The evidence on transmission dynamics of COVID-19: protocol for a series of Systematic Reviews

Protocol for a living evidence review (Version 3: 1 December 2020)

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Keywords

COVID-19; SARS-CoV-2; Transmission.

This protocol has been replaced as the number of reviews has increased and as the evidence has emerged. Protocols have been modified for systematic reviews on the detection and transmission of SARS-CoV-2. The transmission areas include airborne, contact and droplet, orofecal, vertical, fomite and asymptomatic and presymptomatic transmission. We also study transmission on aircraft and cruise ships and the relationship of viral cultures to PCR thresholds. Protocols are regularly updated and outputs recorded at https://www.cebm.ox.ac.uk/research/transmission-of-sars-cov-2

Updated protocols are made available: Transmission of SARs-COV-2: Updated Protocols for a series of systematic reviews. figshare. Preprint. https://doi.org/10.6084/m9.figshare.19229754.v3

Background

COVID-19 is a new disease, distinct from other diseases caused by coronaviruses, such as Severe Acute Respiratory Syndrome (SARS) and Middle East Respiratory Syndrome (MERS). The SARS-CoV-2 virus spreads rapidly. At present, there are no therapeutics or vaccines proven to treat or prevent COVID-19, although national governments, WHO and partners are working urgently to coordinate the response and rapid development of prevention, control and management measures on many fronts.

The overarching aim of the WHO's global Strategic Preparedness and Response Plan for COVID-19[1] is to control COVID-19 by suppressing transmission of the virus and preventing associated illness and death. However, transmission of the SARS-CoV-2 virus and the disease it causes is poorly understood, and public health measures for restricting transmission are based on limited information with relatively few systematic reviews on the transmission of the SARS-CoV-2 virus available.

Given the novelty of the disease and its cause, early reliance on models of spread is based on what is known of the dynamics of other respiratory infections, especially those due to other coronaviruses and influenza. One of the most important aspects of these uncertainties regards the modes and circumstances of transmission of newly identified agents. As a result, research is ongoing throughout the world across various disciplines with the aim of understanding SARS-CoV-2 modes of transmission, complemented with rapid publications. As a result, there is a need to continuously and systematically conduct reviews of publicly available studies with the latest knowledge from publications to inform WHO recommendations using the most up-to-date information.

Objectives

Objectives are to provide a rapid summary and evaluation of relevant data on transmission of SARS-CoV-2, report important policy implications, and highlight areas of research urgently needed. These transmission areas include airborne, contact and droplet, orofecal, vertical, fomite and other modes such as urine and blood and body fluids.

[1] Operational planning guidance to support country preparedness and response. Geneva: World Health Organization; 2020
https://www.who.int/publications/i/item/draft-operational-planning-guidance-for-un-country-teams

Modes of transmission for SARS-CoV-2[2] [3]

Respiratory droplets are >5-10 µm in diameter. Respiratory droplets that include virus can reach the mouth, nose or eyes of a susceptible person and can result in infection.

- Respiratory droplets <5µm in diameter are referred to as droplet nuclei or aerosols. Airborne transmission is the spread of an infectious agent caused by the dissemination of aerosols that remain infectious when suspended in air over long distances and time.
- Close or direct contact transmission occurs with an infected person who has respiratory symptoms. ● Respiratory secretions or droplets can contaminate surfaces and objects, creating fomites (contaminated surfaces).
- Orofecal transmission occurs where the virus in fecal particles can pass from one person to the mouth of another. Main causes include lack of adequate sanitation and poor hygiene practices. Fecal contamination of food is another form of orofecal transmission.
- Intrauterine/ mother to child transmission of SARS-CoV-2 from infected pregnant women to their fetuses (vertical transmission).
- Bloodborne or body fluid transmission.

Subgroups:

Where feasible will assess transmission outcomes by setting:healthcare facilities, community settings and the environment. We will report the evidence from studies with the results of reverse transcriptase polymerase chain reaction (RT-PCR) where reported by cycle threshold, time from symptom onset and live culture of SARS-CoV-2 by transmission mode. Evidence from studies comparing culture with other means of diagnosis is not usually mode of transmission-specific. Updates of the culture review will be carried out alongside and in parallel with mode of transmission study extraction for all modes. **Methods**

Search Strategy

The following electronic databases are searched, with searches being updated approximately each month starting from 1 December 2020 with screening every three months unless stated otherwise: LitCovid, medRxiv, Google Scholar and the WHO Covid-19 database. Search terms are Covid-19, SARS-CoV-2, transmission, and appropriate synonyms. The reference lists of included studies are searched for additional relevant studies.

Priorities for searching will be agreed with the study funder.

Study inclusion and exclusion

Eligible studies are on any potential mode of transmission, including droplet, airborne, fomite, fecal-oral, bloodborne, vertical or other. Studies can be observational including case series, ecological, or prospective;

[2] Transmission of SARS-CoV-2: implications for infection prevention precautions: https://www.who.int/news-room/commentaries/detail/transmission-of-sars-cov-2-implications-for-infection-prevention-precautions

[3]Infection Prevention and Control of Epidemic-and Pandemic-prone Acute Respiratory Infections in Health Care. Geneva: World Health Organization; 2014 (available at https://apps.who.int/iris/bitstream/handle/10665/112656/9789241507134_eng.pdf;jsessionid=41AA684FB64571CE8D8A453C4F2B2096?sequence=1).

[4]Jefferson T; Spencer EA; Brassey J; Heneghan C. Viral cultures for COVID-19 infectious potential assessment – a systematic review. Clinical Infectious Diseases 2020 (in press).

or interventional including randomised trials and clinical reports, outbreak reports, case control studies, experimental studies, non-predictive modelling.

Studies on factors influencing transmission are included, such as location settings, meteorological or immunological factors. Studies incorporating models to describe observed data are included. Studies reporting solely predictive modelling are excluded.

Data extraction

Study data are extracted into data extraction templates Table 1 (study characteristics) and Table 2 (methodological quality of studies) and Table 3 (summary of main findings). References are included in alphabetical order as a webappendix that facilitates updating. We follow PRISMA reporting guidelines as [5] indicated for systematic or scoping reviews where applicable (PRISMA checklist) Extraction is performed by one author and checked by a second author. Where there is disagreement, a third author arbitrates.

Quality assessment

Included studies quality is assessed based on a modified Quadas-2 tool using five criteria: (1) a clearly defined setting; (2) demographic characteristics or sampling procedures adequately described; 3) follow-up duration sufficient for the outcomes; (4) the transmission outcomes assessed adequately; (5) main biases that are threats to validity taken into consideration. Quality assessment is performed by one author and checked by a second author. In the case of disagreement a third author arbitrates, or for culture *Data synthesis and reporting*

Outcomes are specified within each review. We summarise data narratively and report the outcomes as stated in the paper, including quantitative estimates where feasible and relevant. We report the detection of a live culture of SARS-CoV-2 when reported (see also *sub groups*). Where possible, compatible datasets may be pooled for meta-analysis. We may write to authors for clarification of data, and also report research and policy implications.

Continual data release

Summary descriptions of important relevant research papers identified are summarised in the tracker and corresponding folders in an ongoing manner. As important new data accumulates, we produce a report as an individual rapid review and aim to make all our work available by depositing the review findings on the Oxford Research Archive.[6]

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[5] Tricco AC, Lillie E, Zarin W et al. PRISMA extension for scoping reviews (PRISMA-ScR): checklist and explanation. Ann Intern Med. 2018,169(7):467-473. doi:10.7326/M18-0850
[6] The Oxford Research Archive. Website. https://ora.ox.ac.uk Accessed 5 October 2020.