

# Healthcare in global crisis: preparations needed during the COVID-19 pandemic

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COVID-19 has led to more than 6 million deaths around the world [1]. Healthcare systems globally, with many already under crisis prior to the pandemic, have been impacted tremendously since the pandemic began. Leadership in each country and globally had to find ways to mitigate surges, while also having effective plans in place for timely responses with adequate access to interventions. As COVID-19 variants [2] surge with a persistent lack of sufficient vaccine coverage, the global healthcare community continues to require a comprehensive multidisciplinary approach to deal with the ongoing COVID-19 pandemic, where vaccination plays a vital role in mitigating the pandemic in addition to nonpharmaceutical interventions and therapeutics. Cooperation is urgently required between nations, community leaders, the scientific and healthcare community, global leaders, and industry to manage COVID-19 variant surges globally, as well as the spread of emerging pathogens, while focusing on prevention, testing, treatment, and healthcare and supply chain infrastructure and development.

*Vaccine Insights* 2022; 1(4), 183–190

DOI: 10.18609/vac.2022.028

The COVID-19 pandemic is far from over and variants continue to evolve and spread globally. Scientists, healthcare professionals, public health officials, policymakers, and leaders face challenges making informed timely decisions and providing evidence-based guidance to guide their constituents and populations.

Since the beginning of the pandemic, non-pharmaceutical interventions (NPIs), also known as public health and social measures (PHSMs), such as hand washing, masks, physical distancing, and lockdowns played key roles in mitigation strategies [3]. We now have vaccines and therapeutics as additional powerful tools to control the pandemic. COVID-19 vaccines have succeeded in decreasing disease severity, viral spread, and mortality. However, inadequate (worldwide and regional) vaccine coverage due to lack of access, vaccine hesitancy [4], and other factors have contributed to COVID-19 surges in many parts of the world, compounded and exacerbated by the spread of new variants. These surges in turn led to severe shortages and in some cases the collapse of healthcare services in areas with low vaccination rates, especially during the delta variant surge. The experience in the southern United States in summer 2021 in states with low vaccination coverage demonstrates how the downstream effects of vaccine hesitancy can cripple local healthcare systems in even the wealthiest of countries [5]. And the experience in many low- and middle-income countries (LMICs) serves as a stark example of the catastrophic results of inadequate COVID-19 vaccine coverage, especially as new variants spread.

In April–May 2021, the delta variant-mediated COVID-19 wave surged in India, leading to mortality that was likely much higher than the officially reported 400,000 deaths [6]. Although the majority of vaccine doses contributed to COVAX were manufactured in India [7], vaccination coverage in this country of approximately 1.4 billion was under 5% at the time [8]. During the peak of infections, there were shortages and outages of oxygen, prompting a public outcry regarding need for critical oxygen supply for

hospitalized patients as well as sick patients needing home oxygen due to inability in obtaining hospital beds. There were also shortages of critical medications and hospital beds. Clinical staff were stretched beyond safe limits. Widespread use of ineffective therapies such as ivermectin, doxycycline, azithromycin, and mixtures of Ayurvedic medicines may have exacerbated the crisis. Updated guidelines were provided at both the national and state levels but were frequently modified and often at variance with each other. Social media became the driver for prescribing practices, which were often not evidence based. Glucocorticoids were frequently misused. In desperation, people purchased novel therapies such as remdesivir and tocilizumab on the open market and at exorbitant prices, but without assurances of origin and quality. By the time the supply chains of oxygen and medications were streamlined and restored, significant damage had been done. India then faced another crisis. An unprecedented wave of COVID-19-associated mucormycosis cases (over 47,000 from May–July 2021) ensued [9], possibly due to overuse of steroids (including dexamethasone or equivalent) and the high diabetes/pre-diabetes prevalence in India, potentially causing an increased number of mucormycosis cases with a case fatality rate of approximately 36.5% [9]. The acute incidence of this epidemic of life-threatening fungal disease created critical shortages and price surges of key antifungals such as amphotericin B and Posaconazole [10].

The disruption of healthcare services due to COVID-19 affected all countries worldwide, with disproportionate impact on LMICs due to chronic suboptimal investments in health infrastructure and less resilience to recover. New surges of COVID-19 and emerging pathogens could cripple countries in the future. In times of medical crisis secondary to COVID-19, irrespective of variants, the healthcare and political leadership in each country and globally must find ways to mitigate surges while also having effective plans in place for timely responses with adequate access to interventions and healthcare.

Countries need to have robust surveillance in place, or they will continue to be unpleasantly surprised at the spread of new variants. Once COVID-19 cases begin to increase, it is critical to take early measures to control disease spread and transmission. Delayed action results in increased cases and mortality as well as severe stress on healthcare systems for all patients and healthcare workers and staff. With oral therapeutics now available in some countries, COVID-19 is being managed effectively in the outpatient setting even for high-risk populations for those who have access to these drugs. Widespread availability and access to these drugs are urgently needed worldwide. However, current oral therapeutics still require patients to present early after symptom onset (within five days of symptoms) and cannot be administered to all due to the potential of drug–drug interactions with some therapeutics. In order to promote early access, best practices and availability of diagnostics, prevention, and therapeutics must be in place and immediately implemented. A linear response to an exponentially increasing threat will result in failure and lead to crisis. We propose the following three-pronged approach:

## PREVENTION

National pandemic preparedness plans should be developed and revised based on lessons learned from prior surges. The World Health Organization (WHO) should continue to assist countries in identifying gaps, establishing best practices, and setting targets for implementation.

Countries should establish, with support as needed from international donors, a sentinel surveillance system that includes routine monitoring and sequencing for variants. This needs to be coupled with tailored and effective community engagement.

COVID-19 vaccines must be universally available, accessible, affordable, and meet necessary safety, quality, and regulatory standards. This will require sustained financial

commitments and increased manufacturing of vaccine products. But, without investment in capacity and infrastructure for countries to manufacture and deliver vaccines, and sustained efforts to gain public trust, vaccine doses will go to waste [11,12]. The latter will require consistent messaging and active engagement of susceptible populations and communities. Incentives should be designed to ensure ease of access to vaccines including transportation to vaccination sites, compensation for time off work to allow for vaccination and days off if needed post-vaccination, and additional methods to mitigate the indirect and out-of-pocket cost of accessing the vaccines.

Vaccines must be affordable, easy to store, and accessible. Policies should be feasible to implement and ensure equity and prioritization of vaccines based on scientific and medical data.

Health systems should be supported or augmented to be able to implement vaccine policies in a timely manner.

Misinformation should be addressed with strong community engagement and co-design of locally appropriate, fact-based messages. Scientific literacy for all policy and country leaders is necessary to guide public messaging. Vaccine hesitancy, willingness to be diagnosed, physical distancing, and mask-wearing are all areas where misinformation has resulted in setbacks in promoting accurate spread of information.

Research into improved vaccine thermostability and innovative methods for real-time extension of shelf-life information on vaccine batches should be encouraged to reduce vaccine wastage and simplified delivery. Vaccines should also be adjusted to new variants as needed.

Vaccination of vulnerable, marginalized, and high-risk populations, including health care and front-line workers, should be a priority.

In countries with large populations, policies such as allocation of vaccines to the private sector need to be mindful of both national and global guidelines to ensure

equitable and efficient distribution to their populations.

Boosters should be considered as per national policy and especially in moderately to severely immunocompromised people and high-risk populations.

With only 22% of the population of low-income countries vaccinated with at least one COVID-19 vaccine dose, wealthier countries must assist in vaccine equity and coverage worldwide [1]. Without vaccine equity and coverage on a global scale, variants will continue to develop and spread, and our current vaccines are at risk of becoming ineffective.

Investments should be made to boost sustainable manufacturing hubs in many low- and middle-income countries (LMICs) for COVID-19 diagnostics, therapeutics and vaccines via technology transfer and capacity strengthening in chemistry, manufacturing and control (CMC) capacity, and other critical infrastructure needed to produce and administer quality interventions [13].

Community participation and political leaders need to emphasize proper mask wearing and COVID-19 protective behavior during surges such as avoiding large gatherings, indoor masking, and physical distancing to achieve control of the pandemic surges. In addition, contact tracing (when possible) and quarantine measures need to be enforced.

Universal availability of adequate PPE including N-95 face masks for health workers and at-risk front-line workers should be prioritized, as well as high risk populations/communities and all front-line workers.

Areas with known low vaccination rates should be targeted for preparatory measures to combat surges, as delineated in the next two sections.

Science and evidence should prevail and dominate the discourse, with attention to making key scientific findings and evidence accessible and understandable to lay audiences. Strong community and leadership support is required to counter COVID-19 misinformation on social media, in open or public forums, and from influential leaders

(politicians, religious leaders, local and community leaders), public protests, information handouts, and other areas where misinformation is also being propagated.

### DIAGNOSIS & TREATMENT

- ▶ Accessing validated rapid diagnostic tests (RDTs), and polymerase chain reaction (PCR) is the first condition for access to treatment. Technical and resourcing support should be provided to ensure wide availability of antigen rapid diagnostic testing including community-based testing and self-testing to capture infections at the earliest stage of detectability so that the most suitable treatment options can be administered.
- ▶ Clinical guidelines should be consistent, evidence-based, widely accessible, and flexible to address local needs of communities. Guidelines should address all patients including hospitalized and outpatients as well as patient contacts.
- ▶ Adequate stocks of essential lifesaving drugs during the pandemic which now include oral antivirals nirmatrelvir/ritonavir and IV antivirals such as remdesivir as well as glucocorticoids such as dexamethasone, immunomodulators such as tocilizumab and baricitinib, currently effective monoclonal antibody cocktails, additional medications such as anticoagulants, antifungals, and antibiotics when needed, and critical oxygen supply must be maintained at levels sufficient to meet surge needs. Antibiotic stewardship should also be maintained during a surge. Key principles of how stocks and supplies can be transferred within a country between highly affected and non-affected regions/states should be investigated and negotiated before any surge. Oral therapeutics, IV remdesivir, and monoclonal antibodies are being used to prevent severe disease and hospitalizations. Methods for rapid and affordable deployment of oral therapeutics and

currently effective monoclonal antibodies, including in low-resource settings, should urgently be designed for those at primary need, i.e., at-risk populations. Efficacious oral treatments for outpatients need an immediate scalable production plan.

- ▶ The supply chain for oxygen (including production, transportation, storage, and distribution) must be prioritized, ensured, and supervised when oxygen supplies are noted to be in shortage. The oxygen shortage that was witnessed in multiple countries during the early part of the pandemic must never be repeated. Critically ill patients struggled to find oxygen for use in hospitals or at home during surges in multiple countries. The allocation of available oxygen supplies need to be managed through planning and monitoring [14].
- ▶ Medication and diagnostic prices in private markets where patients pay out of pocket must be controlled to ensure equitable and affordable access. Home care and triage protocols must be strengthened to ensure timely identification and safe transfer of patients to higher level care when needed.
- ▶ Research into oral treatments is still needed given the limitations of existing options. In addition, treatments may need to be adapted due to variant selection (e.g., monoclonal antibodies), to treat immunosuppressed patients, to prevent resistance development, and, ideally, to prevent or treat post-COVID conditions. Adequate funding to cover those critical research gaps is needed.

## HEALTHCARE INFRASTRUCTURE

Hospital beds, staffing, respiratory equipment, ventilators and supplies that will be needed should be prepared in advance of a COVID-19 surge. Infection Prevention and

Control (IPC) teams in health systems should be adequately resourced to manage IPC supplies [15]. Temporary hospitals for treating mild-to-moderate cases of COVID-19 are also needed when home quarantine is not possible [16].

Adequate staffing of healthcare personnel such as physicians and nurses should be ensured prior to surges. During staff shortages, task shifting plans should be in place to train other healthcare workers, including medical and nursing students and resident trainees, in COVID-19 care. Mental health needs for healthcare worker teams must also be addressed during this time.

Command and control communication systems should be prepared ahead of time to ensure coordination, facilitation, and safe transportation of sick patients from rural areas and homes to hospitals.

Healthcare systems must be strengthened, especially at the primary care level to ensure equitable access to diagnostics, therapies, and vaccines. Healthcare and public health systems should be responsive and able to test, track and treat in a timely manner and have access to tools such as rapid antigen testing (AgRDT).

Capacity for advanced virology (e.g., genomic sequencing) should be considered a necessity and at least 5% of detected samples should be sequenced. The system for pathogen genomic sequencing in LMICs is nascent and will require technical and financial support to achieve these targets.

There is an urgent need to vaccinate equitably to prevent the spread of this pandemic and to ensure therapeutics are readily available worldwide. We need a comprehensive multidisciplinary approach to deal with the ongoing COVID-19 pandemic, where vaccination will play a vital role in mitigating the pandemic in addition to non-pharmaceutical interventions and therapeutics. We must scale up vaccine and therapeutics production, encourage unhindered supply, and ensure that infrastructure for delivery is in place globally. This will require coordination between governments, vaccine producers,

pharmaceutical companies, and community leaders to save lives and ensure equity. In turn, this will prevent the spread of more coronavirus variants and accelerate the decline of the pandemic. In addition, vaccine developers have a moral duty to support vaccination campaigns in LMICs to establish and expand infrastructure and vaccine manufacturing capacities. It is also essential for the current and future global pandemics that intellectual property rights for vaccines and therapeutics that are deemed essential worldwide do not prevent widespread deployment. As part of global efforts for pandemic preparedness, global health leaders and multilateral organizations should leverage on

intellectual flexibility frameworks to ensure equal access for vaccines and therapeutics that are deemed essential.

Simultaneously, as the world's population is yet to be fully vaccinated, we must be prepared to manage cases of COVID-19 with adequate infrastructure, diagnostics and therapeutics. Cooperation and solidarity are urgently required between nations, community leaders, the scientific and healthcare community, global leaders, and industry. The time is now for such a collaboration to address the needs of the healthcare communities worldwide that are being impacted by the ongoing crisis and support the infrastructure that is so desperately needed.

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**Contributions:** Lall B, Chaudhry D., Batista C, Shoham S, and Ergonul O wrote the initial draft. All other authors contributed equally. All named authors take responsibility for the integrity of the work as a whole, and have given their approval for this version to be published.

**Acknowledgements:** None.

**Research ethics statement:** This study did not receive nor require ethics approval, as it does not involve human & animal participants.

**Disclosure and potential conflicts of interest:** The authors report the following competing interests: Bottazzi ME and Hotez PJ are developers of a COVID-19 vaccine construct, which is licensed by Baylor College of Medicine to commercial vaccine manufacturers for scale up, production, testing and licensure. Gursel M participates in one of eight SARS-CoV-2 vaccine development projects supported by The Scientific and Technological Research Council of Turkey (TÜBİTAK) since March 2020. Gilbert S is cofounder of Vaccitech and has a patent on ChAdOx1 nCoV-19 licensed to AstraZeneca. Hassanain M is Founder and Managing Director of SaudiVax. Figueroa JP, Kang G and Kaslow DC are members of the WHO SAGE Working Group on COVID-19 vaccines. Kang G is independent director appointed by the Wellcome Trust, MSD Wellcome Trust Hilleman Laboratories Private Limited and Vice Chair of the Board, Coalition of Epidemic Preparedness Innovations (CEPI). Hotez P is a developer of COVID-19 vaccine constructs which have been licensed by Baylor College of Medicine to commercial vaccine manufacturers for scale up, production, testing and licensure. Hotez P declares that he is a developer of the RBD219-N1C1 and RBD203-N1 technologies, and that Baylor College of Medicine (BCM) licensed RBD219-N1C1 to Biological E, an Indian manufacturer, for further advancement and licensure. Similar licensing agreements are also in place with other partners for both RBD219-N1C1 and RBD203-N1. Kaslow DC reports grants from Bill and Melinda Gates Foundation (BMGF) and grants from CEPI, Kim JH reports personal fees from SK biosciences. Larson H reports grants and honoraria from GlaxoSmithKline for training talks and from Merck as a member of the Merck Vaccine Confidence Advisory Board, grants from J&J outside the submitted work. Wilder-Smith A serves as Consultant to WHO. The views presented here reflect her views and not necessarily those of WHO. Sheahan T reports grants from National Institute of Allergy and Infectious Disease and Fast Grants and research contracts from GlaxoSmithKline, and ViiV Healthcare. Sow S reports grants from Ansun BioPharma, Astellas Pharma, Cidara Therapeutics, F2G, Merck, T2 Biosystems, Shire Pharmaceuticals, Shionogi, and Gilead Sciences, outside the submitted work; and personal fees from Amplify Pharmaceuticals, Acidophil, Janssen Pharmaceuticals, Reviral, Intermountain Healthcare, Karyopharm Therapeutics, Immunome, Celltrion, and Adagio outside the submitted work. All other authors declare no conflict of interests. The authors views and opinions in the Commentary do not necessarily represent the views, decisions, or policies of the institutions, universities, or health systems with which they are affiliated.

**Funding declaration:** The authors received no financial support for the research, authorship and/or publication of this article.

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**Article source:** Invited; externally peer reviewed.

**Submitted for peer review:** Aug 18 2022; Revised manuscript received: Aug 22 2022; Publication date: Sep 16 2022.