Norwegian Institute of Public Health

A systematic and living evidence map on COVID-19

Project information	
Products:	Systematic and living evidence map of evidence on COVID-19. Systematic and living evidence map of guidelines on COVID-19 Systematic reviews on COVID-19
Thematic area:	COVID-19 pandemic
Commisioner:	Norwegian Institute of Public Health
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Mandate

The COVID-19 epidemic has become a pandemic, and there is a need for easy-to-access, quality assessed, up-to-date information. We consider the Division of Infection Control and Environmental Health at the Norwegian Institute of Public Health that provides national guidance, the Directorate of Health, the directors of the hospital trusts and the regional health authorities, health care personnel and the general global public as commissioners of this research map. The WHO Collaborating Center for Infectious Disease, Research Methods and Recommendations and the Michael G. DeGroote Cochrane Canada and GRADE centers at McMaster University support WHO and other stakeholders in optimizing the use of credible research methods to derive evidence-based recommendations.

Aim

We aim to create a systematic and living evidence map providing an up–to-date overview of available scientific publications on coronavirus disease (COVID-19). We will publish updated reports and interactive maps displaying the publications sorted into broad categories with subcategories for publication types and research topics. The map will be globally available, with frequently updated reports.

Our aim is that people can use the map as a basis for study identification when making rapid systematic reviews in response to prioritized questions.

We will conduct rapid systematic reviews following standard methodology for systematic reviews. We will assess and report the risk of bias and provide a brief description of the content of the studies relevant for the particular question. We plan to summarize the main outcomes in meta-analyses where possible and relevant, and grade the certainty of evidence for the the main outcomes. We may also synthesize evidence from qualitative studies for prioritised questions.

In addition, we aim to organize electronically the individual recommendations comprising all WHO and other trustworthy guidelines, in a schematic evidence map based on PICO ontology and linked to the evidence and judgments supporting the recommendations. We aim to

collaborate with groups internationally, to provide updated evidence-based systematic reviews to support guideline development and decision making in health policy and practice.

We aim to collaborate globally to avoid duplication of work, hence when available, we will use existing systematic reviews of high quality to answer the questions of our commissioners. We will make known which questions we are conducting systematic reviews on so others can avoid duplicating our work. The global availability of our map will make it a global public good that everyone can access and use as a basis for information and for their own rapid reviews.

Introduction

Coronavirus disease 2019 (COVID-19) is an infectious disease caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). SARS-CoV-2 is a novel coronavirus in the same family as the coronaviruses causing Middle East Respiratory Syndrome (MERS-CoV) and Severe Acute Respiratory Syndrome (SARS-CoV).

First reported in Wuhan City, China, in December 2019, ostensibly of zoonotic origin (animal to human transmission), the virus spread then rapidly nationwide by human-to-human transmission mainly via respiratory droplets (Wu and McGoogan 2020). The associated increased need for healthcare overwhelmed the available capacity and resources. The first estimates from Wuhan reported that 14% of cases became severely and 5% became critically ill. The early reports of total case-fatality rate was 2.3%, with the case-fatality rate among critically ill patients as high as 49.0% (Wu and McGoogan 2020), and 62.0% in patients admitted to intensive care units (Yang et al. 2020). To date, there is no vaccine and no specific antiviral medicine to prevent or treat COVID-19. Supportive care remains for now the most common form of COVID-19 management.

On the 11th of March 2020 the World Health Organization (WHO) characterized the outbreak of COVID-19 as a pandemic. As of 2nd April there have been more than 1 000 000 COVID-19 cases, with more than 50 000 attributable deaths (https://www.worldometers.info/coronavirus/). WHO identified an immediate and increasing need for information on distinct thematic areas, with subordinate research priorities: the virus natural history, transmission, and diagnostics; treatment; clinical management; data sharing; social sciences responses; and ethical considerations (WHO2020).

New studies and reports are published daily. As publications amass with an increasing amount of institutions and organizations contributing, it is becoming more challenging to keep an overview. The WHO publishes an up-to-date list of all COVID-19 publications, filterable by few overarching topics, and by publication type. As entries are not screened for eligibility, further processing of the entries requires additional laborious efforts (https://www.who.int/emergencies/diseases/novel-coronavirus-2019/global-research-on-novel-coronavirus-2019-ncov).

Our systematic and living evidence maps on COVID-19 research will provide an overview of scientific publications categorized and parsed into more specific subgroups, providing quick access to specific topic-relevant publications. Hence it also visualizes the lack thereof, possibly guiding research to match individual- and population-level needs.

It is common that the headlines of today, or the most recent publication, gets the most attention. With publications of high quality, this may not be a problem. However, when publications on the same question already exist, a synthesis of all available studies will matter more than novelty. Hence, we aim to structure our systematic and living evidence maps so that same interventions or challenges are easily identified together.

Risk of bias assessment of new studies and reports is essential to interpret the authors' results and conclusions. This is equally relevant for reviews that combine individual studies' results in a single estimate. Quality assessment is a demanding and time consuming task, not feasible on the individual level for the clinician, public health expert, or for decision-makers confronted with numerous publications on the daily basis. Therefore, we aim to assess the risk of bias for included studies populating the maps by priority of topic. When it is possible to combine results across multiple studies, we will assess our confidence in these results.

Decision-makers struggle to make informed decision in a timely manner. In times of COVID-19 this is especially demanding with the rapidly unfolding pandemic and a continuously expanding knowledge base. Therefore, our systematic and living research maps will provide a foundation for swift evidence identification. We aim to frequently update the maps with the newest studies. Based on this infrastructure we will publish and update systematic reviews and meta-analyses on prioritised topics.

Furthermore, we are aiming to produce up-to-date, searchable and living maps of all COVID-19 recommendations that are trustworthy and link this information to the evidence and judgments in the above mentioned maps. Our work will emulate the eTB WHO guideline database that has recently been launched in its very first version (https://tuberculosis.evidenceprime.com/) and focus on allowing transparent adaptation and contextualization of recommendations.

Methods

Inclusion criteria for the evidence map

We will include all publications about COVID-19 collected from our regular systematic literature searches. :

We have no limitations on study design and comparisons. We aim to include studies published in all languages.

We aim to include both our own systematic reviews and systematic reviews published by others on COVID-19 in our systematic and living evidence maps.

Literature search for the evidence map

The literature search was peer reviewed by MJ, and dates back to 1st December 2019. We will run searches daily or every other day to include publications as they get published. The search strategy is presented in the box below, the date marked in yellow will be changed for each new search.

(("covid-19"[nm] OR "severe acute respiratory syndrome coronavirus 2"[nm] OR ((Coronavirus[mh] OR "Coronavirus Infections"[mh] OR Coronaviridae[mh:noexp] OR "Coronaviridae Infections"[mh:noexp] OR "corona virus"[tw] OR "corona viruses"[tw] OR coronavir*[tw] OR coronovirus*[tw] OR betacoronavirus*[tw]) AND (novel[tw] OR 2019[tw] OR Wuhan[tw] OR Huanan[tw] OR Hubei[tw])) OR "new coronavirus"[tw] OR "COVID-19"[tw] OR COVID19[tw] OR "SARS coronavirus 2"[tw] OR "severe acute respiratory syndrome coronavirus 2"[tw] OR nCoV[tw] OR 2019nCoV[tw] OR nCoV2019[tw] OR "SARS-CoV-2"[tw] OR "SARS-CoV2"[tw] OR SARSCoV19[tw] OR SARS-CoV19[tw] OR SARS-CoV-19[tw] OR HCoV-19[tw] OR WN-CoV[tw]) AND (2019/12/01:2030/12/31[edat]))

We will search PubMed and supplement by regular updates with material retrieved by searches performed by organizations such as WHO, CDC or others.

When our systematic and living evidence maps on COVID-19 is up and running smoothly, we will consider expanding to include information about ongoing trials and ongoing systematic reviews.

Study selection and categorisation

For the first search, and for each new update of the literature search, two researchers will independently carry out title and abstract screening and also independently assess the full texts of all potentially eligible studies. We will use EPPI-Reviewer 4 (Thomas et al. 2010) for screening for inclusion or exclusion of references, and categorization of all included reference.

We will categorise all included references in the main categories and relevant subcategories according with the framework in appendix 1 below. The main categories are types of publication, types of data, population of interest and topic(s) reported on. The categories and subcategories are presented in appendix 1.

We have drafted the framework from core research questions (prevalence, aetiology, diagnosis, effect of interventions, prognosis and experiences, opinions, norms). We are also inspired by the PRECEPT framework. We aim to provide maps that are easy to understand and navigate. We expect that we will have opportunity to improve the framework based on information and insight gained when reviewing the included publications, and with input from users of the maps, experts in the field and other stakeholders.

Some of the studies will be relevant for several categories in our mapping-system, they will then be categorised to both/several categories.

Most of the included publications will be editorials, commentaries and letters that do not contain primary empirical data. For completeness we will keep these references in the maps. We will consider to flag references without primary data if they are of special interest.

Risk of bias assessment for the evidence map and prioritized systematic reviews

We will use EPPI-reviewer 4 for the assessments of risk of bias and methodological quality. Based on advice from the WHO and Norwegian health authorities, we will prioritize the order in which studies are assessed for risk of bias and considered for synthesising, meta-analysis and grading.

Two researchers will independently assess the risk of bias using study design specific tools, starting with those that reflect the prioritised questions.

We will assess systematic reviews using the ROBIS checklist.

We will assess randomised trials for risk of bias in accordance with the Cochrane risk of bias tool (Higgins et al. 2011). We will assess the following: sequence generation, concealment of allocation, blinding of participants and personnel, blinding of outcome assessor, incomplete outcome data, selective outcome reporting and other risk of bias.

Non-randomised studies of interventions will also be assessed for risk of bias in respect to similarity of baseline characteristics, similarity of baseline outcome data, and contamination. We will rate all items as high risk of bias, unclear, or low risk of bias.

We will assess diagnostic accuracy test studies using the Quality Assessment of Diagnostic Accuracy Studies-2 (QUADAS-2) tool (Whiting et al. 2011).

We will assess prognostic and prevalence studies using the QUIPS tool (Hayden 2013).

We will assess animal studies for risk of bias using OHAT (OHAT/NTP 2015).

We will assess qualitative studies using the adapted Critical Appraisal Skills Program tool for qualitative studies (CASP 2018).

We will assess guideline recommendations using the AGREE or NEATS tools (AGREE 2010).

We will assess in vitro studies and modelling studies using appropriate tools

Data extraction and analysis for systematic reviews

One researcher will extract information from the included studies that are prioritised; another researcher will independently check the data extraction for accuracy and relevance. We will extract data on the following: full reference, location (country) and date of study.

For studies reporting on the effects of interventions, we will extract patient data: on clinical history (if available), age, sex and co-morbidities, geography, ethnicity, and information about the intervention, the comparison where relevant, and the reported outcomes. We will look to the suggested core outcome sets for clinical trial on COVID-19 (Jin 2020) when extracting information on outcomes.

We will consider meta-analysis for the main outcomes as specified by the question asked and the included studies. Meta-analyses are relevant when populations, interventions, comparisons, and outcomes are sufficiently similar. Dichotomous outcomes will be presented as risk ratios (RRs) or odds ratios (ORs) with 95% confidence intervals (CIs). Continuous outcomes will be presented as mean difference between the groups with 95% CIs. Where different scales are used to measure the same outcome, we will calculate standardized mean difference with a 95% CI. We plan to use either EPPI Reviewer 4, Review Manager (The Cochrane Collaboration 2014), or R software (https://www.R-project.org) to generate forest plots and conduct meta-analysis. Attrition will be handled using intention-to-treat analysis. We will use random effects models and evaluate statistical heterogeneity using the Q test and I^2 value.

Considerations for subgroup analysis: Potential subgroups may be on the population-level, such as morbidity groups, genders, or age groups, or on the intervention-level, according to the categories defined in the maps, such as different diagnostic strategies or types of intensive care treatments.

We will also consider collecting data and conduct systematic reviews for other prioritised topics, such as questions on aetiological and prognostic factors, diagnostic tests or strategies and prognosis, and questions that can be answered by overviews of qualitative studies.

Our aim is to conduct a series of overviews that might help inform guideline development and policymaking.

Judgements about the certainty of the evidence using the GRADE approach

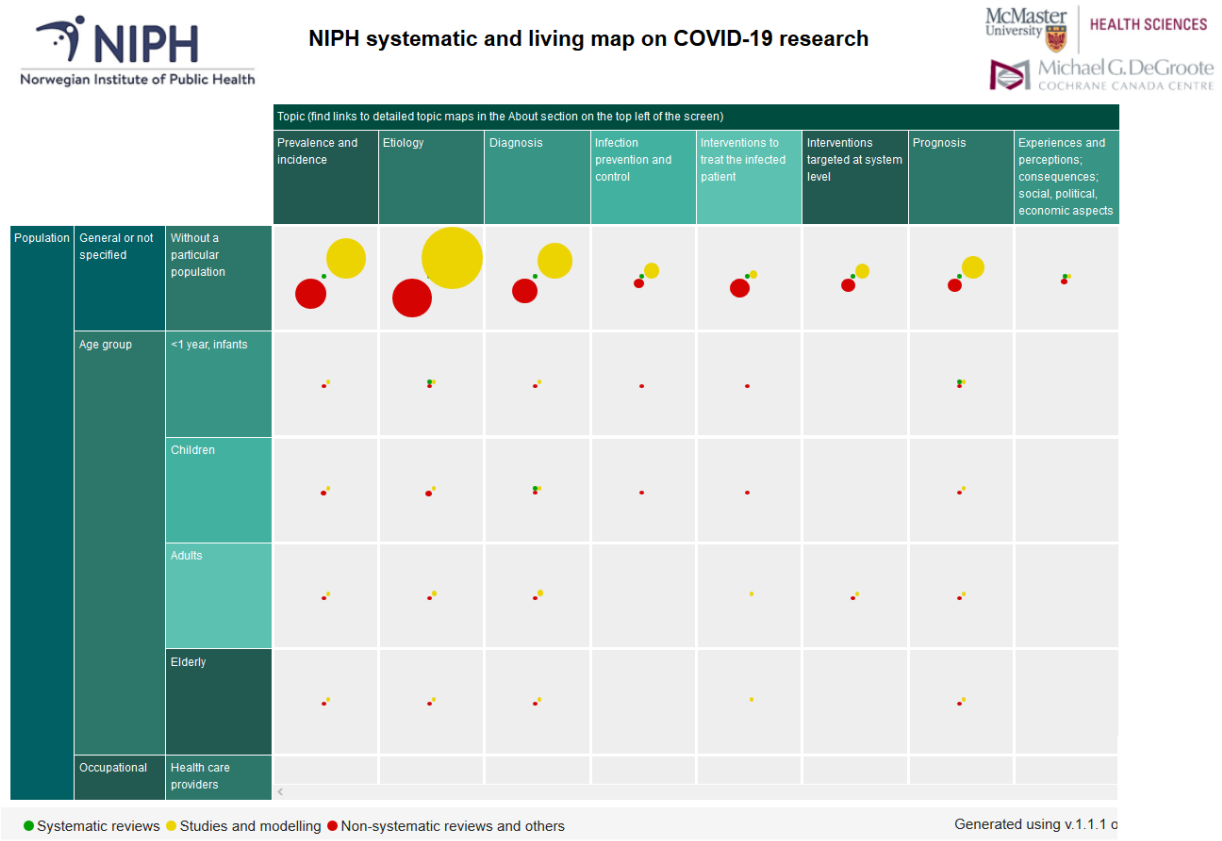
We will synthesize data in both tabular and narrative formats. We will conduct meta-analyses depending on the nature of the collected data. A single reviewer will grade the certainty of the evidence using the GRADE approach and a second reviewer will verify all assessments. If applicable, we will follow published guidance for rating the certainty of the evidence in the absence of a single estimate of effect (Thayer and Schunemann 2016, Murad, Mustafa et al. 2017).We will use the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach (Guyatt et al. 2011).

We will include GRADE Summary of Findings table in the COVID-19 maps. Evidence may also be presented using interactive Summary of Findings (iSoF) or GRADE Evidence Profiles developed in the GRADEpro (www.gradepro.org) software (Guyatt, Oxman et al. 2011, Guyatt, Thorlund et al. 2013) that can be linked to the recommendation maps (see below). These tables are visual tools to quickly and clearly communicate both the effect estimates of the important outcomes and our certainty in these effect estimates. Consistent with the updating of meta-analysis when new studies are added, we will also update the grading of our confidence in the certainty of the evidence.

We will use the GRADE-CERQual approach to assess our confidence in the findings from systematic reviews of qualitative studies. (Lewin et al. 2018).

Systematic and living web-based interactive evidence maps

Based on functionality in EPPI-reviewer 4 we will make included publications easy to identify and access through visual and interactive web-based maps (see figure below). Users can identify the relevant publications that fit the topics and population of interest. We will produce a main map which will give an overview, and we will provide more detailed maps based on more detailed classifications. The users can further sort the publications according to study design through filter functions.



We aim to develop evidence maps that make the distribution of publications on COVID-19 research visible and easy to navigate.

We will display publications according to topics and population of interest in a matrix system. The coloured bubbles in each cell show how many publications there are in each of three main categories of study types (systematic reviews, primary and modelling studies, and non-systematic reviews/ others). By clicking anywhere in a cell, users will access a list of all studies addressing that particular topic and population. By clicking a bubble within that cell, users will find studies of a particular publication type. The "Filter" function makes it possible to sort by more detailed classification of publication types. The list of studies includes for each publication the abstract (if available), URL, DOI, author(s) and source (journal).

We will produce eight maps which will give users access to more detailed information regarding these topics:

- Prevalence and incidence
- Aetiology
- Diagnosis
- Infection prevention and control
- Interventions to treat the infected patient
- Interventions targeted at system level
- Prognosis
- Experiences and perceptions, social, political, economic aspects

We will provide user guides for each map in the About-section in the top left corner of the screen. We ask users and stakeholders to provide feed-back and suggestions for improvements of the maps, so that the maps are as user-friendly and useful as possible.

Review and evaluation of systematic reviews and guideline recommendations

We will conduct ongoing systematic reviews using international standard methodology for reviews and existing guidelines and recommendations regarding COVID19.

Data Sources and Searches for guidelines

We will search the WHO database for guidelines, Medline, EMBASE, CMA Infobase, NHS Evidence Search, TRIP database, the GIN library and the grey literature from 2019 with the assistance of an information scientist. We will combine free text words and medical subject headings (Mesh) indexed terms when applicable, such as "COVID19", "guideline", "recommendation", and "systematic review". The search strategy will be finalized with an information specialist. We will use no language restrictions or time limits.

We will include guidelines and recommendations if they achieve an AGREE II domain score of at least 60% on:
Domain 1: Scope and purpose
Domain 3: Rigour of development
Domain 6: Editorial Independence

Summary of considerations of available evidence for each prioritized question

A summary introduction about the intervention/challenge regarding covid-19 (a few sentences). Then we say how many studies, of what design and how many patients/size of population that are involved, and also how many other publications are available on that particular issue. This introduction should include sentences using our standard formulations from GRADE.

If a systematic review of good quality (quality assessment and description of the review will also be made available) already exists, or several studies are available, then next should be a GRADE-Summary of findings table.

Where no systematic review of good quality is available, but two or more studies on the same main outcome, the forest plot(s) or tabulated descriptions are presented.

They are followed by a description of each of the included studies with risk of bias assessments.

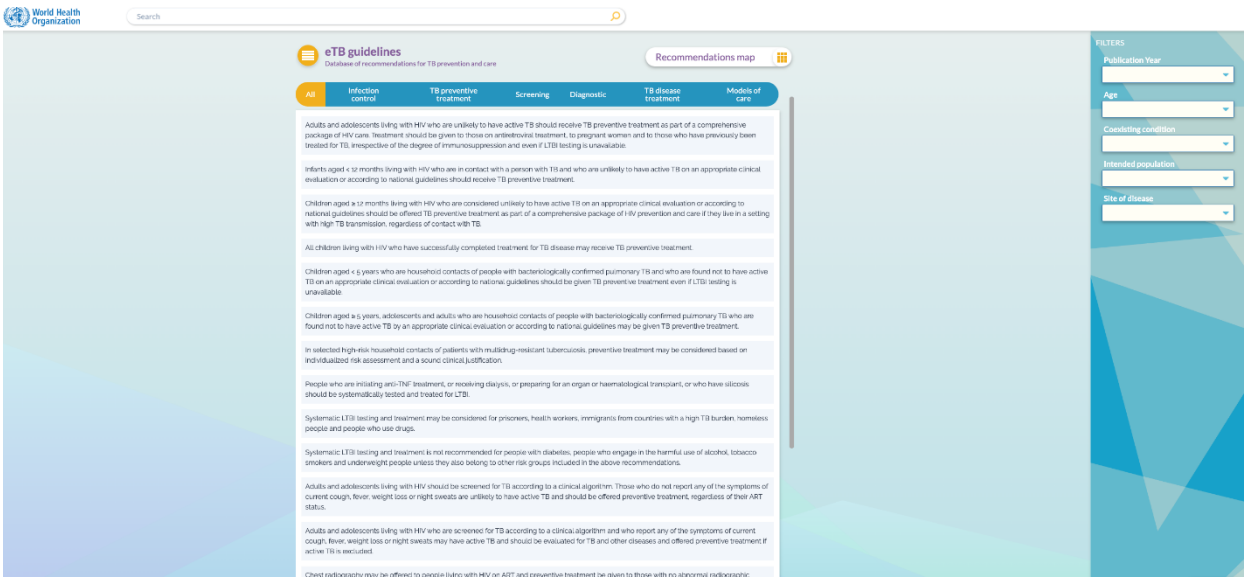
Where relevant, we will also consider including systematic reviews about the same symptoms (e.g. ARDS)/ intervention/ challenge from/about other virus or epidemics. Obviously with a discussion about the indirectness/transferability between them.

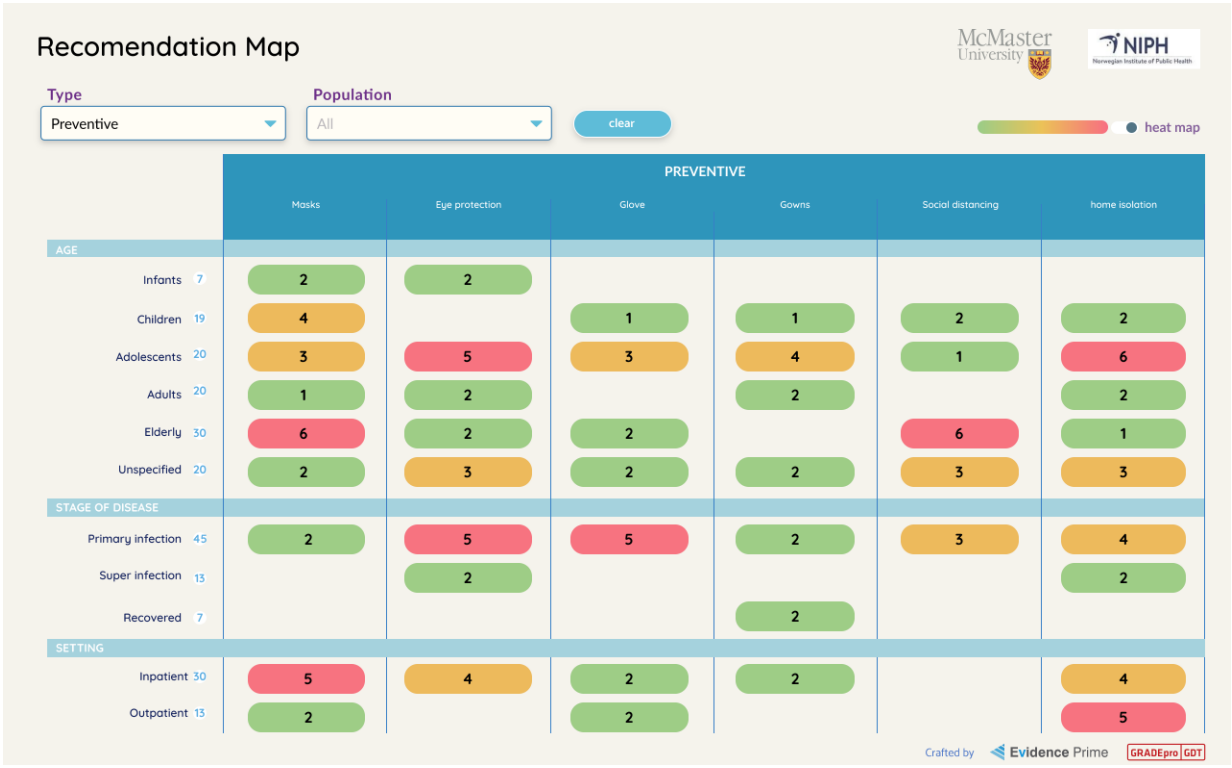
Presentation of the available recommendations

Our goal is to provide electronic access to centralized, live, organized WHO COVID19 and other recommendations and enable two-way iterative interaction between the database and other stakeholders. This will allow, for example, member states or those who adapt or adopt guidelines to access and contribute information of contextualized use of the guideline and help identify priorities for new or updated recommendations. It will also allow us to:

- monitor contributions of member-states
- Ease contextualization of WHO and others' COVID19 guidelines by member states, through the use of GRADE Adolopment and EtD frameworks (please see Appendices 2 and 3)

Example of a recommendation map (https://tuberculosis.evidenceprime.com/ for the WHO database and https://adobe.ly/3azZLEN)





Ultimately, these features will concentrate the dispersed recommendations available across all WHO publications in a single visually attractive and interactive browser-based platform to facilitate use and understanding (this is based on work the McMaster team supported for the WHO EML and GTB platforms). Alternative descriptions of the availability of recommendations for different settings can be built based on the experience our collaborating IT team has with the WHO Essential Medicines list.

These maps will be supported by conceptual frameworks that resemble patient, diagnostic and/or treatment pathways that we are currently developing for WHO. They will be able to show:

- Redundancies in recommendations (as visualized by overlap in PICO components)
- Currency of the recommendation (i.e. when was the recommendation formulated? Is the recommendation or evidence informing it out of date?)
- Repetition or redundancy in evidence (systematic reviews and trials) informing multiple recommendations and patient-important outcomes in the maps
- Gaps in evidence informing recommendations
- Clusters of evidence strengthening recommendation areas
- Connection to the WHO essential medicine lists (to be added)

Adolopment

We are aiming to ease the contextualization and adaptation process of recommendations in a rapid learning health system by encouraging widespread use of adoption and adaptation of recommendations by other stakeholders using the GRADE Evidence to Decision Frameworks (Schünemann 2017).

Guideline recommendations do not serve as dictates, but rather provide a high-level support in the evidence-based decision-making process of providers, patients, policy makers, health systems, and stakeholders. To provide uniform, up-to-date recommendations derived from standardized, transparent methods, while facilitating the necessary contextualization through a process of adolopment to meet the unique needs of the locality, is imperative. The best recommendations flounder in the absence of appropriate contextualization by implementers. This information in turn, provides fruitful learning for the continued refinement of recommendations. This cyclical process can be understood by rapid learning health systems (see figure below below, www.canada.cochrane.org).

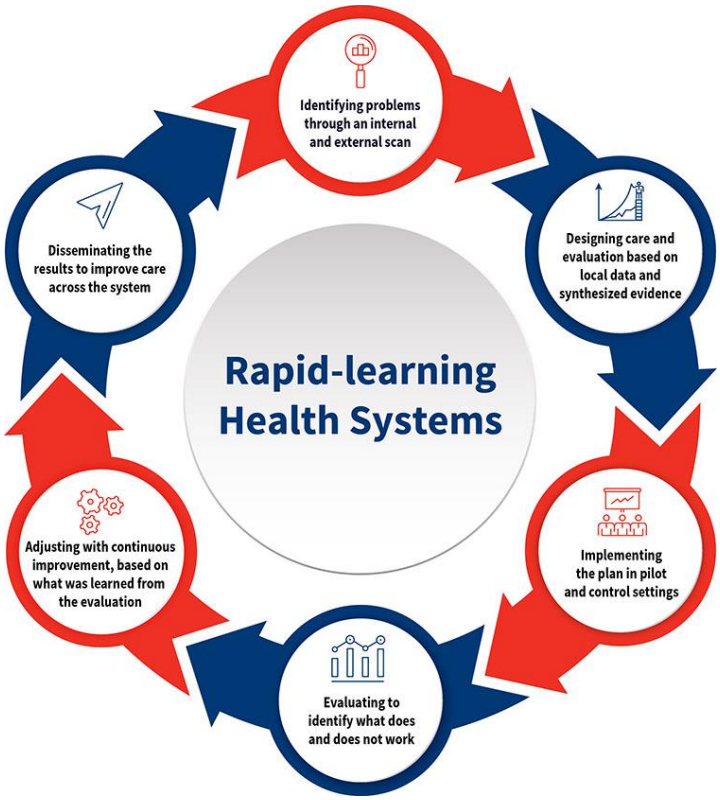
To understand which information is required to implement recommendations by member states and using that information to provide optimal, up-to-date recommendations we suggest making better use of the GRADE Adolopment and EtD frameworks. Using the GRADEpro Adolopment module, member states would be able to access recommendations and provide information on the contextualization of the recommendations to their locality. Member states could organize themselves internally to coordinate the 'live' updates on recommendations (as was seen with adaptations of the Model Essential Medicines List), or appoint a country coordinator in each member state (as was the case with the European Commission Initiative on Breast Cancer). The WHO may also choose to select liaisons analogous to the country level contacts or their equivalents in the ministries of health of member states. Monitoring of feedback can take place in many ways, including at the WHO department or other level.

A concern may arise around the adolopment/implementation of conditional recommendations. A defining feature of GRADE is the separation of judgments on the confidence in the certainty of the evidence from the deemed strength of recommendations; i.e. high confidence in measures of effect do not imply strong recommendations, and strong recommendations can come from low confidence in effect measures. The EtD framework facilitates this judgement

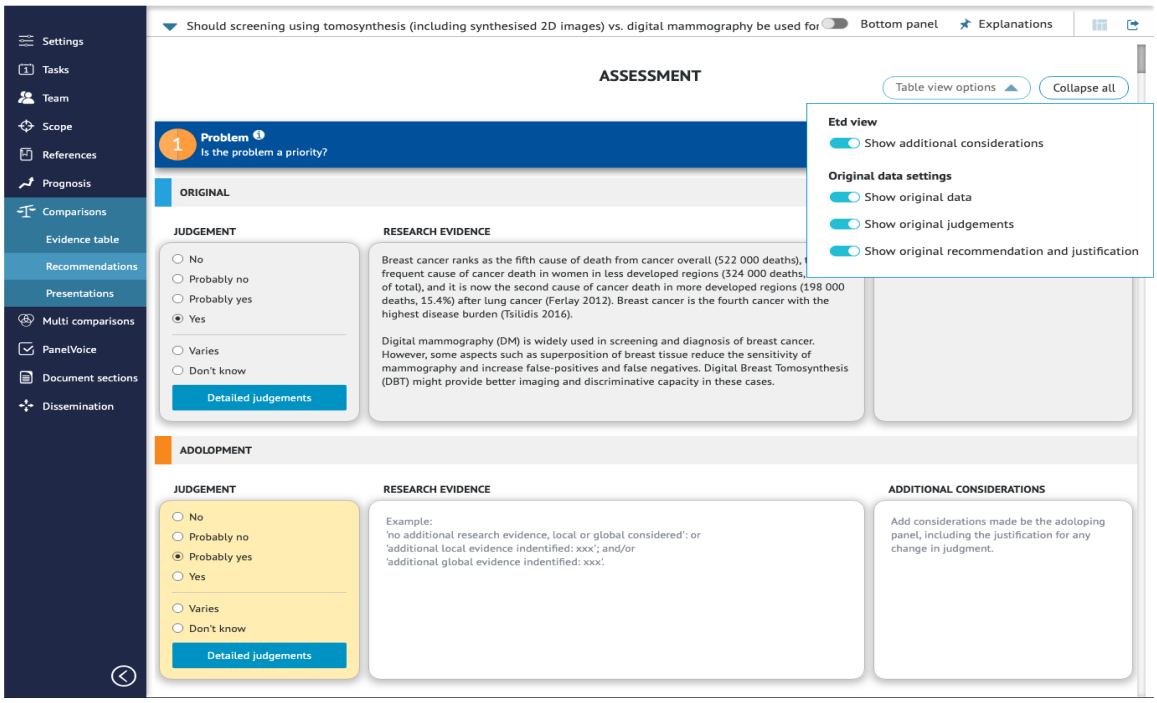
and provides a transparent record of the guideline panel's process of moving from the evidence to a decision. It is important to note that both strong and conditional recommendations require appropriate adolopment. When conditional recommendations are offered, they may depend on local resistance patterns, feasibility or cost. Member countries can utilize the adolopment module to make decisions about whether or not to implement a conditional recommendation and that information can be provided to WHO and other organizations centrally for its COVID19 recommendations updating. This can be done using an approach engrained in rapid learning health systems and leads to living recommendations informed by optimal system information.

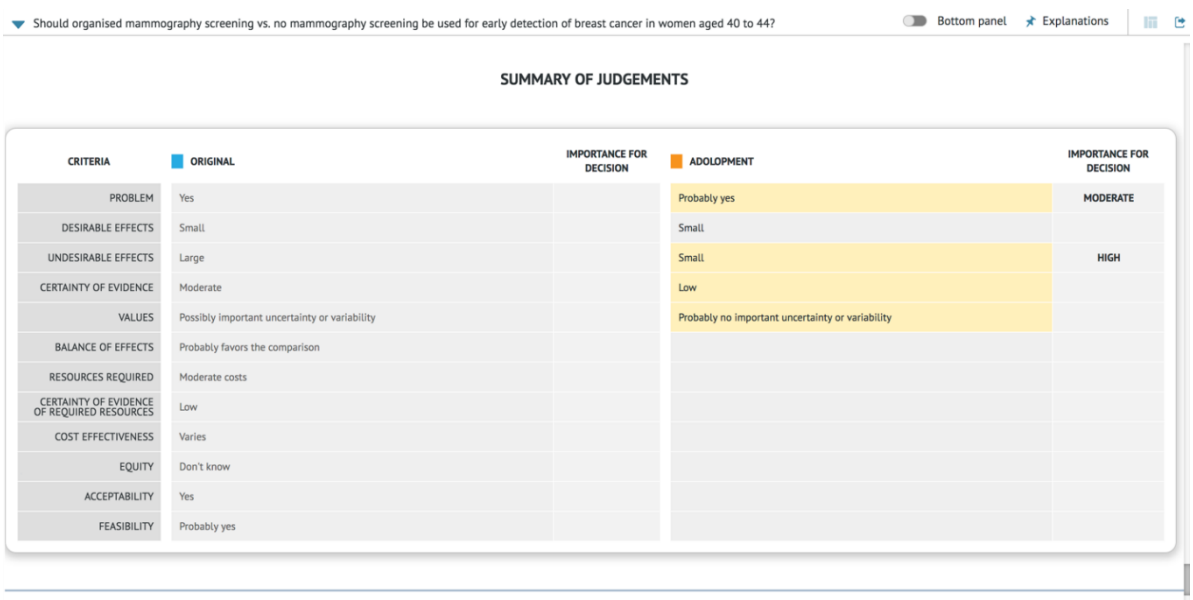
It includes:

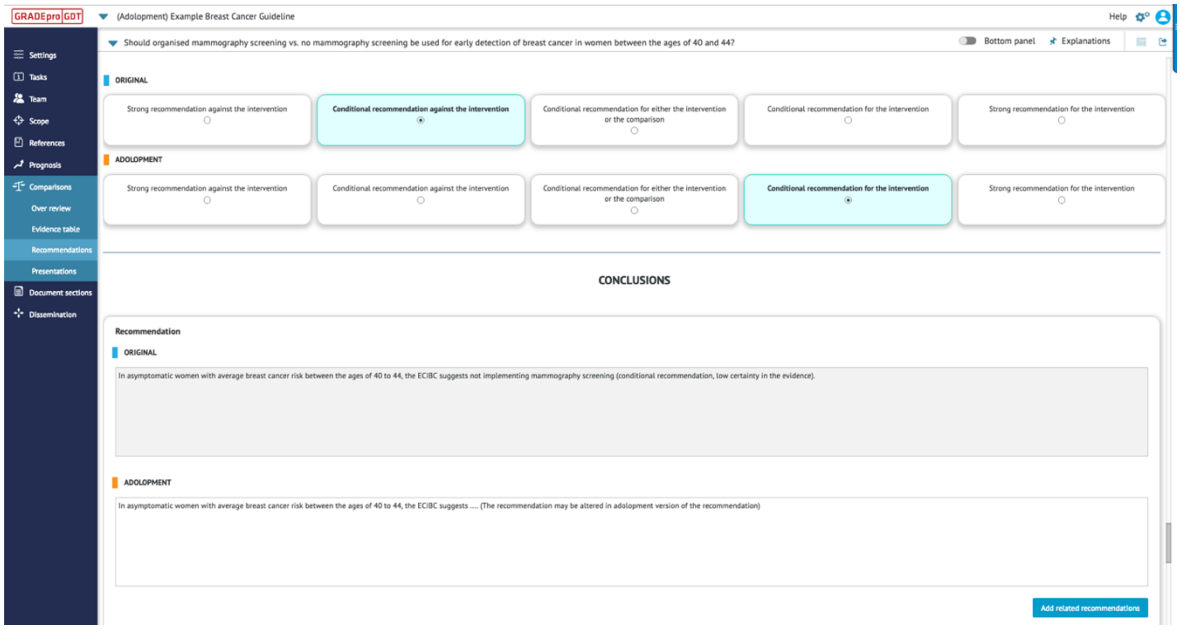
- Engaged patients and other stakeholders
- Digital capture, linkage and timely sharing of relevant data
- Timely production of research evidence
- Appropriate decision supports
- Aligned governance, financial and delivery arrangements
- Culture of rapid learning and improvement: Systems are stewarded at all levels by leaders committed to a culture of teamwork, collaboration and adaptability
- Competencies for rapid learning and improvement



The GRADEpro Adolopment Module for member states, and the potential layout for to visualize country activity (Example from European Commission Breast Guidelines).


Settings
Tasks
Team
Scope
References
Prognosis
Comparisons
Evidence table
Recommendations
Presentations
Multi comparisons
PanelVoice
Document sections
Dissemination
Should screening using tomosynthesis (including synthesised 2D images) vs. digital mammography be used for
Bottom panel
Explanations
ASSESSMENT
Table view options
Collapse all
Etd view
Show additional considerations
Original data settings
Show original data
Show original judgements
Show original recommendation and justification
1
Problem
Is the problem a priority?
ORIGINAL
JUDGEMENT
No
Probably no
Probably yes
Yes
Varies
Don't know
Detailed judgements
RESEARCH EVIDENCE
Breast cancer ranks as the fifth cause of death from cancer overall (522 000 deaths),
frequent cause of cancer death in women in less developed regions (324 000 deaths,
of total), and it is now the second cause of cancer death in more developed regions (198 000
deaths, 15.4%) after lung cancer (Ferlay 2012). Breast cancer is the fourth cancer with the
highest disease burden (Tsilidis 2016).
Digital mammography (DM) is widely used in screening and diagnosis of breast cancer.
However, some aspects such as superposition of breast tissue reduce the sensitivity of
mammography and increase false-positives and false negatives. Digital Breast Tomosynthesis
(DBT) might provide better imaging and discriminative capacity in these cases.
ADOLOPMENT
JUDGEMENT
No
Probably no
Probably yes
Yes
Varies
Don't know
Detailed judgements
RESEARCH EVIDENCE
Example:
'no additional research evidence, local or global considered': or
'additional local evidence indentified: xxx'; and/or
'additional global evidence indentified: xxx'.
ADDITIONAL CONSIDERATIONS
Add considerations made be the adoloping
panel, including the justification for any
change in judgment.


Should organised mammography screening vs. no mammography screening be used for early detection of breast cancer in women aged 40 to 44?
Bottom panel
Explanations
SUMMARY OF JUDGEMENTS
CRITERIA
ORIGINAL
IMPORTANCE FOR DECISION
ADOLOPMENT
IMPORTANCE FOR DECISION
PROBLEM
Yes
Probably yes
MODERATE
DESIRABLE EFFECTS
Small
Small
UNDESIRABLE EFFECTS
Large
Small
HIGH
CERTAINTY OF EVIDENCE
Moderate
Low
VALUES
Possibly important uncertainty or variability
Probably no important uncertainty or variability
BALANCE OF EFFECTS
Probably favors the comparison
RESOURCES REQUIRED
Moderate costs
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES
Low
COST EFFECTIVENESS
Varies
EQUITY
Don't know
ACCEPTABILITY
Yes
FEASIBILITY
Probably yes


TYPE OF RECOMMENDATION
GRADEpro GDT
(Adolopment) Example Breast Cancer Guideline
Help
Should organised mammography screening vs. no mammography screening be used for early detection of breast cancer in women between the ages of 40 and 44?
Bottom panel
Explanations
ORIGINAL
Strong recommendation against the intervention
Conditional recommendation against the intervention
Conditional recommendation for either the intervention or the comparison
Conditional recommendation for the intervention
Strong recommendation for the intervention
ADOLOPMENT
Strong recommendation against the intervention
Conditional recommendation against the intervention
Conditional recommendation for either the intervention or the comparison
Conditional recommendation for the intervention
Strong recommendation for the intervention
CONCLUSIONS
Recommendation
ORIGINAL
In asymptomatic women with average breast cancer risk between the ages of 40 to 44, the ECIBC suggests not implementing mammography screening (conditional recommendation, low certainty in the evidence).
ADOLOPMENT
In asymptomatic women with average breast cancer risk between the ages of 40 to 44, the ECIBC suggests .... (The recommendation may be altered in adolopment version of the recommendation)
Add related recommendations

WHO Model List of Essential Medicines

The WHO Expert Committee on the Selection and Use of Essential Medicines meets every two years to update the Model List of Essential Medicines. The list is used by countries to help develop their own local lists of essential medicine and pave the way to universal health access. As of 2020, more than 135 countries regulalry update their own national lists of essential medicines based on the World Health Organization's model list. This includes countries in both the developed and developing world. The Model List is disseminated to end users through the electronic Essential Medicines List (eEML) of WHO is a comprehensive, freely accessible, online database containing information on essential medicines. The eEML combines detailed medicine information (e.g. pharmaceutical) data with comprehensive evaluation of benefits, arms and costs (e.g. effectiveness, safety, implications for health care systems) information (https://list.essentialmeds.org/). Most importantly the eEML provides the data related to the status of a medicine as an essential medicine. Our collaborating programmers (A. Nowak and colleagues) have created the electronic platform for the WHO essential medicines list through a contract with WHO: https://list.essentialmeds.org/ our plan is to collaborate with the corresponding WHO department which is our sponsor for the WHO collaborating center to integrate a link with the EML.

An emergency session of the Expert Committee was convened in 2010 during the H1N1 pandemic dedicated to the assessment of antivirals (oseltamivir, zanamivir, amantadine and rimantadine). The WHO EML Secretariat is monitoring RCTs and R&D for medicines against COVID-19 or COVID-19 symptoms to identify potential candidates for inclusion on the Model List. The EML Secretariat is ready to convene an emergency meeting of the Expert Committee in the event that highly effective treatments for COVID-19 should be recommended to countries. A rapid turnover of recommendations, following release of trial data, can help media to refocus their communication and countries to prioritize policies that will give access to these treatments. This will be particularly important if other highly-priced medicines being trialled for COVID-19 (eg, tocilizumab and IL-6 or IL-1 inhibitors) demonstrate benefit. Essential medicines status will provide a strong argument in opening up intellectual property of these treatments, favouring large production and distribution.

Our plan is to collaborate with the EML Secretariat, which is the sponsor for the McMaster WHO collaborating center, with two main objectives:

- providing high quality evidence to inform the decision of the WHO Expert Committee if candidate medicines that might be potentially suitable for inclusion in EML are identified
- integrate key information on essential medicines against Covid-19 with the EML. This will ensure that this information will be rapidly disseminating to countries through WHO Regional and Country Offices and to potential end users. Information on essential medicines is included by Wikipedia within all Wikipedia dedicated medicine entries

The programmers are also developing the electronic Essential Diagnostics List (eEDL) which provides another opportunity.

Starting date (for FHI.no):
March 2020

End date: end of the pandemic, including time for evaluation of the pandemic.

Publication and communication
This COVID-19 systematic and living evidence map will be publicly available, with a weekly updated version.

Weekly newsletters will be circulated.

We will make all the rapid systematic reviews that we conduct available, either by publishing on https://www.fhi.no/ or submitting to an international journal. We will also consider writing articles about the map.

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Conflicts of interest:

GEV, HS, SF are members of the GRADE working group and have actively participated in developing the GRADE approach for assessing certainty of evidence.
The GRADEpro app code is co-owned by Evidence Prime that programs it and McMaster University to ensure that the core code of the app remains available in case that Evidence Prime would not continue programming it. The Adolopment app and Panel Voice app for remote collaboration on guidelines is a product of Evidence Prime that will be made available for free to support COVID-19 work described here. The eEML belongs to WHO.
SV is a member of the MAGIC Evidence Ecosystem Foundation.

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Appendix 1: Categories used to map included references

Publication type
Link to map
Systematic review
Non-systematic review **Guidelines/guidance** **Comment/editorial/correspondence/news** **Errata/corrections/comments to specific papers** **Method papers** **Covid-19 epidemiological reports** **Audio or video files** **For discussion** **Other**
Randomised trials **Non-randomised studies with controls** **Non-randomised studies without controls, including observational studies** **Case series/studies n < 11** **Pre-clinical, animal** **Pre-clinical, in vitro** **Modelling** **Qualitative studies** **Protocols**
Data type
Primary data
Secondary data (only for reviews and guidelines)
Modelled/computed
No primary data
Population
Publications without a specified pop.
Age Infants < 1 year Children Adults Elderly
Sex / gender Female Male Other
Health care providers **Other**
Housing pre-existing/setting Homeless

Nursing homes
Refugee camps
Prisons
Other
Health status, pre-existing
Smokers
Pregnant women
Comorbidities unspecified
Cancer
Hypertension
Diabetes
Immunocompromised
Kidney disease
Liver disease
Respiratory disease
Cardiovascular disease
Hospitalised
Intensive care unit
Obesity
Other
Social and economic
Socioeconomic
Low- and middle-income countries
Ethnicity
In quarantine or isolation
COVID-19 status
COVID-19 asymptomatic carriers
COVID-19 minor symptoms
COVID-19 with pneumonia
COVID-19 hospitalised
COVID-19 deaths
COVID-19 intensive care
COVID-19 recovered
Other
Prevalence and incidence (Epidemiology)
Prevalence and incidence
Aetiology
Characteristics of SARS CoV-2
Origin/history of the SARS-CoV-2 epidemic
Sequence analysis, genetics of SARS-CoV-2 (subtypes, serotypes)
Pathogenicity & Virulence
Reservoir
Other/to discuss

Modes of transmission
- Animal to person
- Person-to-person spread of SARS-CoV-2, including R0 (reproductive number/rate)
- Aerosols
- Blood
- Stool
- Via surfaces
- Other/to discuss

Action in humans/ pathophysiology (how SARS-CoV-2 affects humans)
- Incubation period
- Pathophysiology
- Immune response to SARS-CoV-2
- Other

Aetiological factors (non-viral, environemental factos, system, non-individual)

Other

Diagnosis

SARS-CoV-2 PCR detection tests (all phases of diagnostic studies)
- All PCR, RT-PCR
- Other/to discuss

SARS-CoV-2 serologic test
- Diagnostic serological testing
- Protective immunity
- Population-based seroepidemiology

Clinical diagnosis
- Clinical history, symptoms and signs
- Radiological diagnostics (e.g. Chest CT and X-ray)
- Blood tests

Other diagnostic
- Diagnostic triage strategies
- Point of care testing
- Self-testing

Other/to discuss

Treatments

Antiviral agents
- Remdesivir
- Lopinavir
- Ritonavir
- Lopinavir/ritonavir (PLV/r)
- Oseltamivir
- Ganciclovir
- Ribavirin
- Arbidol (Umifenovir)
- Not specified
- Other/to discuss
- Antiviral trx. comb. with other treatment

Other drugs

Corticosteroids Chloroquine Hydroxychloroquine Macrolides Cyclooxygenase-2 inhibitors Sirolimus Traditional medicine Statins Vitamin C Anti-influenza immune plasma Cepharanthine Selamectine Mefloquine ARBs, angiotensin receptor blockers Teicoplanin Troponin I Other/to discuss
Specific intensive/critical care treatments Treatments for acute respiratory distress syndrome (ARDS) Treatments of sepsis Non-invasive ventilation Invasive ventilation Suction Supportive care Other/to discuss
Other treatments Non-pharmacological treatments
Other/to discuss
Infection Prevention and control
Infection prevention and control policies Restriction of domestic movements Quarantine Isolation Restrictions on schools and kinder gardens Work from home Restrictions on businesses Restrictions on events and gatherings Restrictions on int. travel
Physical barriers Use of masks Gloves Other
Behavioral/hygiene Hand washing Anti-bac (hand disinfection) Other
Vaccines

Other IPC
Executive/legislative forms of IPC
Other
Interventions targeted at system level to improve management of the pandemic
Behaviour modification strategies
Case identification
Clinical practice strategies
Contact tracing
Communication and media strategies
Disease control measures delivered by health and public authorities
Disinfection of public spaces, shops, offices
Geographic information systems (GIS) and other IT technologies
Measures taken at health care level
Plans to increase capacity of intensive care
Screening
Surveillance/monitoring
Stocks and supplies
Staff planning
Testing
Triage
Other/to discuss
Prognosis
General prognosis
Prognostic criteria: clinical
Prognostic criteria: lab
Lethality / case fatality rate /infection fatality rate
Complication or disability rate
Other
Experiences and perceptions, social, political, economic aspects
Experiences, understanding, awareness, knowledge, perceptions
Feasibility
Acceptability
Equity
Barriers and facilitators
Advice communication (including the hard to reach)
Population priorities and values
Social media
Other media
Political aspects
Economic aspects
Societal aspects
Ethical issues
Other/to discuss
Collateral consequences

Other, kept for completeness
Kept for completeness