Health Information and Quality Authority

An tÚdarás Um Fhaisnéis agus Cáilíocht Sláinte

Protocol for evidence synthesis support - COVID-19

22 April 2020

Version	1.5

Revision Record	
Revision Date	**Description of change**
22.03.2020	Addition of Appendix 6 Glossary of terms. Clarifications, regarding language restriction and non-peer reviewed articles. Amendments to account for update reviews in Appendix 3, and Section 2.4 Minor clarifications to PCOs for RQ1- RQ5
30.03.2020	Change to reflect that while searches are updated daily, reports are updated only as required. Details on the appraisal of RCTs and modelling studies added to section 2.3. Addition of Review Question 6. Addition of QA questions for modelling studies Additional terms added to Appendix 6
08.04.2020	Change in 'Purpose and Aim' to reflect the development of evidence summaries for IPC. Addition of Review Question 7. Addition of Review Question 8. Changes to Appendix 5 to reflect the development of evidence summaries for IPC and dates applicable to the summary of relevant guidance.
14.04.2020	Update of search strategy section to reflect targeted searches including face mask search. Face mask search strategy added as Appendix 1. Numbering of all appendices updated.
20.04.2020	Addition of Review Questions 9-11, and associated search strategies

Purpose and Aim

The purpose of this protocol is to outline the process by which the health technology assessment (HTA) team, will identify and review relevant evidence to support the Clinical Expert Advisory Group (EAG) in supporting the National Public Health Emergency Team (NPHET), and those responsible for developing national infection prevention control guidance, in their response to COVID-19. The HTA team will develop evidence summaries based on specific research questions (RQs).

1. Process outline

It is important that a standardised approach to the process is developed and documented, to allow for transparency and to mitigate risks which may arise due to changes in staff delivering and/or receiving the information.

Four distinct steps in the process have been identified that will be completed. These are listed below and described in more detail in sections 2.1-2.4.

1. Search relevant databases.
2. Screening of identified studies to match relevant clinical questions.
3. Data extraction and appraisal of included studies.
4. Summarise findings and send to relevant contacts.

2.1 Search of relevant databases

The initial search to identify research on COVID-19, will be conducted on databases from 30 December 2019 to date of commencement of search. The search timeline may be extended if deemed appropriate by the HTA team to address specific RQs that arise. Following this, new searches will be conducted daily to identify newly published articles. The databases will be searched, using the keywords outlined in

Table 1. The search is designed to be narrow in terms of retrieving information relevant to COVID-19 specifically, as opposed to coronavirus more generally. Additionally, targeted searches may be designed and conducted if deemed appropriate by the HTA team to address specific RQs that arise (see Appendix 1). Pre-print servers have been included to capture rapidly emerging evidence that has not yet been published in peer review journals. Support for the conduct of literature searches is being provided by the librarian team from the Royal College of Surgeons in Ireland (RCSI).

Table 1 Search strategy

Database (only those that all HTA have access to in case of team illness)	**Search strategy**
Pubmed	"coronavirus"[MeSH Terms] OR "coronavirus"[All Fields] OR "COVID-19" Filter: humans Filter: 30 December 2019
Embase.com	('coronavirinae'/exp OR 'coronavirinae' OR 'coronaviridae infection'/exp OR 'coronaviridae infection' OR 'coronavirus disease 2019'/exp OR 'coronavirus'/exp OR coronavirus OR 'coronavirus infection'/de) NOT [medline]/lim AND 'human'/de Filter: 30 December 2019
Science direct	"COVID-19" OR "2019 novel coronavirus infection" OR "2019-nCoV"
Cochrane	"coronavirus" OR "COVID-19"
Infectious diseases society of America search of infectious disease journals	coronavirus OR corona virus OR covid-19 https://academic.oup.com/idsa/search-results?allJournals=1&fl_SiteID=5567&page=1&qb=%7b%22ArticleTitle1%22%3a%22coronavirus+OR+corona+virus+OR+covid-19%22%7d&sort=Date+%E2%80%93+Newest+First
NHS Evidence	"COVID-19" OR "2019 novel coronavirus infection" OR "2019-nCoV" Filter: 30 December 2019
Preprint servers (i.e. preliminary reports of work that have not been peer-reviewed)	
medRxiv and bioRxiv	Pre populated search: https://connect.medrxiv.org/relate/content/181
HRB Open	"coronavirus" OR "COVID-19"

2.2 Screening of identified studies to match relevant clinical questions

Each RQ was formulated in line with the most appropriate research question framework to address that question. For example, PICOS (population, intervention, control, outcome, study design) or POS (population, outcome, study design) framework detailed in Appendix 2. The specific RQs are as follows:

RQ1: What is the evidence for asymptomatic transmission of COVID-19?

RQ2: What is the viral load over the course of the infection (including any asymptomatic or pre-symptomatic phase), and the duration of infectivity?

RQ3: What evidence is available to indicate that children spread COVID-19?

RQ4: What is the natural history of COVID-19 infection in children?

RQ5: What is the average length of stay in ICU for affected persons?

RQ6: For individuals who have COVID-19, what clinical samples and collection sites are suitable for SARS-CoV-2 testing?

RQ7: What evidence is available to indicate that routine wearing of face masks by healthy persons in the community reduces the transmission of respiratory pathogens spread via droplet transmission?

RQ8: What is the evidence that universal use of face masks by healthcare workers outside of the clinical space is of value in reducing the transmission of respiratory viruses in health care settings?

RQ9: What is the rate of reinfection/duration of immunity in individuals who recover from a laboratory-confirmed coronavirus infection?
Assessed as five sub questions:

- What is the reinfection rate following recovery from SARS-CoV-2 or other coronavirus infections?
- How quickly does one develop specific antibodies (seroconversion timing) to SARS-CoV-2 or other coronaviruses?
- What proportion of confirmed cases develop these antibodies (seroconversion rate)?
- What is the duration of immunity following seroconversion (duration of detection of serum antibodies and antibody titres over time)?

- Does the seroconversion rate and or timing, and duration of immunity, depend on the severity of the initial infection?

RQ10: Are individuals reinfected with SARS-CoV-2 or other human coronaviruses infectious?

RQ11: Is there evidence for placental transfer of antibodies, from infected mothers, that confers immunity in the newborn?

All potentially eligible papers identified daily in the search strategy will be exported to Endnote and screened against the PICOS or POS, as outlined in the standard associated operating procedure. No language restrictions will be applied, non-English studies will be translated via google translate, and this will be noted as a potential caveat.

2.3 Data extraction and appraisal of included studies

For each study included, data on the study design, participant demographics and clinically relevant data will be extracted as required per each research question. If the paper has not been peer reviewed, this will be noted. For randomised controlled trials (RCTs) the Cochrane risk of bias tool (version 1) will be used as this can be completed more rapidly than the more in depth version 2. ROBINS-I tool (Risk of bias in non-randomized studies - of interventions) will be used for quality appraisal of non-randomised studies, and for systematic reviews AMSTAR-2 will be used. However, the majority of studies are likely to be from case reports and case series, which have been conducted rapidly. No universally accepted quality appraisal tool exists for assessing the methodological quality of studies based on case series. Therefore, these studies will be assessed using criteria outlined in Appendix 3. Appendix 4 outlines the series of questions that will be used to assess the quality of included modelling studies.

2.4 Summarise findings and send to relevant contact

A descriptive overview of the identified evidence to date for each research question will be compiled and sent to the relevant parties in word format. A PRISMA flow chart will not be presented but for the updated reviews, new studies will be clearly highlighted. After the initial review, updates will be sent as new evidence arises.

A template for this summary is provided in Appendix 5.

3. Quality assurance process

Each review question will be led by an experienced systematic reviewer. A second reviewer will be assigned to assist and to provide cover in the event of illness. The second reviewer will be required to read all the key studies and check that the summary accurately reflects the body of literature. All summaries will be reviewed by a senior member of the team, to ensure processes are followed and quality maintained, this will also enable cover to be maintained.

4. Review and Update

Given the rapidly changing environment this protocol will be regarded as a live document and amended when required to ensure it reflects any additional research question added, and any changes made to the outlined processes.

Appendix 1- Additional targeted searches

For RQ7 and RQ8, a combined search for face masks and respiratory infection was conducted by RCSI library.

Domain	Search parameters
Intervention (face masks)	mask*, facemask*, face mask, face masks, medical mask, medical masks, medical facemask, medical face mask, medical face masks, surgical mask, surgical masks, surgical facemask, surgical facemasks, surgical face mask, surgical face masks, N95, N97, N99, FFP, FFP1, FFP2, FFP3, respirator, respirators, respiratory protection, respiratory protective device, face protection, airborne precaution, airborne precautions, droplet precaution, droplet precautions
Outcomes (respiratory viruses)	infection*, respiratory infection*, respiratory tract infection*, acute respiratory infection*, ARI, acute respiratory tract infection*, upper respiratory tract infection*, URTI, common cold, influenza, flu, pandemic influenza, SARS, Severe acute respiratory syndrome, influenza-like illness, ILI, rhinovir*, adenovir*, coronavir*, infectious disease transmission, communicable disease transmission, cross infection*, Pneumovirus Infections, parainfluenza, respiratory syncytial virus, MERS, Middle East Respiratory Syndrome
Study filters	Systematic review, RCTs, non-ramdomised controlled trials
Dates	01.01.2000 to 09.04.2020
Databases	EMBASE, PUBMED, COCHRANE, CINAHL

For RQ9-RQ10 a combined search for human coronaviruses and immunity/re-infection was conducted by the RCSI library.

	Search strategy
1	"coronavirus"[MeSH Terms] OR "coronavir*"
2	"Severe Acute Respiratory Syndrome" or "SARS"
3	"Middle East Respiratory Syndrome" or "MERS"
4	"COVID-19" or COVID19 or nCoV or 2019nCoV or "SARS-CoV-2" or "SARS-CoV2" or "SARS-CoV-1" or "SARS-CoV1" or SARSCoV19 or SARS-CoV19 or SARS-CoV-19 or HCoV-19 or WN-CoV or ((atypical or Wuhan) adj3 pneumonia)
5	"Immun*"
6	"Antibod*"
7	"Immunoglobulin*" or "IgM" or "IgA" or "IgG" or "IgG3" or "IgG4"
8	"Seroconvers*"
9	"Reinfect*" OR "Re-infec*"

10	"Recurrence"[MeSH] or "recurrence"
11	#1 OR #2 OR #3 OR #4
12	#5 OR #6 OR #7 OR #8 OR #9 or #10
13	#11 AND #12
14	#13 AND Filter: humans Filter: 1 January 2000 to 20 April 2020
Databases	EMBASE, PUBMED (Europe PMC)

For RQ11 a combined search for human coronaviruses and placental transmission was conducted by the RCSI Library.

Domain	**Search terms**
Infection terms	"coronavirus"[MeSH Terms] OR "coronavir*" OR "Severe Acute Respiratory Syndrome" or "SARS" OR "Middle East Respiratory Syndrome" or "MERS" OR "COVID-19" or COVID19 or nCoV or 2019nCoV or "SARS-CoV-2" or "SARS-CoV2" or "SARS-CoV-1" or "SARS-CoV1" or SARSCoV19 or SARS-CoV19 or SARS-CoV-19 or HCoV-19 or WN-CoV or ((atypical or Wuhan) adj3 pneumonia)
Transmission /antibody terms	Maternal antibod* OR passive immunity OR Placenta* OR Placental transfer OR placental transmission OR vertical transmission OR Infectious Disease Transmission, Vertical[MeSH] OR pregnan* OR neonat*
Combine with AND	
Filters	Filter: humans Filter: 1 January 2000 to 20 April 2020
Databases	EMBASE, PUBMED (Europe PMC)

Appendix 2 PICOS or POS for each RQ

Review question 1: What is the evidence for asymptomatic transmission of COVID-19?

Table 1: POS for review question one – asymptomatic transmission

Population	Patients (any age) with laboratory-confirmed test for COVID-19 for whom there is evidence that they transmitted the infection to another confirmed case at a time that they were asymptomatic. This will include: a) those who are asymptomatic throughout the course of the disease and b) those in the pre-symptomatic phase of the disease. • Subgroups of interest adults vs children.
Outcomes	Primary Outcomes • numbers of cases reported to be caused by asymptomatic transmission • characteristics of asymptomatic transmissions (for example age, gender, health status of those transmitting infection and the infected) • proportion asymptomatic patients that become symptomatic and how long before symptom onset transmission occurred • any risk factors for asymptomatic transmission e.g. family/household contacts/occupation/health status. Other outcomes of interest: • viral shedding during asymptomatic phase and with asymptomatic cases compared with average viral shedding for symptomatic cases.
Types of studies	**Include:** • Any study that reports on asymptomatic transmission of COVID-19 (this can include the asymptomatic phase of the disease and those who are asymptomatic throughout the disease). • Studies based on models, will be used mainly to ascertain data used for the asymptomatic transmission. Careful quality assurance is required for any modelled transmission outcomes. **Exclude:** • Studies where it is unclear when transmission took place • Studies where COVID-19 was not confirmed with a laboratory test.

Review question 2: What is the viral load over the course of the infection (including in the pre-symptomatic phase), and the duration of infectivity?

Table 2: POS for review question two – viral load and duration of infectivity

Population	Patients (of any age) infected with COVID-19 with information on either viral load during infection (including in the pre-symptomatic phase) or duration of infectivity. ▪ Subgroups of interest adults vs children
Outcomes	Primary outcomes: ▪ Ribonucleic Acid (viral load) during infection (the test used [including cut-off if reported], sample site [e.g. upper/lower respiratory, faecal, urine], test timing [number of days symptomatic pre-testing (if relevant)], clinical characteristics of the population (age, comorbidity) and clinical syndrome associated with COVID-19 (asymptomatic, mild illness, pneumonia, severe pneumonia, ARDS, sepsis, septic shock) ▪ Duration of virus detection (define start as: first confirmed positive test (or symptom onset); use WHO criteria (where reported) for end of detection, that is, two consecutive negative PCR tests 24 hours apart). ▪ Period of infectiousness/infectivity (defined as the time interval during which SARS-CoV-2 may be transferred directly or indirectly from an infected person to another person).
Types of Studies	**Include:** ▪ any study that reports on the viral load or duration of viral detection or infectivity of COVID-19. **Exclude:** ▪ studies where COVID-19 was not confirmed with a laboratory test.

Review question 3: What evidence is available to indicate that children spread COVID-19?

Table 3: POS for review question three – spread of COVID-19 by children

Population	Children (under 18) with a laboratory-confirmed positive test for COVID-19 • Subgroups of interest asymptomatic vs symptomatic (mild, moderate, severe)*
Outcome	Primary outcome: • confirmed transmission of COVID-19 rates • proportion of which are household transmissions • mean time to transmission/symptoms onset.
Types of Studies	**Include:** ▪ any study that reports on transmission of COVID-19 by children. **Exclude:** ▪ studies where COVID-19 was not confirmed with a laboratory test.

* https://www.who.int/publications-detail/clinical-management-of-severe-acute-respiratory-infection-when-novel-coronavirus-(ncov)-infection-is-suspected

Review question 4: What is the natural history of COVID-19 infection in children?

Table 4: POS for review question four – natural history of COVID-19 in children

Population	Children (under 18) with a laboratory-confirmed positive test for COVID-19, irrespective of clinical signs and symptoms. • Subgroups of interest: known immunosuppression / chronic respiratory disease **Exclude:** Those where vertical transmission is suspected that is during the perinatal period (22 weeks gestation to 7 days post-delivery) and/or history of breast-feeding.
Outcome	**Clinical history:** • symptoms (Specify these – fever [peak fever, time to resolution], cough, sore throat, rhinorrhea, dyspnea, diarrohea etc), • chest x-ray findings – pneumonia Y/N • lab findings: WCC / CRP / procalcitonin / influenza test results • evidence of ARDS / sepsis • mortality. **Management:** • symptomatic treatment only • hospitalisation required (duration of admission, requirement for ICU) • requirement for O2 support • requirement for ventilator support (Y/N, number of days support).
Types of Studies	**Include:** • all study types describing natural history of COVID-19 in children. **Exclude:** • studies where COVID-19 was not confirmed with a laboratory test.

Review question 5: What is the average length of stay in ICU for affected persons?

Table 5: POS for review question five – What is the average length of stay in ICU for affected persons?

Population	Patients (of any age) who have a laboratory-confirmed positive test for COVID-19 and have been admitted to ICU, HDU or other critical care setting.
Outcome	**Primary:** • length of stay (discharged or death as endpoint) • breakdown by age and gender, comorbidities. Important to note stage of epidemic, setting and local context.
Types of Studies	**Include:** • all study types providing data on ICU LOS for patients with COVID-19. **Exclude:** • studies in general wards or non-critical care settings • studies where COVID-19 was not confirmed with a laboratory test.

Review question 6: For individuals who have COVID-19, what clinical samples and collection sites are suitable for SARS-CoV-2 testing?

Table 6: PICOS question for review question 6 - For individuals who have COVID-19, what clinical samples and collection sites are suitable for SARS-CoV-2 testing?

Population	Patients (any age) with known COVID-19.
Index test	Any polymerase chain reaction (PCR)-based method for the identification of COVID-19, including real time, or reverse transcriptase PCR, using single or multiple assays. All target genes and primers will be accepted.
Comparators	Oropharyngeal/Nasopharyngeal – compared with an alternative(s) (e.g. lower respiratory tract [expectorated sputum, endotracheal aspirate, or bronchoalveolar lavage in ventilated patient], whole blood, serum, faecal, urine).
Outcome	COVID-19 detection rate Adequate/sufficient sample Test spoilage rate Concordance rate
Study design	**Include:** • cross-sectional studies, prospective or retrospective cohort, case series.

Review question 7: What evidence is available to indicate that routine wearing of masks by healthy persons in the community reduces the transmission of respiratory pathogens spread via droplet transmission?

Table 7: PICOS for review question 7 – What evidence is available to indicate that routine wearing of masks by healthy persons in the community reduces the transmission of respiratory pathogens spread via droplet transmission?

Population	General population/Community dwelling population of all ages
Intervention	• Routine wearing of masks in the community (including in household settings but excluding healthcare settings or high-risk groups (e.g. persons with cancer or CF)) • Mask wearing by pre-symptomatic or asymptomatic persons to prevent transmission of infection • Mask wearing by healthy individuals to prevent acquisition of infection • Comparisons of different types of masks (e.g. surgical vs. cloth) • Comparisons of use in different settings e.g. in public places, using public transport

Outcome	Primary outcome:
	• rates of community transmission of respiratory pathogens (COVID-19, SARS, MERS, influenza) spread by droplet transmission
	  ○ transmission of infection by pre-symptomatic or asymptomatic persons wearing masks
	  ○ acquisition of infection by healthy persons wearing masks.
	
	Secondary outcomes:
	• comparisons of different types of masks
	• adherence rates
	• adverse outcomes, risks or negative effects such as reduced compliance with hand-washing or social distancing measures, use of sub-optimal masks.

Types of Studies	**Include:** • systematic reviews or RCTs that report on outcomes of routine mask wearing in the community or in households. **Exclude:** ▪ studies focusing on mask wearing by symptomatic persons only ▪ case control studies, cohort studies, case series, case reports.

Study design	**Include:** • cross-sectional studies, prospective or retrospective cohort, case series.

Review question 8: What is the evidence that universal use of medical masks by healthcare workers in the healthcare setting is of value in reducing the transmission of respiratory viruses in health care settings?

Table 8: PICOS question for review question 8 – What is the additional effect of healthcare workers wearing medical masks, at all times in the healthcare setting, on the transmission of respiratory viruses?

Population	All healthcare workers (HCWs) working within a residential or acute healthcare environment, in contexts outside of the time during which they are providing direct clinical care for patients with confirmed or suspected respiratory virus infection, that is, delivery of care to patients without confirmed or suspected respiratory virus infection and in the non-clinical healthcare space (e.g. visiting hospital canteen). Residential or acute secondary or tertiary healthcare settings includes (non-exhaustive list): nursing homes, rehab hospitals, acute inpatient settings. **Exclude:** HCWs outside the residential healthcare environment (e.g. at home).
Intervention	Universal face mask (surgical/medical) wearing outside of the context of direct clinical care for patients with confirmed or suspected respiratory virus infection, i.e. wearing a face mask at all times in a residential or acute healthcare environment
Control	▪ Usual care ▪ Targeted face mask use (that is when providing direct clinical care for patients with confirmed or suspected respiratory viruses) ▪ No face mask wearing
Outcome	Primary outcome: ▪ Reduction of transmission of respiratory viruses (for example influenza, respiratory syncytial virus (RSV), SARS infection and MERS-CoV) or reduction in acquisition of influenza-like illness within the healthcare environment (in HCWs and patients) ○ Self-reported and laboratory-confirmed respiratory virus infection rates ▪ Compliance with universal face mask use
Types of Studies	**Include:** ▪ systematic reviews, RCTs, observational studies with a

	control group. **Exclude:** ▪ observational studies without a control group, case reports, editorials, guidelines, public press articles ▪ studies focusing on face mask wearing during clinical care only.

Review questions 9-11: What is the rate of reinfection / duration of immunity in individuals who recover from a laboratory-confirmed coronavirus infection?

Table 9: POS for review questions 9-11 – recovery from coronavirus infection and duration of immunity / protection from reinfection

Population	Individuals (of any age) who were infected with a laboratory-confirmed coronavirus and subsequently recovered (two consecutive negative respiratory RT-PCR tests 24 hours apart and more than 3 days fever-free OR a minimum of seven days after the first positive RT-PCR test in those who clinically improve earlier [WHO criteria]) Coronaviruses include: ▪ SARS-CoV-2 ▪ SARS-CoV-1 ▪ MERS-CoV ▪ Seasonal coronaviruses.
Outcomes	▪ Protection against reinfection ○ Reinfection is defined as a positive respiratory RT-PCR test (with or without symptoms consistent with acute coronavirus infection) following initial recovery. ○ Seroconversion rate and timing after coronavirus infection (seroconversion is the transition from a seronegative [no detectable coronavirus-specific antibodies in the serum] to a seropositive condition [detectable coronavirus-specific antibodies in serum sample]) Typically this involves detection of serum IgM and IgG levels. ▪ Duration of immunity. This includes: ○ duration of detection of serum immunoglobulin levels to specific coronavirus following infection (typically IgG for long-lasting response, IgM can also be detected in early response) ○ serum titres of IgG over time (typically expressed as Geometric Mean Titres [GMTs]) ○ duration of detection of neutralising antibodies ○ serum titres of neutralising antibodies over time ▪ Antibody transmission during pregnancy ▪ Infectiousness during re-infection

	○ Defined as the ability of the virus to spread, directly or indirectly, from a re-infected person to another Subgroups will include the following: ▪ Age and gender ▪ Comorbidities ▪ Severity of initial coronavirus infection ○ Here the association between the severity of initial illness (asymptomatic, mild, severe or critical) and immune response (rate/timing of seroconversion and duration of immunity) will be investigated.
Types of Studies	**Include:** ▪ any study (including systematic reviews) that reports on the immune response (or infectiousness) following recovery from acute coronavirus infections. **Exclude:** ▪ studies where initial infection was not confirmed with a positive molecular test ▪ animal studies.

Appendix 3- Questions to assist with the critical appraisal case report/series for COVID-19

Question	Response
Relevance to Irish system	
Was the study question or objective clearly stated?	
Are the study patients described in sufficient demographically?	
Is the context applicable?	
Study design	
Were there clear criteria for inclusion of the case(s)?	
Did the case series have consecutive inclusion participants?	
Was the condition measured in a standard, reliable way for all participants included in the case series?	
Was the outcome measured in a standard, reliable way for all participants included in the case series?	
Was the statistical analysis appropriate?	
Peer-review status	
Has this study been formally peer-reviewed?	

Appendix 4 -Questions to assist with the critical appraisal of COVID-19 related modelling studies

Quality dimension	Appraisal question	Helper questions
Study relevance		
Population	Is the population relevant?	Are the demographics similar? Are risk factors/behaviours/comorbidities similar?
Setting	Is the context (setting and circumstances) applicable?	Is the geographic location similar? Is the healthcare system similar?
Model structure & data		
Statement of decision problem/objective	Is the model objective clear?	Is there a clear statement of the model objective? Is the scope of the model clear?
Model type/structure	Is the model type and structure clear?	Is the model type stated (e.g. SIR model)? Is a clear model structure presented (e.g. model schematic & equations)? Does the model structure reflect the underlying natural history of disease? Are structural assumptions transparent and justified?
Model data	Are the underlying sources of data reported clearly?	Are the sources of data used to develop the structure of the model specified? Are the lower and upper parameter bounds presented and justified? Where expert opinion has been used, are the methods described and justified?

Assessment of uncertainty	Has model uncertainty been adequately assessed?	Is the model deterministic or stochastic? Has parameter uncertainty been assessed by assignment of probability or statistical distributions? Has the choice of distribution been stated and justified? Is there evidence that structural uncertainties have been addressed via sensitivity analysis? Has heterogeneity been assessed by subgroup analysis?
Model consistency		
Internal consistency	Is there evidence of internal validation?	Is there evidence that the mathematical logic of the model has been tested thoroughly before use? If approximation methods have been employed, has the process and validation of model fit been described sufficiently?
External consistency	Is there evidence of external validation or cross-verification?	Has the model been calibrated against independent data, with any differences been explained and justified? Have the results of the model been compared with those of previous models or published data?
Peer-review status	Has the study been formally peer-reviewed?	

Appendix 5 Template of summary document

Evidence summary for [insert shortened version of RQ]

The Health Information and Quality Authority (HIQA) has developed a series of 'Evidence Summaries' to assist the Clinical Expert Advisory Group (EAG) supporting the National Public Health Emergency Team (NPHET) in their response to COVID-19. These summaries are based on specific research questions (RQs). This evidence summary (InsertRQnumber) was developed to address the following research question:

(InsertRQ)

The processes as outlined in the protocol were followed. Below is the summary of all relevant guidance until XX April 2020.

Results

[For updates only- initial sentence highlighting how many new studies.]

Describe (1 paragraph and in basic terms):

- Total studies included, and number of additional since previous summary
- Relevant study characteristics (e.g. country, setting, epidemic phase)
- Overview of results of individual studies. (each primary outcome in RQ)
- A description of the quality within and across studies (based upon the agreed questions
- Additional subgroups comparison where available, as documented for each RQ

Discussion

Including a summary of the main findings including the limitations of evidence for each main outcome and considering their relevance to the current and evolving Irish setting. (2-3 paragraphs)

Conclusion

[For updates only - A short paragraph focusing on what has changed. May be useful to consider the following three questions: what was known? what does this new evidence add? and what do we still not know?]

Provide a general interpretation of the results in the context of applicability and relevance, and identify where research is lacking. Describe whether the RQ has been adequately addressed by this evidence review. (1 paragraph)

References

References including links to full text or as attachments if not easily accessible

Table 2 Template data extraction table

Author Country Study design	Population setting Patient demographics Clinical characteristics	Primary outcome results

Appendix 6 Glossary of Terms

Incubation period	The time interval between invasion by an infectious agent and appearance of the first signs or symptoms of the disease in question. Includes specification of the relevant sign or symptom because some diseases have several symptoms with different timing, which would result in a different definition of incubation period.
Latent period	The time from infection to onset of infectiousness (may be shorter than incubation)
Serial interval	The period of time between analogous phases of an infectious illness in successive cases of a chain of infection that is spread person to person. For example, the interval between symptom onset in a secondary case and onset in a primary case.
Period of infectiousness (or period of communicability)	The time interval during which an infectious agent may be transferred directly or indirectly from an infected person to another person.
Duration of shedding	Period during which a patient excretes the organism.
Exclusion period	Minimum recommended period for which patients should be excluded from work, school or other childcare setting.
Asymptomatic	Without symptoms throughout the duration of disease.
Pre-symptomatic	The early stages of disease, after transmission has occurred, but symptoms have not yet developed.

Source: Adapted from European Centre for Disease Prevention and Control

https://www.ecdc.europa.eu/sites/default/files/media/en/publications/Publications/systematic-review-incubation-period-shedding-children.pdf

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