COVID-19 COMMUNITY RESOURCE

RESOURCE FOR ACCESS TO COVID-19 MEDICAL TECHNOLOGY

MAY 2021

make medicines affordable
END UNFAIR MONOPOLIES

ITPC
INTERNATIONAL TREATMENT PREPAREDNESS COALITION

ABOUT ITPC

The International Treatment Preparedness Coalition (ITPC) is a worldwide network of community activists unified by our vision of a longer, healthier, more productive life for all people living with HIV (PLHIV). ITPC's mission is to enable communities in need to access optimal HIV treatment. As a grassroots movement based primarily in the Global South, ITPC is the community's voice on HIV treatment and is driven by and committed to the human rights of those most impacted by the HIV epidemic.

ITPC is a global coalition that includes eight regional networks in Africa, Asia, Latin America and the Caribbean, Eastern Europe, and the Middle East. Through its different campaigns, ITPC is committed to providing accurate and timely HIV treatment information that can improve the lives of PLHIV. Many of the tools developed under this program are also intended to be used for advocacy initiatives.

Additional information about ITPC is available at: www.itpcglobal.org

ACKNOWLEDGMENTS

Dedicated to all of the people who lost their lives to COVID-19 and their families and friends.

Written by Tracy Swan, Richard Jeffreys, Morgane Ahmar, Kajal Bhardwaj, Sergey Kondratyuk and Othoman Mellouk

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ABBREVIATIONS

ACT-A	Access to COVID-19 Tools Accelerator
ACTT	Adaptive COVID-19 Treatment Trial
AMC	Advanced Market Commitment
ART	antiretroviral therapy
ARV	antiretroviral
BARDA	Biomedical Advanced Research and Development
BMGF	Bill and Melinda Gates Foundation
CDC	Centers for Disease Control
CDSCO	Central Drugs Standard Control Organization
CEPI	Coalition for Epidemic Preparedness Innovations
CL	compulsory license
COVID-19	coronavirus disease 2019
CPAP	continuous positive airway pressure
CTAP	Coronavirus Treatment Acceleration Program
DCGI	Drug Controller General of India
DCV	daclatasvir
ddPCR	droplet digital PCR
DoD	Department of Defense
EC	European Commission
EMA	European Medicines Agency
EU	European Union
EUA	Emergency Use Authorization
FDA	US Food and Drug Administration
FDAs	Food and Drug Authorities/Administrations
FIND	Foundation for Innovative Diagnostics
GAVI	Global Alliance for Vaccines and Immunizations
GFATM	Global Fund to Fight AIDS, Tuberculosis and Malaria
GSK	GlaxoSmithKline
HCV	hepatitis C virus
HCW	healthcare workers
ICER	Institute for Clinical and Economic Review
IFR	infection fatality rate
IP	intellectual property
IVA	Inclusive Vaccines Alliance
JAK	Janus kinases
J & J	Johnson and Johnson
LMIC	low- and middle-income countries
LPV/r	lopinavir/ritonavir
MERS	Middle East Respiratory Syndrome
MIS-C	Multisystem Inflammatory Syndrome in Children
mRNA	messenger RNA
MSF	Médecins Sans Frontières

ABBREVIATIONS

NDRA	National Drug Regulatory Authority
NIAID	National Institute of Allergy and Infectious Diseases
NIH	National Institutes of Health
OWS	Operation Warp Speed
PCR	polymerase chain reaction
PPE	personal protective equipment
RDIF	Russian Direct Investment Fund
SARS	Severe Acute Respiratory Syndrome
SOC	standard of care
SOF	sofosbuvir
STATs	signal transducer and activator of transcription proteins
TB	tuberculosis
TRIPS	Trade-Related Aspects of Intellectual Property Rights
UN	United Nations
US	United States
USAMRID	US Army Medical Research Institute of Infectious Diseases
VL	voluntary license
VRC	Vaccine Research Center
WHO	World Health Organization
WTO	World Trade Organization

PART
ONE

INTRODUCTION AND PURPOSE

> **It will irrevocably rewrite the way the world thinks about global health. It will reshape the relationship between health and finance and economics.**
>
> **Peter Sands, Executive Director of the Global Fund**

COVID-19 has revealed – and drastically worsened – economic and social inequality on a global scale. Governmental decisions to prioritize economic recovery over public health have had disastrous results for both. The pandemic highlights the desperate need to shift from the status quo of patent monopolies towards the right to health for all human beings.

Activists have a prime opportunity to prevent pharmaceutical corporations and others from additional profiteering at the expense of global public health – and people's lives. As COVID-19 sweeps across the world, it unveils a collective failure to ensure that all people can benefit from advances in prevention, diagnosis and treatment. Instead of a profit-based, nationalistic response, we need a global, rights-based, public health approach to conquer the threat of COVID-19 – as well as existing diseases and future pandemics.

This guide was developed to promote universal access to affordable COVID-19 testing, vaccines, and effective treatment. It includes information about SARS-CoV-2 (the virus that causes COVID-19) – how it is transmitted and how it can be prevented; the importance of human rights in the context of public health measures; symptoms and outcomes of COVID-19, types of tests, vaccines and research on treatments, including how to assess the quality of clinical trials and their results, and strategies for overcoming intellectual property (IP), regulatory and other barriers.

Information about COVID-19 is likely to be updated frequently. Always check for current information.

PART
TWO

HISTORY OF COVID-19

Coronaviruses, which were named for their resemblance to a crown, can infect animals and people. The first human coronaviruses were described over 50 years ago; some cause the common cold in people, while others cause more serious, potentially life-threatening illnesses.[1] Severe Acute Respiratory Syndrome (SARS) and Middle East Respiratory Syndrome (MERS) are members of the coronavirus family. Both of these viruses jumped from animals (SARS, possibly from bats to civet cats; MERS, possibly from camels) to people, as has the severe acute respiratory syndrome-related coronavirus 2 (SARS-CoV-2), which causes the illness coronavirus disease 2019 (COVID-19).

Although a coronavirus that is 96.2% identical to SARS-CoV-2 has been found in Chinese horseshoe bats, and other closely related coronaviruses in pangolins, more research is needed to identify the animal source.[2] It is not known exactly when or how SARS-CoV-2 made its leap into human beings. The first reported cases occurred in late 2019, and the virus was identified in January 2020. By March of 2021, it had spread to nearly 114 million people in over 200 countries, causing over 2,528,000 deaths. [3, 4] The coronavirus mutates rapidly, and since it has infected millions of people in a short time, it has had many opportunities to mutate. Some of these mutations have led to variants of the virus – new versions that may be more contagious, cause more serious illness and /or can elude immune responses. In 2020 and 2021, several variants were identified that have since spread from country to country – and are now being transmitted in the community – raising alarm that these variants could escape vaccine-induced and natural immune responses to other versions of the virus.

COVID-19 antibody, antigen and viral load tests are available; some are more reliable than others. Yet access to testing in many countries remains inadequate, which allows the virus to continue spreading from people who are unaware that they have it (since many people never have symptoms). It is not clear whether, and for how long, antibodies will confer immunity to COVID-19, especially in people who were asymptomatic. [5, 6]

By the third quarter of 2020, there were already more than 3,118 planned, ongoing and completed clinical trials for COVID-19. [7] During the fourth quarter of 2020 and into 2021, safe, effective coronavirus vaccines were approved with record-breaking speed, building on years of taxpayer funded research, and there are more vaccines in the pipeline. Despite this progress, nearly two million people lost their lives to COVID-19 in 2020.

[1] https://journals.lww.com/pidj/pages/articleviewer.aspx?year=2005&issue=11001&article=00012&type=Fulltext

[2] https://www.sciencemag.org/news/2020/06/nih-halted-study-unveils-its-massive-analysis-bat-coronaviruses

[3] https://covid19.who.int

[4] https://coronavirus.jhu.edu/map.html

[5] https://www.nature.com/articles/s41591-020-0965-6

[6] https://www.medrxiv.org/content/10.1101/2020.06.13.20130252v1

[7] https://clinicaltrials.gov/ct2/results?cond=COVID-19&Search=Apply&recrs=b&recrs=a&recrs=f&recrs=d&age_v=&gndr=&type=&rslt=

Global initiatives and public-private partnerships have been developed to prevent, diagnose and treat COVID-19, with the promise of access for all – but within the context of pharmaceutical business as usual. To counter this, India and South Africa have asked the World Trade Organization (WTO) for a temporary waiver of patent obligations under the TRIPS Agreement for COVID-19 vaccines – but Canada, the EU (with the exception of Spain) and the UK have strongly opposed the waiver, preventing these countries from providing affordable versions of these vaccines.

A global response to the pandemic is being coordinated through the Access to COVID-19 Tools Accelerator; its COVAX facility expects to provide 1.8 billion coronavirus vaccine doses in 2021 although this may not be possible, since India cancelled vaccine exports.[8] COVAX – and its market-based approach to vaccine access – have been increasingly criticized, both for the strong influence of the private sector and private foundations, such as the Bill and Melinda Gates Foundation – and for its limited consultation with civil society organizations and community groups. The call for a 'people's vaccine' – available to all, at no cost, has also gained momentum in the global South and across movements for access to medicines.

In addition to vaccines, a continuum of public health measures and tailored medical care are needed to treat COVID-19 – a strategy that relies on ramping-up affordable, reliable rapid testing and providing supportive care, oxygen and widespread access to medicines that have yet to be discovered. Ideally, a safe, tolerable and effective antiviral could treat asymptomatic or mild COVID-19 cases, limit its transmission, and prevent people from progressing to more serious illness. Individualized, more intensive treatment for people with severe COVID-19 may remain necessary – hopefully, for far fewer people as access to vaccines increases.

Trials are exploring repurposed drugs to treat COVID-19, since this can be done far more quickly – and less expensively – than developing new ones. Although hydroxychloroquine and remdesivir have garnered huge media attention, hydroxychloroquine has been proven ineffective in people with severe COVID-19 and is no longer recommended in the US.[9, 10] Remdesivir's benefits are modest - people who were hospitalized recovered more quickly if they received it in clinical trials, but it did not lower the death rate. The nearly 12,000-person international WHO SOLIDARITY Trial, which is looking at several different treatments in people hospitalized with COVID-19, found no benefit to remdesivir – it did not shorten duration of hospitalization, nor did it have an impact on the need for ventilation or the death rate (although Gilead has questioned the SOLIDARITY result, saying that it is inconsistent with results from other clinical trials – and made a $1.2 billion dollar agreement to provide remdesivir to the EU after it saw the unpublished SOLIDARITY results).[11, 12, 13]

[8] https://www.who.int/news/item/24-02-2021-covid-19-vaccine-doses-shipped-by-the-covax-facility-head-to-ghana-marking-beginning-of-global-rollout

[9] https://www.nih.gov/news-events/news-releases/hydroxychloroquine-does-not-benefit-adults-hospitalized-covid-19

[10] https://www.fda.gov/drugs/drug-safety-and-availability/fda-cautions-against-use-hydroxychloroquine-or-chloroquine-covid-19-outside-hospital-setting-or

[11] https://www.kff.org/news-summary/who-addresses-pushback-on-solidarity-trial-interim-results-some-experts-say-remdesivir-still-potentially-effective-in-early-infection/

[12] https://www.ft.com/content/d7ecca00-9cd1-4fff-bba0-567a0027c9db

[13] https://www.reuters.com/article/us-health-coronavirus-gilead-remdesivir/analysis-sales-of-first-big-covid-19-drug-remdesivir-may-disappoint-idUSKBN2711FG

Gilead's unwillingness to share its intellectual property (IP) on remdesivir has kept prices high and severely limited access in high-income countries while it instituted measures to control the market in low- and middle-income countries (LMIC). This has led to sharp criticism from civil society – and government actions to increase access. Three patent oppositions on remdesivir have been filed by Fundacion GEP in Argentina, while the Hungarian government authorized Richter, a local manufacturer to produce generic remdesivir; and, on 31 December, 2020, the Russian Federation's government issued a compulsory license (CL) on six Eurasian remdesivir-related patents, enabling Pharmasyntez to manufacture generic remdesivir in Irkutsk. [14, 15, 16, 17]

Only one treatment, a widely available and cheap steroid, dexamethasone, has significantly improved survival among people hospitalized with severe COVID-19. In the meantime, other medicines – which have received far less attention – may prove to be effective.

Assessing trial results is challenging in the context of a pandemic, but it is especially important to avoid subjecting people to suboptimal vaccines and/or therapies, and to get information on production costs and capacity as well as potential access barriers.

PART THREE

TRANSMISSION OF COVID-19

Although SARS-CoV-2 can be transmitted by virus that is on surfaces (when a person touches something contaminated before touching their eyes, nose or mouth), it is primarily airborne, spread in poorly ventilated indoor spaces. When an infected person coughs, sneezes, sings, speaks or even exhales, virus-laden droplets – and much smaller particles, called aerosols – enter the air. Aerosols can linger in the air for a much longer time and travel further than larger, heavier droplets.[18, 19] The coronavirus spreads when droplets and/or aerosols are inhaled, or if they land inside another person's eyes, nose or mouth.

Ultimately, coronavirus infection depends on a few factors: the transmissibility of circulating viral variants, the infected person's viral load and the amount of droplets and/or aerosols they produce, the amount of virus that is in these droplets and/or aerosols, its ability to bind to and enter human cells; the amount of time that another person is exposed to an infected person, and the setting they are in - whether they are masked or unmasked, outside or inside, and how well-ventilated indoor spaces are. Generally, close contact – enough to spread the virus – is considered as being within 2 meters of a person who is infected, for at least 15 minutes although new, more infectious coronavirus variants may be transmitted more quickly.

COVID-19 is most likely to be transmitted within a few days after someone becomes infected, often by people who don't have symptoms yet (called pre-symptomatic transmission). COVID-19 is also transmitted by people who are infected, but don't have symptoms (called asymptomatic transmission), and by people with mild symptoms (called oligosymptomatic transmission), as well as by people who have fallen ill.

[14] https://www.fgep.org/category/oposiciones-a-patentes/

[15] https://www.reuters.com/article/us-health-coronavirus-remdesivir-richter-idUSKBN26S283

[16] https://publication.pravo.gov.ru/Document/View/0001202101050003

[17] https://pharmasyntez.com/en/press-center/news/the-first-large-scale-batch-of-remdeform-inn-remdesivir-the-drug-to-treat-covid-19-is-ready-for-prod/

[18] https://www.who.int/news-room/commentaries/detail/modes-of-transmission-of-virus-causing-covid-19-implications-for-ipc-precaution-recommendations

[19] https://www.nytimes.com/2020/07/04/health/239-experts-with-one-big-claim-the-coronavirus-is-airborne.html?action=click&algo=top_conversion&block=trending_recirc&fellback=false&imp_id=529807577&impression_id=1424110&index=9&pgtype=Article&region=footer&req_id=52183512&surface=most-popular

PART
FOUR

PREVENTING COVID-19

Unless effective vaccines, rapid testing and contact tracing are widely available, and support is provided for people who need to quarantine, the epidemic will be difficult to control. Up to 45% of people with COVID-19 do not have symptoms and are likely to be unaware that they are infected.[20] Testing is not always available, and access may be limited to people who have symptoms. It may take several days for results, during which asymptomatic transmission can occur.

Without a vaccine, the most effective ways for people to prevent COVID-19 are by:

- Wearing a close-fitting mask that covers the mouth and nose or a disposable mask with a cloth mask over it in public places, especially indoors;
- Avoiding crowded indoor spaces;
- Keeping two meters (six feet) away from other people ('social distancing') – and avoiding close contact with people who are sick;
- Staying home if you feel ill, or if you have been notified that a contact has tested positive for COVID-19;
- Getting tested if you have been at risk or feel ill, and remaining isolated until you receive the results (and if they are positive, remain at home and away from other people until a healthcare provider advises that you are no longer infectious)
- Frequently washing your hands for at least 20 seconds with soap and water or using hand sanitizer that is at least 60-70% alcohol;
- Not touching your eyes, nose and mouth unless you have just washed your hands.

As discussed in the next section, people's ability and capacity to comply with these preventive measures are often dictated by their means and privilege.

[20] https://www.acpjournals.org/doi/10.7326/M20-3012

PART
FIVE

COVID-19 AND HUMAN RIGHTS

COVID-19 has magnified the fissures in society. It has seen marginalized communities, who were already on the edge, taking the hardest economic hit, getting stuck at the back of the line for vital services and getting scapegoated for the crisis.

Yet the crisis has also seen the most excluded communities being, once again, the first to step up to help - rooted in their expertise from experience, in their empathy and in their insistence that health for all and a recovery for all is possible.

Winnie Byanyima, Executive Director, UNAIDS

In the year since COVID-19 has spread across the globe, harsh inequities and human rights violations have become visible – and have been worsened – in nearly every country. The governmental response to COVID-19 prevention has been to institute varying degrees of lock-down; some were ill-timed, either starting too early or too late, and/or lifted too early to ease economic consequences - or governments have relied on ineffective, non-evidence based half-measures. In some places, lockdowns violated human rights or reinforced discrimination and bigotry in the guise of public health, leading to even more misery. [21, 22, 23, 24]

Country responses have included mandatory quarantine, isolation and testing, breaches of confidentiality and privacy; these relied heavily on criminal penalties and law enforcement agencies. Police brutality and violence have been reported in several countries and are particular concerns for already marginalised groups such as lesbian, gay, bisexual and transgender (LGBT) people, migrants, sex workers and people who use drugs. [25, 26] This has left tens of thousands of people deprived of their liberty without access to information, often in inhumane conditions, without appropriate safeguards against ill-treatment". [27, 28]

[21] https://www.nytimes.com/2020/07/06/world/europe/coronavirus-roma-bulgaria.html

[22] https://www.newsbreak.com/news/0OquSrFq/ramadan-begins-amid-lockdowns-bigotry

[23] https://www.dw.com/en/european-police-used-racial-discrimination-when-enforcing-coronavirus-lockdowns-amnesty-international/a-53931040

[24] http://opiniojuris.org/2020/06/09/a-comparative-analysis-of-covid-19-responses-and-their-effects-on-human-rights-protections-in-east-africa/ On first glance, these restrictions seem necessary, proportionate and non-discriminatory, but, their execution indicates otherwise. They have a disproportionate effect on the poor. Pregnant women have died because they had to walk long distances to get to hospitals due of the bans on public transport. Those who leave home have to get a travel permit from the Resident District Commissioners offices, though some communities do not have access to these offices. Radio education has become an alternative to classroom education, as not every household has electricity, a laptop or personal computer and access to study materials delivered by the Local Council (LC) system. If schools remain closed for the rest of the academic year, it will set back an entire generation of young people.

[25] http://opiniojuris.org/2020/06/09/a-comparative-analysis-of-covid-19-responses-and-their-effects-on-human-rights-protections-in-east-africa/ Additionally, both the local defense units (LDUs) and the army in Uganda has been implicated in shooting a deaf man and trespassing in people's homes under the guise of enforcing the lockdown and curfews. Some citizens have been jailed for violating curfews and social distancing rules in the name of public health. The Ugandan government has not sufficiently ensured access to health care or provided technology and internet for students who's schooling is falling behind. Rather, it has used the regulations to impose the strong arm of force on its citizens.

[26] https://blog.petrieflom.law.harvard.edu/2020/06/04/south-africa-global-responses-covid19/ People have also questioned the deployment of the South African National Defence Force (SANDF) to affected communities. There have been a significant number of cases reported of police and army brutality, including at least 11 deaths...The anti-repression working group of the C-19 People's Coalition Civil — an alliance of over 300 organizations — and the SA Human Rights Commission have been involved in monitoring cases of police and army brutality. There have also been a number of illegal evictions of people occupying municipal land, despite a legal prohibition on evictions during lockdown. In one instance a court application halted evictions in a community outside Cape Town.

[27] https://www.amnesty.org/en/documents/amr01/2991/2020/en/

[28] https://www.washingtonpost.com/world/middle_east/israel-is-using-cellphone-surveillance-to-warn-citizens-you-may-already-be-infected/2020/03/19/68267294-69e7-11ea-b199-3a9799c54512_story.html. Israel is using cellphone surveillance to warn citizens: You may already be infected. South Korea's government posts a "travel log" of patients before they were diagnosed with the virus, retracing their steps using tools such as GPS phone tracking, credit card records and surveillance video. Singapore hosts a website that includes the age, gender and occupation of all its coronavirus patients and where they traveled recently. China's massive surveillance state, which utilizes tools including facial-recognition technology and the Communist Party's neighborhood committees, has been mobilized to keep close tabs on all movement and enforce quarantines and other measures.

The gendered impact of the pandemic and government responses to it has been noticeable, with reports of increased domestic violence.[29] In poor countries, where governments are not able to replace lost income, people were forced to go without food and essential medicines including HIV antiretrovirals, prophylaxis and treatment for TB and malaria and methadone, due to fear of arrest for violating lockdowns.[30, 31] In addition, stigma and discrimination against people who test positive for COVID-19 and their families have been widely reported.

> **I still go out, I still have sex, because if I don't, I'll die of hunger.** [32]
>
> **Stefany Gonçalves, transgender sex worker in Brazil**

As lockdowns are eased or lifted, COVID-19 has flared up again. It has become apparent that while theoretically everyone may be at risk, the narrative of an equal opportunity virus rings false as class, race, gender, poverty and many other factors make some much more vulnerable than others. Standard public health guidance for re-opening includes wearing masks, physical distancing, hand hygiene, restricting interactions and avoiding visits to crowded spaces. These measures were devised by and for privileged people. In many places, they are not possible – people cannot afford to forgo work, not everyone has access to running water, and many people live in multigenerational homes or overcrowded conditions, such as in prisons, where physical distancing and self-isolation are not possible. At the other end of the spectrum, governments or local leaders have pushed against scientific information encouraging people to ignore any prevention advice or shun mask wearing, isolation or any other restrictions.

Vulnerability to COVID-19 is further exacerbated by existing inequities and inequalities. COVID-19 has had a vastly disproportionate impact on people who are poor and/or belong to a racial, ethnic, religious or other minority. They often lack access to regular healthcare and treatment for conditions that cause severe illness from COVID-19. There has not been adequate or in some cases, any government attention to, and commitment of public resources for mitigating the impact of COVID-19 on these communities; this has been reflected by disproportionate rates of severe COVID-19, hospitalization and death among certain groups. For the elderly, who appear to be the most at risk, advice or government policies aimed at prevention rarely goes beyond isolation; there is also little information or inquiry into elder abuse and violence in homes and communities. While the increased risk for healthcare workers has focussed attention on doctors and nurses, the risk for a wide array of frontline workers such as cashiers, cleaners and other hospital staff has been largely unaddressed.

[29] https://blog.petrieflom.law.harvard.edu/2020/06/04/south-africa-global-responses-covid19/ The lockdown has had a particularly negative effect on women, especially with respect to vulnerability to domestic violence. Until recently, women were not allowed out of homes to report violence; nonetheless, reports of domestic violence have risen sharply.

[30] https://www.scielo.br/scielo.php?pid=S0102-311X2020000805013&script=sci_arttext&tlng=en

[31] https://blog.petrieflom.law.harvard.edu/2020/06/04/south-africa-global-responses-covid19/ There has been a massive increase in food insecurity and hunger (which was already very high). The closure of schools risks disadvantaging a generation of learners and increasing inequality in educational outcomes, and the phased re-opening of schools has been highly contested. There are over 70 water-stressed communities, and generally sanitation and access to water are suboptimal in poor communities. Livelihoods and food systems have been disrupted, and there is growing evidence that other health care services and programs, including HIV, TB, sexual and reproductive health care are being adversely affected.

[32] https://www.theguardian.com/global-development/2020/may/21/if-i-dont-have-sex-ill-die-of-hunger-covid-19-crisis-for-rios-trans-sex-workers

In several countries, governments have been criticized for concealing crucial information about the pandemic from the public. There have been reports of journalists being censored for highlighting gaps and problems in government responses.[33] Under-reporting of COVID-19 cases, deaths and disaggregated data and analysis continue to hinder the response in several countries.

Health systems, which were often underfunded, have been overwhelmed by large numbers of people requiring intensive care and lengthy hospitalisation as the effect of COVID-19 is becoming increasingly obvious. An even greater concern are the diseases that have only been addressed through concerted global efforts over the past few decades - HIV, TB and malaria. Models of COVID-19's impact on health systems and services predict that deaths from HIV, TB and malaria could double over the next 12 months, with 534,000 additional AIDS-related deaths, 525,000 additional deaths from TB, and 382,000 additional deaths from malaria.[34] Already, 106 countries where there are Global Fund-supported programs have reported disruptions to HIV, TB and malaria programs, including ARV stockouts, increased stigma and discrimination, difficulty sustaining TB treatment, and delays in malaria prevention, testing and treatment; an estimated $28.5 billion is needed to help programs mitigate the effects of COVID-19 over the next year. [34]

THE POWER OF COMMUNITY

> **For people living with HIV, ART is our lifeline. If you mess with my treatment, you are violating my right to life... In just four weeks, we contacted 700 people, delivered ART to about 200 people, and referred more than 50 or 60 to the nearest ART centre.** [35]
>
> **Loon Gangte, Delhi Network of Positive People (DNP+)**

Even in the context of an unfolding pandemic and government responses that perpetuate inequalities and human rights violations, communities of people living with HIV, people with TB, people who use drugs, sex worker groups and women's organisations have become lifelines for their communities.

They have been delivering food, money, medicines and providing all manner of support, while taking personal risks during and after lockdowns. Although community groups have effectively become frontline workers, national- and international-level pandemic responses have become characterised by a lack of participation of, and consultation with community groups, NGOs and civil society.

[33] https://www.article19.org/resources/brazil-82-attacks-on-journalists-covering-the-coronavirus-pandemic/

[34] https://www.theglobalfund.org/media/9819/covid19_mitigatingimpact_report_en.pdf?u=637285811880000000

[35] Interview with Loon Gangte of DNP+ (whose members delivered ARVs on their motorbikes during the lockdown in India).

Key Recommendations from Community Groups ITPC-LATCA Consultation, June 2020

- Focus on COVID-19 care and the clinical status of people with HIV; implement ART supply plans and maintain home delivery with a peer strategy for emotional support where appropriate.
- Encourage, implement and strengthen advocacy, reporting and action on demands for basic needs, through agreements between civil society, cooperative agencies and the government sector for comprehensive care of people living with HIV and key populations.
- Implement strategies to prevent violence against women, people living with HIV and people who are members of key populations in national COVID-19 response plans.
- Leaders in the region need to implement advocacy strategies to maintain access to and availability of medicines without discrimination among the most vulnerable sectors - with the support of governments.
- Generate and implement community-based tools for collecting information on people living with HIV and key populations, which can be implemented by communities and their strategic allies, to contribute to meeting their basic needs.
- Carry out demand communication campaigns from community-based organizations that demonstrate the situation of intra-family violence in communities of people living with HIV and other key affected populations in Latin America.

Recommendations from Global Fund Regional Platform Community Survey: The Situation Of Key Populations In The Context Of Covid-19 In The MENA Region by ITPC-MENA

Information	• Adopt innovative methods to provide rapid and accurate information • Adapt material to target key populations • Translate information into local languages • Effective distribution of material in areas in which virtual communication is lacking • Share information through local and regional platforms
PLWHIV	• Provision of PPE and hygiene kits for health workers • More collaboration at regional level • Referral system specific to PLWHIV to avoid disruption of services • Provision of food services • Supply of medications, especially for PLHIV, for a period of several months to avoid stock-outs • Financial support for PLWHIV to access HIV services, testing and treatment • Psycho-social support for PLWHIV
Key Populations	• Provision of PPE and hygiene kits for health workers • More collaboration at regional level • Development of regional action plan w/ involvement from both political and religious leaders to lessen stigma and discrimination • Referral system specific to key populations • Provision of food services to vulnerable populations • Financial Support to key populations • External funding to all NGOs, especially the small ones who work in the field • Assist NGOs in enabling psycho-social support for key populations • Provision of shelters for vulnerable populations, especially for those affected by unemployment and violence • Provision of hygiene kits, especially in areas where social distancing is difficult.

PART
SIX

CORONAVIRUS VACCINES

An ideal vaccine would be cheap, relatively easy to manufacture, distributable without requiring a cold chain, administered via single injection, well tolerated and protective against SARS-CoV-2 infection (or, less optimally, COVID-19 disease).

The urgency of the need to quell the pandemic and return society to a semblance of normalcy prompted scientists and regulators to drastically truncate the typical timeline for vaccine development. Over the course of 2020, multiple vaccine candidates progressed through early-phase clinical trials into large studies assessing efficacy against COVID-19 disease. At the start of 2021, several COVID-19 vaccines have been authorized for use in different countries around the world (see Table 1, Leading COVID-19 Vaccines).

HOW VACCINES WORK

Vaccines work by inducing immune responses capable of recognizing and responding to a given pathogen. Important components of the immune response include T cells and B cells; the latter are responsible for producing antibodies, Y-shaped proteins capable of binding to pathogens in ways that inhibit replication and trigger the destruction of pathogen-infected cells. Antibodies capable of inhibiting pathogens such as SARS-CoV-2 are referred to as "neutralizing" and are widely considered to represent the ideal immune response for preventing infection. T cells and B cells can persist in a long-term "memory" state after exposure to a vaccine or infection, retaining an ability to respond rapidly if they re-encounter the pathogen that they recognize.

The significant efficacy demonstrated by multiple COVID-19 vaccines indicates that protective immunity against SARS-CoV-2 is achievable. Information on the types of immune responses that were associated with protection has yet to be published, but the consensus among scientists is that neutralizing antibodies are likely to have been key. This view is based on evidence from animal studies [36,37,38] and research assessing whether antibody responses reduce the risk of reinfection by SARS-CoV-2.[39]

WHY IT TAKES TIME TO DEVELOP VACCINES

The timeline for developing an effective vaccine is typically measured in years or decades. A critical factor for determining the speed of development is the degree of understanding of the parameters of protective immunity. In HIV, for example, uncertainty about how to protect against the infection has so far stymied efforts to create a vaccine. The shortest recorded period from creation of a vaccine to approval for human use is four years (for a candidate vaccine for the mumps).[40] The reason it takes time is that multiples steps are required to ensure the composition of a vaccine is safe and functional, including evaluations of the manufacturing process by regulators and preclinical research conducted in laboratory and animal models.

[36] https://science.sciencemag.org/content/early/2020/05/19/science.abc4776

[37] https://science.sciencemag.org/content/early/2020/07/01/science.abc5343

[38] https://science.sciencemag.org/content/early/2020/05/19/science.abc6284

[39] https://www.nejm.org/doi/10.1056/NEJMoa2034545

[40] https://www.history.com/news/mumps-vaccine-world-war-ii

Human clinical research then follows, typically proceeding from small phase I trials to assess safety and immunogenicity (ability of the vaccine to induce the desired immune response) through to phase II evaluations in greater numbers of people, culminating in large phase III efficacy trials designed to prove whether the vaccine protects against the targeted infection or disease. Phase III efficacy trials generally require thousands of participants. Review and approval by regulatory agencies and oversight bodies such as Institutional Review Boards (IRBs) is necessary for each trial. Substantial funding is also a requisite for the process to proceed smoothly.

For SARS CoV-2, the traditional timeline for vaccine development has been compressed in a number of ways. For example, animal studies were undertaken in parallel with phase I trials rather than serving as a gatekeeper for human testing. Single trials are also incorporating multiple phases e.g. phase I/II, which involves recruiting increasing numbers of participants as safety and immunogenicity milestones are met rather than conducing individual discrete trials for each phase. Flexible "adaptive" trial designs are being employed to allow researchers to tweak ongoing research as new information becomes available, without compromising the integrity of the data that is being collected.

VACCINE CANDIDATES

The starting pistol for the race to develop vaccines against COVID-19 was the important and laudable online publication of the genetic sequence of the SARS-CoV-2 virus genome by scientists in China on January 10, 2020.[41] Scientists were able to quickly use the genetic code to generate SARS-CoV-2 antigens for inclusion in vaccine constructs, with many developers focusing on the spike protein due to evidence that it represents the major target for neutralizing antibody responses.[42]

The first two COVID-19 vaccine candidates entered clinical trials in mid-March, just 66 days after the SARS-CoV-2 virus genome was published, breaking all previous records. Since that time, there has been an explosion of research involving multiple vaccine constructs. In an historic achievement, an increasing number of vaccines have demonstrated efficacy in preventing symptomatic COVID-19 (particularly severe cases) in large, successfully executed trials that represent a testament to the commitment of all involved including scientists, medical staff, community members and hundreds of thousands of volunteer participants.

The efficacy of different vaccines has varied, but importantly there have so far been no confirmed cases of COVID-19 severe enough to cause hospitalization in any vaccine recipient. It is less clear whether vaccination can prevent acquisition of SARS-CoV-2 infection – some limited data suggests this may be possible, but more information is needed. Table 1 summarizes information on the leading COVID-19 vaccines with available efficacy results.

[41] https://virological.org/t/novel-2019-coronavirus-genome/319

[42] https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)31208-3/fulltext

Table 1: Leading COVID-19 Vaccines

Manufacturer	Name/type of vaccine	# of doses	# of recipients in efficacy trials	Protection against hospitalization or death	Protection against severe disease	Efficacy against mild disease
Pfizer/ BioNTech	BNT162b2 (tozinameran) mRNA	2	~22,000	100%	9 cases in placebo arm, 1 case in vaccine arm	95% [43]
Moderna	mRNA-1273 mRNA	2	~15,000	100% [44]	30 cases in placebo arm, 0 in vaccine arm	94.1% [45]
AstraZeneca	ChAdOx1, AZD1222, Covishield (in India) Chimpanzee adenovirus vector	2	~8,000	100%	10 cases in placebo arm, 0 cases in vaccine arm	62.1% (2 standard doses), 90.0% (low dose followed by standard dose when given at least 12 weeks apart), 70.4% (overall), [46, 47] No efficacy against mild/moderate disease in South Africa [48, 49]
Johnson & Johnson	Ad26.COV2.S Adenovirus serotype 26 (Ad26) vector	1	~22,000	100%	85% (across United States, Latin America & South Africa)	72% in United States, 66% in Latin America, 57% in South Africa [50]
Gamaleya National Research Centre for Epidemiology and Microbiology	Gam-COVID-Vac (Sputnik V) Adenovirus Ad26 and Ad5 vectors	2	~16,000	100%	20 cases in placebo arm, 0 in vaccine arm	91.6% [51]
Novavax	NVX-CoV2373 Recombinant protein + Matrix M adjuvant	2	~9,700	100%	2 cases in placebo arms, 0 cases in vaccine arms	89.3% in UK, 60% in South Africa (HIV- negative participants) [52, 53]
Sinovac Biotech Ltd.	CoronaVac Whole-killed vaccine	2	~7,000	100%	N/A	50.65% for all cases, 83.70% for cases requiring medical treatment (Brazil), 91.25% all cases (Turkey) [54]

[43] https://www.nejm.org/doi/full/10.1056/NEJMoa2034577

[44] One possible but not fully confirmed case of severe COVID-19 requiring hospitalization in an mRNA-1273 vaccine recipient is reported in the US FDA briefing document (page 27): https://www.fda.gov/media/144434/download

[45] https://www.nejm.org/doi/full/10.1056/NEJMoa2035389

[46] https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)32661-1/fulltext

[47] https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3777268

[48] https://www.medrxiv.org/content/10.1101/2021.02.10.21251247v1

[49] https://www.statnews.com/2021/02/07/south-africa-halts-rollout-of-astrazenecas-covid-19-vaccine-after-shot-falters-against-variant/

[50] https://www.jnj.com/johnson-johnson-announces-single-shot-janssen-covid-19-vaccine-candidate-met-primary-endpoints-in-interim-analysis-of-its-phase-3-ensemble-trial

[51] https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)00234-8/fulltext

[52] https://ir.novavax.com/news-releases/news-release-details/novavax-covid-19-vaccine-demonstrates-893-efficacy-uk-phase-3

[53] In an analysis including 148 participants living with HIV, efficacy diminished to 49.4%. Further details and potential explanations for lack of evidence of efficacy in the HIV+ cohort are not yet available.

[54] http://www.sinovac.com/?optionid=754&auto_id=922

Efficacy has also been reported for several vaccines developed in China. CanSino's vaccine uses an adenovirus vector; the rest of the Chinese vaccines are based on a traditional approach using a killed form of the SARS-CoV-2 virus, but details remain lacking. The Indian company Bharat Biotech is developing an inactivated vaccine named Covaxin that has been granted emergency authorization in India. Bharat Biotech announced that the vaccine was 78% effective effective against mild, moderate and severe COVID-19 in phase III.[55]

The vaccines made by Moderna and Pfizer/BioNTech use a novel approach: genetic code in the form of messenger RNA, which delivers the SARS-CoV-2 spike protein to cells (stimulating them to produce it; when spikes or their fragments poke out of these cells, it elicits an antibody response). These vaccines appear to offer the highest degree of protective efficacy against symptomatic COVID-19. However, these vaccines have burdensome refrigeration requirements and the Pfizer/BioNTech vaccine requires low-dead space syringes. Notably, all the leading vaccines appear to offer strong protection against severe manifestations of COVID-19.

Overall, vaccine safety profiles are reported to be favorable, with the exception of rare blood clots and low platelets, which are associated with vaccines from AstraZeneca and Johnson and Johnson (see Box). The most common adverse events include transient injection site pain, muscle soreness, headaches and malaise. There are concerns about potential rare allergic reactions to the Moderna and Pfizer/BioNTech vaccines and these reactions need to be monitored for after immunization.[56] Trials of the AstraZeneca vaccine were briefly paused due to two cases of nerve disorders, but the events were ultimately deemed unrelated to vaccination.[57] In India, a trial participant hospitalized for 10 days with a severe adverse event (acute neuroencephalopathy) is suing vaccine producer Serum Institute of India - who has threatened to sue the study participant to the shock of bioethicists and scientists.[58, 59]

VACCINES AND RARE BLOOD CLOTS

A very rare but dangerous side effect, blood clots with low platelets, has been reported among recipients of the AstraZeneca and Johnson and Johnson coronavirus vaccine. These extremely rare events have mainly occured among women under age 60, leading to age-based restrictions in some countries. Regulators in the EU, South Africa, the UK and the US are monitoring these events, and have added cautions to vaccine labeling, including signs and symptoms of rare blood clots with low platelets - but all agree that the benefits of the vaccines outweigh risks.

There are concerns and uncertainties about whether the first wave of COVID-19 vaccines will be able to protect against new variants of SARS-CoV-2 that are emerging around the world, especially in South Africa, where B.1.351, a variant with reduced susceptibility to some antibodies, is circulating (see Table 1).[60] In a relatively small trial involving 2,026 participants in South Africa, the AstraZeneca vaccine failed to demonstrate protective efficacy against symptomatic COVID-19, and this outcome was driven by a lack protection against the B.1.351 variant of SARS CoV-2. The trial population was young and no cases of severe disease requiring hospitalization occurred, so it was not possible to answer the question of whether the vaccine might protect against severe manifestations of infection with the B.1.351 variant. South Africa has suspended use of AstraZeneca's vaccine.

In contrast, vaccines made by Johnson & Johnson and Novavax have demonstrated efficacy in trials in South Africa, albiet at somewhat reduced levels compared to results in other locations (see Table 1). Several vaccine manufacturers have published evidence that reduced susceptibility will not eliminate efficacy due to the high titers of neutralizing antibodies induced by immunization.[61, 62]

[55] https://indianexpress.com/article/explained/covaxin-phase-3-data-coronavirus-variants-7283792/
[56] https://acaai.org/news/acaai-provides-further-guidance-risk-allergic-reactions-mrna-covid-19-vaccines
[57] https://www.nytimes.com/2020/10/23/health/covid-vaccine-astrazeneca-johnson-and-johnson.html
[58] https://www.livelaw.in/news-updates/madras-high-court-notice-sii-dcgi-icmr-volunteer-alleging-side-effects-covishield-trial-170095
[59] https://timesofindia.indiatimes.com/india/covid-19-siis-threat-to-sue-vaccine-volunteer-alarms-scientists/articleshow/79501112.cms
[60] https://science.sciencemag.org/content/371/6528/448.full
[61] https://www.biorxiv.org/content/10.1101/2021.01.25.427948v1
[62] https://www.biorxiv.org/content/10.1101/2021.01.27.427998v1

In addition, vaccine-mediated protection against severe COVID-19, hospitalization and death has so far been maintained even in locations where new SARS-CoV-2 variants are predominating. As a precaution, work is already underway to produce vaccines specifically designed to induce immune responses against emerging SARS-CoV-2 variants. [63]

Comprehensive information on these COVID-19 vaccines, including the countries where they have been given full approval or emergency authorization, is available from the frequently updated New York Times Vaccine tracker.[64] AVAC also maintains a helpful summary pipeline, which offers descriptions of the various technologies employed. [65]

RESOURCES FOR FOLLOWING COVID-19 VACCINE DEVELOPMENT

There are several excellent online resources providing regularly updated information on the pipeline, including the WHO, *New York Times*, and *Regulatory Focus*:

https://www.who.int/publications/m/item/draft-landscape-of-covid-19-candidate-vaccines
https://www.nytimes.com/interactive/2020/science/coronavirus-vaccine-tracker.html
https://www.raps.org/news-and-articles/news-articles/2020/3/covid-19-vaccine-tracker

MAKING VACCINES ACCESSIBLE

Multiple efforts are underway to facilitate large-scale production of efficacious COVID-19 vaccines. The WHO, in partnership with the CEPI and Gavi, has formed the COVAX facility, which aims to provide access to for the highest risk populations globally. [66] Currently, however, COVID-19 vaccine distribution is mirroring the inequities that occurred when combination antiretroviral therapy for HIV first became available, with millions of vaccinations occurring in resource-rich countries and essentially none in the global south. COVAX published their first interim distribution and global supply forecasts on February 3, 2020, [67] highlighting that attempts are underway to begin to address the problem but a vast amount of work remains to be done.

A very broad coalition of over 140 global leaders, experts, elders and advocates have issued a call for a "people's vaccine" and requested guarantees that COVID-19 vaccines, diagnostics, tests and treatments are "provided free of charge to everyone, everywhere." [68] The People's Vaccine Alliance has noted that, as of February 4, 2021, a total of 108 million COVID-19 vaccine doses have been given across 67 countries but only 4.4% were in developing countries. [69] The alliance is demanding suspension of intellectual property rules, sharing of technology and ending of monopolies in an effort to accelerate the equitable distribution of COVID-19 vaccines.

Currently, information on vaccine pricing is limited; pharmaceutical corporations have insisted that pricing and other contract details remain secret.

[63] https://www.bloomberg.com/news/articles/2021-02-04/pfizer-pfe-moderna-mrna-race-to-make-vaccines-for-covid-variants
[64] https://www.nytimes.com/interactive/2020/science/coronavirus-vaccine-tracker.html
[65] https://www.avac.org/resource/cheat-sheet-covid-19-vaccine-pipeline
[66] https://www.statnews.com/2020/06/26/who-partners-unveil-ambitious-plan-to-deliver-2-billion-doses-of-covid-19-vaccine-to-high-risk- populations/
[67] https://www.who.int/news/item/03-02-2021-covax-publishes-first-interim-distribution-forecast
[68] https://www.unaids.org/en/resources/presscentre/pressreleaseandstatementarchive/2020/may/20200514_covid19-vaccine
[69] https://www.epmmagazine.com/news/supply-of-covid-19-vaccines_1/

Table 2: Prices for Approved and Experimental COVID-19 Vaccines [70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81] (as of February 3, 2021)

Product	Price(s) per dose, by country/COVAX
Pfizer/BioNTech (BNT162b2)	EU: $14.70 US:$19.50 COVAX: "not for profit price" amount unspecified
AstraZeneca/Oxford (AZD1222)	EU: $2.10 US: $4.00 Thailand $5.00
Serum Institute of India (Covishield)	Bangladesh: government price $4; private market price $8 COVAX: up to $3 India: government price $3- $4; private market price $6 -$8 South Africa: $5.25 ($3/dose under the African Union Agreement) Uganda: $7 per dose
Moderna (m-RNA-1273)	EU: $18 US: $15
Gamaleya (Sputnik-V)	"less than $10"
Sinovac (Coronavac)	Brazil: $10.30 China (Government price): $30.57 Indonesia: $13.57 Thailand $17 Ukraine $18
Sinopharm (Inactivated vaccines)	China (Government price): $30.57
CanSino (Ad5-nCoV)	Not available
Bharat Biotech (Covaxin)	$4.05
Novavax (NVX-CoV2373)	US: $16
Johnson and Johnson (JNJ-78436735)	EU: $8.50 US: $10.00
Sanofi/GSKh	EU: $10.50 US: $9.30
CureVac CVnCoV	EU: $11.84

[70] https://www.nytimes.com/2021/01/28/world/europe/vaccine-secret-contracts-prices.html

[71] https://www.reuters.com/article/health-coronavirus-safrica-vaccines/update-3-south-africa-to-pay-525-a-dose-for-astrazeneca-vaccine-from-indias-sii-idUSL1N2JW0KI

[72] https://www.theguardian.com/world/2020/dec/18/belgian-minister-accidentally-tweets-eus-covid-vaccine-price-list

[73] https://www.livemint.com/science/health/coronavirus-vaccine-to-cost-rs-219-292-to-govt-rs-438-584-in-private-market-serum-institute-of-india-11609760249328.html

[74] https://timesofindia.indiatimes.com/india/experts-question-govt-vaccine-purchase-price-say-its-higher/articleshow/80260579.cms

[75] https://www.business-standard.com/article/current-affairs/coronavirus-vaccine-moderna-pfizer-to-oxford-covaxin-vaccine-price-who-gets-it-first-other-faqs-on-covid-vaccine-120112000362_1.html

[76] https://www.pfizer.com/news/press-release/press-release-detail/pfizer-and-biontech-reach-agreement-covax-advance-purchase

[77] https://sputnikvaccine.com/newsroom/pressreleases/ministry-of-health-of-nicaragua-has-authorized-the-use-of-sputnik-v/

[78] https://www.reuters.com/article/us-health-coronavirus-ukraine-vaccine-idUKKBN294150?edition-redirect=uk

[79] https://riotimesonline.com/brazil-news/rio-business/coronavac-to-be-four-times-more-costly-than-flu-vaccine/

[80] https://www.thejakartapost.com/news/2020/10/13/covid-19-vaccine-to-be-priced-at-rp-200000-per-dosage-bio-farma.html

[81] https://www.globaltimes.cn/content/1210093.shtml

Intellectual property (IP) monopolies can create supply problems – in this case, with desperately needed coronavirus vaccines. In January 2021, countries were scrambling to avert emergence and spread of coronavirus variants – especially those that are both more transmissible and render vaccines less effective – by vaccinating as many people as quickly as possible. Pfizer reduced – and delayed – anticipated shipments to Canada and the EU after closing its plant in Belgium to upgrade production capacity in January. At the same time, after delivering far fewer vaccine doses than the EU expected, AstraZeneca cited production problems, saying delivery dates were "targets, rather than promises." [82] Unexpected delays in, and smaller than anticipated deliveries of coronavirus vaccines slowed vaccination efforts in Canada and the EU.

Moderna announced that it would not enforce its COVID-19-related patents during the pandemic, and willingness to grant licenses after the end of the pandemic (although no definition or timeframe was given). [83] However, as noted by civil society, know-how, technology and other aspects of vaccine development production would still be protected under IP rules.[84]

PART SEVEN

TESTING FOR COVID-19

TARGET PRODUCT PROFILE

The ideal target product profile for a diagnostic test is cheap, rapid, easily administered in multiple settings and highly accurate (sensitive and specific). Sensitivity is a test's capacity to correctly identify a true positive result, while specificity reflects a test's capacity to identify true negative result. There are some circumstances where it may be reasonable to accept lower accuracy if a test is rapid and easy to administer (e.g. suitable for home use).[85] For SARS-CoV-2 testing, optimal approaches should involve minimal sample handling in order to reduce exposure to the virus.

DIAGNOSTIC TESTING

There are a bewildering number of diagnostic tests for COVID-19, the majority based on detecting the genetic material (RNA) of the SARS-CoV-2 virus using polymerase chain reaction (PCR) technology. The PCR approach amplifies any RNA in samples that matches known segments of SARS-CoV-2 RNA as a means to detect the presence of the virus. Typical PCR approaches require a process of repeated heating and cooling (thermal cycling) and take one to four hours.

[82] https://www.cnbc.com/2021/01/29/eu-publishes-astrazeneca-vaccine-contract-as-battle-over-supplies-heats-up.html
[83] https://investors.modernatx.com/node/10066/pdf
[84] https://www.doctorswithoutborders.org/what-we-do/news-stories/news/msf-modernas-decision-not-enforce-covid-19-vaccine-patents-during
[85] https://www.nytimes.com/2020/07/03/opinion/coronavirus-tests.html

At least two companies, Abbott and Cepheid, have developed all-in-one PCR devices that accelerate the process and reduce the required time to less than an hour. In the case of Cepheid – known for marketing its cartridge-based GeneXpert system for detecting drug-resistant tuberculosis – the company is charging a price of $20 for 145 eligible developing countries, drawing the ire of activists. The price is six times what the test costs to manufacture, leading to demands for significant price reductions, including a global civil society campaign for a top price of $5.[86, 87]

Additional SARS-CoV-2 RNA tests in development use technologies that avoid the need for thermal cycling, potentially making the suitable for point-of-care (POC) application. These include loop-mediated isothermal amplification (LAMP)-based approaches, and combinations of LAMP with Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR) technology (a gene editing technique). [88, 89]

The standard approach for SARS-CoV-2 RNA testing involves the use of nasopharyngeal swabs that go along the passageway that connects the base of the nose to the back of the throat, but several research teams have advanced saliva-based approaches that may have the potential to offer similar accuracy with greater rapidity and convenience. On August 15, 2020, the US FDA granted emergency use authorization for the SalivaDirect COVID-19 diagnostic test.[90] The SalivaDirect test was developed at Yale School of Public Health and funded by the US National Basketball Association and the National Basketball Players Association; it is open-source, 94% accurate, and expected to be priced at $10 per test.[91, 92]

The ACT Accelerator has forged global partnerships for improving access to rapid testing in low- and middle-income countries; although the Global Fund has contributed $50 million, and Abbott and SD Bioscience have agreed to a $5 price ceiling for their tests, only 120 million tests will be provided over a six-month period.[93]

Importantly, detection of virus RNA does not always mean that fully intact infectious virus is present. Furthermore, false negative results are also possible, with the risk increasing over time after onset of symptoms.[94] Evidence indicates that false negative results have contributed to anecdotal reports of possible reinfection after recovery from COVID-19. For example, reports of cases of reinfection in South Korea appeared to be explained by false negative PCR results being followed by additional positive test results that did not reflect the presence of transmissible virus (reinfection with SARS-CoV-2 is possible, especially with a new variant).[95]

[86] https://www.treatmentactiongroup.org/statement/treatment-action-group-statement-on-the-high-price-of-cepheids-xpert-test-for-covid-19/

[87] https://healthpolicy-watch.news/medecins-sans-frontieres-announces-campaign-for-5-covid-19-test-on-tuberculosis-testing-platform/

[88] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7346719/

[89] https://www.nature.com/articles/s41587-020-0513-4

[90] https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-issues-emergency-use-authorization-yale-school-public-health

[91] https://eu.usatoday.com/story/sports/nba/2020/08/15/fda-approves-covid-19-saliva-test-developed-yale-nba-nbpa-aid/5590452002/

[92] https://publichealth.yale.edu/news-article/27120/

[93] https://www.who.int/news/item/28-09-2020-global-partnership-to-make-available-120-million-affordable-quality-covid-19-rapid-tests-for-low--and-middle-income-countries

[94] https://www.cdc.gov/mmwr/volumes/70/wr/mm7008a3.htm?s_cid=mm7008a3_w

[95] https://www.sciencenews.org/article/coronavirus-covid19-reinfection-immune-response

In addition to testing for SARS-CoV-2 RNA, it is also possible to detect virus antigens. Antigens are virus proteins or protein fragments that are recognized by the immune system. The tests use antibodies that are reactive to SARS-CoV-2 proteins to flag their presence in samples. Fewer antigen tests are available or in development and, while they can potentially be cheaper and more easily scalable for point-of-care use, they are generally much less sensitive than PCR tests (meaning there is a greater risk of false negative results). [96]

FIND maintains an online database of diagnostic tests and publishes evaluations of test performance.[97] Many commercial manufacturers have developed diagnostics, and individual laboratories can also be authorized to conduct their own in-house tests. The development of more rapid tests is a major research focus.[98]

ANTIBODY- WHICH ONES, AND DO THEY CONFER IMMUNITY?

Antibody testing – also referred to as serology – is designed to detect whether a person has developed antibodies that specifically target SARS-CoV-2. These tests are generally not used for diagnosis, because it takes days to weeks after SARS-CoV-2 infection for the immune system to generate virus-specific antibodies.[99]

ABOUT ANTIBODIES

Antibodies are Y-shaped proteins produced by B cells in response to infection. The first type to be generated after an exposure to a pathogen are called immunoglobulin M or IgM for short. Later in the course of infection, B cells switch to producing IgG antibodies and IgA antibodies, with the latter preferentially distributed at mucosal surfaces. IgG and IgA antibodies are typically more effective at binding and neutralizing their targets compared to IgM. Most antibody tests look for the presence of IgG antibodies.

Evidence indicates that recovery from COVID-19 and the generation of antibodies leads to protective immunity in most cases for at least six months. [100, 101]

A number of research papers have raised concerns that antibody levels may decline precipitously in the months after recovering from COVID-19 [102, 103, 104] but immunologists note that this is not atypical of the kinetics of an immune response to a pathogen that has not previously been encountered.[105]

[96] https://www.sciencemag.org/news/2020/05/coronavirus-antigen-tests-quick-and-cheap-too-often-wrong
[97] https://www.finddx.org/covid-19/pipeline/
[98] https://www.nature.com/articles/d41586-020-02140-8
[99] https://www.nature.com/articles/s41591-020-0897-1
[100] https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2021.26.5.2100092
[101] https://www.nejm.org/doi/10.1056/NEJMoa2034545
[102] https://www.medrxiv.org/content/10.1101/2020.07.09.20148429v1
[103] https://www.nature.com/articles/s41591-020-0965-6
[104] https://www.nejm.org/doi/full/10.1056/NEJMc2025179
[105] https://www.nytimes.com/2020/07/22/health/covid-antibodies-herd-immunity.html

An analysis of the presence of antibody titers in a cohort of 19,860 individuals conducted by researchers at Mount Sinai Hospital in New York found that they were stable over a three month period and correlated with neutralization activity against SARS-CoV-2 in laboratory tests.[106] The persistence of antibodies may also vary depending on the part of SARS-CoV-2 that they target, with some studies suggesting that antibody responses to a part of the spike protein called the receptor binding domain (RBD) are more robust than those against the nucleocapsid protein.[107]

There are many different antibody tests available, which vary in the important parameters of sensitivity and specificity. There are ongoing evaluations of COVID-19 antibody tests being carried out by researchers,[108] the U.S. Food and Drug Administration (FDA)[109] and FIND.[110] A major concern with antibody testing is that even with relatively high sensitivity, false positives can occur at a problematic frequency when the prevalence of the disease in the population is low.[111]

One widely publicized proposal for assisting countries in emerging from COVD-19 lockdowns involves providing "immunity passports" to people who display antibody responses to SARS-CoV-2. The idea is based on the assumption that such individuals would be able to resume normal activities without risk. Unfortunately, the uncertainty about the extent and duration of immunity and the potential for false positive antibody responses make this proposal a non-starter, in addition to concerns about discrimination, privacy and practicality.[112]

At the current time the primary role for antibody testing is for conducting population-based surveys of exposure to SARS-CoV-2 and for monitoring responses to vaccines.

VIRAL LOAD

The term viral load is familiar to those involved in HIV care, because a variety of well-established tests are available that quantify the amount of HIV RNA in blood samples in order to monitor the effectiveness of treatment. Assessments of SARS-CoV-2 viral load are being carried out by researchers, both in order to understand the pathogenesis of COVID-19 and to monitor antiviral effects of candidate therapeutic interventions. However, it's important to appreciate that experience with methods for measuring SARS-CoV-2 viral load is much more limited than is the case for HIV.

There are two main methods for quantifying the amount of SARS-CoV-2 RNA in samples. The most common uses the PCR test to amplify viral RNA from samples, then employs a formula to calculate how much RNA was present based on how many PCR cycles of heating and cooling were necessary to detect the RNA. An alternate method called droplet digital PCR (ddPCR) distributes a sample across thousands of tiny wells and tags any viral RNA that is present with fluorescent signal that allows machine-based counting of fluorescent droplets to quantify the amount of viral RNA. Studies suggest the results produced by the two methods generally correlate, but ddPCR is more sensitive for detecting low levels of SARS-CoV-2 RNA.[113]

[106] https://www.medrxiv.org/content/10.1101/2020.07.14.20151126v1
[107] https://www.nytimes.com/2020/07/26/health/coronvirus-antibody-tests.html
[108] https://www.medrxiv.org/content/10.1101/2020.04.25.20074856v2
[109] https://www.fda.gov/medical-devices/emergency-situations-medical-devices/eua-authorized-serology-test-performance
[110] https://www.finddx.org/covid-19/sarscov2-eval-immuno/
[111] https://www.cdc.gov/coronavirus/2019-ncov/lab/resources/antibody-tests-guidelines.html
[112] https://www.nature.com/articles/d41586-020-01451-0
[113] https://academic.oup.com/cid/article/71/15/793/5812997

Published evidence indicates that viral load in respiratory tract samples peaks around the time that symptoms begin and declines within one to three weeks.[114] Higher viral loads at hospital admission have been associated with worse outcomes, including higher risk of mortality.[115, 116] However, viral load levels can be similar between asymptomatic and symptomatic individuals, underscoring the possibility of asymptomatic transmission.[117]

Studies are evaluating the role of viral load monitoring in assessing the effectiveness of treatments for COVID-19. Evidence to date is limited. For example, while a large U.S.-based efficacy trial of the antiretroviral drug remdesivir reported a slight but significant improvement in recovery time,[118] viral load results were not included. A prior trial in China was unable to demonstrate a statistically significant effect of remdesivir on SARS-CoV-2 viral load compared to placebo.[119]

WHAT TESTS DO WE NEED

All forms of SARS-CoV-2 testing could benefit from improvements in standardization, ease of use, rapidity of results, affordability and applicability to multiple settings including home and point of care. Intensive work is happening in this area, and the FDA recently initiated a new effort to support the development of COVID-19 diagnostic tests "that can be performed entirely at home or in other settings besides a lab, such as offices or schools, and that could be available without a prescription."[120]

PART EIGHT

NATURAL HISTORY OF COVID-19

The natural history of COVID-19 is complex and variable. Overall, an estimated 80% of people do not develop serious illness. Of the remaining 20%, an estimated 15% develop severe disease and 5% may become critically ill. The time to severe illness ranges from 5-12 days, with some people worsening rapidly.[121]

Up to 45% of people may not have any symptoms, while others remain ill for months, with what has been referred to as lingering, or long COVID.[122, 123, 124] The risk factors for lingering COVID-19 have not been identified. Symptoms, ranging from mild to severe, include fever, night sweats, dry cough, shortness of breath and difficulty breathing, racing heartbeat, hypertension, headache, severe fatigue, anxiety, difficulty sleeping confusion, difficulty with memory and concentration, muscle and body aches, pain in the hands and feet, ringing in the ears, dizziness and gastrointestinal problems.[125, 126, 127] Currently, it is not known how long these symptoms will last.

[114] https://www.journalofinfection.com/article/S0163-4453(20)30449-7/fulltext
[115] https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30232-2/fulltext
[116] https://academic.oup.com/cid/article/doi/10.1093/cid/ciaa851/5865363
[117] https://www.nejm.org/doi/full/10.1056/NEJMc2001737
[118] https://www.nejm.org/doi/full/10.1056/NEJMoa2007764
[119] https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)31022-9/fulltext
[120] https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-posts-new-template-home-and-over-counter-diagnostic-tests-use-non
[121] https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-guidance-management-patients.html
[122] https://www.acpjournals.org/doi/10.7326/M20-3012
[123] https://www.theatlantic.com/health/archive/2020/06/covid-19-coronavirus-longterm-symptoms-months/612679/
[124] https://docs.google.com/document/d/1KmLkOArlJem-PArnBMbSp-S_E3OozD47UzvRG4qM5Yk/edit#
[125] https://directorsblog.nih.gov/2020/09/03/citizen-scientists-take-on-the-challenge-of-long-haul-covid-19/
[126] https://www.sciencemag.org/news/2020/07/brain-fog-heart-damage-covid-19-s-lingering-problems-alarm-scientists
[127] https://elemental.medium.com/new-survey-identifies-98-long-lasting-covid-symptoms-87935b258a3e

At first, COVID-19 was considered mainly as a respiratory infection, but it has become clear that it is a systemic disease, with gastrointestinal, cardiac, renal, neurological, and vascular involvement.[128, 129] Severe COVID-19 can lead to cardiac, kidney, and liver injury, cardiac arrhythmias, rhabdomyolysis, coagulopathy, and strokes, and it can precipitate cytokine storm – an inflammatory response during which the immune system attacks cells and tissues – especially in the lungs.[130]

- Children are less likely to become seriously ill from COVID-19, but they are vulnerable to a range of consequences, including poverty, violence, loss of a parent or other family members, death from vaccine-preventable diseases and disruption of their education.[131] Although it is rare, some children who have COVID-19 fall ill with a rare condition called Multisystem Inflammatory Syndrome in Children (MIS-C), which causes widespread inflammation including in the heart, lungs, kidneys, brain, skin, eyes, or gastrointestinal tract, usually within two to four weeks after having COVID-19. Although it can become very serious, even fatal, MIS-C is usually treatable if it is caught early; symptoms may include fever, abdominal pain and vomiting, diarrhea, neck pain, rash, bloodshot eyes and being extra tired.[132]

The overall fatality rate from COVID-19 is difficult to determine, for several reasons, including that there are large numbers of people who have never been tested, and because the risk of death varies by age and other factors, including access to healthcare and improvements in treatment. Studies from different parts of the world estimate an infection fatality rate (IFR; the proportion of people who will die from the infection, including people who were asymptomatic and those who were not tested) of 0.5% to 1%.[133] A current estimate of the fatality rate from Geneva, Switzerland, ranges from 0.64% overall to 5.6% among people age 65 and above.[134]

Most people will fall ill within 4-5 days after they were exposed to COVID-19, but it may take up to 14 days before symptoms develop.[135] Symptoms include:

- Fever
- Chills
- Dry cough
- Appetite loss
- Fatigue
- Muscle or body aches
- Headache
- New loss of taste or smell
- Sore throat
- Congestion or runny nose
- Nausea or vomiting
- Diarrhea
- Conjunctivitis
- Skin rash
- Shortness of breath or difficulty breathing
- Discolored fingers or toes.[136, 137]

[128] https://www.health.harvard.edu/diseases-and-conditions/covid-19-basics
[129] https://www.acpjournals.org/doi/10.7326/M20-2003
[130] https://www.nejm.org/doi/full/10.1056/NEJMcp2009575
[131] https://www.un.org/sites/un2.un.org/files/policy_brief_on_covid_impact_on_children_16_april_2020.pdf
[132] https://www.cdc.gov/coronavirus/2019-ncov/daily-life-coping/children/mis-c.html
[133] https://www.nature.com/articles/d41586-020-01738-2
[134] https://osf.io/wdbpe/
[135] https://www.health.harvard.edu/diseases-and-conditions/covid-19-basics#:~:text=Recently%20published%20research%20found%20that,as%2013%20days%20later.
[136] https://www.cdc.gov/coronavirus/2019-ncov/symptoms-testing/symptoms.html
[137] https://www.who.int/emergencies/diseases/novel-coronavirus-2019/question-and-answers-hub/q-a-detail/q-a-coronaviruses

Although there is no formal consensus, most people with COVID-19 are considered not to be contagious 10 days after they have stopped having symptoms, including fever, or after having two negative viral load test results at least 24 hours apart (although poor access to testing makes this impossible in many places).[138, 139]

COVID-19 and HIV

COVID-19 has a huge impact on people living with HIV, as well as the global goals and targets for ending the epidemic. A double whammy of funding gaps and COVID-19-related disruptions to ART and HIV services has prevented the world from achieving the UNAIDS 90-90-90 targets for ending AIDS by 2030. [140] Globally, in 2020, 73 countries reported being at risk of antiretroviral (ARV) drug stockouts; in 24 of them, which are home to 8.3 million people who receive ARVs, stock reached critically low levels or stock-outs have occurred. Transportation shutdowns, late delivery - and limited access to healthcare during lockdowns – threaten to undo global progress against AIDS.[141]

People living with HIV who are on ART and virally suppressed are not at higher risk of becoming infected with COVID-19 than the general public. However, people with a low CD4 cell count (<350 cells/mm^3, and especially <50 cells/ mm^3) or a low CD4 cell nadir (<200 cells/mm^3), people who are not taking ART – including those who are undiagnosed - and those with comorbidities or a recent opportunistic infection are at higher risk for severe illness and death from COVID-19. [142, 143]

COVID-19 outcomes among people living with HIV differ. Also, this data is from 2020 – and standard for care for COVID-19 has improved since the beginning of the COVID-19 pandemic, which is likely to have a positive effect on survival rates.

In Cape Town, South Africa, where prevalence of HIV is high, data from nearly 13,000 people with COVID-19 who were treated in the public sector revealed that mortality from COVID-19 was two to three times higher among people living with HIV – regardless of viral suppression – than among HIV-negative people. (In contrast, the risk of death was much higher among people over age 50 and people with diabetes (even if well-controlled), hypertension and kidney disease.[144]

In New York, where COVID-19 was prevalent, and HIV rates are high, a study comparing COVID-19 outcomes among 204,583 people, 2,410 of them living with HIV, reported that a higher proportion of people living with HIV were hospitalized, admitted to intensive care, and died than people who did not have HIV -especially those with a CD4 cell count of <500 cells/mm^3.[145] Another study, also done in New York, followed 2,988 people living with HIV who were diagnosed with COVID-19. Although diagnosis rates did not differ by HIV status, people living with HIV were more likely to develop severe disease and be hospitalized, especially those with a CD4 cell count of <500 cells/mm^3. Both studies reflected demographic differences due to structural racism that has created health disparities in the US: Black and Hispanic people were more likely to have HIV and COVID-19 than their White counterparts.[146]

A UK analysis of COVID-19 outcomes reported a higher death rate among people living with HIV versus those who were HIV-negative, even after taking obesity, poverty, smoking and ethnicity into account – although Black people living with HIV were at higher risk of death from COVID-19 than those of other races/ethnicities.[147] A different analysis of 47,592 people, 122 of them living with HIV, who were hospitalized with COVID-19 in the UK, found a higher death rate among people living with HIV, regardless of age.[148]

[138] https://www.health.harvard.edu/diseases-and-conditions/if-youve-been-exposed-to-the-coronavirus
[139] https://medicalxpress.com/news/2020-04-covid-contagious-longer.html
[140] https://www.unaids.org/sites/default/files/media_asset/2020_global-aids-report_en.pdf
[141] https://www.who.int/news/item/06-07-2020-who-access-to-hiv-medicines-severely-impacted-by-covid-19-as-aids-response-stalls
[142] https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa1339/5903368
[143] https://onlinelibrary.wiley.com/doi/10.1111/hiv.13037
[144] https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa1198/5899044
[145] https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa1793/6012626
[146] https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2775827
[147] https://www.thelancet.com/journals/lanhiv/article/PIIS2352-3018(20)30305-2/fulltext
[148] https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa1605/5937133

PART NINE

STANDARDS FOR EVIDENCE: ASSESSING RESEARCH IN THE CONTEXT OF A PANDEMIC

Trials need to answer questions about drug safety, efficacy and, in the context of a global pandemic, feasibility. But an overwhelming volume of research – sometimes of poor quality, in small numbers of people and without adequate peer review – and the high stakes involved with finding vaccines and a treatment for a global pandemic – have led to a confounding array of science-by-press-release. Understanding trial design is essential for interpreting results.

SIMPLE QUESTIONS ABOUT COVID-19 TREATMENT TRIALS

The desperation for a pandemic-halting cure and financial high stakes involved with COVID-19 vaccine and drug development call for rigorous assessment of clinical trial design and results. The gold standard for establishing cause and effect between an intervention and an outcome is a randomized, controlled trial, because this design minimizes bias. These trials lay the foundation for additional research of the safety and effectiveness of treatment for COVID-19 – and other illnesses – across different populations and under different circumstances.

Was the trial randomized?
Assigning people to a treatment by chance instead of selecting them based on how severe their illness is, their age and other criteria minimizes bias.

Was the trial controlled?
If a new treatment is not compared with anything else, either a placebo or the current standard-of-care, it will not be possible to tell whether it improved or worsened outcomes.

Was the trial blinded?
In a double-blinded trial, neither the study participant or the research staff know whether the person is getting the experimental drug vs. standard of care or placebo. As an example, people who are known to be getting an experimental drug might be monitored more closely than those getting the standard of care; double-blinding is done to avoid bias, by ensuring that all participants receive the same amount of care.

Knowing the trial's main question, called the primary endpoint, is important because it was planned to answer that specific question (as well as secondary endpoints), rather than others that may be added after it is completed.

The trial's primary endpoint needs to address the most important question. For example, does the drug cure people? Do people who get the drug live longer? Does the drug help people leave the hospital sooner? Does the vaccine prevent people from becoming seriously ill?

What did the drug or vaccine do?
Did it save lives, prevent people from worsening or becoming infected, shorten the duration of symptoms?

How were results analyzed; intent-to-treat includes everyone in the trial and is the most reliable/rigorous way to analyze results. A per-protocol analysis only includes those who remained in the trial – there could be a big difference in the results, for example, if there is a high dropout or fatality rate. The drug will look far more effective if per protocol analysis is used.

Was there a post-hoc analysis? Sometimes, if a trial does not come out the way sponsors expected it to, they will do a post-hoc analysis (which means after the event, especially with the false or misleading assumption that what happened has a logical relationship with the event it follows). For example, if the trial showed that the drug did not reduce the overall death rate, a sponsor might decide to do a post-hoc analysis to find out if deaths were reduced within a small group of people, such as those under age 25.

SIMPLE QUESTIONS ABOUT COVID-19 TREATMENT TRIALS (continued)

How many people were in the study?
The size of the trial matters, as well as the types of people who participated in it. The study has to be large enough and designed – called 'powered' - to yield statistically significant results- that is, that the result is not by chance. As an example, a trial of the AstraZeneca coronavirus vaccine in South Africa was small (just over 2,000 people), with an average age of 30 – people who are unlikely to fall seriously ill, require hospitalization, or die from COVID-19. There were no cases of severe COVID-19 in the trial – including among people who got placebo. Although the study found that the vaccine was not effective for preventing infection with the B.1.351 variant, it could not shed light on whether the vaccine prevented serious illness, hospitalization and death because it was too small.[149]

Who was the drug or vaccine studied in, where was it studied (age, race, sex and other baseline characteristics) **and will it work for everyone/ those who need it most?**
Coronavirus variants have emerged in Brazil, India, the UK and the US. Trials that do not include people at risk for or infected with these variants will not produce useful information about how to effectively prevent and treat them. Older people (age >65 years), pregnant women and people with underlying medical conditions (hypertension, diabetes -especially if it is poorly controlled or uncontrolled - obesity, chronic kidney or liver disease, chronic obstructive pulmonary disease, serious cardiovascular disease, sickle cell disease, transplant recipients and other people with weakened immune systems) are more likely to have severe disease from COVID-19.[150, 151, 152] In the US, cardiovascular disease, diabetes and chronic lung disease increased the odds of hospitalization from COVID-19 by six-fold, and death by 12-fold.[153]

Sponsors may be reluctant to enroll people with poor prognostic factors because they can make drugs or vaccines look less effective. But is particularly important to have information about safety and efficacy of new drugs and vaccines in these groups, since their side effects may be worse or they may be less effective. Phase IIb/ and phase III trials, where an effective dose has been established and some drug interactions are known, may be the best entry point for people with pre-existing conditions, although compassionate use/named patient protocols should also be in place to create access for people who are unable to enroll in, or are ineligible for clinical trials.

In the US, far higher rates of COVID-19 - and serious illness and death resulting from it - have been reported among Black and Latinx people; this is likely to be driven by structural racism more than biological vulnerability.[154, 155] Similar findings have been reported in the UK, where Black, Asian and Hispanic people are more likely to acquire COVID-19.[156] Sponsors need to ensure adequate representation in COVID-19 trials so that results are relevant across racial and ethnic groups; in particular, there may be variability in vaccine safety and immunogenicity amongst people with different ethnicities.[157]

- Sex: women are less likely to die from COVID-19 than men (although the pandemic has increased rates of gender-based violence and deepened existing social and economic inequalities for women and girls).[158, 159]
- Other factors are yet to be identified, but once known, they should be considered when designing trials and interpreting their results.

[149] https://www.nejm.org/doi/10.1056/NEJMoa2102214
[150] https://storage.googleapis.com/stateless-bhekisisa-website/wordpress-uploads/2020/06/94d3ea42-covid_update_bhekisisa_wc_3.pdf
[151] https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-at-increased-risk.html
[152] https://www.cdc.gov/coronavirus/2019-ncov/cases-updates/special-populations/pregnancy-data-on-covid-19.html
[153] https://www.cdc.gov/mmwr/volumes/69/wr/pdfs/mm6924e2-H.pdf
[154] https://www.scientificamerican.com/article/why-racism-not-race-is-a-risk-factor-for-dying-of-covid-191/
[155] https://jamanetwork.com/journals/jama/fullarticle/2766098
[156] https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370(20)30148-6/fulltext
[157] https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370(20)30148-6/fulltext
[158] https://globalhealth5050.org/covid19/sex-disaggregated-data-tracker/
[159] https://www.unwomen.org/-/media/headquarters/attachments/sections/library/publications/2020/policy-brief-the-impact-of-covid-19-on-women-en.pdf?la=en&vs=1406

SIMPLE QUESTIONS ABOUT COVID-19 TREATMENT TRIALS (continued)

Did the drug or vaccine work equally well for everyone in the study?
If not, who was it most effective for?

What stage of the disease was studied?
Different approaches to treating COVID-19, based on its manifestations and severity, are necessary. Antivirals tend to be most effective when taken earlier; sometimes an effective drug might be used too late- or a drug that does not work or is poorly tolerated among people with a mild illness could be life saving for people with severe COVID-19. For example, in the UK RECOVERY trial, dexamethasone significantly improved survival among people with severe COVID-19 who were on mechanical ventilators or receiving oxygen, but it did not help people with milder illness.

Did the people in the study have similar baseline characteristics and a similar disease stage?
If not, it will be difficult to interpret results unless the trial was designed to take these factors into account (called stratification); as an example, some trials have included people on ventilators along with those with less severe forms of COVID-19, or people with poor prognostic factors with younger and healthier people.

Can the drug be used with other medicines, especially those that people take for chronic illnesses?
Drug interactions can make medicines less effective – and lead to drug resistance – or worsen side effects. Information about how medicines can be used, and options for switching is important for people living with HIV and many other conditions requiring daily medication.

PART TEN

TARGET PRODUCT PROFILE FOR COVID-19 TREATMENT

Ideally, treatments for COVID-19 would be oral and/or inhalable, cheap to produce, easy to manufacture, distribute and administer; safe, tolerable and effective in infants, children and adults (including during pregnancy and breastfeeding), the elderly and people with pre-existing conditions. Treatment should work across the spectrum of COVID-19, by preventing infection, illness, progression to serious illness - and by curing people who have developed more serious illness or lingering symptoms. In addition, treatment needs to have limited drug interactions so it can be used with other medicines (including, but not limited to, TB and malaria prophylaxis and treatment, HIV antiretrovirals, methadone, buprenorphine, antihypertensives, psychiatric medicines, hormonal contraception, insulin and other antidiabetic agents).

PART
ELEVEN

EXISTING TREATMENT FOR COVID-19

One of the complexities of treating - and developing therapies for - COVID-19 is when to intervene. In general, antivirals work best when given early, but many people with COVID-19 may not have symptoms, or may have only a mild, self-limiting illness. By the time they seek health care, antivirals may be less effective. In contrast, immunotherapies are best used later in the course of COVID-19, in people who have developed overactive immune responses; using them pre-emptively could thwart the immune system's defenses against the virus.

It is likely that a combination of drugs- and approaches- will be needed to treat COVID-19. Some scientists suggest that there are three stages of COVID-19 illness. Stage one, which is early infection, can cause cold- or flu-like symptoms as the virus is multiplying. At this stage, monoclonal antibodies may be useful for preventing progression to more serious illness – and antivirals are most likely to be effective. The hallmarks of stage two, the pulmonary phase, are coughing, shortness of breath, low levels of oxygen; blood clotting may also occur. At this point, treatment may include blood thinners, antivirals and therapies for lung function. During stage three, called hyperinflammatory, an overactivated immune system can cause 'cytokine storms' leading to kidney and heart damage as the body attacks itself; antivirals and immunomodulators have been used to treat people in stage three.[160]

PART
TWELVE

SUPPORTIVE CARE

Healthcare workers (HCW) need - and deserve – safe working conditions for delivering quality care to people with COVID-19 and other illnesses. Although data are scarce, WHO estimates that in some countries, 1 of 10 HCW have been infected with SARS-CoV-2.[161] As of June 3rd, 2020, an estimated 450,000 HCW were infected worldwide.[162] An analysis of data from over 2 million US and UK users of the COVID-19 Symptom Study app found a 3-fold higher risk for COVID-19 among frontline HCW versus the general public. The risk increased to five-fold among HCV who were Black, Asian and other ethnic minorities – and was even greater among those who lacked adequate access to personal protective equipment (PPE).[163]

There are currently no recommended treatments for people with mild COVID-19. The standard of care is resting at home, drinking ample fluids and using fever reducers if needed. People who are elderly and/or have pre-existing conditions should consult a healthcare provider and be closely monitored, including with a pulse oximeter (a non-invasive fingertip device that measures blood oxygen levels) in case their illness worsens.

The standard of care for people who are hospitalized with moderate to severe/ critical COVID-19 has evolved, as healthcare providers learn from one another. It may include essential medicines, such as fever reducers, pain relievers, anticoagulants and antibiotics for bacterial pneumonia, as well as oxygen to help with breathing.[164,165]

[160] https://journals.physiology.org/doi/pdf/10.1152/physrev.00020.2020
[161] https://www.weforum.org/agenda/2020/04/10-april-who-briefing-health-workers-covid-19-ppe-training/
[162] https://www.covid-action.net/Kieran-Baker/update-up-to-450000-health-care-workers-worldwide
[163] https://www.thelancet.com/journals/lanpub/article/PIIS2468-2667(20)30164-X/fulltext
[164] https://apps.who.int/iris/bitstream/handle/10665/325771/WHO-MVP-EMP-IAU-2019.06-eng.pdf?ua=1
[165] https://files.covid19treatmentguidelines.nih.gov/guidelines/covid19treatmentguidelines.pdf

OXYGEN CONCENTRATORS

In contrast to heavy oxygen tanks, which need to be transported to and refilled at central stations and may explode or catch fire, oxygen concentrators are suitcase or briefcase-sized devices that filter the air and concentrate oxygen, delivering it via a thin tube that can be pressurized with a continuous positive airway pressure (CPAP) machine. Oxygen concentrators run on electricity, batteries or generators; in places where there is an unstable power supply, they may require voltage stabilizers. Currently, there is a global shortage of these devices, due to increased need (estimated at 88,000 large cylinders for every million cases per week, globally), limited number of suppliers, rising prices (up to $2000) and delivery delays.[166]

In addition to HCW and essential medicines, a range of equipment is needed to deliver supportive care, including (but not limited to) PPE, medical monitoring equipment (pulse oximeters, thermometers and other devices used to track vital signs), nasal prongs and tubing, tanks, concentrators and CPAP machines to deliver oxygen, ventilators, and supplies to administer intravenous medicines and fluids.

PART THIRTEEN

ANTI-INFLAMMATORY AND IMMUNE-BASED THERAPIES FOR COVID-19

The only treatment that has been found to significantly reduce mortality among hospitalized people with COVID-19 is the anti-inflammatory corticosteroid dexamethasone. In the large, randomized RECOVERY trial in the United Kingdom, oral or intravenous dexamethasone at 6 mg once daily for up to 10 days reduced mortality by about a third in people receiving mechanical ventilation and by about one fifth among those receiving oxygen without invasive mechanical ventilation.[167] In contrast, there was no benefit from dexamethasone observed in participants who were not receiving any form of respiratory support, and a hint of slightly elevated risk of mortality (17.8% versus 14.0%) although this did not reach statistical significance.

Dexamethasone is off patent and considered affordable in most countries, having been in use since the 1960s and included in the WHO Model List of Essential Medicines since 1977. [168]

The dexamethasone results are consistent with the idea that COVID-19 has three stages, with mild symptoms in stage one and inflammation beginning in stage two, progressing to a more severe immune overreaction consisting of hyperinflammation and excessive production of potentially damaging immune system proteins called cytokines (cytokine storm) in stage three. The anti-inflammatory, immune-suppressive effect of dexamethasone was helpful in stages two and three but may be counterproductive during stage one when an immune response to SARS-CoV-2 is being initiated.

In essence, the evidence suggests that initiation of anti-inflammatory, immune-suppressive interventions have to be timed to allow the early development of immune responses to SARS-CoV-2 (because in most people these immune responses will prevent severe disease) but prevent or ameliorate the excessive immune reaction that can cause tissue damage and mortality in a minority of people with COVID-19.

[166] https://www.nytimes.com/2020/06/23/health/coronavirus-oxygen-africa.html

[167] https://www.nejm.org/doi/full/10.1056/NEJMoa2021436

[168] https://www.who.int/news-room/detail/16-06-2020-who-welcomes-preliminary-results-about-dexamethasone-use-in-treating-critically-ill-covid-19-patients

A range of other anti-inflammatory approaches are being investigated for COVID-19 treatment. Additional corticosteroids in clinical trials include prednisone, hydrocortisone and methylprednisolone. More recently developed drugs that target various steps in inflammatory pathways are also being tested. Janus kinases (JAK) and signal transducer and activator of transcription proteins (STATs) transmit immune-activating signals inside cells and JAK/STAT inhibitors such as ruxolitinib, tofacitinib, peficitinib and baricitinib block this activity. Baricitinib was evaluated in combination with remdesivir in the Adaptive COVID-19 Treatment Trial 2 (ACTT-II), a large randomized study sponsored by the National Institute of Allergy and Infectious Disease (NIAID) in the US; overall, adding baricitiib to remdesivir shortened median recovery time among hospitalized people by a day, although the benefits were greater for people who required supplemental oxygen or non-invasive ventilation, with a median time to recovery shortened from 18 to 10 days. [169, 170, 171]

Upstream of JAK/STAT signaling are cytokines that interact with cytokine receptors on the outside of immune cells in order to deliver activating messages. A variety of antibody-based therapies target either cytokines or cytokine receptors in order to interfere with these interactions and dampen immune activation.

Tocilizumab is an antibody that inhibits the activity of the pro-inflammatory cytokine IL-6 by binding to the IL-6 receptor (IL-6R) on cells. Cohort studies have suggested tocilizumab may have benefit among people with severe COVID-19 including those requiring mechanical ventilation.[172, 173] A trial in people with early-stage pneumonia did not show evidence of efficacy.[174] On July 29, 2020, Roche released news from the phase III COVACTA study of tocilizumab (trade name Actemra) in hospitalized people with severe COVID-19 pneumonia. It did not improve clinical status or reduce mortality.[175] A phase III study of a different antibody targeting IL-6R—sarilumab (trade name Kevzara)—was stopped early after failing to demonstrate any effect among people on ventilators.[176] In the U.S., the negative findings have caused the government's Biomedical Advanced Research and Development Authority (BARDA) to cease supporting studies of Actemra and Kevzara for COVID-19. [177]

However, later trials have suggested that the timing of treatment with tocilizumab and sarilumab and combinations with other treatments can influence how effective they are. The RECOVERY trial conducted a randomized evaluation of tocilizumab among participants whose condition deteriorates despite other interventions; it reported that tocilizumab reduced mortality among people hospitalized with severe COVID-19.[178, 179] In January 2021, UK health authorities issued an interim position statement encouraging tocilizumab or sarilumab for people with severe pneumonia from COVID-19, provided that treatment is started within 24 hours of intensive care admission.

[169] https://clinicaltrials.gov/ct2/show/NCT04401579
[170] https://www.nih.gov/news-events/news-releases/baricitinib-plus-remdesivir-shows-promise-treating-covid-19
[171] https://www.nejm.org/doi/full/10.1056/NEJMoa2031994
[172] https://www.thelancet.com/journals/lanrhe/article/PIIS2665-9913(20)30173-9/fulltext
[173] https://academic.oup.com/cid/article/doi/10.1093/cid/ciaa954/5870306
[174] https://www.reuters.com/article/us-health-coronavirus-roche-hldg/roche-rheumatoid-arthritis-drug-fails-to-help-covid-19-patients-in-italian-study-idUSKBN23O3GG
[175] https://www.roche.com/media/releases/med-cor-2020-07-29.htm
[176] https://www.fiercepharma.com/pharma/sanofi-regeneron-s-kevzara-trial-covid-19-comes-to-a-screeching-halt-after-no-benefit-found
[177] https://www.biocentury.com/article/305872
[178] https://www.recoverytrial.net/for-site-staff
[179] https://www.recoverytrial.net/files/recovery-press-release-tocilizumab_final.pdf

In a pre-print report from the REMAP-CAP trial, combining one of these immune modulators with a corticosteroid reduced the death rate by 24 percent (from 35.8 percent to 27 percent) – a strategy that could avert 1 of every 12 deaths in this group. In addition, people who received one of these immunomodulators recovered more quickly.[180, 181]

Anakinra is a modified version of a protein that inhibits interactions between IL-1R and the proinflammatory cytokines IL-1α and IL-1β. Published results from a small cohort studies have associated anakinra administration with reduced disease severity. [182, 183, 184] and multiple randomized controlled trials are now underway. [185]

Additional anti-inflammatory approaches under investigation include adalimumab, an antibody inhibitor of the cytokine TNF-α, and CD24Fc, a protein that interferes with the ability of certain danger-associated molecules that trigger inflammation. [186]

ANTIVIRAL CYTOKINES

The interferon family of cytokines are being pursued as immune-based therapeutics for COVID-19 due to their ability to exert antiviral effects. SARS-CoV-2 appears to have evolved the ability to subvert production of interferons, [187, 188] which are normally a key component of innate cellular antiviral responses. Type I and Type III interferons have been shown to inhibit SARS-CoV-2 infection in laboratory studies. [189]

Interferon β 1a (an approved therapy for multiple sclerosis) is undergoing the most extensive investigation in human studies of COVID-19. Positive impacts on viral shedding, hospital discharge rates and mortality have been reported from small randomized trials [190, 191] but the large WHO Solidarity trial found no clinical benefit from its use. [192, 193, 194] The U.S. National Institutes of Health (NIH) has announced that their Adaptive COVID-19 Treatment Trial 3 (ACTT-3) will test the combination of subcutaneous interferon β 1a and remdesivir in over 1,000 hospitalized adults. [195]

A company that manufactures an aerosol formulation of interferon β 1a delivered by nebulizer, Synairgen, has reported reductions in severe disease in a trial involving 101 hospitalized people with COVID-19. [196] A larger phase III randomized controlled trial is now underway. [197]

Less information is available on alpha interferon [198] but several randomized trials are ongoing.

[180] https://www.cas.mhra.gov.uk/ViewandAcknowledgment/ViewAlert.aspx?AlertID=103134
[181] https://www.medrxiv.org/content/10.1101/2021.01.07.21249390v1
[182] https://www.thelancet.com/journals/lanrhe/article/PIIS2665-9913(20)30164-8/fulltext
[183] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7252085/
[184] https://www.pnas.org/content/early/2020/07/21/2009017117
[185] https://clinicaltrials.gov/ct2/results?cond=CoVID&term=Anakinra&cntry=&state=&city=&dist=
[186] https://academic.oup.com/ofid/article/7/7/ofaa219/5851926
[187] https://www.sciencedirect.com/science/article/pii/S0168170220308170
[188] https://www.biorxiv.org/content/10.1101/2020.05.11.088179v1
[189] https://jvi.asm.org/content/early/2020/07/16/JVI.00985-20
[190] https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)31042-4/fulltext
[191] https://aac.asm.org/content/early/2020/07/08/AAC.01061-20
[192] https://www.who.int/emergencies/diseases/novel-coronavirus-2019/global-research-on-novel-coronavirus-2019-ncov/solidarity-clinical-trial-for-covid-19-treatments
[193] https://www.who.int/emergencies/diseases/novel-coronavirus-2019/global-research-on-novel-coronavirus-2019-ncov/solidarity-clinical-trial-for-covid-19-treatments
[194] https://www.who.int/emergencies/diseases/novel-coronavirus-2019/global-research-on-novel-coronavirus-2019-ncov/solidarity-clinical-trial-for-covid-19-treatments
[195] https://www.nih.gov/news-events/news-releases/nih-clinical-trial-testing-remdesivir-plus-interferon-beta-1a-covid-19-treatment-begins
[196] https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(20)30511-7/fulltext
[197] http://www.pharmatimes.com/news/synairgen_begins_large-scale_trial_of_inhaled_covid-19_treatment_1361172
[198] https://www.frontiersin.org/articles/10.3389/fimmu.2020.01061/full

CONVALESCENT PLASMA AND MONOCLONAL ANTIBODIES

Convalescent plasma comprises antibodies sampled from people who have recovered from COVID-19. There is a long history of the use of convalescent plasma to treat viral infections, including recent experience with Ebola.[199, 200] Exploratory uncontrolled studies suggested possible therapeutic efficacy in people with COVID-19 [201, 202, 203, 204] but results from larger trials – including the UK RECOVERY trial – have failed to demonstrate benefit. [205, 206, 207] Convalescent plasma was granted emergency authorization for use by the U.S FDA in late 2020, but the agency has since limited the indication to plasma containing high titers of antibodies for the treatment of hospitalized patients early in the disease course or with impaired antibody immunity. [208]

Convalescent plasma can be thought of as an antibody soup containing a mix of antibodies of varying activity targeting multiple different parts of the virus (referred to as polyclonal antibodies). Modern technology also allows the identification of anti-SARS-CoV-2 monoclonal antibodies by essentially fishing out the most potent individual antibodies from the soup and manufacturing them for therapeutic use. There are multiple examples of highly potent monoclonal antibodies that have been identified, and several are advancing into clinical testing. [209, 210, 211, 212]

Bamlanivimab (also known as LY-CoV555) is a monoclonal antibody targeting the SARS-CoV-2 spike protein manufactured by Eli Lilly and Company. In a dose-ranging study, intravenous infusion of 2800mg of the antibody was associated with evidence of accelerated SARS-CoV-2 viral load decline. [213] A trial conducted by the U.S. NIH in people hospitalized with COVID-19 (ACTIV-3) was stopped due to lack of efficacy, [214, 215] but an outpatient study (ACTIV-2) remains ongoing. In an efficacy trial undertaken by the NIH's COVID-19 Prevention Network (CoVPN), bamlanivimab significantly reduced the risk of contracting symptomatic COVID-19 among residents and staff at long-term care facilities. [216]

The FDA issued an emergency use authorization for bamlanivimab on November 9, 2020, [217] which was revoked on April 16, 2021, due to the increase of SARS-CoV-2 variants that are resistant to bamlanivimab when it is used alone, although the combination of bamlanvimab and etesevimab is still available under EUA. [218]

[199] https://www.trasci.com/article/S1473-0502(16)30200-2/fulltext
[200] https://www.jci.org/articles/view/138003
[201] https://www.pnas.org/content/117/17/9490
[202] https://onlinelibrary.wiley.com/doi/full/10.1002/jmv.25882
[203] https://jamanetwork.com/journals/jama/article-abstract/2763983
[204] http://www.haematologica.org/content/early/2020/07/20/haematol.2020.261784
[205] https://www.bmj.com/content/371/bmj.m3939
[206] https://www.nejm.org/doi/full/10.1056/NEJMoa2031304
[207] https://www.recoverytrial.net/news/statement-from-the-recovery-trial-chief-investigators-15-january-2021-recovery-trial-closes-recruitment-to-convalescent-plasma-treatment-for-patients-hospitalised-with-covid-19
[208] https://www.fda.gov/news-events/fda-brief/fda-brief-fda-updates-emergency-use-authorization-covid-19-convalescent-plasma-reflect-new-data
[209] https://www.sciencemag.org/news/2020/05/race-antibodies-stop-new-coronavirus
[210] https://jamanetwork.com/journals/jama/fullarticle/2767383
[211] https://jamanetwork.com/journals/jama/fullarticle/2768115
[212] https://www.cell.com/trends/pharmacological-sciences/fulltext/S0165-6147(20)30166-8
[213] https://www.nejm.org/doi/full/10.1056/NEJMoa2029849
[214] https://www.nejm.org/doi/full/10.1056/NEJMoa2033130
[215] https://www.nih.gov/news-events/news-releases/results-nih-sponsored-activ-3-trial-published
[216] https://www.globenewswire.com/news-release/2021/01/25/2163897/0/en/Analysis-Demonstrates-Effectiveness-of-LY-CoV555-Antibody-in-Preventing-Symptomatic-COVID-19.html
[217] https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-authorizes-monoclonal-antibody-treatment-covid-19
[218] https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-revokes-emergency-use-authorization-monoclonal-antibody-bamlanivimab

The European Medicines Agency (EMA) announced they are reviewing data on the use of monoclonal antibodies for COVID-19.[219]

Eli Lilly and Company has also studied bamlanivimab in combination with a second monoclonal antibody, etesevimab (LY-CoV016). In an outpatient population with mild to moderate COVID-19, the combination is reported to have reduced viral loads in nasal swabs and lessened the frequency of hospitalization or death by 70 percent.[220] The results are not yet published. On February 10, 2021, FDA granted an emergency use authorization for the combination of bamlanivimab and etesevimab.[221]

Another lead candidate is Regeneron Pharmaceuticals REGN-COV2, a double antibody cocktail containing casirivimab and imdevimab that is being assessed in phase II/III treatment trials and a phase III prevention trial.[222] Administration is via intravenous infusion or subcutaneous injection. Published interim results from an ongoing outpatient trial indicate reductions in SARS-CoV-viral load.[223] An emergency use authorization for casirivimab and imdevimab was granted by the FDA on November 21, 2020, with the same indication as Eli Lilly and Company's bamlanivimab. Vir and GSK are developing VIR-7831; the 583-person phase III COMET-ICE trial of VIR-7831 was halted in March 2021 after a recommendation from the Independent Data Monitoring Committee when an interim analysis revealed that it was 85 percent effective in reducing hospitalization and death among people with mild-to-moderate COVID-19 who were at risk for severe illness; the partners will apply for emergency use authorization.[224]

Cocktails of more than one monoclonal antibody are important due to SARS-CoV-2 developing resistance to single antibodies, and emergence of variants such as B.1.351, and P.1 which render bamlanivimab ineffective.[225, 226]

Potential drawbacks for monoclonal antibodies include the challenges associated with manufacturing at scale and cost. The antibody proteins have to be produced in vast steel bioreactors, a complex and expensive process. However, there are existing initiatives exploring how to reduce the costs of manufacturing monoclonal antibodies to scale, such as a collaboration between IAVI and the Serum Institute of India that was launched in the context of HIV but may lead to advances that are translatable to COVID-19.[227] IAVI and the Wellcome Trust have collaborated to issue a timely report on strategies for making monoclonal antibodies more affordable and accessible globally.[228]

[219] https://www.ema.europa.eu/en/news/ema-reviewing-data-monoclonal-antibody-use-covid-19

[220] https://investor.lilly.com/news-releases/news-release-details/new-data-show-treatment-lillys-neutralizing-antibodies

[221] https://www.reuters.com/article/us-health-coronavirus-lilly-fda/eli-lillys-antibody-combination-receives-fda-emergency-use-authorization-for-covid-19-idUSKBN2AA02P

[222] https://investor.regeneron.com/news-releases/news-release-details/regeneron-announces-start-regn-cov2-phase-3-covid-19-prevention

[223] https://www.nejm.org/doi/10.1056/NEJMoa2035002

[224] https://www.gsk.com/en-gb/media/press-releases/vir-biotechnology-and-gsk-announce-vir-7831-reduces-hospitalisation-and-risk-of-death-in-early-treatment-of-adults-with-covid-19/

[225] https://www.biorxiv.org/content/10.1101/2020.07.21.214759v1

[226] https://www.biorxiv.org/content/10.1101/2021.02.11.430787v1

[227] https://www.iavi.org/news-resources/press-releases/2018/iavi-and-serum-institute-of-india-to-develop-and-manufacture-globally-affordable-and-accessible-antibody-products-for-hiv

[228] https://www.iavi.org/news-resources/expanding-access-to-monoclonal-antibody-based-products-a-global-call-to-action

ANTIVIRAL TREATMENTS FOR COVID-19

HOPE AND HYPE ARE NOT ANTIVIRALS

As one drug's prospects wane, much ado is made over another, while a steroid steals the show

Hydroxychloroquine, a decades-old oral drug, prevents and treats malaria. Since it has immunomodulatory effects, it is also used for lupus erythematosus and rheumatoid arthritis. Interest in hydroxychloroquine as a potential treatment for COVID-19 was generated by preliminary in vitro and clinical data from small studies in China and an uncontrolled French trial, supporting further research.[229]

An unprecedented, uninformed and continuing endorsement of hydroxychloroquine by former US president Trump (who has a financial stake in Sanofi, which produces a branded version of the drug) led to a run on it, creating shortages among people who rely on it for lupus and rheumatoid arthritis, steep increases in the price of its active pharmaceutical ingredient (API) and deaths among hydroxychloroquine users.[230, 231]

An analysis of registry data, which was quickly discredited, reported a significant increased death rate among people with COVID-19 treated with hydroxychloroquine or chloroquine versus those who were not given these drugs. Nonetheless, a retrospective analysis from the US Veteran's administration reported a higher death rate among people given hydroxychloroquine.[232, 233] Trials paused, restarted and finally stopped or discontinued use of hydroxychloroquine – including the WHO SOLIDARITY Trial, the NIH ORCHID study and the UK RECOVERY trial, all of which determined that hydroxychloroquine was not an effective treatment.[234, 235, 236] In addition, two large, randomized trials of hydroxychloroquine postexposure prophylaxis among people who had household or occupational exposure to COVID-19 reported that it had not preventive benefit.[237, 238] Shockingly, a July 2020 search of currently recruiting COVID-19 trials on www.clinicaltrials.gov found 106 that included hydroxychloroquine.[239] Notably, the Drugs for Neglected Diseases *initiative* is sponsoring ANTICOV, a multi-site adaptive trial which includes hydroxychloroquine in people with mild COVID-19.[240]

In the meantime, dexamethasone, a cheap and widely available steroid, has reduced mortality among people with severe COVID-19 who were either receiving oxygen or invasive mechanical ventilation (although it did not improve survival among people with less serious disease).[241]

[229] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7159849
[230] https://www.nytimes.com/2020/04/06/us/politics/coronavirus-trump-malaria-drug.html
[231] https://www.dicardiology.com/article/fda-reports-deaths-and-injuries-use-antimalarial-hydroxychloroquine-covid-19-patients
[232] https://www.medrxiv.org/content/10.1101/2020.04.16.20065920v2
[233] https://www.cell.com/med/fulltext/S2666-6340(20)30006-4
[234] https://www.nih.gov/news-events/news-releases/nih-halts-clinical-trial-hydroxychloroquine
[235] https://www.who.int/news-room/detail/04-07-2020-who-discontinues-hydroxychloroquine-and-lopinavir-ritonavir-treatment-arms-for-covid-19
[236] https://www.recoverytrial.net/news/statement-from-the-chief-investigators-of-the-randomised-evaluation-of-covid-19-therapy-recovery-trial-on-hydroxychloroquine-5-june-2020-no-clinical-benefit-from-use-of-hydroxychloroquine-in-hospitalised-patients-with-covid-19
[237] https://www.nejm.org/doi/full/10.1056/NEJMoa2016638
[238] https://www.sciencemag.org/news/2020/06/three-big-studies-dim-hopes-hydroxychloroquine-can-treat-or-prevent-covid-19
[239] https://clinicaltrials.gov/ct2/results?cond=covid+19&term=hydroxychloroquine&cntry=&state=&city=&dist=&recrs=a
[240] https://www.sciencemag.org/news/2020/12/first-its-kind-african-trial-tests-common-drugs-prevent-severe-covid-19
[241] https://www.nejm.org/doi/full/10.1056/NEJMoa2021436

RE-PURPOSED DRUGS

Most medicines in trials for COVID-19 treatment were already developed; they may have failed or were approved for use in other diseases; this is known as re-purposing. The advantage to re-purposing drugs, particularly in the context of a pandemic, is the available information on drug safety and interactions, which allows medicines to be developed far more rapidly, and at significantly less expense than new agents.

Some of these drugs are already generic and could be swiftly and affordably mass-produced, but it will be important to ensure adequate supply for people who rely on them to treat other conditions.

REMDESIVIR

Remdesivir was originally developed - and failed - as a treatment for hepatitis C virus (HCV). It has also been studied in Ebola, SARS and MERS; this research received at least US $70 million in government and/or academic funding support.[242, 243] According to experts at the University of Liverpool, a five-day treatment course of remdesivir could be mass-produced at a profit for less than $5.00 (not including its delivery, since it is given as a daily infusion). [244] Remdesivir has secured emergency use authorizations in the US and Canada, conditional approval from the EMA, provisional approval in Australia, restricted emergency use approval in India, and regulatory approvals in Japan and Bangladesh. [245, 246, 247, 248, 249, 250, 251]

Some of Gilead's remdesivir trials used a primary endpoint of clinical improvement/ being able to leave the hospital sooner instead of higher survival rates, appearing to be engineered for calculating pricing and savings for the US healthcare system. Indeed, the company's Chief Executive, Daniel O'Day, said that remdesivir should help reduce hospital costs by $12,000 per person (based on clinical trials in which people taking remdesivir were discharged four days sooner than those receiving the standard of care). [252]

As the last of Gilead's donated remdesivir was distributed in the US, the government announced that it had purchased 500,000 treatment courses – over 90% of what Gilead will produce in July, August and September 2020 – at fixed, non-negotiable prices. [253] Private insurers will pay $3200 per treatment course, while government-sponsored insurance will pay $2,340; it is unclear how the estimated 28 million uninsured people in the US, most of whom are low-income and/or unemployed, will access remdesivir. [254, 255]

[242] https://www.gilead.com/-/media/gilead-corporate/files/pdfs/covid-19/gilead_rdv-development-fact-sheet-2020.pdf
[243] https://www.washingtonpost.com/business/2020/05/26/remdesivir-coronavirus-taxpayers/
[244] http://viruseradication.com/journal-details/Minimum_costs_to_manufacture_new_treatments_for_COVID-19/
[245] https://www.gilead.com/news-and-press/press-room/press-releases/2020/5/gileads-investigational-antiviral-remdesivir-receives-us-food-and-drug-administration-emergency-use-authorization-for-the-treatment-of-covid19
[246] http://www.pmlive.com/pharma_news/japan_follows_us_with_approval_for_gileads_remdesivir_in_covid-19_1340093
[247] http://newsroom.mylan.com/2020-07-06-Mylan-Secures-Regulatory-Approval-for-Remdesivir-Lyophilized-Powder-for-Injection-100-mg-vial-in-India-for-Restricted-Emergency-Use-in-COVID-19-Patients
[248] http://www.pharmatimes.com/news/chmp_backs_approval_of_remdesivir_as_covid-19_treatment_1342952
[249] https://www.pharmaceutical-technology.com/news/australia-tga-remdesivir-approval/
[250] https://www.reuters.com/article/us-health-coronavirus-gilead-sciences-ca/canada-gives-conditional-approval-to-gileads-remdesivir-for-covid-19-idUSKCN24T24W
[251] https://www.thedailystar.net/coronavirus-deadly-new-threat/news/eskayef-starts-distributing-remdesivir-hospitals-coronavirus-treatment-1905523
[252] https://www.wsj.com/articles/covid-19-drug-remdesivir-to-cost-3-120-for-typical-patient-11593428402
[253] https://www.hhs.gov/about/news/2020/06/29/trump-administration-secures-new-supplies-remdesivir-united-states.html
[254] https://www.nytimes.com/2020/06/29/health/coronavirus-remdesivir-gilead.html)
[255] https://www.kff.org/uninsured/issue-brief/key-facts-about-the-uninsured-population/

In other high-income countries with national health systems, remdesivir will also be priced at $2,340 per treatment course – but since Gilead has sold almost the entire supply, they will not be able to access much of it. Experts project $2.3 billion in 2020 remdesivir sales, generating $1.3 billion in profits.[256]

The generics producers who have signed a VL with Gilead plan to charge less than $1,000 per treatment course. Yet in Bangladesh, which can produce (and export) medicines without the patent holder's permission, Eskayef Pharmaceuticals announced that it was producing a generic version of remdesivir on May 8, 2020 and Beximco Pharmaceuticals began producing generic remdesivir after the government issued an emergency decree.[257] It is donating the product to government-funded hospitals and selling to private clinics.[258]

On December 31, 2020, after pressure from activists and generics producers, Russian Prime Minister Mikhail Mishustin signed an order allowing a local producer, Pharmasyntez, permission to mass produce a generic version of remdesivir without the patent holder's consent – a compulsory license. The generic version, called Rendemform, will be priced at approximately $100 per vial (a treatment course requires 6 to 11 vials).[259, 260]

Table 3: Pricing for Generic and Originator Remdesivir [261, 262, 263, 264]

Producer	Product name	Price per 5-day treatment course
Gilead Sciences	Remdesivir	$2,340
Beximco Sciences	Bemsivir	$390
Cipla	Cipremi	$320
Eskayef Pharmaceuticals	Remvir	$960
Hetero	Covifor	$426
Jubliant Life Sciences	JUBI-R	As of 3 August, the company has not disclosed pricing
Mylan	Desrem	$384

However, the SOLIDARITY trial reported that remdesivir use made no difference in duration of hospitalization, need for ventilation or mortality – a claim which Gilead is contesting.[265, 266, 267]

[256] https://www.wsj.com/articles/covid-19-drug-remdesivir-to-cost-3-120-for-typical-patient-11593428402
[257] https://www.thedailystar.net/coronavirus-deadly-new-threat/news/eskayef-first-produce-remdesivir-the-country-1900711
[258] https://www.statnews.com/pharmalot/2020/05/22/gilead-remdesivir-covid19-coronavirus-beximco-patent/
[259] https://meduza.io/en/feature/2021/01/13/uncertain-benefits
[260] https://makemedicinesaffordable.org/russian-government-issues-its-first-ever-compulsory-license-for-covid-19-treatment/
[261] https://www.reuters.com/article/us-health-coronavirus-bangladesh-remdesi/exclusive-bangladeshs-beximco-to-begin-producing-covid-19-drug-remdesivir-coo-idUSKBN22H1DD
[262] https://www.reuters.com/article/us-health-coronavirus-cipla/indias-cipla-prices-its-generic-remdesivir-at-53-34-per-vial-below-rivals-idUSKBN2492Q3
[263] https://mumbaimirror.indiatimes.com/mumbai/other/another-bdesh-firm-offers-remdesivir-for-65-per-vial/articleshow/76272801.cms
[264] https://tbsnews.net/bangladesh/health/remdesivir-will-be-free-covid-19-patients-govt-hospitals-84058
[265] https://www.kff.org/news-summary/who-addresses-pushback-on-solidarity-trial-interim-results-some-experts-say-remdesivir-still-potentially-effective-in-early-infection/
[266] https://www.ft.com/content/d7ecca00-9cd1-4fff-bba0-567a0027c9db
[267] https://www.reuters.com/article/us-health-coronavirus-gilead-remdesivir/analysis-sales-of-first-big-covid-19-drug-remdesivir-may-disappoint-idUSKBN2711FG

FAVIPIRAVIR

The world is awaiting more results on trials of favipiravir, an antiviral drug developed for influenza which has been approved for treating COVID-19 in China, India and Russia. An 80-person COVID-19 treatment trial compared favipiravir plus aerosolized interferon to LPV/r plus aerosolized interferon; people who received favipiravir cleared the virus significantly faster than those treated with LPV/r (a median of 4 days vs. 11 days); they were also significantly more likely to have improved chest imaging.[268, 269, 270] Additional and favorable results have emerged from various sources: a press release issued by Glenmark Pharmaceuticals, an article about a 50-person trial in Bangladesh, and a pre-print about a multi-center observational study in Thailand, along with inconclusive results in a Japanese trial, but data are limited.[271, 272, 273] Favipriavir is being studied in 27 trials in Australia, Bahrain, Bangladesh, Brazil, Canada, Egypt, France, Germany, Iran, Italy, Mexico, Romania, Saudi Arabia, Thailand, Turkey, the UK and the US.[274]

Notably, favipiravir causes birth defects in animals and is therefore not recommended during pregnancy; it causes increased blood uric acid levels and is not recommended for people who have or have had gout or high levels of uric acid; it also causes diarrhea and liver enzyme elevations, and it cannot be co-administered with the TB drug pyrazinamide.[275]

In India, favipiravir has not yet been added to the Ministry of Health's Clinical Management Protocol, due to lack of sufficient evidence of clinical benefit. Nonetheless, a price war has already begun among generics producers.

Table 4: Pricing for Generic Favipiravir [276]

Producer	Product name	Price per 200 mg tablet	Price per 6-day treatment course*	Price per 14-day treatment course*
Glenmark Pharma	Fabiflu	$1.37 at launch; dropped to $1.00	$58	$122
Cipla	Ciplenza	.91	$52	$111
Hetero	Favivir	.79	$45	$96
Brinton Pharma	Faviton	.79	$45	$96
Jenburkt Pharma	Favivent	.52	$30	$63

*Different doses have been used in clinical trials; pricing is based on a twice-daily 1800 mg loading dose, followed by a twice-daily dose of 800 mg for 6 to 14 days (total of 58 to 122 pills).

[268] https://www.sciencedirect.com/science/article/pii/S2095809920300631
[269] https://academic.oup.com/jac/article/75/7/2013/5838326
[270] https://www.medrxiv.org/content/10.1101/2020.06.24.20133249v3
[271] https://www.trialsitenews.com/the-dhaka-trial-clear-cut-evidence-favipiravir-effective-against-covid-19-with-compelling-results/
[272] https://www.biospace.com/article/glenmark-pharmaceutical-s-antiviral-drug-favipiravir-hits-the-mark-in-small-phase-iii-covid-19-study/
[273] https://www.reuters.com/article/us-health-coronavirus-fujifilm/after-early-hype-japans-homegrown-covid-19-drug-hope-avigan-faces-rocky-future-idUSKCN24T0YM
[274] https://clinicaltrials.gov/ct2/results?term=COVID-19&cond=favipiravir&Search=Apply&recrs=b&recrs=a&recrs=d&age_v=&gndr=&type=&rslt=
[275] https://www.cdc.gov.tw/File/Get/ht8jUiB_MI-aKnlwstwzvw
[276] https://www.cnbctv18.com/healthcare/covid-19-treatment-as-more-companies-launch-favipiravir-price-war-may-intensify-6491641.htm

IVERMECTIN

Ivermectin is an antiparasitic medicine which was developed in the 1970s. Merck's patent expired in 1996 – although there are 101 international patents on it.[277] It is approved in tablet form to treat certain worms (intestinal strongyloidiasis and onchocerciasis), and in a topical formulation for head lice and certain skin conditions. It is also used in animals to prevent and treat parasites. Ivermectin has been studied as a treatment for COVID-19 in 18 randomized controlled trials involving 2,200 people. Initial results are promising; viral clearance and recovery were faster in people who received it, and survival improved. Unfortunately, these trials used different doses and their endpoints also varied; larger trials with consistent dosing and endpoints are needed.

COLCHICINE

Colchicine is an anti-inflammatory medicine used to treat gout, Behçet's disease and a range of other conditions. It was approved in 1961 and there are three international patents on it.[278] It was studied in the 4,500-person COLCORONA trial and was one of the medicines under study in the UK Recovery trial until recruitment was halted when colchicine showed no beneficial effect.[279]

RESOURCES FOR FOLLOWING COVID-19 TREATMENT

There are several online resources, including:

The *New York Times* Coronavirus Drug and Treatment Tracker, Regulatory Focus and STAT COVID-19 Drugs and Vaccines Tracker, available at:

https://www.nytimes.com/interactive/2020/science/coronavirus-drugs-treatments.html
https://www.raps.org/news-and-articles/news-articles/2020/3/covid-19-therapeutics-tracker
https://www.statnews.com/feature/coronavirus/drugs-vaccines-tracker/#treatments

[277] For more information, see https://www.drugpatentwatch.com/p/generic-api/ivermectin
[278] For more information, see: https://www.drugpatentwatch.com/p/generic-api/colchicine
[279] https://www.recoverytrial.net/news/recovery-trial-closes-recruitment-to-colchicine-treatment-for-patients-hospitalised-with-covid-19

PART
FIFTEEN

ACCESS

The scope and severity of COVID-19 have created an unprecedented opportunity to overthrow monopolies created by intellectual property (IP) protection that blocks access to life-saving vaccines and drugs – and to prevent health nationalism.

The world cannot afford COVID-19; a World Bank estimate suggests that the pandemic pushed 71 to 100 million people into poverty in 2020, most of whom are living in South Asia and sub-Saharan Africa. Poverty is going to increase among people in middle-income countries, where an estimated 176 million people will become impoverished.[280]

Unless COVID-19 vaccines and treatments are affordable, governments - and people - will not be able to access them. Médecins Sans Frontières (MSF) has urged world leaders to demanded vaccines be sold at their cost price, citing the billions of dollars of taxpayer money that has subsidized vaccine development.[281]

Not only must tests, vaccines and treatments be affordable, the health systems that deliver them need to be strengthened. COVID-19 is having a huge impact on delivery of care for infectious and chronic conditions; as an example, measles outbreaks are an indicator of a failing healthcare system. WHO and UNICEF have already warned of disruptions and declines in childhood immunizations, including a large drop in the number of children who complete the three doses of diphtheria, tetanus and pertussis – which is a marker for immunization coverage.[282]

Countries have saved millions of dollars by using TRIPS flexibilities. Compulsory licenses have led to price reductions on medicines ranging from 6.7 percent to 98 percent.[283] Granting government use licenses in Thailand led to an estimated 84,158 more people gaining access to seven drugs in just five years, including treatment for HIV and cancer; these health gains translate into a measurable benefit to society of $132.4 million dollars.[284] As another example, a Unitaid-funded ITPC project generated five patent oppositions and one patent withdrawal, achieving an average price reduction of 67% for 15 target ARVs over a three-year period.[285] Such additional savings on generic versions of branded products could be used to shore up healthcare systems, ensuring that public health gains are not lost to COVID-19.

TARGET PRICING

To prepare for future pricing negotiations with manufacturers, it is important to determine the optimal target price for a given medicine. Production costs are an important consideration in calculating the target price. Several factors can influence drug prices, such as a high milligram count, complexity of the production process and sales volume. Experts have been tracking the cost of the active pharmaceutical ingredients (API) for potential COVID-19 treatments, using it to estimate a profitable mass production cost for generic versions of these medicines, including formulation and packaging.

[280] http://pubdocs.worldbank.org/en/461601591649316722/Projected-poverty-impacts-of-COVID-19.pdf
[281] https://www.msf.org/any-future-covid-19-vaccines-must-be-sold-cost
[282] https://www.who.int/news-room/detail/15-07-2020-who-and-unicef-warn-of-a-decline-in-vaccinations-during-covid-19
[283] https://link.springer.com/article/10.1057/s42214-020-00068-4
[284] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3176479/
[285] ITPC Unitaid Project Report: 2015- 2018

As an example, there is a great contrast between Gilead's price for a five-day course of remdesivir and the estimate of profitable generic mass-production: $2,340 versus just $5.58.[286, 287]

Branded or generic drugs and vaccines– what is the difference?

Because of patent monopolies, originator pharmaceutical corporations are the only source for certain vaccines and drugs for at least 20 years. When there are no patent barriers, generics companies can produce their own versions of these products.

To enter the market, generic versions of drugs must have the same quality, strength, efficacy and safety as branded ones. A generic drug must have the same active ingredient as a branded drug, and it must reach the same amount in the bloodstream as the branded version, from the time a person takes it until it passes out of their body (called bioequivalence). Generic versions of branded drugs must be given at the same dose, and by the same route (tablet, syrup, injection). A survey of 2,070 FDA-approved generic drugs reported that they were therapeutically equivalent to originator products.[288]

Usually, the API for originator and generic drugs comes from the same source. Although generic products may have different excipients (ingredients that are used for stability, bioavailability and to enhance overall drug safety or function during storage or use) than branded products, they have the same active ingredient as branded products. Studies of branded vs. generic beta-blockers,[289] glatiramer (used to treat multiple sclerosis),[290] and other medicines for different conditions have reported that effectiveness and tolerability did not differ between versions of these products; globally, millions of people rely on generic versions of HIV antiretrovirals.

Vaccines are considered biologics; generic versions of them, called biosimilars, are subject to different approval criteria than drugs, although the concept is similar. The US FDA requires that biosimilar manufacturers show "…their proposed biosimilar product is highly similar to and has no clinically meaningful differences from the FDA-approved reference product and may rely in part on FDA's previous determination of safety and effectiveness for the reference product for approval." This generally means that biosimilar manufacturers do not need to conduct as many expensive and lengthy clinical trials, potentially leading to faster access to these products, additional therapeutic options, and reduced costs for patients."[291] But in practice, the entry of biosimilars in the US market appears to be slow, hampered in part by the testing requirements in the US FDA's biosimilar guidelines.[292]

Biosimilar guidelines in several countries - as well as guidance provided by the WHO - have been critiqued by health groups in recent years for creating barriers, high costs and extended testing requirements. In 2019, scientists urged the WHO to update its registration guidance for biosimilar products to reflect improvements in the field that could simplify approval procedures, improve access to affordable biosimilars and prevent multinational companies from misusing the WHO guidance to sue developing country governments for approving biosimilars.[293]

[286] https://www.wsj.com/articles/covid-19-drug-remdesivir-to-cost-3-120-for-typical-patient-11593428402
[287] https://www.sciencedirect.com/science/article/pii/S2055664020300182
[288] doi: 10.1345/aph.1M141.
[289] doi: 10.1080/21556660.2018.1423988.
[290] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5700775/
[291] https://www.fda.gov/drugs/biosimilars/biosimilar-development-review-and-approval#process with-covid-19
[292] https://www.raps.org/news-and-articles/news-articles/2020/10/testing-requirements-are-likely-slowing-biosimilar
[293] https://www.healthpolicy-watch.org/wp-content/uploads/2019/04/Memo-on-WHO-Guidelines-on-SBPs-.pdf

INTELLECTUAL PROPERTY ISSUES

Patents...and beyond

Business as usual is unacceptable in the context of a global pandemic. IP protections on life-saving interventions for COVID-19 prevent millions of people from accessing them and has led to shortages and delayed delivery of vaccines. The pandemic may require governments to remove IP barriers to personal protective equipment (PPE), diagnostic kits, vaccines, ventilators and other medical equipment. Governments may have to consider whether patents create barriers to COVID-19 medicines and vaccines, as well as other forms of IP, such as data exclusivity and trade secrets.

Different Types of IP and Their Impact on COVID-19

Patents

Patents impact access to diagnostic tests, vaccines, treatments and medical devices. A patent is a form of IP. It grants the patent holder of any new product or process exclusive rights over the invention, allowing them to prevent any other person from (1) making; (2) using; (3) selling; (4) offering for sale and (5) importing it without the patent holder's permission, usually for 20 years - or even longer. Patents on pharmaceuticals often make them more expensive and less available by preventing or restricting competition from generics manufacturers. In the case of COVID-19, patents on medicines and vaccines cause high pricing and limit supplies, which leads to rationing, black market pricing and shortages.

Data and Market Exclusivity

Data and market exclusivity have been adopted in the wealthiest countries; they are largely spread in developing countries through free trade agreements. They establish marketing monopolies for companies who are the first to develop and introduce a medicine to the market. Usually, generics companies enter the market by providing data showing that their product is comparable to the originator product. But data and marketing exclusivity prevent this. In effect, the originator companies enjoy monopolies ranging from 5 – 11 years, depending on the law in a particular country. During this time, generics cannot be registered - or if they are, they cannot be marketed. This sort of monopoly is also a concern with biologic medicines (such as monoclonal antibodies which are a treatment for COVID-19). It can also apply to off-patent medicines, or those that have not been patented under the strict patent laws of some developing countries. Data and marketing exclusivity can complicate compulsory licensing, by creating barriers to the registration of generic medicines.

Trade Secrets

Trade secrets cover a broad range of information that has commercial value, which companies make reasonable attempts to keep secret, such as the recipe for Coca-Cola. Because of the range of information that can be covered by trade secrets, companies in the health sector are increasingly resorting to this form of IP to prevent competitors, employees, whistle-blowers, public institutions, and governments from releasing or using information that these corporations think should not be made public or used by others. In the context of COVID-19, trade secrets may create barriers to the scale-up and manufacturing of all sorts of health products, due to trade secrets on techniques, methods, compilations, processes and software that are applied in the production of medical devices such as ventilators, diagnostic tests, vaccines or medicines.[294] This can include manufacturing processes, test data, medical formulas, cell lines and other biological resources, chemical formulas, processes for manufacturing and for vaccines and biologic medicines, it can also cover genomic information, and other biological material.[295]

[294] https://www.southcentre.int/wp-content/uploads/2020/04/PB73_The-COVID-19-Pandemic-RD-and-Intellectual-Property-Management-for-Access-to-Diagnostics-Medicines-and-Vaccines_EN-1.pdf

[295] http://infojustice.org/archives/42493

IP barriers: Ventilators, Masks, Tests

Indications that IP barriers would hinder access to COVID-19 prevention, testing and treatment came early in the pandemic. As the first devastating wave of COVID-19 hit Italy, ventilators were in short supply. When researchers working on 3-D printing to increase access to mechanical ventilation approached a company holding patents on ventilator valves, it refused to share this information (nonetheless, they managed to create the design themselves and print valves that allowed more than one person to use a ventilator).[296] Meanwhile, in the Netherlands, Roche was unable to meet the demand for COVID-19 testing kits. The Dutch government demanded the recipe for testing fluid (known as lysis buffer), so that hospitals could make it themselves. It took the threat of legal action from the EU competition authority for Roche to reveal the recipe (which was not patented but was subject to trade secret protection).[297] As the global scramble for N-95 masks was making headlines, a severe shortage in the US led to a public call from a member of the Senate for 3M to release its patents so that competitors could also make masks.[298]

Patenting re-purposed drugs

Research on treatments for COVID-19 has focused largely on existing medicines, in the hope that drugs with established safety profiles and existing manufacturing capacities could be deployed. In April 2020, a study was published, estimating the cost to profitably mass-produce several potentially repurposed drugs that were being studied against COVID-19.[299] It reported that the most promising candidates at the time could be manufactured at very low prices, in the range of $5 to $20 per treatment course, although current prices for these drugs are much higher, particularly in high-income countries. Of the initial set of treatments being investigated, the study showed the potential affordability of several medicines, but this can only be ensured if patent and other IP barriers do not prevent generic production.

Table 5: Estimated Production Costs for Potential COVID-19 Treatment

Product	Dose and Administration	Estimated Production Cost, per treatment course	Estimated Production Cost, per day
Remdesivir	5 days, by infusion Day 1: 100 mg twice-daily Day 2-5 100 mg once daily	$5.58	$0.93
Favipiravir (14 days) 600mg bd	14 days, orally 600 mg twice-daily	$20	$1.45

[296] https://www.theverge.com/2020/3/17/21184308/coronavirus-italy-medical-3d-print-valves-treatments

[297] https://www.ftm.nl/artikelen/roche-releases-recipe-after-public-pressure-while-european-commission-considers-intervention-due-to-coronavirus-test

[298] https://www.courier-journal.com/story/news/2020/04/03/beshear-calls-3-m-release-patent-n-95-respirator-amid-pandemic/5112729002/

[299] http://viruseradication.com/journal-details/Minimum_costs_to_manufacture_new_treatments_for_COVID-19/

Unfortunately, savings on re-purposed drugs are not always passed on. Re-purposing creates an opportunity for patent evergreening, by reformulating existing drugs (as an example, Gilead is developing an intranasal version of remdesivir which could potentially be used for prevention and treatment). There are already pending patent applications and granted patents on several medicines that are used to treat COVID-19, such as remdesivir, favipiravir and tocilizumab.[300] In the case of tocilizumab, the main patent expired in 2015, but evergreening patents continue till 2028. Many of these evergreening patents should not be granted, since the medicines already exist and the patents being granted are for new uses or new forms of them.

Monoclonal antibodies (including tocilizumab and newer ones) that have been approved for treating COVID-19 are biologic medicines. In recent years, apart from patent barriers, regulatory barriers to registering biosimilars or biogenerics have emerged as a key hurdle in bringing in competition. As noted, civil society groups have been advocating with the WHO and other regulatory agencies against overly cumbersome requirements for registering biosimilar products.[301]

Intellectual Property and Vaccines

Patenting activity around vaccines has been increasing over the past few decades.[302] There are thousands of patents and patent applications related to coronavirus vaccines in general.[303] Hundreds of patents have also been filed on mRNA technology (the platform for Moderna and Pfizer/BioNTech vaccines as well as others in the pipeline).[304] The extent to which patents have been filed on COVID-19 vaccines will come to light in late 2021, when patents filed in 2020 will be published (since they are published 18 months after they are filed). Patents on vaccines tend to be over-broad, covering starting materials, vaccine composition, process technologies, methods of use, age groups, doses, administration routes, etc. The complexity of the vaccine patenting landscape is evident from the patent licensing and litigation that emerged in the US even as COVID-19 vaccines were in clinical trials.[305]

Investigations by public interest groups KEI and Public Citizen found that Moderna was not revealing the significant extent of its US government funding in the patents it was filing.[306] Although Moderna released a statement saying it would not be enforcing patents on the COVID-19 vaccine during the pandemic, public interest groups have noted that without a commitment to share their know-how and trade secrets, this non-enforcement pledge provides little hope for quick expansion of manufacturing.[307] Interestingly, in December 2020, the CEO of CureVac, which is developing an mRNA-based coronavirus vaccine, called for the suspension of vaccine patents and the sharing of know-how during the pandemic.[308] But the vast majority of vaccine patent holders have remained dismissive, some aggressively so, of demands to suspend or share their patents.[309] Big pharma associations such as BIO and PhRMA have been lobbying against governments and UN agencies attempting to address IP barriers on COVID-19 technologies.[310]

[300] https://www.theverge.com/2020/3/17/21184308/coronavirus-italy-medical-3d-print-valves-treatments
[301] https://www.twn.my/title2/books/BiologicalDrugs-eng.htm
[302] See: https://www.wipo.int/edocs/pubdocs/en/patents/946/wipo_pub_946_3.pdf
[303] https://www.epo.org/news-events/in-focus/fighting-coronavirus/vaccines-and-therapeutics.html
[304] https://www.nature.com/articles/d41573-020-00119-8
[305] https://www.msn.com/en-us/money/companies/pfizer-biontech-and-regeneron-hit-with-patent-lawsuits-over-covid-19-drugs-and-vaccines/ar-BB19JMp
[306] https://www.keionline.org/33970
[307] https://healthpolicy-watch.news/77521-2/
[308] https://www.stuttgarter-zeitung.de/inhalt.kampf-gegen-corona-curevac-patente-fuer-impfstoffe-aussetzen.568f0c24-6dd1-4724-a46f-8683d53c8444.html
[309] https://www.statnews.com/pharmalot/2020/05/28/who-voluntary-pool-patents-pfizer/
[310] https://www.fdanews.com/articles/201195-phrma-pushes-back-against-wto-proposal-to-eliminate-patents-for-covid-19-products

Profit-driven deals and licenses

Unfortunately, from the very beginning of the COVID-19 outbreak, high-income country governments have hoarded medical supplies, placed excessive bids on them and diverted essential supplies - whether they are masks, diagnostics, medicines or vaccines. This occurred with remdesivir, which is sold by the US multinational company Gilead Sciences. Gilead priced it at $3,120 per 5-day treatment course in the US, where the government purchased nearly the entire stock for its own use, and the EU bought what remained.

To provide remdesivir in developing countries, Gilead entered into voluntary licenses with select generic companies in Egypt, India and Pakistan. Predictably, Gilead excluded several key developing countries from these licenses. Although Gilead claimed that its licenses are based on need, the exclusion of Brazil, Russia and almost all Latin American countries - which have some of the world's burdens of COVID-19 - shows the fallacy of such claims. The extent to which Gilead's licenses will benefit the included countries is also unclear. Indian generics companies that have licenses started production but for several months, the supply was only sufficient for India with small batches making their way to Nepal and Indonesia. The Indian companies put a high price on remdesivir: approximately $70 per vial, or $350 for a 5-day treatment course (or $700 for a 10-day treatment course) although a study estimating production costs found remdesivir, including a 10% profit margin, should not be priced at more than a dollar a day.[311] Thus, in terms of prices and availability, being included in the remdesivir licenses does not meet the requirements of several developing countries. In the meantime, generics companies from Bangladesh have already announced that they are making and exporting remdesivir. To access affordable remdesivir from Bangladesh, countries would have to use compulsory licensing provisions. For tocilizumab, there is only a marketing arrangement between Roche and Indian generic company Cipla, which means that prices remain high and availability low.[312]

The coronavirus vaccine landscape has few licensing deals. The companies have stubbornly stuck to this approach, despite global vaccine shortages. Given that several approved vaccines relied on substantial public investment, either for their development or for conducting the clinical trials that led to their approval, the inability or unwillingness of governments to require technology transfer and non-exclusive licensing to expand manufacturing and supply is of great concern. Where governments have acted, they have opted for measures that suit only themselves. The US has invoked the Defense Production Act, which prioritizes vaccine production only for the US.[313] This has already led to concerns in India, which relies on imports of certain vaccine components from the US [314] (which, after pressure, finally made these supplies available to India during its catastrophic COVID-19 surge). [315] The EU has moved to block exports of the Oxford/AstraZeneca vaccine, which has already impacted shipments to Australia and more recently the UK.[316] The UK, in desperation to maintain its fast-paced vaccination campaign, has even gone to the extent of getting 10 million doses of the Oxford/Astrazeneca vaccine from India, tapping into the only source of supply for developing countries at the moment.[317]

[311] http://viruseradication.com/journal-details/Minimum_costs_to_manufacture_new_treatments_for_COVID-19/

[312] https://www.moneycontrol.com/news/business/companies/cipla-to-distribute-roches-biologics-tocilizumab-and-bevacizumab-in-india-2517611.html

[313] https://www.npr.org/sections/health-shots/2021/03/13/976531488/defense-production-act-speeds-up-vaccine-production

[314] https://www.news18.com/news/india/india-takes-up-export-hurdles-of-vaccine-raw-material-with-us-as-poonawalla-red-flags-covishield-production-3542102.html

[315] https://www.whitehouse.gov/briefing-room/statements-releases/2021/04/25/statement-by-nsc-spokesperson-emily-horne-on-national-security-advisor-jake-sullivans-call-with-national-security-advisor-ajit-doval-of-india/

[316] https://www.cnbc.com/2021/03/22/uk-and-eu-covid-vaccine-export-ban-spat-grows.html

[317] https://www.livemint.com/news/world/serum-institute-of-india-to-send-10-million-doses-of-covid-19-vaccine-covishield-to-uk-report-11614743101765.html

Five million doses of the UK order were delayed due to domestic demand in India, which seemed to cause more consternation in the UK than the fact that it was diverting developing country supplies! [318]

Manufacturing licenses for coronavirus vaccines follow the same approach seen with medicines - secret licenses with multiple restrictions that place profits above public health. Oxford University had originally pledged that its COVID-19 technologies would be available universally on a non-exclusive licensing basis. However, when it came to the vaccine - which was developed with public investments - an exclusive license was granted to AstraZeneca, which then entered into secret licenses with certain vaccine manufacturers in Australia, Brazil, India and South Korea.[319] Of these, only Brazil's Fiocruz made the agreement with AstraZeneca public; a notable provision of the license is, according to AstraZeneca, the COVID-19 pandemic will end in July 2021.[320] AstraZeneca's contract with India's Serum Institute has not been published, though news reports indicate that supply under the contract is limited to 62 developing countries.[321] As Serum Institute commenced production of the Oxford vaccine even before global approvals, it was able to maintain a stockpile that has resulted in some supplies reaching developing countries.[322] However, as India witnesses a second wave, exports have been restricted as domestic demand has increased.[323] Apart from the limited supply, enforcement of the no-profit pricing for the Oxford/AstraZeneca vaccine has ironically been better in developed countries in the EU, and in the UK and the US, who pay between $3 to $4 per dose, while the Philippines, South Africa and Thailand have paid around $5 per dose and Uganda has paid $7 per dose (the vaccine is given as two doses, so the full course costs double these prices).[324]

There is significant capacity to produce vaccines across the globe.[325] As pressure has grown on companies with approved coronavirus vaccines, collaborations are slowly emerging. Pfizer and BioNTech have reportedly entered into deals with several rivals to increase their output.[326] These deals appear to be for last stage fills rather than manufacturing, as the companies appear to be intent on not sharing their know-how or technology.[327] The US government announced that it has boosted infrastructure at Merck so that it can help produce the J&J vaccine.[328] Most of these attempts appear geared towards fulfilling deliveries to developed countries. Vaccine R&D and production capacity also exist across the developing world - as is evident from vaccines emerging from China, India and Russia. Although some companies have entered into licenses with Indian vaccine manufacturers, these deals come with significant restrictions.[329] Meanwhile, Russia's Gamaleya Institute has announced multiple collaborations with companies in developed and developing countries to produce Sputnik V.[330] These collaborations will bear fruit far too late, as second and third waves and new variants of SARS-CoV-2 surge across the globe.

[318] https://www.bbc.com/news/uk-56438629

[319] https://khn.org/news/rather-than-give-away-its-covid-vaccine-oxford-makes-a-deal-with-drugmaker/

[320] https://portal.fiocruz.br/sites/portal.fiocruz.br/files/documentos/contrato_vacina_astrazaneca_fiocruz.pdf

[321] https://www.dnaindia.com/health/report-serum-institute-s-big-announcement-on-coronavirus-vaccine-here-s-when-you-will-get-first-dose-of-covid-19-vaccine-2843088

[322] https://timesofindia.indiatimes.com/india/india-exports-over-twice-the-number-of-doses-used-at-home/articleshow/81540812.cms#:~:text=India%20exports%20over%20twice%20the%20number%20of%20doses%20used%20at%20home,-Rupali%20Mukherjee%20%7C%20TNN&text=MUMBAI%3A%20India%20has%20shipped%20over,drive%20began%20on%20January%2016.

[323] https://www.indiatoday.in/coronavirus-outbreak/story/serum-institute-to-delay-vaccine-exports-over-india-shortage-1781876-2021-03-21

[324] https://www.npr.org/sections/goatsandsoda/2021/02/19/969529969/price-check-nations-pay-wildly-different-prices-for-vaccines

[325] http://vaxmap.org/

[326] https://www.fiercepharma.com/pharma/novartis-signs-up-to-help-produce-pfizer-biontech-covid-19-vaccine

[327] https://medicalxpress.com/news/2021-03-rivals-partners-covid-vaccine.html

[328] https://www.washingtonpost.com/health/2021/03/02/merck-johnson-and-johnson-covid-vaccine-partnership/

[329] https://www.reuters.com/article/health-coronavirus-india-vaccine/factbox-indias-many-covid-19-vaccine-manufacturing-deals-idUSL4N2LK1KJ

[330] https://timesofmalta.com/articles/view/russia-says-sputnik-v-production-deals-reached-in-key-eu-states.858199

What can communities and governments do?

Different strategies can be used to overcome intellectual property barriers that prevent access to COVID-19 technologies. Several countries have recognized the importance of these provisions in the context of COVID-19 and have taken action on the compulsory licensing provisions in their country's patent laws, including Canada, Chile, Colombia, Ecuador, France and Germany.[331, 332] Brazil's parliament is considering a draft law to facilitate faster compulsory licensing for COVID-19 products. Some countries have already issued CLs, such as Israel, which issued a CL for LPV/r as a treatment for COVID-19.[333] Interestingly, shortly after Israel issued the CL, Abbvie, the company holding multiple patents on LPV/r, announced that it would no longer enforce its patents in any country, leading civil society organizations (CSO) to call on their governments to ensure affordable procurement of this second-line HIV drug.

When patents have already been granted, activists may consider filing post-grant patent oppositions or patent invalidations or asking their governments to consider issuing a CL for public non-commercial use. When there are pending patent application(s), in places where patent laws permit it, activists could file pre-grant opposition(s), third party observation(s) or discuss the scientific arguments against granting patent(s) with their national patent office. CSOs in Argentina, India and Thailand have taken action, by filing patent oppositions and patent revocations on patent applications for favipiravir and remdesivir. And as noted, Russia (and Hungary) have issued a CL on remdesivir.

While the emergency use of government use licenses and CLs is well recognized, communities and governments should also be aware that article 73(b) of the TRIPS agreement allows World Trade Organization members to take any action they consider necessary to protect their essential security interests. According to international legal experts, in the current global emergency this exception to the TRIPS agreement would authorize the procurement and manufacture of necessary health products for addressing the COVID-19 pandemic.[334]

[331] https://www.parl.ca/documentviewer/en/43-1/bill/c-13/third-reading#id0etaa

[332] http://patentblog.kluweriplaw.com/2020/04/02/update-on-patent-related-measures-in-germany-in-view-of-corona-pandemic/?doing_wp_cron=1586856780.0804069042205810546875

[333] ttps://www.keionline.org/wp-content/uploads/a-permit-to-the-state-to-exploit-an-invention-pursuant-to-chapter-six-article-three-of-the-patents-law-5727-1967.pdf

[334] https://www.southcentre.int/wp-content/uploads/2020/04/COVID-19-Open-Letter-REV.pdf

GOVERNMENTS NEED TO ACT NOW

1. Identify any existing patents or patent applications and other monopolies on potential medicines, vaccines and other health products for the prevention, diagnosis and treatment of COVID-19.
2. Ensure that evergreening patents on new uses and new forms of existing medicines and vaccines being tested for COVID-19 treatment are not granted.
3. Introduce a simple, easy-to-use mechanism for government use of patented inventions for medicines and medical devices/equipment to address situations similar to COVID-19 by using the provisions of the patent law, or, if necessary, by amending the patent law; the Minister of Health should have full powers to make urgent decisions on such use.
4. If a country has data or marketing exclusivity, introduce a mechanism for waivers of such exclusivity on medicines to address situations similar to COVID-19, including, if necessary, by amending relevant laws and by changing legislation on circulation of medicines; the Minister of Health should have full powers to make urgent decisions on such waivers.
5. Put in place a mechanism for the immediate grant of government use orders and waivers for any IP protection including patents, data exclusivity and trade secrets related to COVID-19 vaccines, tests, treatments and medical devices/equipment that may be approved and procured with state or municipal funds.
6. Create and implement national and regional production plans for any newly approved tests, treatments and vaccines for COVID-1919, including assessing access to raw materials and active pharmaceutical ingredients.
7. Support the proposal at the WTO for a waiver from TRIPS obligations on Covid-19 health technologies.

While there is a clear need to ensure availability and affordability of any newly approved COVID-19 treatments, governments and communities should also consider the need to remove IP barriers on other medicines, as the inevitable long-term impacts from the COVID-19 outbreak emerge. At present, most health budgets and systems are being diverted towards addressing the pandemic; these health budgets are already strained by the high prices of patented medicines for other illnesses. The economic fallout from COVID-19 will increase the need to ensure affordability of all essential medicines in developing countries, therefore it is likely that there will be a need for government use or CL provisions for non-COVID 19 medicines and other health products.

From previous experience with fighting the HIV, HCV and TB epidemics, various barriers can hamper timely access to needed medicines and medical devices, including IP-related monopolies, prolonged procurement procedures and marketing authorization processes, taxation of medicines, disruptions in global supply chain and API manufacturing. These barriers are also likely to arise in the context of the COVID-19 response and should be addressed on a priority basis.

TRIPS Waiver Proposal

The race for IP protections on COVID-19 medical products has directly translated into exorbitant pricing and profiteering. With entire health systems already diverted to COVID-19 and a looming economic crisis, the health budgets of developing countries cannot sustain purchasing high-priced COVID-19 medical products. For vaccine production, an urgent global effort is required to upgrade existing facilities, ensure technology transfer, forecast and set up supply chains for raw materials and much more. For all this, governments and local and regional producers cannot be held for ransom over IP protections; the removal of all relevant IP barriers is required.

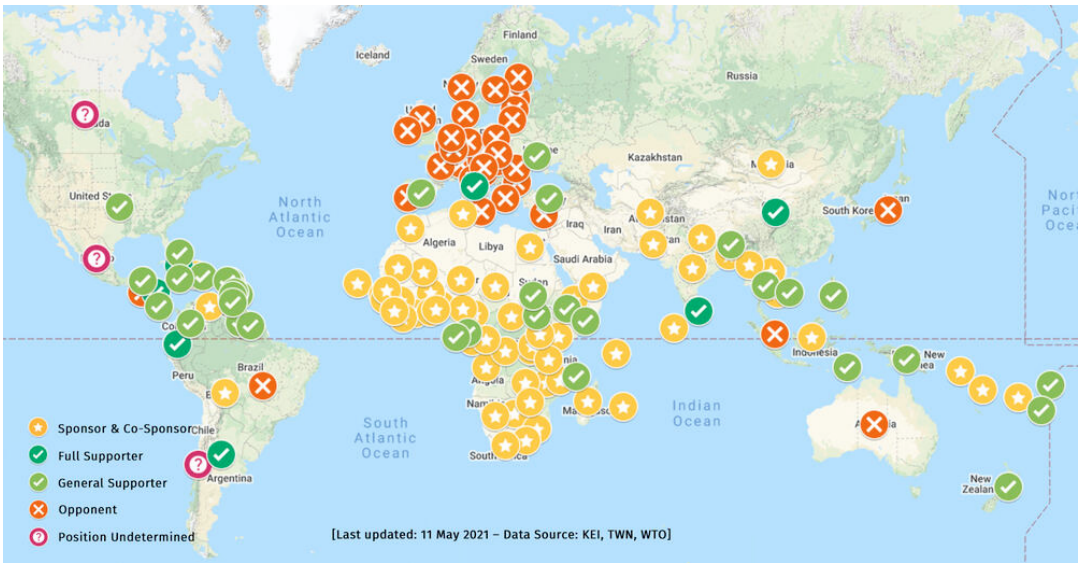
To address these issues, in October 2020, India and South Africa submitted a proposal for a "Waiver from certain obligations of the TRIPS Agreement in relation to the prevention, containment, and treatment of COVID-19" (Waiver Proposal) at the WTO.

Although the TRIPS Agreement contains TRIPS flexibilities that can promote access, WTO members may face complex procedures and legal, institutional and other challenges to effective use of these flexibilities. Adoption of a Waiver at the WTO level will suspend implementation, application and enforcement of relevant provisions of the TRIPS Agreement in relation to prevention, containment, and treatment of COVID-19. It enables an expedited, open and automatic solution to allow uninterrupted collaboration in the development, production and supply of medical products, and to collectively address the global challenge of COVID-19.

The final decision on the Waiver Proposal should be taken by the Ministerial Conference or the General Council.

As the proposal is being discussed, the positions of WTO members follow predictable lines, with most of the developed countries - with the exception of Spain and the US- opposing the request (See Figure 1 [335]), while nearly two-thirds of the WTO membership is now backing the proposal, including the least-developed countries group and the African group, both of which have expressed their support. [336, 337, 338]

Figure 1. Opponents and supporters of the TRIPS waiver [339]



[335] https://www.nature.com/articles/d41573-020-00119-8

[336] https://www.msn.com/en-us/money/companies/pfizer-biontech-and-regeneron-hit-with-patent-lawsuits-over-covid-19-drugs-and-vaccines/ar-BB19JMp

[337] https://ustr.gov/about-us/policy-offices/press-office/press-releases/2021/may/statement-ambassador-katherine-tai-covid-19-trips-waiver

[338] https://english.elpais.com/spanish_news/2021-05-07/spain-backs-bidens-proposal-for-vaccine-patent-waivers.html

[339] https://www.msf.org/countries-obstructing-covid-19-patent-waiver-must-allow-negotiations

PART
SIXTEEN

REGULATORY ISSUES

National Drug Regulatory Authorities (NDRAs), which are often called Food and Drug Authorities/Administrations (FDAs), regulate and oversee the development, approval, manufacturing, importing and marketing of medicines to ensure the safety, efficacy and quality of drugs, vaccines, diagnostics and other medical products. Before drugs reach the market, they must secure regulatory approval. Products for COVID-19 have been approved under EMA conditional approval and/or US FDA (and other countries, some more rigorous than others) emergency use authorization, a mechanism developed to facilitate availability of diagnosis, treatment and prevention of diseases during public health emergencies when certain criteria are met- and there are no adequate, approved or available alternatives. For vaccines, the US FDA requires that at least half of all phase III trial participants are followed for at least two months after vaccination in addition to plans to follow product safety and continue clinical trials.[340]

Expensive and lengthy regulatory process need to be adapted for COVID-19 – especially for biosimilar products (generic versions of vaccines, insulin, interferons and other products that are modeled after therapies using living organisms), which have a separate and more complex approval process than small molecules. The financial investment for registering a product can be a barrier to widespread and rapid access; hopefully WHO and other regulatory agencies will define a harmonized, efficient and rigorous pathway at no cost.[341]

Some changes to improve registration for COVID-19 products have been instituted. WHO has shifted some of the prequalification unit staff to COVID-19 to work on the Emergency Use Listing for diagnostics, and provide expert input on possible therapeutics and vaccines.[342] Several NDRA have worked to hasten access to diagnostics, vaccines and treatments for COVID-19: India's Central Drugs Standard Control Organisation (CDSCO) has implemented new approval, safety and import measures to expedite access to COVID-19 diagnostics, vaccines and treatments.[343] The EMA has created the COVID-19 EMA Pandemic Task Force to enable Member States and the European Commission to take quick and coordinated regulatory action during the pandemic, while the US FDA created the Coronavirus Treatment Acceleration Program (CTAP) to expedite access to new treatments by streamlining its review and advice processes and issued guidance for vaccine development.[344, 345, 346]

Although ending regulatory lag is important, concerns have been raised about increasing political pressure to approve vaccines or study them too widely before adequate data are available on their safety and effectiveness, especially in older people and those with pre-existing conditions. In Russia and China, experimental vaccines have been used on members of the military, which could have disastrous consequences.[347, 348]

[340] https://www.fda.gov/vaccines-blood-biologics/vaccines/emergency-use-authorization-vaccines-explained
[341] http://viruseradication.com/journal-details/Minimum_costs_to_manufacture_new_treatments_for_COVID-19/
[342] https://extranet.who.int/prequal/news/impact-covid-19-prequalification-activities
[343] https://www.emergobyul.com/blog/2020/04/indias-cdsco-responds-covid-19-new-approval-import-and-safety-measures
[344] https://www.ema.europa.eu/en/documents/other/mandate-objectives-rules-procedure-covid-19-ema-pandemic-task-force-covid-etf_en.pdf
[345] https://www.fda.gov/news-events/fda-voices/path-forward-coronavirus-treatment-acceleration-program
[346] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/development-and-licensure-vaccines-prevent-covid-19
[347] http://www.xinhuanet.com/english/2020-08/03/c_139262032.htm
[348] https://edition.cnn.com/2020/06/30/health/china-coronavirus-military-vaccine-intl-hnk-scli/index.html

CONCLUSION

In 2020, the world made a gamble on coronavirus vaccines - with billions of taxpayer dollars. It has paid off, especially for pharmaceutical corporations – a stinging reminder that science is our friend, but the pharmaceutical industry is not. It has refused to share the technology that could enable global access to affordable vaccines. Instead, high-income countries are paying millions to guarantee national vaccine supplies, while pharmaceutical executives reap vast profits from stock option sales - and low-and-middle income countries are left behind.

The consequences of vaccine nationalism, patent monopolies and pharmaceutical profiteering alongside failures to invest in national health systems, poor coordination of essential research on treatment for COVID-19 and inadequate public health measures are already becoming apparent. The failure to control the pandemic and SARS-CoV-2's rapid mutation rate could make the virus difficult to eradicate - while generating endless profits - because vaccines may need constant adjustments to ensure their effectiveness.

In 2021, the world has another chance to turn the pandemic around, if it can outpace viral variants, corruption, inaction and pharmaceutical profiteering - if governments are willing to heed some of the bitter lessons from 2020:

- Medical innovation and technology must reach everyone – no one is safe from coronavirus until all of us are safe;
- Intellectual property protections including patents, trade secrets, copyrights and data exclusivity should not be granted for medical products and technologies (including vaccines, diagnostics, treatments and devices) needed to fight the pandemic;
- WTO members should endorse the proposal from India and South Africa to waive certain TRIPS obligations for COVID-19 prevention, treatment and containment;
- Governments must prioritize human rights and public health – not economics – by fully funding healthcare systems and reclaiming products developed with taxpayer funds for the greater good.
- Governments must place communities at the heart of their pandemic responses; people must be consulted in the design and implementation of prevention, testing and treatment programmes and the delivery of these services, especially for quarantine or isolation requirements.
- Governments in low- and middle-income countries must invest enough to ensure access to COVID-19 medical products for everyone, and enforce and monitor efficient and transparent use of these funds by authorized state bodies/agencies.

APPENDIX: Human Rights Resources

COVID-19 and its human rights dimensions.

ohchr.org/EN/NewsEvents/Pages/COVID-19.aspx

"The Office of the UN High Commissioner for Human Rights notes that, under international human rights law, emergency legislation and measures should be strictly temporary and must remain subject to meaningful legislative and judicial oversight. Promoting human rights now will help societies emerge more resilient from this pandemic in the future. The threats are comprehensive. A society that cannot offer equal treatment for all, including healthcare and social security, will lose its social cohesion and more of its people will fall victim to the virus. A society that surrenders separation of powers may lose sovereign rule altogether. Against threats like these, resilient societies can help advance human rights norms in the aftermath of the pandemic."

https://www.weforum.org/agenda/2020/04/coronavirus-has-exposed-human-rights-gaps-we-need-to-fix-this-covid-19/

"The right to health must guide responses to Covid-19"

"The COVID-19 pandemic has been exacerbated by human rights failures, yet the right to health can provide a framework for assuring that the COVID-19 response serves to realise the right to the highest attainable standard of physical and mental health for all."

"Access to health as human right: As recognised in the International Covenant on Economic, Social and Cultural Rights, the right to health requires that states take steps for the "prevention, treatment and control of epidemic, endemic, occupational and other diseases" and to assure "medical service and medical attention in the event of sickness". The right to health requires that health goods, services, and facilities are available in adequate numbers; accessible on a financial, geographical, and non-discriminatory basis; acceptable, including culturally appropriate and respectful of gender and medical ethics; and of good quality."

https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)31255-1/fulltext

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Policy brief: The impact of COVID-19 on women

https://asiapacific.unwomen.org/en/digital-library/publications/2020/04/policy-brief-the-impact-of-covid-19-on-women

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