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New and updated Cochrane summaries for COVID-19

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Does quarantine, alone or in combination with other public health measures, control coronavirus (COVID-19)?

How effective is screening for COVID-19?

Can travel-related control measures contain the spread of the COVID-19 pandemic?

Does the use of antimicrobial mouthwash or nasal spray by people who are not actively suspected of having COVID-19 - or by their healthcare workers - protect their healthcare workers when they undertake 'aerosol-generating procedures' on them?

What are the benefits and risks of healthcare workers using antimicrobial mouthwashes or nasal sprays to protect themselves when they treat people with COVID-19?

What are the benefits and risks of people with COVID-19 using antimicrobial mouthwashes or nasal sprays to improve their health and protect healthcare workers who treat them?

How accurate is chest imaging for diagnosing COVID-19?

Is plasma from people who have recovered from COVID-19 an effective treatment for people with COVID-19?

Does quarantine, alone or in combination with other public health measures, control coronavirus (COVID-19)?

Authors: Nussbaumer-Streit B, Mayr V, Dobrescu AI, Chapman A, Persad E, Klerings I, Wagner G, Siebert U, Ledinger D, Zachariah C, Gartlehner G

Background

Coronavirus disease 2019 (COVID-19) is caused by a new virus that has spread quickly throughout the world. Most infected people either experience no symptoms or suffer mild, flu-like symptoms, but some become seriously ill, and may die.

There is no vaccine (a medicine that stops people catching a specific disease) for COVID-19, so other ways of

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slowing its spread are needed. One way of controlling the disease is quarantine. This means separating healthy people from other healthy people, who may have the virus after being in close contact with an infected person, or because they have returned from an area with high infection rates. Similar recommendations include isolation (like quarantine, but for people who tested positive for COVID-19) and physical distancing (people without symptoms keep a distance from each other).

What did we want to find out?

We wanted to find out whether and how effectively quarantine stops COVID-19 spreading and if it prevents death. We wanted to know if it was more effective when combined with other measures, and how much it costs.

Study characteristics

COVID-19 is spreading rapidly, so we needed to answer these questions as quickly as possible. This meant we shortened some steps of the normal Cochrane Review process. Nevertheless, we are confident that these changes do not affect our overall conclusions.

We looked for studies that assessed the effect of any type of quarantine, anywhere, on the spread and severity of COVID-19. We also looked for studies that assessed quarantine alongside other measures, such as isolation, physical distancing or school closures. COVID-19 is a new disease, so, to find as much evidence as possible, we also looked for studies on similar viruses, such as SARS (severe acute respiratory syndrome) and MERS (Middle East respiratory syndrome).

Studies measured the number of COVID-19, SARS or MERS cases, how many people were infected, how quickly the virus spread, how many people died, and the costs of quarantine.

Key results

We included 51 studies. Thirty-two studies focused on COVID-19, 14 on SARS, three on SARS plus other viruses, and two on MERS. Most studies combined existing data from multiple sources and assumptions to create a model (a simulation) for predicting how events might occur over time, for people in different situations (called modelling studies). Four COVID-19 studies observed the effects of quarantine (observational studies) on 6064 individuals in China, Greece and Singapore. Twenty-eight COVID-19 studies simulated outbreaks in Algeria, China, Canada, Italy, Kazakhstan, Nepal, UK, USA, Singapore, South Korea, on the cruise ship Diamond Princess, and in a general population. Four studies looked back on the effect of quarantine on 178,122 people involved in SARS and MERS outbreaks. The remaining 15 studies modelled SARS and MERS outbreaks.

The modelling studies all found that simulated quarantine measures reduce the number of people with COVID-19 and the number of deaths. With quarantine, estimates showed a minimum reduction in the number of people with COVID-19 of 44%, and a maximum reduction of 96%. Similarly, with quarantine, estimates of the number of deaths showed a minimum reduction of 31%, and a maximum reduction of 76%. Combining quarantine with other measures, such as closing schools or physical distancing, may be more effective at reducing the spread of COVID-19 than quarantine alone. The SARS and MERS studies agreed with the studies on COVID-19.

Two SARS modelling studies assessed costs. They found that the costs may be lower when quarantine measures start earlier.

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Reliability of the evidence

We are uncertain about the evidence we found for several reasons. The observational studies on COVID-19 did not include a comparison group without quarantine. The COVID-19 studies based their models on limited data and made different assumptions about the virus (e.g. how quickly it would spread). The other studies investigated SARS and MERS so they only provide indirect evidence.

Conclusion

Despite limited evidence, all the studies found quarantine to be important in reducing the number of people infected and the number of deaths. Results suggest that quarantine was most effective, and cost less, when it started earlier. Combining quarantine with other prevention and control measures may have a greater effect than quarantine alone.

This review includes evidence published up to 23 June 2020.

How effective is screening for COVID-19?

Authors: Viswanathan M, Kahwati L, Jahn B, Giger K, Dobrescu AI, Hill C, Klerings I, Meixner J, Persad E, Teufer B, Gartlehner G

Why does screening matter?

Screening aims to identify a condition in people who may not be showing any symptoms. Some people may have the COVID-19 virus but appear healthy or have only mild symptoms. It is important to identify infected people so they can stay away from others and seek appropriate care. Incorrectly identifying COVID-19 in healthy people could lead to unnecessary self-isolation and further tests. Incorrectly identifying no infection in infected people could spread the virus.

Screening for COVID-19 can include temperature checks, or asking about international travel or contact with COVID-19 cases, or rapid tests. Screening can occur over the telephone, online, or in person, in homes, clinics, workplaces, airports or schools.

What did the review study?

We wanted to identify:

· the benefits and negative effects of screening apparently healthy people for COVID-19 infection;

· whether screening can identify those with and without the virus correctly.

To answer these questions rapidly, we shortened some steps of the normal Cochrane Review process. We are confident these changes do not affect our overall conclusions.

What did we do?

We looked for studies that screened people who had not sought care for potential COVID-19 symptoms.

This review includes evidence up to May 2020.

Key results

We found 22 studies; 17 assessed people (cohort studies) and five were computer-generated models (modelling studies). Studies took place in USA, Europe, and Asia.

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Benefits and negative effects

Two modelling studies reported on the benefits and negative effects of screening. One suggested that asking about symptoms at airports may slightly slow, but not stop, the importation of infected people.

Another model reported that weekly or biweekly screening of healthcare workers may reduce transmission to patients and other healthcare workers in emergency departments.

No studies reported on negative effects of screening.

Identification of infected people

Seventeen cohort studies and three modelling studies reported on whether screening can correctly identify those with and without the virus. Studies varied widely in the baseline level of COVID-19, settings, and methods. All cohort studies compared screening strategies to a 'gold standard' test called RT-PCR.

Cohort studies

All screening strategies (17 studies, 17,574 people), incorrectly identified:

· between 20 and 100 out of 100 infected people as healthy;

· between 0 and 38 people out of 100 healthy people as infected

Asking about symptoms (13 studies, 16,762 people), incorrectly identified:

· between 40 to 100 out of 100 infected people as healthy

· between 0 to 34 out of 100 healthy people as infected

Temperature measurements, *asking about international travel*, *exposure to known infected people* and *exposure to known or suspected infected people* (6 studies, 14,741 people), incorrectly identified**:**

· between 77 and 100 out of 100 infected people as healthy

· between 0 and 10 out of 100 healthy people as infected

Asking about symptoms plus temperature measurement (2 studies, 779 people), incorrectly identified:

· between 31 and 88 out of 100 infected people as healthy

· between 0 to 10 people out of 100 healthy people as infected

There was insufficient evidence from two small studies on rapid laboratory tests and repeated symptom assessment to tell how accurate they were in identifying healthy and infected people.

Modelling studies

Three studies modelled entry and exit screening in airports. One study missed 70% of infected travellers. Another detected 90% of infections, but used an unrealistic scenario. The third used very unreliable methods so we cannot use evidence from this study.

How confident are we in the results of the studies?

Our confidence in these findings is limited because most studies did not describe their screening methods clearly, some found very few cases of infections and the types of participants and settings varied greatly, making it difficult to judge whether the results apply broadly.

Authors' conclusions

One-time screening in apparently healthy people is likely to miss people who are infected. We are unsure whether combined screenings, repeated symptom assessment, or rapid laboratory tests are useful.

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As more people become infected, screening will identify more cases. However, because screening can miss people who are infected, public health measures such as face coverings, physical distancing, and quarantine for those who are apparently healthy, continue to be very important.

Can travel-related control measures contain the spread of the COVID-19 pandemic?

Authors: Burns J, Movsisyan A, Stratil JM, Coenen M, Emmert-Fees KMF, Geffert K, Hoffmann S, Horstick O, Laxy M, Pfadenhauer LM, von Philipsborn P, Sell K, Voss S, Rehfuess E

What are travel-related control measures?

To contain the spread of COVID-19, numerous countries have implemented control measures related to international travel. These include:

· complete closure of borders (i.e. a total ban on any border crossings);

· partial travel restrictions (e.g. restrictions on air travel only, or restrictions on travellers from certain countries);

· entry or exit screening (e.g. when travellers are asked about symptoms, examined physically, or tested for infection when leaving or entering a country);

· quarantine of travellers (e.g. when travellers have to stay at home or at a specific place for some time after crossing a border).

Some countries implemented similar travel-related control measures during the recent outbreaks of two related diseases, severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS).

What did we want to find out?

We wanted to find out how effective travel-related control measures are in containing the COVID-19 pandemic. We also wanted to know about the costs of the measures and what effect they have on healthcare and other resource use, as well as potential negative effects, such as feeling isolated.

What we did

We searched for studies on the effects of travel-related control measures on the spread of COVID-19, as well as on SARS and MERS to provide supporting information. Studies had to report how many cases (people with infection) the measures prevented or detected, and whether the measures changed the course of the epidemic. Studies could include people of any age, anywhere. They could be of any design including studies that used 'real-life' data (observational studies) or hypothetical data from computer-generated simulations (modelling studies).

We included studies published up to 26 June 2020.

What we found

We found 25 studies on COVID-19, 10 on SARS and one on both SARS and MERS. Studies took place across the world except for Africa and the eastern Mediterranean.

Twelve studies (11 modelling studies, 1 observational study) on COVID-19 found that restricting cross-border travel at the beginning of an outbreak may reduce new cases by a minimum of 26% to a maximum of 90%, may reduce the number of deaths, may reduce the time to an outbreak by between 2 to 26 days, and may reduce

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the spread and risk of an outbreak. There was also a reduction in imported or exported cases and in growth of the epidemic.

We found 12 studies (11 modelling studies, 6 observational studies) on entry or exit screening, with and without quarantine, to contain the spread of COVID-19. Based on data from three modelling studies, there may be a delay in the time to an outbreak, and between 10% to 53% of infected travellers would be detected. However, the results from the observational studies varied considerably, and we are uncertain about the proportion of people identified accurately as having COVID-19 from these studies.

Only one modelling study examined quarantine measures for COVID-19. It found fewer new cases due to imported cases where 14-day quarantine was in place.

How reliable are these results?

Our confidence in these results is limited for several reasons. Most studies were not based on real-life epidemics but on mathematical predictions. Their results depended on the assumptions that they made, not on real-life data. Also, the studies were very different from each other and their results would probably vary according to the stage of the epidemic, the amount of cross-border travel, other measures undertaken locally, and the extent of implementation and enforcement. Results of entry and exit screening studies might vary according to the screening method used and the level of infection among travellers. Also, some studies were published as 'preprints', which means they did not undergo the rigorous checks of most peer-reviewed studies.

What this means

Overall, travel-related control measures may help to limit the spread of disease across national borders. Cross-border travel restrictions are probably more effective than entry and exit screening. Screening is likely to be more effective if combined with other measures, such as quarantine and observation. We found very little information on travel-related quarantine as a stand-alone measure and no information on costs or negative effects.

Does the use of antimicrobial mouthwash or nasal spray by people who are not actively suspected of having COVID-19 - or by their healthcare workers - protect their healthcare workers when they undertake 'aerosol-generating procedures' on them?

Authors: Burton MJ, Clarkson JE, Goulao B, Glenny A-M, McBain AJ, Schilder AGM, Webster KE, Worthington HV

Why is this question important?

COVID-19 is an infectious disease caused by the SARS-CoV-2 virus. Most people infected with COVID-19 develop a mild to moderate respiratory illness, and some may have no symptoms (asymptomatic infection). Others experience severe symptoms and need specialist treatment and intensive care.

COVID-19 spreads from person to person primarily through droplets that are produced when an infected person coughs, sneezes or talks. A person can also become infected by touching a surface or object that has viral droplets on it, and then touching their own mouth or nose.

Some people with COVID-19 do not have any symptoms, therefore they might not be known to be or suspected of being infected. However, they might still be able to pass the infection on to others. This means that healthcare workers who are treating them may be at risk of catching the infection. Risk of infection may be particularly high when healthcare workers undertake 'aerosol-generating procedures', which are medical

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procedures that cause the patient to produce many small droplets. For example, people who have surgery under general anaesthesia, or people with a lung disease that makes breathing difficult (such as pneumonia), may need to be placed on a ventilator (artificial breathing machine) to help them breathe. This requires a healthcare worker to insert a tube through the patient's mouth, into their airway – a procedure during which many small droplets are likely to be produced by the patient. Similar droplets can be produced during routine dental procedures, such as drilling or scaling of teeth.

Patient or healthcare worker use of antimicrobial mouthwash (to rinse the mouth) or nasal spray (sprayed into the nose) might help to protect healthcare workers against infection by COVID-19. Antimicrobial mouthwash and nasal spray are liquids that kill or stop the growth of micro-organisms such as viruses or bacteria.

As with any medical treatment, antimicrobial mouthwash and nasal spray have potential risks as well as benefits. It is possible that using mouthwash or nasal spray could cause a variety of unwanted (adverse) effects, including irritation, allergic reactions or loss of smell. It may also remove micro-organisms from the mouth or nose that are useful for protecting the body against infection.

We set out to assess the benefits and risks of self-administration of antimicrobial mouthwashes and nasal sprays by patients without a known or suspected COVID-19 infection, or the healthcare workers who treat them with aerosol-generating procedures, by reviewing the research evidence.

How did we search for evidence?

Our team of researchers searched the medical literature for studies that compared the effects of patients or healthcare workers self-administering any antimicrobial mouthwash or nasal spray against using no treatment, water or a salt solution.

What did we find?

We found no completed, or ongoing, studies to include in this review.

What does this mean?

There is currently no evidence relating to the benefits and risks of healthcare workers' or patients' use of antimicrobial mouthwashes or nasal sprays to protect healthcare workers who undertake aerosol-generating procedures on patients without a known or suspected COVID-19 infection.

We need studies to be conducted so that we can answer this important clinical question.

How-up-to date is this review?

We last searched for evidence on 1 June 2020. This review covered research that was available up to that date, but did not consider any evidence that may have been produced since then.

What are the benefits and risks of healthcare workers using antimicrobial mouthwashes or nasal sprays to protect themselves when they treat people with COVID-19?

Authors: Burton MJ, Clarkson JE, Goulao B, Glenny A-M, McBain AJ, Schilder AGM, Webster KE, Worthington HV

Why is this question important?

COVID-19 is an infectious disease caused by the SARS-CoV-2 virus. Most people infected with COVID-19 develop a mild to moderate respiratory illness, and some may have no symptoms (asymptomatic infection). Others experience severe symptoms and need specialist treatment and intensive care.

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COVID-19 spreads from person to person primarily through droplets that are produced when an infected person coughs, sneezes or talks. A person can also become infected by touching a surface or object that has viral droplets on it, and then touching their own mouth or nose.

Healthcare workers who treat people with COVID-19 are at risk of becoming infected themselves. Self-administered use of an antimicrobial mouthwash (to rinse the mouth) or nasal spray (sprayed into the nose) might help healthcare workers to protect themselves against infection. Antimicrobial mouthwashes and nasal sprays are liquids that kill or stop the growth of micro-organisms such as viruses or bacteria.

As with any medical treatment, antimicrobial mouthwashes and nasal sprays have potential risks as well as benefits. It is possible that using mouthwashes or nasal sprays could cause a variety of unwanted (adverse) effects, including irritation, allergic reactions or loss of smell. They may also remove micro-organisms from the mouth or nose that are useful for protecting the body against infection.

To assess the benefits and risks of self-administered antimicrobial mouthwashes and nasal sprays for healthcare workers treating patients with COVID-19, we set out to review the research evidence.

How did we search for evidence?

Our team of researchers searched the medical literature for studies that compared the effects of any antimicrobial mouthwash or nasal spray used by healthcare workers against no treatment, water or a salt solution.

What did we find?

We found no completed studies to include in this review.

We found three studies currently in progress that aim to enrol nearly 700 participants. These studies are investigating the effects of povidone iodine (as a mouthwash and nasal spray), nitric oxide (as a mouthwash and nasal spray) and GLS-1200 nasal spray (though the content of this spray is unclear, and it may not turn out to include an antimicrobial agent).

Two of the studies are randomised controlled trials (clinical, real-life studies where people are randomly put into one of two or more treatment groups). This type of study provides the most robust evidence about the effects of a treatment. The third study is a non-randomised clinical study.

Only one of the ongoing studies specifically states that it will investigate adverse events. It is not clear whether this will include changes in the sense of smell or to the mix of micro-organisms that are present in the mouth or nose, and the consequences of these changes.

What does this mean?

There is currently no evidence relating to the benefits and risks of healthcare workers' use of antimicrobial mouthwashes or nasal sprays to protect themselves when they treat people with COVID-19.

Two randomised controlled trials and one non-randomised study are underway. Once these studies are completed, we will be able to analyse them and include their findings in an updated version of this review.

It is important that future studies collect and analyse information about adverse events. Only one of the ongoing studies we identified specifically states that it will investigate these. If future studies show a beneficial effect of mouthwashes and nasal sprays, it may not be a large effect (very few health interventions have large

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and dramatic effect sizes). It will only be possible to weigh up potentially small benefits against risks if any adverse events that occur are reported in studies.

How-up-to date is this review?

We last searched for evidence on 1 June 2020. This review covered research that was available up to that date, but did not consider any evidence that may have been produced since then.

What are the benefits and risks of people with COVID-19 using antimicrobial mouthwashes or nasal sprays to improve their health and protect healthcare workers who treat them?

Authors: Burton MJ, Clarkson JE, Goulao B, Glenny A-M, McBain AJ, Schilder AGM, Webster KE, Worthington HV

Why is this question important?

COVID-19 is an infectious disease caused by the SARS-CoV-2 virus. Most people infected with COVID-19 develop a mild to moderate respiratory illness, and some may have no symptoms (asymptomatic infection). Others experience severe symptoms and need specialist treatment and intensive care.

COVID-19 spreads from person to person primarily through droplets that are produced when an infected person coughs, sneezes or talks. A person can also become infected by touching a surface or object that has viral droplets on it, and then touching their own mouth or nose.

Administering antimicrobial mouthwash (to rinse the mouth) or nasal spray (sprayed into the nose) to people with COVID-19 might help them fight the infection and prevent them from infecting the healthcare workers who treat them. Antimicrobial mouthwash and nasal spray are liquids that kill or stop the growth of micro-organisms such as viruses or bacteria.

As with any medical treatment, antimicrobial mouthwash and nasal spray have potential risks as well as benefits. It is possible that using mouthwash or nasal spray could cause a variety of unwanted (adverse) effects, including irritation, allergic reactions or loss of smell. It may also remove micro-organisms from the mouth or nose that are useful for protecting the body against infection.

What did we aim to do?

To assess the benefits and risks for patients and healthcare workers of administering antimicrobial mouthwashes and nasal sprays to patients with COVID-19, we set out to review the research evidence. In particular, we wanted to investigate the effects of patient use of antimicrobial mouthwashes and nasal sprays on:

- patient deaths and healthcare needs – including the need for hospitalisation, artificial breathing support, dialysis or haemofiltration (treatments required when the kidneys do not work properly);
- new COVID-19 infections of healthcare workers;
- important adverse effects such as loss of smell;
- change in patients' COVID-19 viral load (the amount of virus in an infected person’s blood); and
- the viral load of droplets produced by patients.

How did we search for evidence?

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Our team of researchers searched the medical literature for studies that compared the effects of any antimicrobial mouthwash or nasal spray administered to patients with COVID-19 against no treatment, water or a salt solution.

What did we find?

We found no completed studies to include in this review.

We found 16 studies currently in progress that aim to enrol nearly 1250 participants. These studies are investigating a range of mouthwashes and nasal sprays.

Fourteen of the studies are randomised controlled trials (clinical, real-life studies where people are randomly put into one of two or more treatment groups). This type of study provides the most robust evidence about the effects of a treatment.

What does this mean?

There is currently no evidence relating to the benefits and risks of patients with COVID-19 using antimicrobial mouthwashes or nasal sprays.

Sixteen randomised controlled trials are underway. Once these studies are completed, we will be able to analyse them and include their findings in an updated version of this review.

It is important that future studies collect and analyse information about adverse events. Few of the ongoing studies we identified specifically state that they will investigate these. If future studies show a beneficial effect of mouthwashes and nasal sprays, it may not be a large effect (very few health interventions have large and dramatic effect sizes). It will only be possible to weigh up potentially small benefits against risks if any adverse events that occur are reported in studies.

How-up-to date is this review?

We last searched for evidence on 1 June 2020. This review covered research that was available up to that date, but did not consider any evidence that may have been produced since then.

How accurate is chest imaging for diagnosing COVID-19?

Authors: Salameh J-P, Leeflang MMG, Hooft L, Islam N, McGrath TA, van der Pol CB, Frank RA, Prager R, Hare SS, Dennie C, Spijker R, Deeks JJ, Dinnes J, Jenniskens K, Korevaar DA, Cohen JF, Van den Bruel A, Takwoingi Y, van de Wijgert J, Damen JAAG, Wang J, McInnes MDF

Why is this question important?

People with suspected COVID-19 need to know quickly whether they are infected, so that they can self-isolate, receive treatment, and inform close contacts. Currently, formal diagnosis of COVID-19 infection requires laboratory analysis of blood or nose and throat samples. The laboratory test, called RT-PCR, requires specialist equipment and takes at least 24 hours to produce a result. Further, RT-PCR is not completely accurate and a second RT-PCR or a different test may be required to confirm the diagnosis.

COVID-19 is a respiratory infection: people with COVID-19 may have a cough, may have difficulty breathing and in severe cases may have COVID-19 pneumonia. Clinicians use chest imaging tests to diagnose COVID-19 disease, when awaiting RT-PCR test results, for example, or when RT-PCR results are negative, and the person has COVID-19 symptoms.

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We wanted to find out how accurate chest imaging is in diagnosing COVID-19 disease in people with known or suspected infection.

What are chest imaging tests?

X-rays or scans produce an image of the organs and structures (heart, lungs and airways) in the chest. They can detect blockages, inflammation and excess fluid.

- X-rays (radiography) use a small amount of radiation to produce a 2-D image. They are usually carried out in hospitals using fixed equipment by a radiographer but may also be carried out using a portable machine.
- Computed tomography (CT) scans use a computer to merge multiple X-ray images taken from different angles to produce a 2-D image that can be converted to a 3-D image. They require highly specialised equipment and are carried out in hospital by a specialist radiographer.
- Ultrasound scans use high-frequency sound waves to produce an image. They can be carried out in hospital or other healthcare settings such as a doctor's surgery or clinic.

What did we do?

We searched for studies that assessed the accuracy of chest imaging to diagnose COVID-19 disease. Studies could include people with either suspected or confirmed COVID-19, based on the results of an RT-PCR or other test. Studies could be of any design and take place anywhere.

What did we find?

We found 84 studies with 8279 people. Studies included either only people with confirmed COVID-19 diagnosis (71 studies, involving 6331 people) or both suspected and confirmed COVID-19 (13 studies, involving 1948 people). Infection was mainly confirmed using RT-PCR.

The majority of studies evaluated chest CT. We found studies from all over the world; 78 studies took place in Asia.

Accuracy of chest imaging for diagnosing COVID-19 in people with confirmed infection

On average, chest CT correctly identified infection in 93% of people with confirmed COVID-19 (65 studies, 5759 people). Chest X-ray correctly identified infection in 82% of people with confirmed COVID-19 (nine studies, 682 people). Lung ultrasound correctly identified infection in 100% of people with confirmed COVID-19 (2 studies, 32 people).

Accuracy of chest imaging for diagnosing COVID-19 in people with suspected or confirmed infection

On average, chest CT correctly identified infection in 86% of people who were infected with COVID-19 (13 studies, 2346 people). However, it incorrectly identified infection in 82% of people who were not infected with COVID-19. We did not find any studies that reported data on lung ultrasound.

How reliable are the results?

Studies reported limited information about how they confirmed COVID-19 diagnosis, how they recruited participants, and they did not always use robust methods. Most studies only included people with a confirmed COVID-19 diagnosis, so we have little information about the ability of chest imaging to rule out COVID-19 in people who are not infected. Also, studies did not report any pre-existing respiratory conditions that might have affected their results. Finally, 25% of studies were published as preprints, which do not undergo the

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same rigorous checks as published studies. We cannot confidently draw conclusions based on the results from studies included in this review.

What does this mean?

The evidence suggests that chest CT and chest X-ray may be good tests for confirming COVID-19 diagnosis in people who have been diagnosed with COVID-19 infection using another test. However, CT scans may be less accurate in confirming or ruling out infection in people with only suspected COVID-19.

We plan to update this review regularly as more research becomes available.

How up-to-date is this review?

The evidence in this Cochrane Review is current to May 2020.

Is plasma from people who have recovered from COVID-19 an effective treatment for people with COVID-19?

Authors: Chai KL, Valk SJ, Piechotta V, Kimber C, Monsef I, Doree C, Wood EM, Lamikanra AA, Roberts DJ, McQuilten Z, So-Osman C, Estcourt LJ, Skoetz N

Coronavirus disease 2019 (COVID-19) is a highly infectious respiratory illness caused by a newly recognised type of coronavirus. Some people have severe infection, leading to hospitalisation, admission to intensive care or death. Currently, no vaccine or specific treatment is available.

People who have recovered from COVID-19 develop natural defences in their blood (antibodies). Antibodies are found in part of the blood called plasma. Plasma from blood donated from recovered patients, which contains COVID-19 antibodies, can be used to make two preparations. Firstly, convalescent plasma, which is plasma that contains these antibodies. Secondly, hyperimmune immunoglobulin, which is more concentrated, and therefore contains more antibodies.

Convalescent plasma and hyperimmune immunoglobulin have been used successfully to treat other respiratory viruses. These treatments (given by a drip or injection) are generally well-tolerated, but unwanted effects similar to those from standard plasma transfusion can occur.

What did we want to find?

We wanted to know whether plasma from people who have recovered from COVID-19 is an effective treatment for people with COVID-19, and whether this causes any unwanted effects.

Our methods

We searched major medical databases for clinical studies on treatment with convalescent plasma or hyperimmune immunoglobulin for people with COVID-19. Studies could be conducted anywhere in the world and include participants of any age, gender, ethnicity or disease severity.

The evidence is up to date to 19 August 2020.

Key results

We included 19 completed studies with 38,160 participants; 36,081 participants received convalescent plasma.

We found two randomised controlled trials (RCTs), with 189 participants; 95 participants received convalescent plasma. RCTs are clinical studies where people are randomly allocated to receive the treatment

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(intervention group) or to receive different or no treatment (control group). Methods used in RCTs are designed to produce the most reliable evidence.

We found eight studies that were not randomised but included a control group of participants who did not receive convalescent plasma (controlled NRSIs), with 2471 participants; 485 participants received convalescent plasma. Because of critical study limitations or missing data, we did not include these studies to evaluate the benefit of convalescent plasma.

The remaining nine studies were not randomised and did not include a control group (non-controlled NRSIs) but provided information about unwanted effects of convalescent plasma for 20,622 of the included participants.

To assess whether convalescent plasma is effective for COVID-19, we evaluated results from the RCTs. The control groups received standard care at the time of treatment without convalescent plasma. There was not enough evidence to determine whether convalescent plasma affected the risk of death at hospital discharge and our confidence in the evidence is low. Convalescent plasma may decrease the need for breathing support, but our confidence in the evidence is low.

To assess whether convalescent plasma causes unwanted effects, we also evaluated nine non-controlled NRSIs. We identified some serious unwanted effects, which could be related to convalescent plasma, including death, allergic reactions or respiratory complications. There was not enough evidence to determine whether convalescent plasma therapy causes serious unwanted events and our confidence in the evidence is low. None of the included studies reported effects on quality of life.

Certainty of the evidence

Our certainty (confidence) in the evidence was low or very low because there were only two RCTs and most studies did not use reliable methods to measure their results. Furthermore, participants received various treatments alongside convalescent plasma, and some had underlying health problems.

Conclusion

We are uncertain whether plasma from people who have recovered from COVID-19 is an effective treatment for people hospitalised with COVID-19 and whether convalescent plasma affects the number of serious unwanted effects. These findings could be related to the natural progression of disease, other treatments or to convalescent plasma. Our searches found 138 ongoing studies, of which 73 are randomised. This is the second update of our review, and we will continue to update this review.

If you have any questions or comments with regard to the above document please feel free to contact me.

Kind regards

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