



Pandemic preparedness and the role of science

EXECUTIVE SUMMARY

Based on consideration by the Scientific Academies of the G20 countries of how the experience of the response to COVID-19 might inform pandemic preparedness in the future, the governments of G20 are urged to undertake the following actions:

- 1. Promote the creation of a global network of surveillance, with agreed criteria to:**
 - Detect emerging unusual clusters of morbidity and mortality that may be the harbingers of a potential new pandemic by:
 - building on existing infrastructures including the global alert and response system for disease outbreaks;
 - promoting enhanced support for systems such as the Epidemic Intelligence from Open Sources initiative (EIOS);
 - developing robust policies and platforms for collating and sharing detailed data - for example on pathogen genomics.
 - Provide molecular epidemiological surveillance for directly transmitted respiratory infections (the most dangerous in terms of rapid spread) and bacterial infections in the context of the spread of antibiotic resistance genes.
 - Strengthen the system for worldwide antimicrobial resistance surveillance.
 - Advvertise, educate and promote support for these, and build capacity and skills for their use.

The network should be underpinned by the governance, infrastructure and skills to interpret, analyse and connect across countries, and to learn from international data.

- 2. Promote the distributed manufacture and delivery of diagnostics, drugs, vaccines, medical supplies and equipment for:**
 - Increased technology and manufacturing capability worldwide, but especially in low and middle-income countries.
 - Streamlined regulatory processes for novel diagnostics, drugs and vaccines.
 - International regulatory agencies to look at the lessons learned from swift development of vaccines in the COVID-19 pandemic and ensure new regulatory processes can be implemented in a timely fashion.
 - Provide an international structure to compile and advise on the sensitivity and specificity of different diagnostic tools.
 - Enhance access to new technologies, accounting for intellectual property, patenting and pricing mechanisms.
- 3. Launch an Intergovernmental Convention that should:**
 - Pave the way to the formulation of an *International Agreement on Pandemic Preparedness and Management*, as recently proposed by more than 20 world leaders.
 - Provide a unique forum to assess the experience of COVID-19 for successes and failures in global cooperation.
 - Discuss the need for incentives and mechanisms to reinforce the International Health Regulations (2005) that must become a sharper instrument for action and more timely reporting of potential outbreaks.

1. INTRODUCTION

A pandemic is the worldwide spread of a new disease. Achieving protection against a pandemic is a public good. Like mitigation of climate change, it is a supranational issue that cannot be left only to national governments. Achieving global health security (including prevention of pandemics) requires reinforced international collaboration to deliver decisions about allocation of limited resources.

2. LESSONS FROM COVID-19 AND PREVIOUS PANDEMICS

The first lesson of pandemic preparedness is that this needs to start long before a new pandemic starts. Countries with recent experience of zoonotic infections that might have become pandemic, such as avian influenza, SARS-1 and MERS, have tended to manage the current pandemic more effectively than those whose public health systems were less experienced and that had received less investment in pandemic preparedness.

Pandemic preparedness starts with rapid and transparent sharing of information and samples, it requires research at great speed and scale, and involves the production and distribution of necessary public health commodities such as vaccines and drugs, protective equipment, and the infrastructure for identification, testing, tracing, isolating, treating and preventing cases, especially considering the routes of disease transmission. Aware of the heavy economic, societal and human impact of pandemics, recommendations aimed at enhancing preparedness have been put forward in the recent past (1 - 4). However, it is clear from the COVID-19 pandemic experience that the recommendations have not been sufficient to mitigate the effects of the pandemic, nor have they been adequately implemented in most countries. Indeed, a major problem in the response to COVID-19 has not been just one of resources, except for drug and vaccine shortages, but also misinformation and unsuccessful global coordination of resource deployment at scale, resulting in a multiplication of parallel efforts.

Preparing for unexpected and difficult-to-predict infectious

diseases to prevent or control outbreaks can be very challenging. Nonetheless, the world has accumulated substantial knowledge and experience from past infectious disease epidemics and pandemics. Great strides have been achieved towards ensuring preparedness and response capacity for potential emerging infectious diseases particularly in high income countries. This was achieved by developing and implementing comprehensive approaches and proactive systems including resource prioritization, substantial investment in scientific research and improvement of research infrastructures, efficient national and international cooperation; effective networks of infectious disease epidemiology and surveillance, research collaboration and enablement of data sharing, therapeutics and vaccine clinical trials, dedicated and committed scientific, medical and political leadership. Unfortunately, progress towards meeting such minimal preparedness, especially in low and middle income countries, is lagging in terms of public health surveillance and outbreak response causing high risk and vulnerability.

2.1. Lessons on pandemic prevention and early detection

A) Preventing the onset of epidemics

Control of infectious diseases depends on preventing new cases of infection. It requires the ability to detect any new or re-emerging pathogens including drug-resistant microbes that represent a challenge for global health. Interactions between humans, domestic and wild animals are important predisposing factors that are influenced, not only by their immediate environment, but also by agricultural practices and cultural attitudes. The frequency of zoonoses will likely increase due to a growing and increasingly mobile human population, climate change, inappropriate use and scarcity of water, consumption of wildlife products, legal and illegal trades of wild animals, and loss of biodiversity. The international community is confronted with two interlinked major challenges, namely *mitigating human vulnerability to pandemics and developing approaches to minimize spillovers from animals and their associated environment to humans*.

Presently, our ability to predict the emergence of a disease in

areas and populations identified as being at high risk is poor and is constrained by knowledge and technological asymmetries, infrastructure, culture, and politics.

Epidemiological surveillance includes the systematic collection, recording, analysis, interpretation, and dissemination of data on communicable diseases that can lead to early warning signals and promote an adequate response. Surveillance must be enhanced in high-risk areas and populations, which may be identified with the support of epidemiological models and experience, including emerging local information and scientific findings on infectiousness of pathogens, information on international trade, mobility, transport, animal breeding, agricultural practices, and loss of biodiversity. The capacity for continuous genetic sequencing, molecular surveillance, structured data and terminology for the use of artificial intelligence must be integrated to enhance the detection of novel pathogens, predict risk, and identify of potential therapeutics.

B) Early detection of the pathogen in animals and humans and predictive models, immediately after an outbreak

Early detection is essential and relies on clinical recognition, mathematical modelling, the rapid availability of trained personnel, and an infrastructure for widespread and rapid testing and tracing. Establishing the capability for contact tracing is particularly important at the beginning of a pandemic. International data sharing must occur rapidly. Early detection can be based on passive surveillance of cases, or on active surveillance of sentinel sites or on new technologies capturing specific symptoms in the population (5). Models based on previous information should be improved by incorporating emerging local information.

Rapid data and sample collection and then their international sharing is key to fighting a pandemic. A global network of clinical and epidemiological surveillance, coupled with the capability for genomic analysis, needs to be managed by highly qualified personnel according to principles of complete transparency of communication. In some countries, essential information to make decisions during the COVID-19 pan-

demic was provided by large cooperative data platforms, with ethics (including consent) and administrative procedures developed in advance.

C) Preventing the spread of epidemics

Containment measures are crucial. Non-pharmaceutical interventions (e.g. testing, quarantine and isolation, physical distancing, masking, handwashing, ventilation hygiene) have proven to be highly effective. To implement such measures better, we need to increase the understanding of infection control, leading to its implementation in a coherent public health response. The refinement of early epidemiological models with the help of data assimilation, filtering via actual observations, and sensitivity analysis may help guide the choice of the most appropriate containment strategies. This needs to be done within the global network mentioned above and detailed below, including a repository of raw data, terminology and procedures for supervision.

Many of the world's epidemics, particularly those transmitted by intermediate hosts, are known to be highly sensitive to long-term changes in climate and short-term fluctuations in the weather. Predictive models should apply environmental data to test for any relationship between local environmental conditions and spread of diseases.

Experts in communication of public health messaging need to be trained in advance and messaging coordinated both nationally and internationally. Variable and inconsistent messaging have undermined compliance with public health precautions and fed scepticism about the safety and effectiveness of vaccines, social distancing and the use of masks. Curtailing the spread of misinformation via social media platforms requires global cyber-regulations and enhanced cybersecurity. The striking progress made in the accelerated development of vaccines for COVID-19 (months rather than years) shows that vaccines can be deployed to prevent recurrent surges of infection in a pandemic, especially when appropriate interventions are taken to delay the reappearance of the disease. This is also true of vaccine adaptation to the emergence of novel strains, which evade protective immunity.

D) Identifying the vulnerable population and determining preventive or mitigating measures

The COVID-19 pandemic has revealed high variability in outcomes based on age, gender, ethnicity, and co-morbidities that need to be better understood.

2.2. Lessons on interventions

Various challenges have become apparent in the COVID-19 pandemic.

Firstly, a striking variability has emerged in the response to infection and in the usefulness of interventions dependent on the stage of the disease. The detection of treatments that worked relied on randomized clinical trials (RCTs) asking simple questions in complex situations. By contrast, small trials, often performed at a single site, were often underpowered and not useful (6).

Parsing and predicting variability of response to the infection has relied on global alliances and pipelines that might be repositioned to gather scientific information across the lifespan of the disease, provide information on the timing of interventions, and accelerate the discovery of novel diagnostic and therapeutic opportunities. Such a coordinated mechanism must align with manufacturing, procurement, distribution, and delivery.

Secondly, the sensitivity of the global supply chain of essential drugs and vaccines to disruption has become evident. International coordination is necessary to address this complex problem that is impacted by funding, distribution infrastructure and politics.

The management of such challenges could be organized by the WHO, leveraging its unique role in establishing norms for global behavior (e.g., data sharing, material transfer agreements, common protocols, and ethics reviews). However, the governance of this complex enterprise would strongly benefit also from the involvement of medical and scientific organizations worldwide as, in its present configuration, WHO is not an operational body and is responsible to its member states. We suggest that this issue be thoroughly analyzed in the light of the COVID-19 experience.

3. PROPOSAL OF ACTIONS

3.1. General actions

Science alone cannot abolish the contribution of poverty and inequality to pandemic vulnerability, as well as to the health, social and economic costs of a pandemic, which have emerged dramatically during COVID-19. However, a scientific assessment of the latter costs would show conclusively that addressing poverty and inequality is now, more than ever, a global priority. Pursuing this challenging goal does require strengthening of national science, technology and innovation systems especially in low and middle income countries. A global effort to narrow the widened income gap caused by COVID-19 is urgently required.

The G20 governments should recognize the need to:

- (i) Provide secure funding to National and International Health Institutions to allow for the provision of transparent, *independent* and accessible public health information to the global community as well as for the best allocation of available resources. This would include investment in basic, translational and implementation research, analysis of public health strategies such as lockdowns and travel restrictions to identify the best sustainable practices that could be harmonized and applied in the future. It should also include a source of current information on the safety and efficacy of new vaccines and drugs and the sharing of sequencing capability to monitor genomic variations in pathogens that may alter infectivity and virulence or change the effectiveness of vaccines or confer resistance to therapeutic drugs. Genomic sequencing allows the rapid development of tools to monitor the spread of the pandemic and the evolution of new strains.
- (ii) Improve communication as well as health and scientific education among the public, addressing areas of misinformation, public scepticism and concern related to the required interventions necessary to control a pandemic, including those that are embedded in culture (e.g. vaccine hesitancy, the wearing of face masks, trust in pharmaceutical companies).

- (iii) Promote research to discover new antimicrobials, promote the reduction in use and more rational deployment of existing antimicrobials, for both human treatment and animal breeding and exclude antimicrobials from use in healthy humans and animals.
- (iv) Extend the deployment of technological innovations (e.g. telemedicine) that may help to provide health assistance and guide resource allocation in the course of pandemics.
- (v) Pay attention to psychological stress associated with pandemics that affect the mental and emotional health of global populations and health care providers.
- (vi) Invest the relatively small amounts of resource necessary to reach a minimum level of preparedness such as to improve outcomes for vulnerable populations when an outbreak occurs.

3.2. Specific actions to improve prevention and early detection

International collaboration of the G20 governments is especially needed to reach the following goals:

- (i) Improve regulation and enforce biosecurity of farmed animals (good husbandry practices) as well as documentation and control of legal and illegal trading of wild animals.
- (ii) Promote the study of emerging infectious diseases under a “One Health” approach. This requires cooperation between medical, veterinary, agricultural and environmental sciences, as well as the establishment of specific research institutions where integrated research can be performed. There should be a reflection on the measures needed to improve the degree of success of the joint efforts of the current WHO, World Organization for Animal Health [formerly the International Epizootic Office (OIE)], Food and Agriculture Organization of the United Nations (FAO), and UN Environmental Programme (7).
- (iii) Propose the creation of an *international network of National Institutes for Infectious Diseases and Infection Con-*

trol. This would update open-access databases and repositories of relevant epidemiological, clinical, and other scientific data collected in each country through the involvement of reference hospitals and other networks in member countries. Real time surveillance would be a key part of data sharing. Transparency of national and local health organizations for the real-time availability and sharing of comprehensive clinical and scientific standardized datasets to WHO to facilitate the work of international experts is necessary.

Specific areas for data collection and sharing include:

- Biology, pathology, and ecology of new microbial pathogens, with special emphasis on rapidly-mutating RNA viruses; ecology of animal carriers and reservoirs; mechanisms of pathogen transmission within and amongst animal species and from animals to humans;
 - Determinants of the onset and spread of zoonoses; information systems on epidemiological surveillance, increasing their inter-operability;
 - Strengthening joint activities to enhance biosafety and biosecurity at the global level;
 - Studies to explain the variability of response to infection.
- (iv) Enhance coordination on research in the following areas:
 - Mechanisms of contagion, assessment of the risk of contagion under different environmental conditions (humidity, temperature, ventilation, distancing), technological innovations of protective equipment.
 - Study of the relationships between climate change and the emergence of microorganisms, including the risk of the appearance of pathogens presently buried in the cryosphere.
 - Innovative technologies to allow for the accelerated development and dissemination of new drugs and vaccines.
 - Development of and global access to a distributed network of vaccine manufacturing facilities, to con-

trol infections. More than ever, vaccines must be considered as a global good for which each country must be the guarantor.

- Development of rapid, simple, efficient, and inexpensive diagnostics and establishment of clear diagnostic criteria.
 - Genomics platforms for systematic assessment of pathogen evolution and host genomics, and development of multi-omics and immunophenotyping pipelines with standardized approaches to sample analysis.
 - Analysis of basic aspects of antigen immunogenicity and immune memory.
 - Transnational platforms for integration of structured data and terminology from questionnaires and electronic health records.
 - Development of animal models using the 3Rs (replacement, reduction and refinement) that can mimic human diseases for pathogenesis study and for drug screening.
- (v) Develop comprehensive industry enabling biotechnology platforms. Industry led initiatives might include building multiple antibody libraries, biobanking of microorganisms, development of viral vector platforms, screening of products and formulations and a facility to achieve good manufacturing practice (GMP) process development, manufacturing scale up and stockpiling of materials for preclinical and clinical trials.

3.3. Specific actions to improve the control of new pandemic diseases

- (i) Refine approaches to screening for new drugs, integrating novel laboratory technologies and preclinical models with experimental medicine approaches and innovative exploratory trial designs. This should be planned on a global basis.
- (ii) Establish several international networks designed to activate rapidly observational cohort studies and large RCTs incorporating digital screening methods and rapid

response evidence- and consensus-based frameworks for immediate treatment. Put in place a funding mechanism - a *research preparedness - response fund* - for vaccine and drug development and the rapid design and implementation of such studies and trials.

- (iii) Establish a streamlined international consultation mechanism for medical professionals to recommend rapidly only those new or repurposed drugs proven to be effective and safe.
- (iv) Increase sequencing capacity to detect viral evolution that may impact the effectiveness of diagnostics, small molecule drugs, immunotherapies and vaccines, and integrate evidence on genotypic evolution with strategies to determine phenotypic properties such as incubation periods, infectiousness, transmissibility and pathogenicity as measured by mortality and morbidity requiring hospitalization.
- (v) Collect pathogen samples where genome data can be linked to location and epidemiological and demographic information about the patient from which the sample was collected. A well curated, interoperable database of such information should be designed and made operational for emerging infections.
- (vi) Establish a global monitoring system to record the long-term sequelae of infection and the comparative safety and duration of efficacy of vaccines and pharmaceuticals.

4. THE NEED FOR AN INTERNATIONAL AGREEMENT ON PANDEMIC PREPAREDNESS AND MANAGEMENT

In view of the above recommendations, we support the launch of an *Intergovernmental Convention* that should pave the way to formulation of an *International Agreement on Pandemic Preparedness and Management*, as recently proposed by more than 20 world leaders (8) and affirmed at the G7 (9). The *Intergovernmental Convention* should provide a unique forum to discuss success and failures emerged from the experience of COVID-19 and the need for incentives and mecha-

nisms to reinforce the International Health Regulations (2005) that must become a sharper instrument for action and more timely reporting of potential outbreaks. *The International Agreement* should be subject to an annual review of the implementation of the commitments and policies agreed upon. While there is great uncertainty about the future threats of infectious diseases, there is much that governments and policymakers can do to prepare. Many of the key choices for governance and regulation are about recognizing the need for a globally integrated approach to tackling infectious diseases. A true “One Health” approach in close cooperation with the WHO, the FAO, the OIE and the UN Environmental Program (UNEP) as well as similar organizations (10), is essential.

While the structuring of an *International Agreement on Pandemic Preparedness* is left to the governments, it should aim (i) to facilitate rapid and efficient implementation of practices based on the best available science and technology and (ii) to de-politicize and integrate public health messaging from a widely accepted source.

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