Rapid reviews on COVID-19: Challenges and Opportunities

Andrea C. Tricco MSc, PhD
St. Michael’s Hospital, Unity Health Toronto
Dalla Lana School of Public Health & IHPME, University of Toronto
Joanna Briggs Institute Centre of Excellence, Queen’s University

Areti-Angeliki Veroniki, MSc, PhD
St. Michael’s Hospital, Unity Health Toronto
IHPME, University of Toronto
Cochrane Statistical Methods Group
Acknowledgement of Traditional Land

The Knowledge Translation Program is located on land now known as Tkaronto (Toronto). Tkaronto is the traditional territory of many groups, including the Mississaugas of the Credit and the Chippewa/ Ojibwe of the Anishnaabe Nations; the Haudenosaunee, and the Wendat. It is now home to many diverse First Nations, Inuit and Métis peoples. We also acknowledge that Tkaronto is covered by Treaty 13 with the Mississaugas of the Credit and The Dish with One Spoon treaty between the Anishinaabe, Mississaugas and Haudenosaunee that connected them to share the territory and protect the land. All Indigenous Nations and peoples, Europeans and newcomers, have been invited into this treaty in the spirit of peace, friendship and respect.

We would like to honour the Elders and Knowledge Keepers, both past and present, and are committed to continuing to learn and respect the history and culture of the communities that have come before and presently reside here.

We acknowledge the harms of the past and present, and we dedicate ourselves to work with and listen to First Nations, Inuit and Métis communities in the spirit of reconciliation and partnership.

We recognize and are grateful to have this opportunity to work on this land, and commit to caring for this land and continuously and actively working towards reconciliation. We recognize that Indigenous practices of health and well-being have been in place in this territory for over 10,000 years and are maintained to this day.
Outline of presentation

• Define rapid reviews

• Describe methods for rapid reviews

• Present a case example on a rapid review
  o COVID-19 diagnostic test accuracy network meta-analysis

• Discuss challenges and opportunities related to rapid reviews
Rapid Reviews
What is a Rapid Review?

If an organization produces rapid reviews for decision-making, then this definition can be used: “A rapid review is a form of knowledge synthesis that accelerates the process of conducting a traditional systematic review through streamlining or omitting a variety of methods to produce evidence for stakeholders in a resource-efficient manner.”

- 5-12 weeks to complete
- Cost $25,000 CAD
How are Rapid Reviews Useful?

- Rapid review-informed decisions helped in savings of approximately $3 million per year in one hospital in Quebec, Canada.
- Rapid HTA in Austria helped inform investment decisions on variety of new health technologies reducing costs in hospitals.
- Useful for decision-makers during urgent situations (e.g., COVID-19).
- Moving away from rapid reviews as a method on its own, more of a framework to situate the knowledge synthesis in.
- Can do systematic review, overviews of reviews, and scoping reviews rapidly.

## What are Rapid Evidence Products?

<table>
<thead>
<tr>
<th>Category</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inventories</td>
<td>Inventories only list the evidence that is available on a given topic. There is no attempt to appraise, summarize or synthesize the evidence for further use, nor is there an attempt to present conclusions or recommendations to the knowledge user.</td>
</tr>
<tr>
<td>Rapid response briefs</td>
<td>Rapid response briefs present a summary of the best available evidence in a synthesized and contextualized manner, in direct response to a decision-maker’s question. They are knowledge translation products created through formal methods to synthesize and appraise the evidence. They do not generate new knowledge but use findings that are already available, especially from existing systematic reviews.</td>
</tr>
<tr>
<td>Rapid reviews</td>
<td>Rapid reviews represent a knowledge generation strategy. They synthesize findings and assess the validity of research evidence using “abbreviated” systematic review methods, modifying these methods to generate evidence in a short time.</td>
</tr>
</tbody>
</table>
Rapid Review steps

- Discuss policy, practice, and clinical implications with caution
- Provide a more streamlined product (e.g., 1-page summaries)
- Limit to basic descriptive summary of studies
- Prioritize type of analysis

![Diagram of Rapid Review steps]

- Develop research question using PICOST
- Determine eligibility criteria using the PICOST research question
- Plan a literature search
- Only register protocol

- Limit literature search (e.g., # of databases, by date, grey lit)
- Use a layered search approach

- Level 1: Titles and abstracts
- Level 2: Full-text articles

- Pilot the form
- Use two reviewers for some of the data points to be abstracted
- Limit to a single reviewer only or single reviewer and one verifier

- Summarize study and patient characteristics
- Prioritize assessment of key sources of bias
- Streamline by limiting to a single reviewer and one verifier
- (Skip this step)

<table>
<thead>
<tr>
<th>Status</th>
<th>Patients, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disposition after evaluation in emergency department</td>
<td></td>
</tr>
<tr>
<td>Hospitalized</td>
<td>377 (66)</td>
</tr>
<tr>
<td>Discharged from emergency department</td>
<td>140 (23)</td>
</tr>
<tr>
<td>Discharged after observation period in emergency department</td>
<td>46 (8)</td>
</tr>
<tr>
<td>Transferred to other health facility</td>
<td>6 (1)</td>
</tr>
<tr>
<td>Died in emergency department?</td>
<td>1 (0)</td>
</tr>
<tr>
<td>Hospitalization?</td>
<td></td>
</tr>
<tr>
<td>Discharged within the first 3 days</td>
<td>112 (30)</td>
</tr>
<tr>
<td>Hospitalized for 4–9 days</td>
<td>187 (50)</td>
</tr>
<tr>
<td>Stayed in the hospital ≥10 days</td>
<td>78 (20)</td>
</tr>
<tr>
<td>Treatment</td>
<td></td>
</tr>
<tr>
<td>Nonoperative</td>
<td>280 (51)</td>
</tr>
<tr>
<td>Surgery</td>
<td>243 (43)</td>
</tr>
<tr>
<td>Transferred to other health facility</td>
<td>6 (1)</td>
</tr>
<tr>
<td>Died</td>
<td>31 (5)</td>
</tr>
</tbody>
</table>
Conduct guidance

- Guidance for conduct of rapid reviews for health policy and systems research developed in collaboration with WHO
- WHO guide recommends researchers tailor methods to needs of decision-makers
- Several ways that rapid reviews can be streamlined to accommodate decision-makers’ needs related to both scope of review and timeliness across all steps of review process

Tricco, A. et al. (2017) WHO
Developing PRISMA-RR, a reporting guideline for rapid reviews of primary studies (Protocol)

Adrienne Stevens¹², Chantelle Garrity¹², Mona Hersi¹, David Moher¹³⁴

¹Ottawa Methods Centre, Clinical Epidemiology Program, Ottawa Hospital Research Institute, Canada;
²TRIBE Graduate Program, University of Split School of Medicine, Croatia;
³Centre for Journalology, Clinical Epidemiology Program, Ottawa Hospital Research Institute, Canada;
⁴School of Epidemiology and Public Health, University of Ottawa, Canada;
Rapid Reviews & COVID-19

Challenges identified:
- Involving all relevant knowledge users (patient partners, clinicians, policy-makers)
- Urgency of the request (5-10 days)
- Finding all relevant evidence (scattered across websites and pre-print servers)
- Interpreting results when clear and direct evidence does not exist
- Sharing the results widely
- Updating reviews on a continuous basis (e.g., living reviews)
Case Example from the "Real World"

COVID-19 rapid antigen & molecular tests: A rapid review with diagnostic test accuracy network meta-analysis (DTA-NMA)
Rapid Review Example

Health Canada and the Public Health Agency of Canada contacted us to lead a review to determine the most sensitive and/or specific rapid test for the diagnosis of COVID-19.

They needed the report as soon as possible.

We set up our team considering to include the policy-makers who requested the evidence, at least one clinician/content expert, two patient partners, content experts, research methodologists, and statisticians.
1. Research Question

- We developed a research question and determined eligibility criteria as follows:
  - **Population**: Adults and/or children screened/suspected for COVID-19
  - **Target condition**: COVID-19 infection
  - **Index tests**: We included studies evaluating one or more commercially available COVID-19 rapid lateral flow antigen test or rapid molecular test (providing a result in ≤1 hour) used for screening of asymptomatic individuals or the diagnosis of COVID-19 infection in symptomatic individuals
  - **Reference Standard**: polymerase chain reaction (PCR) test
  - **Study design**: We included RCTs and observational studies providing the 2x2 table data
  - **Outcome**: Sensitivity and specificity of rapid antigen and molecular tests suitable for screening and diagnosing COVID-19

- Registered our protocol with PROSPERO: CRD42021289712
2. Literature Search Strategy

- We worked with an experienced librarian
- The search was peer-reviewed by another librarian using the Peer Review of Electronic Search Strategies (PRESS) Checklist
- Searched 3 databases:
  - Embase, MEDLINE, and EBM Reviews - Cochrane Central Register of Controlled Trials
  - Completed on September 12, 2021
- We included only primary studies from December 2019 up to September 2021
- Grey literature was not searched
- Limited to English publications with available data for analysis
- Did not contact authors for clarifications
3. Study Selection

- We used a standardized screening form for both levels of screening
  - Level 1: Titles and abstracts
  - Level 2: Full-text articles
- A pilot exercise was completed to calibrate and test the form at each level of screening with all reviewers (i.e., 50 citations at level 1 and 15 articles at level 2)
- We made decisions based on 1 reviewer

4. Data Extraction

- We used a standardized data extraction form
- Performed a pilot exercise to calibrate and test the form with all reviewers using 5 full-text articles
- We made decisions based on 1 reviewer and 1 verifier
5. Risk of Bias Assessment

- This step was not performed
- We plan to assess risk of bias using the QUADAS-2 and QUADAS-C tools for the included studies
6. Data analysis

- Limited to basic descriptive summary of studies
  - Country of conduct and type of rapid test

- Kept the analysis high-level:
  - Random-effects DTA meta-analysis (bivariate model)
  - Random-effects DTA-NMA (Nyaga ANOVA model)

- Estimated sensitivity and specificity for each test along with their 95% credible intervals

- Investigated potential sources of heterogeneity that may influence diagnostic accuracy using:
  - **Subgroup analysis**: symptom status (asymptomatic vs symptomatic), sample type (e.g., saliva, nasal swab), participant type (e.g., general public, healthcare worker), and rapid molecular test category (i.e., rRT-PCR, PT-Isothermal, RT-Lamp)
  - **Meta-regression**: age

- Assessed transitivity based on the distribution of the above potential effect modifiers across test comparisons
7. Summary and Display of Data

- Sent preliminary results and asked for a deep-dive on any key issues from our knowledge users:
  - Health Canada, Public Health Agency of Canada, Ministry of Public Health in Thailand, and Irish Department of Health
- Discussed implications of results with caution
- Provided our knowledge users with a 1-page summary
8. Report Findings

• Used reporting guidelines to ensure transparent and complete reporting of our research approach and findings (e.g., PRISMA-DTA and PRISMA-NMA Checklist)
8. Summarized results

**DTA-NMA results**

**Rapid antigen tests**

**Rapid molecular tests**
Challenges of rapid reviews for COVID-19 during the pandemic

Challenges and study limitations:

- Literature searches are 7 months old and this is a rapidly-moving area
- Staff shortages due to covid-19
- We might have missed studies to contribute to the evidence-base (e.g. 1 reviewer)
- Findings have not been assessed regarding the study risk of bias
- Unclear what variants of SARS-CoV-2 the participants had during these studies
- Transitivity could not be assessed appropriately, since reporting was inadequate in the original studies

A more comprehensive (systematic) review should be completed

- To conduct a full systematic review that will be updated on a continuous basis (i.e., living review)
- To assess methodological quality using the QUADAS-2 and QUADAS-C tools
- To consider the inclusion of both preprints and publications in any language, and to contact the authors for potentially missing or unclear data
- To evaluate the impact of circulating variants, vaccination status, test operator (e.g., nurse, self-testing), who interpreted the results (e.g., nurse, self-testing), and participant age on the accuracy of the individual rapid tests
Opportunities of rapid reviews for COVID-19 during the pandemic

Opportunities:

- Initiated project and submitted results for COVID-19 rapid tests within 8 months
- Registered with PROSPERO to help avoid duplication and increase transparency
- Not fundamentally different from a standard systematic review – but faster
- Matched to decision-making timeframes; provided input to decision-making
- Performed formal comparison of all identified rapid antigen tests and rapid molecular tests using a DTA-NMA
- This work involved two patient partners to ensure patient perspectives are integrated in our research question.
- Will publish these results for transparency and accountability, as well as for knowledge transfer and translation within the fast-moving field of COVID-19
Acknowledgements

Sofia Tsokani
Sharon Straus
Jennifer Watt
Carole Lunny
Paul Khan
Charlene Soobiah
Ahmed Negm
Amanda Doherty-Kirby

Paul Taylor
Jessie McGowan
Julian Little
Patrick Mallon
David Moher
Sabrina Wong
Jacqueline Dinnes
Yemisi Takwoingi

Lynora Saxinger
Adrienne Chan
Wanrudee Isaranuwatchai
Bryn Lander
Adrienne Meyers
Guillaume Poliquin
Thank you!
Questions?

Let’s keep in contact!

@ATricco
@AVeroniki

andrea.tricco@unityhealth.to
areti-angeliki.veroniki@unityhealth.to