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THE PREPRINT SERVER FOR HEALTH SCIENCES

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Relevant disclosures

- Co-founder of medRxiv (contribution without compensation)

Editor's Perspective

The End of Journals

Harlan M. Krumholz, MD, SM

For hundreds of years, medical journals have served as arbiters of the quality of medical research. But the traditional peer-reviewed publication model is fraying. The hierarchical gateway to publication, historically in the hands of experts, is at odds with the ubiquitous democratization of data and information in the 21st century. The impending revolution in the approach to evaluate and disseminate scientific findings is not an indictment of the talent, intentions, or products of editors and reviewers, but rather a response to a model that simply may have run its course given societal and technological change.

The *Circulation: Cardiovascular Quality and Outcomes* team has had the privilege to found and lead this publication. My thoughts about the state of publication derive from my experiences as an editor, an investigator, an avid reader of the medical literature, and a seeker of ways to improve health care. My observations are as much or more about my own journal as they are about others. As our group approaches the end of our terms, it seemed to be a good time to reflect on the state of medical journals.

Journals are facing fundamental challenges that can only be overcome through relentless innovation and a willingness to leave the security of an outdated model. There are at least 9 deficiencies in the current model that fuel the sense that journals as we have known them are approaching their final act.

Too Slow

The publication process is a long one. The time from the initial submission of an article to its publication can be half a year or more. There are exceptions, and some papers are expedited, but that is not the typical experience. Despite efforts to streamline the process, obstacles remain in the timeliness of publication. Improvements such as online posting and digital transactions with reviewers and editors have reduced times, but it still takes many months even for papers that require only a single round of review. Moreover, many contributions are considered by multiple journals and most articles take a year or more to be publicly available. The idea that much of the medical literature lends itself to this leisurely timeline raises the issue that if new knowledge in medicine is not time sensitive, perhaps it is not important enough to be published. Other fields provide the opportunity for public posting of new publications and a public peer review process long before the print version. In the future, these types of delays in the transmission of new knowledge will likely not be acceptable.

Too Expensive

From the perspective of authors, the expense of publishing growing rapidly. Page charges, even from journals that prod profits, drain vital resources from the research enterprise. T funds often must derive from sources other than grants an be an obstacle for many investigators. It is not uncommo publication to cost in the range of $3000 to $5000, part for open access. From the perspective of journals, eve their value derives from content provided by investi from reviewers who donate their time, costs of m model that requires a web presence and an inf editors and staff, along with sales personnel, From the perspective of libraries and subscri the journals can be prohibitive. For the p to articles in journals that do not have o expensive. In the future, medical know sidered a social good and cost barri rent role.

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TOO LIMITED

The configuration of articles within most medical journals prohibits a comprehensive and in-depth approach to a scientific question. The format generally requires the investigators to chunk their work into contributions that fit within 3000 to 5000 words and no more than a handful of tables and images. Supplementary files are allowed, but a published article typically must be limited to executive summary length. Therefore, for substantive investigations, the published work represents only a fraction of the knowledge that was generated to address the research question. But more expansive presentation of findings can, in many cases, have value. In the future, investigators will have the capacity to fit the structure of the presentation of new data to the needs of the project; constraints on format, beyond those that improve readability, will be unnecessary.

TOO UNRELIABLE

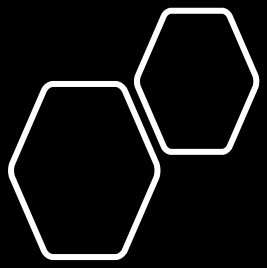
Peer review and the journal decision-making process occur without much external scrutiny and transparency. The way that journals select or eliminate contributions is rarely evaluated and routine metrics of success are absent. It is not unusual for similar-tier journals to arrive at different decisions about the same article. Reviewers donate time, the quality of reviews is variable, and there is little accountability for performance. Moreover, biases can go unappreciated. The impact of articles published in high-profile venues may derive as much from the venue as from the quality of the science. In the future, there will be a growing interest in a more reliable and open process, one that can be subject to iterative improvement and public comment.

TOO FOCUSED ON THE WRONG METRICS

Journals vie for prestige, which brings them attention, authors, and revenue. The impact factor has gained an edge among all potential measures as a means of ranking journals. Many journals are internally and externally judged by their relative position on the impact factor list, which is issued annually to increasing fanfare. The drive toward simplified metrics that inadequately capture the performance of a journal can distort decisions about what to publish and encourage a culture of pandering to the citation rather than seeking to advance scientific knowledge and improve clinical practice. The flaws of the impact factor are well characterized, but its pre-eminence is unquestioned. In the future, the success of a vehicle to communicate scientific information will probably be gauged by much more than a narrow view of performance centered on frequency of citations.

TOO POWERFUL

Except for a few scientific contributions with obvious and substantial importance for clinical practice, acceptance of a contribution involves discretionary decisions. Much like college admissions, editors face thousands of submissions that could qualify for acceptance, and they must make choices for limited spots. That discretion and the importance of publication, particularly among the journals with the greatest prestige, place the editors in a remarkably powerful position. Publication in such a journal can transform a career or influence millions of dollars or more in sales of a product. That concentration of power exerts substantial influence over perspectives and information that are disseminated broadly in the press, and that guide the public and policy makers. In the future, the scientific community may prefer that such influence is more broadly and openly distributed, rather than placed in the hands of the few.



TOO PAROCHIAL

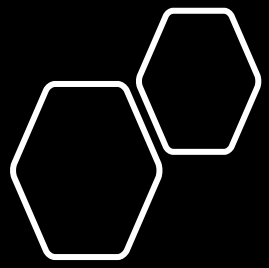
Journals tend to lack diversity in their editorial groups. This applies to sex and race/ethnicity, as well as national origin. Science knows no national boundaries yet journals seem to have national, and sometimes even regional, preferences with regard to their selection of submissions. Given the lack of transparency in the decision-making process, it is difficult to capture data to evaluate this perception, but it is commonly expressed that journals tend to favor contributions from their countries of origin. They may also prefer content that reflects the preferences and interests of their editors. In the future, the value of scientific knowledge will increasingly lie in its evaluation by the larger scientific community, uninfluenced by the imposition of favoritism—implicit or explicit—by a select group.

TOO STATIC

The journal publication is currently a static product, presented as a singular contribution rather than as a living document. It can be corrected or retracted, but it is not interactive and has no capacity for iterative change spurred by input from the larger audience. Many scientific projects might be better presented as an interactive website with the opportunity for the community to probe the findings and provide feedback. Creative visualizations of data are often best presented in ways that allow images to be rotated and manipulated for better understanding. In the future, novel strategies for conveying knowledge and engaging readers will probably emerge, leaving behind the static presentation of results that offers limited options for interactive understanding.

TOO DEPENDENT ON A FLAWED BUSINESS MODEL

Journals have been a good business. For organizations and corporations, they have been cash cows. The model from the author's perspective has been likened to a restaurant in which the customers cook the meal and then pay the bill. Despite the profits, page charges abound and reviewers are unpaid. The contributions in kind to journals are immense. The availability of editorial support that could improve the quality of the contributions is the exception rather than the norm. For those journals with hefty advertising revenues, there are issues—generally unexamined—surrounding conflict of interest. Journals rarely, if ever, expose their advertising revenue sources even as disclosure is mandatory for authors. Almost all journals separate their business and editorial functions, but every editor is aware of which articles are likely to produce revenue through reprints—and which companies support advertisements. In the future, there will likely be interest in business models that rely less on revenues that tax authors and reviewers and depend on support from industry.



CONCLUSIONS

We have arrived at the juncture where medicine and science need new vehicles for the dissemination of knowledge. These new approaches will enable us to separate the wheat from the chaff in order to better serve the public. The question for all of us in medical publishing—and for those who consume medical knowledge—is how that would best be accomplished in a new world that is flat, digital, and transparent.

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EDITOR'S PERSPECTIVE

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Key Words: peer review

The New England Journal of Medicine

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CASE reports, usually published in the "Medical Intelligence" section, should include only the pertinent details of each case and reference to articles reporting closely related cases. A complete review of the literature is rarely desirable. A preliminary report, a very short case report or a description of a technic submitted for publication as a "Brief Recording" should be limited to 1½ double-spaced typewritten pages.

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The *Journal's* masthead does not differentiate among various types of printed medical communication. The understanding is that material submitted to the *Journal* has not been offered to any book, journal or newspaper. If an author willingly and actively has contributed the same material to any other publication – whether as text to a standard medical journal, or as a "letter to the editor," or as a feature in a lay magazine – that understanding has been disregarded. There is no reason whatsoever why controlled-circulation journals should be in a separate category, and any editor of such a journal who "assures" an author to the contrary is guilty of misrepresentation.

Some qualifications, however, are necessary. Part of the ritual of biomedical meetings is the publication of abstracts submitted by authors who seek their 10-minute turn behind the lectern. An exception must therefore be made for abstracts printed in programs of meetings. Also excepted is material that is not really submitted – e.g., when a reporter notes what is said by a speaker at a public meeting. Suppose the speaker is interviewed after the talk and provides additional information. Here a decision may be difficult, but in the *Journal's* opinion the material has been contributed elsewhere if the speaker makes illustrations available to the interviewer, or if the published interview covers practically all the principal points contained in a subsequently submitted manuscript.

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RESEARCH

Publication and reporting of clinical trial results: cross sectional analysis across academic medical centers

Ruijun Chen,[1] Nihar R Desai,[2,3] Joseph S Ross,[3,4,5,6] Weiwei Zhang,[3] Katherine H Chau,[1] Brian Wayda,[7] Karthik Murugiah,[8] Daniel Y Lu,[9] Amit Mittal,[8] Harlan M Krumholz[2,3,5,6]

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ABSTRACT

OBJECTIVE
To determine rates of publication and reporting of results within two years for all completed clinical trials registered in ClinicalTrials.gov across leading academic medical centers in the United States.

DESIGN
Cross sectional analysis.

SETTING
Academic medical centers in the United States.

PARTICIPANTS
Academic medical centers with 40 or more completed interventional trials registered on ClinicalTrials.gov.

METHODS
Using the Aggregate Analysis of ClinicalTrials.gov database and manual review, we identified all interventional clinical trials registered on ClinicalTrials

disseminated results for 2892 (66%) trials, with 1560 (35.9%) achieving this within 24 months of study completion. The proportion of clinical trials with results disseminated within 24 months of study completion ranged from 16.2% (6/37) to 55.3% (57/103) across academic medical centers. The proportion of clinical trials published within 24 months of study completion ranged from 10.8% (4/37) to 40.3% (31/77) across academic medical centers, whereas results reporting on ClinicalTrials.gov ranged from 1.6% (2/122) to 40.7% (72/177).

CONCLUSIONS
Despite the ethical mandate and expressed values and mission of academic institutions, there is poor performance and noticeable variation in the dissemination of clinical trial results across leading academic medical centers.

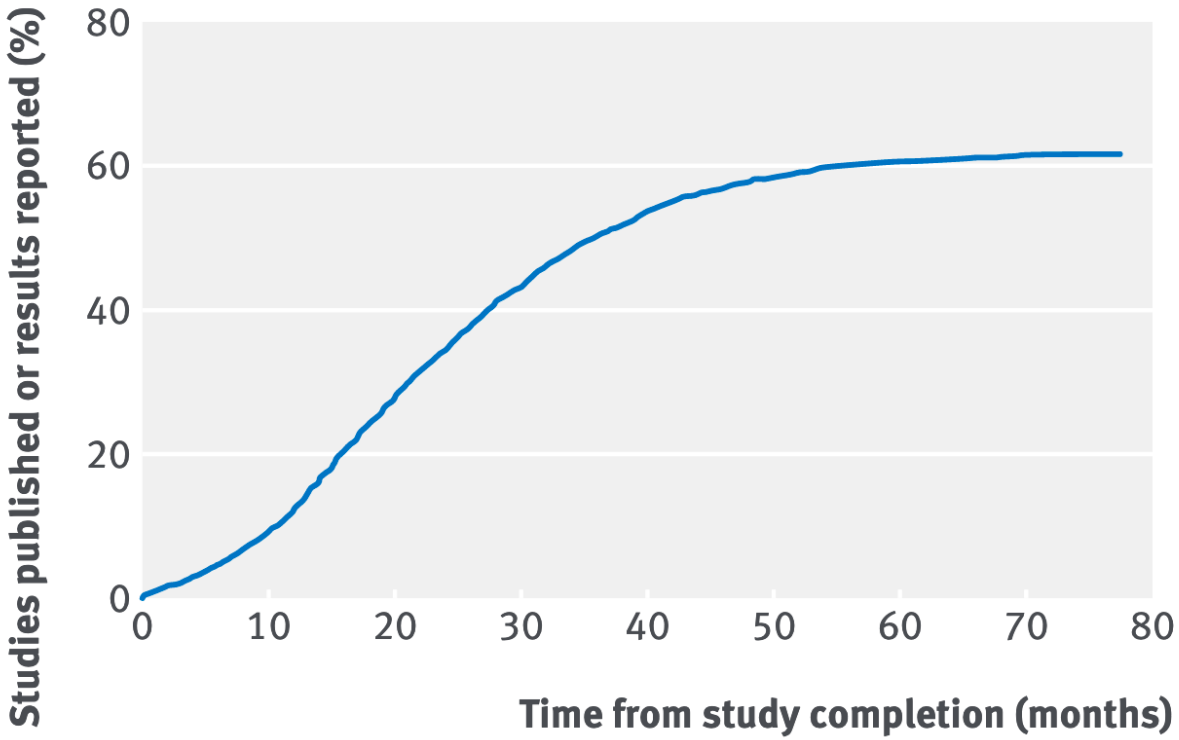


Fig 1 | Time to publication of results or results reporting for completed clinical trials across academic institutions. Of 4347 completed clinical trials, this figure excludes those without dissemination of results (n=1455) as well as those with publication date and results reporting date <0 (n=216)

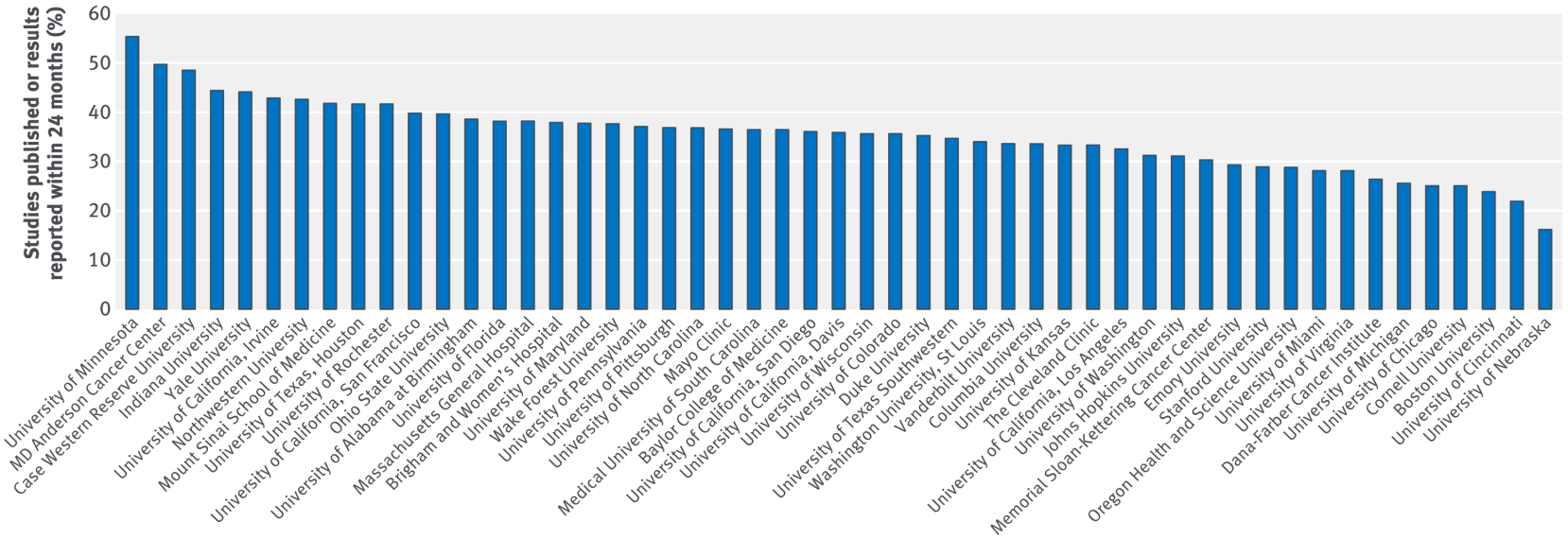


Fig 2 | Rates of dissemination of clinical trial results (publication of results or reporting of results on ClinicalTrials.gov) within 24 months across academic institutions. Of 4347 completed clinical trials, this figure excludes trials without dissemination of results (n=1455) as well as those with publication date and results reporting date <0 (n=216)

May 13, 2013

Time to Publication Among Completed Clinical Trials

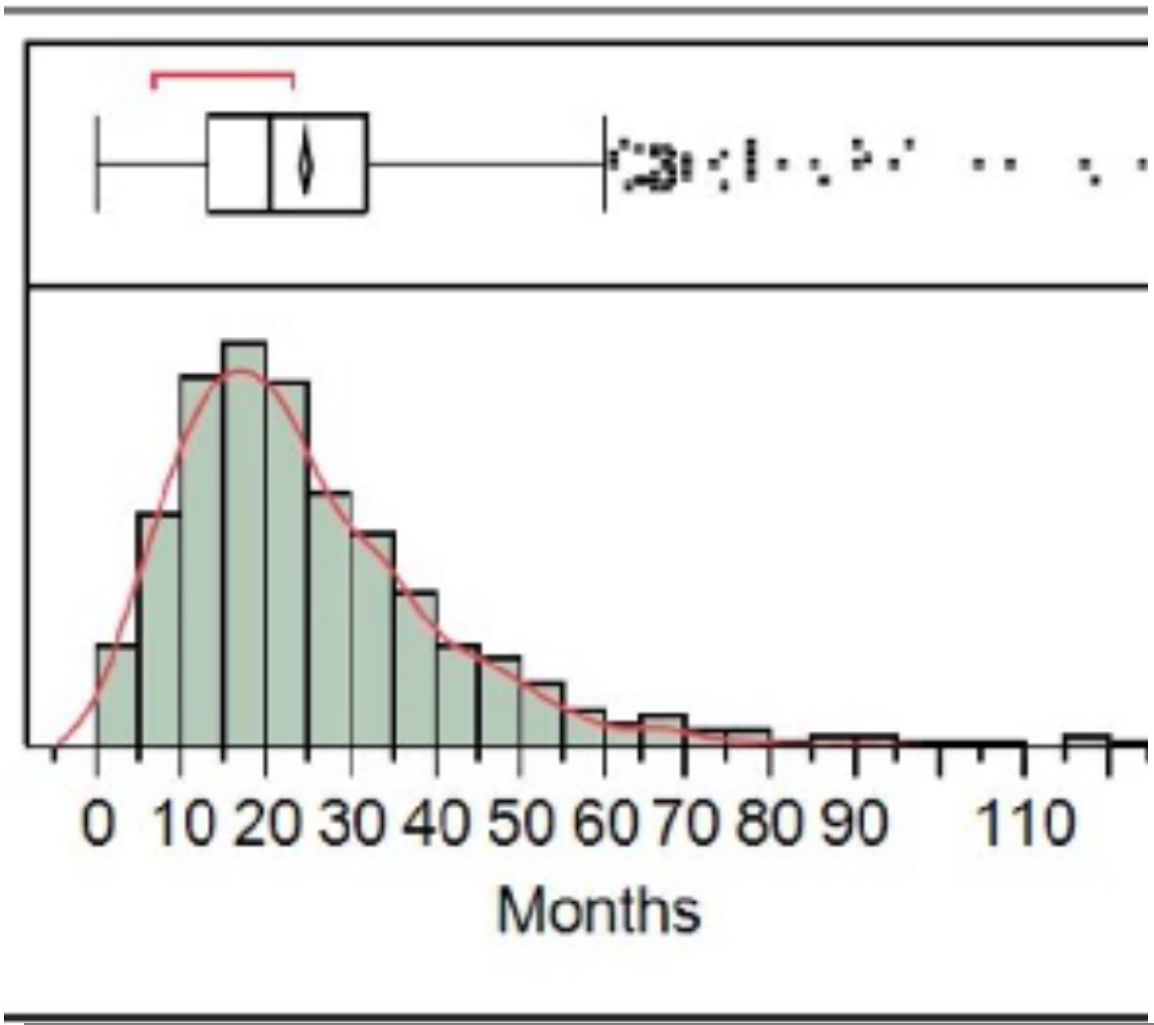
Joseph S. Ross, MD, MHS; Marian Mocanu, MD; Julianna F. Lampropulos, MD; Tony Tse, PhD; Harlan M. Krumholz, MD, SM

» Author Affiliations | Article Information

JAMA Intern Med. 2013;173(9):825-828. doi:10.1001/jamainternmed.2013.136

Prior studies have shown that 25% to 50% of clinical trials are never published.[1-4] However, among those published, we know little about the length of time required for publication in the peer-reviewed biomedical literature after study completion. Ioannidis[5] previously demonstrated that a sample of randomized phase 2 and 3 trials conducted between 1986 and 1996 required nearly 2.5 years for publication, while our more recent study of National Institutes of Health (NIH)-funded trials found that the average time to publication was almost 2 years.[4] We sought to determine time to publication for a recent and representative sample of trials published in 2009.

Time to publication after completion among clinical trials registered in ClinicalTrials.gov and published in the biomedical literature



Median time to publication was 21 months, with an interquartile range of 13 to 32 months

JAMA Oncology | Original Investigation

Delays in the Publication of Important Clinical Trial Findings in Oncology

Lindor Qunaj, BSc; Raina H. Jain, BA; Coral L. Atoria, MPH; Renee L. Gennarelli, MS; Jennifer E. Miller, PhD; Peter B. Bach, MD, MAPP

IMPORTANCE The complete and timely dissemination of clinical trial data is essential to all fields of medicine, with delayed or incomplete data release having potentially deleterious effects on both patient care and scientific inquiry. While prior analyses have noted a substantial lag in the reporting of final clinical study results, we sought to refine these observations through use of a novel starting point for the measurement of dissemination delays: the date of a corporate press release regarding a phase 3 study's results.

OBJECTIVE To measure the length of time elapsed between when a sponsor had results of study findings they deemed important to announce, and when the medical community had access to them.

DESIGN AND SETTING Covering the years 2011 through 2016, we measured the delay from when 8 large pharmaceutical companies issued a press release announcing completed analyses of phase 3 clinical trials in oncology, and the public sharing of those results either on ClinicalTrials.gov or in a peer-reviewed biomedical journal as found via PubMed or Google Scholar. Press releases announcing regulatory steps and presentation schedules for conferences were excluded, as were those announcing results from preclinical trials, follow-up analyses, and studies of supportive care therapies or various modes of infusion for the same therapy.

MAIN OUTCOMES AND MEASURES Time to public dissemination of clinical trial data.

RESULTS Of the 100 press releases in our sample, 70 (70%) reported positive results, but only 31 (31%) included the magnitude of study findings. Through the end of follow-up, 99 (99%) of press releases had an associated peer-reviewed publication, complete data posting to ClinicalTrials.gov, or both, with a median time to reporting of 300 days (95% CI, 263-348 days). Positive findings were reported more quickly than negative ones (median of 272; 95% CI, 211-318 days vs 407; 95% CI, 298-705 days; log-rank $P < .001$).

Supplemental content

The median time from a press release referencing trial results until either publication or posting on ClinicalTrials.gov was 300 days.

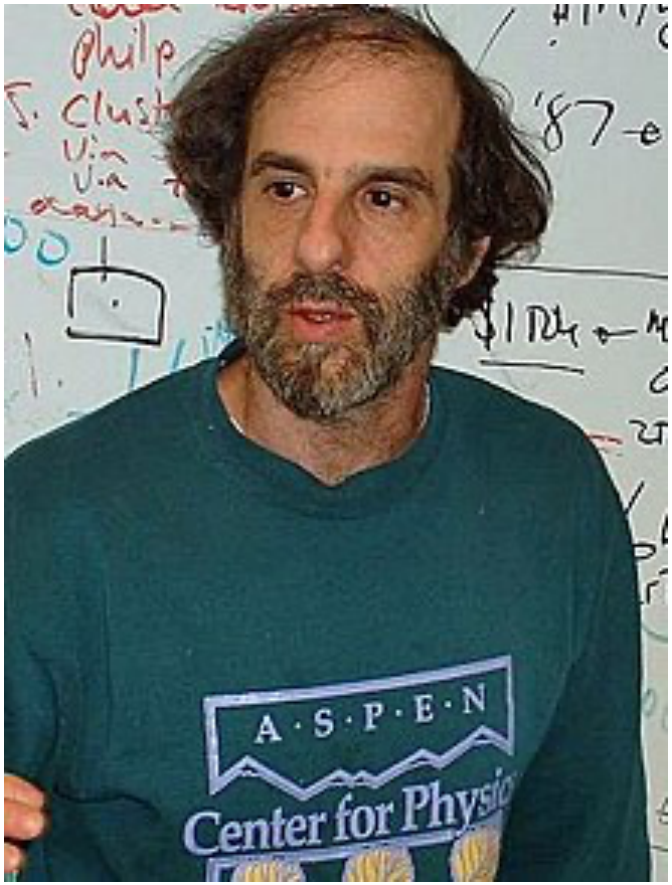
Slow, incomplete, inaccessible

Preprint (n):

a research manuscript yet to be certified by peer review and accepted for publication by a journal

Preprint server (n):

an online platform dedicated to the distribution of preprints

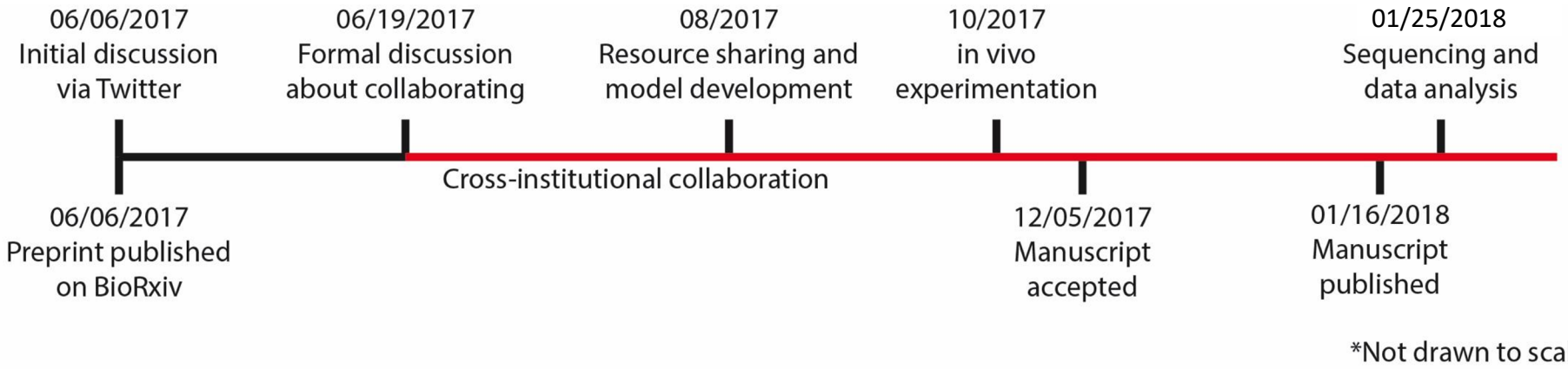


Preprint servers are proliferating

Rapid, early sharing of new science and information

- By removing the lag time to publication, after 10 years there could be a five-fold acceleration in scientific discovery.

  (Steve Quake, Stanford Medicine Big Data 2017 talk)



Source: https://twitter.com/mikefeigin/status/953371916693377024.

medRxiv: a server for health science preprints

- Conceptually and technologically similar to bioRxiv
- Not-for-profit
- A service not a product
- Publisher-neutral
- Operated by CSH Laboratory
- Managed in partnership with BMJ and Yale University
- Launched Q2 2019

Preprints in medicine: potential benefits

Rapid, early sharing of new information

- Establishes provenance of ideas while papers peer reviewed
- Facilitates awareness, prompts scientific feedback
- Enhances collaboration among scientists
- Demonstrates scientific productivity

Make less "publishable" studies more readily available

- Medical education and qualitative research
- Quality improvement & healthcare delivery innovations
- Confirmatory or contradictory results
- Negative or inconclusive research findings

Foster more "complete" results reporting

- Promotes research transparency, particularly for abstract presentations, complements trial registry results reporting
- Links protocols, sensitivity analyses and supplementary materials (not all journals publish)

Preprints in medicine: concerns and perceived risks

Editors worry about:

- Harm to the public from wrong information, magnified by media reporting
- 'Persistent preprints' with results/conclusion that changed after peer review
- Manipulation by commercial interests
- Undermining established medical communication norms
  - Peer-reviewed journals
  - Conferences
  - ClinicalTrials.gov

Authors worry about:

- Journals won't publish their paper if it's preprinted

medRxiv: mitigating concerns and risks

- Submission requirements for authors
- Clear posting criteria – research articles only!
- Established screening process
- Signaling the need for caution when scientists and non-scientists read and review preprints

medRxiv: submission requirements

- Follow ICMJE guidance, including author names, contact info, affiliation
- Funding and competing interest statements
- Statement of IRB / ethics committee oversight
- Study registration when applicable

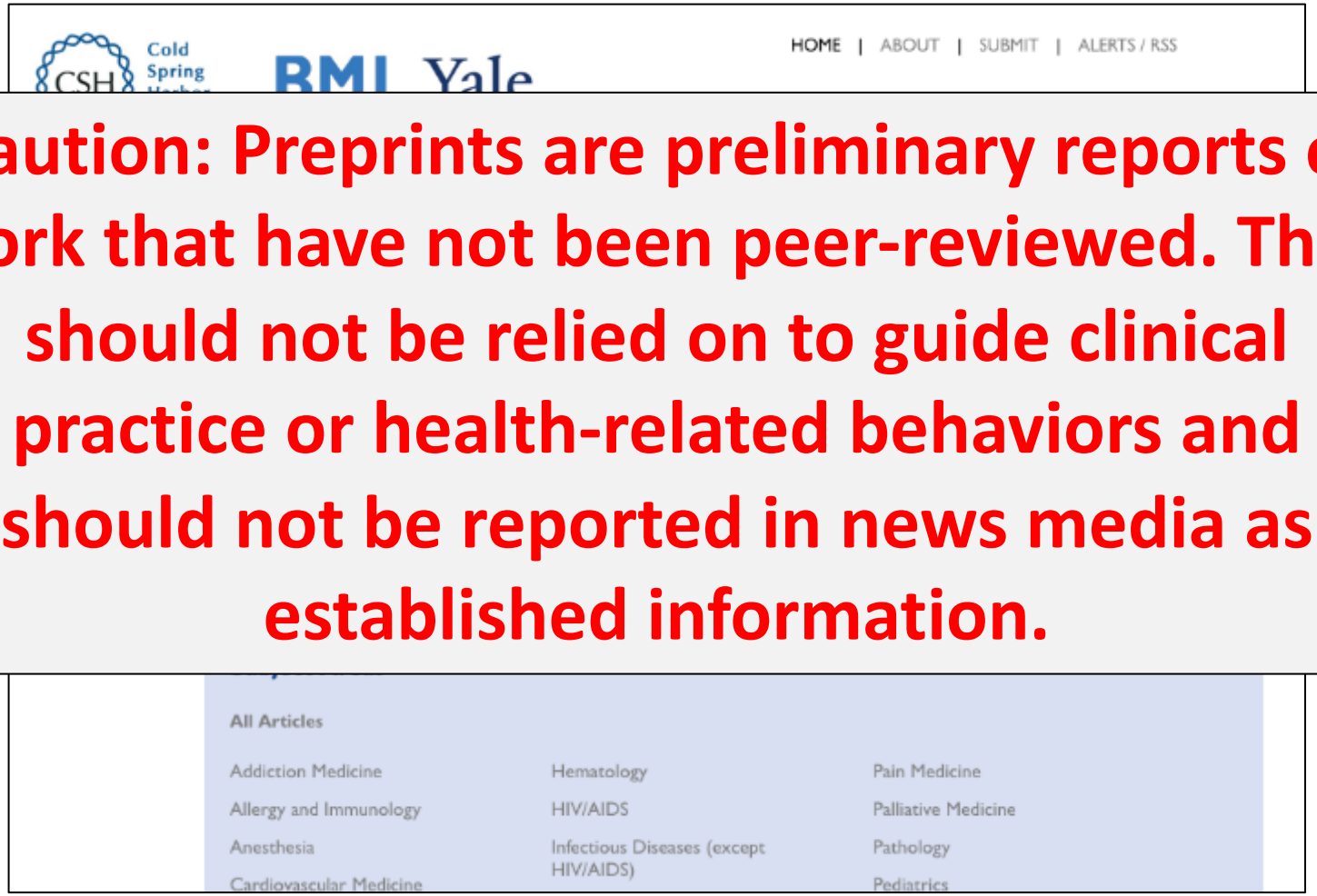
  (ClinicalTrials.gov or other ICMJE approved registry for trials, PROSPERO for reviews)
- Study protocol *
- Data sharing / availability statement *
- EQUATOR Network reporting guidelines checklist(s) *

medRxiv: allowed article types

- Original research in the biomedical sciences, including clinical trials, observational research, surveys, qualitative research, quality improvement and implementation science, policy studies, and medical education
- Systematic reviews and meta-analytic research
- Methodological research
- Data publications
- Protocols (to accompany study preprints)

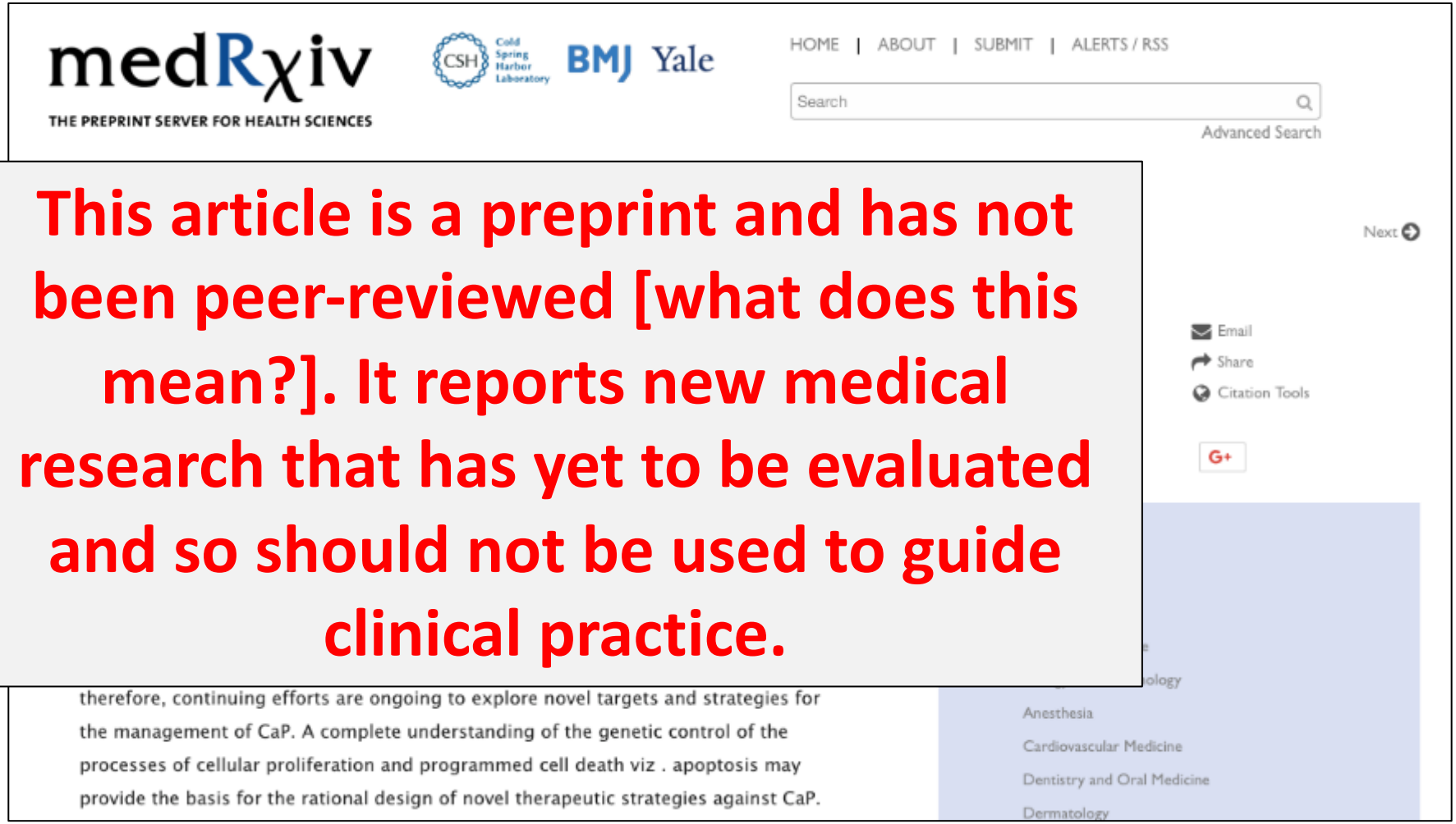
Not Allowed: commentaries, editorials, opinion pieces or essays, letters to editors, narrative reviews, medical-legal research, case reports

medRxiv: urging caution in using preprints

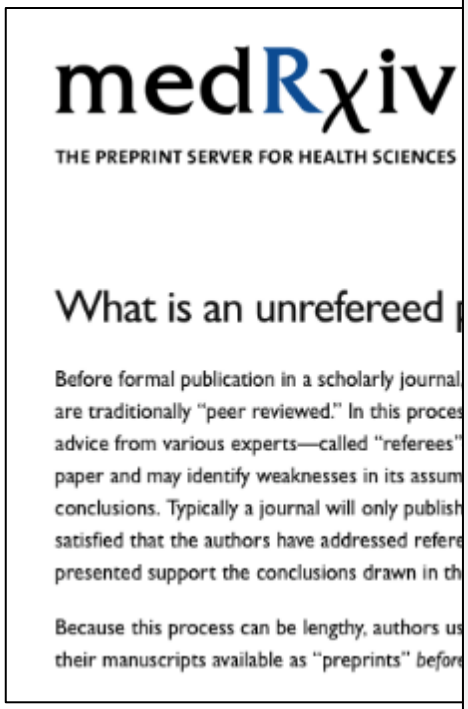


Caution: Preprints are preliminary reports of work that have not been peer-reviewed. They should not be relied on to guide clinical practice or health-related behaviors and should not be reported in news media as established information.

medRxiv: urging caution in using preprints



medRxiv: urging caution in reporting on preprints



medRxiv

THE PREPRINT SERVER FOR HEALTH SCIENCES

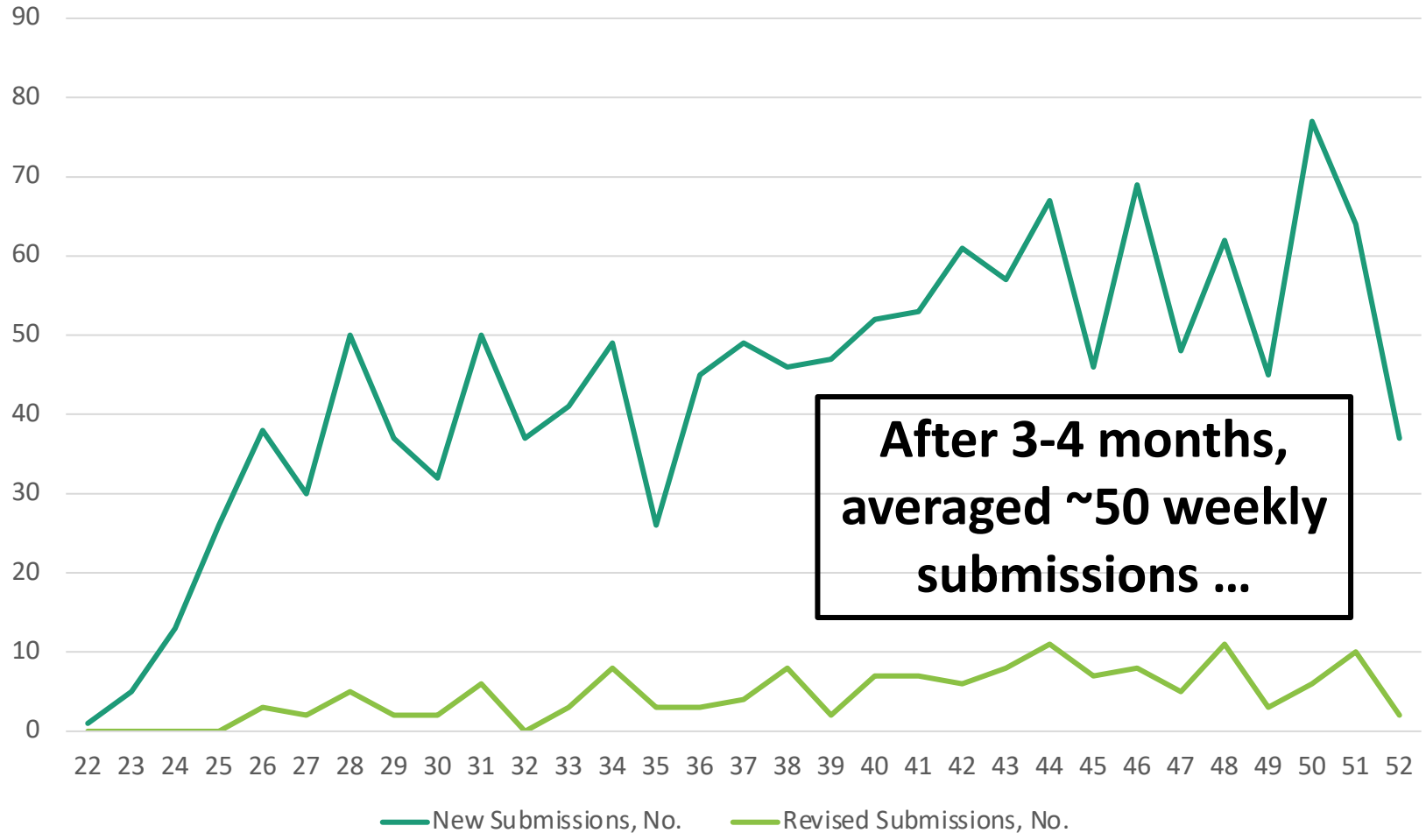
What is an unrefereed

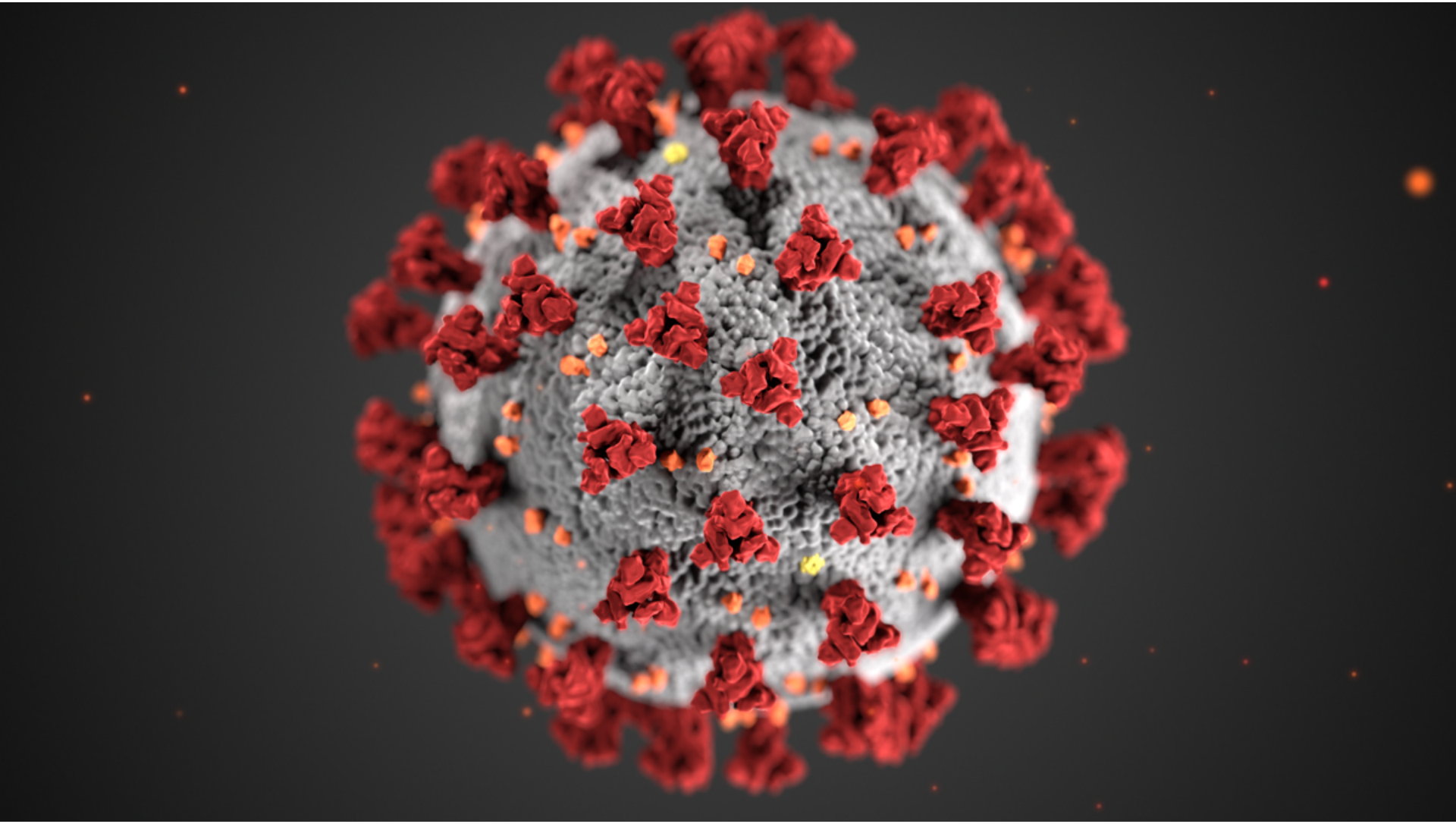
Before formal publication in a scholarly journal
are traditionally "peer reviewed." In this proces
advice from various experts—called "referees"
paper and may identify weaknesses in its assum
conclusions. Typically a journal will only publish
satisfied that the authors have addressed refere
presented support the conclusions drawn in th

Because this process can be lengthy, authors us
their manuscripts available as "preprints" *before*

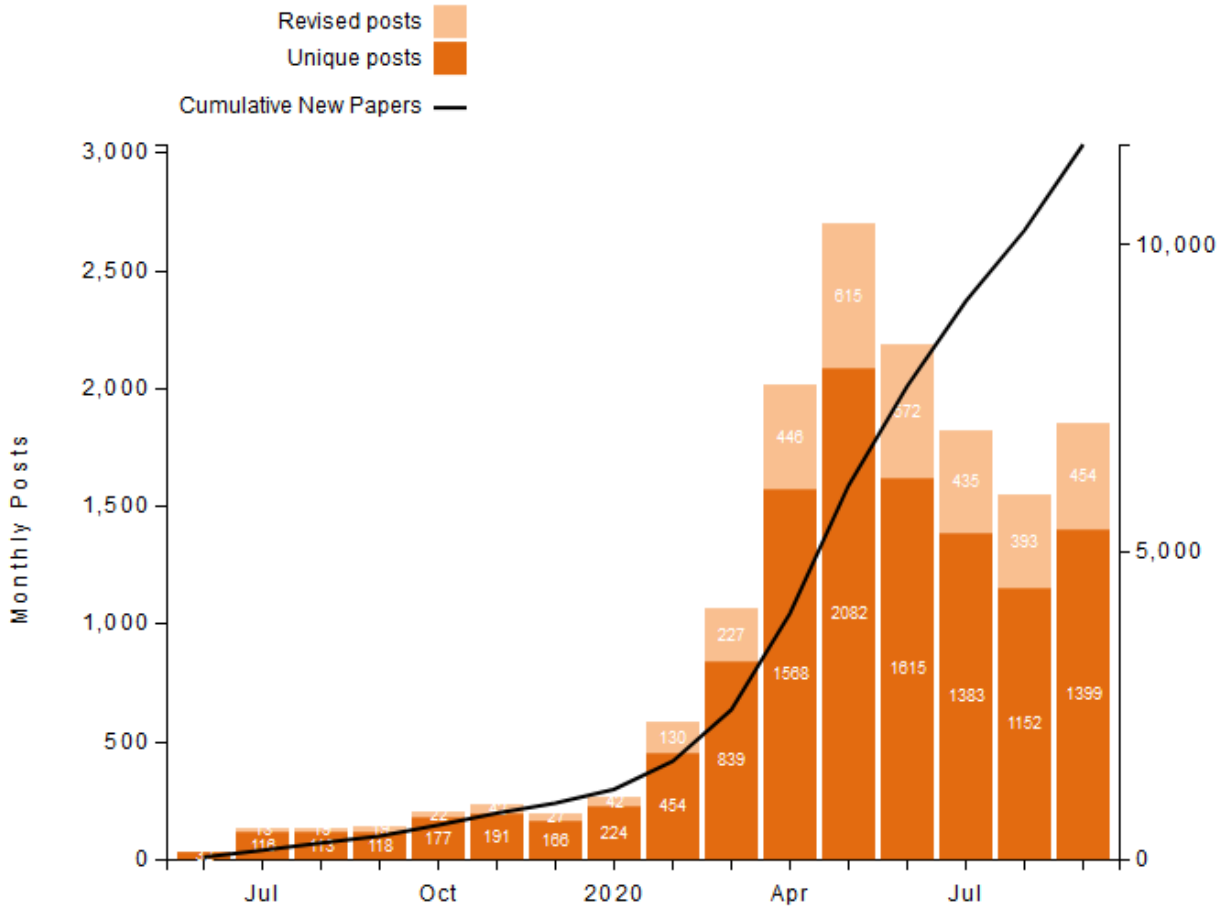
We also urge journalists and other individuals who report on medical research to the general public to consider this when discussing work that appears on medRxiv and emphasize it has yet to be evaluated by the medical community and the information presented may be erroneous.

Weekly submissions (06/05/19 – 12/31/19)





	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep
Average **DAILY** Submissions, No.	7.2	16.2	27.1	52.3	77.1	65.1	58.6	49.5	61.8

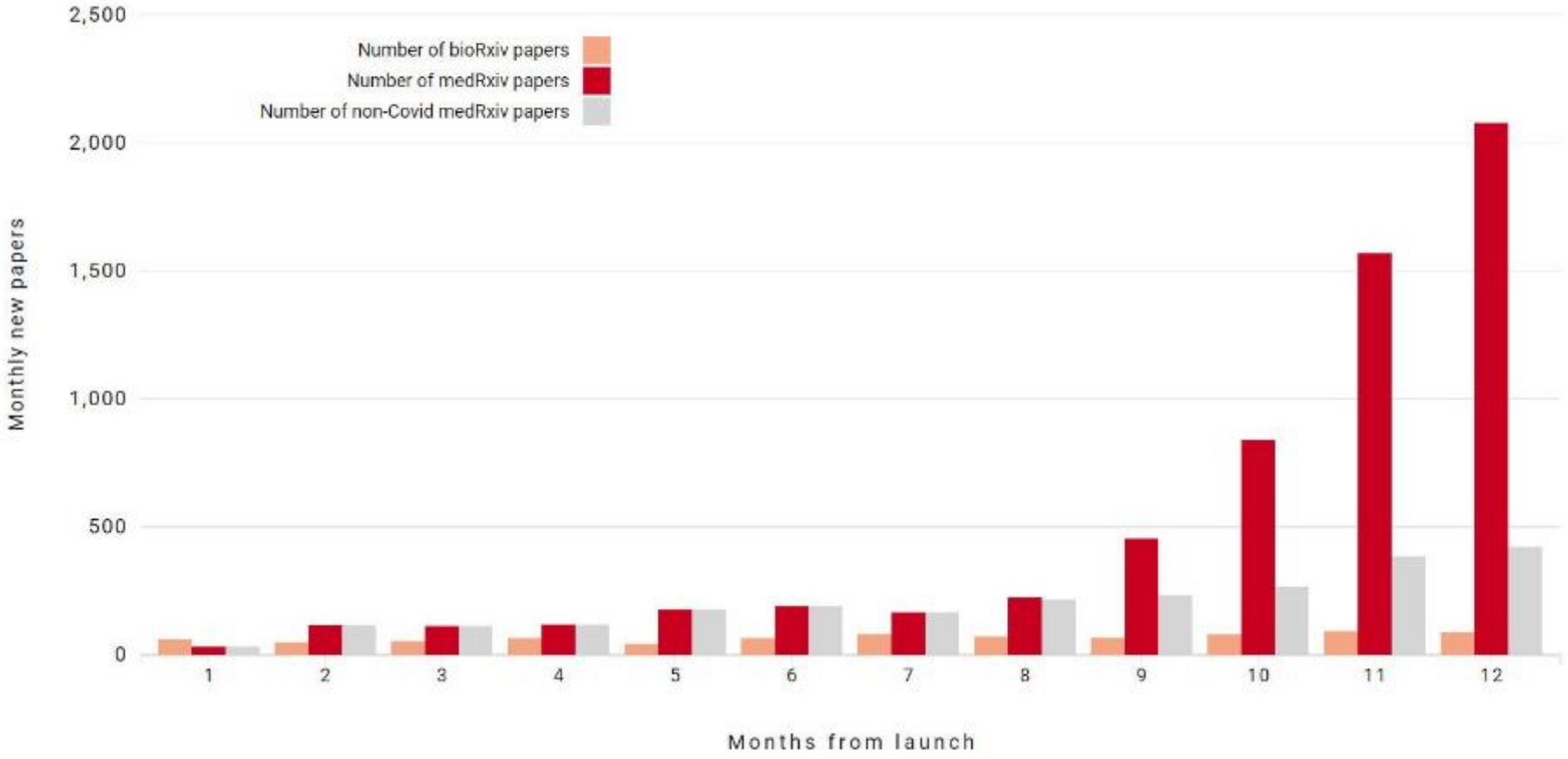


~12000 total papers

~3500 revised

~25% rejected

Content growth comparison by month



>3000 Institutions Represented

Top 10

University of Oxford

University of Cambridge

Stanford University

University College London

King's College London

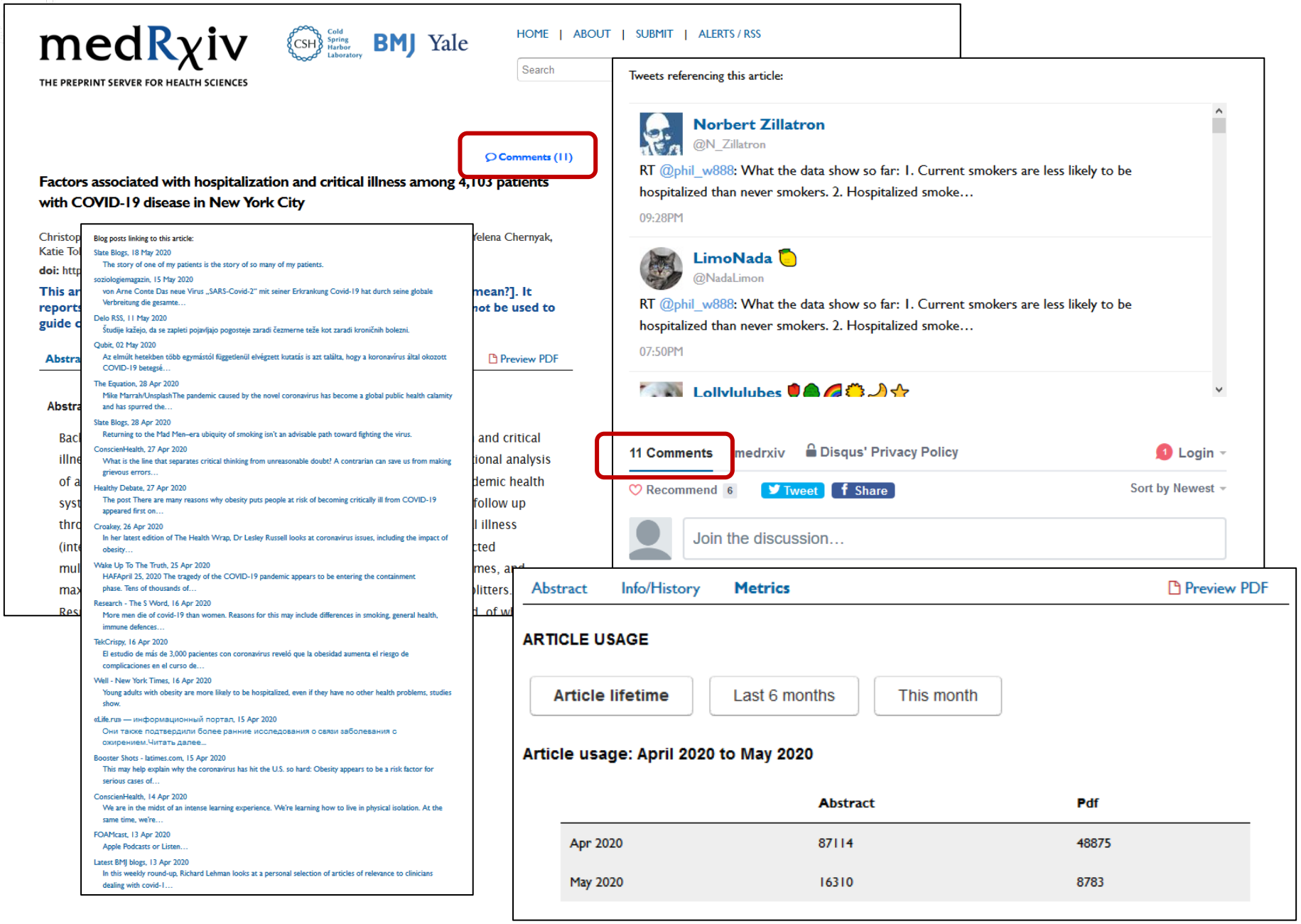
University of Bristol

University of Michigan

Imperial College London

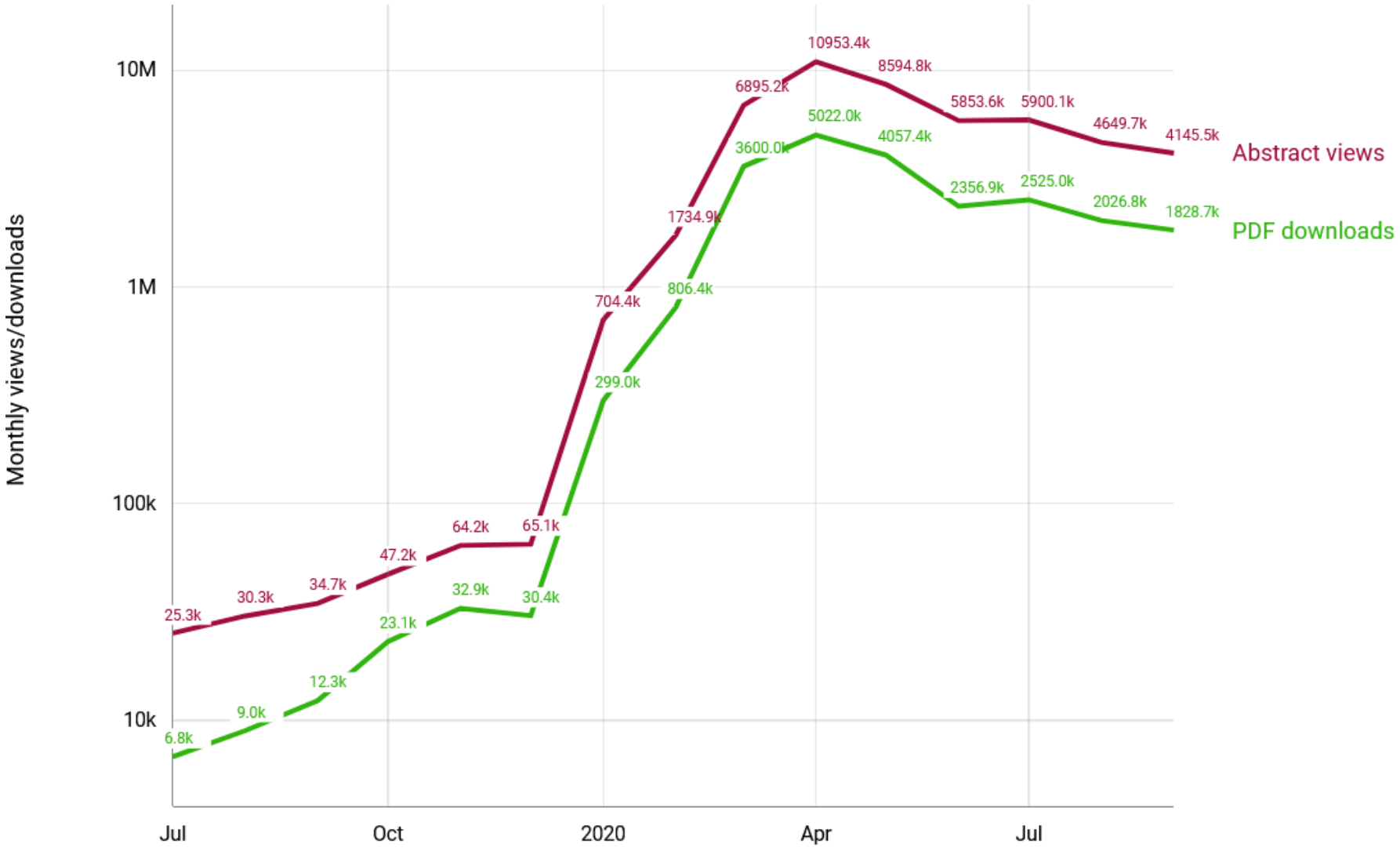
London School of Hygiene and Tropical Medicine

Yale University



Source: Petrilli et. al., https://www.medrxiv.org/content/10.1101/2020.04.08.20057794v1.

Monthly Usage (excluding bots)



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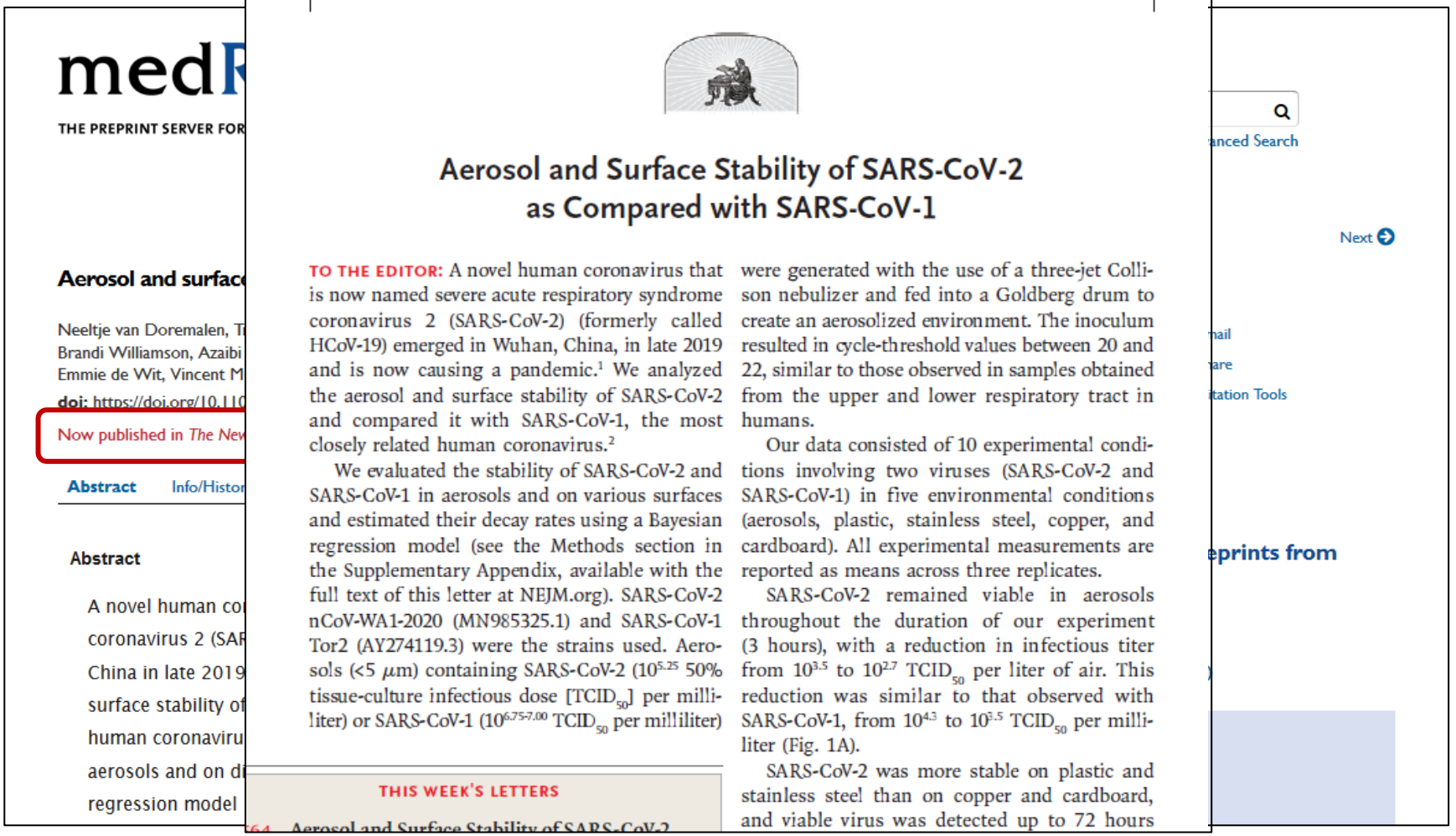

medR

THE PREPRINT SERVER FOR

Aerosol and surfac

Neeltje van Doremalen, T
Brandi Williamson, Azaibi
Emmie de Wit, Vincent M

doi: https://doi.org/10.11

Now published in *The New*

Abstract Info/Histor

Abstract

A novel human co
coronavirus 2 (SAR
China in late 2019
surface stability of
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The NEW ENGLAND JOURNAL of MEDICINE

CORRESPONDENCE

Aerosol and Surface Stability of SARS-CoV-2 as Compared with SARS-CoV-1

TO THE EDITOR: A novel human coronavirus that is now named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (formerly called HCoV-19) emerged in Wuhan, China, in late 2019 and is now causing a pandemic.[1] We analyzed the aerosol and surface stability of SARS-CoV-2 and compared it with SARS-CoV-1, the most closely related human coronavirus.[2]

We evaluated the stability of SARS-CoV-2 and SARS-CoV-1 in aerosols and on various surfaces and estimated their decay rates using a Bayesian regression model (see the Methods section in the Supplementary Appendix, available with the full text of this letter at NEJM.org). SARS-CoV-2 nCoV-WA1-2020 (MN985325.1) and SARS-CoV-1 Tor2 (AY274119.3) were the strains used. Aerosols (<5 μm) containing SARS-CoV-2 ($10^{5.25}$ 50% tissue-culture infectious dose [$TCID_{50}$] per milliliter) or SARS-CoV-1 ($10^{6.75-7.00}$ $TCID_{50}$ per milliliter) were generated with the use of a three-jet Collison nebulizer and fed into a Goldberg drum to create an aerosolized environment. The inoculum resulted in cycle-threshold values between 20 and 22, similar to those observed in samples obtained from the upper and lower respiratory tract in humans.

Our data consisted of 10 experimental conditions involving two viruses (SARS-CoV-2 and SARS-CoV-1) in five environmental conditions (aerosols, plastic, stainless steel, copper, and cardboard). All experimental measurements are reported as means across three replicates.

SARS-CoV-2 remained viable in aerosols throughout the duration of our experiment (3 hours), with a reduction in infectious titer from $10^{3.5}$ to $10^{2.7}$ $TCID_{50}$ per liter of air. This reduction was similar to that observed with SARS-CoV-1, from $10^{4.3}$ to $10^{3.5}$ $TCID_{50}$ per milliliter (Fig. 1A).

SARS-CoV-2 was more stable on plastic and stainless steel than on copper and cardboard, and viable virus was detected up to 72 hours

THIS WEEK'S LETTERS

64 Aerosol and Surface Stability of SARS-CoV-2

Source: van Doremalen et. al., https://www.medrxiv.org/content/10.1101/2020.03.09.20033217v2.

Comments (17)

Effect of Dexamethasone in Hospitalized Patients with COVID-19: Preliminary Report

Peter Horby, Wei Shen Lim, Jonathan Emberson, Marion Mafham, Jennifer Bell, Louise Linsell, Natalie Staplin, Christopher Brightling, Andrew Ustianowski, Einas Elmahi, Benjamin Prudon, Christopher Green, Timothy Felton, David Chadwick, Kanchan Rege, Christopher Fegan, Lucy C Chappell, Saul N Faust, Thomas Jaki, Katie Jeffery, Alan Montgomery, Kathryn Rowan, Edmund Juszczak, J Kenneth Baillie, Richard Haynes, Martin J Landray, RECOVERY Collaborative Group

doi: https://doi.org/10.1101/2020.06.22.20137273

This article is a preprint and has not been peer-reviewed [what does this mean?]. It reports new medical research that has yet to be evaluated and so should *not* be used to guide clinical practice.

Previous
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Posted June 22, 2020.

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COVID-19 SARS-CoV-2 preprints from medRxiv and bioRxiv

ORIGINAL ARTICLE

Dexamethasone in Hospitalized Patients with Covid-19 — Preliminary Report

The RECOVERY Collaborative Group*

Article | Figures/Media | Metrics

July 17, 2020
DOI: 10.1056/NEJMoa2021436

39 References 192 Citing Articles

Abstract

BACKGROUND

Coronavirus disease 2019 (Covid-19) is associated with diffuse lung damage. Glucocorticoids may modulate inflammation-mediated lung injury and thereby reduce progression to respiratory failure and death.

METHODS

In this controlled, open-label trial comparing a range of possible treatments in patients who were

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