

Q&A on COVID-19, HIV and antiretrovirals

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What is causing this new coronavirus pandemic and what is COVID-19?

Coronavirus disease 2019 (COVID-19) is a respiratory tract infection caused by a newly emergent coronavirus, that was first recognized in Wuhan, China, in December 2019. Genetic sequencing of the virus suggests that it is a betacoronavirus closely linked to the SARS virus and is now called SARS-CoV-2.

Are people living with HIV at increased risk of being infected with SARS-CoV-2, the virus causing COVID-19?

People living with HIV (PLHIV) who have not achieved viral suppression through antiretroviral treatment may have a compromised immune system that leaves them vulnerable to opportunistic infections and further disease progression. At present there is no evidence to suggest that there is an increased risk of infection and increased severity of illness for PLHIV and there is currently no reported case of COVID-19 infection among PLHIV, though this can rapidly change as the virus spreads. We know that during the SARS and MERS outbreaks there were only a few case reports of mild disease among PLHIV.

Current clinical data suggest the main mortality risk factors are linked to older age and other comorbidities including cardiovascular disease, diabetes, chronic respiratory disease, and hypertension. Some very healthy people have also developed severe disease from the coronavirus infection.

PLHIV who know their HIV status are advised to take the same precautions as the general population (e.g. wash hands often, cough hygiene, avoid touching your face, social distancing, seek medical care if symptomatic, self-isolation if in contact with someone with COVID-19 and other actions per the government response). PLHIV who are taking ARV drugs should ensure that they have at least 30 days of ARVs if not a 3 to 6-month supply and ensure that their vaccinations are up to date (influenza and pneumococcal vaccines).

It is also an important opportunity to ensure that all PLHIV who are not yet on antiretroviral treatment (ART) start. People who feel they may have been at HIV risk are advised to seek testing to protect against HIV disease progression and complications from any other comorbidities.

- WHO Guidance on the COVID-19 outbreak can be found here: <https://www.who.int/emergencies/diseases/novel-coronavirus-2019>.
- WHO country and technical guidance can be found here: <https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance>.

Can antiretrovirals be used to treat COVID-19?

Several studies have suggested that patients infected with SARS-CoV-2, the virus causing COVID-19, and the related coronavirus infections (SARS-CoV and MERS-CoV) had good clinical outcomes, with almost all cases recovering fully. In some cases, patients were given an antiretroviral drug: lopinavir boosted with ritonavir (LPV/r). These studies were mostly carried out in HIV negative individuals.

It is important to note that these studies using LPV/r had important limitations. The studies were small, timing, duration and dosing for treatment were varied and most patients received co-interventions/co-treatments which may have contributed to the reported outcomes.

While the evidence of benefit of using antiretrovirals to treat coronavirus infections is of very low certainty, serious side effects were rare. Among PLHIV, the routine use of LPV/r as treatment for HIV is associated with several side effects of moderate severity. However, as the duration of treatment in patients with coronavirus infections was generally limited to a few weeks, these occurrences can be expected to be low or less than that reported from routine use.

- WHO updated guidelines on the clinical management of severe COVID-19 can be found here: [https://www.who.int/publications-detail/clinical-management-of-severe-acute-respiratory-infection-when-novel-coronavirus-\(ncov\)-infection-is-suspected](https://www.who.int/publications-detail/clinical-management-of-severe-acute-respiratory-infection-when-novel-coronavirus-(ncov)-infection-is-suspected). These are updated regularly as evidence and experience evolves.

Can antiretrovirals be used to prevent SARS-CoV-2 (virus causing COVID-19) infection?

Two studies have reported the use of LPV/r as post-exposure prophylaxis for SARS-CoV and MERS-CoV. One of these studies suggested that the occurrence of MERS-CoV infection was lower among health workers receiving LPV/r compared to those who did not receive any drugs; the other study found no cases of SARS-CoV infection among 19 PLHIV hospitalized in the same ward of SARS patients, of whom 11 were on antiretroviral therapy. Again, the certainty of the evidence is very low due to small sample size, variability in drugs provided, and uncertainty regarding intensity of exposure.

What studies on treatment and prevention of COVID-19 with antiretrovirals are being planned?

Several randomized trials are planned to assess the safety and efficacy of using antiretroviral drugs – mainly LPV/r – for treating COVID-19, in combination with other drugs. Results are expected from mid-2020 onwards.

What is WHO's position on clinical trials/research while the outbreak is ongoing?

WHO is providing support and direction to the scientific community and welcomes the research and development of effective tests, vaccines, medicines and other interventions for COVID-19.

For public health emergencies, WHO has a systematic and transparent process for research and development, including for clinical trials of new drugs and vaccines. The WHO "R&D Blueprint" for COVID-19, initiated on 7 January 2020, will serve as the global strategy for R&D activities. Its aim is to fast-track the availability of effective tests, vaccines and medicines that can be used to save lives and avert large scale crises.¹ As part of this, WHO is leading the global prioritization of candidate vaccines and therapeutics for development and evaluation. To support testing, WHO convened a scientific advisory group (SAG) to develop guidance on trial designs for experimental vaccines and therapeutics.²³

WHO is actively following the ongoing clinical trials for existing antivirals and other medicines that are being conducted for COVID-19. WHO continues to emphasize that all clinical trials should and must follow stringent ethical and regulatory standards. Regulatory authorities have a role to play to ensure close oversight of all clinical trials that will be undertaken.

What is WHO's position on the use of evidence from early outcomes of research or unproven therapeutics for interventions?

There are many pathogens for which no proven effective intervention exists. For certain pathogens, there may be interventions that have shown promising safety and efficacy in the laboratory and in relevant animal models. In most cases, clinical trials are needed to generate reliable evidence for use in humans before recommendations can be made.

WHO has developed emergency use assessment and listing (EUAL) procedures for candidate medicines and other medical products for public health emergencies. The purpose of this procedure is to provide guidance to national regulatory authorities. This procedure can be used to expedite the availability of medicines in public health emergencies when the community may be willing to accept less certainty about the efficacy and safety of products given the morbidity and mortality of the diseases and the shortfall of treatment and/or prevention options.⁴

WHO emphasizes however, that it is the sole prerogative of Member States whether to allow emergency use of such medicines in their countries.⁵

¹ WHO R&D Blueprint www.who.int/research-observatory/analyses/rd_blueprint

² <https://apps.who.int/iris/bitstream/handle/10665/330692/WHO-HEO-RDBlueprintnCoV-2020.2-eng.pdf>

³ www.who.int/blueprint/15-01-2020-nfr-bp-wg-clinical-trials-ncov.pdf

⁴ Emergency Use Assessment and Listing procedure (EUAL) for candidate medicines for use in the context of public health emergency, www.who.int/medicines/news/EUAL-medicines_7July2015_MS.pdf

⁵ Ibid

In the context of an outbreak characterized by high mortality, it can be ethically appropriate to offer individual patients experimental interventions on an emergency basis outside of clinical trials, provided that:⁶

- 1) no proven effective treatment exists;
- 2) it is not possible to initiate clinical studies immediately;
- 3) data are available providing preliminary support for the intervention's efficacy and safety, at least from laboratory or animal studies, and use of the intervention outside of clinical trials has been suggested by an appropriately-qualified scientific advisory committee based on a favourable risk–benefit analysis;
- 4) the relevant national authorities, as well as an appropriately qualified ethics committee, have approved such use;
- 5) adequate resources are available to ensure that risks can be minimized;
- 6) the patient has given informed consent; and
- 7) the emergency use of the intervention is monitored, and the results are documented and shared in a timely manner with the wider medical and scientific community.

The use of experimental interventions under these circumstances is referred to as “monitored emergency use of unregistered and experimental interventions” (MEURI)⁷.

What is WHO's position on the use of antiretrovirals for the treatment of COVID-19?

Currently, there is insufficient data to assess the effectiveness of LPV/r or other antivirals for treating COVID-19. Several countries are evaluating the use of LPV/r and other antivirals and we welcome the results of these investigations.

Again, as part of WHO's response to the outbreak, the WHO R&D Blueprint⁸ has been activated to accelerate evaluation of diagnostics, vaccines and therapeutics for this novel coronavirus. WHO has also designed a set of procedures to assess the performance, quality and safety of medical technologies during emergency situations.

What is WHO's position on use of corticosteroids for the treatment of COVID-19?

The current interim guidance from WHO on clinical management of severe acute respiratory infection when COVID-19 infection is suspected advises against the use of corticosteroids unless indicated for another reason.⁹

⁶ WHO guidance for managing ethical issues in infectious disease outbreaks, <https://apps.who.int/iris/bitstream/handle/10665/250580/9789241549837-eng.pdf>

⁷ Monitored emergency use of unregistered and experimental interventions (MEURI), <http://www.who.int/ethics/publications/infectious-disease-outbreaks/en/> Chapter 9 MEURI

⁸ <https://www.who.int/blueprint/priority-diseases/key-action/novel-coronavirus/en/>

⁹ Clinical management of severe acute respiratory infection when novel coronavirus infection is suspected, [www.who.int/publications-detail/clinical-management-of-severe-acute-respiratory-infection-when-novel-coronavirus-\(ncov\)-infection-is-suspected](http://www.who.int/publications-detail/clinical-management-of-severe-acute-respiratory-infection-when-novel-coronavirus-(ncov)-infection-is-suspected)

This guidance is based on several systematic reviews that cite lack of effectiveness and possible harm from routine treatment with corticosteroids for viral pneumonia or acute respiratory distress syndrome.¹⁰

If countries use antiretrovirals for COVID-19, are there concerns about treatment shortages for people living with HIV?

Antiretrovirals are an efficacious and highly tolerable treatment for people living with HIV (PLHIV). The antiretroviral LPV/r is currently being investigated as a possible treatment for COVID-19.

If they are to be used for the treatment of COVID-19, a plan should be in place to ensure there is adequate and continuous supply to cover the needs of all PLHIV already using LPV/r and those who will need to begin treatment. However, a relatively small proportion of PLHIV are on regimens which include LPV/r, since it is used as a second-line regimen according to WHO's HIV treatment guidelines. Any country that allows the use of HIV medicines for the treatment of COVID-19 must ensure that an adequate and sustainable supply is in place.

Human rights, stigma and discrimination

As the world scales up public health responses to the COVID19 pandemic, countries are being urged to take decisive action to control the epidemic. The World Health Organization has urged all countries to ensure an appropriate balance between protecting health, preventing economic and social disruption, and respecting human rights.

WHO is working with partners including the UNAIDS Joint Programme and the Global Network of People Living with HIV to ensure that human rights are not eroded in the response to COVID-19 and to ensure that people living with or affected by HIV are offered the same access to services as others and to ensure HIV-related services continue without disruption.

Multi-month prescriptions

Clinically stable adults, children, adolescents and pregnant and breastfeeding women as well as members of key populations (people who inject drugs, sex workers, men who have sex with men, transgender people and people living in prisons and closed settings) can benefit from simplified antiretroviral therapy (ART) delivery models which include multi month prescriptions (from 3-6 month supply) which reduce the frequency of visits to clinical settings and ensures continuity of treatment during possible disruption of movements and clinic schedule during the coronavirus outbreak.

¹⁰ Clinical evidence does not support corticosteroid treatment for 2019-nCoV lung injury, www.thelancet.com/pb-assets/Lancet/pdfs/coronavirus/S0140673620303172.pdf

