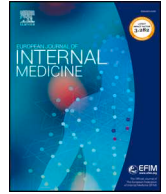




ELSEVIER

Contents lists available at ScienceDirect

European Journal of Internal Medicine

journal homepage: www.elsevier.com/locate/ejim

Letter to the Editor

Need for innovative and timely synthesis of evidence during Covid-19 outbreak

ARTICLE INFO

Keywords:

Evidence-based medicine
Methodology
Covid-19
Meta-analysis

Amid the Covid-19 pandemic, one major challenge for health-care providers is to navigate the outstanding number of new studies released every day, looking for evidence to improve clinical practice. As of May 27th, 2020, a search on Pubmed with the keywords “Covid-19” yielded an impressive number of 16,490 results, mainly retrospective analysis of existing cohorts, commentaries on pathophysiological hypothesis, and evaluation of therapeutic approaches. Such numbers are likely to skyrocket in few weeks, given the unprecedented research efforts ongoing across the world: more than 1,700 studies on Covid-19 are already registered on clinicaltrials.gov [1].

In this scenario, front-line health-care providers and clinicians struggle to keep pace with new evidence, which often needs careful interpretation in view of existing studies. For example, several studies are ongoing evaluating lopinavir/ritonavir in the treatment of Covid-19, but any new findings will have to be compared with the already published randomized controlled trial [2]; only in the last weeks, three studies reported findings on the use of hydroxychloroquine [3,4,8], and others are on the way.

Among uncertainties generated by fragmented evidence, rigorous qualitative and quantitative synthesis methods (i.e. systematic review and meta-analysis) represent an unparalleled ally for translating these investigations effectively into clinical practice. However, in a pandemic landscape, these approaches should be implemented to address the need for rapid inclusion of new relevant studies and to achieve a timely update of the synthesis, regardless of the actual start of the search strategy. Conversely, producing duplicated reviews, with no added value to the existing knowledge, is a practical risk researcher can face, given the dispersion of overwhelming information we are witnessing. To date, more than a thousand reviews on Covid-19, already indexed on Pubmed, are inevitably destined to become shortly outdated.

Therefore, a call for collaborative initiatives among experts is needed to guarantee a better allocation of resources. A thorough search for similar ongoing or published reviews should be conducted before starting a new project; if a similar review is found, authors should pursue in conducting a new one only if the addition of newly published studies is predicted to significantly change the results. Moreover, investigators should share protocols of their reviews, to ease a rapid update. Given the expected high heterogeneity between study settings

and protocols, meta-analyses of individual participant data should be performed, whenever feasible; these would allow more flexible and reliable analysis than study-level meta-analysis. Finally, Living Systematic Reviews [5,7], which are dynamic, frequently-updated review of the literature, is one promising approach that should be strongly considered, and may better meet the need of providing a rapid but rigorous synthesis of constantly updated literature.

We have learned that the fight of a pandemic poses the scientific community in front of the responsibility to provide reliable and scientifically sound answers to an entirely new and unknown disease. Innovative approaches for the synthesis of evidence may represent a fundamental turning point in the battle against Covid-19, and systematic reviews and meta-analysis should timely and appropriately address the urge for answers in the uncharted.

Funding

None.

Declaration of Competing Interest

The authors declare they have no conflict of interest.

References

- [1] [Clinicaltrials.gov](https://clinicaltrials.gov/ct2/results?cond=COVID-19). Search of: COVID-19 - List Results, <https://clinicaltrials.gov/ct2/results?cond=COVID-19>; 2020 [accessed 27 May 2020].
- [2] Cao B, Wang Y, Wen D, et al. A trial of lopinavir–ritonavir in adults hospitalized with severe Covid-19. *N Engl J Med* 2020.
- [3] Geleris J, Sun Y, Platt J, et al. Observational study of hydroxychloroquine in hospitalized patients with Covid-19. *N Engl J Med* 2020. [NEJMoa2012410](https://doi.org/10.1056/NEJMoa2012410).
- [4] 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.
- [5] 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. [M20-1515](https://doi.org/10.1093/ajcp/mkz015).
- [7] Elliott JH, Turner T, Clavisi O, et al. Living systematic reviews: an emerging opportunity to narrow the evidence-practice gap. *PLoS Med* 2014;11:e1001603.
- [8] Tang W, Cao Z, Han M, et al. Hydroxychloroquine in patients with mainly mild to moderate coronavirus disease 2019: open label, randomised controlled trial. *BMJ* 2020;369(m1849).

<https://doi.org/10.1016/j.ejim.2020.06.007>

Received 1 June 2020; Accepted 4 June 2020

0953-6205/ © 2020 European Federation of Internal Medicine. Published by Elsevier B.V. All rights reserved.

Giulio Francesco Romiti^{a,*}, Bernadette Corica^a, Roberto Cangemi^a,
Stefania Basili^a, Valeria Raparelli^b

^a Department of Translational and Precision Medicine – Sapienza, University
of Rome, Rome, Italy

^b Department of Experimental Medicine – Sapienza, University of Rome,
Rome, Italy
E-mail address: giuliofrancesco.romiti@uniroma1.it (G.F. Romiti).

* Corresponding author.