The COVID-NMA initiative

An Evidence Ecosystem for the COVID-19 Pandemic

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Toward a new research ecosystem

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EVIDENCE SYNTHESIS ECOSYSTEM SERIES

Future of evidence ecosystem series: 1. Introduction Evidence synthesis ecosystem needs dramatic change

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Abstract

Objectives: This article presents why the planning, conduct, and reporting of systematic reviews and meta-analyses of therapeutic interventions are suboptimal.

Study Design and Setting: We present an overview of the limitations of the current system of evidence synthesis for therapeutic interventions.

Results: Systematic reviews and meta-analyses are a cornerstone of health care decisions. However, despite the increasing a number of published systematic reviews of therapeutic interventions, the current evidence synthesis ecosystem is not properly addressing stakeholders' needs. The current production process leads to a series of disparate systematic reviews because of erratic and inefficient planning with a process that is not always comprehensive and is prone to bias. Evidence synthesis depends on the quality of primary research, so primary research that is not available is biased or selectively reported raises important concerns. Moreover, the lack of interactions between the community of primary research producers and systematic reviewers impedes the optimal use of data. The context has considerably evolved, with ongoing research innovations, a new medical approach with the end of the one-size-fits-all approach, more available data, and new patient expectations. All these changes must be introduced into the future evidence ecosystem.

Conclusion: Dramatic changes are needed to enable this future ecosystem to become user driven and user oriented and more useful for decision-making. © 2020 Published by Elsevier Inc.

Keywords: Systematic review; Meta-analysis; Evidence synthesis ecosystem; Decision-making; Waste in research; Methods

1. Introduction

The results of more than 30,000 new randomized controlled trials (RCTs) are published every year [1]. Hence, patients, clinicians, clinical practice guideline developers, researchers, policy makers, health system managers, and funders alike find it extremely challenging to consider all the primary research findings on a given topic when making health care decisions [2]. They need a comprehensive, critical, up-to-date synthesis of all available evidence about the efficacy and safety of interventions. Accordingly, systematic reviews (i.e., a systematic identification, appraisal, and synthesis of all relevant prior studies on a specified topic according to a predetermined and explicit method [3]) and meta-analyses (i.e., the statistical aggregation of all relevant prior studies [3]) are a cornerstone of health care decisions [4,5].

Systematic reviews of RCTs have been developed to address this need and are usually considered the highest

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EVIDENCE SYNTHESIS ECOSYSTEM SERIES

Future of evidence ecosystem series: 2. current opportunities and need for better tools and methods

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Abstract

To become user driven and more useful for decision-making, the current evidence synthesis ecosystem requires significant changes (Paper 1. Future of evidence ecosystem series). Reviewers have access to new sources of data (clinical trial registries, protocols, and clinical study reports from regulatory agencies or pharmaceutical companies) for more information on randomized control trials. With all these newly available data, the management of multiple and scattered trial reports is even more challenging. New types of data are also becoming available: individual patient data and routinely collected data. With the increasing number of diverse sources to be searched and the amount of data to be extracted, the process needs to be rethought. New approaches and tools, such as automation technologies and crowdsourcing, should help accelerate the process. The implementation of these new approaches and methods requires a substantial rethinking and redesign of the current evidence synthesis ecosystem. The concept of a "living" evidence synthesis enterprise, with living systematic review and living network meta-analysis, has recently emerged. Such an evidence synthesis ecosystem implies conceptualizing evidence synthesis as a continuous process built around a clinical question of interest and no longer as a small team independently answering a specific clinical question at a single point in time. © 2020 Elsevier Inc. All rights reserved.

Keywords: Systematic review; Evidence synthesis; Clinical study report; Automation; Crowdsourcing; Living network meta-analysis

As presented in paper 1 of the Future of evidence ecosystem series, the current evidence synthesis ecosystem—ecosystem for producing systematic reviews, meta-analyses, and network meta-analyses—requires significant changes to overcome its important drawbacks to adapt to developments in health care and primary research and become more useful in the decision-making process.

In this paper, we will consider how access to new sources and types of data and recent developments of new methods, new technologies, and new tools presents a great opportunity to create and sustain an ecosystem that is better designed to support the production of updated high-quality evidence syntheses.

1. Using all existing sources and types of data

1.1. Searching, using, comparing, and integrating all sources of data

As previously discussed in paper 1, most systematic reviews currently rely on summary data extracted from reports published in peer-reviewed journals or reported in conference abstracts. This approach raises important concerns related to reporting bias [1–4] and lack of

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EVIDENCE SYNTHESIS ECOSYSTEM SERIES

Future of evidence ecosystem series: 3. From an evidence synthesis ecosystem to an evidence ecosystem

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Abstract

The "one-off" approach of systematic reviews is no longer sustainable; we need to move toward producing "living" evidence syntheses (i.e., comprehensive, based on rigorous methods, and up-to-date). This implies rethinking the evidence synthesis ecosystem, its infrastructure, and management. The three distinct production systems—primary research, evidence synthesis, and guideline development—should work together to allow for continuous refreshing of synthesized evidence and guidelines. A new evidence ecosystem, not just focusing on synthesis, should allow for bridging the gaps between evidence synthesis communities, primary researchers, guideline developers, health technology assessment agencies, and health policy authorities. This network of evidence synthesis stakeholders should select relevant clinical questions considered a priority topic. For each question, a multidisciplinary community including researchers, health professionals, guideline developers, policymakers, patients, and methodologists needs to be established and commit to performing the initial evidence synthesis and keeping it up-to-date. Encouraging communities to work together continuously with bidirectional interactions requires greater incentives, rewards, and the involvement of health care policy authorities to optimize resources. A better evidence ecosystem with collaborations and interactions between each partner of the network of evidence synthesis stakeholders should permit living evidence syntheses to justify their status in evidence-informed decision-making. © 2020 Elsevier Inc. All rights reserved.

Keywords: Systematic review; Evidence synthesis ecosystem; Evidence ecosystem; Living evidence; Primary research; Living meta-analysis; Living evidence synthesis; Living systematic review; Living monitoring of quality; Living guidelines

1. Introduction

An accurate, concise, up-to-date, and unbiased synthesis of available evidence is arguably one of the most valuable contributions a research community can offer patients, health care providers, guideline developers, funders, health policymakers or health system managers, and other decision makers [1]. Changes in health care research, advancements in technology, and the development of new methods are converging in new ways to produce higher quality evidence synthesis (i.e., based on more rigorous methods and a timely, comprehensive search) for better health care decision-making. However, these developments imply rethinking the evidence synthesis ecosystem, its infrastructure and management, and to move toward an evidence ecosystem.

For clinical research, we can no longer afford the "one-off" approach of systematic reviews relying on repeated construction and deconstruction of ephemeral review teams in a "staccato" fashion [2]. A system based on multiple initiatives arising from uncoordinated groups of researchers working to answer narrow questions focusing on only some

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0895-4356/

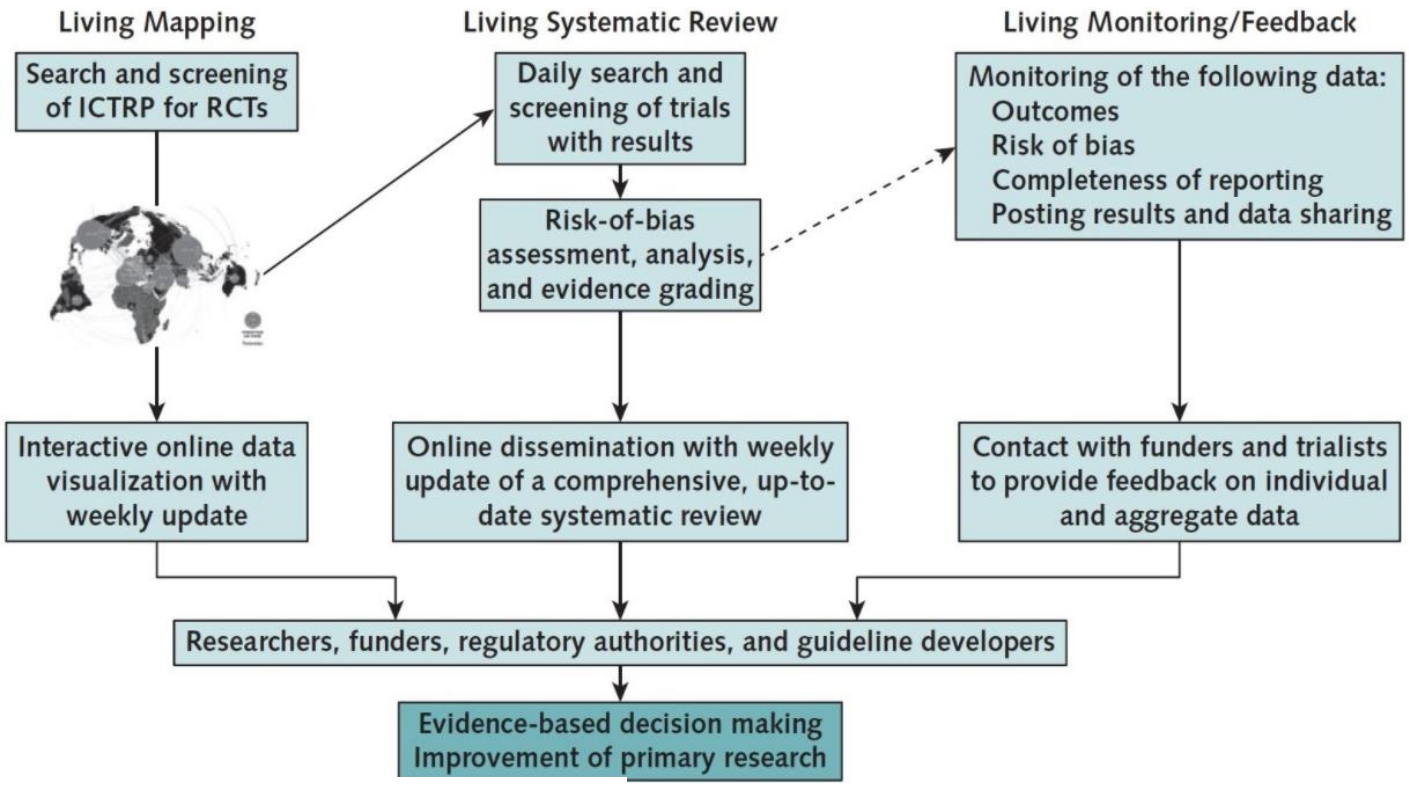
Boutron, Crequit (….), Ravaud. J Clin Epidemiol 2020
Crequit, Boutron (…) Ravaud J Clin Epidemiol 2020
Ravaud, Crequit (…) Boutron. J Clin Epidemiol 2020

Annals of Internal Medicine

IDEAS AND OPINIONS

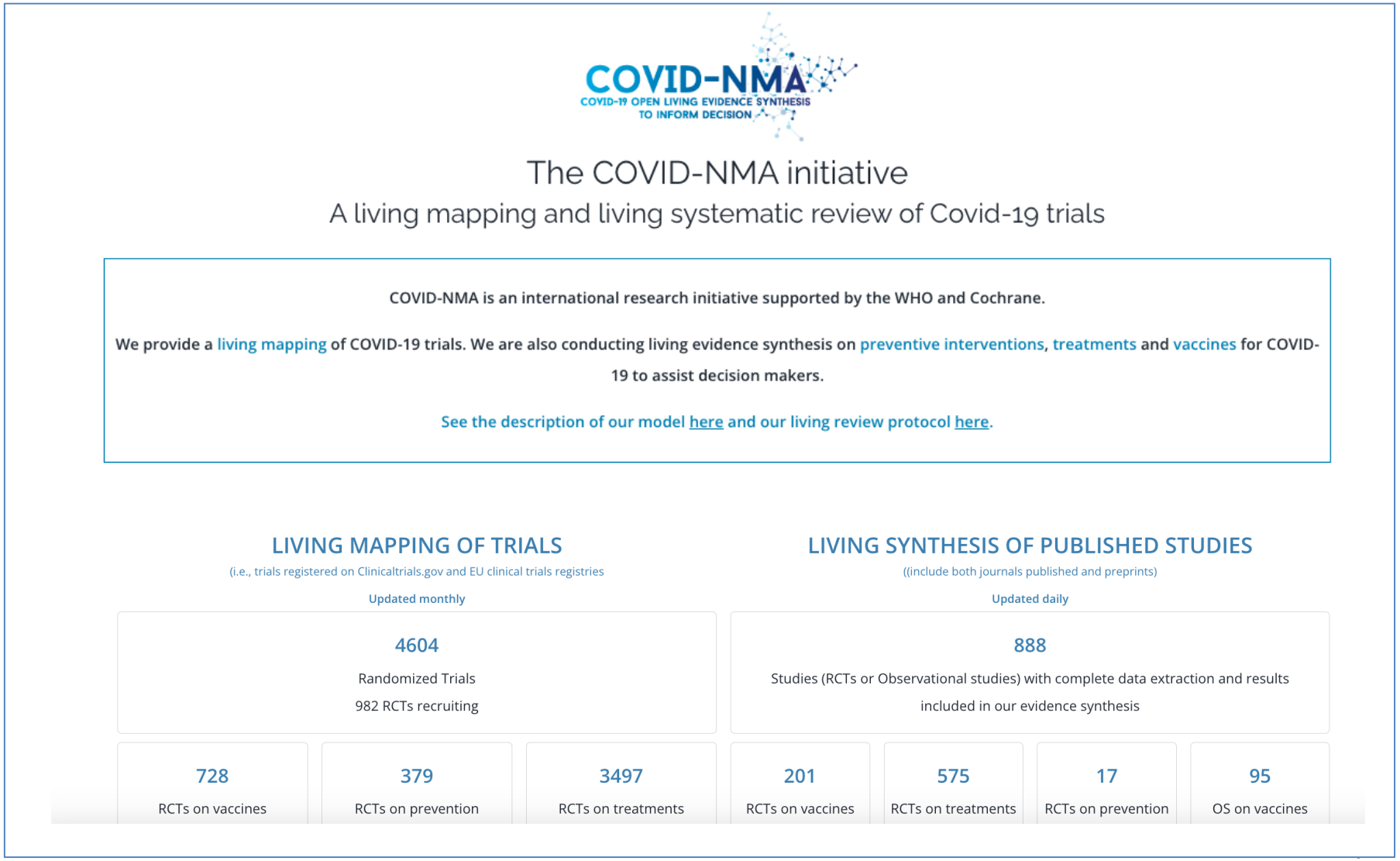
The COVID-NMA Project: Building an Evidence Ecosystem for the COVID-19 Pandemic

Isabelle Boutron, MD, PhD; Anna Chaimani, PhD; Joerg J. Meerpohl, MD; Asbjørn Hróbjartsson, MD, PhD, MPhil; Declan Devane, PhD; Gabriel Rada, MD; David Tovey, MBChB; Giacomo Grasselli, MD; and Philippe Ravaud, MD, PhD, for the COVID-NMA Consortium*



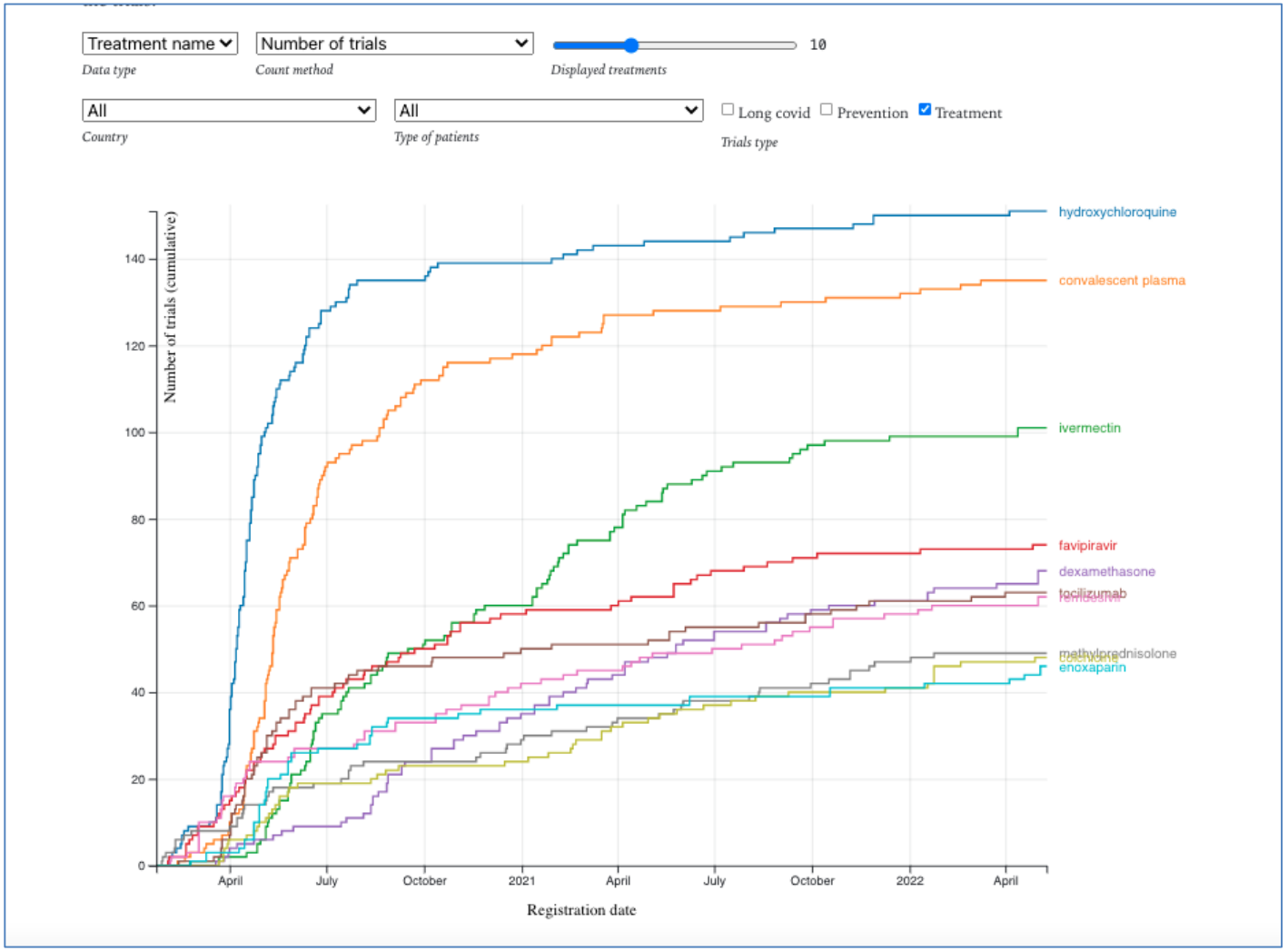
Boutron I, J Clin Epidemiol 2020
Crequit, J Clin Epidemiol 2020
Ravaud J Clin Epidemiol 2020
Boutron, Chaimani, …, Ravaud. Annals Internal Med 2020

All results made available on an open access platform https://covid-nma.com/



VISUALISATIONS: Romain Vuillemot - LIRIS, École Centrale de Lyon; Philippe Rivière - LIRIS, VisionsCarto; Pierre Ripoll - LIRIS, INSA Lyon; Julien Barnier - Centre Max Weber, CNRS.

Living mapping



Nguyen V et al. J Clin Epidemiol 2021

Living review

Contact authors

Preprint updates

External quality control

Form to request for missing data

WHO

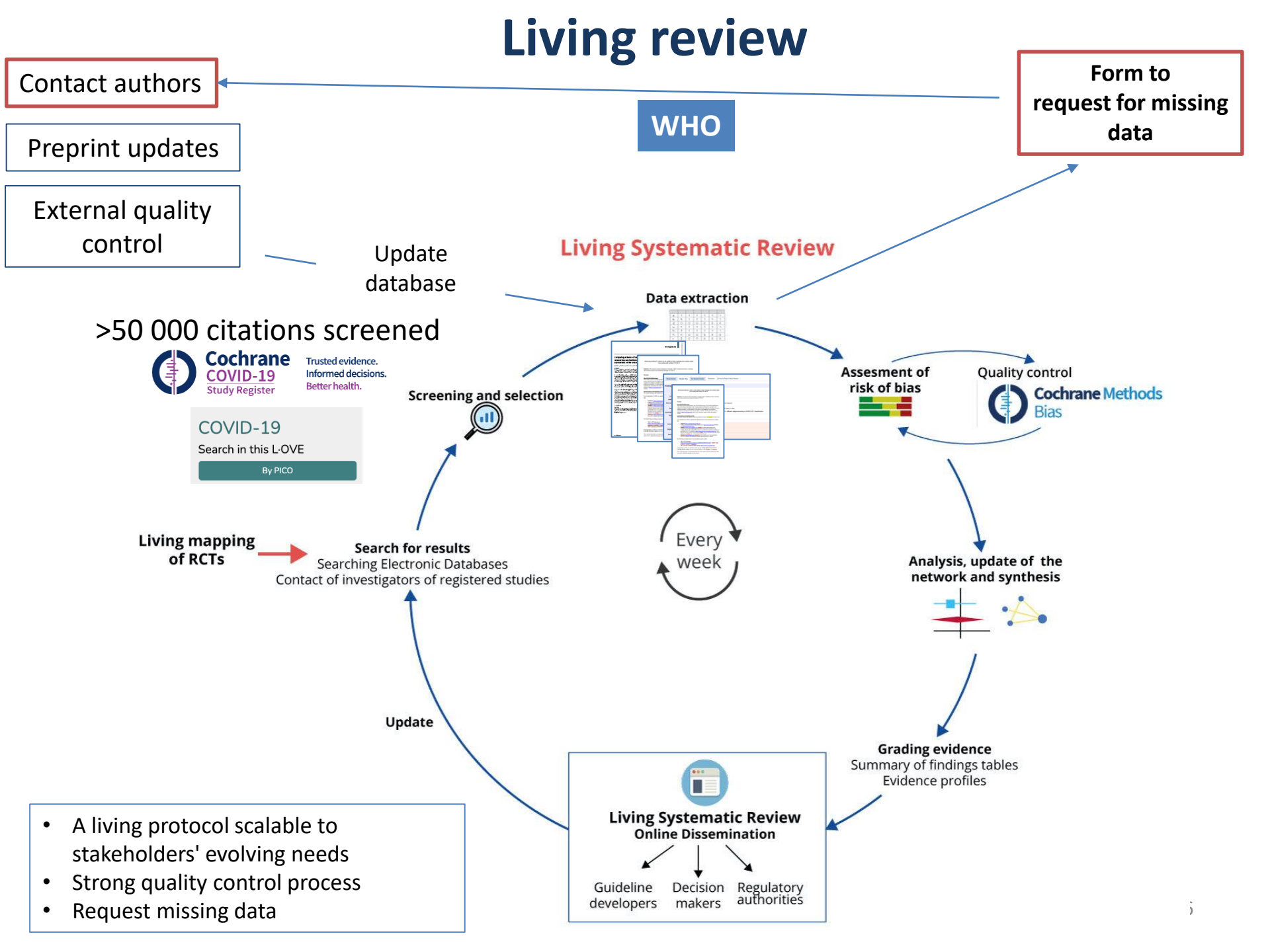
Update database

>50 000 citations screened

Cochrane COVID-19 Study Register — Trusted evidence. Informed decisions. Better health.

COVID-19
Search in this L·OVE
By PICO

Living Systematic Review

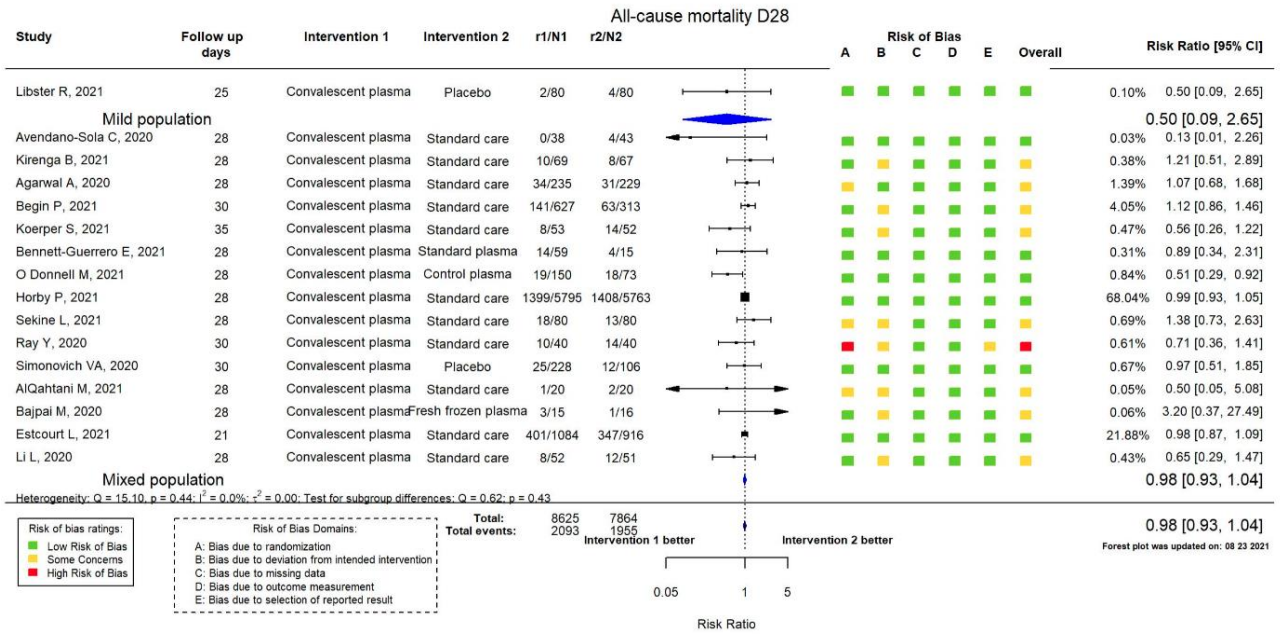


- A living protocol scalable to stakeholders' evolving needs
- Strong quality control process
- Request missing data

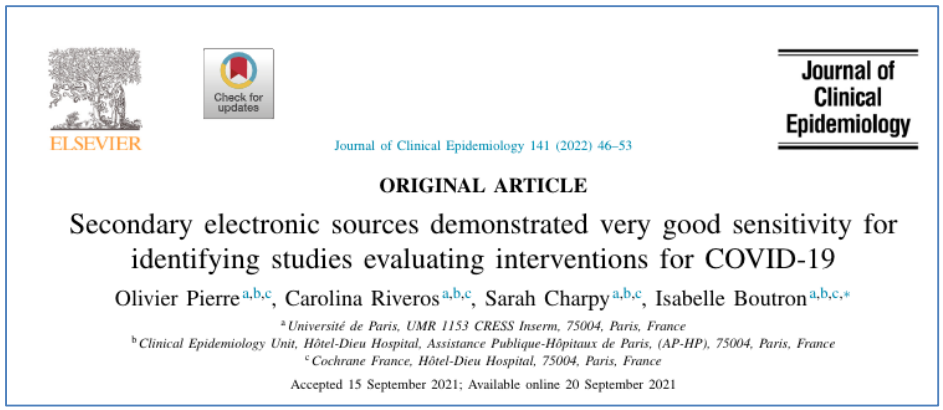
Open access platform

Open acces through the COVID-NMA platform to

- Studies general characteristics
- Detailed risk of bias assessment for all outcomes of interest
- Forest plots for all comparisons and outcome of interest (**> 8000** produced) for about **300 comparisons**
- SoF tables for all comparisons



Balance between speed and quality



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Check for updates

Journal of Clinical Epidemiology 141 (2022) 46–53

Journal of Clinical Epidemiology

ORIGINAL ARTICLE

Secondary electronic sources demonstrated very good sensitivity for identifying studies evaluating interventions for COVID-19

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Accepted 15 September 2021; Available online 20 September 2021

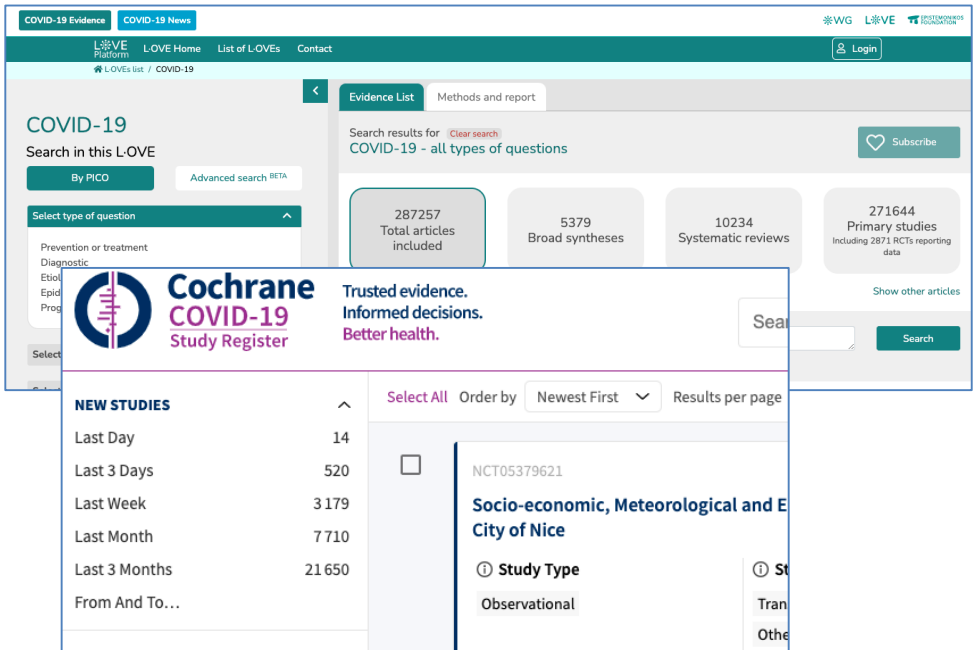
Scientometrics (2021) 126:5285–5304
https://doi.org/10.1007/s11192-021-03900-7

Check for updates

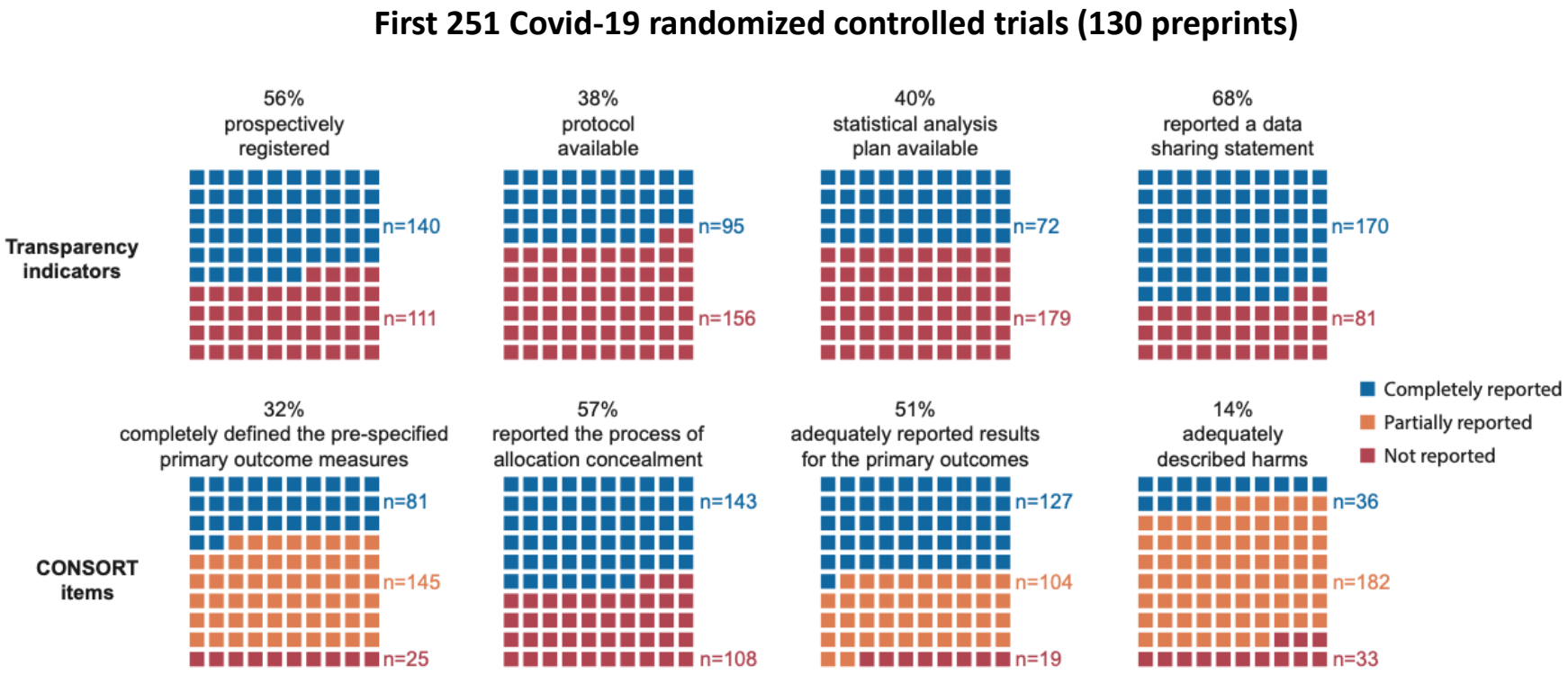
Day-to-day discovery of preprint–publication links

Guillaume Cabanac[1] · Theodora Oikonomidi[2] · Isabelle Boutron[2,3,4]

Received: 7 November 2020 / Accepted: 2 February 2021 / Published online: 18 April 2021



Monitoring trial transparency

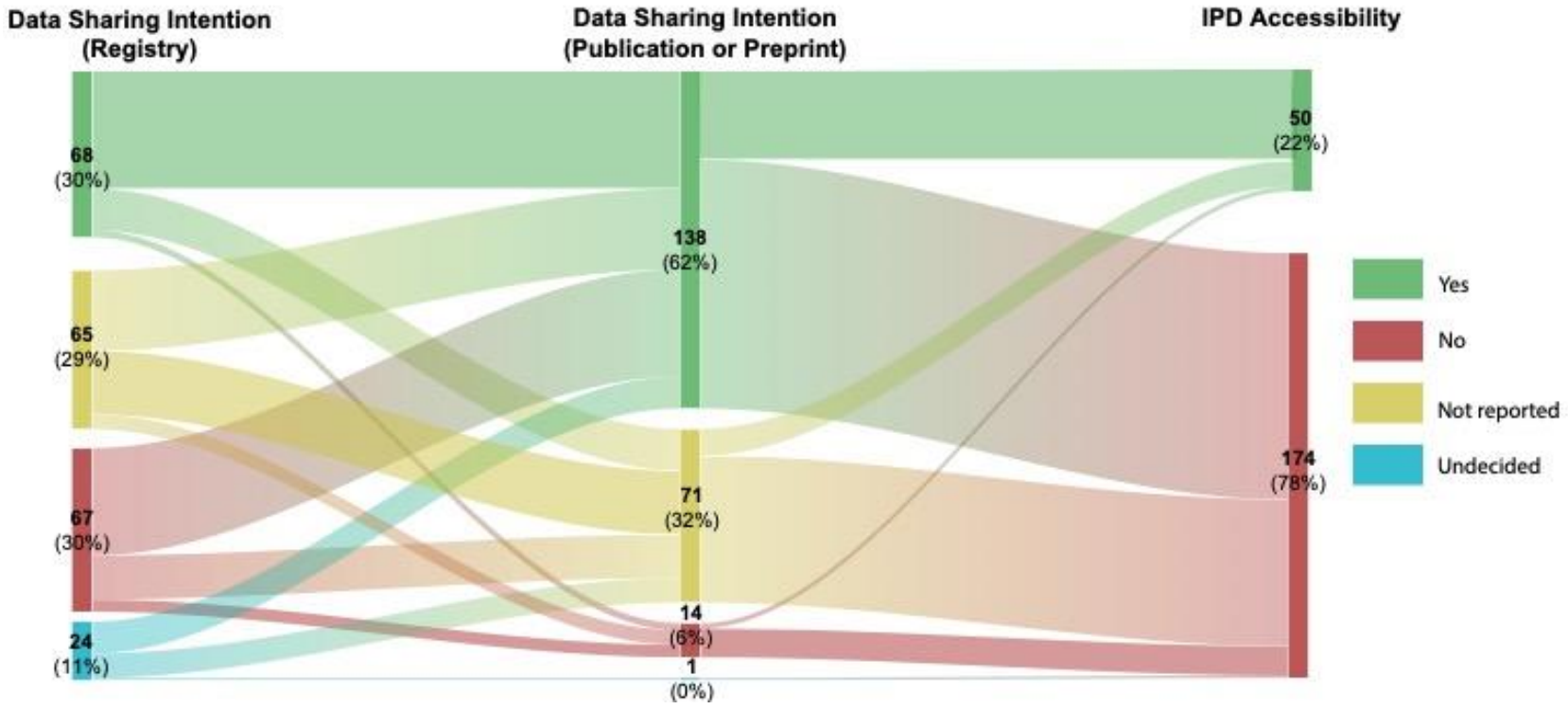


Kapp P, Esmail L, Ghosn L, Ravaud P, Boutron I BMC Med 2022

Access to IPD

224 RCT evaluating pharmacologic treatment for COVID-19 (March 2020 to May 2021)

- Contact authors to access IPD to conduct an IPD-MA
- 2 reminders September 2020 to September 2021
- 54% (n=121) responded to our e-mail
- 22% (n=50/224) IPD was accessible
- Ten RCTs initiated a data sharing process but did not complete the process by December 2021

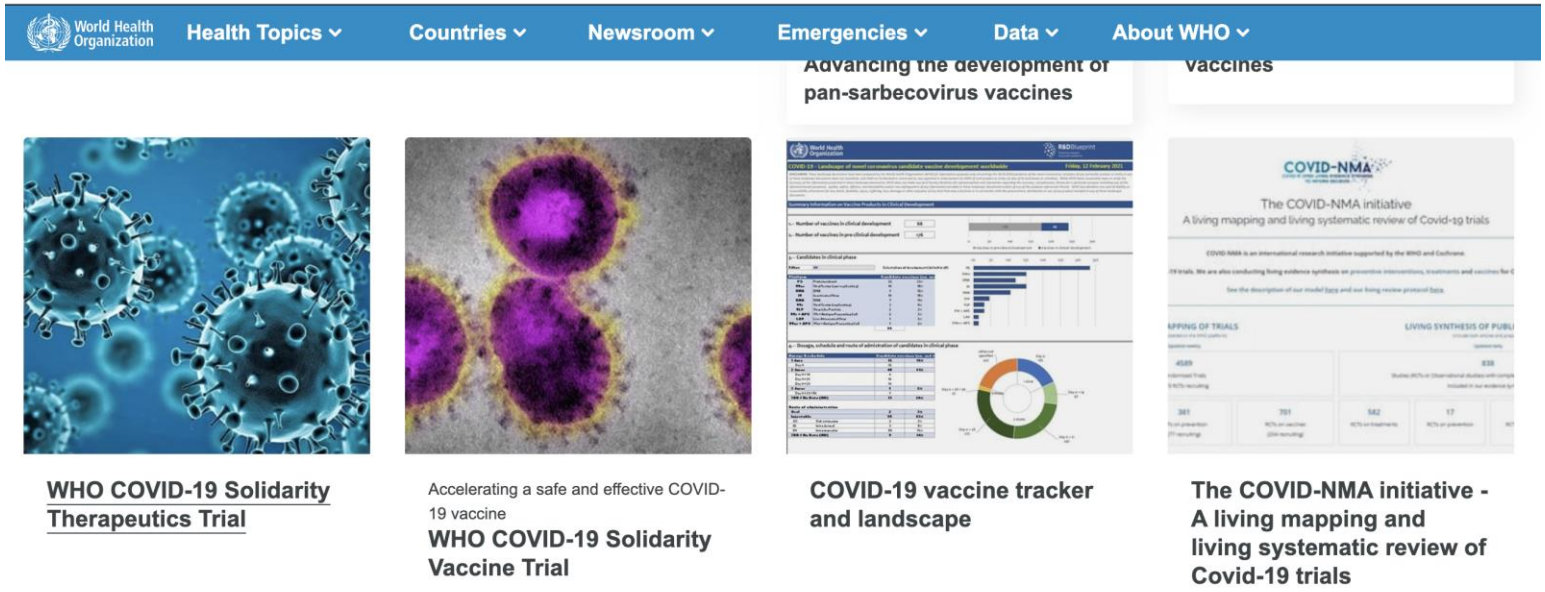


Esmail, Kapp, Assi, Wood, Regan, Ravaud, Boutron JAMA 2023

The *Lancet* Commission on lessons for the future from the COVID-19 pandemic

Jeffrey D Sachs, Salim S Abdool Karim, Lara Aknin, Joseph A
María Fernanda Espinosa, Vitor Gaspar, Alejandro Gaviria,
Muhammad Ali Pate, Gabriela Ramos, K Srinath Reddy, Isr
Lan Xue, Chandrika Bahadur, Maria Elena Bottazzi, Chris E
Emma Torres, Lauren Barredo, Juliana G E Bartels, Neena J
Susan Michie

provides an invaluable source of information on current trials evaluating a range of interventions.[442] COVID-NMA is an example of an international initiative, led by a team of researchers from Cochrane and other institutions, that works in conjunction with WHO to generate up-to-date mapping of evidence from trials regarding COVID-19 drug treatments.[443] COVID-NMA is one of many groups producing living evidence syntheses and improving future research by assessing the methodology and transparency of trials. Clinicians, policy makers, and people wanting to understand the best available evidence should consult robust sources such as this, and should not be swayed by the results of individual trials that have not been subject to such appraisal.[444]



Lessons learned

- **Strategic choices**
  - Large scope
  - Flexibility (e.g., scope, inclusion of observational studies at specific time)
  - Link between mapping and evidence synthesis
  - Appropriate infrastructure
  - Balance between quality (training module, internal quality, external quality control through the Cochrane BMG) and speed (efficient workflow for a weekly update, automation)
  - Open access platform to communicate the results
  - Decision making process relying on a steering committee
  - Development of the appropriate tools and automation to accelerate the process while maintaining quality
  - Systematic assessment of the accuracy of the tools developed

- **Issues**
  - Results communication
  - Funding scheme
  - Granting scheme