

In KEYNOTE 042, the PD-1 inhibitor pembrolizumab produced a significant improvement in survival in patients with advanced NSCLC with PD-L1 expression on 1% or more of tumour cells, but this survival benefit was predominantly driven by patients with PD-L1 expression on 50% or more of tumour cells. Ultimately, findings from IMpower010 support a new role for PD-L1 testing in surgically resected NSCLC, although they underscore the need for additional studies to further define which subpopulations benefit most from adjuvant atezolizumab.

IMpower010 represents an important step forward. In my view, adjuvant atezolizumab should be a new standard of care for patients with surgically resected, PD-L1-positive stage II-IIIa NSCLC after completion of adjuvant chemotherapy, with particular emphasis on those patients with PD-L1 expression on 50% or more tumour cells. In the near future, the therapeutic landscape for resectable NSCLC is likely to become more complicated as additional data emerge from other, ongoing studies of immune checkpoint inhibitors in the adjuvant setting and parallel studies evaluating neoadjuvant approaches. More broadly, the success of adjuvant PD-L1 blockade in patients with NSCLC, along with recent data in melanoma,<sup>10</sup> sets the stage for continued expansion of immune checkpoint inhibitors into the adjuvant setting across disease areas over the ensuing decade.

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## Functioning of the International Health Regulations during the COVID-19 pandemic



When the International Health Regulations (IHR) came into force in 2007, WHO announced that “the global community has a new legal framework to better manage its collective defences to detect disease events and to respond to public health risks and emergencies”.<sup>1</sup> The IHR aim to enable the prevention, detection, and containment of health risks and threats, the strengthening of national capacities for that purpose, and the coordination of a global alert and response system.

In the prolonged and unprecedented COVID-19 pandemic, some have stated that the IHR “are a conservative instrument that constrain rather than facilitate rapid action”.<sup>2</sup> What we, the Review Committee on the Functioning of the IHR (2005) during the COVID-19 Response, found instead was that much of what is in the IHR is well considered, appropriate, and meaningful in any public health emergency. However, many countries only applied the IHR in part, were not sufficiently aware of these

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regulations, or deliberately ignored them,<sup>3,4</sup> and that WHO did not make full use of the powers given to it through the wording and spirit of the IHR. Thus, the IHR are not deficient, but their implementation by member states and by WHO was inadequate. The IHR Review Committee on COVID-19, which consists of 20 experts with diverse health expertise from around the world, derived these findings through a combination of literature review, background information requested from the WHO IHR Secretariat, interviews with experts, statements from member states, and review of IHR articles.

Recognising the limited mandate of the IHR Review Committee on COVID-19, which was focused solely on the IHR-related aspects of the COVID-19 response, we propose that there was a collective failure in three areas: compliance and empowerment; early alert,

notification, and response; and financial and political commitment.

Inadequate compliance of states with obligations under the IHR, particularly on preparedness, contributed to the COVID-19 pandemic becoming a protracted global health emergency. To improve compliance, IHR implementation needs to become a priority at the highest level of government and placed in the context of building a resilient health system in a whole of government approach. This can be supported through, for example, ensuring IHR national focal points are appropriately organised, resourced, and positioned within government, with sufficient seniority and authority, to meaningfully engage with all relevant sectors in crisis response. A robust review and accountability mechanism is also needed for evaluating and jointly improving compliance with

**Panel: Select recommendations of the Review Committee on the Functioning of the International Health Regulations (2005) during the COVID-19 Response to strengthen implementation of the IHR**

**Role and functioning of national focal points**

States parties should enact or adapt legislation to authorise national focal points to perform their functions and to ensure that the national focal point is a designated centre, not an individual, which is appropriately organised, resourced, and positioned within government, with sufficient seniority and authority to meaningfully engage with all relevant sectors.

WHO should assess the performance and functioning of national focal points and report its findings accordingly in WHO's annual report to the World Health Assembly on IHR implementation.

**Core capacity requirements for preparedness, surveillance, and response**

States parties should strive to integrate the core capacities for emergency preparedness, surveillance, and response within the broader health system and essential public health functions, to ensure that national health systems are resilient enough to function effectively during pandemics and other health emergencies.

**Legal preparedness**

States parties should periodically review existing legislation and ensure that appropriate legal frameworks are in place to: manage health risks and health emergencies; foster a whole-of-government approach; and support the establishment and functioning of core capacities.

**National notification and alert system**

States parties should share the relevant public health information, including genomic sequencing data, needed by

WHO to assess the public health risk for a notified or verified event as soon as it becomes available, and continue to share information with WHO after notification or verification so as to allow WHO to conduct a reliable risk assessment. States parties should communicate more proactively through WHO's Event Information Site with both other states and the WHO Secretariat. WHO should monitor and document countries' compliance with their IHR requirements for information sharing and verification requests, and report its findings in WHO's annual report to the World Health Assembly on IHR implementation.

**Risk assessment and information sharing**

WHO should proactively and assertively make use of the provisions in the IHR to share information about public health risks with states parties (including unofficial information from reliable sources without seeking agreement from the states parties concerned) and should report annually to the World Health Assembly on how it has implemented these provisions, including instances of sharing unverified information with states parties through WHO's Event Information Site.

WHO should strengthen its informal interactions with states parties to enable WHO to conduct high-quality rapid risk assessments. To this end, WHO should further develop confidence-building and trust-building mechanisms (eg, periodic conferences, informal information sharing sessions) between itself and the appropriate national focal points or competent authorities, at the global, regional, and country levels.

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### **COVID-19 Emergency Committee and the determination of a Public Health Emergency of International Concern**

WHO should make available to states parties through WHO's Event Information Site all the information and technical documentation it provides to the Emergency Committee for each of its meetings, including findings of rapid risk assessments. WHO should allow sufficient time for Emergency Committee members to deliberate, reach a conclusion, and prepare their advice to the Director-General. Emergency Committee members should not be required to reach a consensus; if there is division, divergent views should be noted in the Committee's report.

For events that may not meet the criteria for a Public Health Emergency of International Concern but may require an urgent escalated public health response, WHO should actively alert the global community. Building on WHO's online Disease Outbreak News, a new World Alert and Response Notice (WARN) system should be developed to inform countries of the actions required to respond rapidly to an event so as to prevent it from becoming a global crisis.

### **Travel measures**

Consideration should be given to clearly defining states parties' responsibilities for implementing isolation and quarantine measures under the IHR on international cruise ships, as well as international contact tracing, and care and repatriation of international cruise ship passengers.

WHO should support research efforts to strengthen the evidence base and its recommendations on the impact and advisability of travel restrictions.

### **Digitalisation and communication**

WHO should develop norms and standards for digital technology applications relevant to international travel, ensuring individual privacy and facilitating equitable access to all persons, including those in low-income countries. This may include the development of digital technologies for contact tracing in the international context, as well as options for the digitalisation of all health forms in the IHR.

WHO should make greater use of digital technology for communication among national focal points and should support states parties in strengthening information technology systems to enable rapid communication between national focal points, WHO, and other states parties.

WHO and states parties should strengthen their approaches to and capacities for information and infodemic management, risk communication, and community engagement to build public trust in data, scientific evidence, and public health measures, and to counter inaccurate information and unsubstantiated rumours.

### **Collaboration, coordination, and financing**

States parties should ensure adequate and sustained financing for IHR implementation at the national and subnational levels

and provide adequate and sustained financing to the WHO Secretariat for its work on preventing, detecting, and responding to disease outbreaks.

States parties should give WHO a clear mandate to proactively support individual states parties when information about high-risk events becomes known to WHO. WHO should further strengthen its work with relevant networks to coordinate and offer immediate technical support in outbreak investigations and risk assessments, and such offers should be accepted by states parties; where such offers are not accepted by states parties, they should promptly provide a written explanation of their position.

WHO should strengthen existing operations through an expanded Global Outbreak Alert and Response Network and by working with Emergency Medical Teams, the Global Health Cluster, and other relevant networks.

WHO and states parties should consider the benefits of developing a global convention on pandemic preparedness and response. Such a convention may include provisions for preparedness, readiness, and response during a pandemic that are not addressed by the IHR, such as, for example, equitable access globally to countermeasures, rapid deployment of WHO teams maintaining the global supply chain, as well as for prevention and management of zoonotic risks.

WHO should facilitate and support efforts to build evidence and research on the effectiveness of public health and social measures during pandemics.

### **Compliance and accountability**

Each state party should inform WHO about the establishment of its national competent authority responsible for overall implementation of the IHR that will be recognised and held accountable for the national focal point's functioning and the delivery of other IHR obligations. WHO, in consultation with member states, should develop an accountability framework for the competent authorities.

WHO should work with states parties and relevant stakeholders to develop and implement a universal period review mechanism to assess, report on and improve compliance with IHR requirements, and ensure accountability for the IHR obligations, through a multisectoral and whole-of-government approach.

WHO should collaborate with international human rights bodies to monitor states parties' actions during health emergencies and to regularly reiterate the importance of respecting international human rights principles, including the protection of personal data and privacy.

IHR=International Health Regulations. These recommendations are selected from the Committee's published 40 recommendations in ten areas.<sup>6</sup>

IHR obligations. Strong accountability mechanisms are crucial since inadequate IHR core capacities can endanger health across the globe. The IHR Review Committee on COVID-19 considers that obligatory periodic reviews of national IHR capacities, including their functionality, would be beneficial. The universal periodic reviews of the Human Rights Council<sup>5</sup> could serve as a guiding example. States also need to ensure that appropriate national legal frameworks are in place to manage health risks and health emergencies and that these accord with the IHR. Intensified international cooperation is required to better support global health protection. The IHR Review Committee on COVID-19 considers developing a global, legally binding convention on pandemic preparedness and response an important step in that direction.

Early alert is important for triggering timely action, notably to enable WHO to use the powers conferred on it by the IHR. But the alarm was not raised effectively by many of the first countries with SARS-CoV-2 transmission and WHO and states did not react early and decisively enough to COVID-19. Early data provided by states to WHO were often incomplete and subsequent data reporting was insufficient. Timely identification of person-to-person transmission, as well as pre-symptomatic and asymptomatic transmission, was one of the biggest challenges. Many countries also struggled to recognise community transmission in time. There was a marked lack of national responses both to WHO's first alerts—eg, published risk assessments and guidance on public health response and statements by the WHO Director-General—and to the Public Health Emergency of International Concern declaration. This is why we believe that a formal intermediate level of alert would not have improved the situation. In our view, better adherence to and use of the existing IHR obligations could have provided more meaningful alert and improved the early response.

Early alert and response require better collaboration, coordination, and more trust between countries and between countries and WHO that can be developed through regular, meaningful, frequent interactions outside of crisis situations. Working through networks such as the Global Outbreak Alert and Response Network or the International Association of National

Public Health Institutes is one step in that direction. We recognise there are tensions between the public health requirements and requirements to avoid unnecessary interference with international traffic. In general, countries that implemented early travel restrictions to reduce importation together with comprehensive public health measures were able to delay the epidemic in their countries. Precautionary travel restrictions are useful early on in some health crises. The longer-term effects of maintaining such restrictions after the early phase need to be considered in the larger context of economic and social impacts. There are also serious human rights considerations attached to implementing strict travel measures with insufficient notice or over long periods of time.

Effective IHR implementation requires political commitment and sustainable financing nationally and internationally. However, political will and financial resources for IHR implementation remain insufficient and inconstant. The IHR Review Committee on COVID-19 requested, for the first time, detailed information on the personnel resources available at WHO for IHR implementation. As of early 2021, roughly 200 full-time staff equivalents were providing WHO's IHR-related functions, with a total estimated staff cost of about US\$42 million.<sup>6</sup> This number is less than the number of staff in some countries' national public health institutes.

In April, 2021, we made 40 recommendations in ten areas to strengthen implementation of the IHR<sup>6</sup> and selected recommendations are listed in the panel. Many of those recommendations have been made before. We largely know what needs to be done to protect health across the globe and across our societies. Action now needs to be taken.

We are members of the Review Committee on the Functioning of the International Health Regulations (2005) during the COVID-19 Response. We declare no other competing interests.

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## Advancing racial and ethnic equity in science, medicine, and health: a call for papers



Racism takes many forms. It can exist in unconscious bias, in outright taunt, or in murder. But racism encompasses more than individual prejudice. Structural racism means that norms embedded in culture, systems, policies, and practices routinely disadvantage racially minoritised groups, perpetuating inequity. For minority ethnic populations, life opportunities are diminished on all fronts, including in education, employment, health care, housing, finance, and justice. Racism is associated with poorer mental and physical health outcomes and complex coping behaviours.<sup>1,2</sup> Structural racism leads to pathways that include segregation to lower-income neighbourhoods, schools, and jobs; violence (sometimes at the hands of authorities such as the police) and incarceration; and inequitable health-care access and poor-quality care.<sup>1,3</sup> For many Indigenous peoples, the legacy of colonisation and loss of land, culture, language, and self-determination is writ large in continued health, social, and economic disadvantage.<sup>4</sup> The pernicious effects of colonialism have also been far-reaching across other cultures and contexts.

Some clinicians may dismiss the notion of structural racism and claim not to distinguish race and ethnicity. But such supposed colour blindness ultimately fails patients. It overlooks how they are harmed by systemic bias and can reinforce these harms.

Structural racism is inherent in medical training, for instance when race is conveyed as a disease risk factor without context, perpetuating stereotypes of some groups as “more diseased than others”.<sup>5</sup> In clinical decision making, race-based diagnostic and treatment algorithms or guidelines can lead to undertreatment or overtreatment, exacerbating disparities. For example, the equation used to estimate glomerular filtration rate (GFR) questionably applies a higher value to Black people. An overestimated GFR in renal impairment could mean receiving nephrotoxic medicine in doses that are too high or not qualifying for renal transplantation, amplifying racial inequity.<sup>6</sup>

The brutal police killings of George Floyd and other African Americans in 2020 marked a turning point in global awareness of racial injustices and their impacts on life outcomes. Prompted by the Black Lives Matter protests in the summer of 2020, the UK Government commissioned a report from the Commission on Race and Ethnic Disparities.<sup>7</sup> The Commission’s report refuted decades of evidence on racial inequities, and disappointingly, downplayed the continued reality of structural and institutional racism in the UK today. Indeed, systemic inequities have aggravated the toll of the COVID-19 pandemic on racially minoritised populations, who have had disproportionately high rates of infection, morbidity, and death.<sup>8</sup>

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