Preprint Servers: improving research transparency or bad idea?

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PHRI Rounds, Wednesday February 9th 2022

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Population Health Research Institute
HEALTH THROUGH KNOWLEDGE

Hamilton Health Sciences

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Disclosures

Speaker and Advisory fees from Otsuka, Bayer, Sanofi, Reata

Funding from Canadian Institutes of Health Research, Kidney Foundation of Canada, Canadian Society of Nephrology, American Society of Nephrology

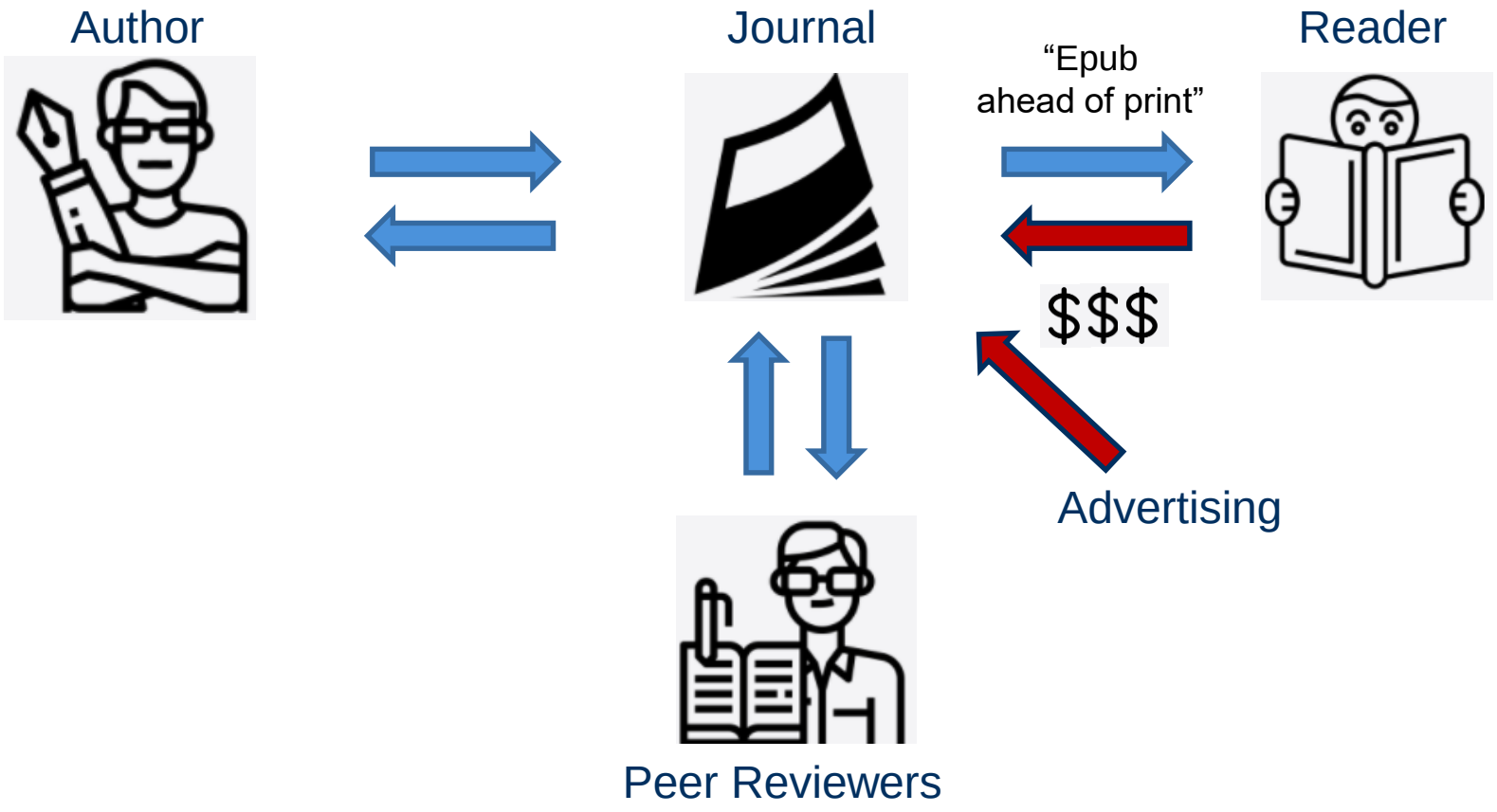
Objectives

1) What is a preprint server and how does it work?

2) What are the potential benefits?

3) What are some concerns or drawbacks?

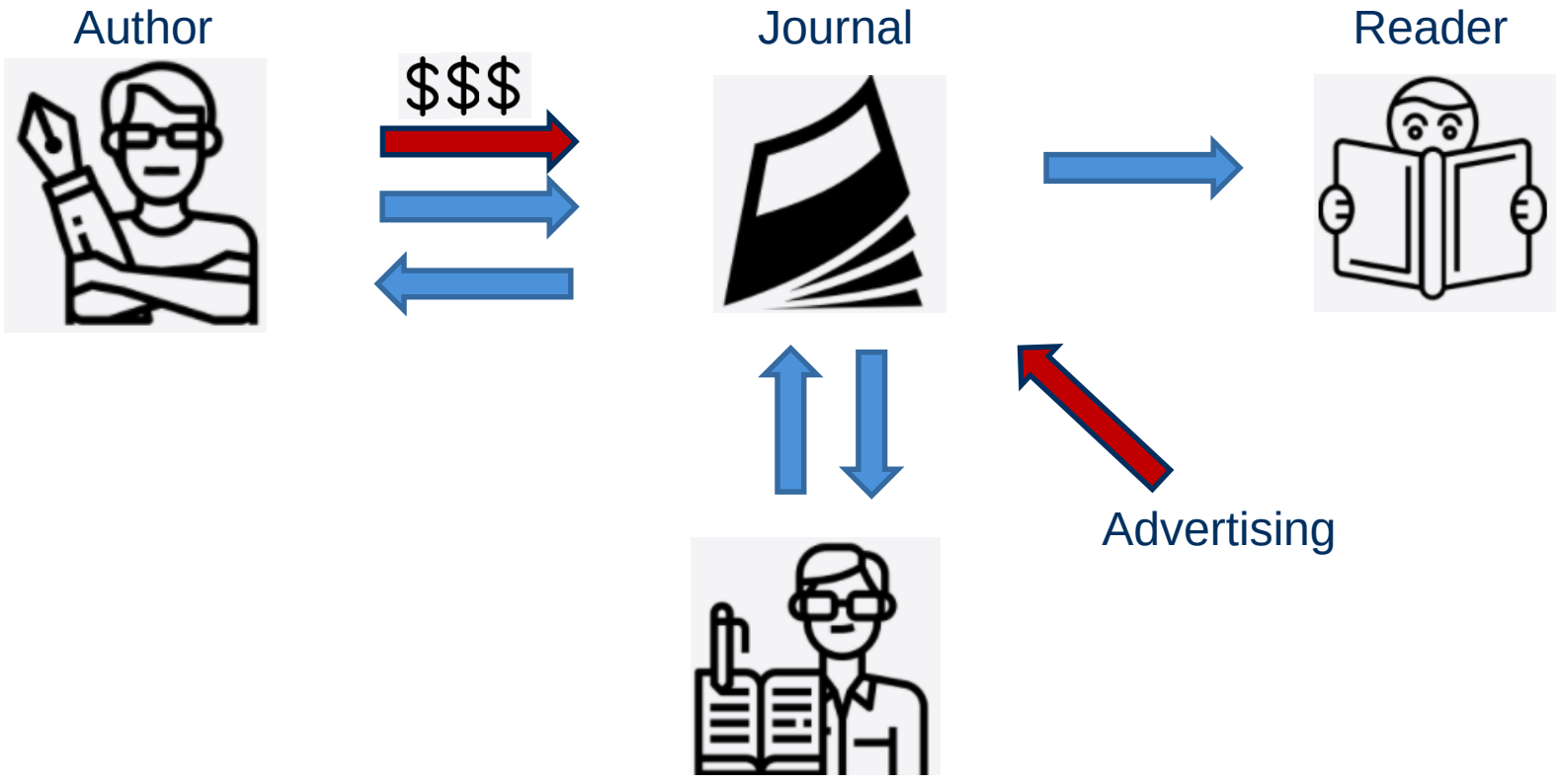
Traditional publication model



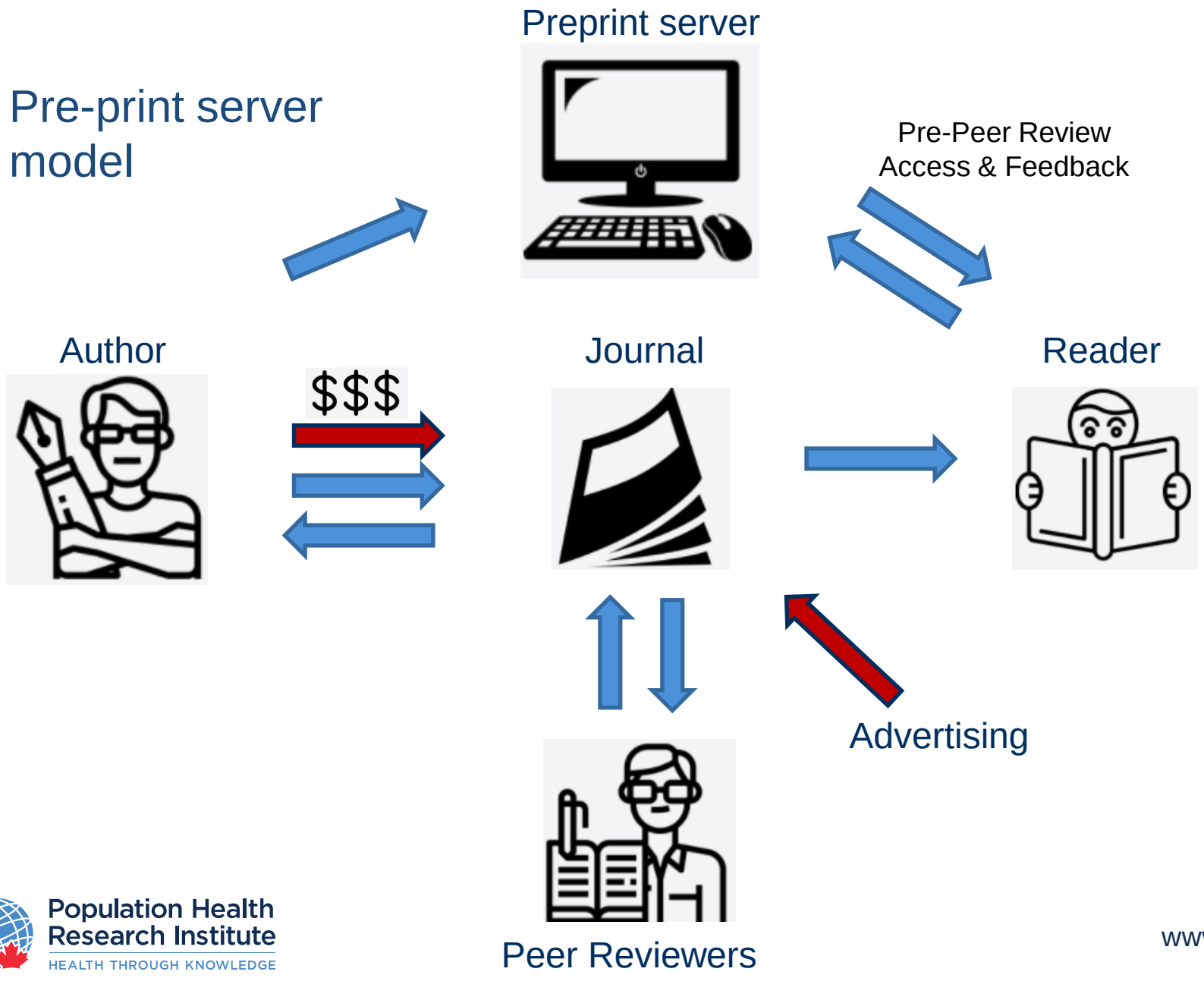
Features of the ideal publication model

- Transparency / Free from bias
- Equity
  - Credit allocation
  - Access / Availability
  - Opportunity to disseminate findings
- Validity / Improve replicability
- Foster collaboration & open debate
- Rapidity
- Permanence, yet correctable
- Promotion/Improve visibility

“Open access” model



Pre-print server model



Goals of Preprint servers

- Provide public access to pre-peer review research
- Establish public record or “provenance” of ideas
- Increase rapidity dissemination
- Improve visibility
- Mitigate publication bias

Preprint servers

arXiv.org

Circa. 1991

RePEc

Circa. 1997

bioRxiv

THE PREPRINT SERVER FOR BIOLOGY

Circa. 2013

PsyArXiv

Circa. 2016

medRxiv

THE PREPRINT SERVER FOR HEALTH SCIENCES

Circa. 2019

Preprints with THE LANCET

Circa. 2018

Cold Springs Harbor Laboratory
Chan Zuckerberg initiative

Common features of preprint servers

- Open access to original research
- Articles are not peer-reviewed, edited, or typeset
- Revised versions post-review are NOT posted
  - Link provided to journal website
- Manually screened for plagiarism, “offensive or non-scientific content”, and “material that might pose a health risk”
- Unique digital object identifier (DOI) and date of posting permanently linked to paper
- Authors may submit revisions or withdraw at any time, but previous submissions remain available as part of the permanent record
- Search engines
- Citable

As an author, why would you preprint?

- Establish providence & prevent scooping
- Increase visibility, improve Altmetric
- Speed up dissemination
- Demonstrate progress in funding applications
- Receive early feedback
- Streamline submission process
- Akin to conference presentation
- Identify potential reviewers from social media

As a journal, concerns about preprints?

- Negatively impact novelty?
- Will they still need us?
  - Demonstrates the need for peer review, curation, editorials, copy editing, quality control, production, dissemination
- Improve peer review?
- Reduce the probability of fraudulent research?
- Increase visibility/ induce hype

As a reviewer, impact from preprints?

- No longer benefit from early access to research
- Crowd-sourced reviews may influence your views

Who accepts Preprinted manuscripts?

Table 1. Preprint policies reported by the top 20 journals in nephrology

Journals that Accept Preprinted Articles	Journals that Do Not Accept Preprinted Articles
American Journal of Nephrology	*Advances in Chronic Kidney Disease*[a]
BMC Nephrology	*American Journal of Kidney Disease*
Canadian Journal of Kidney Health and Disease	*Journal of Renal Nutrition*
CJASN	*Nature Reviews Nephrology*[a]
Clinical Kidney Journal	
Current Opinion in Nephrology and Hypertension[a]	
International Journal of Nephrology and Renovascular Disease	
JASN	
Journal of Nephrology	
Kidney International	
Kidney International Reports	
Kidney International Supplements	
Nephron	
Nephrology, Dialysis and Transplantation	
Pediatric Nephrology	
Seminars in Nephrology	

[a]Only publishes invited reviews.

Who accepts Preprinted manuscripts?

BMJ: *"BMJ fully supports and encourages the archiving of preprints in any recognized, not-for-profit, preprint server."*

NEJM: "NEJM accepts the submission of manuscripts that have previously been posted on a nonprofit preprint server. Authors should notify NEJM of any preprint related to a manuscript submission."

JAMA: *"Manuscripts that have been previously posted on a preprint server may be submitted for consideration for publication. When the manuscript is submitted, authors must provide information about the preprint, including a link to it and a description of whether the submitted manuscript has been revised or differs from the preprint."*

Lancet: *"the Lancet journals initiated a collaboration with the research sharing platform SSRN to offer authors a dedicated preprint area called Preprints with The Lancet."*

Who accepts Preprinted manuscripts?

86% of top 100 clinical journals accept

13% had “case-by-case” policy

Who accepts Preprinted manuscripts?

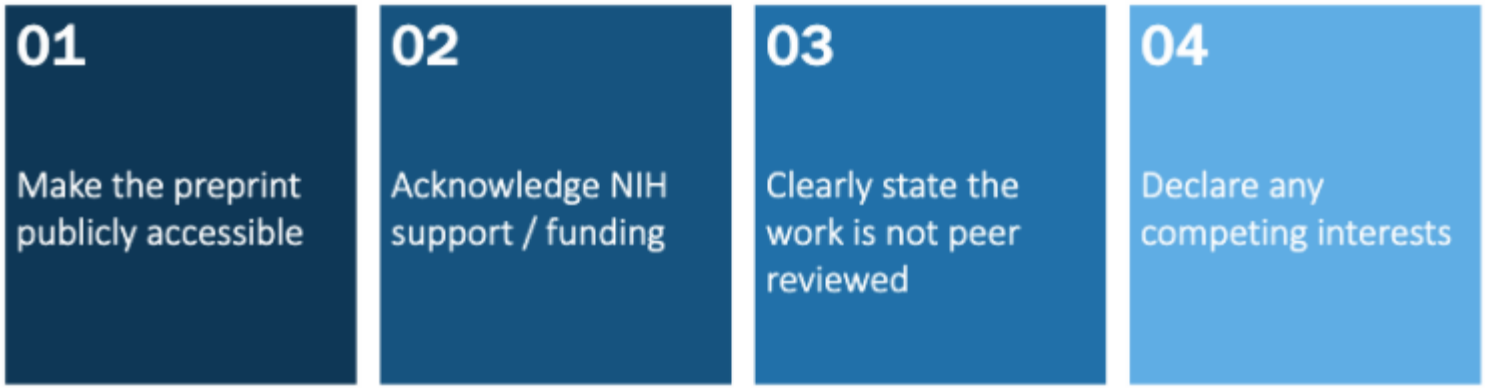
American Society of Nephrology “Kidney Week” & American Heart Association:
Posting of unrefereed manuscripts to a community preprint server by authors will not be considered as prior publication, provided that the following conditions are met:

- During submission, authors acknowledge preprint server deposition.
- Versions of a manuscript that have been altered as a result of the peer review process may not be deposited;
- The preprint version cannot be indexed (e.g., in MEDLINE or PubMed).
- Upon ASN publication, authors are responsible for updating the archived preprint version with a link to the ASN Abstract Supplement PDF.
- The preprint server should meet NIH standards for interim research product repositories.

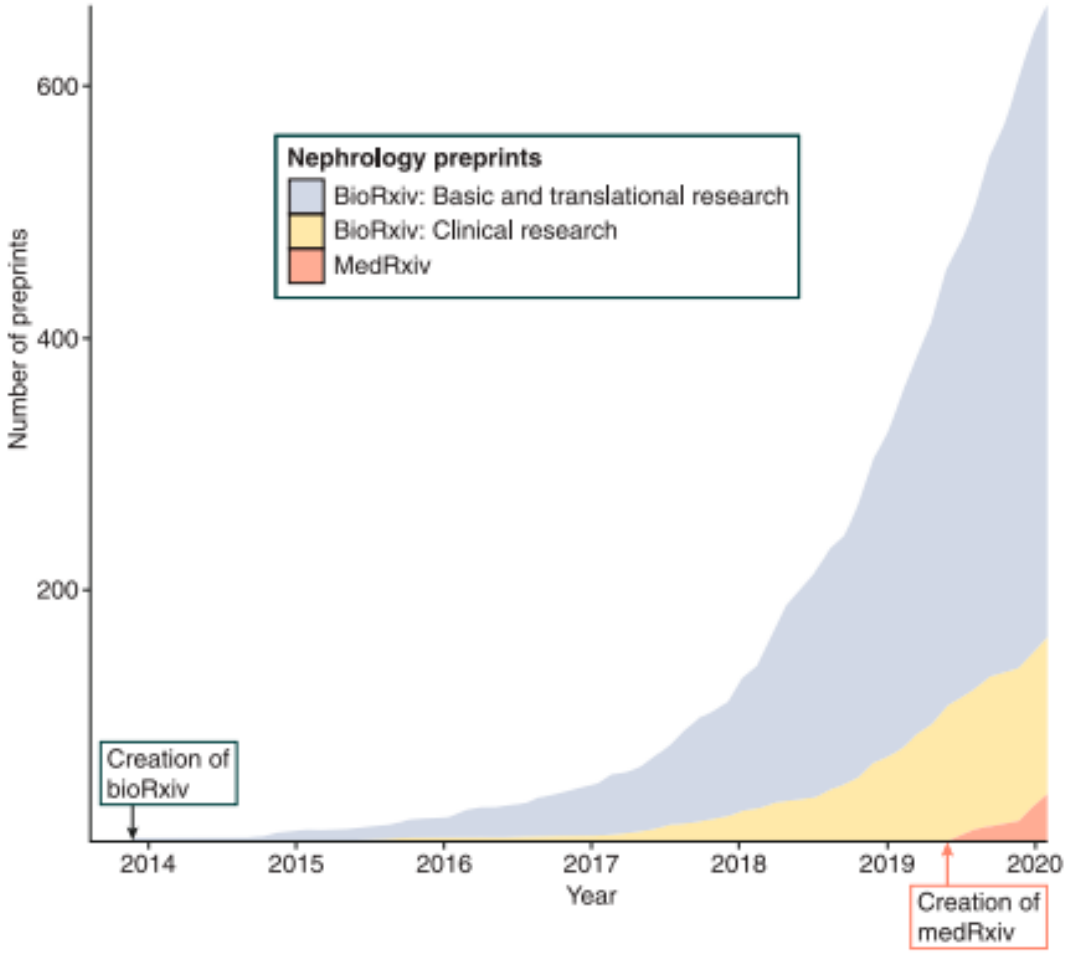
Who accepts Preprinted manuscripts?

CIHR: *Since the early 2000's, CIHR has recognized preprints as an important vehicle for the dissemination of research results. As recognition and support for preprints as legitimate sources for the transmission of scientific knowledge increases, the importance of standards and best practices related to preprints, and preprint servers, must follow. CIHR and other funding agencies are working with key stakeholders to support the development of relevant resources and raise awareness of the role of preprints in the research enterprise.*

NIH: Guidance to investigators



Rapid growth in preprint server use



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Vlasschaert, Lanktree *CJASN* 2021

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Uptake of medRxiv

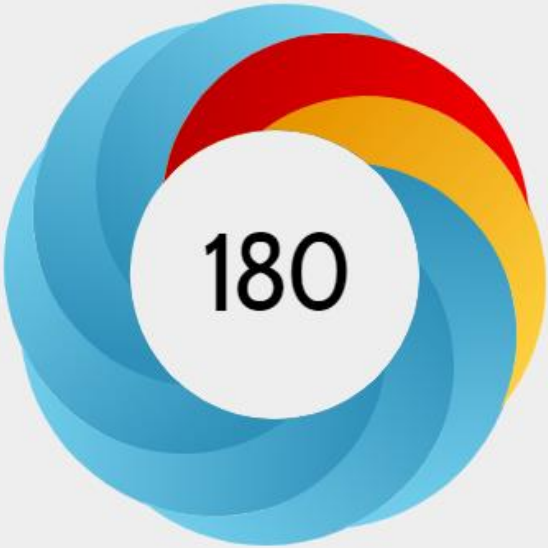
11,164 submissions in the first year
1197 (11%) rejected from posting
18 (0.002%) were subsequently withdrawn

Only 9% had comments posted in medRxiv
(Does not include twitter or blog posts)

Only 10% published in peer-reviewed literature within 1 year

Altmetric

- Measure online presence
- Indicator of impact & interest
- Early, more diverse than citation-based metrics
- Used by journals, institutions, granting agencies



About this Attention Score

In the top 5% of all research outputs scored by Altmetric

MORE...

Mentioned by

11 news outlets
1 blog
132 tweeters

June 30, 2021

Timing and Length of Nocturnal Sleep and Daytime Napping and Associations With Obesity Types in High-, Middle-, and Low-Income Countries

Lap Ah Tse, PhD[1]; Chuangshi Wang, PhD[2]; Sumathy Rangarajan, MSc[3]; et al

» Author Affiliations | Article Information

JAMA Netw Open. 2021;4(6):e2113775. doi:10.1001/jamanetworkopen.2021.13775

Altmetric Scores, Citations, and Publication of Studies Posted as Preprints

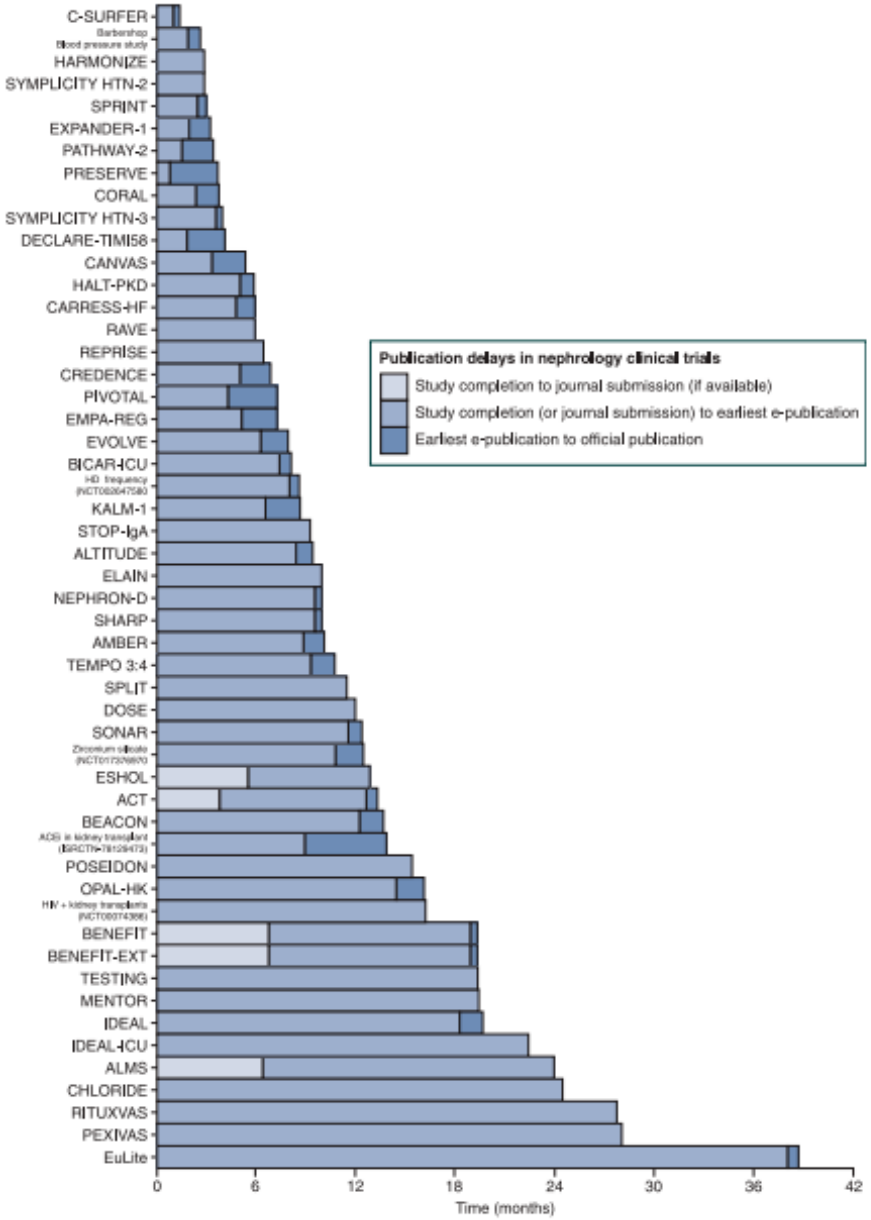
- 776 bioRxiv articles that were subsequently published from Nov 2013-Jan 2017
- for each article, selected up to 5 matching articles published in same issue that were not submitted to a preprint server
- Of preprinted articles:
  bioinformatics (16%), neuroscience (13%), genomics (12%), only 3 were clinical trials
- Preprinted articles had greater Altmetric scores:

  9.5 [IQR 3 to 35] vs 3.5 [IQR 1 to 12] $P < 0.001$
- Preprinted articles had more citations

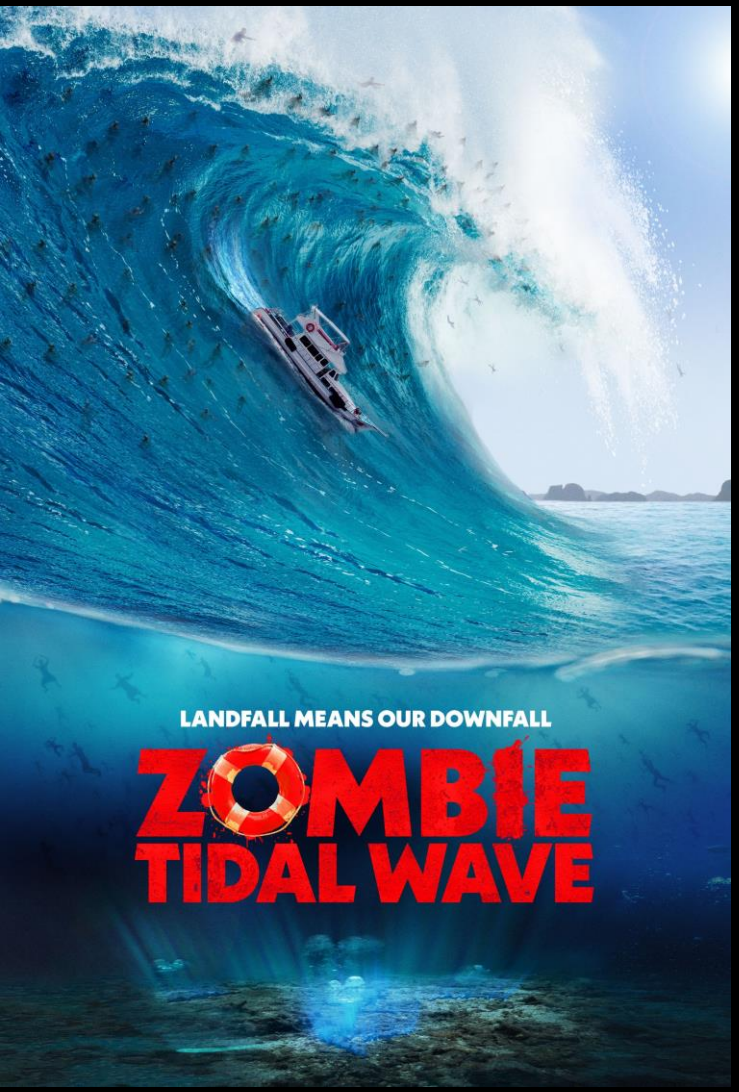
  4 [IQR 1 to 10] vs 3 [IQR 1 to 7] $P < 0.001$

Time from study completion to publication

Median = 300 days



Vlasschaert, Lanktree *CJASN* 2021



Infodemic

Flood of false or misleading information

Preprint servers during COVID-19

>6000 COVID-19 preprints within 4 months of the first confirmed case

accounted for 73% of medRxiv submissions Feb-June 2020

Greater media attention of pre-printed articles in the context of poor understanding of implications of “preprint” science in general population

Misleading titles, false claims

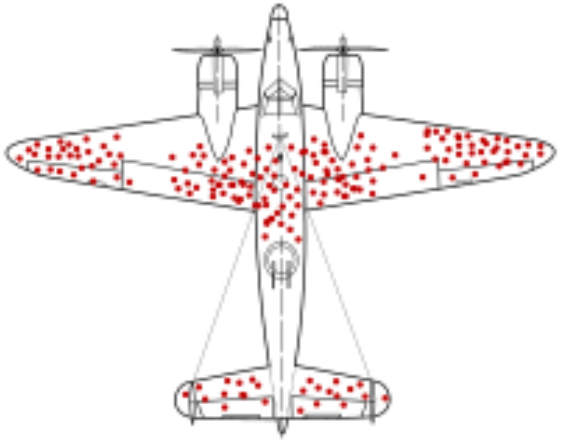
Responsible reporting:

- Emphasis of **“preliminary”**
- Explicitly labelled as “not peer reviewed”
- Include comment from non-conflicted expert

META-RESEARCH ARTICLE

Tracking changes between preprint posting and journal publication during a pandemic

- 14,812 bioRxiv and medRxiv COVID articles Sept 2019-Apr 2020
  - -> 105 preprint-published paper pairs by May 1, 2020
  - -> “randomly selected” 105 preprint-published non-COVID pairs
- Variety of quantitative and qualitative metrics of changes to paper
- No change in # of figures or tables
- Qualitative changes to conclusions:
  - 17.2% of COVID related studies
  - 7.2% of non-COVID related studies



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Brierly *et al*., PLOS Biology 2022

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Preprint servers during COVID-19

Effectiveness of Ivermectin-Based Multidrug Therapy in Severe Hypoxic Ambulatory COVID-19 Patients

Sabine Hazan, Sonya Dave, Anoja W. Gunaratne, Sibasish Dolai, Robert L Clancy, Peter A. McCullough, Thomas J. Borody

medRxiv 2021.07.06.21259924; doi: https://doi.org/10.1101/2021.07.06.21259924

Picked up by **6** news outlets
Blogged by **2**
Tweeted by **3714**

Randomized Controlled Trials of Early Ambulatory Hydroxychloroquine in the Prevention of COVID-19 Infection, Hospitalization, and Death: Meta-Analysis

Joseph A. Ladapo, John E. McKinnon, Peter A. McCullough, Harvey A. Risch

medRxiv 2020.09.30.20204693; doi: https://doi.org/10.1101/2020.09.30.20204693

See more details

Picked up by **12** news outlets
Blogged by **6**
Tweeted by **6609**
On **1** Facebook pages
On **1** videos

Contribution of endogenous and exogenous antibodies to clearance of SARS-CoV-2 during convalescent plasma therapy

Maddalena Marconato, Irene A. Abela, Anthony Hauser, Magdalena Schwarzmüller, Rheliana Katzensteiner, Dominique L. Braun, Selina Epp, Annette Audigé, Jacqueline Weber, Peter Rusert, Emèry Schindler, Chloé Pasin, Emily West, Jürg Böni, Verena Kufner, Michael Huber, Maryam Zaheri, Stefan Schmutz, Beat M. Frey, Roger D. Kouyos, Huldrych F. Günthard, Markus G. Manz, Alexandra Trkola

medRxiv 2021.12.09.21267513; doi: https://doi.org/10.1101/2021.12.09.21267513

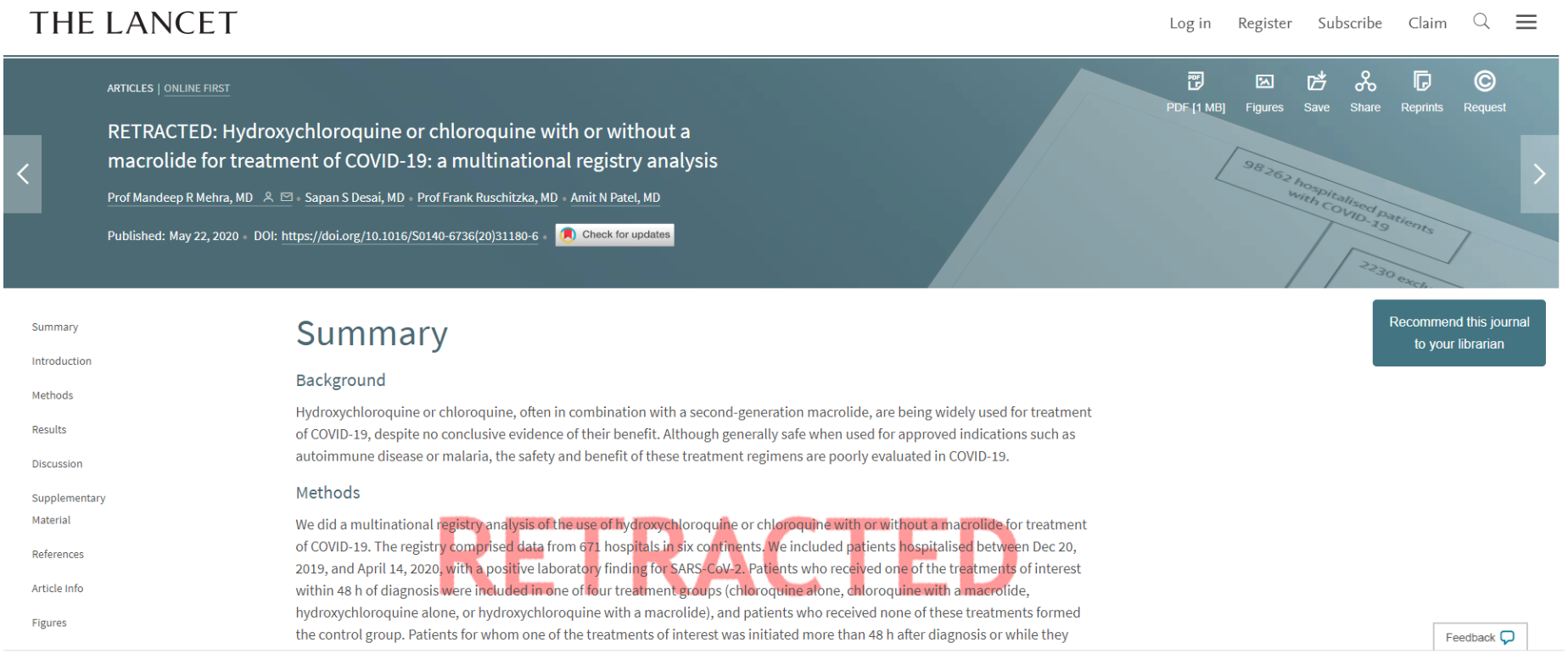
Tweeted by **45**

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.

Risks of preprint servers

- Rapid dissemination of untruths may cause harm
- Apparent “flip-flop” may reduce credibility in eyes of lay audience
- Media may utilize uncredible “experts” for interpretation
- “Research requires scrutiny before public dissemination”
- Over-emphasis of single studies
- Over-emphasis of relative effects without recognition of population and limitations
- Overwhelms with volume
- Disruption of publication primacy
  - Who is first?
  - Favors posting of preliminary results

Surgisphere Scandal



THE LANCET

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ARTICLES | ONLINE FIRST

RETRACTED: Hydroxychloroquine or chloroquine with or without a macrolide for treatment of COVID-19: a multinational registry analysis

Prof Mandeep R Mehra, MD • Sapan S Desai, MD • Prof Frank Ruschitzka, MD • Amit N Patel, MD

Published: May 22, 2020 • DOI: https://doi.org/10.1016/S0140-6736(20)31180-6 • Check for updates

PDF [1 MB] Figures Save Share Reprints Request

98 262 hospitalised patients with COVID-19

2230 excl

Summary
Introduction
Methods
Results
Discussion
Supplementary Material
References
Article Info
Figures

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Summary

Background

Hydroxychloroquine or chloroquine, often in combination with a second-generation macrolide, are being widely used for treatment of COVID-19, despite no conclusive evidence of their benefit. Although generally safe when used for approved indications such as autoimmune disease or malaria, the safety and benefit of these treatment regimens are poorly evaluated in COVID-19.

Methods

We did a multinational registry analysis of the use of hydroxychloroquine or chloroquine with or without a macrolide for treatment of COVID-19. The registry comprised data from 671 hospitals in six continents. We included patients hospitalised between Dec 20, 2019, and April 14, 2020, with a positive laboratory finding for SARS-CoV-2. Patients who received one of the treatments of interest within 48 h of diagnosis were included in one of four treatment groups (chloroquine alone, chloroquine with a macrolide, hydroxychloroquine alone, or hydroxychloroquine with a macrolide), and patients who received none of these treatments formed the control group. Patients for whom one of the treatments of interest was initiated more than 48 h after diagnosis or while they

RETRACTED

Feedback

Published May 22nd, Retracted May 29th

Surgisphere Scandal

This article has been retracted.

ORIGINAL ARTICLE

Cardiovascular Disease, Drug Therapy, and Mortality in Covid-19

Mandeep R. Mehra, M.D., Sapan S. Desai, M.D., Ph.D., SreyRam Kuy, M.D., M.H.S., Timothy D. Henry, M.D., and Amit N. Patel, M.D.

Published May 1st, Retracted June 18th 2020

Red flags?

Collaborators? Where exactly did data come from

- “Cloud” storage of individual-level clinical data?
- Across borders?
- Acknowledgment of hospitals?

History of investigators in data science? Funding?

Turnaround time?

- Mar 15 end of collection time, May 1 publication date
- Securely extracts de-identified patient-level data, data cleaned, QC’d, analyzed, published in weeks?

Red flags?

Ethics assessment even if no individual consent required?

Sharing of data?

Even if not individual-level, hospital-level summary-data?

Inconsistencies between confidence intervals and sample sizes

Unusually small variation in baseline variables between continents

Code? Preprints?

COVID-19 hospitalized case fatality rates were 5.8%

Is this in keeping with other estimates?

Was this a failure of peer review?

Was it a failure of the journal editorial staff?

Could have this been avoided?

Should reviewers or editors be held accountable?

Further evolution of peer-review?

- Unblind reviewers?
  - Accountability
  - Reduce or minimally acknowledge bias
  - Receive credit (publons, $$, reduced publication fees)
  - Blowback
- Crowd sourced reviewers vs. invitation
- Formatting of paper following journal decision
- Sharing of reviews between journals
- Access to data
  - De-identified individual level data vs. summary
- Access to code (github)
- Authorship models

“Democracy is the worst form of government, except for all the others”

- Winston Churchill

FAQs and frequent comments

- Does it really avoid scooping?
- Do journals still look negatively on it?
- Looks like a lot of work?
- It’s too hard to find anything worthwhile
- I can’t be bothered to search the servers
- I can’t be bothered to publicly comment on preprints
- But what about the journals?
- Are preprints ever removed?
- Won’t preprints reduce the originality of reports? Make it “old news”?
- Grant reviewers can’t be expected to review preprints
- Should authors receive credit for work they haven’t pushed through peer review?
- Isn’t twitter just a waste of time?