

COVID-19: The burning questions

Virus transmission, treatment options and long-term immunity are priorities for systematic reviews.

The Systematic and living evidence map of COVID-19 provides an overview of scientific publications categorized in detailed subgroups, providing quick access to specific topic-relevant publications. This makes it easier to produce systematic reviews. The most important questions to answer vary according to whom you ask.

What are the treatment options?

– One of the critical questions is how patients with COVID-19 should be treated and what treatment options should be made available, says Ane-Kristine Finbråten, MD, PhD, junior doctor at the Department of Medicine, Lovisenberg Diaconal Hospital in Oslo.



**Ane-Kristine
Finbråten**

long-term damage after a COVID-19 infection. How does COVID-19 affect the lungs, heart, brain, liver, and other organs in the long run?

COVID-19 is a self-limiting disease in most cases, but some patients become severely ill. What are the factors that determine a worst case scenario, the absolute worst clearly being mortality? Which patients are at risk of developing symptoms that worsen over the course of the disease, and how can these patients be identified? There is a rapid need for prognostic biomarkers. Another important aspect is the possible

Risks and benefits of ICU interventions

– There are several clinically relevant questions not answered by current evidence, says Jon Henrik Laake, MD, PhD, anesthesiologist and senior consultant, Oslo University Hospital.



Jon Henrik Laake

also missing links in the comprehensive management of these patients.

– Oxygen and mechanical ventilation are the only therapeutic options supported by any degree of evidence in COVID-19 patients but there are many knowledge gaps even here. Among these, are the risks and benefits of early vs late intubation, of high-flow nasal cannula and/or non-invasive ventilation vs standard oxygen therapy and a series of other questions related to intensive care. Rehabilitation and after-care are



Frode Forland

media. How many are infected? How many people have had the disease without knowing it? How many need hospitalization? How many will die? And how many will recover and be immune?

We also need better understanding of how the virus is transmitted. How important is asymptomatic and pre-symptomatic spread? And we need to know more about the effects of the different measures that are taken at the individual and societal level to prevent the spread of the virus.

The effects of measures taken

– Right now it seems most important to get rapid and reliable evidence on the prevalence of the disease, says Frode Forland, MD, Specialist Director Infectious Diseases and Global Health at the Norwegian Institute of Public Health. He is part of the leadership group coordinating the corona-outbreak in Norway and is responsible for evidence updates, research and

Immunity after infection?

– The decision of opening up or closing further down society, has direct consequences on the life and death of the inhabitants. Besides, the health consequences of a prolonged lock down on key economic functions of society, are dire. Therefore, the most important questions now are the actual number of infected citizens in affected societies at each stage of the pandemic,



Are Breen

and to what extent immunity is achieved after an infection, says Are Breen, MD, PhD, editor-in-chief at The Journal of The Norwegian Medical Association.

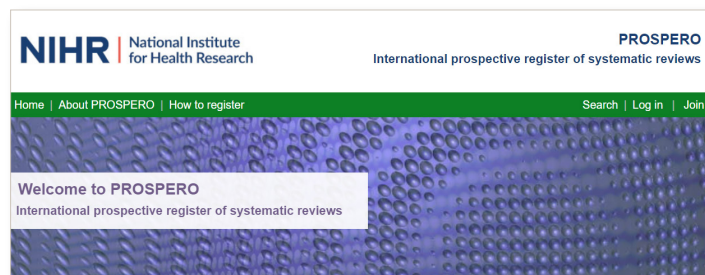
Systematic reviews are needed

Clinicians and policy makers do not have the time to critically read all the original articles published, and systematic reviews may be the best source of evidence.

Systematic reviews underway

Does the profile of the reviews on COVID-19 under production reflect the need for evidence? So far clinical and epidemiological features dominate. Only a few systematic reviews on preventive issues are registered.

As the pandemic develops an increasing number of studies are being published. Many of the individual studies are still small with preliminary results and systematic synthesis of the available evidence is strongly needed. The topics for systematic reviews on COVID-19 under production should ideally reflect the information needed for decision makers.



An indicator of the development in this area and the topics for reviews, can be found in international databases of systematic review protocols. [PROSPERO](#) is such a data base maintained by the Centre for Reviews and Dissemination at the University of York, UK. Researchers around the world are encouraged to register their systematic reviews in PROSPERO when they start, and to record their progress.

Huge spike in April

Until March just two systematic reviews on COVID-19 were registered in PROSPERO in 2020, one on traditional Chinese herbal medicine and one on “the availability, quality and inclusivity of supportive care guidelines in the management of high consequence infectious disease”. [COVID-19 was declared a pandemic](#) 11 March 2020 and over the month of March another 80 reviews were registered.

During April the number of registered systematic reviews on COVID-19 increased week by week. So, by the end of April, a total of 661 systematic reviews were registered.

Clinical and epidemiological features

About half of all registered reviews have focused on the epidemiological and clinical features of COVID-19. This includes prevalence, clinical characteristics, risk factors for severity and mortality, and the long-term outcomes

for individuals with the disease. Studies on diagnostic issues include laboratory analysis, coagulation parameters and radiological imaging.

Several reviews relate to specific patient groups, e.g. children and pregnant women. Others concentrate on comorbidities, e.g. heart disease, obesity, diabetes and neurological disorders.

Treatment

One third of all registered systematic reviews are related to the treatment of infected patients. The following three review groups are approximately the same size and include:

- Reviews on the effect of drugs, like antiviral agents (e.g. remdesivir, lopinavir, ritonavir) and other drugs (e.g. chloroquine, corticosteroids)
- Reviews on the efficacy of traditional Chinese medicine, including herbal medicine formulas
- Other sorts of treatments; oxygenation strategies, ventilation, ICU-treatment, rehabilitation plans etc.

Societal effects

Around one in ten ongoing reviews are studying the mental health and psychosocial problems among healthcare workers and the general population, and coping with the pandemic on a societal level. Among these reviews are also studies on the indirect effect of the corona pandemic on other patient groups (e.g. patients with cancer and waiting for elective surgery), and the information coverage in the media.

Few reviews on prevention

The PROSPERO database includes only a few review protocols on the prevention of Coronavirus infection and public health issues. Among these are studies on contact tracing; the efficacy of face masks; and the effect of water, sanitation and hygiene (WASH) interventions that are commonly implemented as part of emergency response activities (i.e. in response to disease outbreaks) to reduce the risk of disease transmission in a variety of settings particularly in Low and Middle Income Countries. Other examples are reviews on the effects of temperature and humidity on the spread of COVID-19, and ways to organize primary health care services.

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