Health Information and Quality Authority

An tÚdarás Um Fhaisnéis agus Cáilíocht Sláinte

Protocol for evidence synthesis support - COVID-19

25 May 2020

Version	1.6

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
23.04.2020	Addition of Review Question 12 and associated search strategy.
07.05.2020	Addition of quality appraisal tools.
20.05.2020	Addition of Review Question 13 and associated search strategy. Addition of quality appraisal tool for diagnostic accuracy studies.

Purpose and aim

The purpose of this protocol is to outline the process by which the health technology assessment (HTA) directorate in the Health Information and Quality Authority (HIQA) 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. HIQA's 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

A narrow search strategy was initially used to retrieve research relevant to COVID-19 specifically, as opposed to coronavirus more generally. However, this approach has been adapted to incorporate search strategies that are tailored specifically to each research question. Each strategy is developed in collaboration with the Royal College of Surgeons in Ireland (RCSI) librarian. The initial search is conducted by the RCSI librarian and then updated by the HTA directorate, as appropriate. A list of resources that may be routinely searched across the search strategies include:

- PubMed
- Embase
- Europe PMC
- Cochrane Library
- UCL EPPI centre
- NHS Evidence
- NICE UK
- ScienceDirect
- Infectious Diseases Society of America search of infectious disease journals
- HRB Open

- Lenus.

The final search strategy employed for each research question is detailed in Appendix 1.

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?

RQ12: Is performing aerosol generating procedures (AGPs) on patients without clinical features of viral respiratory tract infections associated with airborne transmission to health care professionals?
Assessed as two sub-questions:

- What is the evidence that performance of AGPs on patients without clinical features of viral respiratory tract infection at the time of the procedure is associated with airborne transmission of respiratory viruses to healthcare professionals?
- What is the evidence that performance of AGPs on individuals without clinical features of viral respiratory tract infection at the time of the procedure, is associated with generation of potentially infectious aerosols?

RQ13: What is the diagnostic accuracy of tests for the detection of SARS-CoV-2 using salivary clinical samples compared with nasopharyngeal, oropharyngeal or lower respiratory tract clinical samples?

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. A template for the data extraction table is provided in Appendix 5. 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-randomised studies - of interventions) will be used for quality appraisal of non-

randomised studies, the AMSTAR-2 to appraise systematic reviews, and the Quality Assessment of Diagnostic Accuracy Studies version two (QUADAS-2) will be used to assess explicit studies of diagnostic accuracy. The National Heart, Lung and Blood Institute (NIH) quality assessment tools will be used for appraisal of observational cohort studies and for pre-post studies with no control group, for example, analytical studies. 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 Search strategies

Initial Search strategy for RQ1-5 to identify COVID-19 related evidence (used pre-27 March 2020)

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"

Tailored search strategies

RQ 1: What is the evidence for asymptomatic transmission of COVID-19? (Strategy employed from 27 March 2020)

	PubMed
A	((coronavirus [MeSH]) OR ("coronavirus infections"[MeSH Terms]) OR (coronavirus [All Fields]) OR ("covid 2019") OR ("SARS2") OR ("SARS-CoV-2") OR ("SARS-CoV-19") OR ("severe acute respiratory syndrome coronavirus 2" [supplementary concept]) OR (coronavirus infection) OR ("severe acute respiratory" pneumonia outbreak) OR ("novel cov") OR (2019ncov) OR (sars cov2) OR (cov2) OR (ncov) OR (covid-19) OR (covid19) OR (coronaviridae) OR ("corona virus"))
B	(((asymptomatic OR pre-symptomatic OR presymptomatic))) OR ("Disease Transmission, Infectious"[Mesh] OR "disease transmission" OR infectious[Text Word])
C	A AND B = 4889 ; Limited to Humans from 30/11/2019
	Europe PubMed Central
A	(coronavirus OR covid-19 OR "covid 19" OR "SARS-CoV-2") AND (asymptomatic OR presymptomatic OR infectious)
	A limited to Preprints from 01012020
	EMBASE excl Medline
A	'coronavirinae'/exp OR 'coronavirinae' OR 'coronaviridae infection'/exp OR 'coronaviridae infection':ti,ab,kw OR 'coronavirus'/exp OR coronavirus:ti,ab,de,kw OR 'coronavirus infection'/de OR SARS-VoV-2:ti,ab,kw OR covid-19:ti,ab,kw OR covid19:ti,ab,kw
B	(asymptomatic OR pre-symptomatic OR presymptomatic):ti,ab,kw OR 'disease transmission'/exp OR disease NEXT/2 transmission OR infectious:ti,ab,de,kw
C	A AND B; Limited to HUMAN, YEAR 2020, excluding MEDLINE

RQ 2: What is the viral load over the course of the infection (including in the pre-symptomatic phase), and the duration of infectivity? (Strategy employed from 27 March 2020)

	PubMed
A	((coronavirus [MeSH]) OR ("coronavirus infections"[MeSH Terms]) OR (coronavirus [All Fields]) OR ("covid 2019") OR ("SARS2") OR ("SARS-CoV-2") OR ("SARS-CoV-19") OR ("severe acute respiratory syndrome coronavirus 2" [supplementary concept]) OR (coronavirus infection) OR ("severe acute respiratory" pneumonia outbreak) OR ("novel cov") OR (2019ncov) OR (sars cov2) OR (cov2) OR (ncov) OR (covid-19) OR (covid19) OR (coronaviridae) OR ("corona virus"))
B	("Viral Load"[Mesh] OR ("viral load"[Text Word] OR "viral burden"[Text Word] OR "virus titer"[Text Word]) OR infectivity[Text Word] OR Virulence[Mesh] OR virulence[Title/Abstract])
C	A AND B
	C Limited to HUMAN, from 30112019 to 27032020
	Europe PubMed Central
A	(coronavirus OR covid-19 OR "covid 19" OR "SARS-CoV-2") AND ("viral load" OR infectivity OR virulence)
	EMBASE
A	('coronavirus'/exp OR coronavirus:ti,ab,de,kw OR 'coronavirus infection'/exp OR covid19:ti,ab,de,kw OR 'covid 19':ti,ab,kw OR 'covid-19' OR 'covid 2019' OR 'sars cov 2':ti,ab,kw OR '2019 ncov':ti,ab) OR 'novel coronavirus':ti,ab,kw
B	'virus load'/exp OR (viral NEXT/1 load) OR infectivity:ti,ab,de,kw OR virulence:ti,ab,kw
C	**A AND B ; Limited to HUMAN, YEAR 2020, both Embase and MEDLINE**

Search updated from April 1 2020.

#	PubMed
1	"coronavirus"[MeSH Terms] OR "coronavirus infections"[MeSH Terms] OR "coronavirus"[All Fields] OR "covid 2019"[All Fields] OR "SARS2"[All Fields] OR "SARS-CoV-2"[All Fields] OR "SARS-CoV-19"[All Fields] OR "coronavirus infection"[All Fields] OR "severe acute respiratory"[All Fields] OR "pneumonia outbreak"[All Fields] OR "novel cov"[All Fields] OR "2019ncov"[All Fields] OR "sars cov2"[All Fields] OR "cov2"[All Fields] OR "ncov"[All Fields] OR "covid-19"[All Fields] OR "covid19"[All Fields] OR "coronaviridae"[All Fields] OR "corona virus"[All Fields] OR "severe acute respiratory syndrome coronavirus 2"[Supplementary Concept]
2	"Viral Load"[MeSH Terms] OR "Viral Load"[Text Word] OR "viral burden"[Text Word] OR "virus titer"[Text Word] OR "infectivity"[Text Word] OR "virulence"[MeSH Terms] OR "virulence"[Title/Abstract] OR "Virology"[MeSH Terms] OR "disease transmission, infectious"[MeSH Terms] OR "virus shedding"[MeSH Terms] OR "Virology"[Title/Abstract] OR

	"virologic*"[Title/Abstract] OR "cultur*"[Title/Abstract] OR "virus burden"[Title/Abstract] OR "viral detect*"[Title/Abstract] OR "virus detect*"[Title/Abstract] OR "RNA"[Title/Abstract] OR "RNA"[Title/Abstract] OR "ribonucleic acid"[Title/Abstract] OR "Cycle threshold"[Title/Abstract] OR "Ct value"[Title/Abstract] OR "Infectiousness"[Title/Abstract] OR "transmiss*"[Title/Abstract] OR "shedding"[Title/Abstract] OR "Virus clearance"[Title/Abstract] OR "Viral clearance"[Title/Abstract] OR "virus load"[Title/Abstract] OR "virus titre"[Title/Abstract] OR "viral dynamic"[Title/Abstract]
3	#1 AND #2
	Limits: Human, from 2020
	EMBASE
1	('coronavirus'/exp OR coronavirus:ti,ab,de,kw OR 'coronavirus infection'/exp OR covid19:ti,ab,de,kw OR 'covid 19':ti,ab,kw OR 'covid-19' OR 'covid 2019' OR 'sars cov 2':ti,ab,kw OR '2019 ncov':ti,ab) OR 'novel coronavirus':ti,ab,kw
2	('virus load'/exp OR (viral NEXT/1 load) OR infectivity:ti,ab,kw OR virulence:ti,ab,kw OR 'virology'/exp OR 'virus detection'/exp OR 'rna'/exp OR 'disease transmission'/exp OR 'virus shedding'/exp OR virology:ti,ab,kw OR virologic*:ti,ab,kw OR cultur*:ti,ab,kw OR 'virus burden':ti,ab,kw OR 'viral detect*':ti,ab,kw OR 'virus detect':ti,ab,kw) OR 'rna':ti,ab,kw OR 'ribonucleic acid':ti,ab,kw OR 'cycle threshold':ti,ab,kw OR 'ct value':ti,ab,kw OR 'infectiousness':ti,ab,kw OR 'transmiss*':ti,ab,kw OR 'shedding':ti,ab,kw OR 'virus clearance':ti,ab,kw OR 'viral clearance':ti,ab,kw OR 'virus load':ti,ab,kw OR 'virus titre':ti,ab,kw OR 'viral dynamic':ti,ab,kw OR 'virus dynamic':ti,ab,kw
3	**#1 AND #2**
	Limits: Human, Embase and Medline, from 2020
	Europe PubMed Central
1	(coronavirus OR covid-19 OR "covid 19" OR "SARS-CoV-2") AND ("viral load" OR "infectivity" OR "virulence" OR "virus load" OR "Infectiousness" OR "viral Shedding" OR "virus shedding") AND (SRC:PPR) AND (FIRST_PDATE:2020)

RQ 6: For individuals who have COVID-19, what clinical samples and collection sites are suitable for SARS-CoV-2 testing? (Strategy employed from 31 March 2020)

	PubMed
A	((coronavirus [MeSH]) OR ("coronavirus infections"[MeSH Terms]) OR (coronavirus [All Fields]) OR ("covid 2019") OR ("SARS2") OR ("SARS-CoV-2") OR ("SARS-CoV-19") OR ("severe acute respiratory syndrome coronavirus 2" [supplementary concept]) OR (coronavirus infection) OR ("severe acute respiratory" pneumonia outbreak) OR ("novel cov") OR (2019ncov) OR (sars cov2) OR (cov2) OR (ncov) OR (covid-19) OR (covid19) OR (coronaviridae) OR ("corona virus"))
B	(nasopharyngeal[Text Word] OR oropharyngeal[Text Word] OR faecal[Text Word] OR stool[Text Word] OR sputum[Text Word] OR urine[Text Word] OR blood[Text Word] OR serum[Text Word] OR swab[Text Word] OR sample[Text Word])
C	"Diagnosis"[Mesh] OR "diagnosis"[Subheading] OR "Early Diagnosis"[Mesh] OR Diagnosis[Text Word] OR diagnostic[Text Word] OR sensitivity[Text Word]
D	A AND B AND C From November 2019, humans only
	Europe PMC 2020 diagnostic Preprints
A	("COVID-19" OR "SARS-CoV-2" AND (diagnosis OR diagnostic OR sensitivity) AND (nasopharyngeal OR oropharyngeal OR faecal OR stool OR sputum OR urine OR blood OR serum OR swab OR sample))
	EMBASE limited to Human, from year 2020
A	'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 OR 'sars cov 2':ti,ab,kw
B	**nasopharyngeal**:ti,ab,de,kw OR **oropharyngeal**:ti,ab,de,kw OR **faecal**:ti,ab,de,kw OR **stool**:ti,ab,de,kw OR **sputum**:ti,ab,de,kw OR **urine**:ti,ab,de,kw OR **blood**:ti,ab,de,kw OR **serum**:ti,ab,de,kw OR **swab**:ti,ab,de,kw OR **sample**:ti,ab,de,kw
C	'diagnostic test'/exp OR diagnosis:ti,ab,de,kw OR diagnostic:ti,ab,de,kw OR sensitivity:ti,ab,kw
D	**A AND B AND C**
	NHS EVIDENCE Dec2019-Mar2020
	(Coronavirus OR COVID 19 OR SARS Cov 19) AND (diagnostic OR diagnosis) AND (nasopharyngeal OR oropharyngeal OR faecal OR stool OR sputum OR urine OR blood OR serum OR swab OR sample)

RQ7: 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?

RQ 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?

(Combined Strategy employed from 9 April 2020 – CINAHL was searched in addition to the strings presented below; however the string is not presented)

	PubMed
A	(((mask OR masks OR facemask OR facemasks OR "face mask" OR "face masks" OR "medical mask*" OR "medical face mask*OR "surgical mask*" OR "surgical face mask* OR N95 OR N97 OR N99 OR FFP OR FFP1 OR FFP2 OR FFP3 OR respirator OR respirators OR "respiratory protection" OR "respiratory protective device" OR "face protection" OR "airborne precaution*" OR "droplet precaution*")))
B	((randomized controlled trial[Publication Type] OR (randomized[Title/Abstract] AND controlled[Title/Abstract] AND trial[Title/Abstract])OR randomized controlled trials as topic[mh] OR "clinical trial" OR clinical trial[Publication Type]) OR "systematic review" OR "Systematic Review" [Publication Type])
C	A AND B ; Limit Human, 2000 to 2020
	EMBASE
A	mask OR masks OR facemask OR facemasks OR (face NEXT/1 mask*) OR (medical NEXT/1 mask*) OR (surgical NEXT/1 mask*) OR n95 OR n97 OR n99 OR ffp OR ffp1 OR ffp2 OR ffp3 OR respirator OR respirators OR (respiratory NEXT/1 protection) OR (respiratory NEXT/1 protective NEXT/1 device*) OR (face NEXT/1 protection) OR (airborne NEXT/1 precaution*) OR (droplet NEXT/1 precaution*)
B	'randomized controlled trial'/exp OR (randomized NEXT/1 controlled) OR (controlled NEXT/1 trial) OR (clinical NEXT/1 trial) OR 'clinical trial'/exp OR 'systematic review'/exp OR (systematic NEXT/1 review)
C	A AND B; Limited to Embase only excl Medline, 2010 to 2020 only
	COCHRANE LIBRARY and CENTRAL REGISTRY OF CLINICAL TRIALS
A	mask OR masks OR facemask OR facemasks OR (face NEAR/1 mask*) OR (medical NEAR/1 mask*) OR (surgical NEAR/1 mask*) OR n95 OR n97 OR n99 OR ffp OR ffp1 OR ffp2 OR ffp3 OR (respirator NEAR/3 protection) OR (respirators NEAR/3 protection) OR (respiratory NEAR/1 protection) OR (respiratory NEAR/1 protective NEAR/1 device*) OR (face NEAR/1 protection) OR (airborne NEAR/1 precaution*) OR (droplet NEAR/1 precaution*)

Review question 9-10: Covid-19 immunity and re-infection; Strategy employed from 18 April 2020

	PubMed
A	"coronavirus"[MeSH Terms] OR coronavirus [All Fields] OR "Severe Acute Respiratory Syndrome"[All Fields] OR "SARS"[All Fields] OR "Middle East Respiratory Syndrome"[All Fields] OR "MERS"[All Fields] OR "COVID-19"[All Fields] OR ("COVID-19"[Supplementary Concept] OR "COVID-19"[All Fields] OR "covid19"[All Fields]) OR "SARS-CoV-2"[All Fields] OR "SARS-CoV2"[All Fields] OR "SARS-CoV-1"[All Fields] OR "SARS-CoV1"[All Fields] OR SARS-CoV-19[All Fields] OR HCoV-19[All Fields]
B	Immunity[Mesh] OR immunity[All Fields] OR Antibodies[Mesh] OR antibodies[All Fields] OR antibody[All Fields] OR "Immunoglobulin*"[All Fields] OR "IgM"[All Fields] OR "IgA"[All Fields] OR "IgG"[All Fields] OR "IgG3"[All Fields] OR "IgG4"[All Fields] OR "seroconversion"[Mesh] OR seroconversion[All Fields] OR reinfection[All Fields] OR reinfections[All Fields] OR "Recurrence"[MeSH] OR "recurrence"[All Fields]
C	A AND B, limit humans, 2000 to 2020
	EMBASE
A	'coronavirus'/exp OR coronavirus OR 'coronavirus infection'/de OR 'severe acute respiratory syndrome'/exp OR acute NEXT/1 respiratory NEXT/1 syndrome OR covid19:ti,ab,kw OR 'covid-19*':ti,ab,kw OR 'COVID-2019*' OR 'sars-cov-2' OR sars2:ti,ab,kw OR '2019-ncov' OR 'SARS-CoV-2019' OR 'SARS-CoV-19' OR 'SARS-CoV-2019' OR 'severe acute respiratory syndrome':ti,ab,kw OR 'severe acute respiratory syndrome'/exp OR 'SARS coronavirus'/exp OR SARS:ti,ab,kw OR 'Middle East respiratory syndrome'/exp OR MERS:ti,ab,de,kw
B	Immunity:ti,ab,de,kw OR 'immunity'/exp OR 'antibody'/exp OR antibody:ti,ab,de,kw OR antibodies:ti,ab,de,kw OR 'immunoglobulin'/exp OR immunoglobulin:ti,ab,de,kw OR immunoglobulins ti,ab,de,kw OR IgM OR IgA OR IgG OR IgG3 OR IgG4 OR 'seroconversion'/exp OR seroconversion:ti,ab,de,kw OR 'reinfection'/exp OR reinfection:ti,ab,de,kw OR reinfections:ti,ab,de,kw OR 'recurrent disease'/exp OR recurrence :ti,ab,de,kw
C	A AND B; limit human, 2000 to 2020
	EuropePMC
A	("2019-nCoV" OR "2019nCoV" OR "COVID-19" OR "SARS-CoV-2" OR "Coronavirus" OR "coronaviruses" OR "SARS-CoV" OR "MERS-CoV" OR "Severe Acute Respiratory Syndrome" OR "Middle East Respiratory Syndrome" OR MERS OR SARS) AND (immunity OR antibody OR antibodies OR immunoglobulin OR immunoglobulins OR IgM OR IgA OR IgG OR IgG3 OR IgG4 OR seroconversion OR reinfection OR reinfections OR recurrence) AND (SRC:PPR)

Review question 11: Placental transmission; Strategy employed from 20 April 2020

	PubMed
A	"coronavirus"[MeSH Terms] OR coronavirus [All Fields] OR "Severe Acute Respiratory Syndrome"[All Fields] OR "SARS"[All Fields] OR "Middle East Respiratory Syndrome"[All Fields] OR "MERS"[All Fields] OR "COVID-19"[All Fields] OR ("COVID-19"[Supplementary Concept] OR "COVID-19"[All Fields] OR "covid19"[All Fields]) OR "SARS-CoV-2"[All Fields] OR "SARS-CoV2"[All Fields] OR "SARS-CoV-1"[All Fields] OR "SARS-CoV1"[All Fields] OR SARS-CoV-19[All Fields] OR HCoV-19[All Fields]
B	(((((((("maternal antibody"[All Fields] OR "maternal antibodies"[All Fields]) OR "passive immunity"[All Fields]) OR ((((("placenta"[MeSH Terms] OR "placenta"[All Fields]) OR "placentas"[All Fields]) OR "placenta s"[All Fields]) OR "placentae"[All Fields])) OR (((((((("placenta"[MeSH Terms] OR "placenta"[All Fields]) OR "placental"[All Fields]) OR "placentally"[All Fields]) OR "placentals"[All Fields]) OR "placentation"[MeSH Terms]) OR "placentation"[All Fields]) OR "placentations"[All Fields]) OR "placentitis"[All Fields])) OR ((("gravidity"[MeSH Terms] OR "gravidity"[All Fields]) OR "pregnant"[All Fields]) OR "pregnants"[All Fields])) OR ((("pregnancy"[MeSH Terms] OR "pregnancy"[All Fields]) OR "pregnancies"[All Fields]) OR "pregnancy s"[All Fields])) OR (((((((("infant, newborn"[MeSH Terms] OR ("infant"[All Fields] AND "newborn"[All Fields])) OR "newborn infant"[All Fields]) OR "neonatal"[All Fields]) OR "neonate"[All Fields]) OR "neonates"[All Fields]) OR "neonatality"[All Fields]) OR "neonatals"[All Fields]) OR "neonate s"[All Fields])) OR "vertical transmission"[All Fields]) OR "infectious disease transmission, vertical"[MeSH Terms]
C	A AND B, limit Humans, 2000-2020
	EMBASE excl Medline
A	'coronavirus'/exp OR coronavirus OR 'coronavirus infection'/de OR 'severe acute respiratory syndrome'/exp OR acute NEXT/1 respiratory NEXT/1 syndrome OR covid19:ti,ab,kw OR 'covid-19*':ti,ab,kw OR 'COVID-2019*' OR 'sars-cov-2' OR sars2:ti,ab,kw OR '2019-ncov' OR 'SARS-CoV-2019' OR 'SARS-CoV-19' OR 'SARS-CoV-2019' OR 'severe acute respiratory syndrome':ti,ab,kw OR 'severe acute respiratory syndrome'/exp OR 'SARS coronavirus'/exp OR SARS:ti,ab,kw OR 'Middle East respiratory syndrome'/exp OR MERS:ti,ab,de,kw
B	(maternal NEXT/1 antibody) OR (maternal NEXT/1 antibodies) OR (passive NEXT/1 immunity) OR placenta OR placental OR (vertical NEXT/1 transmission) OR pregnant OR pregnancy OR neonate OR neonatal
C	A AND B, limit Humans, 2000-2020
	EuropePMC
A	("2019-nCoV" OR "2019nCoV" OR "COVID-19" OR "SARS-CoV-2" OR ("wuhan" AND "coronavirus") OR "Coronavirus" OR "Corona virus" OR "corona-virus" OR "corona viruses" OR "coronaviruses" OR "SARS-CoV" OR "Orthocoronavirinae" OR "MERS-CoV" OR "Severe Acute Respiratory Syndrome" OR "Middle East Respiratory Syndrome" OR ("SARS" AND "virus")) AND (placenta OR placental OR maternal

	OR pregnant OR pregnancy OR neonate OR neonatal OR "vertical transmssion")
B	Preprints

Review question 12: What is the evidence that performance of AGPs on patients without clinical features of viral respiratory tract infection at the time of the procedure is associated with airborne transmission of respiratory viruses to healthcare professionals? (b) What is the evidence that performance of AGPs on individuals without clinical features of viral respiratory tract infection at the time of the procedure, is associated with generation of potentially infectious aerosols? (Strategy employed from 23 April 2020)

	PubMed
A	"coronavirus"[MeSH Terms] OR "coronavirus" OR "Severe Acute Respiratory Syndrome" OR "Severe Acute Respiratory Syndrome"[Mesh] 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 influenza [Text Word] OR parainfluenza OR flu OR "influenza-like" OR ILI OR "respiratory syncytial virus" OR measles OR mumps OR rubella OR varicella OR "chickenpox" OR adenovir* OR rhinovir* OR "common cold" OR pneumovir* OR "viral respiratory" OR "viral infection" OR "viral disease" OR "acute respiratory infection" OR ARI OR "respiratory tract infection" OR URTI
B	AGP* OR "aerosol generating procedure" OR "aerosol-generating procedure" OR intubation OR extubation OR ventilation OR NIV OR HFOV OR OR BiPAP OR BPAP OR CPAP OR suction OR tracheotomy OR tracheostomy OR bronchoscopy OR drill OR drilling
C	A AND B
D	Transmission OR "cross infection" OR "Infectious Disease Transmission, Patient-to-Professional"[Mesh] OR "Disease Transmission, Infectious"[Mesh] OR (infection[Title/Abstract] AND transfer[Title/Abstract]) OR transmittal OR "infection rate" OR "infection risk" OR nosocomial OR "exposure"
E	"viral load" OR "infectious aerosol*" OR "infectious airborne" OR "viable virus" OR "viral RNA" OR "RNA in aerosol*" OR "Ribonucleic Acid" OR nucleotides OR "vir* fragment" OR "respiratory pathogen" OR "airborne pathogen" OR "airborne virus"
F	D OR E
G	C AND F, limit Humans
	EMBASE
A	coronavirus OR coronaviruses OR Severe NEXT/1 Acute NEXT/1 Respiratory NEXT/1 Syndrome OR SARS OR Middle NEXT/1 East NEXT/1 Respiratory NEXT/1 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 influenza OR parainfluenza OR flu OR "influenza-like" OR ILI OR "respiratory syncytial virus" OR measles OR mumps OR rubella OR varicella OR "chickenpox" OR adenovirus OR adenoviruses OR rhinovirus OR rhinoviruses OR "common cold" OR pneumovirus OR "viral respiratory" OR "viral infection" OR "viral disease" OR "acute respiratory infection" OR ARI OR "respiratory tract infection" OR URTI

B	**[**AGP* OR "aerosol generating procedure" OR "aerosol-generating procedure" OR intubation OR extubation OR ventilation OR NIV OR HFOV OR OR BiPAP OR BPAP OR CPAP OR suction OR tracheotomy OR tracheostomy OR bronchoscopy OR drill*]
C	A AND B
D	"viral load" OR "infectious aerosol*" OR "infectious airborne" OR "viable virus" OR "viral RNA" OR "RNA in aerosol*" OR "Ribonucleic Acid" OR nucleotides OR "vir* fragment" OR "respiratory pathogen" OR "airborne pathogen" OR "airborne virus"
F	C AND D , limit Humans, Exclude MEDLINE, EMBASE only records
	Cochrane Library, Cochrane Reviews, Registry of Clinical Trials
A	coronavirus OR coronaviruses OR Severe NEAR/1 Acute NEAR/1 Respiratory NEAR/1 Syndrome OR SARS OR Middle NEAR/1 East NEAR/1 Respiratory NEAR/1 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 influenza OR parainfluenza OR flu OR "influenza-like" OR ILI OR "respiratory syncytial virus" OR measles OR mumps OR rubella OR varicella OR "chickenpox" OR adenovirus OR adenoviruses OR rhinovirus OR rhinoviruses OR "common cold" OR pneumovirus OR "viral respiratory" OR "viral infection" OR "viral disease" OR "acute respiratory infection" OR ARI OR "respiratory tract infection" OR URTI
B	AGP OR aerosol NEAR/1 generating OR intubation OR extubation OR ventilation OR NIV OR HFOV OR BiPAP OR BPAP OR CPAP OR suction OR tracheotomy OR tracheostomy OR bronchoscopy OR drills OR drilling
C	A AND B
D	Transmission OR cross NEAR/1 infection OR infection NEAR/3 transfer OR transmittal OR "infection rate" OR "infection risk" OR nosocomial OR "exposure" OR "viral load" OR "infectious aerosol*" OR "infectious airborne" OR "viable virus" OR "viral RNA" OR "RNA in aerosol*" OR "Ribonucleic Acid" OR nucleotides OR "respiratory pathogen" OR "airborne pathogen" OR "airborne virus"
E	C AND D
	EuropePMC
A	(airborne OR aerosol OR ventilation) AND (transmission OR nosocomial OR infection) AND (virus OR viral OR influenza OR coronavirus OR Covid*) Limit to Preprints, all years

RQ13: What is the diagnostic accuracy of tests for the detection of SARS-CoV-2 using salivary clinical samples compared with nasopharyngeal, oropharyngeal or lower respiratory tract clinical samples?

PubMed
"coronavirus"[MeSH Terms] OR "coronavirus infections"[MeSH Terms] OR "coronavirus"[All Fields] OR "covid 2019"[All Fields] OR "SARS2"[All Fields] OR "SARS-CoV-2"[All Fields] OR "SARS-CoV-19"[All Fields] OR "coronavirus infection"[All Fields] OR "severe acute respiratory"[All Fields] OR "pneumonia outbreak"[All Fields] OR "novel cov"[All Fields] OR "2019ncov"[All Fields] OR "sars cov2"[All Fields] OR "cov2"[All Fields] OR "ncov"[All Fields] OR "covid-19"[All Fields] OR "covid19"[All Fields] OR "coronaviridae"[All Fields] OR "corona virus"[All Fields] OR "severe acute respiratory syndrome coronavirus 2"[Supplementary Concept]
"nasopharyngeal"[Text Word] OR "oropharyngeal"[Text Word] OR "swab"[Text Word] OR "salivary"[Text Word] OR "saliva"[Text Word] OR "sample"[Text Word] OR "sputum" [Text Word]
"Diagnosis"[Mesh] OR "diagnosis"[Subheading] OR "Early Diagnosis"[Mesh] OR Diagnosis[Text Word] OR diagnostic[Text Word] OR sensitivity[Text Word] OR Detection[Text Word] OR specificity[Text Word] OR accuracy[Text Word] OR rate[Text Word]
#1 AND #2 AND #3
Limit #4 Human
Limit #5 PubMed publication year
Embase
'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 OR 'sars cov 2':ti,ab,kw OR SARS-CoV-2:ti,ab,kw OR SARS-CoV-19:ti,ab,kw
nasopharyngeal:ti,ab,de,kw OR oropharyngeal:ti,ab,de,kw OR swab:ti,ab,de,kw OR sample:ti,ab,de,kw OR sputum:ti,ab,de,kw OR saliva:ti,ab,de,kw OR salivary:ti,ab,de,kw
'diagnostic test'/exp OR diagnosis:ti,ab,de,kw OR diagnostic:ti,ab,de,kw OR sensitivity:ti,ab,de,kw OR detection:ti,ab,de,kw OR specificity:ti,ab,de,kw OR accuracy:ti,ab,de,kw OR rate:ti,ab,de,kw
#1 AND #2 AND #3
Limits: Human
Limits : November 2019 to 2020
Europe PMC
(("COVID-19" OR "SARS-CoV-2") AND (diagnosis OR diagnostic OR sensitivity OR detection OR specificity OR rate OR accuracy) AND (nasopharyngeal OR oropharyngeal OR saliva OR salivary OR sputum OR swab OR sample))
Limits: Preprints AND 2020
NHS Evidence
(Coronavirus OR COVID 19 OR SARS Cov 19) AND (diagnostic OR diagnosis OR detection OR sensitivity OR specificity OR rate OR accuracy) AND (nasopharyngeal OR oropharyngeal OR sputum OR swab OR sample OR saliva OR salivary)
Limits: December 2019

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 o transmission of infection by pre-symptomatic or asymptomatic persons wearing masks o 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.

Review question 12: Is performing AGPs on patients without clinical features of viral respiratory tract infections associated with airborne transmission to health care professionals?

Table 10: PICOS questions for review question 12 (a) What is the evidence that performance of AGPs on patients without clinical features of viral respiratory tract infection at the time of the procedure is associated with airborne transmission of respiratory viruses to healthcare professionals? (b) What is the evidence that performance of AGPs on individuals without clinical features of viral respiratory tract infection at the time of the procedure, is associated with generation of potentially infectious aerosols?

(a)	
Population	HCPs performing AGPs on patients with no clinical features of viral respiratory tract infection* at the time of the procedure. AGPs included are limited to higher risk procedures involving the respiratory system namely: tracheal intubation, manual ventilation before intubation, non-invasive ventilation tracheotomy and other intubation related procedures, and AGPs used in dental, maxillofacial and otolaryngology surgery.
Exposure	HCPs performing an AGP on patients with no clinical features of viral respiratory tract infection at the time of the procedure.
Controls	HCPs performing AGPs on patients with a diagnosis of viral respiratory tract infection at the time of the procedure. HCPs performing procedures other than AGPs.
Outcome	Infection rate in HCPs. Risk of transmission from patient to HCP.
Study design	**Include:** Reviews, cross-sectional studies, prospective or retrospective cohort, case-control studies.
(b)	
Population	Patients and people with no clinical features of viral respiratory tract infection* at the time they are undergoing an AGP procedure.

	AGPs included are limited to higher risk procedures involving the respiratory system namely: tracheal intubation, manual ventilation before intubation, non-invasive ventilation tracheotomy and other intubation related procedures, and AGPs used in dental, maxillofacial and otolaryngology surgery.
Exposure	Performance of an AGP on patients and people in any setting.
Comparator	Baseline (before AGP) air sample.
Outcome	**Primary:** Detection of viable virus in generated aerosols. **Secondary:** Molecular detection of viral material in generated aerosols.
Study design	**Include:** Reviews, experimental studies with human subjects **Exclude:** Studies with animals and simulations without human subjects.

* Viral respiratory tract infection caused by, for example SARS-CoV2, SARS-CoV1, MERS-CoV, influenza, respiratory syncytial virus (RSV), measles virus, mumps virus, rubella, varicella zoster, adenoviruses and rhinoviruses.

Review question 13: What is the diagnostic accuracy of tests for the detection of SARS-CoV-2 using salivary clinical samples compared with nasopharyngeal, oropharyngeal or lower respiratory tract clinical samples?

Table 11: PICOS question for review question 13 - What is the diagnostic accuracy of tests for the detection of SARS-CoV-2 using salivary clinical samples compared with nasopharyngeal, oropharyngeal or lower respiratory tract clinical samples?

Population	Patients (any age) tested for COVID-19 ▪ Categorised as paediatric (aged <18 years) and adult (aged ≥18 years), where possible
Index test	▪ Salivary sample*
Reference test	▪ Nasopharyngeal and/ or Oropharyngeal sample* ▪ Lower respiratory tract sample (for example bronchoalveolar lavage or expectorated sputum)*
Outcome	Any measure reflective of diagnostic accuracy, including: ▪ Rates of detection or non-detection ▪ Sensitivity ▪ Specificity ▪ Positive predictive value ▪ Negative predictive value ▪ Likelihood ratio ▪ Area under the Receiver Operating Curve ▪ Diagnostic odds ratio Any measure of influencing factors beyond diagnostic accuracy, including: ▪ Adequate/sufficient sample ▪ Test spoilage rate ▪ Patient and/or provider acceptability ▪ Cost per unit test
Study design	▪ Diagnostic accuracy studies ▪ Cross-sectional studies ▪ Prospective or retrospective cohort studies ▪ Case series

*With polymerase chain reaction (PCR) testing

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 11 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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