The Cochrane Covid LSR experience

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Informed decisions.
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Conflicts of interest

Employed by Cochrane

Author of Cochrane Reviews

Editor for Cochrane Airways Group

Author on MECIR standards & Handbook chapters

Associate Editor for Research Integrity & Peer Review

PRISMA extension for Protocols, Abstracts, Harms, IPD

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Since April 2020, Cochrane has published

Rapid Reviews	Living Reviews	Intervention reviews	Qualitative	Overviews
Quarantine	Convalescent plasma	PPE	Infection prevention control	Interventions for heavy menstrual bleeding available during pandemics
Universal screening	Signs and symptoms (dx)	ENT/Oral health suite on antimicrobial mouth washing (x 3)		
Travel bans	Antibody tests (dx)			
Video calls	Rapid point of care tests (dx)			
Ash for handwashing				
Oxygen targets				
Digital contact tracing				

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Perfect fit? Covid 19 & criteria for when to do LSR

1. Question of particular importance to decision-makers
2. Uncertainty in existing evidence base
3. Emerging evidence likely to impact on interpretation

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Living versus updated

While core review methods are not fundamentally different to other Cochrane Reviews, LSRs additionally include explicit, transparent and pre-specified decisions on:

- how frequently new evidence is sought and screened; and
- when new evidence is incorporated into the review

In Covid 19 updating triggers need to balance number of factors

Convalescent plasma & Covid 19

Contains antibodies from blood donated by patients recovered from Covid 19

Used during Spanish Flu pandemic to boost immune system response – role in Covid?

April 2020 – protocol received from Cochrane Haematology:

Criteria for considering studies for this review

Types of studies

To assess the benefits and safety of convalescent plasma for the therapy of COVID-19 we plan to include randomised controlled trials (RCTs) only, as such trials, if performed appropriately, currently give the best evidence for experimental therapies in highly controlled therapeutic settings. When RCT data are available, we will use the common methods recommended by the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2019), as specified in the following description of the methods.

If there is insufficient evidence (very low-quality evidence or no evidence) available from RCTs to answer this review's questions we will include prospective controlled non-randomised studies of interventions (NRSIs), including quasi-randomised controlled trials (e.g. assignment to treatment by alternation or by date of birth), controlled before-and-after (CBA) studies, and interrupted time series (ITS) studies. In that case, we will use the methods proposed in the *Cochrane Handbook for Systematic Reviews of Interventions* for the inclusion of NRSIs in systematic reviews (Reeves 2017).

If there is insufficient evidence (very low-quality evidence or no evidence) available from RCTs and NRSIs we will include prospective observational studies with a control group and will adapt the methods for the inclusion of NRSIs in systematic reviews as specified by the *Cochrane Handbook for Systematic Reviews of Interventions* as well (Reeves 2017).

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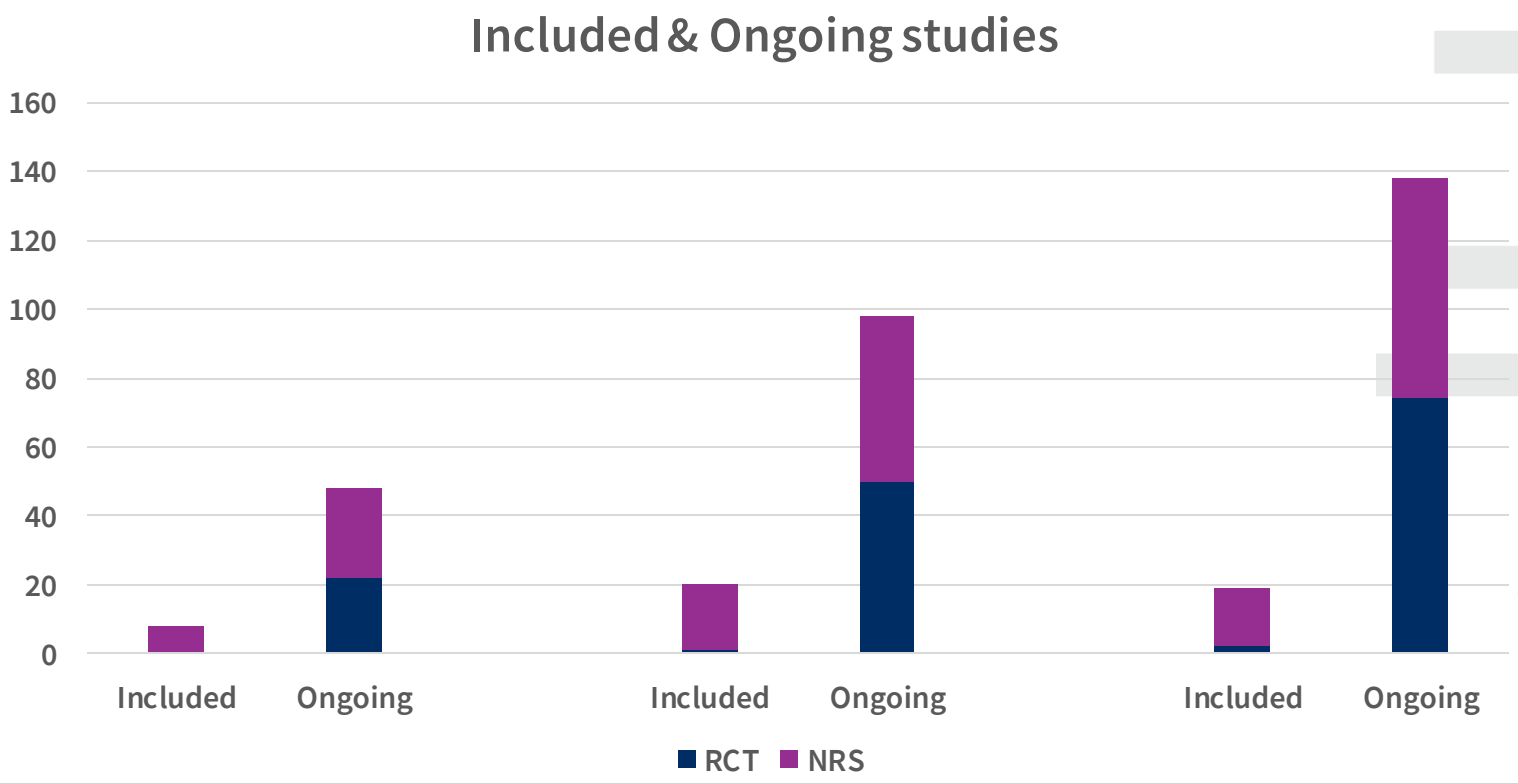
Hierarchical approach

Committed authors to look for alternative sources of evidence

Eligibility criteria & methods changing with incremental improvements in study design, understanding of disease & treatment

Growing N RCTs registered, but still only few provide data

Convalescent plasma by study design (included & ongoing over time)



POLICY FORUM

RESEARCH ETHICS: COVID-19

Against pandemic research exceptionalism

Crises are no excuse for lowering scientific standards

By **Alex John London**[1] *and* **Jonathan Kimmelman**[2]

The global outbreak of coronavirus disease 2019 (COVID-19) has seen a deluge of clinical studies, with hundreds

tists stated, "Given the urgency of the situation, some limitations…may be acceptable, including the small sample size, use of an unvalidated surrogate end point, and lack of randomization or blinding" (*1*). The perception that core methodological components

'…challenges that rigorous methods address do not disappear in the face of urgent need. Small studies that build on basic science and pre-clinical research in early phases of drug development routinely generate signals of promise that are not confirmed in subsequent trials.'

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Impact on conclusions limited so far, why not lengthen updating cycles?

Refresh intelligence on status of ongoing studies with adaptive designs

Healthy dose of realism (Press, Preprints & Politicians)

Important insights emerging about ongoing RCT evidence & contact with study investigators

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Learning (1)

Match ambition with time

Trust & communication within team critical

Technology needs refinement for LSR

Risks/benefits of using preprints: rapid access versus reliability

Choose source of evidence according to breadth of question

- Topic specific registers (e.g. Covid 19 Register) might be enough

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Learning (2)

Build in opportunity to revisit question/methods:

- Case definition (different subgroups?)
- Core Outcome Set development
- Communication with study investigators

Implement changes to protocol in good faith & report them honestly

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Learning (3)

Deciding what parts of protocol to change & when to update can still be hard: ask for help

Study identification & data collection is continual process, write up is not

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Thank you