CORONAVIRUS UPDATE 22

The Solidarity Trial

'Solidarity' is an international clinical trial to help find an effective treatment for COVID-19, launched by the WHO and partners. Find out which therapies are included in the trial. MORE

Transmission scenarios

Measures to reduce transmission

Guidance for the faith community

EPI•WiN

World Health Organization

For the latest data, please access:

- WHO situation dashboard
- WHO situation reports
- UNWFP world travel restrictions

Current global situation

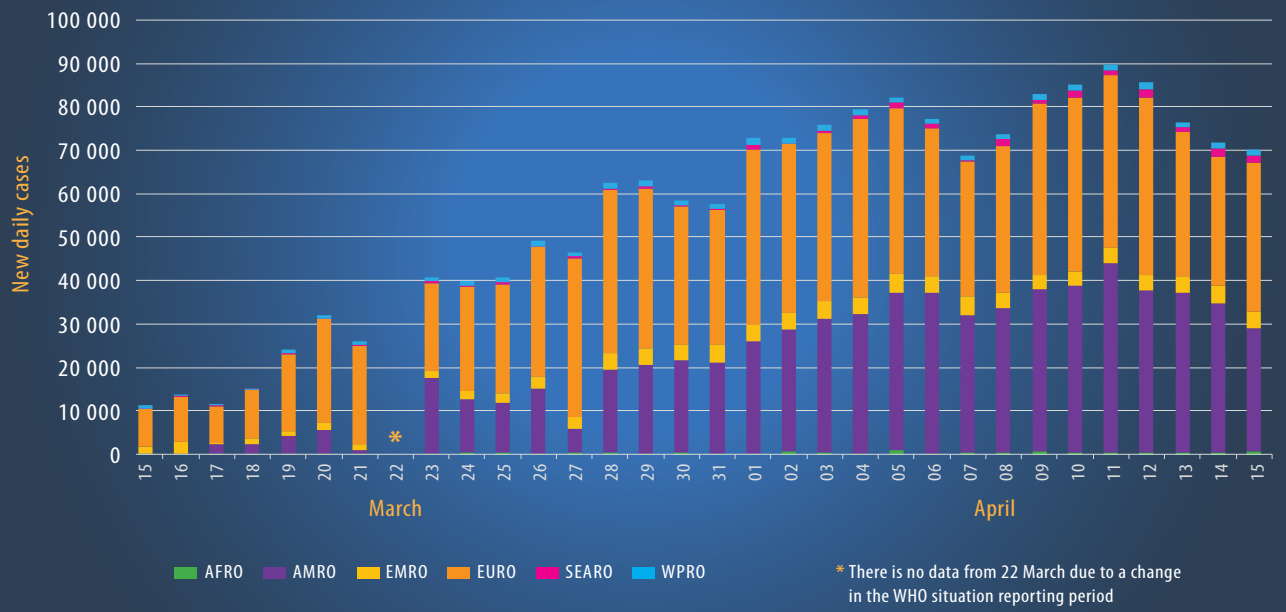
- Nearly **2 million** confirmed cases
- More than **123 000** deaths
- USA has more than 575 000 confirmed cases – the most in the world

Top ten countries with the highest number of new cases

COUNTRY	NEW REPORTED CASES IN LAST 24HRS
United States of America	24 446
France	5 483
United Kingdom	5 252
Turkey	4 062
Russian Federation	3 388
Spain	3 045
Italy	2 972
Germany	2 486
Islamic Republic of Iran	1 574
Canada	1 360

Data as of 15.04.20

Number of new cases of COVID-19 per day, by WHO Region



EPI•WIN

World Health Organization

Public health objectives of a COVID-19 response

1

Slow & stop transmission, prevent outbreaks and delay spread

2

Provide optimized care for all patients, especially the seriously ill

3

Minimize the impact of the epidemic on health systems, social services and economic activity

Reference: The Strategic Preparedness and Response Plan for COVID-19

Measures to reduce transmission of COVID-19

Public health and social measures must be implemented at ALL times with careful consideration given to the local context and any potential harm that may arise.

Personal measures
PHYSICAL DISTANCING

Aim: to protect the individual & close contacts

Public setting measures
MASS GATHERINGS, SCHOOLS, WORKPLACES

Aim: to reduce mixing healthy and sick & increase physical distancing in public areas

Movement reduction measures
NATIONAL & INTERNATIONAL

Aim: to reduce movement of the virus – introduction & re-introduction in healthy population

Protection measures
VULNERABLE PEOPLE, FRONTLINE RESPONDERS & ESSENTIAL SERVICE WORKERS

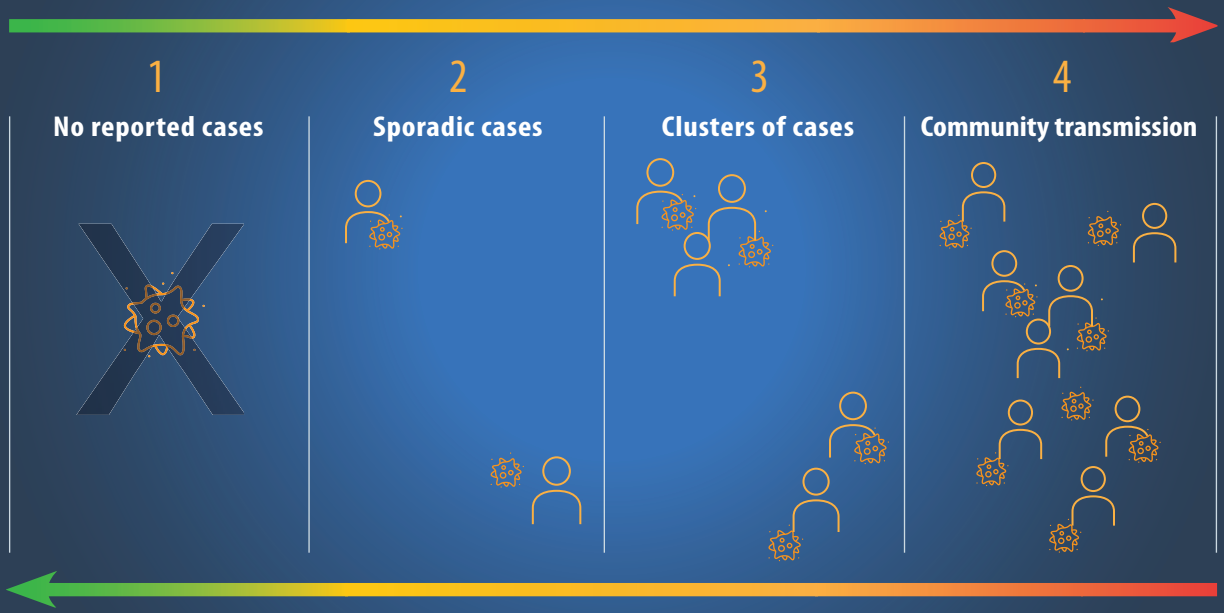
Aim: to mitigate impact on society by protecting vulnerable groups

EPI•WiN

World Health Organization

Four scenarios for COVID-19 response

WHO has described 4 transmission scenarios* to be considered while planning a COVID-19 response



* *Countries could experience 1 or more of the transmission scenarios at the subnational level*

What is the Solidarity Trial being coordinated by WHO?

The Solidarity Trial is a large international clinical trial to help find an effective treatment for COVID-19, launched by the World Health Organization and partners.

The trial will compare four treatment options against standard of care, to assess their relative effectiveness against COVID-19. By enrolling patients in multiple countries, the Solidarity trial aims to rapidly discover whether any of the drugs slow disease progression or improve survival. Other drugs can be added based on emerging evidence. Over 90 countries have confirmed their participation in the trial.[1,2]

The four most promising therapies included in the trial are:

1) Remdesivir

2) Lopinavir/Ritonavir

3) Lopinavir/Ritonavir with interferon beta and

4) Chloroquine

[1] *https://www.sciencemag.org/news/2020/03/who-launches-global-megatrial-four-most-promising-coronavirus-treatments*
[2] *https://www.who.int/emergencies/diseases/novel-coronavirus-2019/global-research-on-novel-coronavirus-2019-ncov/solidarity-clinical-trial-for-covid-19-treatments*

THE SOLIDARITY TRIAL

Repurposing drugs for COVID-19: the four most promising therapies

No 1. Remdesivir

Developed by Gilead to treat Ebola and related viral diseases

An experimental medicine with no established efficacy or safety for the treatment of any condition, as yet.

Mechanism of Action

Stops viral replication by inhibiting a key viral enzyme, RNA-dependent RNA polymerase. In animal studies it has been shown to reduce the severity of disease, viral replication, and damage to the lungs in MERS and be superior to lopinavir/ritonavir plus Interferon Beta B1 therapy.[1,2] Remdesivir is highly active against COVID-19 virus in vitro.[3]

Relevant clinical studies to date

Remdesivir was developed to treat Ebola but efficacy was not proved in clinical trials in the Democratic Republic of Congo.[4]

Ongoing clinical studies of Remdesivir and COVID-19

Gilead study in patients with moderate disease: NCT04292730. Gilead study in patients with severe disease: NCT04292899. NIAID study: NCT04280705 INSERM study: 2020-000936-23. China study in patient with mild/moderate disease: NCT04252664. China study in patients with severe disease: NCT04257656

[1] *https://www.pnas.org/content/pnas/117/12/6771.full.pdf*

[2] *https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6954302/*

[3] *https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7054408/pdf/41422_2020_Article_282.pdf*

[4] *https://www.nejm.org/doi/full/10.1056/NEJMoa1910993*

THE SOLIDARITY TRIAL

Repurposing drugs for COVID-19: the four most promising therapies

No 2. Lopinavir / ritonavir

Developed by Abbot Laboratories. FDA approved in 2000

A fixed-dose drug combination used to treat HIV. It is widely available and can be manufactured to large scale and used immediately.

Mechanism of Action

Both of these drugs are viral protease inhibitors. They block the enzyme that breaks down proteins into smaller pieces that are needed to make new virus. When lopinavir (the more potent of the two) is given alone, only low levels of the drug appear in the blood. This is because it is broken down by an enzyme in the human liver and intestines called cytochrome P450 3A4 (CYP3A4). Lopinavir is given along with a small dose of ritonavir which is also an inhibitor of CYP3A4. This prevents the rapid breakdown of the lopinavir and boosts its blood levels.

Relevant clinical studies to date

Lopinavir/ritonavir has previously been tried for the treatment of SARS and MERS (serious illnesses also caused by Coronaviruses) but the studies were inconclusive.[1,2]

It was also tried for the treatment of severe COVID-19 in China. 199 patients were either given standard care or standard care plus lopinavir/ritonavir. There was no significant difference between the groups. It is thought that the drug treatment may have started too late in these patients with severe disease.

[1] *Chu CM, Cheng VC, Hung IF, et al. Role of lopinavir/ritonavir in the treatment of SARS: initial virological and clinical findings. Thorax 2004;59:252-256*

[2] *Kim UJ, Won E-J, Kee S-J, Jung S-I, Jang H-C. Combination therapy with lopinavir/ritonavir, ribavirin and interferon-a for Middle East respiratory syndrome. Antivir Ther 2016;21:455-459*

[3] *Cao B, Wang Y, D Wen, et al. A trial of lopinavir-ritonavir in adults hospitalized with severe Covid-19. NEJM. March 18 2020. DOI: 10.1056/NEJMoa2001282*

THE SOLIDARITY TRIAL

Repurposing drugs for COVID-19: the four most promising therapies

No 3. Lopinavir/ritonavir + interferon beta

A fixed-dose drug combination used to treat HIV. Please see previous slide.

To be given together with Interferon Beta 1b a drug used to treat multiple sclerosis. Like the lopinavir/ritonavir it is widely available, can be manufactured to scale and used immediately.

Mechanism of Action

Please see previous slide for MoA of lopinavir/ritonavir. Interferons (INFs) are a class of proteins called cytokines that are produced by cells in response to viruses. They signal to other cells around them to heighten their anti-virus defenses. Their name comes from their ability to "interfere" with virus replication. Other coronaviruses, such as the one that causes MERS, have been shown to weaken the natural INF response and lead to weakened immune defense against the virus.[1] One INF known as Beta 1b has shown the greatest inhibition of MERS coronavirus.[1] Studies in animal models have indicated that IFN β1b also results in less severe disease and pathology during MERS treatment.[2]

Relevant clinical studies to date

A clinical trial of lopinavir/ritonavir and IFN β1b in the treatment of Middle Eastern Respiratory Syndrome (MERS) is ongoing (the MIRACLE trial).[1]

[1] *https://trialsjournal.biomedcentral.com/track/pdf/10.1186/s13063-017-2427-0*

[2] *https://academic.oup.com/jid/article/212/12/1904/2911949*

THE SOLIDARITY TRIAL

Repurposing drugs for COVID-19: the four most promising therapies

No 4. Chloroquine

A drug first synthesised in 1934. Has been used to prevent and treat malaria and to treat auto-immune diseases.

It is widely available and can be manufactured to scale and used immediately.

Mechanism of Action

Chloroquine has antiviral and anti-inflammatory properties. Its mechanisms of action against viruses includes increasing pH in the compartments of the cell containing the virus (the endosome) and impairing virus release from cells.[1] It also allows zinc to enter cells and to inhibit viral RNA-dependent RNA polymerase.[2] Its anti-inflammatory mechanism of action is through suppression of Tumour Necrosis Factor (TNFα) a cytokine involved in systemic inflammation.

Chloroquine effectively inhibits the COVID-19 virus in vitro.[3]

Relevant clinical studies to date

Gao et al reported (18 Feb 2020) that chloroquine had been found to be superior to standard care in treatment of COVID-19 but no data has been shown to date.[4] Over 23 clinical trials of chloroquine in COVID-19 are currently ongoing in China alone.[5]

[1] *https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(03)00806-5/fulltext*

[2] *https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2973827/*

[3] *https://www.nature.com/articles/s41422-020-0282-0*

[4] *https://www.jstage.jst.go.jp/article/bst/14/1/14_2020.01047/_pdf/-char/en*

[5] *https://pubmed.ncbi.nlm.nih.gov/32173110/*

Clinical studies of the 4 drugs outside of the Solidarity Trial

- **Remdesivir, 9 studies**
  https://clinicaltrials.gov/ct2/results?cond=COVID-19&term=lopinavir%2Fritonavir&cntry=&state=&city=&dist=&Search=Search
- **Lopinavir / ritonavir, 18 studies**
  https://clinicaltrials.gov/ct2/results?cond=COVID-19&term=lopinavir%2Fritonavir&cntry=&state=&city=&dist=&Search=Search
- **Interferon, 16 studies**
  https://clinicaltrials.gov/ct2/results?cond=COVID-19&term=interferon&cntry=&state=&city=&dist=&Search=Search
- **Chloroquine, 14 studies**
  https://clinicaltrials.gov/ct2/results?cond=COVID-19&term=lopinavir%2Fritonavir&cntry=&state=&city=&dist=&Search=Search

Other drugs for COVID-19 under investigation

- **Azithromycin, 7 studies**
  https://clinicaltrials.gov/ct2/results?cond=COVID-19&term=azithromycin&cntry=&state=&city=&dist=&Search=Search
- **Darunavir, 3 studies**
  https://clinicaltrials.gov/ct2/results?cond=COVID-19&term=darunavir&cntry=&state=&city=&dist=&Search=Search
- **Favipiravir, 2 studies**
  https://clinicaltrials.gov/ct2/results?cond=COVID-19&term=favipiravir&cntry=&state=&city=&dist=&Search=Search
- **Hydroxychloroquine, 26 studies**
  https://clinicaltrials.gov/ct2/results?recrs=&cond=COVID-19&term=hydroxychloroquine&cntry=&state=&city=&dist
- **Oseltamivir, 5 studies**
  https://clinicaltrials.gov/ct2/results?cond=COVID-19&term=oseltamivir&cntry=&state=&city=&dist=&Search=Search
- **Xiyanping, 2 studies**
  https://clinicaltrials.gov/ct2/results?cond=COVID-19&term=xiyanping&cntry=&state=&city=&dist=&Search=Search
- **Yinhu Qingwen, 2 studies**
  https://clinicaltrials.gov/ct2/results?cond=COVID-19&term=yinhu+qing+wen&cntry=&state=&city=&dist=&Search=Search

EPI-WIN collaboration with the faith community

WHO is working with religious leaders, faith-based organizations and faith communities to:

- share best practices and experiences and
- co-develop practical guidance and recommendations to support the special role of religious leaders, faith-basedvtions, and faith communities in COVID-19 education, preparedness, and response
- EPI-WIN relies on existing trusted networks within the faith community to share and amplify messages and guidance, reaching thousands of people worldwide

Related resources:

Learn more about WHO's collaboration with the faith communtity

New! Practical considerations and recommendations for Religious Leaders and Faith-based Communities in the context of COVID-19

- Access the publication
- Access the risk assessment tool
- Access the decision tree

Safe Ramadan practices in the context of COVID-19

EPI•WIN

World Health Organization

Information resources

WHO WhatsApp messaging service
Receive the latest news and information on COVID-19. To subscribe:
text 'hi' to +41 79 893 1892

New EPI-WIN website
Access to timely, accurate, and easy-to-understand advice and information from trusted sources
www.who.int/epi-win