

# **Planning Cochrane's Editorial Response to COVID in 2021 & Beyond**

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# 1 Aims of this paper

The number of COVID-19 reviews Cochrane has already published, the number requiring regular updating, and the priority areas we could still cover are potentially unsustainable. This paper aims to set out Cochrane's priorities for our response to COVID in 2021 and beyond.

This will enable us to:

- consider future submissions/proposals against select priority areas
- identify evidence synthesis gaps within our priority areas and actively commission reviews in areas of need

We acknowledge that the COVID-19 pandemic is a rapidly evolving situation and we aim to retain flexibility to allow us to respond to changing and emerging priorities.

## 2 Background

In 2020, Cochrane's editorial response to the COVID-19 pandemic was coordinated centrally. Cochrane Review Groups (CRGs) collaborated with Cochrane's Central Editorial Service to publish reviews addressing stakeholder needs as they emerged in the early months of 2020. Large, highly organised review teams collaborated to produce reviews addressing priorities in treatment, prevention, and diagnostics.<sup>1</sup> The editorial service team was expanded to manage the volume of work, and a panel of consumers was established to provide input on reviews that were managed centrally. Associate Editors from the CRG Networks were instrumental in providing quality assurance on these reviews. The [COVID-19 Review Bank](#) documented priority questions for evidence syntheses whether they were being addressed within Cochrane or elsewhere, to reduce duplication.

Keeping pace with the evolving evidence base for COVID-19 has presented challenges in deciding which review questions to prioritise and in balancing speed with rigour. The [COVID-19 study register](#) has been a major source of evidence for these reviews, yet also served to highlight the vast number of studies still being indexed every week. We now need to plan our approach to producing new and updated reviews in 2021 and the years to come. This requires us to take stock of the reviews we have, how we identify and address emerging and long-term priorities in COVID-19, and how CRGs and the Central Editorial Service work together to achieve this.

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<sup>1</sup> Hilton J, Flemyng E, Soares-Weiser K. COVID-19: working together and making a difference for decision-makers. *Cochrane Database of Systematic Reviews* 2020, Issue 12. Art. No.: ED000150. DOI: 10.1002/14651858.ED000150.

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## 3 What have we covered?

Mapping our published reviews to topic domains identified in July 2020<sup>2</sup>, there is good coverage of infection prevention (including an update of the physical interventions review from the Acute Respiratory Infections Group<sup>3</sup>), public health measures, and diagnostics. Two Network Meta-Analyses led by Cochrane France on treatment and prevention are now underway.

Reviews managed through the Central Editorial Service have included a few therapeutic questions to date. We are anticipating the publication of a steady number of pairwise intervention reviews (e.g. IL-1 agonists, antiplatelets, inhaled corticosteroids) in addition to updates of reviews of prophylactic anticoagulants and neutralising monoclonal antibodies. A review of chloroquine/hydroxychloroquine managed by the Infectious Diseases Group published in February 2021. Reviews of IL-6 agonists and convalescent plasma are Living Systematic Reviews.

## 4 What can we tell from the reviews we have published so far?

We have addressed diverse and often complex review questions. This has required us to make technological changes, accommodate new methods and reporting guidance to support the publication of Rapid Reviews. We have worked with teams developing Living Systematic Reviews to support expedited updating processes. Recently completed methodological research comparing preprints with published articles will help us to develop appropriate guidance for the inclusion, appraisal and synthesis of preprint articles.<sup>4</sup> It is likely that further reviews of public health measures in 2021 will need to incorporate evidence from study designs that we have not currently developed robust guidance for, notably modelling studies.

Commissioning decisions took in to account our relationship with external partners, recruitment of able, well-resourced review teams, and commitment from a central editorial team. We have built on good community relationships with CRGs, methods groups and CRG Network editorial teams in the form of the Associate Editors. A Public Health 'Hub' was led by the Public Health and Health Systems Network, Lisa Bero and Co-ordinating Editor of the Public Health Group, Luke Wolfenden. This is a sound basis on which to proceed with continued engagement with WHO to ensure that our coverage continues to reflect national and global policy-maker priorities.

In 2020, the response from CRGs to working with us on COVID-19 reviews and our expansion of the Central Editorial Service enabled us to achieve much. In 2021 resources will need to be managed

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<sup>2</sup> [https://covidreviews.cochrane.org/sites/covidreviews.cochrane.org/files/public/uploads/covid-19\\_priorities\\_13\\_july\\_2020.pdf](https://covidreviews.cochrane.org/sites/covidreviews.cochrane.org/files/public/uploads/covid-19_priorities_13_july_2020.pdf)

<sup>3</sup> Jefferson T, Del Mar CB, Dooley L, Ferroni E, Al-Ansary LA, Bawazeer GA, et al. Physical interventions to interrupt or reduce the spread of respiratory viruses. *Cochrane Database of Systematic Reviews* 2020, Issue 11. Art. No.: CD006207. DOI: 10.1002/14651858.CD006207.pub5

<sup>4</sup> <https://medrxiv.org/cgi/content/short/2021.04.12.21255329v1>

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carefully in anticipation of the planned editorial pilot. We will need to make careful decisions relating to which reviews we prioritise and how they are managed. The Editorial Board has proven to be an effective advisory group as we navigate challenges and we should continue to recruit their time and expertise in our response to COVID-19.

## 5 How should we plan for 2021 and beyond?

To address key priorities, we will need to:

- Respond to user demand – several COVID-19 reviews currently in progress have been commissioned directly by national and international guideline bodies, and we will continue to respond with agility to the needs of our stakeholders.
- Monitor emerging priorities by making use of the outputs of a range of COVID-19 prioritization panels, in particular the horizon scanning work of COVID-END, to identify the topics for which living syntheses are most needed.<sup>5</sup>
- Identify evidence synthesis gaps and avoid duplication of effort by monitoring high-quality outputs from other evidence synthesis groups.<sup>6</sup>
- Be flexible and recognise that as our understanding of COVID-19 has evolved so have our priorities, and this evolution is likely to continue over the coming months and years.
- Play to Cochrane’s strengths – we have a community of CRGs, skilled Associate Editors, good links with WHO, access to consumers and to methodological expertise through the Methods Support Unit, and we have demonstrated capacity to manage reviews centrally with specialist methods e.g. Diagnostic Test Accuracy, complex reviews (of observational studies) in public health, Network Meta-Analyses, Prognosis and Mixed methods.
- Maintain communication with CRGs who have already registered and produced COVID-19 reviews, or who are interested in proceeding with COVID-19 reviews.
- Base decisions about which reviews to commission and update on the balance between time and effort required with priority to end users, external partners and stakeholders.
- Improve coverage of topics relevant to low resource settings, especially generic medicines and access to vaccines.
- Review priorities regularly with the Editorial Board and continue to seek advice on submissions and reviews in process as needed.
- Align effort to produce reviews with attempts to secure funding opportunities: current resourcing of COVID review teams is unlikely to be stable over 2021, and funding sources will be needed to target support for priority reviews.
- Work closely with teams of researchers involved with the German CEO Sys consortium to publish full systematic reviews of therapeutics.
- Look to invite submissions from other teams already preparing reviews in priority areas to publish through Cochrane.
- Explore the potential for surveillance of the COVID-19 study register to help inform when large influential studies deliver results against priority review areas.

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<sup>5</sup> <https://www.mcmasterforum.org/networks/covid-end/resources-to-support-decision-makers/horizon-scans-for-emerging-issues>

<sup>6</sup> <https://www.mcmasterforum.org/networks/covid-end/resources-to-support-decision-makers/Inventory-of-best-evidence-syntheses>

- Lengthen updating cycles for living reviews as studies deliver more definitive results, and evidence stabilises.
- Monitor emerging priorities as the long-term impact of the pandemic and its impact become clear e.g. morbidity of disease, infection and treatment, mental health impacts, novel therapeutics or diagnostics.
- Maintain good communication with the Knowledge Translation Department to identify how to disseminate the COVID-19 reviews we publish.

## 6 Priorities for 2021 and beyond

The COVID-19 pandemic is not just a crisis of public health, but one of inequality<sup>7 8</sup> and misinformation.<sup>9</sup> We can expect that access to effective medicines in COVID-19, including vaccines, and the continued supply of generic medicines used for indications other than COVID-19, to be compromised in many low and middle income countries.<sup>10</sup> Furthermore, in many high income countries disparities of income, employment, and housing have increased risks from both the virus and the public health measures intended to arrest its transmission.<sup>11 12</sup> Allied to this, increased use of advertising space on social media platforms by anti-vaccine organisations has fostered distrust,<sup>13</sup> one of many factors cited as barriers to uptake of deployed COVID-19 vaccines.<sup>14</sup> Social media played a particularly important role in accelerating the promotion of chloroquine as an effective treatment of COVID-19 in the early months of 2020 before large scale randomised trials proved its lack of effect on mortality.<sup>15</sup>

Retaining a focus on effects of public health measures will continue to be an important part of Cochrane's continued response to the pandemic, and a proposal to support methodological development of public health reviews in 2021 could include some financial support for new or updated COVID-19 reviews. We will continue to consider public health reviews of interventions that may have large-scale impact, reviews of public health measures specific to healthcare settings and reviews with clear implications for health equity. The emergence of multiple SARS-CoV-2 variants of concern and the

<sup>7</sup> <https://www.cdc.gov/coronavirus/2019-ncov/community/health-equity/race-ethnicity.html>

<sup>8</sup> Burki T. COVID-19 among American Indians and Alaska Natives. *Lancet Infect Dis.* 2021 Mar;21(3):325-326. doi: 10.1016/S1473-3099(21)00083-9. PMID: 33639126.

<sup>9</sup> [https://www.who.int/health-topics/infodemic#tab=tab\\_1](https://www.who.int/health-topics/infodemic#tab=tab_1)

<sup>10</sup> Lancet Commission on COVID-19 Vaccines and Therapeutics Task Force Members. Urgent needs of low-income and middle-income countries for COVID-19 vaccines and therapeutics. *Lancet.* 2021 Feb 13;397(10274):562-564. doi: 10.1016/S0140-6736(21)00242-7. Epub 2021 Jan 28. PMID: 33516284; PMCID: PMC7906712.

<sup>11</sup> Bamba C, Riordan R, Ford J, et al The COVID-19 pandemic and health inequalities. *Journal of Epidemiology and Community Health* 2020;74: 964-968.

<sup>12</sup> Glover et al. A framework for identifying and mitigating the equity harms of COVID-19 policy interventions. *Journal of Clinical Epidemiology* 2020 (128): 35-48.

<sup>13</sup> Jamison AM, Broniatowski DA, Dredze M, Wood-Doughty Z, Khan D, Crouse Quinn S. Vaccine-related advertising in the Facebook Ad Archive. *Vaccine* 2020; 38, 3: 512-520.

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[https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment\\_data/file/952716/s0979-factors-influencing-vaccine-uptake-minority-ethnic-groups.pdf](https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/952716/s0979-factors-influencing-vaccine-uptake-minority-ethnic-groups.pdf)

<sup>15</sup> Gould S, Norris SL. Contested effects and chaotic policies: the 2020 story of (hydroxy) chloroquine for treating COVID-19. *Cochrane Database of Systematic Reviews* 2021, Issue 1. Art. No.: ED000151. DOI: 10.1002/14651858.ED000151.

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potential changes in transmissibility, virulence and vaccine efficacy has been identified as a clear priority for primary and secondary research<sup>16</sup>. We are working to commission scoping reviews of the transmission characteristics and impact on public health and health systems of new variants of concern, with the aim of informing future evidence syntheses in this area. Publishing reviews which address these questions will require us to continue to use a flexible review structure in our software and our publishing systems.

Adopting an equity lens<sup>17</sup> can help us achieve two objectives in support of decision-making. Firstly, it can help us identify questions that are most relevant to disadvantaged populations, and secondly it can contextualise results and help us understand differential outcomes for interventions which are demonstrated to be effective against COVID-19. We can also mitigate some of the long-term consequences of unequal access to life-saving knowledge and of rapidly shared misinformation. We have demonstrated an ability to produce trusted information quickly, but we need to ensure global relevance in our continued response to COVID-19.

Decisions to update COVID-19 reviews published in 2020 may be informed by this document but should be considered independently. The decision framework informing review updates in a pandemic context, in particular living systematic reviews, have been covered in separate manuscripts<sup>18</sup>. These decisions are made following dialogue and mutual agreement between author and editorial team and are dependent on ongoing stakeholder demand and the emergence of new evidence likely to change the review conclusions. In the fast-evolving COVID-19 evidence landscape, review updates may be required frequently for some topics where the evidence base is growing rapidly. For example, the global use of rapid point of care tests has increased substantially since the publication of the first version of the Cochrane review of their diagnostic accuracy<sup>19</sup>, and the evidence base has expanded quickly as more test evaluations are published. There is a clear need to maintain this review at frequent intervals. Other reviews, however, such as the review of the accuracy of antibody tests<sup>20</sup>, whilst topical at the time of publication, no longer serve the same use for stakeholders (we note that this may change with changes in test application and technologies).

Regular communication between the Deputy Editor in Chief, Editorial Service, Editorial Board and CRGs and Networks will be necessary to achieve a reasonable balance of priorities covered by any new and updated reviews. Ongoing dialogue with relevant CRGs will be required to ensure appropriate division of reviews overseen centrally and those overseen by CRGs. By centrally coordinating this approach, we will be able to support efforts to identify and secure funding for teams preparing reviews in these areas:

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<sup>16</sup> <https://www.ecdc.europa.eu/en/covid-19/variants-concern>

<sup>17</sup> <https://training.cochrane.org/handbook/current/chapter-16>

<sup>18</sup> Iannizzi C, Dorando E, Burns J, Weibel S, Dooley C, Wakeford H, Estcourt LJ, Skoetz N, Piechotta V. Living systematic reviews in the context of rapidly emerging diseases: challenges and lessons learned. 2021. *Under review*.

<sup>19</sup> Dinnes J, Deeks JJ, Adriano A, Berhane S, Davenport C, Dittrich S, et al. Rapid, point-of-care antigen and molecular-based tests for diagnosis of SARS-CoV-2 infection. *Cochrane Database of Systematic Reviews* 2020, Issue 8. Art. No: CD013705.

<sup>20</sup> Deeks JJ, Dinnes J, Takwoingi Y, Davenport C, Spijker R, Taylor-Phillips S. Antibody tests for identification of current and past infection with SARS-CoV-2. *Cochrane Database of Systematic Reviews* 2020, Issue 6. Art. No.: CD013652. DOI: 10.1002/14651858.CD013652. Accessed 19 May 2021.

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## 1. Vaccines and immunity

As vaccines are developed and approved for use against COVID-19 and new SARS-CoV-2 variants of concern emerge, reviews should be considered against the following themes:

### 1.1 Effectiveness & safety

A living Network Meta-Analysis led by Cochrane France will answer the question of vaccine effectiveness against serious illness from COVID-19 and harms. The team have mapped the studies in this area, and this will also provide an opportunity to keep the analyses updated as trial endpoints are reached. The uncertain impact of emerging SARS-CoV-2 variants on vaccine effectiveness will mean that it is crucial that this living NMA is kept up to date. Tracking vaccine effectiveness as variants emerge will be key to informing policy decisions and the need for vaccine ‘editing’ and booster vaccinations. Extending the review question further to include harms identified through post-marketing surveillance would also be of interest, as well as data included in submissions to regulatory procedures.

### 1.2 Global rollout & uptake

COVID-19 vaccines can require ultra-cold chains, restricting their deployment to settings where the necessary infrastructure exists to ensure optimal distribution, storage and safe handling procedures.<sup>21</sup> Reviews that consider equity in the storage, distribution dosing and effectiveness of vaccines should be commissioned. Synthesis of the barriers and facilitators to vaccine uptake, health system capacity and communication strategies around vaccine hesitancy are needed. Consultation with the Cochrane Equity Methods Group and Cochrane’s Geographic Groups in regions most affected by these issues will help to refine these priorities further.

### 1.3 Immunity

The duration of immunity following both infection and vaccination are key unknowns, and prognosis reviews addressing these questions are anticipated from the Cochrane Haematology Group. The effects of vaccines in clinically vulnerable, immunosuppressed populations are uncertain since they were not recruited to early efficacy studies. Reviews commissioned to date will assess immune response in these populations, as well as adverse effects. The immune response to both vaccination and disease as new variants emerge is a priority for Cochrane. In addition to the NMA cited in 1.1, the commissioned scoping review on variants of concern discussed above aims to inform other reviews in this field.

## 2. Generic medicines

Even with concerted efforts to establish a global supply of COVID vaccines<sup>22</sup>, stark differences in their rollout across the world are likely to persist for many months or even years.<sup>23</sup> This and the likely endemic nature of the SARS-CoV-2 virus<sup>24</sup> make the evaluation of low-cost treatments such as corticosteroids

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<sup>21</sup> Wouters OJ, Shadlen KC, Salcher-Konrad M, Pollard AJ, Larson HJ, Teerawattananon Y, Jit M. Challenges in ensuring global access to COVID-19 vaccines: production, affordability, allocation, and deployment. *Lancet*. 2021 Mar 13;397(10278):1023-1034. doi: 10.1016/S0140-6736(21)00306-8. Epub 2021 Feb 12. PMID: 33587887

<sup>22</sup> <https://www.who.int/initiatives/act-accelerator/covax>

<sup>23</sup> <https://ourworldindata.org/covid-vaccinations> (date accessed 5<sup>th</sup> March 2021)

<sup>24</sup> Torjesen I. Covid-19 will become endemic but with decreased potency over time, scientists believe. *BMJ*. 2021 Feb 18;372:n494. doi: 10.1136/bmj.n494. PMID: 33602668.

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(inhaled and systemic), colchicine, ivermectin, azithromycin, (hydroxy)chloroquine, and antiplatelets a particularly important priority.

Several medicines currently being trialled in COVID-19 studies already have established indications and are included on the WHO Essential Medicines list.<sup>25</sup> Heightened interest in the potential for low-cost medicines to treat COVID-19 can impact on supply and access to these medicines for other conditions.<sup>26</sup> Diversion of these medicines away from established indications is double-edged: low-cost medicines are denied to those who rely on them and they are repurposed for uncertain benefit in treating COVID-19. Reviews are needed to better inform treatment recommendations.

As part of a consortium led by Cochrane Germany ('CEOSys'), teams of German researchers are preparing systematic reviews on a range of therapeutics driven by commissioner demand (German Federal Ministry of Health). Non-overlapping reviews will be brought into the Editorial Service that cover many low-cost generic medicines. The submission of several of these reviews is driven by the release of data from high-quality trials (e.g. RECOVERY) to optimise the utility of these reviews to readers. Review questions not currently being prepared by the CEOSys teams which fit in to this category could also represent an excellent opportunity to work with review teams from low- and middle- income countries. Financial awards could also be offered to incentivise production of these reviews.

### 3. Mental health

The impacts of lockdown, grief and anxiety over the course of the pandemic will likely endure.<sup>27</sup> A complex picture of the impact the pandemic has had on people with pre-existing mental health disorders is emerging,<sup>28</sup> and the urgent medical response to the pandemic has left mental health service provision in many countries severely disrupted.<sup>29</sup>

Our published reviews in this field have focused on mitigation of the mental health impacts of the pandemic and the effect of restrictions to reduce transmission on people's mental health. The Cochrane Mental Health and Neuroscience Network is in a good position to help identify relevant review questions. The Common Mental Disorders Group has begun to scope out review questions that are likely to be relevant from their existing portfolio. There will be a need to coordinate with the group as they identify COVID specific and broader review questions that could be done.

Among the topic areas that we would expect to see covered would be review questions addressing the impact of the pandemic on:

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<sup>25</sup> <https://www.who.int/publications/i/item/WHOMVPEMPIAU2019.06> (date accessed 5th March 2021)

<sup>26</sup> <https://www.commonwealthfund.org/blog/2020/covid-19-highlights-problems-our-generic-supply-chain>

<sup>27</sup> Pfefferbaum B, North CS. Mental Health and the Covid-19 Pandemic. *N Engl J Med.* 2020 Aug 6;383(6):510-512. doi: 10.1056/NEJMp2008017. Epub 2020 Apr 13. PMID: 32283003.

<sup>28</sup> Pan KY, Kok AAL, Eikelenboom M, Horsfall M, Jörg F, Luteijn RA, et al. The mental health impact of the COVID-19 pandemic on people with and without depressive, anxiety, or obsessive-compulsive disorders: a longitudinal study of three Dutch case-control cohorts. *Lancet Psychiatry.* 2021 Feb;8(2):121-129. doi: 10.1016/S2215-0366(20)30491-0. Epub 2020 Dec 8.

<sup>29</sup> <https://www.who.int/news/item/05-10-2020-covid-19-disrupting-mental-health-services-in-most-countries-who-survey>

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- Children/young people
  - Front-line workers
  - Seniors
  - People experiencing intimate partner abuse

Conditions that will likely be addressed include anxiety/depression; complex post-traumatic stress disorder, suicidality, self-harm; alcohol and substance misuse and sleep disorders. Mental health impacts could also be incorporated into any updates of reviews of public health measures in preparation for any future outbreaks.

## 7 Longer-term health impacts

We are at too early a stage to understand the long-term effects of COVID-19 and public health measures to control it. A watching brief is needed in the years to come to ensure that we can identify how COVID-19 affects those who have lived through it. At the beginning of the pandemic COVID-19 was largely thought of as an acute respiratory disease. Since then, it has become increasingly clear that it affects more than one body system over the course of the disease, and that public health measures to reduce community transmission risk increasing economic, social and health disparities in the future.

As with the 1918 influenza pandemic, there are likely to be sequelae that emerge at a distance of many years after people recover from infection.<sup>30</sup> The involvement of neurological, respiratory and cardiovascular systems in COVID-19, and the experiences of people with long COVID will need to be captured by our reviews in the long term. Health and social inequalities prior to the pandemic have exacerbated risks of the disease and widened further since. We should be open to reviews of interventions, diagnosis, prognosis and qualitative evidence playing a role in informing healthcare and policy decisions in the future.

Cochrane demonstrated agility in responding to the COVID-19 pandemic. Working with its community of contributors in geographic groups and CRGs, we identified and produced high priority, high quality reviews. Cochrane needs to retain as much of the agility it demonstrated in 2020 as possible in order to address diverse questions that meet the needs of external users of our evidence as the world lives with the continuing effects of the COVID-19 pandemic.

## 8 Recommendations:

- Decisions to update COVID-19 reviews published in 2020 may be informed by this document but should be considered independently and made according to the review's individual priority status in the changing evidence landscape

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<sup>30</sup> <https://www.newstatesman.com/politics/health/2020/10/scars-long-covid>

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- Decisions regarding new reviews submitted the Central Editorial Service should be assessed against the priority areas of vaccines and immunity, generic medicines and mental health outlined in this document.
  - Reviews should be commissioned where there are evidence synthesis gaps in our priority areas. This may be via Cochrane Review Groups and their Networks, Cochrane Geographic Groups, Cochrane Fields, or external author teams.
  - We should monitor emerging priorities by making use of the outputs of a range of COVID-19 prioritization panels, in particular the horizon scanning work of COVID-END, to identify the topics for which living syntheses are most needed
  - We should endeavour to avoid duplication of effort where possible by monitoring high-quality outputs from other evidence synthesis groups