



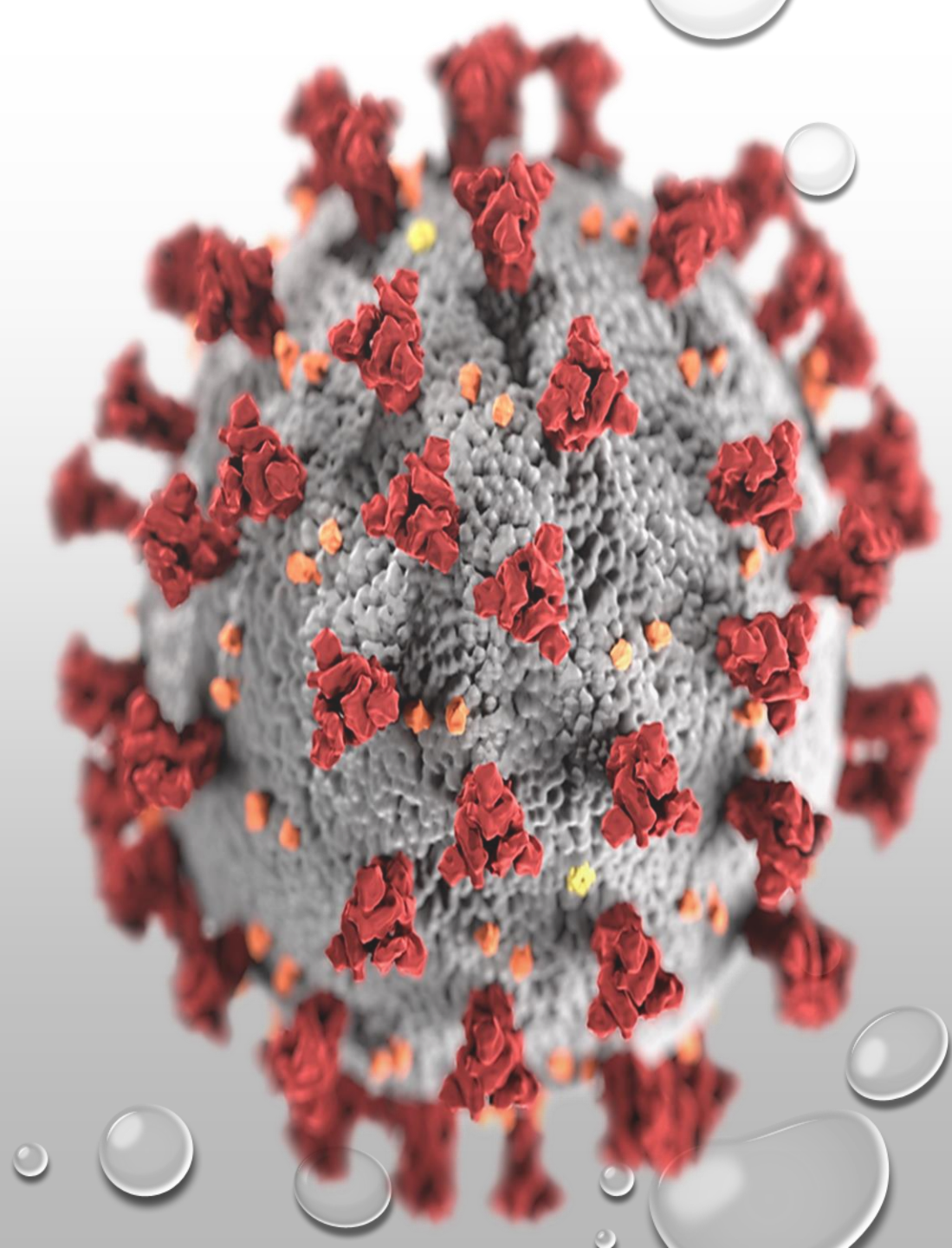
SOLIDARITY CLINICAL TRIAL FOR COVID-19 TREATMENT – A SYSTEMATIC REVIEW

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What is Coronavirus?

COVID-19 is an infectious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-COV-2), first identified in December 2019 in Wuhan, the capital of china's Hubei province and has since spread globally, resulting in the ongoing 2019-20 coronavirus pandemic.

The official names covid-19 were issued by the who on 11 February 2020. WHO chief Tedros Adhanom Ghebreyesus explained: CO for corona, VI for virus, D for disease and 19 for when the outbreak was first identified (31 December 2019).



What is Solidarity Trial?

- To increase the chances of success, WHO is facilitating interactions between 300 scientists, developers and funders to support coordination, and/or provide common platforms for working together to increase the likelihood that one or more safe and effective treatment/vaccines will soon be available to all for COVID-19. They called this study the “solidarity trial.”
- The trial was announced on 18 march 2020. This trial will compare four treatment options against standard of care, to assess their relative effectiveness against COVID-19.
- On 13 may 2020, ICMR has fast-tracked the roll out of global solidarity trial, to help find an effective treatment for COVID-19.



METHODOLOGY

I have conducted a systematic review to summarize and critically analyse all the published scientific articles regarding the COVID-19.

This review aims to provide the evidence on the effective treatment and the availability of vaccine of covid-19.

This can provide meaningful information for future research related to this topic and may support government decision-making on strategies to handle this public health emergency at the community, national, and international levels.

RATIONALE

To deal with COVID-19, WHO considered the need for speed and scale in the trial. The solidarity trial will help to reduce the time taken by 80%. This will help to facilitate the rapid worldwide comparison of unproven treatments and will overcome the risk of multiple small trials which not generate the strong evidence needed to determine the relative effectiveness of potential treatments. (who, Solidarity” clinical trial for COVID-19 treatments, 2020)

RESEARCH QUESTION →

How effective is the solidarity clinical trial for COVID-19?

OBJECTIVE {

To understand the solidarity trial.

To know the available treatment of COVID-19 and compare their effectiveness against COVID-19.

To know the availability of safe and effective vaccine for COVID-19.

Participation in Solidarity Trial

Over 400 hospitals in 35 countries are actively recruiting patients and nearly 3500 patients have been enrolled from 17 countries. Overall, over 100 countries have joined or expressed an interest in joining the trial, and WHO is actively supporting 60 of them with:

- Ethical and regulatory approvals of the WHO core protocol;
- Identification of hospitals participating in the trial;
- Training of hospital clinicians on the web-based randomization and data system;
- Shipping the trial drugs as requested by each participating country.

WHO is also inviting developers and companies to collaborate on ensuring affordability and availability of the treatment options if they prove effective.

Information is till 31 May 2020



THE FOUR TREATMENT OPTIONS AGAINST STANDARD OF CARE, TO ASSESS THEIR RELATIVE EFFECTIVENESS AGAINST COVID-19

Remdesivir	Chloroquine and Hydroxychloroquine	Lopinavir and Ritonavir	Interferon- β in combination with Lopinavir and Ritonavir
Manufactured to treat Ebola in 2014, it has since been used to treat MERS and SARS.	These 2 generic drugs are used to treat malaria and rheumatology conditions.	The combination (brand name – Kaletra) is a licensed treatment for HIV.	Interferon beta – 1a is used to treat multiple sclerosis.
In phase 3 clinical trial of remdesivir, hospitalized patients with advanced COVID-19, recovered 50 percent faster than similar patients who received placebo and half were	HCQ and CQ are primarily accepted as effective drugs for COVID-19. On 19 May 2020, Dr. M C Mishra, former director of AIIMS in Delhi said that “There have been reports	This combination started when there were only 500 COVID-19 cases worldwide. There is currently no strong evidence for the efficacy of lopinavir and ritonavir	UK-based Synairgen began the phase 2 and 3 trials of SNG001, a special inhalation formulation of interferon- β in patients with COVID-19.

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Remdesivir	Chloroquine and Hydroxychloroquine	Lopinavir and Ritonavir	Interferon- β in combination with Lopinavir and Ritonavir
discharged from the hospital within 2 weeks.	of some patients developing cardiac arrhythmias due to HCQ which can cause sudden cardiac death.”	in the treatment of COVID-19.	
US drug – maker Gilead Sciences had signed agreements allow the companies – Cipla, Hetero Labs, Jubilant Lifesciences, and Mylan and Ferozsons Laboratories, to manufacture remdesivir for distribution in 127 countries.	However, on 25 May the Executive Group of the trial has implemented a temporary pause of the hydroxychloroquine arm within the Solidarity Trial while the safety data is reviewed by the Data Safety Monitoring Board.	Studies are still ongoing, and there's still a possibility this combination could show some benefit. As with other antivirals, this drug would likely work better if given earlier in the disease course.	Also for this drug combination, the trial is ongoing to know its effectiveness to treat COVID-19.

How the Solidarity Trial works?

- Adults (age ≥ 18 years) with COVID-19 admitted to participant hospitals can join this study.
- Eligible patients will have to sign the consent to show they understand the possible risks and benefits of joining the study. The medical team responsible for each patient will check whether any of the study treatments would be unsuitable.
- After those checks, brief identifying details and any other conditions are digitally recorded for the patient, who is then randomly allocated to one of the study options:
 - Local standard of care,Or local standard of care plus one of
 - Remdesivir

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- Chloroquine or hydroxychloroquine
 - Lopinavir with ritonavir
 - Lopinavir with ritonavir plus interferon beta-1a.
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- Neither the patient nor the medical staff choose which of the study options a patient will receive, as a computer makes this allocation at random.
 - Critical anonymized information for the trial will only be collected at the randomization stage and when the patient is discharged or dies: which study drugs were given (and for how many days); whether ventilation or intensive care was received (and, if so, when it began), date of discharge, or date and cause of death while still in hospital.
 - Interim trial analyses are monitored by a global data and safety monitoring committee, which is an independent group of experts.

What other treatments are available?

There is currently no treatment specifically approved for COVID-19, and no cure for an infection, although experimental treatments are tested to see how effective they are. Examples of therapies used for these illnesses include:

- **Antiviral or Retroviral Medications** – Research for potential treatment is started in January 2020. and several antiviral drugs are in clinical trials.
- **Breathing support, such as Mechanical Ventilation** – Most cases of COVID-19 are not severe enough to require mechanical ventilation, but some of the cases are.
- **Steroids** – WHO and NIH do not oppose the use of NSAIDs, and the FDA also said that there is no evidence that NSAIDs worsen COVID-19 symptoms.
- **Blood plasma transfusions** – The convalescent plasma therapy aims at using antibodies from the blood of a recovered Covid-19 patient to treat those critically affected by the virus. The therapy can also use to immunise those at a high risk of contracting the virus such as health workers, families of patients and other high-risk contacts.

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Vaccine for COVID - 19

- For COVID-19, there are over 120 vaccines being developed across the world now, some from scratch, some from existing molecules developed for other diseases.
- There are currently more than 110 teams in contention, speeding up efforts to produce a ready vaccine. Some have reached the clinical trial stage; others have shown a little less than favorable results.
- A vaccine would normally take years, if not decades, to develop. But in this case, researchers hope to achieve the same amount of work in just a few months. Most experts think a vaccine is likely to become available by mid-2021.
- The same is the case with Indian vaccine, as experts say that it is still in the nascent stage and it will take a while before we see conclusive development. A lot of vaccines are in the development phase in India as well, and medicinal trials are also going on for treatment.

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- As of May 24, there were at least 10 vaccines in human trials, according to the WHO:

Moderna's RNA Vaccine: The Massachusetts-based biotech company Moderna Inc. has already successfully completed phase 1 trials of its vaccine candidate and is all set to begin the phase 2 trial on 600 healthy individuals in the month of July.

Pfizer-BNTECH vaccine : On 29 May Pfizer believes that a COVID-19 vaccine could be ready by the end of October 2020, reported the Times of Israel, citing Albert Bourla, the CEO of the firm. Pfizer is working with German firm BNTECH for several possible vaccines in Europe and the United States.

Oxford University and AstraZeneca Plc Vaccine: Their experimental vaccine was highly looked forward to ever since the trials began in April. Oxford scientists said a million doses of their COVID-19 vaccine could be ready as early as September.



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CanSino Biologics Inc and Beijing Institute of Biotechnology

Vaccine: They also proceed to the stage 2 of the study. CanSino makes its vaccine using a genetically modified cold-causing virus to carry the genetic material of the novel coronavirus, similar to the approach employed by oxford.

Wuhan Institute of Biological Products/Sinopharm: They had also reach to a phase II trial. They are developing an inactivated vaccine using non-living viruses, bacteria or other pathogens that have lost disease-producing capacity to stimulate the immune system to develop an immune response.

Beijing Institute of Biological Products/Sinopharm: They had entered phase II clinical trials. A vaccine could be ready for the market as early as the end of this year or early 2021, according to the May 29 post on Chinese social media platform WeChat.



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Sinovac: Sinovac started developing the inactivated vaccine against COVID-19 in January this year in collaboration with academic research institutes in China. On 31 May as per a Sky News report, Luo Baishan, a researcher at Sinovac, said, “it must be successful...99 per cent sure.” The company has reached stage 2 of its vaccine trial, with more than 1000 volunteers participating. The company is in preliminary talks to hold stage 3 trials – the final part of the process in the UK.

Novavax COVID-19 vaccine: On May 25, Novavax announced in a press release that it had begun Phase 1/2 trial of its COVID-19 vaccine candidate in Australia. The preliminary results of Phase 1 trial are expected in July 2020, after which Phase-2 trials will begin in multiple countries, including the US. In the meantime, Novavax has bought Czech republic-based Praha Vaccines, a unit of India's Cyrus Poonawalla Group, which also owns Serum Institute, in Pune.



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Institute of Medical Biology, Chinese Academy of Medical Sciences: They are developing the inactivated vaccine against Covid-19. Currently they are in the phase 1 trial of clinical evaluation.

Inovio Pharmaceuticals: Inovio Pharmaceuticals has reported promising data from the preclinical studies of its Covid-19 vaccine candidate, in mice and guinea pigs. The company expects to report preliminary safety and immune responses data from a Phase I clinical trial in June. Furthermore, a Phase II/III efficacy trial has been planned for launch in July/August, pending regulatory approval.



CONCLUSION

At the end of the report, I want to conclude that Solidarity Trial is a large international clinical trial to help find an effective treatment for COVID-19, launched by the WHO and partners.

Till now as per the WHO, there is no specific treatment for COVID-19. To manage the patients WHO recommended four treatment options against standard of care: Remdesivir, Chloroquine and Hydroxychloroquine, Liponavir/Ritonavir, and Liponavir/Ritonavir combined with Interferon beta.

The antiviral drug Remdesivir shows some positive result, it reduced the duration of recovery by 4 days. The phase 3 clinical trial of Remdesivir is started, said to be the final step in the process of the drug approval. However, WHO temporary pause the use of hydroxychloroquine within the solidarity trial on 25 May while the safety data is reviewed by the Data Safety Monitoring Board.

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For Lopinavir/Ritonavir and their combination with Interferon- β , the trial is ongoing and there is currently no strong evidence to prove their efficacy to treat COVID-19.

Patients are also managing with Antiviral or Retroviral medications, Mechanical Ventilation, Steroids and Blood plasma transfusions. The convalescent plasma therapy showed some improvement in patients' condition. Now, several countries are seriously looking at plasma therapy as a potential treatment for COVID-19 including India.

The virus spreads easily and the majority of the world's population is still vulnerable to it. A vaccine would provide some protection by training people's immune systems to fight the virus so they should not become sick. The reason behind the rush is a staggering number of covid-19 cases (6,229,895) and death toll (372,888) globally, in India alone, there are 151,876 corona cases as of May 31.

Information is till 31 May 2020



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THANK YOU

