responsible for the content of this manuscript.

Requests for reprints should be addressed to Barry R. Meisenberg, MD, Anne Arundel Medical Center, Luminis Health System, 2001 Medical Parkway, Annapolis, MD, 21401-1595.

E-mail address: Meisenberg@AAHS.org

without clinical trials or clinical trial evidence. Based on scientific concepts of inflammatory pathophysiology or clinical impressions derived from anecdotal cases, anti-inflammatory disease modulators and putative antiviral agents were moved into the armamentarium early on. Given the variability of clinical course, it is not surprising that some concluded that these agents are beneficial, even if the “negative” clinical trial comes limping along months later.¹² It seems that “confirmation bias,” in addition to the previously mentioned “action bias,” emerges with pandemic. As a result, the distance between therapies based on physiologic frameworks or in vitro findings and the patient’s medication list is shorter and truer now than in recent times.

In truth, medical practice has always been idiosyncratic or inclined to be dominated by influential voices. Indeed, the entire *materia medica* for influenza in 1918 was not evidence-based and included items like strychnine, digitalis, antiseptic gargles, and blood-letting.¹³ What was not noxious was worthless. It is also true that professional journals have never entirely been free from bad data, bad method, or dishonest publication. But what is different now is the sheer amount of “alternative” learning and the speed of its dissemination. We have come to expect better from our learning sources and habits 102 years after the Great Influenza. We are after all schooled in scientific medicine.

Medical staffs around the world deserve admiration for being engaged in learning and hungry for data. But one can lament without being dismissive or harshly critical. We can demand in this next phase of pandemic more discretion from ourselves and discernment by editors and gatekeepers. To repurpose a popular aspirational phrase making the internet rounds, “We’re all in this together.”

A recent newspaper article highlighted the internal disagreements medical staffs have over therapeutic interventions: “study it” versus “just do it.”¹⁴ However, a recent essay argues that the dichotomy between “learning” and “doing” may be a false one if we learn to study smarter.¹⁵

We have struggled emotionally and even physically through the first phase of this pandemic. When the storm made landfall, we were without the tools we needed. Those of us in a position to forge new tools by initiating standardization and planning and completing well-designed clinical trials should make it a priority to do so. We owe it to each other and to the public to be more scientific, more judicious, and more discriminating. We are indeed “all in this together.”

Barry R. Meisenberg, MD

Chair, Department of Medicine and
Medical Director Research Institute, Anne
Arundel Medical Center, Luminis Health
System, Annapolis, Md

References

- Rosenberg ES, Dufort EM, Udo T, et al. Association of treatment with hydroxychloroquine or azithromycin with in-hospital mortality in patients with COVID-19 in New York State. *JAMA* 2020;323(24):2493–502. <https://doi.org/10.1001/jama.2020.8630>.
- Conrad J. *Nostromo: A Tale of the Seaboard*. Available at: https://planetpdf.com/planetpdf/pdfs/free_ebooks/Nostromo_NT.pdf. Accessed August 25, 2020.
- Thomas K, Fink S. FDA “grossly misrepresented” blood plasma data, scientists say. Available at: <https://www.nytimes.com/2020/08/24/health/fda-blood-plasma.html?action=click&module=Top%20Stories&pgtype=Homepage> Accessed August 25, 2020.
- Desai A, Warner J, Kuderer N, et al. Crowdsourcing a crisis response for COVID-19 in oncology. *Nat Cancer* 2020;1:473–6.
- Xu XL, Han MF, Li TT, et al. Effective treatment of severe COVID-19 patients with tocilizumab. *Proc Natl Acad Sci U S A* 2020;117(20):10970–5. <https://doi.org/10.1073/pnas.2005615117>.
- Liang W, Guan W, Chen R, et al. Cancer patients in SARS-CoV-2 infection: a nationwide analysis in China. *Lancet Oncol* 2020;(3):335–7 [21].
- 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 [retracted June 4, 2020]. *Lancet*. doi: 10.1016/S0140-6736(20)31180-6.
- Seongman B, Kim M, Kim JY, et al. Effectiveness of surgical and cotton masks in blocking SARS-CoV-2: a controlled comparison in 4 patients (letter) [retracted July 7, 2020]. *Ann Intern Med*. doi:10.7326/M20-1342.
- Mehra MR, Desai SS, Kuy S, Henry TD, Patel AN. Retraction: cardiovascular disease, drug therapy, and mortality in COVID-19. *N Engl J Med* 2020;382:2582. <https://doi.org/10.1056/NEJMoa2007621>.
- Swift J. *The Examiner*, ed. Addison J. November 2, 1710: 15. Available at: <https://play.google.com/books/reader?id=KigTAAAAQAAJ&hl=en&pg=GBS.PA15>. Accessed August 21, 2020.
- Zhou F, Yu T, Fan G, et al. Clinical course and risk factors for mortality of adult in patients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet* 2020;395:1054–62.
- Roche provides an update on the phase III COVACTA trial of Actemra/RoActemra in hospitalized patients with severe COVID-19 related pneumonia. Available at: <https://www.roche.com/dam/jcr:6d8de90d-2e31-43c8-b4e1-0a24a2675015/en/29072020-mr-covacta.pdf>. Accessed August 28, 2020.
- Friedlander AF, McCord CP, Sladen FJ, Wheeler GW. The epidemic of influenza at Camp Sherman, Ohio. *JAMA* 1918;71(20):1652–6.
- Dominus S. The COVID drug wars that pitted doctor vs. doctor. *New York Times*. Available at: <https://www.nytimes.com/2020/08/05/magazine/covid-drug-wars-doctors.html>. Accessed August 28, 2020.
- Angus DC. Optimizing the trade-off between learning and doing in pandemic. *JAMA* 2020;323(19):1895–6.