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The role of diagnostics in covid-19 and future pandemics

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About this report

“The role of diagnostics in covid-19 and future pandemics” is a report by Economist Impact produced as part of The Economist Group’s Vaccine Ecosystem Initiative. This Initiative examines what we have learnt from the herculean efforts and collaboration that has taken place between sectors and governments during the pandemic caused by SARS-CoV-2. The Vaccine Ecosystem Initiative will explore avenues for building resilience and enabling equitable global access to vaccines, and to safeguard against future vaccine-preventable illnesses. Our focus is on the five pillars that support the ecosystem: Research & Development; Manufacturing; Procurement, Pricing & Finance; Distribution, Logistics & Supply Chain Management; and User Acceptance & Uptake.

In addition, we will be looking at key cross-cutting issues that are crucial to the ecosystem, such as diagnostics. In this report we look at the role that in vitro diagnostics (IVD) have played in the covid-19 pandemic. We examine how that role has evolved, as well as the challenges and lessons learnt that may help us tackle future pandemics and other vaccine-preventable illnesses.

Our report focuses on two types of covid-19-related IVD methods:

- **Diagnostic tests:** These detect specific components of the SARS-CoV-2 virus and can be used to diagnose an infection. They include molecular tests (which detect viral genetic material) and antigen tests (which detect viral surface proteins).
- **Serology/antibody and other acquired immune response tests:** These detect antibodies to SARS-CoV-2 (such as IgM or IgG antibodies) or measure different types of immune response to the virus (such as the T cell response).

This report is based on a review of published literature and data, as well as insights gained from interviews with experts in the field. We would like to express our sincere thanks the following experts for sharing their knowledge and experience (in alphabetical order):

- Dr Kenneth Fleming, Chair of the *Lancet* Commission on diagnostics and Emeritus Fellow, Green Templeton College, University of Oxford, UK
- Dr Laura Kahn, Co-founder of the One Health Initiative, US, and Advisory Council Member of The Vaccine Ecosystem Initiative
- Professor Madhukar Pai, Canada Research Chair in Epidemiology & Global Health, and Associate Director, McGill International Tuberculosis Centre, Canada
- Dr Bill Rodriguez, Chief Executive Officer, FIND, Switzerland

The Vaccine Ecosystem Initiative is led by Dr Mary Bussell, who oversaw and edited this report. The report was written by Dr Alicia White and Dr Rosie Martin with contributions and assistance from Bettina Redway, Elly Vaughan and Janet Clapton, and copy-edited by Maria Carter. We are grateful for collaborative discussions with our Economist Intelligence colleagues, Dr Mark Whitten and Angela Kustas.

The Vaccine Ecosystem Initiative is supported by our founding sponsors MSD, a research-intensive biopharmaceutical company and leader in vaccines, and BD (Becton, Dickinson and Company), a leading global medical technology company, along with our silver sponsor, Siemens Healthineers.

The findings and views expressed in this report do not necessarily reflect the views of the sponsors or the experts we interviewed. Economist Impact bears sole responsibility for the content of this report.

Executive summary

Diagnostics have played and continue to play a fundamental role in combatting the covid-19 pandemic globally – from identifying the causative pathogen, to tracking and interrupting the spread of disease, from informing vaccine design and research to monitoring variants of concern. Progress in covid-19 diagnostics has happened at a rate that was previously unthinkable. In less than a year from identification of the causative organism at the start of 2020, all 194 World Health Organization (WHO) member states were reported to have the capability to test for SARS-CoV-2.

Despite this, the covid-19 pandemic has also shed light on long-standing gaps in diagnostic preparedness and equitable access to diagnostics. The importance of diagnostics has historically been under-appreciated, and therefore its provision under-resourced. In order to prevent future pandemics it is likely that even more rapid development, evaluation and implementation of accurate in vitro diagnostics will be necessary, all the more so for novel diseases that can be spread by asymptomatic or pre-symptomatic individuals, as with covid-19.

A number of key actions are required to strengthen diagnostic preparedness and response. These include:

- **Continuing and improving disease surveillance.** The surveillance systems put in place after the SARS outbreak facilitated the rapid detection of the first cases of covid-19 in China. The availability of advanced sequencing techniques allowed identification of the novel pathogen and development of diagnostic tests within weeks of its emergence. Unfortunately, this was still not sufficient to curtail its spread on a global scale, hence the need for strengthening protocols for detection of novel threats and testing in outbreak areas in the future. Current surveillance systems tend to focus on known pathogens and known disease presentations; they must become more active and comprehensive, and encompass regular monitoring of potential emerging zoonotic diseases among wild animals and livestock.
- **Investing in diagnostic research and development (R&D).** For infectious diseases such as tuberculosis (TB) and many neglected tropical diseases that have been known for centuries there are still few simple, rapid, accurate point-of-care (POC) in vitro diagnostic tests. The rapid and successful development of a wide array of covid-19 diagnostics demonstrates what should be possible for other diseases. Progress is being made but it could be accelerated through greater prioritisation and investment. In addition to high-throughput laboratory-based methods, innovations that allow decentralised testing, and that do not require expensive laboratory facilities and equipment or highly trained staff, will be very beneficial for low- and middle-income countries (LMICs) and even hard-to-reach communities in high-income countries. Priority should also be given to platform technologies that can be rapidly adapted to new pathogens. Given the sheer volume of tests carried out worldwide during the pandemic, more sustainable and environmentally friendly diagnostic solutions should be factored in.

- **Formalising flexible but rigorous regulation pathways to allow rapid diagnostic authorisation.** The pandemic forced regulatory authorities to use streamlined versions of their usual approval processes, allowing diagnostic tests to be brought onto the market quickly. These processes may still be needed if new SARS-CoV-2 variants emerge that cannot be detected by the existing tests. They should incorporate mechanisms to assess emerging evidence on tests, so that authorisations can be rapidly revoked or altered as required. Formalising these pathways will enable better responses to future pandemic threats.
- **Diversifying diagnostic technologies, suppliers and manufacturers.** The bottlenecks seen in the diagnostic supply chain during covid-19 illustrate the need for a broader range of technologies, including those that are less reliant on proprietary reagents. Diversification of manufacturing centres and supply sources could also help alleviate bottlenecks, and contribute to reducing inequity of access to testing in regions where such facilities are currently limited.
- **Expanding laboratory capabilities and capacity worldwide.** Countries have struggled to reach the unprecedented levels of testing needed to control the pandemic. As a result, many have expanded their laboratory capabilities and capacity, which could leave a long-term legacy of strengthened health systems that are better able to detect and deal with current and future health threats (both communicable and non-communicable) and move us closer towards universal healthcare. Improvements must address not only laboratory facilities, but also the wider infrastructures needed to support them, such as staff training, quality assurance systems, IT systems and equipment maintenance.
- **Making improvements to computational systems and data sharing.** Timely sharing of genomic sequencing data for SARS-CoV-2 facilitated the development of diagnostic tests and vaccines, as well as epidemiological tracking. For the first time, data sharing enabled an almost real-time perspective on progress of the disease, usage of tests and demand. This has strengthened global efforts to contain covid-19, and it could do the same for other diseases. Robust data collection allows monitoring and linkage of diagnostic data to public health measures, such as contact tracing, localised testing and lockdown measures. Alongside expanding genomic sequencing capability globally, strengthened computational capabilities are needed to analyse the data generated and identify new variants as they arise. A well-governed network of biobanks for the collection and sharing of samples of these new variants is also important for the rapid development and evaluation of diagnostic tests. Some of these systems are being developed, but it is important that they are maintained in the long term.
- **Facilitating combined purchasing and improving financing mechanisms.** Pooled procurement through the multilateral Covid-19 Supply Chain System (CSCS) enabled LMICs to obtain lower prices and purchase an average of 55% of their covid-19 diagnostic supplies. Similar mechanisms should be explored in the longer term, with better financing mechanisms for capital-intensive activities like building laboratories and purchasing equipment. These steps are crucial for addressing inequitable access to testing.

While the pandemic has had a devastating impact, it may yet prove to be a catalyst for positive change if some of the systems being put into place to combat it are maintained, and these lessons learned.

Holistic systems that integrate diagnostics and diagnostic data with appropriate public health measures and access to vaccines and therapeutics are crucial going forward to bring an end to this pandemic – and for application to future pandemics. It is in the interest of the health of all nations to ensure equitable access to pathogen surveillance and diagnostics globally, as well as vaccines, to ensure protection against such threats.

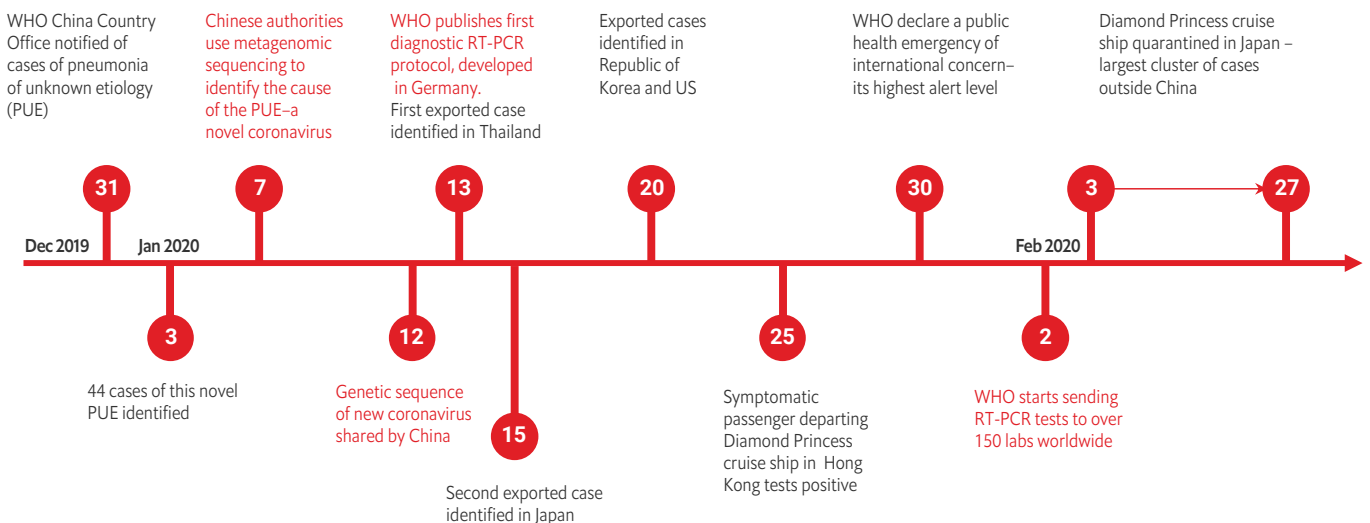
The start of the pandemic and SARS-CoV-2 diagnostics

Diagnostics and diagnostic surveillance have played a key role in the covid-19 pandemic from the very start. After the 2003 SARS-CoV (severe acute respiratory syndrome coronavirus) outbreak, China established a passive surveillance system for pneumonia of unknown etiology (PUE).¹ The system requires clinicians to alert an expert consultation committee when they detect a PUE, then the committee decides whether to report the case to the PUE surveillance system. Any such reports trigger an investigation by the China Center for Disease Control and Prevention (CDC), to determine whether the PUE was caused by an avian influenza virus, SARS-CoV or Middle East respiratory syndrome coronavirus (MERS-CoV). Although the system detects many PUEs, according to a 2016 study in two hospitals, around 13% are unreported.¹

Great credit is due to the doctor who alerted the authorities to the first cases of the PUE that occurred in Wuhan, Hubei province, China, in December 2019 – which led to the current pandemic. Four cases were associated with a seafood market and triggered the PUE surveillance mechanism. The China CDC was alerted at the end of December and began investigations with local authorities. Figure 1 shows key events in the two months after this point.²⁻⁵

Figure 1: Timeline of SARS-CoV-2 identification, spread and early diagnostic milestones

Numbers represent dates; text in red indicates timeline events directly related to diagnostics.





Early molecular tests and WHO diagnostic guidance

The causative organism for these cases of pneumonia was identified as a novel coronavirus. This happened about a week after the disease being notified to the China CDC, through the use of metagenomic sequencing,^{2,6} which simultaneously determines the genetic sequences of microorganisms in clinical samples that may contain a mix of unknown pathogens. Once the genetic sequence of the novel coronavirus, which we now call SARS-CoV-2, was made publicly available, laboratories began to design their own nucleic acid amplification tests (NAATs) within days, using reverse-transcription polymerase chain reaction (RT-PCR) to detect the virus. The first laboratory assay to detect it was developed and validated by 13 January 2020, by a group of European scientists, led by the German Center for Infection Research (Deutsches Zentrum für Infektionsforschung (DZIF)) at Charité Universitätsmedizin Berlin. The World Health Organization (WHO) adopted their protocol as a guideline for other laboratories,⁷⁻¹⁰ and began to purchase the necessary supplies. By early February 2020 they were shipping RT-PCR tests to laboratories around the world.⁹

Unfortunately, despite the seemingly rapid identification of the pathogen and early development of tests, the virus had already spread beyond China's borders. The first case was identified outside the country on 13 January 2020, in Thailand.

WHO provided its first interim guidance on laboratory testing four days later, on 17 January 2020. It recommended that testing for the novel virus should rely on NAATs, such as RT-PCR.¹¹ As the tests for SARS-CoV-2 were being developed, organisations such as WHO and the US Food and Drug Administration (FDA) utilised emergency use mechanisms to expedite access to them – as was later done for the vaccines.^{12,13} The FDA granted the US CDC with emergency use authorisation (EUA) to distribute an RT-PCR assay for SARS-CoV-2 in February 2020.¹⁴ The first commercial tests were available in March 2020.^{15,16}

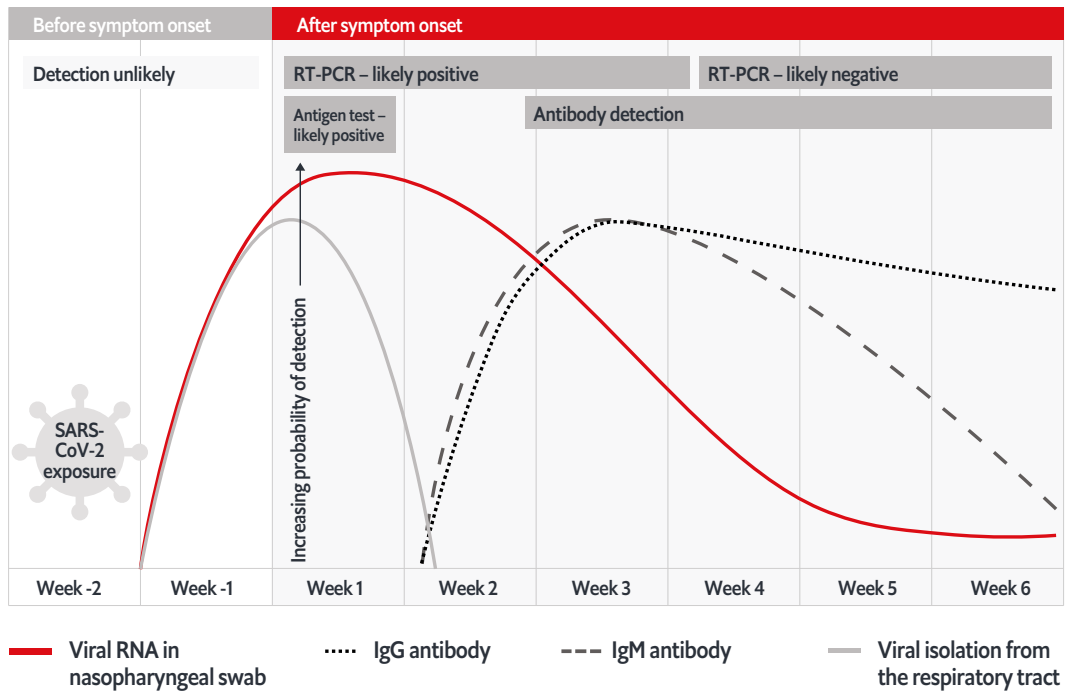
By 21 March 2020, the global picture had worsened. It was clear that the demand for testing would outstrip capacity. WHO issued recommendations to prioritise the testing of vulnerable people and healthcare workers, and first cases occurring in outbreaks in closed settings (such as schools) where testing facilities were limited.¹⁷ This recommendation remains in place (as of interim guidance produced on 25 June 2021) where resources are tight.¹⁸

As well as PCR-based tests, researchers also developed methods to rapidly assess whether a person was infected based on antigen testing, and also to detect antibody responses to infection. Table 1 and Figure 2 summarise the different diagnostic tests for SARS-CoV-2; their development and roles are discussed below.

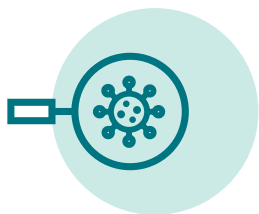
Table 1: Types of IVD tests to detect SARS-CoV-2 infection

Type of test	Examples	Type of sample required	Included in WHO's Essential Diagnostics List 2021	Mechanism of test	Drawbacks of test
Molecular	NAATs such as RT-PCR	Wide range of samples, usually nasopharyngeal or oropharyngeal swabs	Yes	Detects viral RNA (such as the gene encoding the spike (S) protein)	<p>Requires sophisticated laboratory techniques and specialist staff</p> <p>Can have relatively long turnaround (from sample collection to delivery of results)</p> <p>May detect people who have been infected but are no longer infectious</p>
Antigen	Rapid diagnostic tests, such as lateral flow tests	Wide range of samples, usually nasal, nasopharyngeal or oropharyngeal swabs	Yes	Most identify the nucleocapsid (N) protein, produced by the virus when it replicates	There is no antigen amplification, thus can produce more false negative results in early stages of infection or if inadequate swab
Antibody/serology	Tests that detect immunoglobulins IgA, IgG, IgM, or the T-cell response	Blood from blood draw or finger stick	No	Identify immune responses to infection, usually to viral S or N proteins	Not currently able to easily distinguish between natural immunity due to infection and immunity from vaccination, nor determine when infection occurred

Figure 2: Ability of different tests to detect SARS-CoV2 infection relative to time of infection and symptom onset



Time intervals are estimates, to indicate differences in ability to detect viral genetic material, antigens and antibodies over time.¹⁹



Antigen testing

The first antigen-based test was given emergency use authorisation by the US FDA on 8 May 2020, about four months after SARS-CoV-2 was first identified.²⁰ This test provided a result within minutes but still required specialist laboratory equipment.

Since then, the number of antigen tests available has proliferated. Most use nasal, nasopharyngeal or oropharyngeal swabs. Some are analysed in a laboratory and are useful for high-throughput testing; but many are designed for rapid, point-of-care (POC) or near-patient use, requiring just the use of a handheld or benchtop reader, or no additional equipment at all. Most rapid antigen tests are cheaper than RT-PCR, costing only USD \$5–15 per test.²¹ They are also suitable for mass production and mass distribution.

These features are beneficial, of course, but there are limitations. For instance, the tests detect viral proteins without amplification, which makes them less sensitive than RT-PCR, so they produce a higher rate of false negative results. Conversely, RT-PCR, while being very sensitive, can pick up low levels of viral material in people who are no longer infectious.

A Cochrane review (including evidence published up to November 2020) found that most rapid POC antigen tests have high specificity, correctly giving negative results in 99.6% of people without the SARS-CoV-2 infection (according to RT-PCR) on average.²² However, the tests' ability to correctly identify people with the infection (their sensitivity) varied according to the brand of test, as well as the characteristics of the population being tested. Pooling the results from available studies, the tests were found to be more sensitive in:

- people with symptoms (72.0%) (compared to those without (58.1%))
- the first week after symptom onset (78.3%) (compared to the second week after onset (51.0%))
- people with more viral genetic material in their sample (an indicator of higher viral load).

The third finding suggests that rapid antigen tests may be better for identifying those individuals who are most infectious. In support of this, some studies found that the rapid tests are also more sensitive in clinical samples containing viable SARS-CoV-2 virus that is capable of replicating in cells in the laboratory (an indicator of infectiousness), than in samples which contain viral genetic material but not viable virus.²³⁻²⁵ A strategy of regular, rather than one-off, antigen testing has been suggested as a way to reduce the chance of missing people who may be infected but not yet infectious.²³

RT-PCR is still the gold standard for diagnosis, but rapid antigen tests have great value in certain situations. They allow tests to be performed in settings without any laboratory infrastructure, and some of them can be used by the public for self-testing. This makes them particularly useful in schools, for example, and in remote or resource-limited areas.

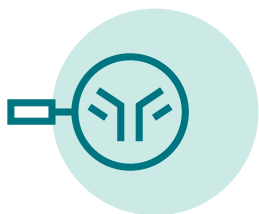


Rapid antigen tests are reported to be available worldwide, and have received various regulatory authorisations from organisations such as:

- Agência Nacional de Vigilância Sanitária (Anvisa, the Brazilian Health Regulatory Agency)
- European CE Marking for IVD devices (CE IVD)
- Saudi Food and Drug Authority (FDA)
- US FDA
- WHO.²¹

As of 6 August 2021 there were reported to be 380 commercially available rapid antigen tests (according to the European Commission COVID-19 In Vitro Diagnostic Devices and Test Methods Database).²⁶ Of these tests, 114 (30%) met the criteria to be included in the “common” list of rapid antigen tests that are considered appropriate for use in European Union (EU) Member States to inform public health measures. To be included, the tests must:

- be performed by a trained healthcare personnel or trained operators
- carry CE marking to indicate that they conform with all relevant EU regulations (a legal requirement to market tests in the region)
- have as a minimum a sensitivity of 90% and a specificity of 97%
- have been validated by at least one EU Member State (and have appropriate study documentation).



Antibody testing

Both laboratory-based and rapid POC antibody testing have been developed to detect immune response to SARS-CoV-2. In the months before vaccines received emergency authorisations, antibody testing allowed public health officials to monitor how many people had been infected with SARS-CoV-2.²⁷ The tests are not currently able to easily distinguish between immune responses due to vaccination versus responses to natural infection, therefore they are less useful markers of a population’s exposure to infection as vaccination levels increase.

Antibody tests have other potential uses, such as detecting past SARS-CoV-2 infections in people who have symptoms suggestive of covid-19 but who tested negative with other tests, or in those in whom the viral load is too low to be detected (due to late presentation).

In the early stages of the pandemic it was hoped that identifying people who had been infected using antibody tests would reassure them that they might have some immunity against reinfection, especially those in high-risk occupations (such as healthcare workers). However, at that stage it was unclear what level of protection was provided by previous infection, or how long any protection would last, or whether it would prevent individuals from spreading the disease.

More recent evidence suggests that previous infections provide a high degree of protection from



reinfection, for at least 6–8 months in most adults.²⁸ However, it is not yet known how long this protection lasts. The level of protection in elderly people is much lower, and may be impacted by the emergence of new SARS-CoV-2 variants. WHO noted that as of May 2021 the precise mechanisms of protection were still not well understood,²⁸ therefore it was difficult to determine the extent to which the current antibody tests are true indicators of immunity. However, evidence on the immunological markers which predict protection is accumulating,²⁹ therefore this could change in the future.

Because of this uncertainty some bodies such as the US FDA currently recommend against using antibody tests to evaluate a person's level of immunity or protection from covid-19.³⁰ However, anecdotal evidence suggests that antibody tests have been used by some as a proxy measure of protection. In Iran for, example, in early 2021 when vaccination rates were very low (only 1% of the population had received at least one dose of a covid-19 vaccine by the end of April 2021³¹), a news report suggested that the tests were being used by young people as informal "immunity passports", to get around restrictions on social distancing.³² In India, some people have reportedly used the tests to find out whether they have developed an immune response after being vaccinated.³³

Overall, antibody tests have not been adopted as widely as the molecular and antigen tests, but they do have specific uses, particularly in research. There are studies underway that aim to understand how the antibody response to SARS-CoV-2 infection and vaccination changes over time, and that are exploring which characteristics of the response predicts whether someone is protected against infection (the "correlates of protection").²⁹ Once the correlates of protection are understood, as well as feeding into how the outcomes of clinical trials of vaccines are assessed, it has been suggested that antibody testing might be used to identify people with suboptimal responses to vaccination, to better target booster vaccinations in countries where a decision is made to provide these.³⁴



Key challenges for diagnostic testing as an early line of defense

In the early stages of the pandemic, testing was one of the few lines of defence – a way of finding the ‘unseen enemy’ and cutting off its ability to infect others by allowing the infected individuals it identified to be isolated, their known contacts to be quarantined, and appropriate personal protective equipment (PPE) to be worn by those who had to come into contact with them. Testing increased our understanding of the speed with which the virus was spreading and the effectiveness of public health measures.

Testing was not without its challenges, however. RT-PCR can only be carried out by specialist staff using specialist equipment and, therefore it is relatively expensive.³⁵ In its basic form, RT-PCR involves multiple time-consuming processes to detect and amplify viral RNA.³⁵ As the true scale of the SARS-CoV-2 threat became apparent, the race was on to develop commercial tests for detecting it – tests that were faster and simpler, using platforms that enabled mass testing.

Different groups developed a variety of approaches and, as with vaccine development, this proved to be beneficial. It allowed laboratories with different equipment and processes to perform tests using the systems they already had in place. The fact that the various techniques used a range of reagents and raw materials went some way towards mitigating global depletion of supplies, although this still became an issue because of the vast numbers of tests needed.

There were some teething problems with the quality of the tests. For example, some of the early RT-PCR test kits produced by the US CDC had contaminated reagents, which meant that laboratories had to send samples to the central US CDC for testing; this delayed diagnosis and may have allowed infections to spread.³⁶⁻³⁸ The shortage of tests in March 2020 led the US FDA to relax its restrictions, allowing individual states to authorise laboratory-developed tests for local use and manufacturers to distribute tests prior to receiving formal emergency use authorisation.³⁹ However, because of concerns about fraudulent tests and inaccurate (false positive) results from antibody tests, the restrictions were tightened in late May, and 27 antibody tests were removed from the market in the US.³⁹ India was also impacted by test quality issues. It started using rapid antibody test kits in early 2020, but some states reported that the accuracy was very low; these kits went on to fail quality checks conducted by the Indian Medical Research Council (IMRC). As a result, India cancelled an order for half a million rapid antibody tests in April 2020.⁴⁰

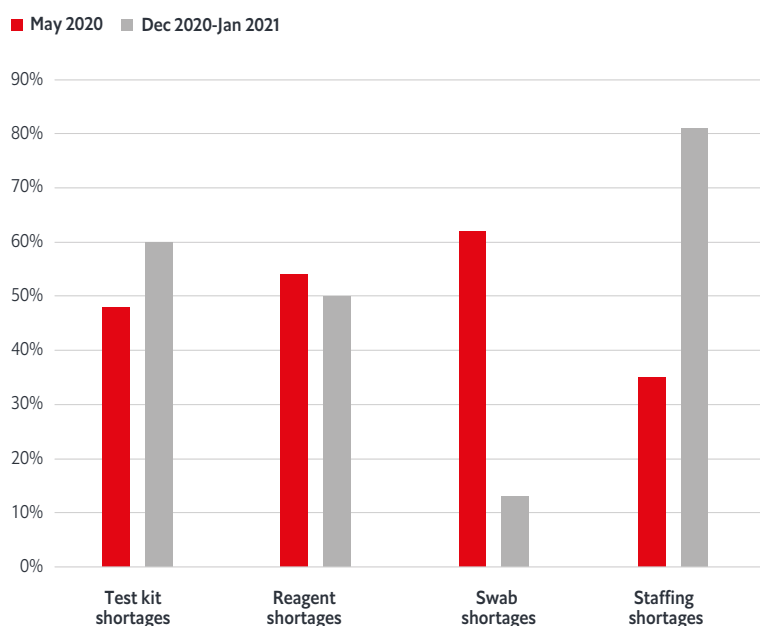
When tests became available that were suitable for widespread use, a further challenge became apparent – supporting the sheer volume of testing required. Various approaches were used to achieve this, including repurposing equipment,⁴¹ using laboratories not usually used for routine clinical testing (such as university laboratories),⁴² creating mobile testing sites,⁴³ re-deploying trained staff and training volunteers. In situations in which only low numbers of tests were expected to be positive, samples were pooled together for initial RT-PCR testing – another resource saving strategy.⁴⁴

A worldwide survey of members of the American Association for Clinical Chemistry (AACC), representing commercial, hospital and public health laboratories, showed how testing for SARS-CoV-2 expanded.⁴⁵ At the beginning of February 2020, less than 20% of laboratories offered covid-19 diagnostic testing, but by the beginning of January 2021 this had increased to 92%.

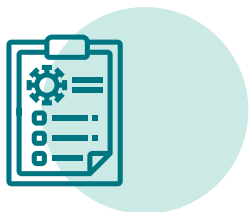
As the need for testing rose even more, global demand exceeded supply, a problem exacerbated by transport restrictions.⁹ Companies also struggled to meet the high demand for tests (and analysers) and often had distribution problems.^{46, 47} Even in high-income countries, there were challenges with

supply chains and staff shortages. Data collected by the AACC suggest that many US laboratories experienced shortages of test kits and reagents up to the end of 2020. In May 2020, there were also problems with the supply of swabs, but they largely resolved by the end 2020. Conversely, staff shortages worsened over this time (see Figure 3).

Figure 3: Challenges faced by US laboratories in SARS-CoV-2 testing



These were just some of the issues that hampered efforts to achieve full testing capacity. In late autumn 2020, such shortages forced health systems across the US to limit testing^{41, 48} To alleviate the impact of this, some healthcare providers diversified the testing platforms they used at different sites,⁴¹ and resources were redirected from other forms of testing. The picture was similar outside the US.⁴⁵ The UK, for example, faced a bottleneck in laboratory capacity in September 2020.⁴⁹ This was attributed to staff shortages, as well as increased demand, and some tests had to be sent abroad for processing.



WHO guidance on national testing

As of October 2021, WHO interim guidance on national SARS-CoV-2 testing strategies (published June 2021) recommends that anyone who meets the criteria for suspected covid-19 disease should be tested, regardless of whether they have had a vaccination or have previously had the disease.¹⁸ It states that NAATs such as RT-PCR are the reference standard for diagnosis of SARS-CoV-2 infection, and that antigen tests are not meant to replace NAAT but can be implemented as a complementary strategy. In particular, high-quality rapid antigen tests performed by trained operators are an alternative in settings where NAATs are unavailable, or where turnaround times

are too long (over 48 hours). The most recent WHO guidance on rapid antigen testing from October 2021 specifies (compared to NAATs) that they should have a minimum:

- sensitivity of 80%
- specificity of 97%.⁵⁰

It notes that rapid antigen tests perform best in individuals with high viral load, early in the course of infection, and are most reliable in settings where the prevalence of SARS-CoV-2 infection is 5% or over. In settings where the prevalence of SARS-CoV-2 is lower than this they recommend that NAATs are used for first-line testing, or for confirming positive rapid antigen test results. In symptomatic individuals with a negative rapid antigen test result, confirmatory testing with NAAT or repeat antigen testing should be considered based on clinical factors, availability of testing, and local prevalence.⁵⁰

As of October 2021, WHO does not currently recommend widespread screening of people without symptoms of covid-19 with molecular tests or antigen tests, other than people with known close contact with individuals who have probable or confirmed covid-19, or those in frequently exposed groups, such as healthcare workers.^{50,51} This is because of the limited evidence currently available on its benefits and cost-effectiveness in low-risk populations, the cost associated with such testing, and the risk of diverting resources from testing of higher priority groups. WHO states that countries should only consider widespread screening of people who are asymptomatic if they continue to prioritise timely and reliable testing of suspected cases.¹⁸ They must also make sure there are appropriate human and financial resources in place to support both the testing and its consequences (e.g. reporting, isolation, contact tracing and follow-up).

Some high-income countries that have the resources to do so have been using antigen tests for widespread screening. Among them is the UK, where self-testing with rapid antigen tests at home is common. Tests can be obtained at no cost to the user in the community or online, and people with no symptoms (including young people aged 11 and over) are encouraged to test twice weekly and record their results online.⁵² Those who test positive are recommended to have confirmatory RT-PCR testing.⁵³

WHO does not recommend antibody testing for the diagnosis of covid-19, because of the time it takes for antibodies to be produced.¹⁸ However, it notes that the tests are important for detecting past infections and have value for research and surveillance.

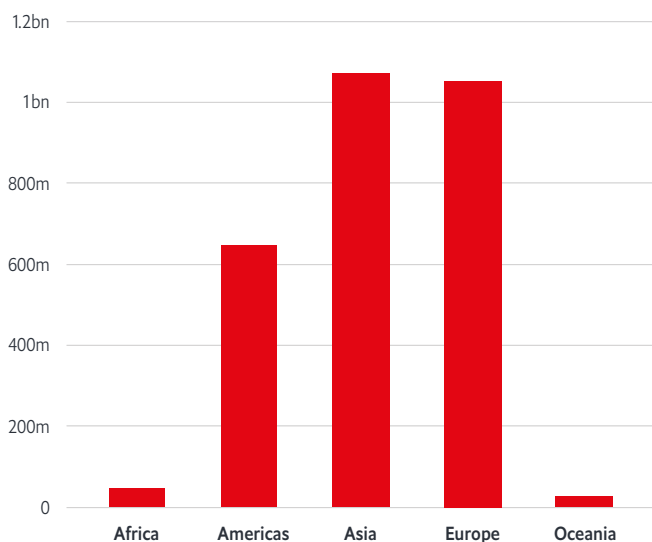
Unprecedented testing volume and data collection globally

According to Our World in Data, more than 2.8 billion RT-PCR and antigen tests for covid-19 had been carried out worldwide by 30 July 2021.³¹ This is probably an underestimate, because some countries do not report results from both types of test, while others only report the number of people tested rather than the number of tests performed.

The volume of testing varies widely by region, with Asia performing the most tests in total – over one billion since the start of the pandemic – followed by Europe and the Americas, with Africa and Oceania trailing behind (see Figure 4).

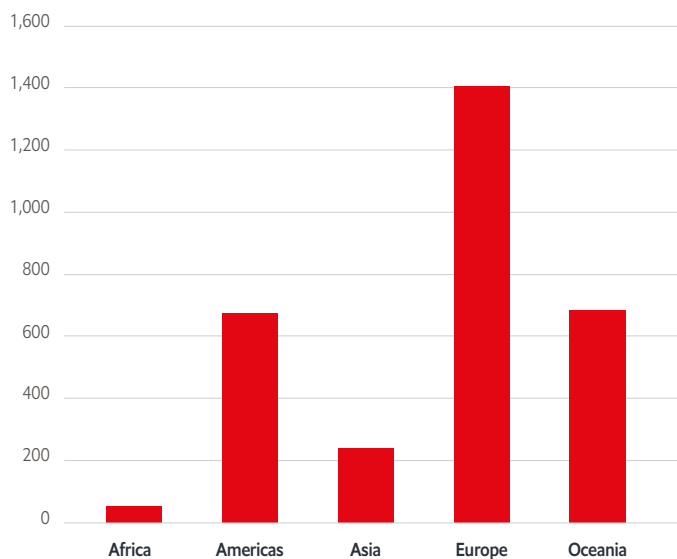


Figure 4: Total SARS-CoV-2 tests performed by region up to 30 July 2021



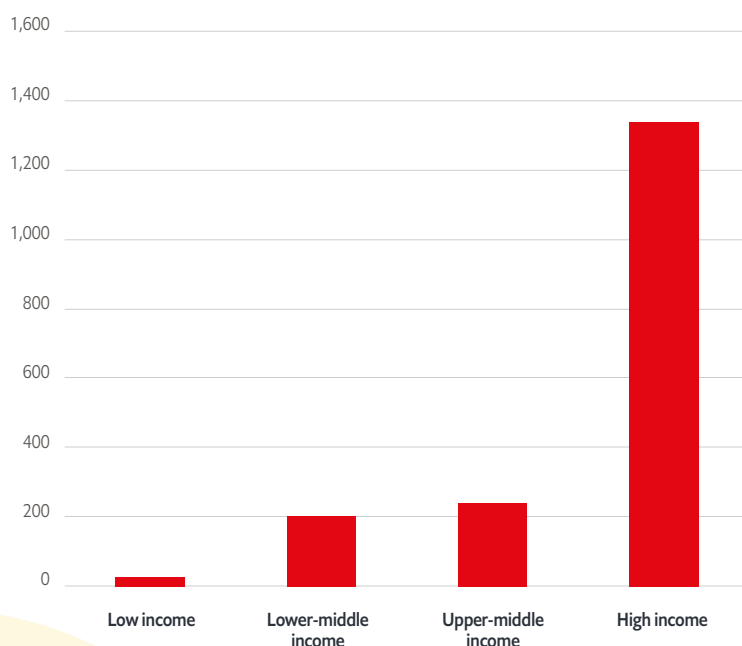
Even after standardising for population size there is considerable variation in testing rates, as shown in Figure 5. Europe has carried out the most extensive testing, having done enough tests to cover every person in its population at least once (1,405 tests per 1,000 people). Oceania and America are next with 686 and 673 per 1,000 people, respectively. Then come Asia and Africa, at 240 and 53 per 1,000, respectively. These rates also vary across countries within these regions.

Figure 5: Total SARS-CoV-2 tests performed per 1,000 population by region up to 30 July 2021



There are also dramatic differences in test rates for countries in different income bands. Throughout the pandemic thus far, the total tests performed per 1,000 people are over 50 times higher in high-income countries than in low-income countries (1,339 compared with 24, respectively) (see Figure 6).

Figure 6: Total SARS-CoV-2 tests performed per 1,000 population by country income band up to 30 July 2021



As well as the unprecedented levels of testing, it is worth noting the extraordinary feat achieved in collecting data for the virus. This is the first time that diagnostics data have been available on such a large scale, throughout the world, almost on a real-time basis. The Our World in Data site collates global data on covid-19, including on testing, and updates it on a daily basis.

Madhukar Pai, Canada Research Chair in Epidemiology & Global Health, and Associate Director, McGill International Tuberculosis Centre, says this is ground-breaking and contrasts significantly with data collection for other diseases. He says: "I still can't tell you how many TB tests have been done in India yesterday, or last month, or last year. I just don't know. Nobody's tracking them, let alone putting them on our dashboard or a public website. So [covid-19 testing] is the only diagnostic in the world – in the global health space – where we almost have real-time information on the number of tests being done, positivity rate, and so on. Which is just mind boggling, that in all these years, we've never invested in a diagnostics reporting system globally." Professor Pai highlights digital connectivity as one of the essential requirements for diagnostic tests going forward.



Laboratory testing capacity

High-income countries have been able to increase their laboratory capacity for covid-19 testing significantly since the start of the pandemic. In the UK, the estimated daily capacity for RT-PCR tests has increased 27-fold in the past 16 months – from just over 26,000 tests per day on the 10 April 2020 to over 708,000 on 8 August 2021.⁵⁴ The latter capacity figure was about 2.6 times test utilisation at that point, with about 270,000 tests recorded as being conducted on 8 August 2021. This was a vastly improved situation compared to mid-September 2020, when the utilisation of test capacity was almost 100% (around 250,000 test capacity and utilisation).

Estimated daily laboratory-based antibody-testing capacity has also grown substantially, increasing from 500 tests per day to just over 120,000 between early April 2020 and early August 2021. Antibody testing is far less widely used than PCR testing, with a total of about 4.5 million tests performed in the UK compared to over 115 million RT-PCR tests by the start of August 2021.⁵⁴

Although not conducted in laboratories, the use of rapid antigen tests provides another indication of the demand for testing. In England, rapid antigen tests using lateral flow were in use from late October 2020.⁵⁵ In these tests, the sample flows sideways (laterally) from one end of a membrane to another. If specific viral antigens are present in the sample they bind to antibodies immobilised on the membrane, resulting in the appearance of a simple indication (usually a coloured line) that shows the presence of the virus.

The volume of rapid antigen tests carried out in England was initially lower than that for RT-PCR tests, but at the start of 2021 their use increased rapidly.⁵⁵ Now daily lateral flow test volume exceeds that of RT-PCR. In the week of 22–28 July 2021, 3.8 million rapid antigen tests were performed and reported in England – an average of just under 550,000 per day – reported to be more than twice the volume of RT-PCR tests carried out in England in the same period (1.5 million tests).⁵⁵ This is unsurprising given the easy availability of these tests, and government policy encouraging twice weekly testing in people with no symptoms (who outnumber those with symptoms). In total, between the start of the pandemic and 28 July 2021, about 124 million rapid antigen tests were carried out and reported in England. In other countries, the use of antigen tests varies depending on individual national recommendations and availability.

In contrast, the onslaught of covid-19 has highlighted the lack of laboratory capacity in low- and middle-income countries (LMICs). India, despite having a population over 20 times that of England (about 1.4 billion), only has about double England's molecular testing capacity, carrying out 1.5 million tests per day at the start of May 2021 compared to 0.7 million in England.^{54,56} The surge in infections from the Delta variant meant that, despite having just over 2,500 molecular testing laboratories and deploying three-shift patterns, testing reached its limit in India in early May 2021.

In February 2020, only two laboratories in WHO's Africa region were able to diagnose covid-19 using RT-PCR.⁹ With support from WHO, this number went up to 750 laboratories by mid-November 2020. However, testing remains relatively low. Using data from Our World in Data, Economist Impact calculated test rates of different regions compared to Africa, and found that the overall test rate per 1,000 population is 26 times higher in Europe, 13 times higher in the Americas and Oceania, and more than 4 times higher in Asia (see Figure 5).

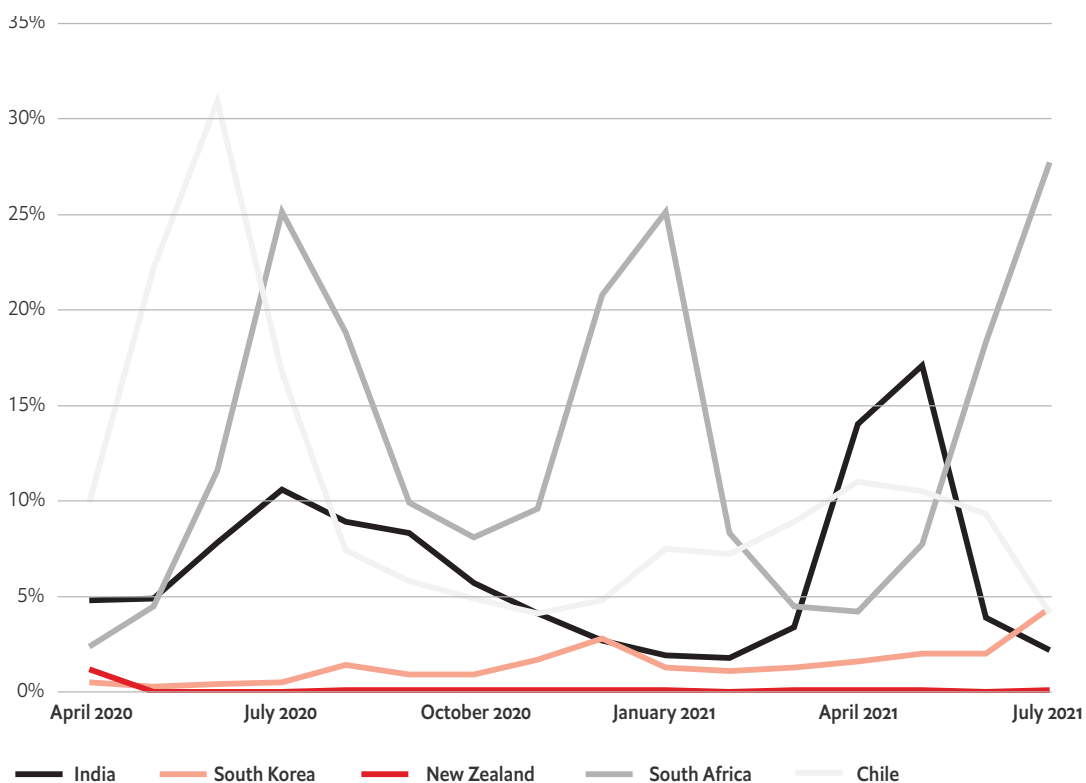


According to their metrics, one way of determining that the infection is under control occurs when less than 5% of tests are positive over a two-week period.⁵⁷ Rates in excess of 5% suggest that only a fraction of true covid-19 cases are being captured, thus testing is not sufficient. This criterion assumes that surveillance and testing of suspected infections is comprehensive (estimated to require testing of around one person per 1,000 population each week).

By 1 August 2021, there were 47 countries with positivity rates of 5% and above (according to Our World in Data). These comprised 15 countries in Asia, 13 in Africa, 12 in the Americas, 6 in Europe, and 1 in Oceania. As can be seen from Figure 7, the positivity rate for countries such as South Africa, Chile and India has changed dramatically over time. South Korea maintained a positivity rate of less than 5% until nearly the end of July 2021.³¹

Our analysis of the data suggest that 62 countries had spent at least half of the time from March 2020 to 1 August 2021 with a positivity rate above 5% (based on daily positivity rates, and excluding countries reporting less than 100 days of data). Notably this group includes the US and 15 other high-income nations. Only 12 countries have spent less than 10% of this time with positivity rates over 5%; this includes a small group of countries, including New Zealand, that had not reported a positivity rate of in excess of 5% up to 1 August 2021.

Figure 7: Average monthly test positivity rate in selected countries (April 2020 - July 2021)



Covid-19 has underscored issues of laboratory capacity in existence long before the arrival of SARS-CoV-2. In 2018, Kenneth Fleming, Emeritus Fellow of Green Templeton College, University of Oxford, led a series of articles in the *Lancet* highlighting the under-resourcing of laboratory medicine and pathology in LMICs. As a result, the *Lancet* set up a Diagnostics Commission, chaired by Dr Fleming, to explore the situation in detail and identify solutions. The recently published findings of the Commission show that almost half of the global population (47%) has little or no access to diagnostic testing.⁶⁰

The expansion of laboratory capacity is clearly challenging, and must be addressed in order to ensure that countries are capable of dealing with not just covid-19 but any future pandemic as well as communicable and non-communicable diseases.

Professor Pai highlights the wider long-term benefits of building molecular testing capacity as a result of covid-19. “The beauty of molecular testing,” he says, “is that it is disease agnostic. So long as you know the target you’re amplifying – it doesn’t matter if it’s a virus, bacterium, parasite – you can do them all. You can even do cancer genetics with it, so it’s not limited to infectious diseases. So this molecular capacity, that every country in the world was forced into rapidly building up, no matter where they had started, I would love to see that after this pandemic dies down it leaves that infrastructure in place, so that more and more of the essential diagnostics lists can be delivered to people in countries. That would be a positive legacy.”

Box 1: A closer look at South Korea

South Korea was one of the first countries to be exposed to covid-19. Its first imported case was reported on 20 January 2020. By the end of March 2020, the country had carried out 40 times more tests per capita than the US.⁵⁸ The country had learnt many lessons from dealing with the MERS outbreak in 2015, leading to reforms that put it in a good place for coping with the new pandemic.⁵⁸ It was able to control the disease without using some of the drastic public health measures needed in other countries. Part of this success was due to good use of diagnostics. This involved:

- obtaining SARS-CoV-2 viral samples from China at an early stage
- developing diagnostic tests before the first local covid-19 case was confirmed
- working closely with local biotechnology companies early on to ensure an adequate supply of tests to allow rapid scale-up
- building innovative high-capacity screening facilities, such as drive-through centres and specially designed positive-pressure booths* to protect healthcare workers
- screening at strategic locations such as airports and hospitals.

However, even South Korea's ability to control the virus was impacted by the Delta variant. Cases rose from late June 2021, and its test positivity rate crept above 5% in late July.³¹ As of 11 August, only 16% of the population was fully vaccinated, with another 26.5% being partly vaccinated.³¹

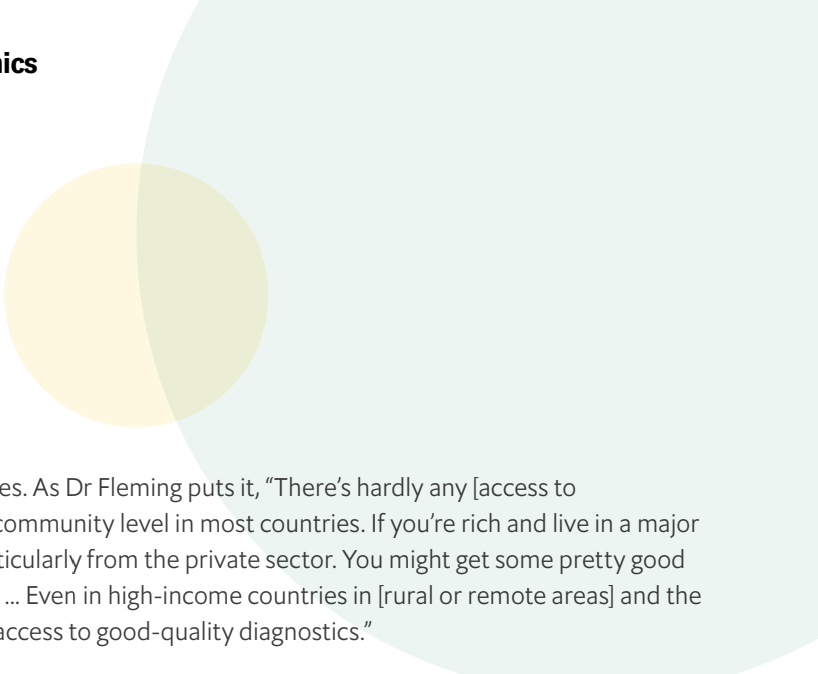
**Positive-pressure booths are sealed units in which the internal air pressure exceeds that of outside air. Therefore, no air- or droplet-borne viral particles can flow in.⁵⁹ The person being tested stands outside of the booth and the healthcare worker stands inside and performs the swab while wearing gloves integrated into the side of the booth. This means that there is no direct contact between the person being tested and the healthcare worker.*



Inequity of access: a challenge for diagnostic testing as well as vaccines

In parallel with vaccines, access to diagnostic tests is not equitable across the world. Most African countries, in particular, have struggled to get access to tests.³¹ This is due to a range of challenges such as a lack of:

- financial resources to buy tests
- reagents (including difficulties in importing and transporting temperature-sensitive reagents)⁶¹
- laboratory facilities for conducting tests
- ability to get the samples to a laboratory
- trained laboratory staff
- infrastructure (such as reliable power supply)
- local manufacturing capacity.



There is also inequity *within* countries. As Dr Fleming puts it, “There’s hardly any [access to diagnostics] at the primary care or community level in most countries. If you’re rich and live in a major city, then you might get access, particularly from the private sector. You might get some pretty good diagnostics, but elsewhere, nothing ... Even in high-income countries in [rural or remote areas] and the urban poor in cities don’t get good access to good-quality diagnostics.”

The UN convened a covid-19 Supply Chain Task Force in early April 2020 to establish the Covid-19 Supply Chain System (CSCS).⁶² It aimed to combat the challenges experienced during the pandemic,⁶³ and has already improved access to diagnostic tests for LMICs. The task force was co-chaired by WHO and the World Food Program (WFP) and included representatives from a wide range of organisations including UNICEF, the World Bank, the Global Fund, and various UN bodies and non-governmental organisations. The CSCS allows countries to request essential supplies, including diagnostics. Funding comes from sources such as WHO, the Global Fund and the Bill & Melinda Gates Foundation. The consolidated requests are sent to purchasing consortia, who coordinate purchasing and allocate purchased supplies based on need. The system also organises the distribution of supplies using multiple established distribution channels. Any country can apply to the CSCS, but most of the supplies are directed to LMICs.⁶⁴ By the end of February 2021, LMICs reported accessing over half of their covid-19 diagnostic supplies (55%) via the initiative. By consolidating orders, the CSCS was able to obtain some of the lowest prices on the market.

As of the end of 2020, about 71 million diagnostic tests and kits were supplied to 161 countries by the CSCS, at a cost of US\$450 million.⁶⁵ Figure 8 shows the value of the diagnostics procured through the CSCS, for each WHO region. Brazil had the largest procurement (US\$100 million) – the total spend was almost four times that of the next largest spend (Nigeria, US\$27 million).

Figure 8: Value of SARS-CoV-2 diagnostic tests and kits procured via the CSCS by WHO region (US\$ million)

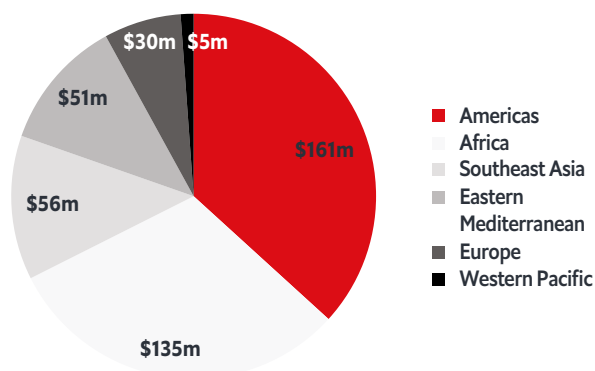


Figure 9: Value of SARS-CoV-2 diagnostic tests and kits procured via the CSCS by test type (US\$ million)

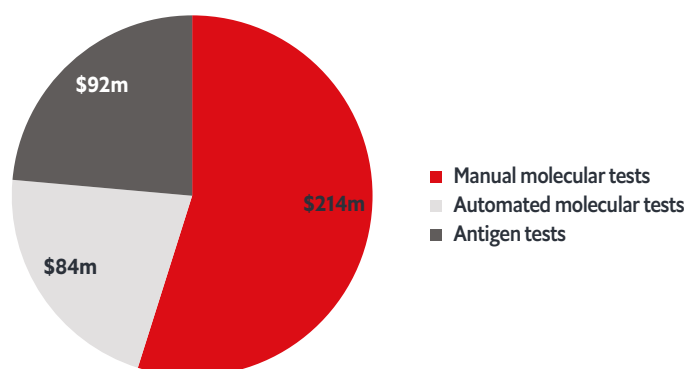


Figure 9 shows the value of the products procured according to the type of test. The largest spend was on manual (unautomated) molecular tests. Part of the reason for this was because (as of January 2021) there were no shortages of these tests and quantities were unrestricted.⁶⁶ In contrast, at the start of 2021 there were limited supplies of automated molecular tests; only LMICs and selected small high-income island states were permitted to procure them, albeit in limited quantities, through the CSCS. WHO has laid out target product profiles for the covid-19 diagnostic tests it considers to be a priority, to guide product development and evaluation.⁶⁷

At the end of December 2020, over a third of the diagnostic supplies purchased via CSCS (38%, representing 28% of the total value purchased) had yet to be delivered. The delays have been attributed to long lead times and insufficient supply of the key diagnostics. A WHO-commissioned analysis of the CSCS identified other issues with the supply of diagnostics:

- relatively few suppliers and high barriers to market entry, resulting in oligopolies.
- complicated purchasing and distribution as diagnostics are regulated products.
- limited product interchangeability.⁶⁸

The assessment also came up with recommendations for diagnostics procurement in the future. These include:

- setting clear technical specifications and testing protocols.
- increasing purchasing power (e.g. through volume guarantees, increasing organisation of buyers, and establishing lead buyers and shared strategies).
- convening pandemic response leaders to establish mechanisms for determining allocations.
- allocating sufficient resources to allow timely assessment of novel products
- providing a global overview of the evolving market situation for essential products updated in real-time.⁶⁸

“There is hardly any [access to diagnostics] at the primary care or community level in most countries.”

Dr Kenneth Fleming, Chair of the *Lancet* Commission on diagnostics and Emeritus Fellow, Green Templeton College, University of Oxford, UK

Overall, the analysis suggested that the CSCS is needed and should be continued, although there was room for improvement. The Access to COVID-19 Tools Accelerator (ACT-A) diagnostics pillar is another mechanism that aims to provide LMICs with funding for and access to tests. This pillar is co-convened by FIND (the Foundation for Innovative New Diagnostics) and the Global Fund, working with WHO. Other participant organisations include Africa CDC, the Bill & Melinda Gates Foundation, the Clinton Health Access Initiative (CHAI), and Unitaid. Up to the end of June 2021 ACT-A had procured over 84 million molecular tests and antigen tests.⁶⁹ They estimate that 500 million tests will be needed by the end of 2021,⁷⁰ and they aim to procure US\$2.4 billion worth of tests to help all LMICs to achieve sufficient testing.⁶⁹

There have already been improvements. By 9 August 2021, Africa CDC reported that almost 59.5 million tests were carried out across Africa.⁷¹ This figure is much higher than the 9 million tests reported a year previously for the continent.⁷² South Africa carried out the most tests in the region (15.3 million), followed by Morocco (7.3 million), Egypt (3.5 million), Ethiopia (3.1 million), Nigeria (2.6 million), Tunisia (2.3 million), Kenya (2.2 million), Rwanda (2.2 million), Zambia (2.1 million) and Cameroon (1.8 million).⁷¹ These ten countries accounted for over 70% of the tests performed in the region at that time point.

Ethiopia is a good example of a low-income country that has scaled up diagnostic testing in response to covid-19. Laboratory capacity had been increasing in the years before the pandemic, in line with International Health Regulations. Its successful expansion programme during the pandemic saw an increase in the number of laboratories able to perform RT-PCR tests from zero, at the start of the pandemic, to 65 – within just 10 months.⁷³ The key factors for adapting so many laboratories included:

- a strong laboratory coordination network
- utilisation of non-virologic laboratories
- establishing quality assurance checks
- establishing local production of laboratory reagents and consumables to strengthen weak supply chains
- training new and existing staff with support from international experts
- receiving support from WHO.



Other examples include Benin, which in March 2020 had just one laboratory that was capable of testing for the virus. By October 2020 it had a nationwide network of 13 laboratories with this capability.⁷⁴ This allowed them to achieve rates of testing above WHO's suggested minimum threshold of 1 test per 1,000 population per week.

Another factor that can impact the availability of diagnostic tests is a lack of local manufacturing capacity, especially when international transport and supply chains are disrupted like they have been during the pandemic. According to FIND, as of July 2021 there were only two manufacturers of diagnostic tests for SARS-CoV-2 in Africa, while Oceania had five.⁷⁵ This was in contrast to the 386 test manufacturers in Asia (largely China and South Korea), 200 in Europe, and 94 in the Americas. The development of manufacturing centres in under-served regions, such as Africa, may help to mitigate this risk and increase global manufacturing capacity.

Professor Pai commented, "This is going to come back and bite you during this crisis. Without decentralized manufacturing capabilities you are at the mercy of [the manufacturing countries]. And then things like trade wars, export bans, all sorts of complex supply chain issues, and inflation of costs start. So I think the decentralized manufacturing of tests, I would argue, is as important as decentralized manufacturing of vaccines, and [potentially] much easier."

There has been some progress in this direction. FIND, working with industry partners and donors, have helped establish three new manufacturing sites across South America, Africa and India.⁷⁶ Bill Rodriguez, the CEO of FIND, said that non-traditional emerging markets are maturing rapidly, partly because of covid-19, with strengthening of procurement systems and better information on demand

for diagnostic tests. He observed that industry is now paying a lot of attention to the needs and opportunities in these markets.

While expansion of covid-19 testing is important, careful management is essential for ensuring that such access is provided without having a significant negative impact on other public health programmes.⁷⁷ In response to the pandemic, the Global Fund said that up to 10% of the grants allocated to individual countries to combat HIV, TB and malaria can be used for the covid-19 response. If countries wish to purchase rapid antigen tests, then further flexibility in the allocation of these funds can be agreed. It is predicted that there will be a knock-on effect from this reallocation of resources which will add to the negative impact of covid-19 on access to antiretroviral medication for HIV, the detection, diagnosis and treatment of TB, and the distribution of mosquito nets for malaria prevention. As a result, mortality rates from HIV, TB and malaria could increase in high-burden settings, a negative impact which could be of the same order of magnitude or even greater than the direct impact of covid-19 in some countries.⁷⁸

An ongoing role for diagnostics in covid-19

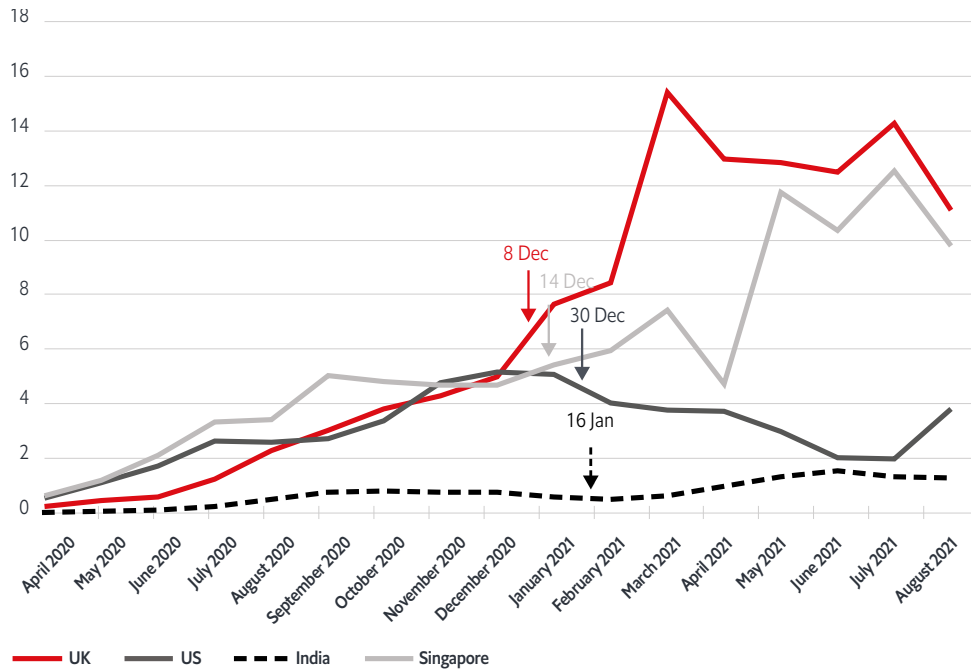
With several vaccines being rolled out widely, it was expected that the need for diagnostic testing would decline, but on the whole this has not been the case. As can be seen from Figure 10, the US had a reduction in the rate of testing after vaccines began to roll out at the end of 2020. However, in countries such as the UK, Singapore and India, testing has generally increased since rollout. This may be because of the emergence of new variants, which are more transmissible. Testing remains a crucial part of limiting the influx of cases now that countries are opening up their borders, particularly with respect to variants of concern.

As Dr Rodriguez puts it “People were hopeful that we’re entering into a phase of the pandemic where testing would have a narrower role as vaccinations rolled out, but it’s now clear to everyone, we’re not close to the end of this pandemic. There’s an increased awareness that we need to refocus our energies on testing. There’s a clear need for more access to rapid tests. There’s an ongoing need for continued PCR testing and expanding the capacity to run those tests throughout the world. And now there’s a growing need for genomic sequencing around the world.”

“People were hopeful that we’re entering into a phase of the pandemic where testing would have a narrower role as vaccinations rolled out , but it’s now clear to everyone, we’re not close to the end of this pandemic... we need to refocus our energies on testing.”

Bill Rodriguez, CEO of FIND

Figure 10: Average daily covid-19 tests per thousand people by month for selected countries before and after vaccine rollout



Arrows indicate the date on which vaccine rollout began for each country shown

Even if vaccination leads to a sustained reduction in cases and in the need for diagnostic tests, it is worth noting that widespread vaccine coverage may take years to achieve in some places. For example, rollout forecasts from April 2021 predicted that much of Latin America will not have widespread vaccination until the middle of 2022 (or even later), that large parts of Asia will not have widespread vaccination until late 2022 or early 2023, and that it will not happen in most African countries until early 2023.⁷⁹

Monitoring SARS-CoV-2 variants

As with other similar pathogens, the genetic makeup of SARS-CoV-2 changes over time. Mutations that occur in a virus produce variants of that virus, simply referred to as variants. Some genetic changes don't affect how a virus behaves, but others can increase its ability to spread, or alter the severity of illness, or make it more difficult to prevent or treat. Variants in the latter category are classified as either variants of interest or variants of concern (see Box 2 for definitions). WHO encourages countries to strengthen their surveillance and sequencing capabilities so they can systematically track and report transmission of variants locally, and identify any unusual epidemiological events (such as clusters of particularly severe cases).

A naming system for variants has now been adopted, using the Greek alphabet. As of 10 November 2021 there were four variants of concern as specified by WHO: Alpha, Beta, Gamma and Delta. There were also two variants of interest: Lambda and Mu. In addition, there were 6 variants that required enhanced monitoring.⁸⁰

Box 2: WHO definitions of variants of interest and concern

Variant of interest A SARS-CoV-2 variant that:

- has genetic changes that are predicted or known to affect virus characteristics such as transmissibility, disease severity, immune escape, diagnostic or therapeutic escape; and
- has been identified to cause significant community transmission or multiple covid-19 clusters in multiple countries with increasing relative prevalence, alongside increasing numbers of cases over time or other apparent epidemiological impacts that suggest an emerging risk to global public health.⁸⁰

Variant of concern A SARS-CoV-2 variant that meets the criteria for being a variant of interest, and is also associated with at least one of the following (at a level that has global public health significance):

- increase in transmissibility or detrimental change in covid-19 epidemiology
- increase in virulence or change in clinical disease presentation
- decrease in effectiveness of public health and social measures or available diagnostics, vaccines or therapeutics.⁸⁰

Collating data on variants

Prompted by the outbreak of avian H5N1 influenza in 2006, the Global Initiative on Sharing Avian Influenza Data (GISAID) was created to facilitate rapid sharing of data on the genetic sequences of circulating influenza viruses.⁸¹ It provides an international open access database, to which scientists can submit and access genetic sequences. It facilitates open sharing by having data-sharing agreements that:

- protect owners' intellectual property rights to the data
- provide transparency on the use of the data
- set out guidelines for the way in which the owners and submitters of the data are acknowledged and recognised.⁸¹

This central portal for genetic information has hastened the ability of researchers to pool and analyse global data on SARS-CoV-2. When covid-19 started spreading, the GISAID team recognised the important role their database could play in hosting genetic information on SARS-CoV-2. They set up a platform for the data, known as EpiCoV, and it has become the largest repository of such information worldwide.⁸² As of 27 July 2021, it included just under 2.4 million sequences from countries around the world.⁸³ GISAID-affiliated scientists have also provided training on genetic sequencing and the use of the database for other scientists in regions that have less experience.

Improvements in genomic sequencing technology and capabilities worldwide have made the technique quicker, cheaper and more scalable. The covid-19 pandemic has allowed the technology,

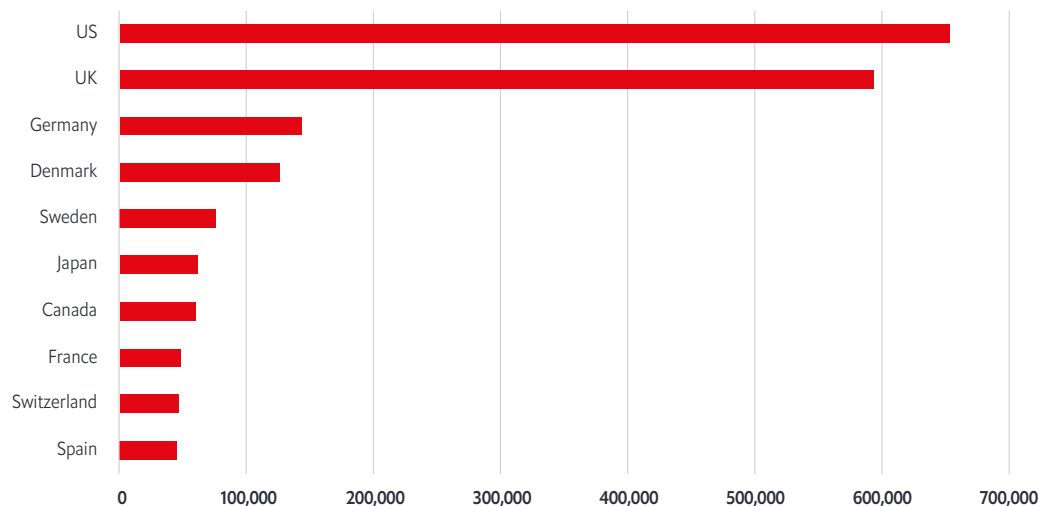
for the first time, to be used in almost real-time to monitor and inform a pandemic response. The information gained from sequencing has been – and will continue to be – used to:

- study disease epidemiology (including identifying the origin of cases)
- inform diagnostic approaches
- help develop vaccines.

The US and UK have submitted the most genomes to GISAID by a large margin. All of the top submitting countries are in North America and Europe (see Figure 11). At the other end of the spectrum, 37 countries or territories with covid-19 cases have not submitted any genomes. The majority of these are small nations, and have only small numbers of cases, yet the group does include some countries and territories with relatively large populations and over 100,000 cases. These include:

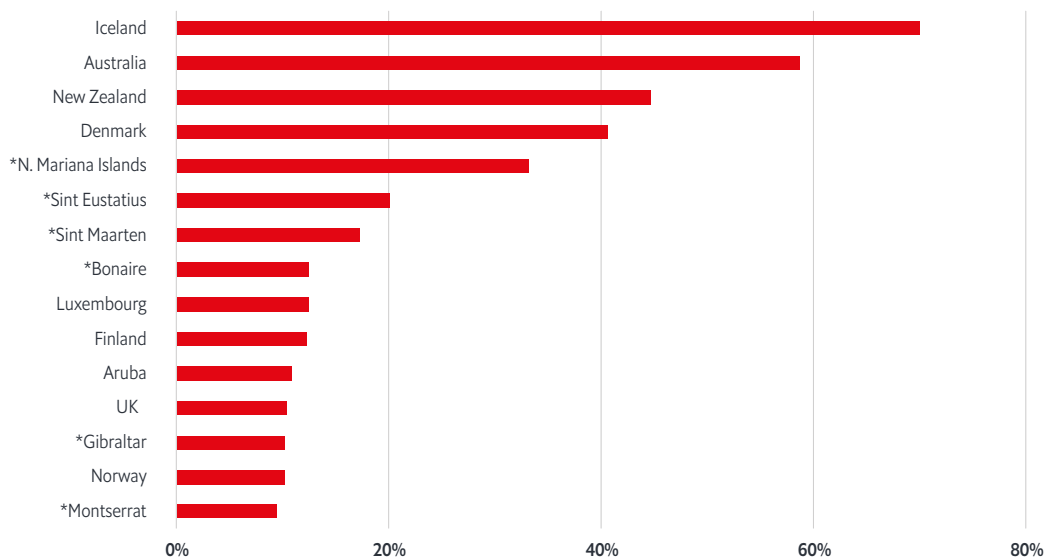
- Kyrgyzstan (population of about 6.6 million in 2021, reporting over 158,000 cases)
- Puerto Rico (population of about 2.8 million in 2021, reporting over 143,000 cases)
- Namibia (population of about 2.6 million in 2021, reporting over 116,000 cases).⁸⁴

Figure 11: SARS-CoV-2 genome sequences shared through GISAID (top 10 countries, through 27 July 2021)



In terms of the percentage of cases sequenced and shared, Iceland is at the forefront. It has sequenced around 70% of its cases – not surprising given the country’s strong sequencing infrastructure and capabilities. Next in line are Australia and New Zealand (around 59% and 45% of cases sequenced, respectively; see Figure 12). The vast majority of countries have sequenced and shared less than 10% of their cases.

Figure 12: SARS-CoV-2 genome sequences shared through GISAID (top 15 countries, through 27 July 2021)



*Countries with fewer than 500 genomes shared.

Over the period between 10 January 2020 and 27 July 2021, sequencing has also varied by region:⁸³

- In WHO’s South-east Asian region, Thailand had sequenced and shared the highest proportion of cases, despite only doing so for 0.37%.
- The situation is similar in the Eastern Mediterranean region, with the highest proportion sequenced and shared in Qatar (1.29%). Iran sequenced and shared only 0.01%, despite reporting over 3.6 million cases.
- Africa has an unexpectedly high level of sequencing and sharing compared to some regions. The highest proportion was seen in The Gambia (7.27%). Other than The Gambia and Mauritius, the remaining countries have rates below 5%. Several countries have shared no sequenced genomes (including Namibia, as mentioned above).
- In the Americas, some of the Caribbean islands (with relatively few cases) top the table for proportion of cases sequenced and shared, peaking at 20% for Sint Eustatius. Among the larger (non-island) nations, Canada leads at 4.25%, but the US (reporting over 34 million cases) has only sequenced and shared 1.91%.

An important caveat to these figures is that sharing sequences via GISAID is voluntary, therefore some countries may be sequencing a greater proportion of their cases than suggested by the GISAID data. Singapore, for example, currently sequences virus from every confirmed case of covid-19, although (as of 10 January 2021) only 47% of cases from the previous 3 months were shared through GISAID. Singapore routinely uses the data to link cases, identify clusters, and determine possible transmission chains – seemingly one of the few countries in the world to do this.⁸⁵

While GISAID has the largest number of complete covid-19 sequences, it is not the only sequence repository. Some sequences are shared elsewhere. GenBank is one of them. It is run by the US National Center for Biotechnology Information, and as of 27 July 2021 contains just under 1 million SARS-CoV-2 nucleotide sequences, of which about 40% are complete; around 38% come from the USA.⁸⁶ If the sequence data in this repository from the US is completely non-overlapping with that in GISAID, then this would increase the proportion of US cases sequenced and shared to about 3%.

Europe also has its own sequence repository, the European covid-19 data portal, which is organised by the European Molecular Biology Laboratory's (EMBL's) European Bioinformatics Institute, on behalf of the European Commission and in liaison with EU Member States and research partners.⁸⁷

The centralised collection of global sequencing data is of great value because it allows variant spread to be monitored over time. For example, the data from GISAID show that in the week starting 26 July 2021 the Delta variant represented about 85% of SARS-CoV-2 sequences reported worldwide, in contrast to 0.1% in the week starting 15 March 2021.⁸⁸

Infrastructure needs to be built to ensure equitable access to sequencing

Within countries, laboratories that have genomic sequencing capability have banded together, with the aim of providing SARS-CoV-2 sequencing close to the sample source, and to facilitate rapid and open data sharing for use by policy makers. For example, in the UK the Coronavirus Disease 2019 (COVID-19) Genomics UK Consortium (COG-UK) was launched in March 2020,⁸⁹ and the Network for Genomic Surveillance in South Africa (NGS-SA) was launched in May 2020.⁹⁰

There are no specific recommendations for the percentage of cases that should be sequenced; the figure varies according to the intended purpose of the sequencing, as well as contextual issues.⁶¹

In order to implement sequencing, countries need sufficient funding for the technology (both consumables and sequencing devices), as well as the infrastructure and human resources to support it. This includes sufficiently high-performance computational systems and suitably trained staff.⁶¹ Because the cost of putting all these components in place is high, it is likely that not all countries will be able to do so. Collaboration between countries is needed, therefore, to ensure that a network of laboratories is established that can provide sequencing capacity for countries where this is lacking. This will enable a robust public health response to existing and emerging threats.

One case in point is Africa. Up to the latter half of 2020, 72% of the continent's capacity for genome sequencing was sited in four countries, namely South Africa, Kenya, Nigeria and Morocco.⁹¹ The majority of this capacity (about 83%) was within private institutions. In response, a programme to build

a collaborative pathogen genomic sequencing network was launched in late 2020 by WHO and Africa CDC.⁹² The Africa Pathogen Genomics Initiative was set up to provide national public health institutes with next-generation sequencing technologies, as well as a data-sharing platform and staff training.⁹¹

This network will inform public health surveillance and outbreak investigations, and improve disease control and prevention. Initiated in 2021, it is a 4-year partnership between the Africa CDC Institute of Pathogen Genomics, the US CDC and the Bill & Melinda Gates Foundation, in addition to a number of private companies that are providing sequencing equipment, reagents and computational support.

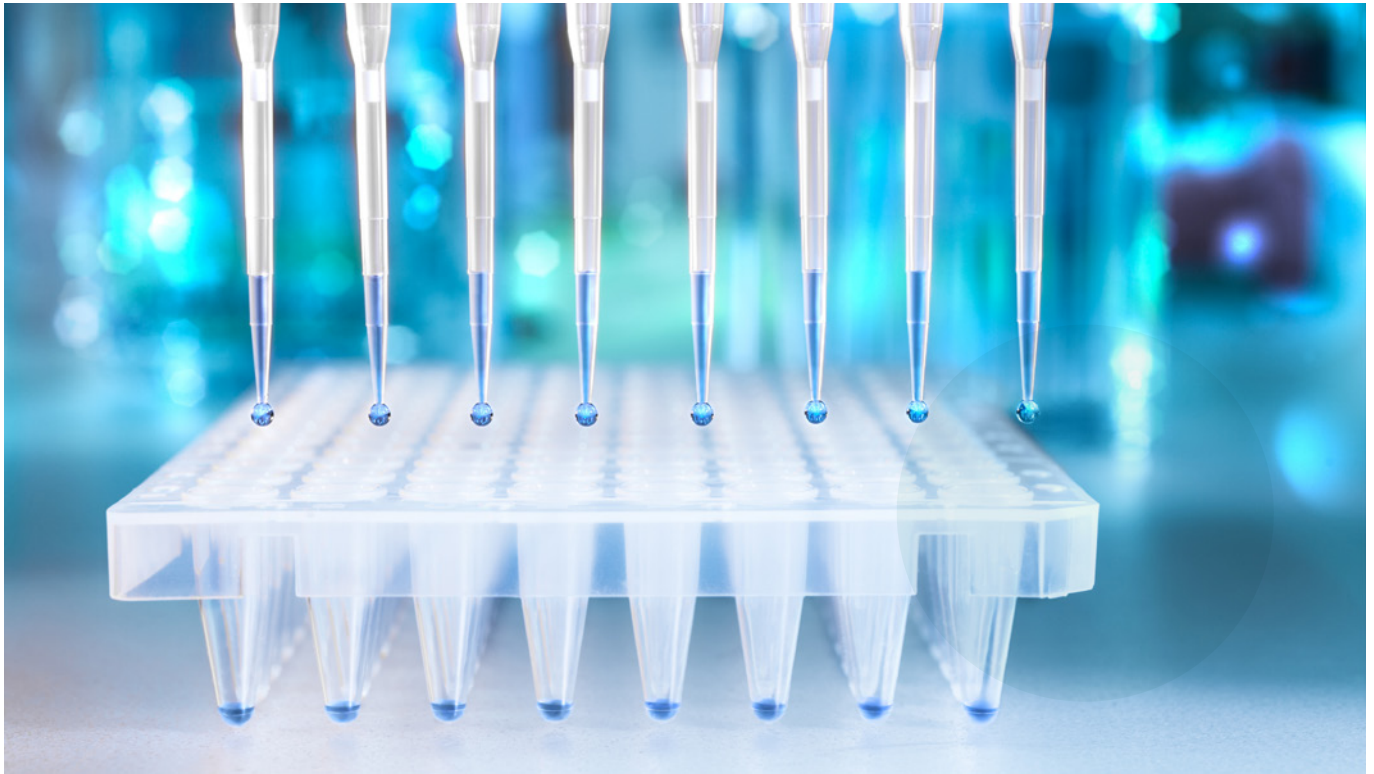
Monitoring variants' impact on test performance and vaccine efficacy

In order to work, RT-PCR relies on the ability of short synthetic pieces of DNA (called primers) to bind to a virus' genetic material; and in order to bind strongly and work well, these primers must perfectly complement the corresponding section of viral sequence. If a viral sequence changes at the primer binding sites, then RT-PCR may not work as well, or it may fail altogether, giving false negative results. To reduce this risk, multiplex PCR tests target more than one region of the viral genome, in case one of the primers fails. Ongoing international monitoring of changes in the viral genome is vital to ensure that tests continue to detect infections accurately. Platforms already exist to facilitate sharing of this information.

Some changes to the viral genome result in changes to the proteins it produces, with potential implications for the accuracy of both antibody and antigen tests, and the effectiveness of vaccines. Antibody tests determine whether a person has existing antibodies to SARS-CoV-2 proteins; they utilise synthetic SARS-CoV-2 proteins, such as the spike (S) protein. If someone has been infected with a virus with proteins that have changed, the antibodies they generate may not bind well to the synthetic proteins used in the test. Similarly, antigen tests work by using synthetic antibodies to bind to SARS-CoV-2 proteins present in patient samples. Again, if the proteins change, the test may not work as well, resulting in false negatives.

Vaccines work by inducing an immune response to SARS-CoV-2 material (usually viral proteins) in the vaccine recipient. Thus, if the SARS-CoV-2 proteins alter over time in the circulating viral strains, these variants may no longer be recognised as well by the immune system, making existing vaccines less effective. This is why some vaccines have lower effectiveness against infections caused by the Beta and Delta variants,^{93,94} although they do still seem to offer protection against severe outcomes such as hospitalisation or death.⁹³ Monitoring changes in the viral genome enables decisions to be made about whether vaccines will need to be adapted going forward.

In addition to data on genomic sequences, access to high-quality, well-characterised samples of SARS-CoV-2 virus variants are also essential for assessing how well diagnostic tests can detect them – a major challenge.⁹⁵ An initiative has been set up by the European Biobanking and Biomolecular Resources Research Infrastructure (BBMRI) and the International Society for Biological and Environmental Repositories (ISBER) to connect biobanks that collate data on samples related to covid-19 for researchers and industry scientists.^{96,97} It uses the existing BBMRI-European Research Infrastructure Consortium (ERIC) Directory, which holds information about biobanks that are willing to share their data and samples. Although the directory is open to global biobanks, as of early October 2021 the majority listed were located in Europe; only a small number of these specified that they provide samples of the viral pathogen itself.⁹⁸



Disease surveillance

In the past 20 years, humans have been threatened by several new infectious diseases, and new strains of existing diseases (such as SARS, H1N1 influenza, MERS, Ebola, Zika and most recently covid-19). These diseases were all initially found in animals, before crossing the species barrier to infect, and then be transmitted by, humans; these diseases are referred to as zoonoses.⁹⁹ The emergence of new infectious diseases like these is becoming more common.¹⁰⁰

Spatial analysis suggests that new infectious diseases are most likely to emerge in areas where population density is high (or growing), in forested tropical regions that are undergoing changes of land use (such as logging or mining), or where there is a rich supply of wildlife (potential hosts).¹⁰⁰ Mapping these factors suggests that the risk for emerging diseases is highest in developing countries at lower latitudes, such as India, China, sub-Saharan Africa and some areas in Latin America. It is telling that Wuhan, where covid-19 originated, lies in one of these predicted higher-risk areas. Yet, despite the location of these hotspots, surveillance and research efforts tend to focus on higher income regions in Europe, North America, Australia and some parts of Asia.¹⁰⁰ Laboratory capabilities in these hotspots should be strengthened in order to facilitate regular high-quality surveillance testing.

There are reported to be no formal surveillance systems in place that routinely carry out broad, active pathogen surveillance in humans and domestic animals alongside clinical assessment for emerging and re-emerging viral diseases.¹⁰¹ There are surveillance systems specifically for viruses that are transmitted by arthropods (such as insects). There is also a global early warning surveillance

system for detecting disease outbreaks, but it does not actively look for emerging pathogens. Other surveillance systems focus on specific diseases or pathogens such as influenza. As a result, there have been calls for a global multisectoral surveillance network that will actively search for the spillover of pathogens from animal populations on an ongoing basis, with a focus on geographical hotspots. This would complement and build on existing surveillance of both humans and animals.

Such a network would require investment, as Laura Kahn, Co-Founder of the One Health Initiative, points out. In some countries, veterinary capacity lags behind public health capability. Dr Kahn notes that – for wildlife in particular – there has been a lack of motivation to carry out surveillance. “For farmers,” she says, “if their animals start dying they have an incentive to investigate ... For wildlife there isn’t much surveillance. Nobody owns them and there isn’t a clear financial incentive to do so, so the argument that we need to spend money to monitor their wellbeing is a difficult one ... The money currently spent on monitoring wildlife and the environment is minimal compared to what is spent on the human system.” The economic impact of covid-19 may play a part in making the case for investment, in order to address this imbalance.

“For wildlife there isn’t much surveillance. Nobody owns them and there isn’t a financial incentive to do so.”

Laura Kahn, Co-Founder, One Health Initiative

How has the use and role of diagnostics evolved during the current pandemic?

The speed at which diagnostic tests for SARS-CoV-2 were developed and evolved has been impressive, as is the array of tests available. “There has been breathtaking innovation,” observes Professor Pai, “within a year [we had] brand new rapid, point-of-care [antigen] tests, and now new point-of-care molecular diagnostics – tests which combine multiple infections in one cartridge – have been designed. And just wonderful innovation around easier sample collection methods ... It’s also been breathtaking to see the level of interest in testing. People have wanted testing, which was very, very uncommon before the pandemic, and even public knowledge about testing [has increased]. So I think public discourse or awareness about the properties and importance of diagnostic testing has dramatically increased.”

According to PATH (Program for Appropriate Technology in Health), a non-profit organisation working towards elimination of health inequities through innovation and partnership, as of 20 July 2021, over 1,200 diagnostic tests for SARS-CoV-2 had been authorised worldwide by at least one regulatory authority.¹⁰² The manufacturers of the majority of these tests are based in the US, China, South Korea and India.

With the speed of development and fast-track regulatory approval systems, perhaps it is inevitable that over time some tests have been superseded or have been found to not be sufficiently accurate. As of 4 August 2021 for example, the FDA revoked five emergency use authorisations for covid-19 tests; this contrasts with only 11 revocations in the previous 5 years.¹⁰³ It is clear that it is very important to have ongoing monitoring of test performance as new information becomes available, as well as the ability to revoke authorisations as required.

“There has been breathtaking innovation. It’s also been breathtaking to see the level of interest in testing.”

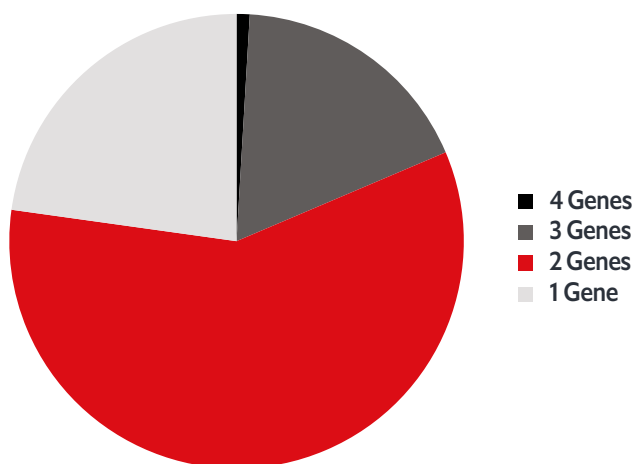
Madhukar Pai, Canada Research Chair in Epidemiology & Global Health, Associate Director, McGill International TB Centre

Ongoing monitoring is also important for determining whether new variants are a threat to the performance of diagnostic tests. Concerns that new variants will evade detection have led PATH to collate data on the impact of variants on diagnostic tests for their diagnostics dashboard. This includes data about the viral gene or protein targeted by the test (most tests target the spike (S) or nucleocapsid (N) genes or proteins, or both). In most cases, it is predicted that the existing tests will be able to detect currently known variants, based on what is known about the tests' targets. For example, most POC antigen tests target a part of the N protein where few mutations have been found, so these are predicted to still be reliable.¹⁰⁴ However, in only a minority of cases has test performance against variants been verified independently or reported by manufacturers.

In order to reduce the chances of failing to detect new variants, molecular tests have become more sophisticated. The original tests only targeted single sites, but over two-thirds of the tests now target at least two genes (see Figure 13).¹⁰⁵ It is likely that these multi-gene tests will become standard. Some newer tests also combine molecular analysis for SARS-CoV-2 with other respiratory pathogens (such as influenza) to allow the two to be differentiated or to identify co-infections.¹⁰⁶

Tests have also become easier to perform in terms of sample collection, the use of automation to allow high-throughput testing, and the development of rapid POC options for molecular, antigen and antibody tests. For molecular and antigen testing, a variety of sample types have been investigated, with nasopharyngeal and oropharyngeal swabs being common. Tests that rely on anterior nasal swabs – rather than deeper, more uncomfortable nasal swabs – have also been developed. In an attempt to make testing more acceptable, saliva-based tests are a particularly attractive option. They are now available and are analysed by RT-PCR. In Scotland these tests can be bought from pharmacies, then carried out at home and sent to a laboratory as proof of infection status for travel purposes.¹⁰⁷

Figure 13: Proportion of SARS-CoV2 RT-PCR tests targeting different numbers of gene sites



While most tests undergo manual processing by trained professionals, fully automated tests and self-testing kits are now available.⁷⁵ These are welcome innovations given the shortage of laboratory staff and low global supplies of PPE. There are other techniques that allow a one-step process for identifying SARS-CoV-2 RNA, such as reverse-transcriptase loop-mediated isothermal amplification (RT-LAMP) and clustered regularly interspaced short palindromic repeats (CRISPR) technology.¹⁰⁸

There are also POC molecular tests, which provide results within minutes, without the need for a laboratory or refrigeration of kit reagents.¹⁰⁹ For example, in February 2021 the US FDA gave their first authorisation for an over-the-counter molecular test.¹¹⁰ The test has connectivity to an app, which will eventually allow results to be reported to the public health authorities. POC molecular tests have also been deployed in Sangamner, a subdistrict in India, where previously there was only a single RT-PCR machine and technician for a population of 140,000.¹⁰⁹ The RT-PCR service was so overwhelmed that the turnaround time for tests was between 8 to 10 days. With help from PATH and The Rockefeller Foundation, the molecular POC tests are now used for over half (55%) of tests in the region; the remainder are rapid antigen kits.¹⁰⁹

This is an encouraging illustration of the use of cutting edge technology in an LMIC, but it isn't routine. Dr Rodriguez describes it thus: "We have a lot of new technologies in the world, platforms that can be used for low cost to detect a number of conditions, many of which are in hospitals in high-income countries. But those technologies haven't reached the rest of the world. We need to accelerate [their] development". Dr Fleming agrees with the importance of the POC technologies: "We have to find some ways of getting diagnostics out there and democratizing access, getting them out of the hospital system into the community ... The speed of technological change is quite extraordinary, and I think it is coming."

Other innovations are being developed to address the issue of how to rapidly scale up laboratory capacity. One such initiative has developed a proof-of-concept shipping container laboratory for covid-19 testing to address this problem.¹¹¹⁻¹¹³ The laboratory uses hardware, chemical reagents and ancillary supplies which are widely available (so called "open" systems), and do not need to come from a specific manufacturer or source, thus reducing the risk of supply chain issues. This contrasts with some commercial laboratory-based covid-19 test equipment which can only use the test manufacturer's kits and reagents, so called "closed" systems, which are often highly automated and have a high-throughput.¹¹⁴

Each of these container laboratories can process 2,400 tests a day, and only requires one person to operate it. Because the mobile labs are in standard shipping containers, they can (theoretically) be easily transported, offering a level of flexibility in location and type of use (e.g. to provide extra

laboratory capacity at an existing site or at a site with no nearby laboratory, or onsite at large workplaces or educational facilities). The crates can be stacked, thus creating larger testing centres, and later dismantled and moved as needed. Currently, the containers need to be connected to both electricity and water supplies, so they are inappropriate for settings that lack these facilities.

Box 3: Wastewater surveillance—insights into SARS-CoV-2 at the community level

Diagnostic tests are also being used in ways that many of us may not have anticipated. Sewage, or wastewater, surveillance has been previously used to detect polio outbreaks. It is currently used in 55 countries to monitor community spread and identification of new covid-19 variants, without relying on testing individual people.¹¹⁵ It measures the extent of community infections, including asymptomatic cases, which is particularly useful in areas where people are reluctant to be tested. Genomic sequencing of samples from sewage can quickly identify the presence of new strains or known variants of concern. This type of testing is useful for informing local public health guidelines and policy, and for determining when strains are no longer in circulation. It complements individual-level SARS-CoV-2 surveillance testing.¹¹⁶

There are national and regional systems for monitoring SARS-CoV-2 in sewage in a range of countries, such as Finland, Hungary, Luxembourg, the Netherlands, Spain, Turkey, the US, Canada, Australia and the UK.¹¹⁷ Researchers at the University of California have created a dashboard of global efforts in wastewater monitoring.¹¹⁵ This highlights the lack of such monitoring in LMICs, possibly in some areas due to lack of good sanitation systems. In Africa, for example, monitoring is limited to South Africa, Nigeria, Kenya and Ghana. For countries that have sewage systems, it offers the potential for less test-intensive monitoring of infection rates.

What has covid-19 taught us about future pandemics?

The covid-19 pandemic has shed light on a long-standing problem – the fact that diagnostics has been under-appreciated and under-resourced. Despite the critical role of diagnostics in achieving the UN’s Sustainable Development Goal of ensuring healthy lives for all, it is telling that that diagnostics and diagnostic capacity are not explicitly mentioned among the targets for monitoring progress (unlike medicines and vaccines). WHO first issued its Essential Medicines list in 1977, but it took 40 years for it to issue its Essential Diagnostics List (the EDL) – first published in 2018.^{118, 119} To date, only India is reported to have developed a national list;¹²⁰ the equivalent system in Nigeria is reported to be in the final stages of approval.¹²¹

The covid-19 pandemic has had a devastating impact, yet it may prove to be a catalyst for change. In vitro diagnostics, in particular, have played and continue to play a crucial role, from identifying the causative pathogen, to tracking and interrupting the spread of disease, from informing vaccine design to monitoring variants of concern.

Progress in covid-19 diagnostics has happened at a rate that was previously unthinkable. In less than a year, from the start of 2020 when the causative organism was first identified, to the end of 2020, all 194 WHO member states were reported to have the capability for testing for SARS-CoV-2.⁹ In order to prevent future pandemics it is likely that even more rapid development, evaluation and implementation of accurate in vitro diagnostics will be necessary, all the more so for novel diseases that can be spread by asymptomatic or presymptomatic individuals, as with covid-19.¹²²

“Pandemics don't create new problems in the world. They just reveal all of the challenges around testing that we've known about in other diseases for a long time.”

Bill Rodriguez, CEO of FIND

Even before the covid-19 pandemic, outbreaks of diseases such as Ebola and Zika highlighted the importance of diagnostics, and the gaps that existed in diagnostic preparedness.¹²³ However, to a large extent these challenges remain unresolved. The global impact of covid-19 in human and economic terms may drive home lessons for addressing other vaccine-preventable illnesses and future pandemics. A number of key actions are required to strengthen diagnostic preparedness and response. These include:

Continuing and improving disease surveillance. The surveillance systems put in place after the SARS outbreak facilitated the rapid detection of the first cases of covid-19 in China. The ability to rapidly undertake metagenomic sequencing allowed identification of the novel pathogen and development of RT-PCR diagnostic tests within weeks of its emergence. Unfortunately, even this rapid detection and identification was not sufficient to curtail its spread on a global scale, hence the need for strengthening protocols for rapid implementation of testing in outbreak areas in the future. Current surveillance systems tend to focus on known pathogens and known disease presentations; they must become more active and comprehensive, and encompass regular monitoring of potential emerging zoonotic diseases among wild animals and livestock.

Investing in diagnostic R&D. For infectious diseases such as TB and many neglected tropical diseases that have been known about for centuries there are still few simple, rapid, accurate POC in vitro diagnostic tests. The rapid and successful development of a wide array of covid-19 diagnostics demonstrates what should be possible for other diseases. Progress is being made but it could be accelerated through greater prioritisation and investment. In addition to high-throughput laboratory-based methods, POC innovations that allow decentralised testing, and that do not require expensive laboratory facilities and equipment or highly trained staff, will be very beneficial for LMICs and even hard-to-reach communities in high-income countries. Priority should also be given to platform technologies that can be rapidly adapted to new pathogens. Given the sheer volume of tests carried out worldwide during the pandemic, more sustainable and environmentally friendly diagnostic solutions should be factored in.

Formalising flexible but rigorous regulation pathways to allow rapid diagnostic authorisation. The pandemic forced regulatory authorities to use streamlined versions of their usual approval processes, allowing diagnostic tests to be brought onto the market quickly. These pathways may still be needed if new variants emerge that cannot be detected by the existing tests. They should incorporate mechanisms to assess emerging evidence on tests, so that authorisations can be rapidly revoked or altered as required. Formalising these pathways will enable better responses to future pandemic threats.

Diversifying diagnostic technologies, suppliers and manufacturers. The bottlenecks seen in the supply chain during covid-19 illustrate the need for a broader range of technologies, including technologies that are less reliant on proprietary reagents. Diversification of manufacturing centres and supply sources could help to reduce inequity of access to diagnostic testing in regions where these facilities are currently limited.

Expanding laboratory capabilities and capacity worldwide. Countries have struggled to reach the unprecedented levels of testing needed to control the pandemic. As a result, many have expanded their laboratory capabilities and capacity, potentially leaving a long-term legacy of

strengthened health systems that are better able to detect and deal with current and future health threats (both communicable and non-communicable) and move us closer towards universal healthcare. Improvements must address not only laboratory facilities, but also the wider supporting infrastructures, such as staff training, quality assurance systems, IT systems and equipment maintenance.

Making improvements to computational systems and data sharing. Timely sharing of genomic sequencing data for SARS-CoV-2 facilitated the development of diagnostic tests and vaccines, as well as epidemiological tracking. For the first time, data sharing enabled an almost real-time perspective on progress of the disease, usage of tests and demand. This has strengthened global efforts to contain covid-19, and it could do the same for other diseases. Robust data collection allows monitoring and linkage of diagnostic data to public health measures, such as contact tracing, localised testing and lockdown measures. Alongside expanding genomic sequencing capability globally, strengthened computational capabilities are needed to analyse the data generated and identify new variants as they arise. A well-governed network of biobanks for the collection and sharing of samples of these new variants is also important for the rapid development and evaluation of diagnostic tests. Some systems are now in place, but it is important that they are maintained in the long term.

Facilitating combined purchasing and improving financing mechanisms. Combined purchasing through the CSCS enabled LMICs to obtain lower prices and purchase an average of 55% of their covid-19 diagnostic supplies. Similar mechanisms should be explored in the longer term, with better financing mechanisms for capital-intensive activities like building laboratories and purchasing expensive equipment, to complement community-based diagnostic approaches. These steps are crucial for addressing inequitable access to testing.

The pandemic has emphasised – in no uncertain terms – the importance of diagnostics. The knowledge and mechanisms needed to strengthen the diagnostics ecosystem globally are developing, including the *Lancet* Commission on Diagnostics, WHO's Essential Diagnostics List and the partnerships being built through the work of organisations such as FIND.

Holistic systems that integrate diagnostics and diagnostic data with appropriate public health measures and access to vaccines and therapeutics are crucial going forward to bring an end to this pandemic – and for application to future pandemics. Pathogens such as SARS-CoV-2 know no borders in our increasingly interconnected world. Therefore it is in the interest of all nations to ensure equitable access to pathogen surveillance and diagnostics globally, as well as vaccines, to ensure protection against such threats.

References

1. Xiang N, Song Y, Wang Y, et al. Lessons from an active surveillance pilot to assess the pneumonia of unknown etiology surveillance system in China, 2016: the need to increase clinician participation in the detection and reporting of emerging respiratory infectious diseases. *BMC Infectious Diseases*. 2019;19(1):770.
2. WHO. Novel Coronavirus (2019-nCoV): Situation Report - 1. Geneva: 2020. Available from: https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200121-sitrep-1-2019-ncov.pdf?sfvrsn=20a99c10_4. (Accessed on 16 August 2021).
3. WHO. Timeline: WHO's COVID-19 response [Internet]. Geneva: World Health Organization. Available from: <https://www.who.int/emergencies/diseases/novel-coronavirus-2019/interactive-timeline>. (Accessed on 17 August 2021).
4. Holshue ML, DeBolt C, Lindquist S, et al. First Case of 2019 Novel Coronavirus in the United States. *New England Journal of Medicine*. 2020;382(10):929-36.
5. Moriarty L, Plucinski M, Marston B, et al. Public Health Responses to COVID-19 Outbreaks on Cruise Ships — Worldwide, February–March 2020. *MMWR Morb Mortal Wkly Rep*. 2020;69:347-52.
6. Zhu N, Zhang D, Wang W, et al. A Novel Coronavirus from Patients with Pneumonia in China, 2019. *New England Journal of Medicine*. 2020;382(8):727-33.
7. Corman VM, Landt O, Kaiser M, et al. Detection of 2019 novel coronavirus (2019-nCoV) by real-time RT-PCR. *Eurosurveillance*. 2020;25(3):2000045.
8. Corman VM, Bleicker T, Brünink S, et al. Diagnostic detection of Wuhan coronavirus 2019 by real-time RT-PCR. Berlin: 2020. Available from: https://www.who.int/docs/default-source/coronaviruse/wuhan-virus-assay-v1991527e5122341d99287a1b17c111902.pdf?sfvrsn=d381fc88_2. (Accessed on 16 August 2021).
9. WHO. A look inside laboratories responding to COVID-19 [Internet]. Geneva: World Health Organization. Available from: <https://www.who.int/news-room/feature-stories/detail/a-look-inside-laboratories-responding-to-covid-19>. (Accessed on 16 August 2021).
10. DZIF. Researchers develop first diagnostic test for novel coronavirus in China [Internet]. Berlin: Deutschen Zentrums für Infektionsforschung. Available from: <https://www.dzif.de/en/researchers-develop-first-diagnostic-test-novel-coronavirus-china>. (Accessed on 17 August 2021).
11. WHO. Laboratory testing of 2019 novel coronavirus (2019-nCoV) in suspected human cases: interim guidance, 17 January 2020. Geneva: 2020. Available from: [https://www.who.int/publications/i/item/laboratory-testing-of-2019-novel-coronavirus-\(2019-ncov\)-in-suspected-human-cases-interim-guidance-17-january-2020](https://www.who.int/publications/i/item/laboratory-testing-of-2019-novel-coronavirus-(2019-ncov)-in-suspected-human-cases-interim-guidance-17-january-2020). (Accessed on 21 October 2021).
12. WHO. Emergency use listing [Internet]. Geneva: World Health Organization. Available from: <https://www.who.int/teams/regulation-prequalification/eul>. (Accessed on 16 August 2021).
13. FDA. In Vitro Diagnostics EUAs [Internet]. US Food & Drug Administration; (last updated 24 May 2021). Available from: <https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/in-vitro-diagnostics-euas>. (Accessed on 16 August 2021).
14. US CDC. CDC Diagnostic Tests for COVID-19 [Internet]. US Centers for Disease Control and Prevention. Available from: <https://www.cdc.gov/coronavirus/2019-ncov/lab/testing.html>. (Accessed on 16 August 2021).
15. Roche's cobas SARS-CoV-2 Test to detect novel coronavirus receives FDA Emergency Use Authorization and is available in markets accepting the CE mark [press release]. Roche, 13 March 2020. Available from: <https://www.roche.com/media/releases/med-cor-2020-03-13.htm>.
16. WHO. WHO Emergency Use Listing for In vitro diagnostics (IVDs) Detecting SARS-CoV-2. Geneva: 2020. Available from: <https://www.who.int/publications/m/item/200922-eul-sars-cov2-product-list>. (Accessed on 21 October 2021).
17. WHO. Laboratory testing strategy recommendations for COVID-19: interim guidance. Geneva: 2020. Available from: <https://www.who.int/publications/i/item/laboratory-testing-strategy-recommendations-for-covid-19-interim-guidance>. (Accessed on 21 October 2021).
18. WHO. Recommendations for national SARS-CoV-2 testing strategies and diagnostic capacities: interim guidance. Geneva: World Health Organization, 2021. Available from: <https://www.who.int/publications/i/item/WHO-2019-nCoV-lab-testing-20211-eng>. (Accessed on 21 October 2021).

19. Sethuraman N, Jeremiah SS, Ryo A. Interpreting Diagnostic Tests for SARS-CoV-2. *JAMA*. 2020;323(22):2249-51.
20. Hahn SM, Shuren JE. Coronavirus (COVID-19) Update: FDA Authorizes First Antigen Test to Help in the Rapid Detection of the Virus that Causes COVID-19 in Patients [Internet]. US Food and Drug Administration. Available from: <https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-authorizes-first-antigen-test-help-rapid-detection-virus-causes>. (Accessed on 21 October 2021).
21. WHO. The selection and use of essential in vitro diagnostics. Geneva: 2021. Available from: <https://www.who.int/publications/i/item/9789240019102>. (Accessed on 21 October 2021).
22. Dinnes J, Deeks JJ, Berhane S, et al. Rapid, point of care antigen and molecular based tests for diagnosis of SARS CoV 2 infection. *Cochrane Database of Systematic Reviews*. 2021(3).
23. Pickering S, Batra R, Merrick B, et al. Comparative performance of SARS-CoV-2 lateral flow antigen tests and association with detection of infectious virus in clinical specimens: a single-centre laboratory evaluation study. *Lancet Microbe*. 2021;2(9):e461-e71.
24. Kohmer N, Toptan T, Pallas C, et al. The Comparative Clinical Performance of Four SARS-CoV-2 Rapid Antigen Tests and Their Correlation to Infectivity In Vitro. *J Clin Med*. 2021;10(2).
25. Pekosz A, Parvu V, Li M, et al. Antigen-Based Testing but Not Real-Time Polymerase Chain Reaction Correlates With Severe Acute Respiratory Syndrome Coronavirus 2 Viral Culture. *Clin Infect Dis*. 2021.
26. European Commission. COVID-19 In Vitro Diagnostic Medical Devices [Internet]. European Commission. Available from: https://covid-19-diagnostics.jrc.ec.europa.eu/devices?manufacturer&text_name&marking=Yes&rapid_diag=1&format&target_type=6&search_method=AND#form_content. (Accessed on 21 October 2021).
27. Watson J, Richter A, Deeks J. Testing for SARS-CoV-2 antibodies. *BMJ*. 2020;370:m3325.
28. WHO. COVID-19 natural immunity [Internet]. World Health Organization; (last updated 10 May 2021). Available from: https://www.who.int/publications/i/item/WHO-2019-nCoV-Sci_Brief-Natural_immunity-2021.1. (Accessed on 21 October 2021).
29. WHO. Correlates of Protection - Will emerging data allow increased reliance on vaccine immune responses for public health and regulatory decision-making? [Internet]. Geneva: World Health Organization. Available from: <https://www.who.int/news-room/events/detail/2021/09/03/default-calendar/save-the-date---will-emerging-data-allow-increased-reliance-on-vaccine-immune-responses-for-public-health-and-regulatory-decision-making>. (Accessed on 21 October 2021).
30. FDA. Antibody Testing Is Not Currently Recommended to Assess Immunity After COVID-19 Vaccination: FDA Safety Communication [Internet]. US Food and Drug Administration; (last updated 19 May 2021). Available from: <https://www.fda.gov/medical-devices/safety-communications/antibody-testing-not-currently-recommended-assess-immunity-after-covid-19-vaccination-fda-safety>. (Accessed on 21 October 2021).
31. Our World in Data. Coronavirus Pandemic (COVID-19) [Internet]. Our World in Data. Available from: <https://ourworldindata.org/coronavirus>. (Accessed on 21 October 2021).
32. Jafari S. Covid-19: Positive test results are the new VIP party pass in Iran. 6 February 2021. Available from: <https://www.middleeasteye.net/news/covid-iran-antibody-test-party-vip-pass>. (Accessed on 21 October 2021).
33. Jamal S, Pingali V, Rayapati A, et al. A look at the usage of Antibody tests to determine level of immunity against COVID-19 after vaccination: A recent trend in India. *Infection Control and Hospital Epidemiology*. 2021.
34. Public Policy Projects. The role of antibody testing within the Covid-19 vaccination programme [Internet]. Public Policy Projects. Available from: <https://publicpolicyprojects.com/publications/the-role-of-antibody-testing-within-the-covid-19-vaccination-rollout/>. (Accessed on 21 October 2021).
35. OECD. Testing for COVID-19: How to best use the various tests? [Internet]. OECD; (last updated 4 December 2020). Available from: <https://www.oecd.org/coronavirus/policy-responses/testing-for-covid-19-how-to-best-use-the-various-tests-c76df201/>. (Accessed on 21 October 2021).
36. Patel NV. Why the CDC botched its coronavirus testing [Internet]. MIT Technology Review; (last updated 5 March 2020). Available from: <https://www.technologyreview.com/2020/03/05/905484/why-the-cdc-botched-its-coronavirus-testing/>. (Accessed on 21 October 2021).
37. Cohen J. The United States badly bungled coronavirus testing—but things may soon improve [Internet]. *Science Magazine*; (last updated 28 February 2020). Available from: <https://www.sciencemag.org/news/2020/02/united-states-badly-bungled-coronavirus-testing-things-may-soon-improve>. (Accessed on 21 October 2021).
38. Guglielmi G. The explosion of new coronavirus tests that could help to end the pandemic [Internet]. *Nature*; (last updated 17 July 2020). Available from: <https://www.nature.com/articles/d41586-020-02140-8>. (Accessed on 21 October 2021).
39. Sharp J, Kenyatta K. The Cost of Speed: FDA Regulatory Flexibilities During the Coronavirus Pandemic [Internet]. The

- Commonwealth Fund; (last updated 20 August 2020). Available from: <https://www.commonwealthfund.org/blog/2020/fda-regulatory-flexibilities-during-coronavirus-pandemic>. (Accessed on 21 October 2021).
40. BBC. Coronavirus: India cancels order for 'faulty' China rapid test kits. 28 April 2020. Available from: <https://www.bbc.com/news/world-asia-india-52451455>. (Accessed on 21 October 2021).
 41. Chamala S, Flax S, Starostik P, et al. Optimizing COVID-19 testing capabilities and clinical management using pathology informatics. *JAMIA Open*. 2020;3(4):523-9.
 42. UCL. UCL and London partners bolster UK's COVID-19 testing capacity [Internet]. London: University College London; (last updated 8 October 2020). Available from: <https://www.ucl.ac.uk/news/2020/oct/ucl-and-london-partners-bolster-uks-covid-19-testing-capacity>. (Accessed on 21 October 2021).
 43. Touron P, Siatka C, Pussiau A, et al. A mobile DNA laboratory for forensic science adapted to coronavirus SARS-CoV-2 diagnosis. *Eur J Clin Microbiol Infect Dis*. 2021;40(1):197-200.
 44. ECDC. COVID-19 testing strategies and objectives. European Centers for Disease Prevention and Control, 2020. Available from: https://www.ecdc.europa.eu/sites/default/files/documents/TestingStrategy_Objective-Sept-2020.pdf. (Accessed on 21 October 2021).
 45. AACC. COVID-19 Survey Results [Internet]. Washington, DC: American Association for Clinical Chemistry. Available from: <https://www.aacc.org/science-and-research/covid-19-resources/aacc-covid-19-testing-survey/full-survey-results>. (Accessed on 17 August 2021).
 46. Krouse S, Terlep S. Why Is It Hard to Get a Rapid Covid-19 Test? The Machines Are in Short Supply. 12 August 2020. Available from: https://www.wsj.com/articles/rapid-response-covid-19-test-makers-face-outrage-demand-11597231427?mod=article_inline. (Accessed on 21 October 2021).
 47. Colchester M. Europe's Covid-19 Testing Programs Creak as Demand Surges. 7 October 2020. Available from: <https://www.wsj.com/articles/europes-coronavirus-testing-programs-creak-as-demand-surges-11602071893>. (Accessed on 21 October 2021).
 48. Frosch D. Covid-19 Testing Is Hampered by Shortages of Critical Ingredient. 22 September 2020. Available from: <https://www.wsj.com/articles/covid-19-testing-is-hampered-by-shortages-of-critical-ingredient-11600772400>. (Accessed on 21 October 2021).
 49. Wise J. Covid-19: What's going wrong with testing in the UK? *BMJ*. 2020;370:m3678.
 50. WHO. Antigen-detection in the diagnosis of SARS-CoV-2 infection. Geneva: World Health Organization, 2021. Available from: <https://www.who.int/publications/i/item/antigen-detection-in-the-diagnosis-of-sars-cov-2infection-using-rapid-immunoassays>. (Accessed on 6 October 2021).
 51. WHO. Recommendations for national SARS-CoV-2 testing strategies and diagnostic capacities. World Health Organization, 2021. Available from: <https://www.who.int/publications/i/item/WHO-2019-nCoV-lab-testing-2021.1-eng>. (Accessed on 21 October 2021).
 52. NHS. Regular rapid lateral flow coronavirus (COVID-19) tests [Internet]. London: UK National Health Service. Available from: <https://www.nhs.uk/conditions/coronavirus-covid-19/testing/regular-rapid-coronavirus-tests-if-you-do-not-have-symptoms/>. (Accessed on 16 August 2021).
 53. NHS. Positive test result for coronavirus (COVID-19) [Internet]. London: UK National Health Service. Available from: <https://www.nhs.uk/conditions/coronavirus-covid-19/testing/test-results/positive-test-result/>. (Accessed on 3 September 2021).
 54. UK Health Security Agency. Testing in United Kingdom [Internet]. GOV.UK. Available from: <https://coronavirus.data.gov.uk/details/testing>. (Accessed on 21 October 2021).
 55. UK Department of Health & Social Care. Weekly statistics for rapid asymptomatic testing (England): 22 July to 28 July 2021. 2021. Available from: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1008939/rapid_testing_22_to_28_july_2021_2.pdf. (Accessed on 21 October 2021).
 56. Indian Council of Medical Research. Advisory for COVID-19 testing during the second wave of the pandemic. Indian Council of Medical Research, 2021. Available from: https://www.icmr.gov.in/pdf/covid/strategy/Advisory_COVID_Testing_in_Second_Wave_04052021.pdf. (Accessed on 21 October 2021).
 57. WHO. Public health criteria to adjust public health and social measures in the context of COVID-19. World Health Organization, 2020. Available from: https://apps.who.int/iris/bitstream/handle/10665/332073/WHO-2019-nCoV-Adjusting_PH_measures-Criteria-2020.1-eng.pdf?sequence=1&isAllowed=y. (Accessed on 21 October 2021).
 58. Kim J-H, An JA-R, Oh SJ, et al. Emerging COVID-19 Success Story: South Korea Learned the Lessons of MERS [Internet]. *Exemplars in Global Health*. Available from: <https://www.exemplars.health/emerging-topics/epidemic-preparedness-and-response/covid-19/south-korea>. (Accessed on 21 October 2021).
 59. Choi S, Han C, Lee J, et al. Innovative screening tests for COVID-19 in South Korea. *Clin Exp Emerg Med*. 2020;7(2):73-7.

60. Fleming KA, Horton S, Wilson ML, et al. The *Lancet* Commission on diagnostics: transforming access to diagnostics. *The Lancet*. 2021.
61. WHO. Genomic sequencing of SARS-CoV-2: a guide to implementation for maximum impact on public health. World Health Organization, 2021. Available from: <https://www.who.int/publications/i/item/9789240018440>. (Accessed on 21 October 2021).
62. The Yellow House. Assessment of the COVID-19 Supply Chain System: Executive summary slide deck. Geneva: World Health Organization, 2021. Available from: <https://www.who.int/publications/m/item/assessment-of-the-covid-19-supply-chain-system-executive-summary-slide-deck>. (Accessed on 21 October 2021).
63. WHO. COVID-19 Supply Chain System: Requesting and receiving supplies. World Health Organization, 2021. Available from: <https://www.who.int/publications/m/item/covid-19-supply-chain-system-requesting-and-receiving-supplies>. (Accessed on 21 October 2021).
64. The Yellow House. Assessment of the COVID-19 Supply Chain System: Executive Summary. Geneva: World Health Organization, 2020. Available from: <https://www.who.int/publications/m/item/assessment-of-the-covid-19-supply-chain-system-executive-summary>. (Accessed on 21 October 2021).
65. The Yellow House. Assessment of the COVID-19 Supply Chain System: Full report slide deck. Geneva: 2021. Available from: <https://www.who.int/publications/m/item/assessment-of-the-covid-19-supply-chain-system-full-report-slide-deck>. (Accessed on 21 October 2021).
66. WHO. Procurement Considerations for COVID-19 Diagnostics. World Health Organization, 2021. Available from: https://www.who.int/docs/default-source/coronaviruse/procurement-considerations-for-covid-19-diagnostics.pdf?sfvrsn=70a480ce_16. (Accessed on 21 October 2021).
67. WHO. Target product profiles for priority diagnostics to support response to the COVID-19 pandemic v1.0. World Health Organization, 2021. Available from: https://cdn.who.int/media/docs/default-source/blue-print/who-rd-blueprint-diagnostics-tpp-final-v1-0-28-09-jc-ppc-final-cmp92616a80172344e4be0edf315b582021.pdf?sfvrsn=e3747f20_1&download=true. (Accessed on 21 October 2021).
68. The Yellow House. Assessment of the Covid-19 Supply Chain System (CSCS): Summary Report. Geneva: 2021. Available from: <https://www.who.int/publications/m/item/assessment-of-the-covid-19-supply-chain-system-report>. (Accessed on 21 October 2021).
69. ACT-Accelerator Partners. Quarterly Update Q2: 1 April - 30 June 2021 Geneva: 2021. Available from: <https://www.who.int/publications/m/item/act-accelerator-quarterly-update-q2-1-april---30-june-2021>. (Accessed on 21 October 2021).
70. FIND. ACT-Accelerator Diagnostics Pillar: Progress [Internet]. Geneva: FIND. Available from: <https://www.finddx.org/covid-19/act-accelerator-progress/>. (Accessed on 21 October 2021).
71. Africa CDC. Africa CDC COVID-19 Dashboard [Internet]. Africa Centres for Disease Control and Preventions. Available from: <https://africacdc.org/covid-19/>. (Accessed on 21 October 2021).
72. Reuters. 10 countries account for 80% of Africa COVID-19 testing: Africa CDC [Internet]. Reuters. Available from: <https://www.reuters.com/article/us-health-coronavirus-africa-testing-idUSKCN2521QZ>. (Accessed on 21 October 2021).
73. Kebede A, Lanyero B, Beyene B, et al. Expanding molecular diagnostic capacity for COVID-19 in Ethiopia: operational implications, challenges and lessons learnt. *The Pan African medical journal*. 2021;38:68-.
74. WHO. Benin boosts COVID-19 response with increased testing [Internet]. World Health Organization; (last updated 23 October 2020). Available from: <https://www.afro.who.int/news/benin-boosts-covid-19-response-increased-testing>. (Accessed on 21 October 2021).
75. FIND. Test Directory [Internet]. Geneva: FIND. Available from: https://www.finddx.org/test-directory/?_region=africa. (Accessed on 21 October 2021).
76. Unitaid. FIND and Unitaid invest to support technology transfer and boost local production of COVID-19 rapid tests in low- and middle-income countries [Internet]. Unitaid; (last updated 15 July 2021). Available from: <https://unitaid.org/news-blog/find-unitaid-technology-transfer-covid-19/#en>. (Accessed on 21 October 2021).
77. The Global Fund. COVID-19 Response: Scaling-Up Testing with Antigen-Detection Diagnostics [Internet]. The Global Fund; (last updated 30 November 2020). Available from: <https://www.theglobalfund.org/en/sourcing-management/updates/2020-11-30-covid-19-response-scaling-up-testing-with-antigen-detection-diagnostics/>. (Accessed on 21 October 2021).
78. Sands P. HIV, tuberculosis, and malaria: how can the impact of COVID-19 be minimised? *Lancet Glob Health*. 2020;8(9):e1102-e3.
79. EIU. The EIU's latest vaccine rollout forecasts [Internet]. The Economist Intelligence Unit; (last updated 28 April 2021). Available from: <https://www.eiu.com/n/eiu-latest-vaccine-rollout-forecasts/>. (Accessed on 21 October 2021).

80. WHO. Tracking SARS-CoV-2 variants [Internet]. World Health Organization. Available from: <https://www.who.int/en/activities/tracking-SARS-CoV-2-variants/>. (Accessed on 12 November 2021).
81. GISAID. Enabling rapid and open access to epidemic and pandemic virus data [Internet]. GISAID. Available from: <https://www.gisaid.org/about-us/mission/>. (Accessed on 21 October 2021).
82. Maxmen A. One million coronavirus sequences: popular genome site hits mega milestone [Internet]. Nature; (last updated 23 April 2021). Available from: <https://www.nature.com/articles/d41586-021-01069-w>. (Accessed on 21 October 2021).
83. GISAID. Index [Internet]. GISAID. Available from: <https://www.gisaid.org/index.php?id=208>. (Accessed on 21 October 2021).
84. UN Department of Economic and Social Affairs Population Dynamics. World Population Prospects 2019 [Internet]. United Nations Department of Economic and Social Affairs Population Dynamics. Available from: <https://population.un.org/wpp/>. (Accessed on 21 October 2021).
85. Tan WM. Median and 90th percentile turnaround time to obtain virus whole genome sequencing result from time of COVID-19 test [Internet]. Ministry of Health Singapore; (last updated 6 July 2021). Available from: <https://www.moh.gov.sg/news-highlights/details/median-and-90th-percentile-turnaround-time-to-obtain-virus-whole-genome-sequencing-result-from-time-of-covid-19-test>. (Accessed on 21 October 2021).
86. NCBI Virus. SARS-CoV-2 Data Hub [Internet]. Available from: <https://www.ncbi.nlm.nih.gov/labs/virus/vssi/#/sars-cov-2>. (Accessed on 27 July 2021).
87. COVID-19 Data Portal. COVID-19 Data Portal [Internet]. European Commission, EMBL-EBI and partners. Available from: <https://www.covid19dataportal.org/>. (Accessed on 21 October 2021).
88. GISAID. Map of tracked variant occurrence [Internet]. Available from: <https://www.gisaid.org/hcov19-variants/>. (Accessed on 21 October 2021).
89. The COVID-19 Genomics UK (COG-UK) consortium. An integrated national scale SARS-CoV-2 genomic surveillance network. *The Lancet Microbe*. 2020;1(3):e99-e100.
90. Msomi N, Mlisana K, de Oliveira T, et al. A genomics network established to respond rapidly to public health threats in South Africa. *The Lancet Microbe*. 2020;1(6):e229-e30.
91. Makoni M. Africa's \$100-million Pathogen Genomics Initiative. *The Lancet Microbe*. 2020;1(8):e318.
92. WHO. COVID-19 genome sequencing laboratory network launches in Africa [Internet]. World Health Organization; (last updated 10 September 2020). Available from: <https://www.afro.who.int/news/covid-19-genome-sequencing-laboratory-network-launches-africa>. (Accessed on 21 October 2021).
93. Lopez Bernal J, Andrews N, Gower C, et al. Effectiveness of Covid-19 Vaccines against the B.1.617.2 (Delta) Variant. *N Engl J Med*. 2021;385(7):585-94.
94. AstraZeneca. Vaxzevria is highly effective after one dose against severe disease or hospitalisation caused by Beta and Delta variants of concern [Internet]. AstraZeneca; (last updated 23 July 2021). Available from: <https://www.astrazeneca.com/media-centre/press-releases/2021/vaxzevria-is-highly-effective-after-one-dose-against-severe-disease-or-hospitalisation-caused-by-beta-and-delta-variants-of-concern.html>. (Accessed on 21 October 2021).
95. Peeling RW, Boeras D, Wilder-Smith A, et al. Need for sustainable biobanking networks for COVID-19 and other diseases of epidemic potential. *The Lancet Infectious Diseases*. 2020;20(10):e268-e73.
96. Catchpole D, Florindi F, Ahern C, et al. Expanding the BBMRI-ERIC Directory into a Global Catalogue of COVID-19-Ready Collections: A Joint Initiative of BBMRI-ERIC and ISBER. *Biopreservation and Biobanking*. 2020;18(5):479-80.
97. Vandenberg O, Martiny D, Rochas O, et al. Considerations for diagnostic COVID-19 tests. *Nature Reviews Microbiology*. 2021;19(3):171-83.
98. BBMRI-ERIC, ISBER. BBMRI-ERIC Directory [Internet]. Graz, Austria: BBMRI-ERIC. Available from: <https://www.bbmri-eric.eu/services/isber-biobank-collaboration/>. (Accessed on 6 October 2021).
99. Smith KF, Goldberg M, Rosenthal S, et al. Global rise in human infectious disease outbreaks. *Journal of The Royal Society Interface*. 2014;11(101):20140950.
100. Jones KE, Patel NG, Levy MA, et al. Global trends in emerging infectious diseases. *Nature*. 2008;451(7181):990-3.
101. Carroll D, Morzaria S, Briand S, et al. Preventing the next pandemic: the power of a global viral surveillance network. *BMJ*. 2021;372:n485.
102. PATH. Global Availability of COVID-19 Diagnostic Tests [Internet]. Seattle, WA: PATH; (last updated 20 July 2021). Available from: <https://www.path.org/programs/diagnostics/covid-dashboard-global-availability-covid-19-diagnostic-tests/>. (Accessed on 7 October 2021).
103. FDA. Historical Information about Device Emergency Use Authorizations [Internet]. US Food and Drug Administration;

- (last updated 29 September 2021). Available from: <https://www.fda.gov/medical-devices/emergency-use-authorizations-medical-devices/historical-information-about-device-emergency-use-authorizations#ivd>. (Accessed on 21 October 2021).
104. PATH. Implication of variants on COVID-19 antigen test detection [Internet]. PATH. Available from: <https://www.path.org/programs/diagnostics/covid-dashboard-implication-variants-covid-19-antigen-test-detection/>. (Accessed on 21 October 2021).
 105. PATH. Implications of variants on COVID-19 molecular test detection [Internet]. PATH. Available from: <https://www.path.org/programs/diagnostics/covid-dashboard-implications-variants-covid-19-molecular-test-detection/>. (Accessed on 21 October 2021).
 106. Cepheid. SARS-CoV-2 Test Information [Internet]. Cepheid. Available from: <https://www.cephheid.com/en/tests/Critical-Infectious-Diseases/Xpert-Xpress-SARS-CoV-2-Flu-RSV>. (Accessed on 21 October 2021).
 107. Newington Pharmacy. COVID-19 Saliva PCR Testing Edinburgh [Internet]. Newington Pharmacy. Available from: <https://www.newingtonpharmacy.org.uk/services/covid-19-saliva-pcr-testing-edinburgh/>. (Accessed on 21 October 2021).
 108. Broad Institute. Questions and Answers about CRISPR [Internet]. Available from: <https://www.broadinstitute.org/what-broad/areas-focus/project-spotlight/questions-and-answers-about-crispr>. (Accessed on 21 October 2021).
 109. Dominic N. Decentralizing testing for COVID-19 and beyond [Internet]. PATH; (last updated 29 July 2021). Available from: <https://www.path.org/articles/decentralizing-testing-covid-19-and-beyond/>. (Accessed on 21 October 2021).
 110. FDA. Coronavirus (COVID-19) Update: FDA Issues Authorization for First Molecular Non-Prescription, At-Home Test [Internet]. US Food and Drug Administration; (last updated 5 March 2021). Available from: <https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-issues-authorization-first-molecular-non-prescription-home-test>. (Accessed on 21 October 2021).
 111. King's College London. First-ever shipping container labs for COVID-19 testing [Internet]. King's College London; (last updated 21 May 2020). Available from: <https://www.kcl.ac.uk/news/first-ever-affordable-shipping-container-labs-for-covid-19-testing>. (Accessed on 21 October 2021).
 112. Walker KT, Donora M, Thomas A, et al. CONTAIN: An open-source shipping container laboratory optimised for automated COVID-19 diagnostics. *bioRxiv*. 2020:2020.05.20.106625.
 113. Open Cell. Press Release: CONTAIN - Mobile COVID-19 Testing Lab [Internet]. Open Cell; (last updated 21 May 2020). Available from: <https://www.opencell.bio/news-old/press-release>. (Accessed on 21 October 2021).
 114. Martell A, Parker N. The U.S. has more COVID-19 testing than most. So why is it falling so short? [Internet]. Reuters; (last updated 27 July 2020). Available from: <https://www.reuters.com/article/us-health-coronavirus-usa-testing-insight/USKCN24S19H?> (Accessed on 6 October).
 115. UC Merced Researchers. COVIDPoops19 Dashboard [Internet]. Available from: <https://www.covid19wbec.org/covidpoops19>. (Accessed on 21 October 2021).
 116. US CDC. Overview of Testing for SARS-CoV-2 (COVID-19) [Internet]. US Centers for Disease Control and Prevention; (last updated 2 August 2021). Available from: <https://www.cdc.gov/coronavirus/2019-ncov/hcp/testing-overview.html>. (Accessed on 21 October 2021).
 117. Naughton CC, Roman FA, Alvarado AGF, et al. Show us the Data: Global COVID-19 Wastewater Monitoring Efforts, Equity, and Gaps. *medRxiv*. 2021:2021.03.14.21253564.
 118. WHO. First-ever WHO list of essential diagnostic tests to improve diagnosis and treatment outcomes [Internet]. World Health Organization. Available from: <https://www.who.int/news/item/15-05-2018-first-ever-who-list-of-essential-diagnostic-tests-to-improve-diagnosis-and-treatment-outcomes>. (Accessed on 21 October 2021).
 119. WHO. WHO Model Lists of Essential Medicines [Internet]. World Health Organization. Available from: <https://www.who.int/groups/expert-committee-on-selection-and-use-of-essential-medicines/essential-medicines-lists>. (Accessed on 21 October 2021).
 120. Boehme C, Hannay E, Pai M. Promoting diagnostics as a global good. *Nature Medicine*. 2021;27(3):367-8.
 121. Pai M. To Improve Access To Diagnostics, Countries Must Adapt The WHO Essential Diagnostics List [Internet]. Forbes; (last updated 1 February 2021). Available from: <https://www.forbes.com/sites/madhukarpai/2021/02/01/who-essential-diagnostics-list-expands-to-include-covid-19-and-much-more/?sh=256484373323>. (Accessed on 21 October 2021).
 122. WHO. Q&A: How is COVID-19 transmitted? [Internet]. Geneva: World Health Organization. Available from: <https://www.who.int/vietnam/news/detail/14-07-2020-q-a-how-is-covid-19-transmitted>. (Accessed on 7 October 2021).
 123. Kelly-Cirino CD, Nkengasong J, Kettler H, et al. Importance of diagnostics in epidemic and pandemic preparedness. *BMJ Global Health*. 2019;4(Suppl 2):e001179.

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