EVIDENCE FOR BIG DECISIONS

Better evidence, better decisions, better lives

Decision-makers lack timely, user-ready evidence for major decisions

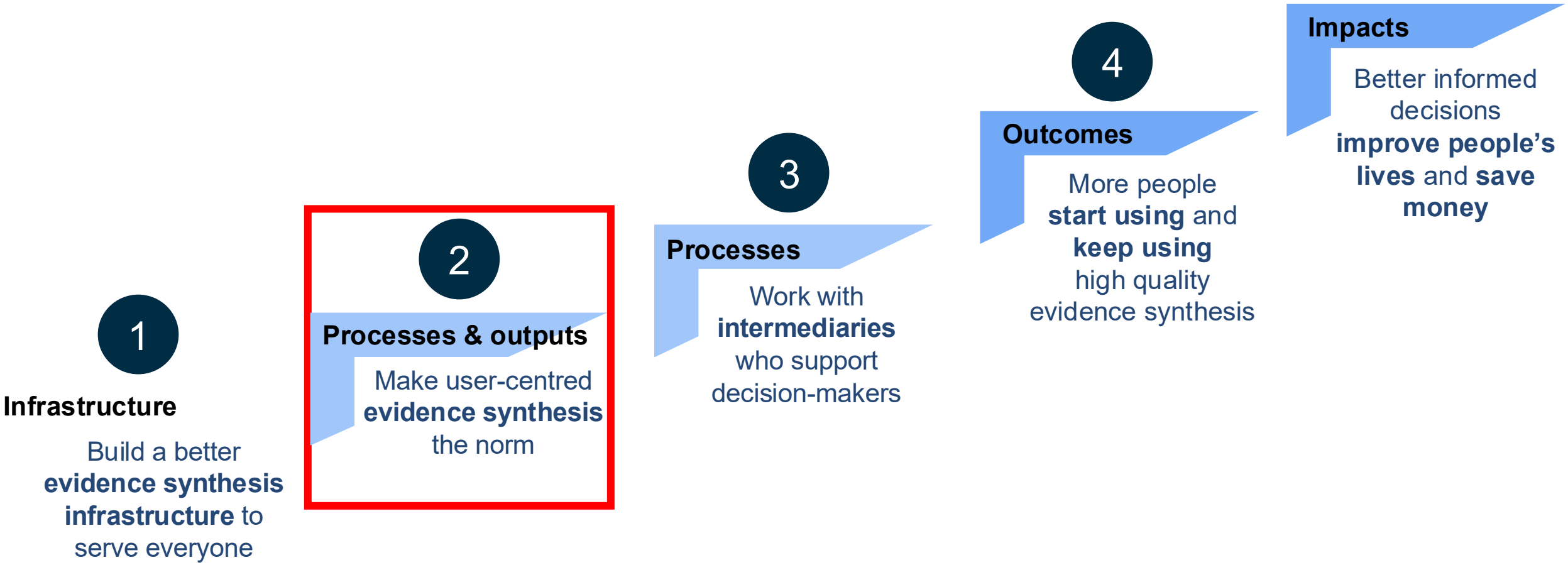
High-stakes challenges (climate, conflict, inequality, pandemics) demand fast and trust-worthy evidence

ESIC envisions a step-change: AI-enabled synthesis designed to serve real-world needs

ESIC positions evidence for big decisions as central to overcoming the fragmented and inefficient status quo

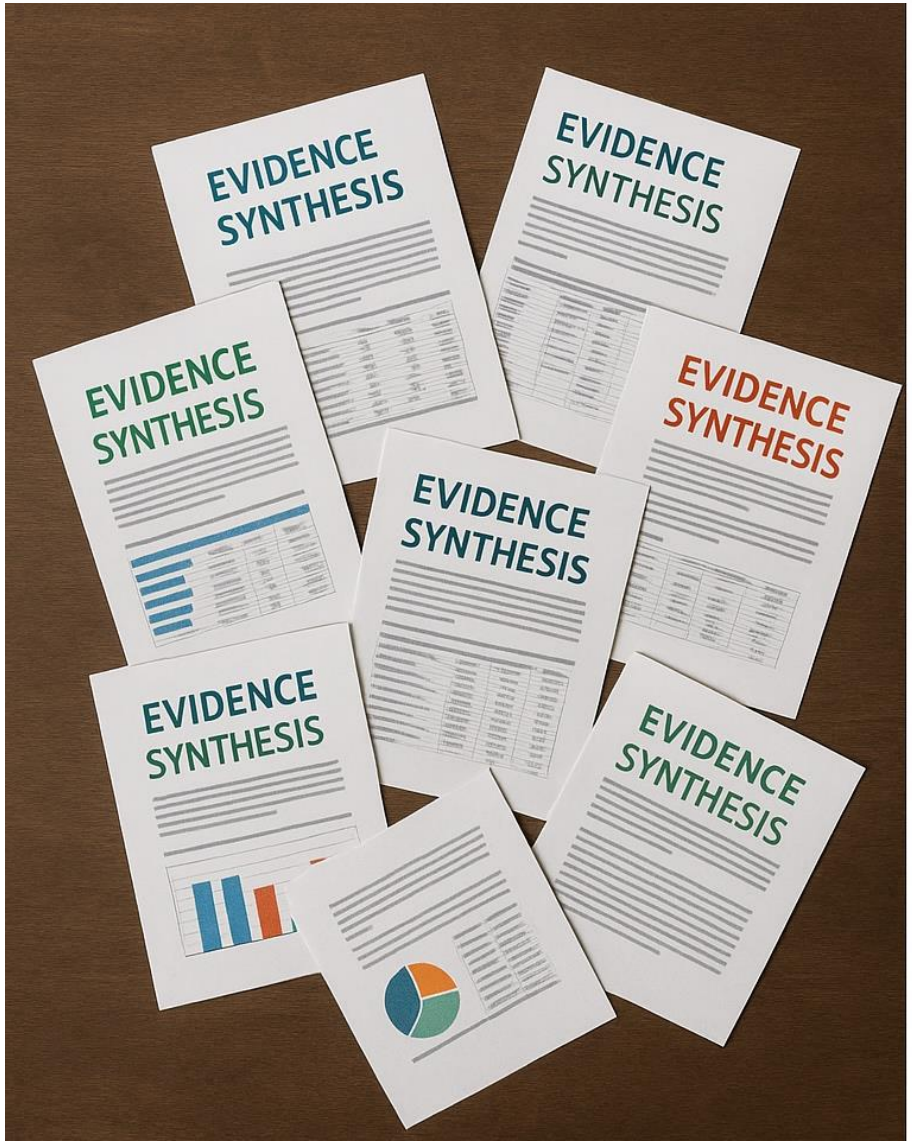
The new norm: timely, affordable, co-produced and embedded into decision-making

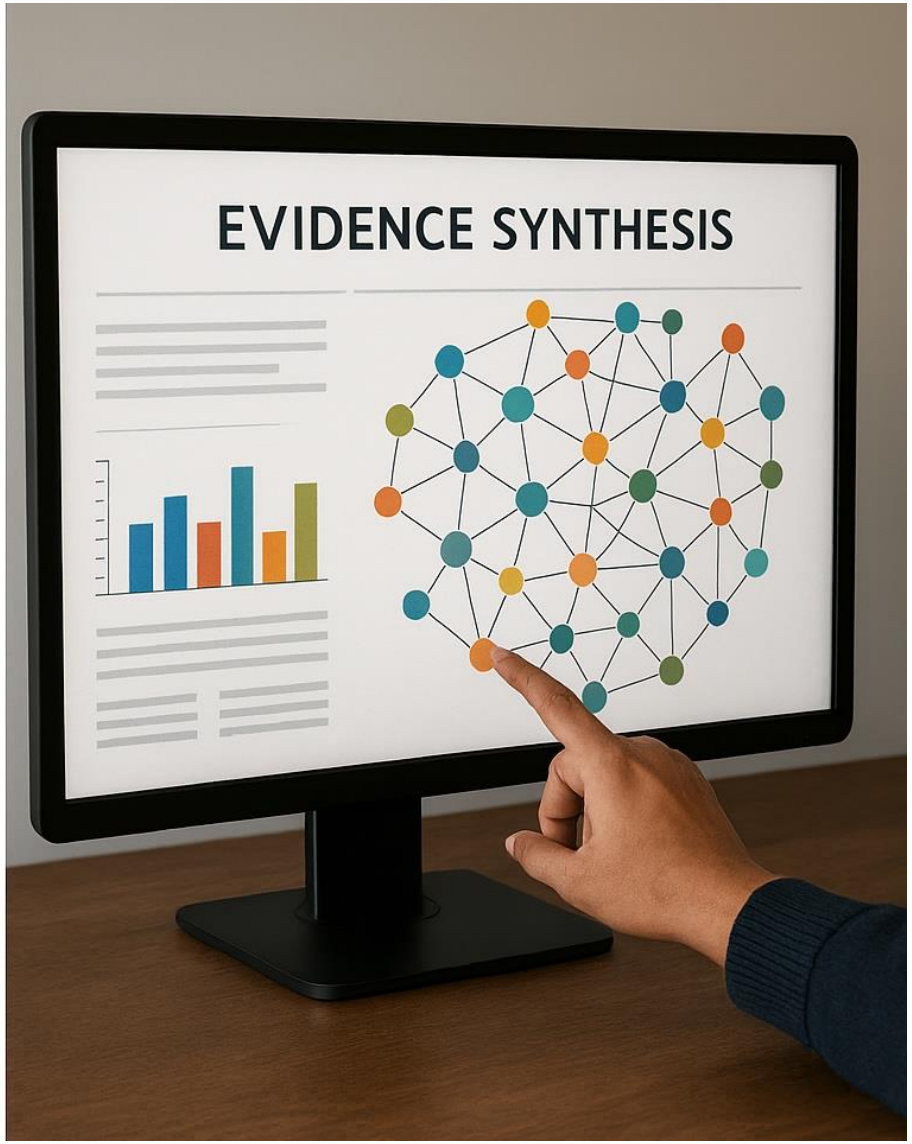
ESIC: a cornerstone of the global evidence architecture



Principles: the 'SHOW ME the evidence' features

‘Business as usual’ falls short





Different names, shared aspirations

Defining policy-scale synthesis?

Policy-scale synthesis is the systematic integration of diverse evidence streams aligned to policy-relevant intervention or outcome families, often spanning multiple domains.

They are designed to be iteratively updated and provide decision-ready, actionable insights.

Depending on context and topic, these syntheses may be modular and combinable (e.g., in social policy), or more holistic (e.g., COVID-19 network meta-analysis).

What does ‘policy-scale’ add?

Policy questions require navigating multiple syntheses → Alignment to real policy agenda

Decision-makers seek evidence organised around real-world challenges → Multiple and clustered intervention and outcome categories

Real world problems are cross-cutting → Modular and combinability

Are they different to current products?

Existing product	Description	How 'policy-scale' could be different
Umbrella reviews/reviews of reviews	Reviews of systematic reviews/syntheses: aggregates multiple reviews on related topics	Policy-scale synthesis actively reorganises and harmonises across intervention families, outcomes, and contexts, enabling modular recombination
Evidence databases/registries (e.g. PROSPERO, Epistemonikos)	Valuable and structured collections of evidence, not synthesis; requires user navigation; no interpretation	Provides interpretation, insight, and guidance, not just storage — and aligns to policy families
EGMs/living maps	Descriptive, useful for finding and navigating evidence, does not answer synthesis questions	interprets impacts, implementation and contextual factors (and possibly cost) not just location of evidence
Guidelines and toolkits (e.g. EEF)	Curated actionable summaries	Perhaps the same/similar? Major difference is in active approach to combination, integration and transparent metadata across sectors?

Policy-scale at different levels

Decision scale	Use of synthesis	Users	Example
Policy area	Resource allocation and strategy	Senior political, policy and public service leaders	Reduce crime and deliver fair and efficient justice
Goal	What approach to take	Senior managers of public services and political leaders	Reduce harm from violent extremism
Options	What specific interventions to use	Managers of public service	Prevent violent radicalization
Intervention	How to do a specific intervention most (cost) effectively	Staff of public services	Counter-narratives for the prevention of violent radicalisation

Different models, shared aspirations

Model	Sector	Synthesis Format	What It Enables
COVID-NMA	Health	Unified, living evidence synthesis	Real-time view of COVID-19 treatment and vaccine effectiveness
Teaching & Learning Toolkit	Education	Linked, user-facing toolkit	Compare interventions by impact, cost & evidence strength
Global SDG Synthesis Coalition	Multi-sector (SDGs)	Modular syntheses by thematic buckets	Actionable insights across SDG themes using mixed methods

The COVID-NMA initiative

Isabelle Boutron

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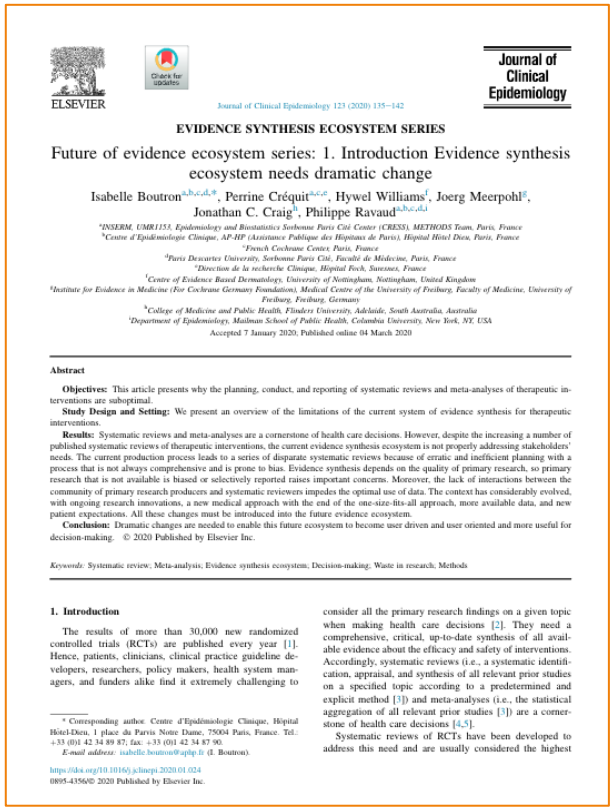
Cochrane France
Université Paris Cité, INSERM,

Toward a new research ecosystem



Journal of Clinical Epidemiology 123 (2020) 135–142

EVIDENCE SYNTHESIS ECOSYSTEM SERIES

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

Isabelle Boutron[a,b,c,d,*], Perrine Créquit[a,c,e], Hywel Williams[f], Joerg Meerpohl[g], Jonathan C. Craig[h], Philippe Ravaud[a,b,c,d,i]

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Accepted 7 January 2020; Published online 04 March 2020

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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0895-4356/

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EVIDENCE SYNTHESIS ECOSYSTEM SERIES

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

Perrine Créquit[a,b,c], Isabelle Boutron[a,b,d,e], Joerg Meerpohl[f], Hywel C. Williams[g], Jonathan Craig[h], Philippe Ravaud[a,b,c,d,i,*]

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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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0895-4356/

Journal of Clinical Epidemiology 123 (2020) 153–161

EVIDENCE SYNTHESIS ECOSYSTEM SERIES

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

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Accepted 7 January 2020; Published online 06 March 2020

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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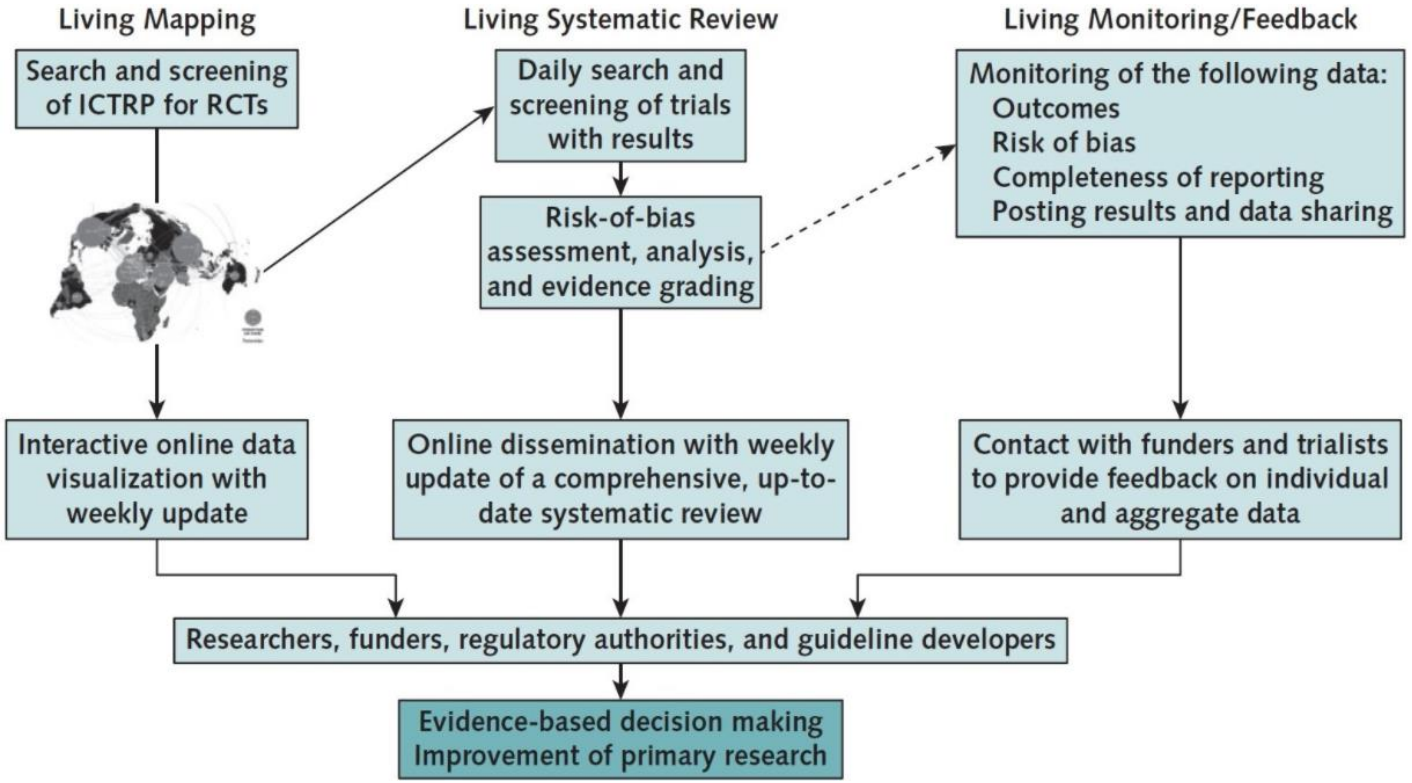
https://doi.org/10.1016/j.jclinepi.2020.01.027
0895-4356/

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*



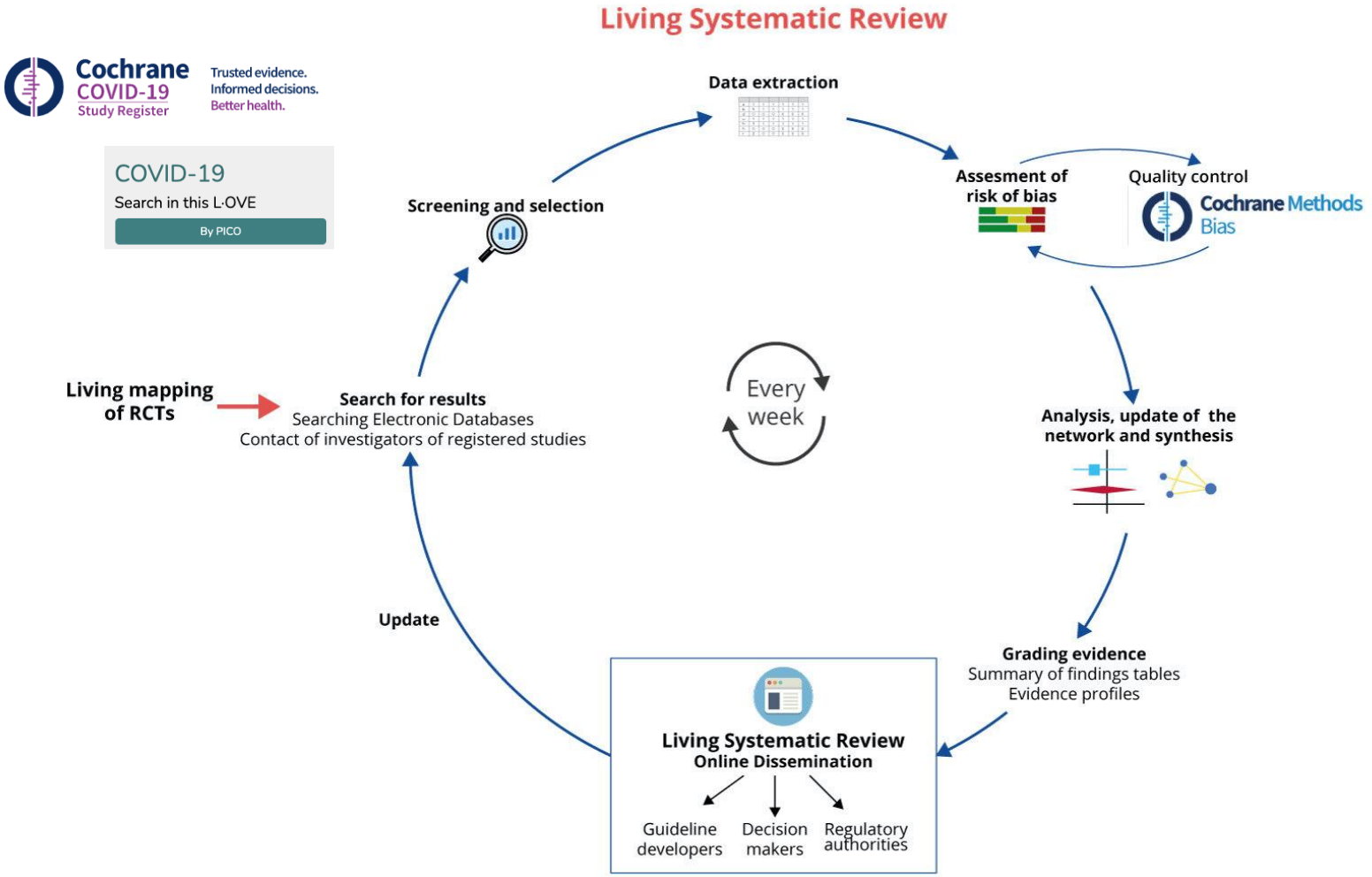
Scope: All treatments and vaccins for COVID-19

Boutron, …, Ravaud. Annals Internal Med 2020

Living systematic review

- A living protocol scalable to stakeholders' evolving needs
- Strong quality control process
- Development of tools: preprint tracker
- Contact of trialists at the outset
- Request missing data

>43 000 citations screened



Results communication: Open access plateform

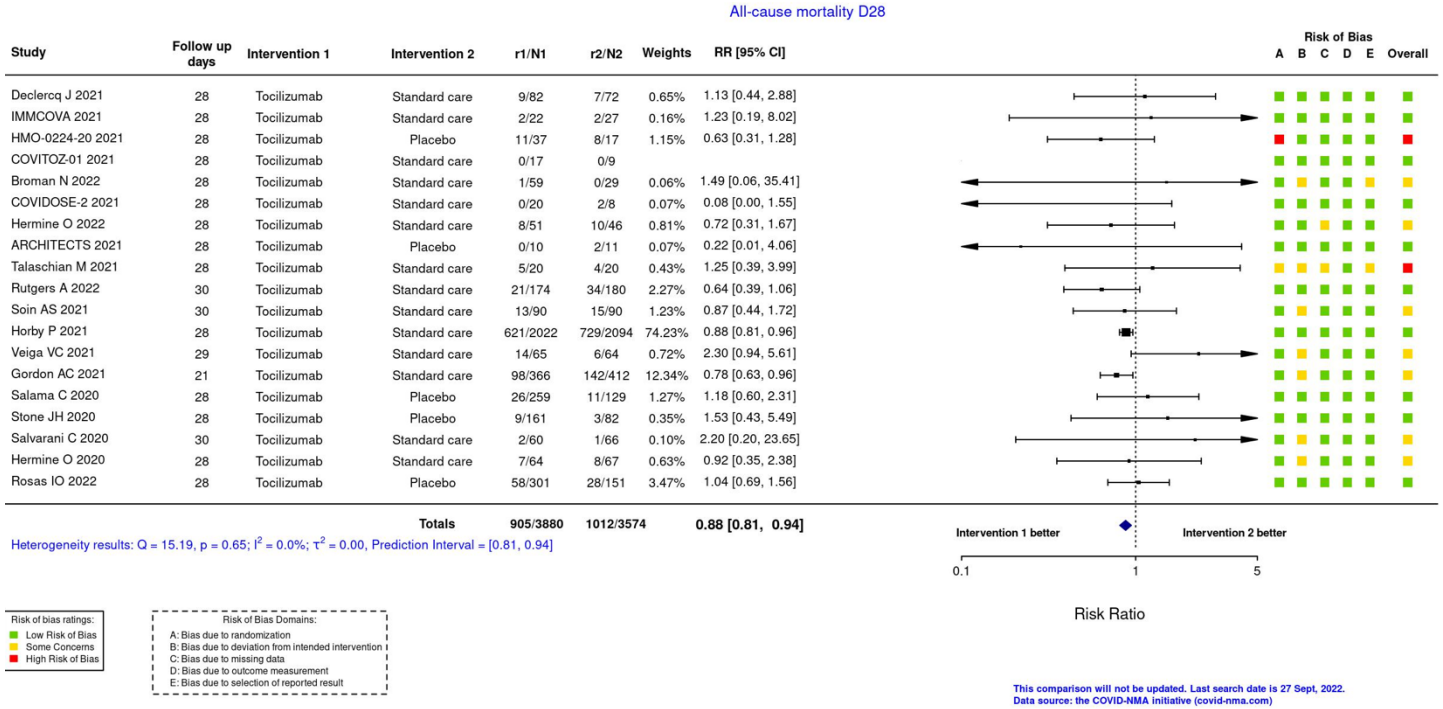
The COVID-NMA plateform: covid-nma.com

Study general characteristics

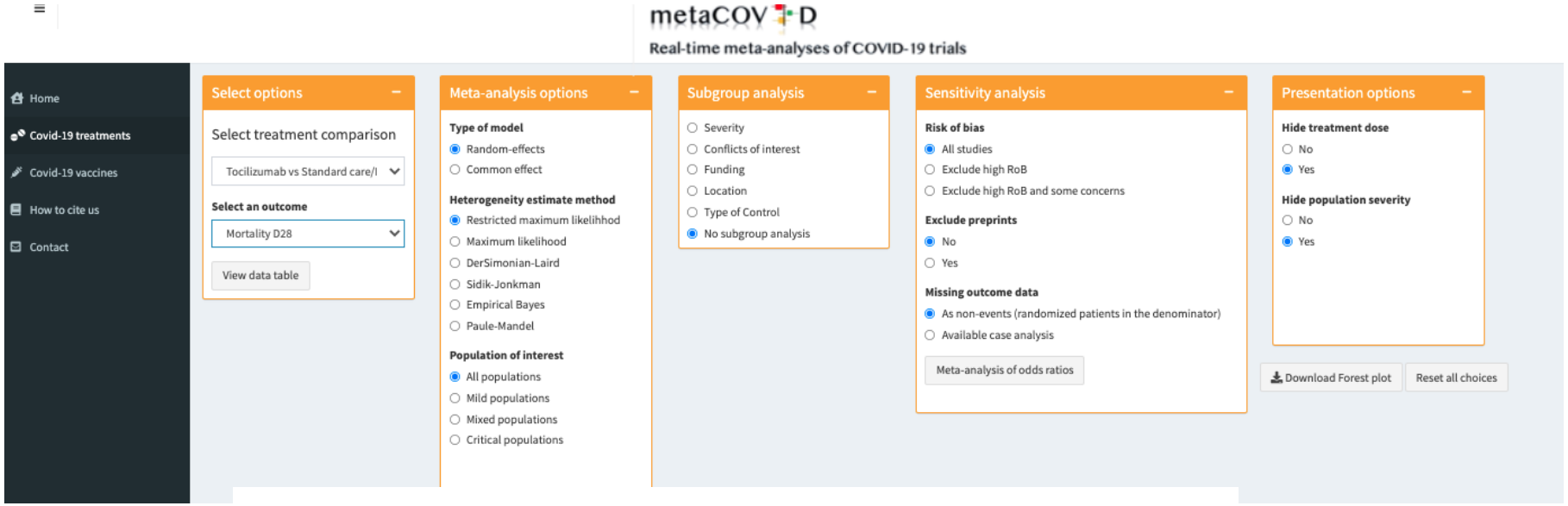
Risk of bias assessment with justification for all outcomes

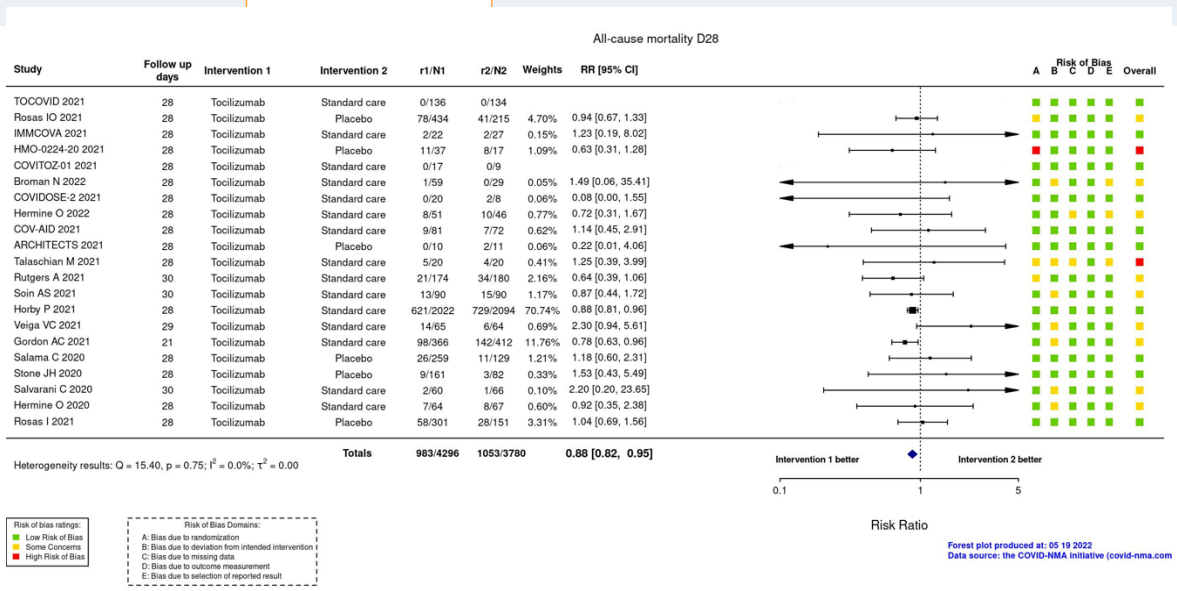
Forest plots

Grading of the evidence (SOF tables)



Tools to allow stakeholders to perform their own analyses

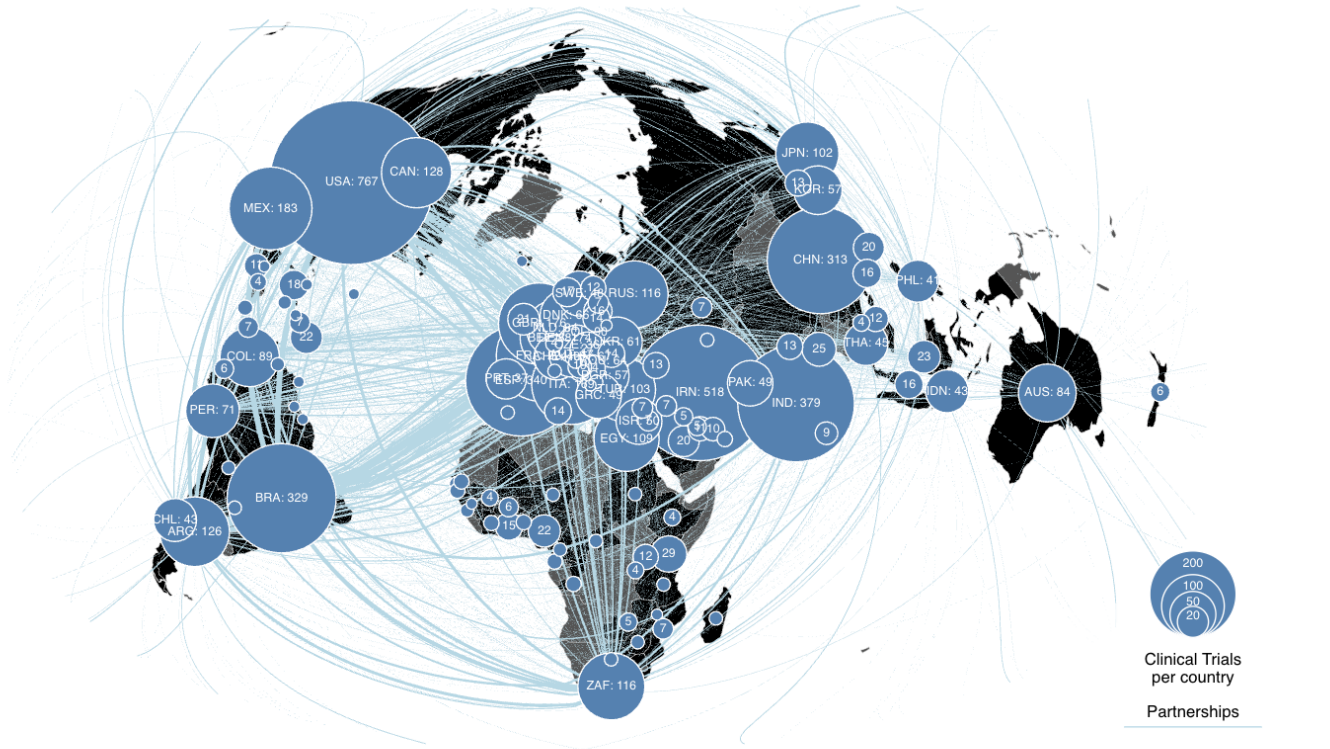




Evrenoglou T, Boutron I, Chaimani A, Res Synth Methods

Living Mapping

▼ Map



Download the data

▼ Table

Show full table

Treatment (per arm)	Sample size	Severity at enrollment	Sponsor/Funder	Reg. number
(1) Nirmatrelvir + ritonavir *vs* (2) Nirmatrelvir + ritonavir *vs* (3) Placebo	900	Patients recovered from covid	Kanecia Obie Zimmerman	NCT05595369
(1) Imidazolyl ethanamide pentandioic acid *vs* (2) Placebo	233	Mild	Valenta Pharm JSC	NCT05216497
(1) Isotretinoin *vs* (2) Isotretinoin *vs* (3) Standard of care	100000	Critical	Kafrelsheikh University	NCT04353180
(1) Interferon gamma *vs* (2) Standard of care	630	Healthy volunteers	SPP Pharmaclon Ltd.	NCT05054114
(1) Fluticasone *vs* (2) Standard of care	500	Mild	University of Medicine and Pharmacy at Ho Chi Minh City	NCT05054322
(1) Baricitinib *vs* (2) Placebo	480	Moderate/severe	Incepta Pharmaceuticals Ltd	NCT05056558
(1) Platelet rich plasma *vs* (2) Placebo	30	Patients recovered from covid	Stanford University	NCT04406584
(1) Masitinib *vs* (2) Masitinib *vs* (3) Masitinib *vs* (4) Placebo	78	Mild/moderate	AB Science	NCT05047783
(1) Isotretinoin + tamoxifen *vs* (2) Isotretinoin + tamoxifen	160	Severe/critical	Kafrelsheikh University	NCT04389580
(1) Placebo	400	Healthy volunteers	Chumakov Federal Scientific Center for Research and Development of Immune-and-Biological Products	NCT05046548
(1) Stri formula *vs* (2) Placebo	598	Mild/moderate	Eyecheck, Inc.	NCT05046561
(1) Placebo	300	Healthy volunteers	Sinocelltech Ltd.	NCT05043285
(1) Placebo	300	Healthy volunteers	Sinocelltech Ltd.	NCT05043311
(1) Probiotic streptococcus salivarius k12 *vs* (2) Standard of care	50	Mild/moderate	King Edward Medical University	NCT05043376
(1) Mib-626 *vs* (2) Mib-626 *vs* (3) Placebo	50	Moderate/severe	Metro International Biotech, LLC	NCT05038488
(1) Acteev masks *vs* (2) Face mask	1600	Health workers	Ascend Performance Materials	NCT05036941
(1) Physiotherapy *vs* (2) Olfactory training *vs* (3) Standard of care	75	Patients recovered from covid	Université de Montréal	NCT05037110
(1) Placebo	50	Healthy volunteers	Biocad	NCT05037188

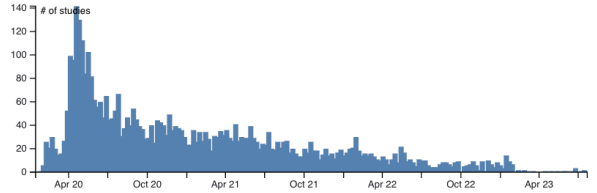
Filters

All trials selected (**4256**) | Reset all

Search…

Ex: Interferon, antiviral, Spain, Assistance Publique, EUCTR2020…

▼ Registration date

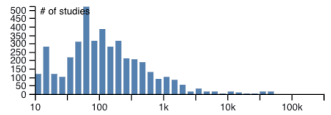


To filter by Registration dates, click and drag to create a range.

▼ Inclusion age

- ☑ minimum 18 yo (3,922 studies)
- ☑ less than 18 yo (330 studies)
- ☑ N/A (4 studies)

▼ Sample size



▼ Recruitment status

- ☑ Completed (1,574 studies)
- ☑ Not recruiting (853 studies)
- ☑ Recruiting (815 studies)
- ☑ Terminated (403 studies)
- ☑ Unknown (362 studies)
- ☑ Withdrawn (191 studies)
- ☑ Not reported (35 studies)
- ☑ Suspended (23 studies)

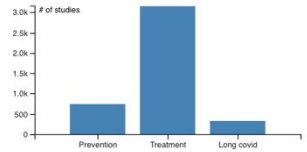
▼ Publication status

- ☑ Not published (3,427 studies)
- ☑ Published (829 studies)

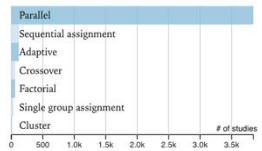
▼ Registry status

- ☑ No results posted (3,838 studies)
- ☑ Results posted in the registry (418 studies)

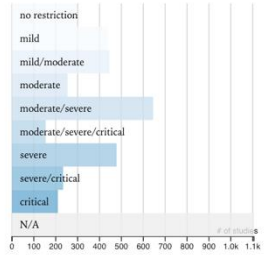
▼ Study aim



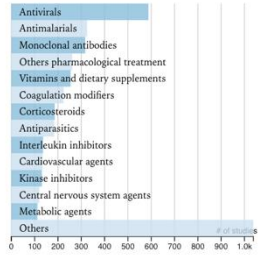
▼ Design



▼ Disease severity



▼ Type of pharmacological treatment



Conclusion

>900 studies were identified, extracted, assessed for risk of bias and analyzed

> 4634 registered trials extracted

The protocol and the platform considerably evolved over time

- Inclusion of observational data to assess vaccine effectiveness against variants
- Reduction of the scope for analyses where appropriate

Wide use of the data

health
Department:
Health
REPUBLIC OF SOUTH AFRICA

2030 NDP

South African National Department of Health
Brief Report of Rapid Review
Component: COVID-19

TITLE: REMDESIVIR FOR COVID-19: EVIDENCE REVIEW OF THE CLINICAL BENEFIT AND HARM

Date: 15 FEBRUARY 2022 *(sixth update of the initial 16 April 2020 rapid review report)*

Key findings

- We conducted a rapid review of available clinical evidence about use of remdesivir, with or without other medicines, for patients with COVID-19.
- We identified a systematic review including eleven RCTs (n=8137) which includes the latest trial data in an cohort of ambulatory patients (www.covid-nma.com).
- Remdesivir is likely to make little or no difference to all-cause mortality at 14 to 28 days, when initiated in hospitalised patients (RR 0.90 95% confidence interval (CI) 0.73 to 1.11, six trials, n = 7553, *moderate certainty evidence due to imprecision).*
- One study in ambulatory patients found a reduction in the composite end-point of hospitalisation and death at 28 days (RR 0.28 CI 0.1 to 0.74), although both treatment and placebo arms recorded no deaths by 28 days.
- Remdesivir is not associated with an increased risk of adverse events compared with placebo (RR 1.00 95% CI 0.91 to 1.11, 4 trials, n = 2752, *low certainty evidence* due to risk of bias in included trials and unexplained heterogeneity).
- We identified no reports of clinical trials with remdesivir specifically conducted in paediatric patients with COVID-19, but did note that the trial conducted in ambulatory patients included a small number of patients (n=8) aged between 12 and 18 years.

Appendix 3: Forest plots for Cochrane Living Meta-analysis: Remdesivir 10 or 5 days vs Placebo for Moderate/Severe COVID-19

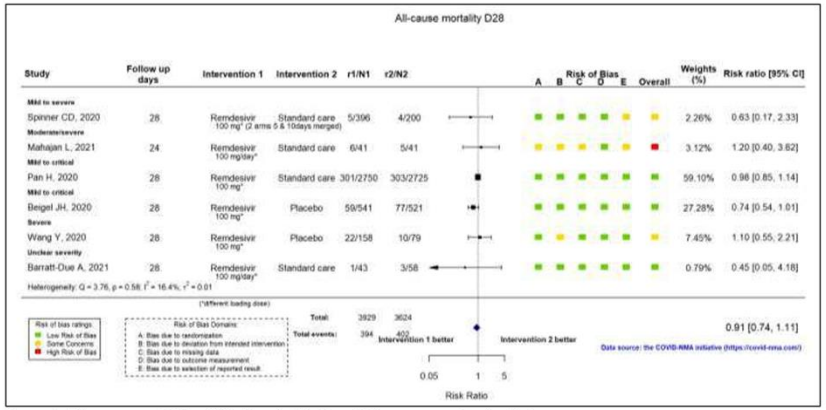


Figure 1: All-cause mortality, D28; Remdesivir 5 or 10 days versus standard of care

SDGs

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targets!

What is a policy-scale question/scope?

Partnerships Pillar (SDG 17): whole of SDG17; it was broad and shallow; findings ended up general and not actionable.

Peace Pillar (narrower focus on priorities in SDG 16.1 and 16.4 – homicides and conflict-related deaths): Still not perfect but a narrower scope enabled clearer framing and (hopefully) more useful and actionable findings.

- A single synthesis trying to cover an entire SDG goal or pillar may risk:
- Conceptual overload (too many interventions, mechanisms, outcomes)
- Methodological sprawl (wide-ranging evidence bases across sectors)
- Practical failure (inability to produce actionable insights)

Combinable SDG16 ‘buckets’ example

Bucket (Intervention / thematic family)	Relevant SDG targets	Cross-pillar relevance	Possible policy-scale scope / relevance
Violence prevention & protection	**16.1, 16.2, 16.4**	People, Prosperity	• Homicides and conflict-related deaths • Violent crime reduction • Child protection systems • Trafficking / organised crime disruption • Community safety & situational prevention • Safe schools / youth violence prevention
Equitable & just societies	**16.3, 16.6, 16.7**	People, Prosperity	• Justice system reform & access to justice • Legal aid, ADR • Transparency, accountability & anti-corruption • Inclusive governance & public administration reform
Legal identity	**16.9**	Peace, People	• National ID / CRVS system strengthening • Social registry interoperability • Foundational identification for service access, inclusion & social protection
Violence against women & children	**SDG 16, SDG 5**	Peace, People	• VAWC legal frameworks & enforcement • Multisectoral service delivery models • Prevention programming • Safe reporting mechanisms • Survivors’ rights & protection systems

How to operationalise?

‘Manufacturing’ pipelines and infrastructure

- Define policy priority families (sectoral and regional hubs)
- Agree taxonomies for repositories (or clever tech-based means of aligning different taxonomies)
- Define core outcomes and contextual metadata
- Conduct modular syntheses (aligned in approach and with an eye on combinability, across sectors, hubs and work packages)
- Generate dashboards and toolkits
- Maintain via living review processes
- Support intermediaries
- Evaluate uptake and update priorities