The Independent Panel FOR PANDEMIC PREPAREDNESS & RESPONSE

COVID-19: State of the Pandemic

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This briefing paper addresses COVID-19's impact and opportunities and challenges in the response to the pandemic.

Long after the 1918-19 influenza pandemic claimed the lives of 50-100 million people globally[1] and on the heels of SARS-CoV-1 affecting more than 8000 patients across 26 countries on five continents[2], World Health Organization member states agreed a substantially new set of measures to detect, assess, and respond to public health events, including by declaration of a Public Health Emergency of International Concern (PHEIC). These International Health Regulations (IHR) (2005) [3] for the first time created a legally binding global instrument able to respond to global health emergencies of any type and was designed to build member state capacities.

The IHR (2005) sought to define a PHEIC precisely instead of using the term 'pandemic' which was subject to a range of definitions. The WHO describes a PHEIC as a situation[4] that "is serious, unusual, or unexpected; carries implications for public health beyond the affected State's national border; and may require immediate international action." Following IHR (2005) adoption, PHEICs have included an outbreak of H1N1 influenza (2009), polio resurgence (2014), Ebola Virus Disease (EVD) in West Africa (2014), Zika virus outbreaks (2016), and EVD in the Democratic Republic of Congo.

The coronavirus disease (COVID-19) caused by a novel coronavirus (SARS-CoV-2) first identified in late 2019 was declared a PHEIC by the WHO on January 30th 2020[5]. As of September 17, 2020, over 29 million cases and 940,000 deaths have been reported across over 200 countries, regions and territories[6].

The COVID-19 pandemic is an explosive – but not an unpredictable – shock.

Common among animals, such as bats, there are many types of coronavirus. Like 60-75% of new infectious diseases[7], coronaviruses can spillover from their animal hosts into humans (so-called "zoonotic infections") – as six types of coronavirus had previously been known to do. Often, coronaviruses cause minor symptoms, accounting for about 15% of cases of the common cold. But like SARS-CoV-1, SARS-CoV-2 poses a more serious threat.

In late 2019, the seventh coronavirus – SARS-CoV-2 – likely jumped from animals to humans and then spread from human-to-human[8]. Though the origin of COVID-19 is still being traced, a major outbreak occurred after several people were exposed to SARS-CoV-2 at a market in Wuhan City, China. This outbreak followed after a series of hospitalizations of patients with acute respiratory distress symptoms in December 2019[9].

[1] Morens, D.M. and Taubenberger, J.K., 2018. Influenza cataclysm, 1918. *The New England journal of medicine*, *379*(24), p.2285.
[2] Peiris, J.S., Yuen, K.Y., Osterhaus, A.D. and Stöhr, K., 2003. The severe acute respiratory syndrome. *New England Journal of Medicine*, *349*(25), pp.2431-2441.

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There were clear signs SARS-CoV-2 would have explosive spread. The reproduction number, or Ro, describes the expected number of infections produced by a primary case in a completely susceptible population. The Ro was 2.4 at the onset of the Wuhan outbreak[10] – meaning one person with the virus would infect another 2-3 people, and those 2-3 people would go onto infect another 2-3 people, and so forth. From Wuhan, a major domestic and international transportation hub, the virus likely traveled in its human hosts to several cities – and from there to other parts of the world. In just a few months, SARS-CoV-2 had spread rapidly across the world.

SARS-CoV-2 transmits by direct contact with people who have the infection, including breathing in the droplets from the nose or mouth of a person who is infected. While the majority of transmission appears to occur person-to-person via infected droplets, there is evidence to show that prolonged exposure to high concentrations of virus left on surfaces (from a few hours to a few days) can also increase the risk of infection. Aerosol transmission (outside of aerosol generating procedures) is being studied and has not yet been ruled out[11,12].

When SARS-CoV-2 enters the upper respiratory tract, the virus begins replicating. The immune system responds by creating antibodies that bind the virus, preventing replication, and deploying other immune system cells that attempt to destroy the virus itself. If not stopped by the body's immune response, the virus can then enter the lower respiratory tract, including the lungs. This can then lead to inflammation, affecting a person's ability to breathe leading to severe COVID-19 disease[13].

For the majority of people, SARS-CoV-2 infection leads to no symptoms or only mild symptoms (e.g. sore throat), affecting the upper respiratory tract. But, patients with certain risk factors are more likely to develop moderate or severe (and potentially fatal) disease impacting the lower respiratory tract (e.g. viral pneumonia, acute respiratory distress syndrome) requiring oxygen therapy and sometimes breathing support from ventilators and other forms of intensive care. Those aged 65 and above, particularly above age 80, are at higher risk of severe disease[14]. Those with cardiovascular disease, diabetes, obesity and chronic lung disease are also at higher risk of severe disease with these patients up to 12 times more likely to die if infected with COVID-19[15]. Those providing care, including unprotected frontline and

[3] https://www.who.int/ihr/publications/9789241580496/en/
[4] https://www.who.int/ihr/procedures/pheic/en/
[5] https://www.who.int/publications/m/item/covid-19-public-health-emergency-of-international-concern-(pheic)-global-research-and-innovation-forum
[6] https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200831-weekly-epi-update-3.pdf
[7] Taylor, L., Latham, S., & woolhouse, M. (2001). Risk factors for human disease emergence. Philosophical Transactions Of The Royal Society B: Biological Sciences, 356(1411), 983-989. http://dx.doi.org/10.1098/rstb.2001.0888
[8] Horton R. The COVID-19 Catastrophe. What's Gone Wrong and How to Stop it Happening Again. 2020.
[9] Exemplars in Global Health COVID-19 Repository.
[10] Kucharski A, et al. Early dynamics of transmission and control of COVID-19. Lancet Infectious Diseases. 11 March 2020.
[11] https://www.sciencedirect.com/science/article/pii/S0269749120325392?via%3Dihub
[12] https://wwwnc.cdc.gov/eid/article/26/9/20-1788_article
[13] https://www.sciencedirect.com/science/article/pii/S2090123220300540
[14] https://www.cdc.gov/mmwr/volumes/69/wr/mm6928e1.htm?s_cid=mm6928e1_w
[15] https://www.cdc.gov/mmwr/volumes/69/wr/mm6924e2.htm?s_cid=mm6924e2_w

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community health workers[16] and those living in the same households as people with COVID-19 are at increased risk of infection and developing severe disease due to higher exposure to the virus.

The COVID-19 infection fatality ratio is estimated to range 0.5 to 1%, while case fatality ranges from 0.1% to over 25% depending on the country[17]. The mortality rate is higher amongst older adults, especially those with pre-existing conditions, and as a result older adults account for a greater proportion of total deaths: in one study, over 80% of people who died of COVID-19 were 65 years or older[18]. As with past epidemics, mortality rates are also higher where health care systems are weaker, and amongst marginalized populations, including "essential service" workers, those living in poverty, and racial and ethnic minorities, whose underlying conditions (e.g. heart disease) have gone untreated due to limited and unequal access to primary health care[19].

The COVID-19 pandemic has cast a long shadow: it hasn't only devastated our immune systems, it has devastated our health, economic and social systems.

The COVID-19 pandemic hasn't only devastated immune systems, it has devastated health systems. Unprotected health workers have fallen sick, health systems have been overwhelmed, and people have been afraid to go to hospitals and clinics to seek care for malaria, treatment for chronic diseases, immunizations and other non-COVID-19 services. As of September 2020, 90% of countries have reported disruptions to essential health services[20]. It is projected that COVID-19's disruption of health systems will lead to hundreds of thousands to millions of non-COVID-19 deaths among patients with HIV, TB, malaria, as well due to excess child and maternal mortality[21].

The virus has cast a dark shadow over our economies. Restaurants and small businesses have closed. Sporting events and other mass gatherings were banned. Millions have lost their jobs and too many have been driven into hunger. The world could experience its deepest recession since the Second World War[22]. High-income countries have deployed more than 9 trillion dollars in economic stimulus[23] and low-income countries have struggled to stabilize their economies[24]. These shocks will have long lasting effects.

COVID-19 has also deepened inequities. The pandemic has exacerbated xenophobia. School terms ended suddenly leaving hundreds of millions of the poorest children without access to education.

[16] https://jamanetwork.com/journals/jama/fullarticle/2769693
[17] https://www.who.int/news-room/commentaries/detail/estimating-mortality-from-covid-19
[18] https://www.kff.org/coronavirus-covid-19/issue-brief/what-share-of-people-who-have-died-of-covid-19-are-65-and-older-and-how-does-it-vary-by-state/
[19] Horton R. The COVID-19 Catastrophe. What's Gone Wrong and How to Stop it Happening Again. 2020.
[20] https://www.who.int/news-room/detail/31-08-2020-in-who-global-pulse-survey-90-of-countries-report-disruptions-to-essential-health-services-since-covid-19-pandemic
[21] https://gh.bmj.com/content/5/7/e003430
[22] https://www.worldbank.org/en/publication/global-economic-prospects
[23] -https://blogs.imf.org/2020/05/20/tracking-the-9-trillion-global-fiscal-support-to-fight-covid-19
[24] https://www.uneca.org/sites/default/files/PublicationFiles/eca_covid_report_en_24apr_web1.pdf

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COVID-19 has placed heavier burdens and risks on women, especially those in caregiving roles[25,26]. The virus has had little mercy on the poor in urban and rural communities, those with mental health disorders and disabilities, racial and ethnic minorities, refugees, prisoners, and essential workers, who have all been hard-hit.

New tools can slow the virus and save lives, but there is no 'magic bullet'.

Along with non-pharmaceutical interventions (NPIs), there are vaccine candidates in development[27,28], efforts to make diagnostic testing more accessible, and many treatment trials underway. Together, these interventions will help further prevent COVID-19 transmission and reduce mortality rates.

Non-pharmaceutical interventions, when combined, can significantly reduce the spread of the SARS-CoV-2. These NPIs include cleaning and disinfecting surfaces[29], hand washing, widespread and appropriate face mask, and physical distancing. Other actions carried out by the public health system, include surveillance (widespread community screening and testing to identify cases), providing supportive case isolation (quarantining suspected or confirmed cases for an incubation period), and high-quality, intense, and wide-reaching contact tracing (retrospectively identifying the source of infection, and those who may have come across the source)[30]. When combined and widely adopted, these interventions have significantly reduced SARS-CoV-2 spread and mortality from COVID-19[31].

Medical countermeasures can further complement actions by the public and public health action.

Vaccine and prophylactic therapy trials are underway. As of September 4, 2020, there are no recommended prevention therapies for COVID-19, though a few preventative prophylactic drugs are in clinical trials. Over 170 vaccine candidates are also being developed, though some estimates suggest that a vaccine may not be licensed until early- or mid-2021.

The next breakthrough will likely be in testing. Outbreaks start and stop in communities. Widespread, community-based COVID-19 testing is critical for understanding and slowing the spread of COVID-19. Initial testing approaches (e.g. based on Polymerase Chain Reaction) have required significant laboratory infrastructure, including the need for specialized staff and specimen collection materials, which are still unevenly distributed around the world and within countries. However, new high performance, rapid-diagnostic antigen tests have tremendous potential because they bring tests to people rather than waiting for people to be brought to tests. Rapid diagnostic tests have the potential to improve testing

[25] https://www.exemplars.health/emerging-topics/epidemic-preparedness-and-response/covid-19/appendix/perspectives/thread?forumId=9&threadId=30
[26] https://www.foreignaffairs.com/articles/world/2020-07-15/melinda-gates-pandemics-toll-women
[27] https://www.gavi.org/vaccineswork/covax-explained
[28] https://www.who.int/docs/default-source/coronaviruse/novel-coronavirus-landscape-covid-19-(4).pdf
[29] https://www.cdc.gov/coronavirus/2019-ncov/prevent-getting-sick/prevention.html
[30] https://www.thelancet.com/pdfs/journals/laninf/PIIS1473-3099(20)30512-0.pdf
[31] https://www.exemplars.health/emerging-topics/epidemic-preparedness-and-response/covid-19

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access, reduce costs and save time – thereby improving early detection and isolation of cases and helping reduce SARS-CoV-2 transmission.

Several treatments are being studied. A review of data from controlled trials showed that current therapies used to treat COVID-19 are demonstrating varying effects[32]. It is important to note, antiviral, steroid-based, convalescent plasma and other drug therapies combined with supportive care like oxygen therapy and ventilatory support can improve outcomes and reduce the risk of death especially amongst sub-groups of moderate to severely ill COVID-19 patients.

None of these medical countermeasures will be a 'magic bullet.' For even as vaccines, tests and treatments are created, producing billions of them, delivering them, and ensuring their uptake by all who need it will remain a challenge.

Some countries have dealt with the virus well and the world should be asking what can be learned from these outliers?

The ultimate goal of COVID-19 response is to control the virus, save lives and protect livelihoods. Emerging success stories in COVID-19 response have been identified amongst countries in every region of the world and at various levels of economic development. These positive outliers or exemplar countries[33] have managed to suppress the virus – or eliminate it for periods. The science shows exemplar countries do 10 essential things to prevent, detect and respond to COVID-19:

PREVENT:

- Communicate with the public clearly and consistently.
- Implement strong border controls[34]
- Adopt universal masking in healthcare[35],[36] and community settings[37].

DETECT:

- Report standardized COVID-19 test figures daily.
- Prioritize widespread community-based screening[38] and testing to identify case clusters and prevent wider transmission.
- Trace and monitor the contacts of new cases within 72 hours at least 80% of the time[39].

[32] https://covid-19tracker.milkeninstitute.org/
[33] https://www.exemplars.health/emerging-topics/epidemic-preparedness-and-response/covid-19
[34] Han et al. Lessons learnt from easing COVID-19 restrictions: an analysis of countries in Asia and Europe. Lancet. 2020 (forthcoming)
[35] https://jamanetwork.com/journals/jama/fullarticle/2768533
[36] https://www.cdc.gov/mmwr/volumes/69/wr/mm6935e2.htm
[37] https://www.who.int/docs/default-source/coronaviruse/corrigendum-to-ig-2020-4-ipc-masks-2020-06-05-pp-15-16-2020-06-06-e.pdf
[38] https://www.nejm.org/doi/full/10.1056/NEJMc2014960
[39] https://apps.who.int/iris/rest/bitstreams/1277773/retrieve

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- Support exposed and infected patients to remain physically distanced (e.g. with financial support).

RESPOND:

- Prepare health systems to accommodate at least a 20% increase in COVID-19 cases.
- Rapidly surge facility- and community-based health workers[40,41,42] along with health and social services to meet demand.
- Leverage telemedicine and community-based strategies to sustain essential health services for non-COVID conditions (e.g. malaria/HIV/TB, reproductive care, vaccinations, non-communicable diseases)[43].

Countries have shown that by applying these evidence-based response strategies it is possible to effectively manage COVID-19: achieving viral suppression or even elimination for certain periods of time. These exemplars offer hope. But their practices must be adopted widely and prioritized, financed and implemented sufficiently.

The history of pandemics is repeating itself: we are leaving people behind again.

The idea that the wealthy and privileged will gain access to life-saving tools like vaccines, testing or treatments, while the poor and marginalized will get excluded from these tools is the story of every pandemic humanity has faced[44]. Efforts like the Access to COVID-19 Tools Accelerator, are working to speed up access to COVID-19 diagnostics, therapeutics and vaccines. But many health systems are still overwhelmed, with low-income regions disproportionately impacted due to shortages of facility-based and community-based health workers, oxygen treatment, ventilators, testing, and personal protective equipment[45,46,47, 48]. The most marginalized people are being left behind yet again in the response to COVID-19. To avoid mistakes of past pandemic responses that led to widening inequalities, equity must be the top priority in COVID-19 policy, financing and implementation[49, 50,51].

In summary, the spread of SARS-CoV-2 has been explosive but not unpredictable. COVID-19 has claimed too many lives and devastated health systems, economies and societies. The pandemic has also

[40] https://www.globalfinancingfacility.org/sites/gff_new/files/documents/Webinar-Summary-Note-Role-of-Community-Based-PHC-in-COVID-19.pdf
[41] https://gh.bmj.com/content/5/6/e002550?rss=1
[42] https://blogs.bmj.com/bmj/2020/03/27/prevent-detect-respond-how-community-health-workers-can-help-fight-covid-19/
[43] https://gh.bmj.com/content/5/7/e003430
[44] "Infections and Inequalities: the modern plagues". (6th ed.) Farmer, P. (2001).
[45] https://www.who.int/initiatives/act-accelerator
[46] https://www.medrxiv.org/content/10.1101/2020.07.03.20145763v1
[47] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7410474/
[48] https://www.cgdev.org/publication/protecting-community-health-workers-ppe-needs-and-recommendations-policy-action
[49] https://time.com/5843232/raj-panjabi-time100-coronavirus/
[50] https://www.wbur.org/cognoscenti/2020/07/22/covid-19-remdesivir-aids-africa-cameron-nutt-wilfredo-matias-robert-bonacci-meredith-kernan
[51] https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)30893-X/fulltext

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exacerbated inequities that exist between and within countries. Evidence-based, effective actions by the public and public health action has proven to slow the spread of the virus and reduce mortality. Medical countermeasures like vaccines, diagnostics and therapies have the potential to further strengthen the COVID-19 response. None of these countermeasures will be a 'magic bullet', as once developed they need to be scaled to reach all in need. Some countries have dealt with the virus well. These positive outliers offer strategies and lessons that should be adopted widely. As with past pandemics, the response to COVID-19 is widening inequities, excluding poor and marginalized people from access to life-saving services. Equity must be the top priority in COVID-19 policy, financing and implementation to ensure no one is left behind in the response to the pandemic.

At the dawn of the 21st century, the world finds itself in an age of pandemics. COVID-19 is not the first pandemic – it will not be the last. It may not be long before the world faces the next pandemic. The task at hand is to learn lessons at this stage of COVID-19 pandemic to strengthen the world's response to its next stage – and ensure we are all better prepared for future pandemics.

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