**Evidence Map and Evaluation of the COVID-19 Synthesis Research**

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# Important Dates

Evidence published up to \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

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# Rationale

This research aligns with the Public Health Risk Sciences (PHRS) Division priorities, which include enhancing and guiding public health decision-making and policies by providing the authoritative analyses, recommendations, and scientific collaborative services (using methods such as epidemiological studies and knowledge synthesis) to address the current pandemic of COVID-19 in Canada and around the globe.

Background

This is evidence mapping of the synthesis research on the COVID- 19 pandemic. Synthesis research includes several methodologies including systematic reviews, meta-analysis, scoping reviews, rapid reviews, umbrella reviews, etc. COVID-19 is an ongoing public issue that is affecting the lives of many and it was declared as a global pandemic on March 11, 2020, by the World Health Organization (WHO). The literature on COVID-19 is being published at a very fast pace and increasingly there are a variety of research syntheses published, however, the quality is highly variable. The goal of this project is to identify, evaluate, and map the quantity, characteristics (topic and outcomes), and quality of the synthesis research on COVID-19.

The emerging sciences group within the Public Health Risk Sciences (PHRS) Division conducts a daily scan of entire literature surrounding COVID-19 using artificial intelligence (AI) based software called, DistillerSR. Pre-prints and published literature are gathered from various databases and organized in DistillerSR. Synthesis research is identified using an AI tool from our COVID-19 library.

Study Question

What are the characteristics and quality of the COVID-19 synthesis research?

Planned Study outputs

1. Examine the quality (AMSTAR) by publication vs. prepublication.
2. Find the proportion of reviews that do not meet minimum quality criteria.
3. Map out the type and topics and outcomes covered by the reviews.

# Methods

## Review Team Expertise & Responsibilities

|  |  |  |
| --- | --- | --- |
| **Member** | **Organization** | **Project Role** |
| Lisa Waddell | PHRS/NML | Project lead/synthesis expertise/reviewer |
| Tricia Corrin | PHRS/NML | Project lead/synthesis expertise/reviewer |
| Austyn Baumeister | PHRS/NML | Reviewer |
| Muhammad Hamzah Abid | PHRS/NML | Reviewer |

## 

## Search Strategy/Databases

## A daily scan of the literature (published and pre-published) is conducted by the emerging sciences group. The scan has compiled COVID-19 literature since the beginning of the outbreak and is updated daily. Searches to retrieve relevant COVID-19 literature are conducted in Pubmed, Scopus, BioRxiv, MedRxiv, ArXiv, SSRN, Research Square, and cross-referenced with the literature on the WHO COVID literature list, and COVID-19 information centers run by Lancet, BMJ, Elsevier, and Wiley. The daily summary and full scan results are maintained in a RefWorks database and an excel list that can be searched. Targeted keyword searching is conducted within these databases to identify relevant citations on COVID-19 and SARS-COV-2. Synthesis research is identified using an AI tool from our COVID-19 library.

## Review Management & Analysis

### **DistillerSR will be used to manage and categorize all types of reviews mentioned above within the**Data Extraction - General Form Synthesis Research.**Based on the type of review, descriptive analysis, and the heat chart of findings will be done by all the reviewers. The date range from which the author(s) conducted their literature search, if identified, will also be noted. Also, we aim to do the review process with the most recent to the least recent synthesis research. Therefore, articles will be reviewed from higher to lower RefID.**

## Relevance Screening

All the synthesis research in DistillerSR within **the**Data Extraction - General Form Synthesis Research will be reviewed by each reviewer. This form includes screening questions that consider the inclusion and exclusion criteria below. This will be followed by the application of the AMSTAR-2 Form (see appendix 2).

### Inclusion/exclusion criteria

1. Timeframe – All years (no exclusions)
2. Location – Global (no exclusions)
3. Study Design – All (all review literature)
4. Document Type – Review articles other than Literature/Narrative/Comprehensive Reviews
5. Disease/Pathogen – all type of findings regarding COVID-19 circulating strain SARS-CoV-2, will be captured in this review.

Data Mapping/Extraction Form

After relevance screening and AMSTAR-2 application, reviewers will categorize and extract outcomes from each type of review. The parental category of each review will include reviews that examine the risk factors, interventions, and methods for diagnosing COVID-19. Within these categories, each review will be designated by the type of risk factor/population/outcome, interventions (therapeutic and public health), and diagnosis methods/purpose. Within each sub-category, it will also be noted if meta-regression or meta-analysis is done for each outcome. The data mapping/extraction categories and outcomes form is in appendix 3. To visualize this mapping, please see the flowchart in appendix 4.

Risk of Bias Assessment (RoBA)

RoBA will be done in this project as AMSTAR-2 Form will be applied to all the synthesis research collected in the DistillerSR. AMSTAR-2 allows us to determine the quality of the review by examining if researchers of each review had a priori protocol, extensive search strategy with at least 2 reviewers, performed a RoBA, etc.

Guide to AMSTAR-2

AMSTAR 2 is a critical appraisal tool for a systematic review of randomized and non-randomized studies of healthcare interventions. We intend to extend the use of AMSTAR-2 to healthcare and public health questions addressed using synthesis research on COVID-19 (systematic reviews, meta-analysis, rapid reviews, living systematic review, scoping reviews, umbrella reviews, etc.). To accommodate this there are a few variations needed in the signaling criteria to accommodate non-intervention questions and the addition of NA is required in some additional questions e.g. Risk of Bias to accommodate synthesis designs e.g. scoping reviews where the risk of bias is not conducted.

The first level data extraction tool will be with questions that identify the type of synthesis research, search dates, coverage, AMSTAR-2, foci, and outcomes reported in the review. For synthesis reviews that are part of a current umbrella review, data will be extracted for relevant outcomes using a repeatable data capture tool. Please see the appendix 2 for the full AMSTAR-2 form that will be used for this review.

AMSTAR-2 Overall Confidence Rating

Based on questions and signaling criteria, this tool will also allow us to grade the quality of the evidence for the rapid and systematic reviews thus, meta-analysis. The confidence rating can be high, medium, and low. See appendix 5 for the criteria of each rank level. For this evidence mapping, we will have downgrade options for some of the AMSTAR-2 questions. One “downgrade” equates to a 1.0 and one “partial yes” equates to 0.5 lower grading score in the overall ranking for the quality of each review. Therefore, high ranking captures scores of 0, 0.5 and 1.0 downgrades. Medium ranking captures scores from more than 1 to less than or equal to 5. Lastly, low ranking is for any review that has more than five downgrades.

Appendix 1: Relevance Screening Form

|  |  |  |
| --- | --- | --- |
| **Question** | **Options** | **Additional Notes** |
| **Relevance Verification:**  The first few questions are designed for verification of the relevance of the article. If any exclusion criteria are selected please indicate the article is excluded before submitting the form. | | |
| What type of review is this (as defined by the author)? | 1. Systematic Review 2. Systematic review –meta analysis (SR-MA) 3. Rapid Review 4. rapid review - meta analysis 5. Meta-analysis 6. Scoping Review 7. Umbrella Review 8. Living Systematic Review 9. Living SR-MA 10. Other \_\_\_TXT   NOT a form of synthesis research (EXCLUDE) | If the article is not a form of synthesis research, then exclude and state the reason for doing so.  Narrative, comprehensive and traditional literature reviews should be excluded.  Definitions for each type of review is in **appendix 6.**  .  Use the "Other" option only if the researchers give a unique term to their synthesis research but use a proper systematic methodology. |
| Is the review about COVID-19? | 1. Yes (proceed) 2. No (exclude) | If the review is not about COVID-19 then click the “No” option and submit the form. |
| Is the review in English or French? | 1. English 2. French 3. Other \_TXT | If “yes” then, proceed to further evaluate the review otherwise if “no” then, tag it to exclude. |
| Is the research pre-print or Published? | 1. Pre-print 2. Published |  |
| What type of review is this after evaluating the paper? | 1. Systematic Review 2. Systematic review –meta analysis (SR-MA) 3. Rapid Review 4. rapid review - meta analysis 5. Meta-analysis 6. Scoping Review 7. Umbrella Review 8. Living Systematic Review 9. Living SR-MA 10. Other \_\_\_TXT   NOT a form of synthesis research (EXCLUDE) | If the article is not a form of synthesis research, then exclude and state the reason for doing so.  Narrative, comprehensive and traditional literature reviews should be excluded.  Definitions for each type of review is in **appendix 6.** |

Appendix 2: AMSTAR-2 Form

|  |  |  |
| --- | --- | --- |
| Question | Answers | Signalling Criteria |
| 1. Did the research questions and inclusion criteria for the review include the components of PICO? | * Yes * No | YES: All components of a PICO/ PECO or other question was well defined  NO: The question is not well defined or clearly  stated. |
| 2. Did the report of the review contain an explicit statement that the review methods were  established prior to the conduct of the review and did the report justify any significant deviations from the protocol? | * Yes * Partial Yes * No | **Yes** includes the above points + synthesis/meta-analysis plan, investigation of heterogeneity plan and justification for deviations from the protocol.  **Partial Yes (ALL present)**: authors stated the protocol was written *a priori* and included ALL: review question, search strategy, inclusion/exclusion criteria, and risk of bias assessment (only for systematic reviews).  No: the authors do not mention creating a protocol prior to initiation of the review. |
| 3. Did the review authors use a comprehensive literature search strategy? | * Yes * Partial Yes * No | **Yes:**   * reference lists of included studies are searched (less important for COVID), * trial registries are searched (if healthcare intervention), * consulted experts in the field (we are the experts), * where relevant, searched for grey literature, conducted search within 24 months of completion of the review   **Partial Yes (ALL 3 present)**:   * At least 2 databases were searched, * the search string (keywords) are included * any restrictions are justified (e.g. language)   No: no search strategy reported. |
| If you answered NO to any from Q1-3, please STOP reviewing this work and exclude the review. | * EXCLUDE: please justify \_\_\_\_\_\_\_ * \_ | Exclude: This review **doesn’t meet the minimum criteria** to be one of the synthesis research methods included in this project. |
| 4. Did the review authors explain their selection of the study designs for inclusion in the review? | * Yes * No | For Yes, the review should satisfy ONE of the following:   * Explanation for including only RCTs * OR Explanation for including only NRSI * OR Explanation for including both RCTs and NRSI |
| 5. Did the review authors perform study selection in duplicate? | * Yes * No (down grade) | For Yes, either ONE of the following:   * at least two reviewers independently agreed on selection of eligible studies   and achieved consensus on which studies to include   * OR two reviewers selected a sample of eligible studies and achieved good agreement (at least 80 percent), with the remainder selected by one reviewer. |
| 6. Did the review authors perform data extraction in duplicate? | * Yes * No (down grade) | For Yes, either ONE of the following:   * at least two reviewers achieved consensus on which data to extract from included studies * OR two reviewers extracted data from a sample of eligible studies and achieved good agreement (at least 80 percent), with the remainder extracted by one reviewer. |
| 7. Did the review authors provide a list of excluded studies and justify the exclusions? | * Yes * Partial Yes * No (down grade) | For Partial Yes:   * provided a list of all potentially relevant studies that were read in full-text form but excluded from the review (We discussed a PRISMA diagram, list of relevant studies in languages not included)   For Yes, must also have:   * Justified the exclusion from the review of each potentially relevant study |
| 8. Did the review authors describe the included studies in adequate detail? | * Yes * Partial Yes * No (down grade) | For Partial Yes (ALL the following):   * described populations * described interventions * described comparators * described outcomes * described research designs   For Yes, should also have ALL the following:   * described population in detail * described intervention in * detail (including doses where * relevant) * described comparator in detail * (including doses where * relevant) * described study’s setting * timeframe for follow-up |
| 9. Did the review authors use a satisfactory technique for assessing the risk of bias (RoB) in individual studies that were included in the review? | * Yes * Partial Yes * No (down grade) * NA (scoping review)   Specify the ROB tool used: textbox | **RCT:**  For Partial Yes, must have assessed RoB from   * unconce aled allocation, and * lack of blinding of patients and assessors when assessing outcomes (unnecessary for objective outcomes such as all cause mortality)   For Yes, must also have assessed RoB from:   * allocation sequence that was not truly random, and * selection of the reported result from among multiple measurements or analyses of a specified outcome   **Non-Randomised Studies:**  For Partial Yes, must have assessed RoB:   * from confounding, and * from selection bias   For Yes, must also have assessed RoB:   * methods used to ascertain exposures and outcomes, and * selection of the reported result from among multiple measurements or analyses of a specified outcome |
| 10. Did the review authors report on the sources of funding for the studies included in the review? | * Yes * No | Must have reported on the sources of funding for individual studies included in the review. Note: Reporting that the reviewers looked for this information but it was not reported by study authors also qualifies **(Important for therapeutics, vaccines and diagnostic tests)** |
| Q11. If meta-analysis was performed did the review authors use appropriate methods for statistical combination of results? *(If they did some correctly and others were incorrect – select NO.)* | * Yes * No (down grade) * No meta-analysis conducted | **RCTs**  For Yes:  The authors justified combining the data in a meta-analysis   * AND they used an appropriate weighted technique to combine study results and adjusted for heterogeneity if present. * AND investigated the causes of any heterogeneity   **Non-Randomised Studies:**  The authors justified combining the data in a meta-analysis   * AND they used an appropriate weighted technique to combine study results, adjusting for heterogeneity if present * AND they statistically combined effect estimates from NRSI that were adjusted for confounding, rather than combining raw data, or justified combining raw data when adjusted effect estimates were not available * AND they reported separate summary estimates for RCTs and NRSI separately when both were included in the review |
| 12. If meta-analysis was performed, did the review authors assess the potential impact of RoB in individual studies on the results of the meta-analysis or other evidence synthesis? | * Yes * No * No meta-analysis conducted   (will not be commonly reported) | For Yes:   * included only low risk of bias RCTs * OR, if the pooled estimate was based on RCTs and/or NRSI at variable RoB, the authors performed analyses to investigate possible impact of RoB on summary estimates of effect |
| 13. Did the review authors account for RoB in individual studies when interpreting/ discussing the results of the review? | * Yes * No * NA (scoping review) | For Yes:   * included only low risk of bias RCTs * OR, if RCTs with moderate or high RoB, or NRSI were included the review provided a discussion of the likely impact of RoB on the results |
| 14. Did the review authors provide a satisfactory explanation for, and discussion of, any heterogeneity observed in the results of the review? | * Yes * No (down grade) | For Yes:   * There was no significant heterogeneity in the results * OR if heterogeneity was present the authors performed an investigation of sources of any heterogeneity in the results and discussed the impact of this on the results of the review   Even for scoping reviews authors should discuss variability between some outcomes, even if it is not the quantitative measurements within studies. |
| 15. If they performed quantitative synthesis did the review authors carry out an adequate investigation of publication bias (small study bias) and discuss its likely impact on the results of the review? | * Yes * No * N/A No meta-analysis conducted | For Yes:   * performed graphical or statistical tests for publication bias and discussed the likelihood and magnitude of impact of publication bias |
| 16. Did the review authors report any potential sources of conflict of interest, including any funding they received for conducting the review? | * Yes * No | For Yes:   * The authors reported **no competing interests** OR * The authors described their funding sources and how they managed   potential conflicts of interest |
| Overall ranking of the quality of the review | * Low (>5 down grades) * Medium (>1 to ≤5 down grades) * High (≤1 down grades) | There are 7 downgrades available in the tool (if this is a systematic review)/ 6 if no MA and 5 if it is a scoping review. We are suggesting the following guideline, but as a reviewer you can choose to downgrade further based on the review not meeting other factors in this checklist. |

Appendix 3: Data Mapping/Extraction Form

|  |  |  |
| --- | --- | --- |
| **Parent Categories Form** | **Sub-forms/Outcome(s)** | **Additional Notes** |
| **Data Categorization:**  This form with all the options will allow the reviewers to map/categorize and retrieve appropriate risk factors, population, outcome, interventions, etc. data useful for the end-users. | | |
| 1. Reviews that that examine the impact (mortality), outcome (anxiety level), or description (prevalence, lab findings) | **Population**   * Infant (newborn – 23 months) * Children (2-17 years) * Adults (18-64 years) * Elderly (65 or above) * General * Pregnant women * Healthcare workers * Fetus   **Risk factors/Exposure**   * Metabolic syndromes (Diabetes) * Immunocompromised (HIV, auto-immune, cancer, transplant) * Age * Sex * Mental Health (anxiety, depression, etc) * Hypertension * Smoker (former, current) * COPD * Asthma * Cystic Fibrosis * ACE II inhibitors or blockers * Birth * Quarantine * Cardiac conditions * Pandemic * Asymptomatic * Disability * Temperature/Climate * Endocrine conditions * Kidney problems * N/A   **Outcome(s)**   * Mortality * Severity of Symptoms * Susceptibility * Prevalence * Transmission * Risk of hospital admission * Risk of ICU admission * Antibody levels * Mental Health * Lab findings * Symptoms * Disability * ARDS * Birth type * Complications * CT findings   Comments (optional)\_\_\_TXT | Use age grouping as expressed by authors  Use general population where no population is specified    Use quarantine for studies of mental health  Use pandemic for studies of mental health in healthcare workers (ex. depression in healthcare workers during the pandemic  Choose N/A if it is just a population and an outcome  **Severity of symptoms** = mild versus severe cases  **Susceptibility** = likelihood of acquiring disease  Mental health outcome includes anxiety, depression, diet, exercise, alcohol intake.  **Prevalence** = is theproportion of a population of a population who have a specific characteristic in each time period |
| 1. Reviews of interventions for controlling disease or to provide treatment. | **Intervention Type**   * Anti-virals * Hydroxy chloroquine * Remdesivir * Kaletra (Lopinavir and Ritonavir) * Vitamins * Procedure * Traditional Medicine * Treatments (general) * Ventilation * Face masks * Isolation/Quarantine * Contact tracing * Rehabilitation * Pre-exposure prophylaxis * Steroids * Facility closures (schools, workplaces, etc.)   **Population**   * Children (2-17 years) * Adults (18-64 years) * Elderly (65 or above) * General * Pregnant women * Diabetes * ARDS * Thrombosis * Severe COVID-19 * Critically ill COVID-19 patients * Recovered   **Outcomes**   * Mortality * Severity * Disability * Morbidity * Treatment * Days of illness * Pneumonia * Viral replication   Comments (optional)\_\_\_TXT |  |
| 1. Review of methods for diagnosing, triaging, and telemedicine. | **Method type**   * Polymerase Chain Reaction (PCR) * Computed Tomography (CT) Scans * CT (AI algorithm) * Best practices and clinical guidelines * Procedures * Services and programmes * Serology (population screening) * Serology (infection detection)   **Context**   * Surgery * Patient care * Rehabilitation   **Purpose**   * Diagnosis (accuracy) * Diagnosis (agreement) * Transmission risk (population level) * Transmission risk (person-to-person) * IPAC * Triage   Comments (optional)\_\_\_TXT |  |
| For each outcome, was there meta-regression or meta-analysis?   1. Yes 2. No   **Note**: this question applies to the outcomes of all the categories  [**“Permanently add an answer to this question**](https://covid.evidencepartners.com/Submit/DataExtraction.php?formid=5&levelid=2&refid=220&qa=0&refid_search=) **“ option is available under each sub-form/outcome.** | | |

Appendix 4: Data Mapping/Extraction Flowchart

**Data Mapping of Reviews**

**Reviews of Interventions**

**Reviews of risk factors or exposure**

**Reviews of Methods**

**Context**

**Method Type(s)**

**Purpose**

**Population**

**Risk factor/Exposure**

**Outcome(s)**

**Population**

**Intervention Types**

**Outcome(s)**

Appendix 5: AMSTAR-2 Overall Confidence Rating of the Review

**High**

* Less than or equal to one downgrade: the systematic review provides an accurate and comprehensive summary of the results of the available studies that address the question of interest

**Medium**

* More than one but less than or equal to five downgrades: the systematic review has more than one weakness but no critical flaws. It may provide an accurate summary of the results of the available studies that were included in the review

**Low**

* More than five downgrades: the review has many non-critical flows and may not provide an accurate and comprehensive summary of the available studies that address the question of interest

Appendix 6: Definitions of Reviews

**Systematic Review** – as per Cochrane, a systematic review (SR) identifies, appraise, and synthesize all the empirical evidence that meets pre-specified eligibility criteria to answer a specific research question. SR uses explicit, systematic methods that are selected with a view aimed at minimizing bias, to produce reliable findings to reach certain conclusions.

**Rapid Reviews** – as per Cochrane, it is a form of knowledge synthesis that accelerates the process of conducting a traditional systematic review through streamlining or omitting specific methods to produce evidence for stakeholders.

**Meta-Analysis** – as per the Cochrane library, meta-analysis is when results of the individual studies are combined to produce an overall statistic. This can be done by collecting data from more than one trial and combining them to generate an average result. This aims to provide a more precise estimate of the effects of an intervention and to reduce uncertainty.

**Scooping Review**– this type of review aims to map all the existing literature concerning volume, nature, and characteristics of the primary research (Arksey and O'Malley,2005). These reviews examine the extent, range, and nature of research activity in a topic area; determine the value and potential scope and cost of undertaking a full systematic review; summarize and disseminate research findings and identify research gaps in the existing literature.

**Umbrella review** – as per Joanna Briggs Institute reviewer’s manual, this is a review of all other types of reviews. It compiles all the evidence from existing reviews on a topic to give a high-level overview.

**Living Reviews** - as per the Cochrane library, these types of reviews are either a form of rapid or systematic review which is continually updated, incorporating relevant new evidence as it becomes available and this process is monitored actively.

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