Considerations for diagnostic COVID-19 tests

Olivier Vandenberg[1,2,3]✉, *Delphine Martiny*[4], *Olivier Rochas*[5], *Alex van Belkum*[6]✉ *and Zisis Kozlakidis*[7]

Abstract | During the early phase of the coronavirus disease 2019 (COVID-19) pandemic, design, development, validation, verification and implementation of diagnostic tests were actively addressed by a large number of diagnostic test manufacturers. Hundreds of molecular tests and immunoassays were rapidly developed, albeit many still await clinical validation and formal approval. In this Review, we summarize the crucial role of diagnostic tests during the first global wave of COVID-19. We explore the technical and implementation problems encountered during this early phase in the pandemic, and try to define future directions for the progressive and better use of (syndromic) diagnostics during a possible resurgence of COVID-19 in future global waves or regional outbreaks. Continuous global improvement in diagnostic test preparedness is essential for more rapid detection of patients, possibly at the point of care, and for optimized prevention and treatment, in both industrialized countries and low-resource settings.

During a pandemic there are multiple concurrent clinical priorities, including the need to understand the pathophysiology of the disease, optimized patient care and prevention of future infections[1]. The detection and characterization of the etiological agent or its immunological consequences in the host are the necessary starting points[2]. Being able to define the pathogen, biologically and genetically, and whether it is inducing (protective) immunity are key in the development of protective and curative protocols against future persisting disease. The current diagnostic procedures are twofold. First there is the direct detection of (parts of) the virus. This can be done by culture of the virus, detection of one or more of its proteins and, the method used most frequently during the present pandemic, direct detection of nucleic acids or detection via amplification of nucleic acids. The latter are what are currently called 'molecular tests'. Immunological tests detect the consequences of infection by the virus in the host. This is most frequently focused on the detection of virus-specific antibodies, whereas some specialized laboratories may also be capable of defining the cellular immune response. Here we will mostly focus on the nucleic amplification tests, with illustrations of how immune tests may complement molecular tests in several cases.

Diagnostics can be used in various manners, the so-called use cases. These include triage of symptomatic individuals in an epidemic or endemic setting, triage of at-risk presymptomatic and symptomatic individuals in endemic settings, confirmatory testing, diagnosis of symptomatic individuals in endemic or epidemic settings, differential diagnosis in endemic or epidemic settings, testing of patients with previous exposure to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2; the cause of the coronavirus disease 2019 (COVID-19) pandemic), surveillance at sites of previous or potential outbreaks and environmental monitoring (Foundation for Innovative New Diagnostics (FIND)). The use case determines the way in which diagnostic tests are used optimally[3].

The ongoing COVID-19 pandemic has underpinned the central position of diagnostic testing in outbreak control[4]. Ending the pandemic involves the accurate application of diagnostic testing in high volumes and the rapid use of the results to help implement the appropriate therapy and prevent further spread. The value of integrated diagnostics in the management of the current COVID-19 wave and possible future COVID-19 waves is high, especially for the molecular detection of the virus, and for the qualification and quantification of the immunological host response[5]. The rapid implementation of COVID-19 tests requires critical assessment and adequate 'jumping' of the initial hurdles during the developmental and regulatory process. Test design, validation and verification, emergency use approval and the manufacturing of test kits in (very) high numbers are just a few examples of such obstacles. From the perspective of a routine-diagnostic microbiology laboratory, the setting up of high-throughput diagnostic pipelines, the logistics involved and the optimization of pragmatic use of test results were encountered as important problems during the first wave of the ongoing COVID-19 pandemic.

✉*e-mail: olivier.vandenberg@lhub-ulb.be; alex.vanbelkum@biomerieux.com*

https://doi.org/10.1038/s41579-020-00461-z

Ultimately, optimized diagnostic tools will provide guidance in the development of therapeutics and vaccines (FIG. 1). Diagnostic lessons learnt during the first wave of the COVID-19 pandemic should be used to help prepare for the next wave, which is anticipated by many.

In this Review we address early COVID-19 test design and the design-, development-, production- and distribution-associated hurdles. We discuss the importance of quality control and options for mass production as well as the practical issues around broad and rapid implementation of entirely new tests that have not undergone classic evaluation and validation. We also estimate the effect of new-generation COVID-19 tests on laboratory medicine practice, the need for new approaches towards biobanking and the economic consequences of the pandemic. Of note, we focus on molecular assays, with limited presentation and explanation of serological tests.

COVID-19 testing

SARS-CoV-2 is an RNA virus, and thus all available RNA detection formats can potentially be applied to detect the virus[6]. For adaption towards the more frequently used diagnostic DNA detection formats, the viral genome needs to be transcribed into a DNA complement by reverse transcriptase. Currently, the preferred SARS-CoV-2 test is DNA amplification by PCR, and the real-time versions of such tests were among the earliest available. Such tests were previously developed during the emergence of SARS-CoV and Middle East respiratory syndrome coronavirus (MERS-CoV), and therefore a PCR-based testing approach for SARS-CoV-2 was an obvious route to take[7]. Moreover, monitoring the host response is important in identifying individuals who have already been infected with SARS-CoV-2 as well as for assessing future vaccine efficacy. For that purpose, again similarly to tests previously developed for SARS-CoV and MERS-CoV, a broad variety of tests detecting specific SARS-CoV-2 antigens and antibodies were developed. Over the past months, all currently available technologies have been exploited to rapidly develop highly sensitive and highly specific detection and characterization assays for SARS-CoV-2. In this section we briefly discuss these test formats, but we will not consider functional tests that assess virus inactivation or the therapeutic effect of cellular immune responses[1]. Such assays are mostly limited to highly specialized laboratories and do not yet have a major impact on current global health-care practice.

Diagnostic tests developed and their application. Direct diagnostic testing to detect active SARS-CoV-2 infections mostly involves reverse transcriptase real-time PCR (rtPCR), although different molecular technologies, such as CRISPR-mediated detection or loop-mediated isothermal amplification, have also been applied[8–12]. Operation and application of these molecular tests is in keeping with those for previously developed tests that detect infectious agents[13].

Moreover, rapid antigen detection tests have also been developed to detect active infection, although a limited number of such tests are available[14,15]. However, in comparison with rtPCR, rapid antigen detection tests lack sensitivity, and owing to the increased risk of false-negative results, they are considered as an adjunct to rtPCR tests[16,17]. Olfactory tests using electronic 'noses' or even dogs have also been presented, but these tests are not yet directly applied in patient care[18,19].

Antibody testing can have a mostly complementary role to rtPCR tests in the diagnosis of COVID-19, at approximately 10 days or more after the onset of symptoms, in assessing past infections and defining the dynamics of the individual humoral responses in individual patients or in patient cohorts undergoing certain forms of treatment[20,21]. Immune-based assays, such as lateral flow assays, are usually designed for detecting human IgA, IgM and/or IgG antibodies or virus antigens[22,23]. Targets for the tests have been identified by comparative screening for genomic regions that have a low mutation frequency to avoid primer and antibody mismatches, and enhance test quality and stability[24]. Hundreds of such diagnostic tests have now been developed (Supplementary Table 1), and technical reviews of their comparative performance assessment have been published recently[25–32]. Very recently, the *Journal of Clinical Microbiology* dedicated nearly an entire issue to COVID-19 testing[33].

Data are available on more than 240 Emergency Use Authorization (EUA)-level COVID-19 diagnostic tests (as of 5 September 2020), and the number of commercially manufactured COVID-19 molecular tests and the number of commercially manufactured immunoassays are approximately equivalent. FIND is or has been assessing more than 800 diagnostic assays, more than 250 of which are so-called rapid tests taking less than 30 minutes to generate a result. The use of immunoassays at the point of care (POC) remains to be universally accepted as part of the postrestriction COVID-19 control strategy[34]. It is important to note that all novel tests urgently need useful clinical cut-off values to help enhance their medical value[35]. At present, negative results in either of these test types do not completely rule out current or past infections owing to possible false-negative results[36,37]. Whether COVID-19 tests need to be quantitative or qualitative is subject to continued debate[38]. Quantitative test results may be a prerequisite for the choice of COVID-19 treatment strategy, for treatment follow-up or for the support of vaccine trials.

Author addresses

[1]Innovation and Business Development Unit, Laboratoire Hospitalier Universitaire de Bruxelles — Universitair Laboratorium Brussel, Université Libre de Bruxelles, Brussels, Belgium.
[2]Center for Environmental Health and Occupational Health, School of Public Health, Université Libre de Bruxelles, Brussels, Belgium.
[3]Division of Infection and Immunity, Faculty of Medical Sciences, University College London, London, UK.
[4]Department of Microbiology, Laboratoire Hospitalier Universitaire de Bruxelles — Universitair Laboratorium Brussel, Université Libre de Bruxelles, Brussels, Belgium.
[5]Strategic Intelligence, Corporate Business Development, bioMérieux, Chemin de L'Orme, France.
[6]Open Innovation and Partnerships, bioMérieux, La Balme Les Grottes, France.
[7]Laboratory Services and Biobank Group, International Agency for Research on Cancer, World Health Organization, Lyon, France.

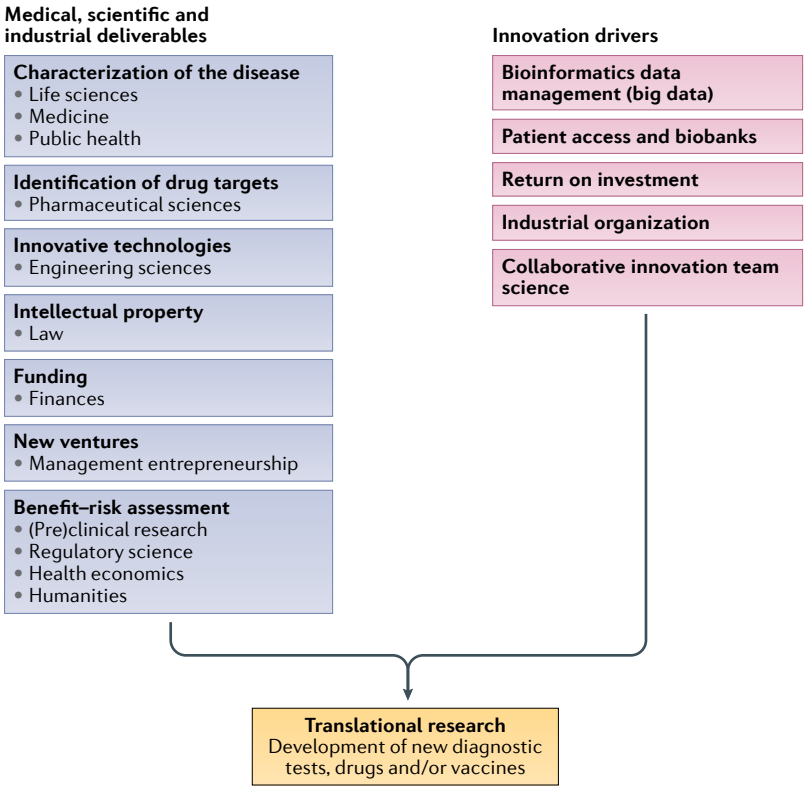

Fig. 1 | **Advancing translational medicine.** A schematic overview of the key innovation drivers, technologies, institutes and partners needed for the development of new diagnostic tests, drugs and/or vaccines. The boxes on the left identify some of the important medical, scientific and industrial deliverables where an interconnected approach covering each steps from fundamental research to commercialization is needed. Translational medicine relies on the interconnection of multidisciplinary teams of life scientists able to translate basic scientific discoveries into changes in clinical practice supported by expertise from engineering, law and financial sciences. The most important facilitators are indicated in each box. The column on the right lists the innovation drivers. Current innovation drivers combine the ability to process large amounts of data and to facilitate access to biological material through easy access to a biobank. The intense collaboration between academia and industry, with detailed sharing of research goals and directions during the coronavirus disease 2019 (COVID-19) pandemic, through the identification of an optimal collaborative approach capitalizing on the strengths of both made possible the rapid development of new diagnostic tests, drugs and possible vaccines against COVID-19.

Another important aspect is surveillance: the rapid and continuous detection efforts aimed at early recognition, isolation and treatment of those infected with the virus[29]. When an infection has been diagnosed, usually on the basis of a combination of clinical parameters (for example, fever, sore throat or loss of smell and taste) and a direct COVID-19 test, search and control policies will be initiated for the detection of those people who were in recent direct contact with the patient and who will then be subjected to confinement and/or COVID-19 testing. For adequate surveillance and tracing, both regionally and globally epidemiological virus typing is important. Next-generation nucleotide sequencing is used to define polymorphisms and to define interrelatedness between virus strains[39,40]. Such approaches have been instrumental in defining the global spread of the virus and may also help to define virus variants with different biological capacities (for example, ease of spread, pathogenicity and tissue tropism). Metagenomic next-generation nucleotide sequencing can also be used diagnostically for virus detection in patients[41] or in environmental samples (such as wastewater)[42].

Considerations for the development, production and distribution of diagnostic COVID-19 tests. The superficial sketch of test design provided in the previous subsection represents only the first steps in test development. Initial design, experimental small-scale laboratory validation and, if at all possible, clinical evaluation using high-quality and patient specimens are followed by industrial scale-up. The test format needs to be compatible with large-scale production, which in the case of COVID-19 was possible for tests that were supported on pre-existing platforms[43]. Any test that was developed rapidly but was not applicable on an existing instrument had a substantial disadvantage to reach the market[44]. Possible exceptions are tests that are presented in a platform-agnostic layout and that can be combined with any type of instrument already available to laboratory-based diagnosticians[45].

Moreover, instruments and tests need to be abundantly available at a local and global scale to ensure scale-up of clinical testing. The preavailability of a platform also enables the broad geographical spread of the test. If an installed base of instruments already exists, then new tests in the already existing format can be rapidly and reliably added to the testing repertoire of a laboratory. In such cases, assay transport and storage are two remaining hurdles, and test distribution in itself may be an important obstacle. The shelf life of a test, the temperature tolerance of the test components and simple characteristics such as the size and weight of the package are all important parameters in the perceived ease of distribution. Once the instrument and assays are available to users, instrument availability and human expertise may still be limiting factors in high-throughput test application[46]. Finally, there needs to be a balance between the laboratory test capacity and the number of requests for tests, and the fluctuation in the number of tests requested and changes in priority test recommendations pose additional problems. It is clear that the entire global population cannot be tested (repeatedly) at the same time, and choices need to be made to prioritize patient groups or groups at increased risk of being infected (for example, health-care workers)[47]. When these groups have been identified, sampling processes (and their logistics) need to be designed and implemented. Simplicity of sampling and homogeneity of the sample itself are important parameters to consider, and other sources, such as saliva, have been considered as alternative specimens for COVID-19 testing[48]. Testing of sample pools has been suggested as a solution to minimize test costs while maintaining test sensitivity and specificity, specifically in settings where the incidence of infection is low[49]. Pooling of samples may generally induce practical pretesting burden and may lower traceability, and thus sample pooling should perhaps be restricted to times of reagent shortage. The jury is still out on whether pooling is diagnostically robust and cost-effective, with conflicting reports having been

published[50–52]. In addition, the current consensus is that individual laboratories should perform validation studies before embarking on large-scale pooling strategies[52].

Many 'diagnostic streets' or drive-through test facilities were established as soon as COVID-19 tests became available, and many laboratories opted for externalization of testing (using tents, dedicated buildings and separation between sample taking and actual testing)[53]. Finally, there is a continuous need for means of rapid and reliable result dissemination, an issue that is covered in privacy loopholes but also the need to use test results beyond the privacy of an individual patient.

Test results are key in surveillance and outbreak management and should be used to inform infection prevention measures. Diagnostic tests need careful consideration and validation before being launched. This is often underestimated and underappreciated by scientists and the community, and involves processes that are costly and time-consuming.

Quality control of COVID-19 testing

The EUA by the US Food and Drug Administration (FDA) covers for most of the more common test quality parameters (for example, sensitivity, specificity, positive and negative predictive values, robustness and reproducibility). More than 160 tests have been approved and provided with the EUA label, and more than 80% of these were molecular tests, with the rest being antibody detection assays and a small number of antigen detection tests (Supplementary Table 1). In addition, the provision of positive control templates was effectively implemented by the European Virus Archive goes Global (EVAg) project, supplying specific products such as RNA transcripts for assays through its online catalogue by mid-January 2020 (REFS[54,55]). Technical qualification data, based on the use of cell culture materials and synthetic nucleic acid constructs, as well as results from exclusivity testing of 75 clinical samples, were included in the first diagnostic protocol provided to the WHO on 13 January 2020. The efficient collaboration within an informal network comprising clinical laboratories servicing consortia of hospitals, academic groups and test manufacturers (forged through previous recent outbreaks and/or operational consolidations) represented a key element in the European response against COVID-19 by promoting the development of new diagnostic tools while supporting acute clinical and international needs (for example, COMBACTE[56]).

On 4 February 2020, the FDA issued an EUA for the COVID-19 rtPCR assay developed by the US Centers for Disease Control and Prevention (CDC), thereby enabling CDC-qualified laboratories to perform the test[57]. Unfortunately, and despite this EUA registration, as described in a news article, there were problems with one of the reagents described in the CDC protocol, partially blocking rapid implementation of the test or leading to retraction of test results. On 29 February 2020, new guidance was issued for laboratories to be able to develop and implement COVID-19 molecular diagnostic tests before obtaining EUA[58–61] (see also Supplementary Table 1). The relative technical ease with which such diagnostic tests could be designed and the stable nature of the target genetic material of the pathogen were contributing factors to test quality and reproducibility, which resulted in various tests being developed within a few months (BOX 1). Diagnostic testing without quality control at all levels (from design up and until end use) is without value and results in abuse of valuable and possibly scarce resources.

Test sensitivity and specificity

The analytical specificity of a molecular COVID-19 test is its ability to determine exclusively the analyte it intends to measure in the presence of off-target templates or interfering substances under well-controlled laboratory conditions. The analytical sensitivity of an assay often describes the lowest amount of analyte that can be accurately measured through an assay. Adequate analytical specificity and sensitivity will in the end lead to optimal clinical performance. For molecular COVID-19 tests, the quality and relevant abundance of RNA in collected samples (which is heavily dependent on the type and site of collection) are crucial for the sensitivity of the assays[62,63]. For example, the rate of rtPCR detection of SARS-CoV-2 in patients with COVID-19 is as high as 93% in bronchoalveolar lavage fluid, but is 72% in sputum and 63% in nasopharyngeal swabs, while it is only 32% in pharyngeal swabs and 29% in stool[64]. A later, small hospital cohort study among patients with laboratory-confirmed COVID-19 reported that the positivity rate of rtPCR for SARS-CoV-2 is 15–30% in blood and 14–38% in rectal swabs[65]. In this study, blood samples were obtained from 23 patients, and rectal swabs were obtained from 15 patients. The analytical sensitivity of the new molecular tests was reported to be high from the outset, even though a number of studies had to use target material from cultures of Vero cells or synthetic viral DNA fragments owing to the regulatory inability to access samples from the early infected populations in China[45]. This validation was repeated with clinically available samples from infected patients in Europe and other geographical regions, including North America and South America. This implies that for none of the currently used COVID-19 tests is the absolute sensitivity (RNA genomes per millilitre) known because there simply is not a clear gold standard for testing available for a pathogen that has been known for about half a year. It has to be emphasized that even 'poor but cheap' tests

Box 1 | **Defining the clinical validation of diagnostic tests**

Clinical validation of diagnostic tests, as considered in this Review, involves assessing the performance of the test in comparison with a reference test that is capable of assigning the sample status without error. The generic validation of a novel technology should be performed on a larger scale, ideally in multiple laboratories, and should include a much more comprehensive investigation of the critical parameters relevant to the specific technology to provide the highest chance of detecting sources of variation and interference. The competence of testing and calibration via new laboratory-developed methods or acquired methods adopted by the laboratory may also be appropriate if they are sufficiently validated. Laboratories have to validate all non-standard methods, and all standard methods used outside their intended scope. This covers both laboratory-based methods and predictive models using diagnostic data to predict the severity of disease, for instance[171]. For amplifications and modifications of standard methods, it has to be confirmed that the methods are fit for the intended use through the provision of a well-recorded, validation protocol and resulting outcomes.

may be of diagnostic significance if the shortcomings of the tests are well considered[66]. It is relevant to note that it is difficult to obtain precise test quality data on locally used tests in China. Many molecular assays have been developed in China, and only a few of them have obtained FDA EUA accreditation (for example, the tests developed by Xiamen Zeesan Biotech, Jiangsu Cowin Biotech and Bioperfectus Technologies; see In Vitro Diagnostics EUAs). In general, the limitations of many of the published validation studies for COVID-19 diagnostic tests were low sample numbers, the differences in the processes for collection, storage and processing of samples before the diagnostic tests (preanalytical bias) and the lack of validation by independent third parties. All of the studies were performed using disperse clinical parameters, a feature also hampering the development of diagnostic tests during previous coronavirus outbreaks[13]. These are not necessarily new aspects[67], although the need for timely delivery of new diagnostic assays allowed them to re-emerge. An entirely novel aspect during this outbreak was the widespread use of preprint servers for sharing research data before peer-review (for example, medRxiv or bioRxiv), where studies appeared evaluating the relative performances of different diagnostic technologies[68]. Still, caution should be exercised with interpretation of non-peer-reviewed manuscripts, and whether easier access to technical and comparative information has been instrumental in getting the tests to the market sooner or increasing their end-user adoption remains to be addressed[69]. Finally, it is very important to note that no biological tests have 100% sensitivity and 100% specificity, which needs to be considered when diagnostic results are translated into clinical practice.

COVID-19 testing in low-resource settings

The WHO ASSURED criteria define the markers that affect availability of diagnostic testing in remote settings. Affordability, sensitivity, specificity, user-friendliness, rapidity and robustness, being free of equipment and being easily deliverable to end users are the key drivers towards diagnostic readiness under difficult circumstances. In addition, the clinical validation in low-resource settings needs to establish diagnostic performance in the target population with its co-endemic diseases, some of which may be seasonal or geographically disperse[70]. Most of the laboratories located in low-resource settings may not possess the costly platforms needed to run well-performing commercial tests. Also, underfunded rural clinics or laboratories in politically unstable environments may face very specific local problems[71]. In addition, to comply with Standards for Reporting of Diagnostic Accuracy Studies (STARD) guidelines[72], studies should actively observe and record the operational characteristics (sensitivity, specificity, precision and on on) of a COVID-19 diagnostic test. Environmental stability requirements must be contextual too. For example, stability testing should include 'open pouch' scenarios; that is, opening the package or 'prefilling' of test tubes and leaving them on the bench (in a humid tropical environment) pending reception of samples[73]. Shelf life is an important determinant of usefulness under such conditions. The user-friendliness of the test must also be assessed according to specific criteria for low-resource settings and not using, for example, a European-context method (SKUP)[74]. Most of the POC immunoassays detecting COVID-19 antigens or antibodies (which are frequently used in low-resource settings) are still being validated by FIND. There are substantial information and expertise gaps between laboratories in industrialized countries versus those in low-resource settings even in the case that the latter have access to diagnostic tests[75]. The positioning of the use cases as defined above differs depending on the financial status of the laboratory.

Mass production of tests

Infectious disease outbreaks tend to be categorized as low-frequency, high-impact supply chain-disruptive events[76]. They represent a supply chain risk characterized by long-term disruption and unpredictable scaling; simultaneous disruption in the supply chain (for example, manufacturing) and the population (for example, pandemic); and simultaneous disruptions in supply, demand and logistic infrastructure[77]. This disruption was palpable for COVID-19 diagnostic tests both in the manufacturing disruption observed and in the downstream logistics infrastructure delivering diagnostic tests to the end users. The tight interoperability of the supply chain as well as the initial (physical and economic) lockdown of China, representing a low-tier supply base for a large part of the manufacturing operations globally, meant that manufacturing would be one of the hardest-hit economic sectors[78,79]. Therefore, a dual bottleneck emerged early on in the pandemic in terms of sourcing the biological materials as well as sourcing the primary sources for manufacturing. The shortage of reagents and disposables is one of the most obvious later-stage problems once an outbreak becomes more widespread and ultimately pandemic[80,81]. In such instances it may become mandatory for manufacturers to start sharing production processes and recipes for reagents[82].

A number of governmental interventions, including direct financial investments, loans and the appointment of special COVID-19 functionaries (with responsibilities for obtaining tests, instruments, vaccines and informing the public, among functions) and policymakers, were initiated to support manufacturing capacity. In the USA, congressional lawmakers introduced legislation to alter the regulatory framework governing laboratory-developed tests[83]. The interventions further included active scouting and import of resources outside usual territories, the continued operation of manufacturing businesses, mobilization towards critical supplies, including the repurposing of manufacturing capacity, and planning for further support in the post-COVID-19 era[84,85]. However, the rapid publication of formal guidelines does not necessarily equate to an increased production capacity for diagnostic tests, as the production of such tests tends to have a particular technological specification and complex manufacturing, and thus manufacturing flexibility and scalability are harder to achieve[86,87]. During a pandemic, the disease burden limits the availability of personnel, and the need to work under protected conditions (masks and suits) does not promote

efficiency. Besides the supply chain issue, intellectual property has been an issue leading to the lack of testing. In the Netherlands, Roche finally revealed the contents of its lysis buffer but only after forceful public uproar[82].

However, the severe initial manufacturing disruption seems to have been temporary[88] (BOX 2). It has currently been overcome through existing networks, expertise and industrial capacity, in addition to regulatory and governmental support[89,90]. Still, sterile swabs for sampling the throat and/or nasopharynx are in very high demand globally, which is sometimes a limiting factor, and test penetration in, for instance, Africa is far from complete[91,92]. Of note, problems of test penetration and availability needed to be solved in the USA and other industrialized countries as well[93,94]. However, regional success stories involving, for instance, local test or tool production were reported from South Africa and Rwanda[95,96]. Although some initial cost estimates of the COVID-19 disruption in the health-care industry have been published[97–99], they are likely to be too preliminary at this point in terms of their accuracy. Estimating the costs of such a complex industrial pivoting is difficult as it affects at a minimum the costs of developing and generating new products, the transformation of the production lines and any potential losses from established products not manufactured during the given period[1]. Mass production of diagnostic tests is complex, and mass use of such tests relies on high-level expertise in the end-user laboratory.

Implementation of new tests

Owing to the different health-care models that coexist in Europe, the local testing strategies included decentralized and fully centralized strategies, with a range of in-between solutions, but they were always anchored on diagnostics[92]. The availability of large-scale testing is crucial for monitoring progression or decline of the outbreak and for informing the lockdown exit strategy. Testing capacity has grown in Europe, but at markedly different rates between countries (FIG. 2). Whereas the UK government centralized all testing in a number of reference laboratories[100], Germany relied on a clinical laboratory network that enabled the detection of the virus in collected samples within 2.5 hours[101]. Either way, by combining different levels of expertise, consolidated laboratories not only processed large volumes of samples but also supported surveillance systems[102]. Although the best surveillance system still needs to be defined, the setting up of networks of regional sequencing centres hosted in academic institutions and/or public health agencies provided a close-to-real-time sequencing facility that enabled genomic data to be interpreted and used locally for epidemiological monitoring[103]. The large-scale use of such sequencing centres in Europe for the assessment of how the virus interacts with host cofactors and the health consequences of COVID-19 are continuously expanded and improved[104].

In low-resource settings, health authorities face many challenges in terms of the implementation of testing, including the lack of infrastructure, trained personnel, reagents and state-of-the-art equipment, which hampers widespread COVID-19 testing and surveillance. In this context, the WHO rapidly called for research on POC diagnostics for use at the community level[105]. Despite the support provided by the Africa Centres for Disease Control and Prevention and the WHO in the supply of testing equipment and reagents, such provisions often did not reach remote areas owing to severe shortages. In other developing regions, similar initiatives were promoted by regional and international health surveillance institutes. In South-East Asia this was pushed, for instance, by the Vietnam National Steering Committee[106], whereas, for instance in South America, the state of São Paulo in Brazil actively supported the use of diagnostics in maintaining social distancing guidelines[107]. Still, and despite this type of support, suboptimal and delayed diagnostics in many developing regions and consequent problems in the efficacy of disease suppression were expected[108–110]. In addition, focusing on COVID-19 tests resulted in a decrease in the availability of tests for HIV-1 infection, malaria and tuberculosis. This destabilizes these three targets and will prevent the reaching of the 2030 Sustainable Development Goals of ending the epidemics of these diseases[111]. As articulated recently in a news article by several ethicists "crises offer no excuse for the lowering of scientific standards"[112]. In the case of COVID-19, the proliferation of new diagnostics that have been validated only by small studies may result in the diversion of already scarce resources and even guide towards ineffective practices[112]. The need for the development of new tests with high internal standards of quality controls and well-validated processes remains ever present. Finally, it is important to consider that COVID-19 testing negatively affects normal routine diagnostics as, for example, laboratory budgets and resources need to be reallocated[3].

Laboratory medicine

Multiplexed, clinically integrated diagnostics. The COVID-19 pandemic has repositioned laboratory medicine at the centre of health-care systems. The further expansion of testing capacity at the primary care level will be a key step for the rapid detection and identification of individuals who have COVID-19 and will thus help to prevent onward community transmission[113]. However, such a systematic expansion of rapid diagnostic capacity requires the development of rapid POC tests

Box 2 | **COVID-19 and supply chain logistics**

The supply lines for diagnostic tests were severely hampered for a few months globally (February to April 2020), while alternative models of operation were sought. As disasters have happened previously, the resilience of logistics and supply lines had been studied (primarily for natural disasters, such as floods, earthquakes and wars[88]). These included exploring the optimal choice of 'logistics service providers' to prepare for disasters[89], and studying the optimal 'temporary facility location' problem to cope with disasters[90]. However, the scenarios were investigated for a defined scale and geography, not considering a pandemic, which is rarer yet more disruptive. For the post-coronavirus disease 2019 (COVID-19) era, the demand for different public health interventions is complemented by a surge in testing, with confinement again being possible but only as a measure of last resort. This demand combined with further lockdown poses a great logistical challenge as the right supplies would need to reach their designated laboratory destination within a short time frame, and supply chains need to remain active while the testing policy is upheld and then be able to dissipate supplies equally rapidly[172].

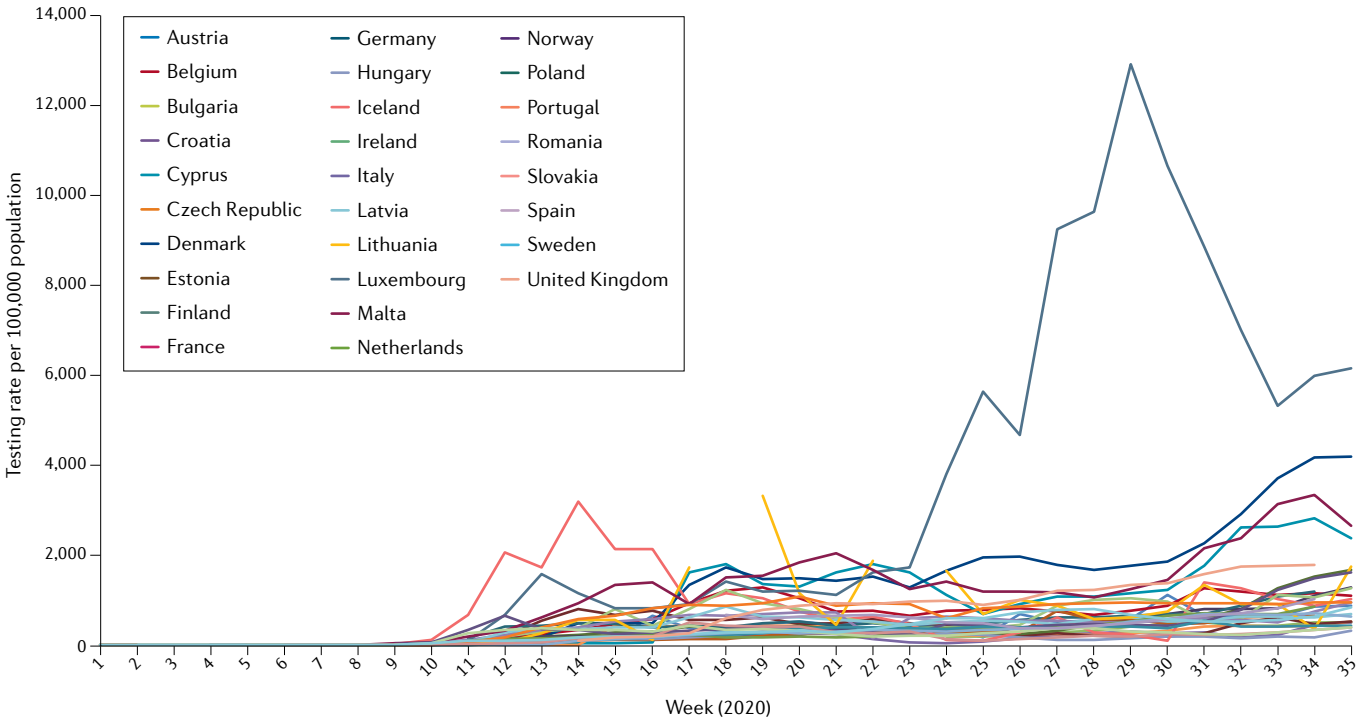

Fig. 2 | **Survey of weekly COVID-19 testing figures.** The graph shows the testing rate per 100,000 population for coronavirus disease 2019 (COVID-19) by week and by member states of the European Union and the European Economic Area, and the United Kingdom. Data provided by the European Centre for Disease Prevention and Control.

with sensitivity and specificity comparable to those of the laboratory-based molecular diagnostic tests[16]. Another important requirement for the expansion is that the test formats are easily scalable to keep up with the varying number of tests to be performed on a daily basis[114]. Scalability of tests may be cumbersome in developing settings because of budget limitations and lack of availability of certain types of test formats[115]. Testing of subpopulations that are at high risk (for example, patients who have received an organ transplant[116]) is a priority to optimize patient management. A plausible first-line clinical approach for the rapid detection of a possible respiratory infection in such patients would involve clinical examination and POC tests that simultaneously target several respiratory pathogens (such as coronavirus, influenza A virus, influenza B virus and respiratory syncytial virus), or multiplex PCR that targets additional respiratory pathogens for patients who are severely ill. In addition to improving patient management, such tests would also prevent unnecessary isolation as well as decrease the use of antibiotics[117,118]. Indeed, international guidelines recommend empirical use of antibiotics for all severely ill patients with suspected COVID-19 and therefore more antibiotics are prescribed than usual, which might further contribute to the emergence of antimicrobial and antifungal resistance[119–121].

In low-resource settings, the first-line approach could be similar to the strategy described above (that is, clinical assessment and POC tests). This is mostly feasible in places where the required structures and resources already exist; for example, where diagnostics are already implemented for the surveillance and control of other pathogens (for example, for HIV-1, Ebola virus and *Mycobacterium tuberculosis*); however, as mentioned above, the reallocation of limited resources towards COVID-19 testing might hinder surveillance programmes for the other pathogens[122]. Perhaps one approach to enhance the diagnostic capacity in low-resource settings would be to increase self-collection of samples. Throat and nasal swabs have been shown to be a reliable alternative, and in this way access to tests is achievable and exposure of health-care workers to potentially infected patients can be reduced[123]. As noted previously, high-quality clinical specimens are of key diagnostic importance, and even small changes in quality can generate false-negative or false-positive results. In the absence of reliable and/or any testing capacity, triage based on clinical case definition or presumptive diagnosis should be prioritized[124–126].

New biomarkers. In the case of a positive COVID-19 test result, the routine implementation of further tests to assess cardiac and respiratory risk factors, which might define the potential gravity of the COVID-19 progression, will be of high medical value for patient management and treatment decisions. Given the rapid accrual of high volumes of clinical data, artificial intelligence (AI) and machine learning approaches that integrate clinical and laboratory data will need to be developed[102,127], with a particular emphasis on high-risk patient groups[128,129]. The integration of tests that would allow the monitoring of the dynamics of the patients' global microbial flora and/or the identification of new markers into the laboratory workflow through AI is key[130,131]. Some mature AI solutions are ready for application to support patient care[132] or clinical decision-making, for example

Box 3 | **The impact of new digital technologies**

During the ongoing coronavirus disease 2019 (COVID-19) pandemic, digital technologies became vital for both social health and economic performance[173]. Rapid developments in the field of artificial intelligence (AI) and machine learning for screening of the population and assessing COVID-19 risk factors (not wearing face masks, having been exposed to known patients, fever, cough and son on) have been observed. This was really the first time in the history of acute infectious research where AI and machine learning were prominently exploited from the initial discovery of the pathogen onward. In China and elsewhere, new AI-powered smartphone applications (apps) are used to monitor the health of individuals and track the geographical spread of the virus[174]. Such apps aim to predict which populations and communities are most susceptible to the negative effects of an infectious disease outbreak, to enable patients to receive real-time information from their medical providers, to provide people with updates about their medical condition without them having to visit a hospital in person and to notify individuals of potential infection hotspots so those areas can be avoided. Similar initiatives are under way in several countries (for example, in South Korea[175]). The real value of these efforts is that digital technologies can offer monitoring in real time, enabling authorities to be more proactive. However, regarding the concerns raised about data protection, the European Union has been advocating voluntary apps and rejected the option of geolocation in favour of the use of a more privacy-friendly Bluetooth technology. Careful pilot studies and risk assessments need to be performed before widespread application of apps[176]. Still, their use is considered key in easing lockdowns, although their successful application has thus far been seen only in Singapore and South Korea.

by reducing antibiotic use[133] (BOX 3). More tools that improve the use of clinical and epidemiological big data will become increasingly available[134,135] and are currently being developed by laboratory scientists together with data scientists and software developers.

New biomarkers are not only crucial for patient management by facilitating early diagnosis of severe COVID-19, they are also important in the development of a COVID-19 vaccine, as they can accelerate clinical trials, reduce costs, guide participant selection, reduce patient safety risks and enable easier verification of the mechanism of action.

COVID-19 and public health-centred surveillance. The ability to directly connect laboratory-produced data (for example, viral genomic data) and records from the laboratory information system[136] to national public health surveillance systems or international networks will be crucial in the control of COVID-19 (FIG. 3). To achieve this, routine testing would need to take place during and outside lockdown periods. In addition, the relevance of transmission via non-symptomatic or mildly symptomatic individuals needs to be clarified, especially in children and young adults[137]. The integration of syndromic POC testing results and sequencing in real time will support the delivery of refined maps to track community spread and potential hospital transmission chains. Such an integration of genomic data will help to identify viral mutations, and combined with health data could inform the assessment of the viral genome correlations with clinical outcomes. Thus, surveillance based on syndromic diagnoses and local and international epidemiological tracing systems enables the investigation of the geographical dynamics of COVID-19 and other respiratory diseases on a large scale (for example, see Syndromic Trends). Such a strategy was shown to be effective in low-resource settings, during the Ebola outbreaks, by facilitating rapid detection of individual patients and equally rapid detection of their contacts, thereby suppressing the spread of infections (the so-called search-and-destroy strategy)[138]. A similar system has already been shown to be efficient for other respiratory diseases and to complement existing data hubs that focus on pathogen epidemiology and antibiotic resistance[139]. Diagnostic COVID-19 testing should be a key determinant in the process of decision-making around confinement of individuals or groups of individuals. This has not been established on a global scale, and even regionally diagnostic testing may be insufficient to warrant obligatory confinement[140,141].

Therefore, integrating antimicrobial resistance monitoring with COVID-19 surveillance through a close collaboration between the pre-existing surveillance networks seems more than warranted[142]. To date, the use of smartphones and specific smartphone applications for surveillance has not advanced much, mainly owing to ethical objections that were raised[143]. Finally, decentralized testing is urgently needed, as this will shorten the time between sampling and a diagnostic result, optimize contact tracing among patients and possibly even lower the overall costs[144].

Clinical and population cohorts and the role of biobanking. In an effort to tackle the multifactorial aspects of COVID-19, an ensemble of large-scale, well-balanced and representative cohorts of individuals who have or have not been affected by SARS-CoV-2 and non-affected individuals, with particular attention to high-risk populations, has already been catalogued in the European Union. These have been assembled rapidly with use of existing research infrastructures such as biobanks under the pan-EU Biobanking and Biomolecular Resources Research Infrastructure (BBMRI-ERIC)[145]. Similar efforts have been reported in Taiwan, Nigeria and several regions in the Asia Pacific region[146–148] (see also the International Society for Biological and Environmental Repositories (ISBER) town hall meeting "The COVID-19 impact part 1: preparedness and response across Indo-Pacific rim and China"). In low-resource settings, where such infrastructures are available and are supported for the long term, an effort to assemble clinically relevant cohorts is also ongoing[149] and in many cases is associated with a governance framework that is increasingly amenable to the sharing of samples and data[150].

However, risks can also be associated with the collection and processing of large volumes of human biospecimens, whether for diagnostic, therapeutic or research purposes. For example, a proportion of the biosamples from patients with cancer, which continue to be collected and stored in biobanks during the pandemic, could possibly be infected with SARS-CoV-2. Therefore, although biobanking is scientifically and clinically relevant[151,152], some biosafety concerns remain[153]. The availability of high volumes of specimens is also expected to support high-throughput metagenomics technologies[154], but such methods need to be validated by regulatory agencies[155,156]. However, discussions regarding the financial viability of many sample collections in the post-COVID-19 era as well as the degree of availability of those collections to industrial partners are ongoing.

Economic consequences and new business models. Economic aspects concerning diagnostics during the COVID-19 pandemic are complex and multifactorial. Influence by governments, cost-effectiveness of the workflow in laboratories, technological readiness, the need for investment in laboratory tools, academic and industrial funding levels, the need for substantial upscaling of tests and required improvement in data management and IT logistics all have important financial consequences. Hence, COVID-19 led simultaneously to two opposite consequences for laboratory medicine activities. On one hand, microbiology departments faced

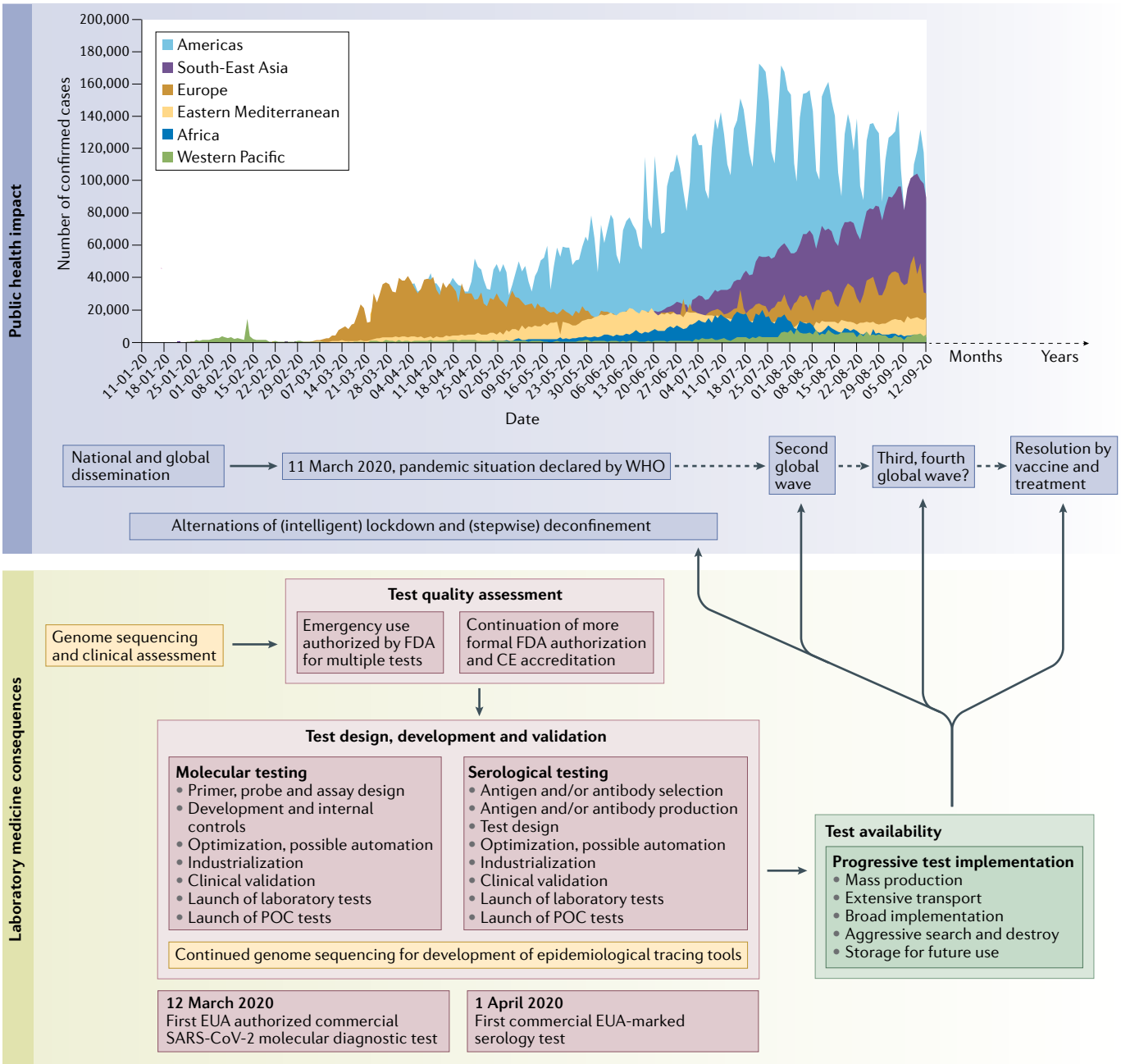

Fig. 3 | **Public health impact and laboratory medicine consequences of COVID-19.** The top panel provides an overview of the national and global dissemination of coronavirus disease 2019 (COVID-19), the declaration of a pandemic state, the implementation of lockdown measures and confinement, the achievement of viral sequencing and clinical assessment, and the concurrent development of diagnostic tools and their progressive implementation on the indicated timescale. The graph shows the number of confirmed COVID-19 cases by date of report and WHO region from 11 January to 31 August 2020 (from WHO Coronavirus Disease (COVID-19) Dashboard). The bottom panel shows the need for quality assessment during the route towards design and development of diagnostic tests, the test quality assessment stage and the stage during which test is formally quality approved and globally available for clinical and epidemiological use. Key ingredients and characteristics of the currently most used test formats are provided, and the continuous need for test refinement based on viral evolution is underscored. The bottom and top boxes are linked by the association between global waves of infection, vaccine development and the production, fine-tuning and degree of availability of large volumes of diagnostic tests needed for appropriate clinical care. EUA Emergency Use Authorization; FDA, US Food and Drug Administration; POC, point of care; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

a huge increase in their diagnostic activities related to the number of patients with suspected COVID-19 (REF.[157]), and sometimes this even led to the requisition of equipment and reagents from other disciplines. On the other hand, the activities of clinical laboratories not directly related to COVID-19 dropped substantially, including, for instance, genetic testing, which had to adapt to a different, remote-based service model[158]. Moreover, owing to the lockdown, ambulatory activities effectively stopped[159,160], which resulted in an immediate economic impact for health-care organizations[161]. As a further example, the stock option of large private laboratory consortia, at the firm level, dropped during the peak of COVID-19, probably owing to the capital intensity from the surge in testing demands[162]. A similar picture was also observed at the hospital level, with a drop of routine activity[163] and the acute need for reallocation of staff and services[161]. These effects were already put forward a few years ago, yet only as a theoretical framework and not tested under pressure[164].

Considering these factors, COVID-19 has changed the health-care business models of clinical laboratories with basic academic health sciences, public health surveillance and the industry. The pandemic can also act as a catalyst, increasing the speed at which promising diagnostic tests move through the academic pipeline into clinical applications, hopefully maintaining the breadth of creative approaches. This includes global activities such as the Innovative Medicines Initiative (IMI), which offers a realistic framework to foster public-private partnerships. The current VALUE-Dx project provides a good example of a platform where industry and non-industry partners collaborate in the development of improved in vitro diagnostics. A priority would be to make IMI fitter for purpose by balancing public health interests on one side and industry interests on the other, while avoiding excessive bureaucracy as imposed by the current IMI rules, especially in times of pandemics. As another example, in the USA the substantial costs for an individual patient (related to diagnostic tests, treatment and hospitalization) and, more specifically, the out-of-pocket costs for underinsured or uninsured patients have initiated strong social debate. The *New York Times* and various scientists presented the US health-care cost prices as unregulated, opaque and quite unpredictable[165–167]. Thus, questions on the delivery of open, transparent, consistent and controlled costs of health care in the context of the COVID-19 pandemic will become a pillar in forthcoming electoral campaigns. Despite initial problems with testing ingredients, the CDC is currently working with state health departments to collect all SARS-CoV-2 laboratory testing data for further consolidation and interpretation at various quality and medical levels[168]. Finally, diagnostic activities in low-resource settings must be made more impactful and better suited for local populations; this could include relatively small-scale but dedicated and adapted test validation activities between industrial and academic partners.

The urgency of the ongoing COVID-19 pandemic forced all the major players in health care to develop or acquire their novel tests quickly and often without serious discussion regarding the price of the individual test. However, the scale of investment needed to combat COVID-19 is certainly ambitious and one of the key economic requirements for the immediate future, and new public–private partnerships are vital, whether this involves drug, vaccine and/or test development. Unlocking additional financing sources, acknowledging the imperative to link financial returns to the providers of capital and the creation of profitable, sustainable financing structures are key in such initiatives[169]. Health considerations (for example, the mental health of staff and risk of burnout) will directly affect performance and thus the profitability of a company and therefore should be incorporated into financial analysis[170]. Positive assessment of such health impacts can provide a competitive advantage, especially ahead of a potential second COVID-19 wave. Obviously, personal health should be prioritized over 'company well-being', without ignoring the fact that company productivity will affect competitive advantage and unemployment levels.

Concluding remarks

Diagnostic tools for COVID-19 were developed just before and during the first global wave of the disease. For forthcoming resurgences of COVID-19, the current tools can be used immediately and mostly quantitatively, thus enabling the rapid detection of new infected individuals, their isolation and the implementation of confinement measures. However, further optimization of tests and more extensive clinical and epidemiological validation, including formal FDA approval, are still needed. In addition, biobanks and the following up of actual patients are still lacking, and AI and machine learning tools need to be developed and applied to data interpretation (BOX 3). Finally, and of utmost importance, diagnostic tests have optimal value only when the community is fully engaged and individuals comply with and participate in confinement measures and adequately use personal protective equipment. There needs to be global solidarity towards test access, and, importantly, infection control and diagnostic interventions need to be strongly intertwined to optimally combat current and future pandemics. Diagnostics should guide the choice of therapy and follow-up of therapy success.

Published online: 14 October 2020

1. Weissleder, R., Lee, H., Ko, J. & Pittet, M. J. COVID-19 diagnostics in context. *Sci. Transl Med.* **12**, eabc1931 (2020).
2. Zhu, N. et al. A novel coronavirus from patients with pneumonia in China, 2019. *N. Engl. J. Med.* **382**, 727–733 (2020).
3. Oh, J. et al. National response to COVID-19 in the Republic of Korea and lessons learned for other countries. *Health Syst. Reform.* **6**, e1753464 (2020).
4. Phua, J. et al. Intensive care management of coronavirus disease 2019 (COVID-19): challenges and recommendations. *Lancet Respir. Med.* **8**, 506–517 (2020).
5. Wölfel, R. et al. Virological assessment of hospitalized patients with COVID-2019. *Nature* **581**, 465–469 (2020).
6. Guglielmi, G. Testing times. *Nature* **583**, 506–509 (2020).
7. Johani, S. & Hajeer, A. H. MERS-CoV diagnosis: an update. *J. Infect. Public Health* **9**, 216–219 (2016).
8. Lalli, M. A. et al. Rapid and extraction-free detection of SARS-CoV-2 from saliva with colorimetric LAMP. Preprint at *medRxiv* https://doi.org/10.1101/2020.05.07.20093542 (2020).
9. Kitagawa, Y. et al. Evaluation of rapid diagnosis of novel coronavirus disease (COVID-19) using loop-mediated

isothermal amplification. *J. Clin. Virol.* **129**, 104446 (2020).
10. Lamb, L. E., Bartolone, S. N., Ward, E. & Chancellor, M. B. Rapid detection of novel coronavirus/severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) by reverse transcription-loop-mediated isothermal amplification. *PLoS ONE* **15**, e0234682 (2020).
11. Huang, Z. et al. Ultra-sensitive and high-throughput CRISPR-powered COVID-19 diagnosis. *Biosens. Bioelectron.* **164**, 112316 (2020).
12. Guo, L. et al. SARS-CoV-2 detection with CRISPR diagnostics. *Cell Discov.* **6**, 34 (2020).
13. Loeffelholz, M. J. & Tang, Y. W. Laboratory diagnosis of emerging human coronavirus infections - the state of the art. *Emerg. Microbes Infect.* **9**, 747–756 (2020).
14. Lambert-Niclot, S. et al. Evaluation of a rapid diagnostic assay for detection of SARS-CoV-2 antigen in nasopharyngeal swabs. *J. Clin. Microbiol.* **58**, e00977-20 (2020).
15. Nagura-Ikeda, M. et al. Clinical evaluation of self-collected saliva by RT-qPCR, direct RT-qPCR, RT-LAMP, and a rapid antigen test to diagnose COVID-19. *J. Clin. Microbiol.* **58**, e01438-20 (2020).
16. Mertens, P. et al. Development and potential usefulness of the COVID-19 Ag Respi-strip diagnostic assay in a pandemic context. *Front. Med.* **7**, 225 (2020).
17. Mak, G. C. et al. Evaluation of rapid antigen test for detection of SARS-CoV-2 virus. *J. Clin. Virol.* **129**, 104500 (2020).
18. Jendrny, P. et al. Scent dog identification of samples from COVID-19 patients - a pilot study. *BMC Infect. Dis.* **20**, 536 (2020).
19. Walker, H. J. & Burrell, M. M. Could breath analysis by MS could be a solution to rapid, non-invasive testing for COVID-19? *Bioanalysis* https://doi.org/10.4155/bio-2020-0125 (2020).
20. Caini, S. et al. Meta-analysis of diagnostic performance of serological tests for SARS-CoV-2 antibodies up to 25 April 2020 and public health implications. *Euro Surveill.* **25**, 23 (2020).
21. Siracusano, G., Pastori, C. & Lopalco, L. Humoral immune responses in COVID-19 patients: a window on the state of the art. *Front. Immunol.* **11**, 1049 (2020).
22. Ong, D. S. Y., de Man, S. J., Lindeboom, F. A. & Koeleman, J. G. M. Comparison of diagnostic accuracies of rapid serological tests and ELISA to molecular diagnostics in patients with suspected COVID-19 presenting to the hospital. *Clin. Microbiol. Infect.* https://doi.org/10.1016/j.cmi.2020.05.028 (2020).
23. Van Elslande, J. et al. Diagnostic performance of 7 rapid IgG/IgM antibody tests and the Euroimmun IgA/IgG ELISA in COVID-19 patients. *Clin. Microbiol. Infect.* **26**, 1082–1087 (2020).
24. Penarrubia, L. et al. Multiple assays in a real-time RT-PCR SARS-CoV-2 panel can mitigate the risk of loss of sensitivity by new genomic variants during the COVID-19 outbreak. *Int. J. Infect. Dis.* **97**, 225–229 (2020).
25. Cheng, M. P. et al. Serodiagnostics for severe acute respiratory syndrome-related coronavirus-2: a narrative review. *Ann. Intern. Med.* **173**, 450–460 (2020).
26. Younes, N. et al. Challenges in laboratory diagnosis of the novel coronavirus SARS-CoV-2. *Viruses* **12**, E582 (2020).
27. Bohn, M. K. et al. Molecular, serological, and biochemical diagnosis and monitoring of COVID-19: IFCC taskforce evaluation of the latest evidence. *Clin. Chem. Lab. Med.* https://doi.org/10.1515/cclm-2020-0722 (2020).
28. Shi, J., Han, D., Zhang, R., Li, J. & Zhang, R. Molecular and serological assays for SARS-CoV-2: insights from genome and clinical characteristics. *Clin. Chem.* **66**, 1030–1046 (2020).
29. Lee, C. Y., Lin, R. T. P., Renia, L. & Ng, L. F. P. Serological approaches for COVID-19: epidemiologic perspective on surveillance and control. *Front. Immunol.* **11**, 879 (2020).
30. Montesinos, I. et al. Evaluation of two automated and three rapid lateral flow immunoassays for the detection of anti-SARS-CoV-2 antibodies. *J. Clin. Virol.* **128**, 104413 (2020).
31. Lippi, G., Mattiuzzi, C., Bovo, C. & Plebani, M. Current laboratory diagnostics of coronavirus disease 2019 (COVID-19). *Acta Biomed.* **11**, 137–145 (2020).
32. Lippi, G. & Plebani, M. The critical role of laboratory medicine during coronavirus disease 2019 (COVID-19) and other viral outbreaks. *Clin. Chem. Lab. Med.* **58**, 1063–1069 (2020).
33. McAdam, A. J. Special issue on diagnostic testing for severe acute respiratory syndrome coronavirus 2 and lessons from this pandemic. *J. Clin. Microbiol.* **58**, e01324-20 (2020).
34. World Health Organization. Advice on the use of point-of care immunodiagnostic tests for COVID-19. https://apps.who.int/iris/handle/10665/331713 (2020).
35. Woloshin, S., Patel, N. & Kesselheim, A. S. False negative tests for SARS-CoV-2 infection - Challenges and implications. *N. Engl. J. Med.* **383**, e38 (2020).
36. Kucirka, L. M., Lauer, S. A., Laeyendecker, O., Boon, D. & Lessler, J. Variation in false-negative rate of reverse transcriptase polymerase chain reaction-based SARS-CoV-2 tests by time since exposure. *Ann. Intern. Med.* **173**, 262–267 (2020).
37. Dellière, S. et al. Evaluation of COVID-19 IgG/IgM rapid test from Orient Gene Biotech. *J. Clin. Microbiol.* **58**, e01233-20 (2020).
38. D'Cruz, R. J., Currier, A. W. & Sampson, V. B. Laboratory testing methods for novel severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2). *Front. Cell Dev. Biol.* **8**, 468 (2020).
39. Lu, R. et al. Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. *Lancet* **395**, 565–574 (2020).
40. Chan, J. F. et al. A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. *Lancet* **395**, 514–523 (2020).
41. Van Tan, L. et al. SARS-CoV-2 and co-infections detection in nasopharyngeal throat swabs of COVID-19 patients by metagenomics. *J. Infect.* **81**, e175–e177 (2020).
42. Daughton, C. G. Wastewater surveillance for population-wide Covid-19: the present and future. *Sci. Total Environ.* **736**, 139631 (2020).
43. Esbin, M. N. et al. Overcoming the bottleneck to widespread testing: a rapid review of nucleic acid testing approaches for COVID-19 detection. *RNA* **26**, 771–783 (2020).
44. Mukattash, T. L. et al. Willingness and readiness to test for COVID-19; a qualitative exploration of community pharmacists. *Int. J. Clin. Pract.* https://doi.org/10.1111/ijcp.13620 (2020).
45. Chan, M., Koo, S. H., Jiang, B., Lim, P. Q. & Tan, T. T. Comparison of the Biofire FilmArray respiratory panel, Seegene AnyplexII RV16, and Argene for the detection of respiratory viruses. *J. Clin. Virol.* **106**, 13–17 (2018).
46. Choi, S. A hidden key to COVID-19 management in Korea: public health doctors. *J. Prev. Med. Public Health* **53**, 175–177 (2020).
47. Wang, D. et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. *JAMA* **323**, 1061–1069 (2020).
48. McCormick-Baw, C. et al. Saliva as an alternate specimen source for detection of SARS-CoV-2 in symptomatic patients using Cepheid Xpert Xpress SARS-CoV-2. *J. Clin. Microbiol.* **58**, e01109-20 (2020).
49. Ben-Ami, R. et al. Large-scale implementation of pooled RNA extraction and RT-PCR for SARS-CoV-2 detection. *Clin. Microbiol. Infect.* **26**, 1248–1253 (2020).
50. Brynildsrud, O. COVID-19 prevalence estimation by random sampling in population - optimal sample pooling under varying assumptions about true prevalence. *BMC Med. Res. Methodol.* **20**, 196 (2020).
51. Abid, S. et al. Assessment of sample pooling for SARS-CoV-2 molecular testing for screening of asymptomatic persons in Tunisia. *Diagn. Microbiol. Infect. Dis.* **98**, 115125 (2020).
52. Mallapaty, S. The mathematical strategy that could transform coronavirus testing. *Nature* **583**, 504–505 (2020).
53. Shah, A. et al. Drive-through testing: a unique, efficient method of collecting large volume of specimens during the SARS-CoV-2 (COVID-19) pandemic. *Mayo Clin. Proc.* **95**, 1420–1425 (2020).
54. Poljak, M. et al. Clinical evaluation of the Cobas SARS-CoV-2 test and a diagnostic platform switch during 48 hours in the midst of the COVID-19 pandemic. *J. Clin. Microbiol.* **58**, e00599-20 (2020).
55. Corman, V. M. et al. Detection of 2019 novel coronavirus (2019-nCoV) by real-time RT-PCR. *Euro Surveill.* **25**, 2000045 (2020).
56. Kostyanev, T. et al. The innovative medicines initiative's new drugs for bad bugs programme: European public–private partnerships for the development of new strategies to tackle antibiotic resistance. *J. Antimicrob. Chemother.* **71**, 290–295 (2016).
57. Mitchell, S. L. et al. Understanding, verifying and implementing Emergency Use Authorization molecular diagnostics for the detection of SARS-CoV-2 RNA. *J. Clin. Microbiol.* **58**, e00796-20 (2020).
58. Freire-Paspuel, B. et al. Evaluation of nCoV-QS (MiCo BioMed) for RT-qPCR detection of SARS-CoV-2 from nasopharyngeal samples using CDC FDA EUA qPCR kit as a gold standard: an example of the need of validation studies. *J. Clin. Virol.* **128**, 104454 (2020).
59. Hogan, C. A. et al. Comparison of the Accula SARS-CoV-2 test with a laboratory-developed assay for detection of SARS-CoV-2 RNA in clinical nasopharyngeal specimens. *J. Clin. Microbiol.* **58**, e01072-20 (2020).
60. Basu, A. et al. Performance of Abbott ID NOW COVID-19 rapid nucleic acid amplification test in nasopharyngeal swabs transported in viral media and dry nasal swabs, in a New York City academic institution. *J. Clin. Microbiol.* **58**, e01136-20 (2020).
61. Ward, S., Lindsley, A., Courter, J. & Assa'ad, A. Clinical testing for Covid-19. *J. Allergy Clin. Immunol.* **146**, 23–34 (2020).
62. Loeffelholz, M. J. et al. Multicenter evaluation of the Cepheid Xpert Xpress SARS-CoV-2 test. *J. Clin. Microbiol.* **58**, e00926-20 (2020).
63. Lieberman, J. A. et al. Comparison of commercially available and laboratory developed assays for in vitro detection of SARS-CoV-2 in clinical laboratories. *J. Clin. Microbiol.* https://doi.org/10.1128/JCM.00821-20 (2020).
64. Wang, W. et al. Detection of SARS-CoV-2 in different types of clinical specimens. *JAMA* **323**, 1843–1844 (2020).
65. To, K. K. et al. Temporal profiles of viral load in posterior oropharyngeal saliva samples and serum antibody responses during infection by SARS-CoV-2: an observational cohort study. *Lancet Infect. Dis.* **20**, 565–574 (2020).
66. Ramdas, K., Darzi, A. & Jain, S. 'Test, re-test, re-test': using inaccurate tests to greatly increase the accuracy of COVID-19 testing. *Nat. Med.* **26**, 810–811 (2020).
67. Spencer, S. et al. Consistency of influenza A virus detection test results across respiratory specimen collection methods using real-time reverse transcription-PCR. *J. Clin. Microbiol.* **51**, 3880–3882 (2013).
68. Van Kasteren, P. B. et al. Comparison of commercial RT-PCR diagnostic kits for COVID-19. Preprint at *bioRxiv* https://doi.org/10.1101/2020.04.22.056747 (2020).
69. Vabret, N., Samstein, R., Fernandez, N. & Merad, M., Sinai Immunology Review Project, Trainees & Faculty. Advancing scientific knowledge in times of pandemics. *Nat. Rev. Immunol.* **20**, 338 (2020).
70. Ombelet, S. et al. Clinical bacteriology in low-resource settings: today's solutions. *Lancet Infect. Dis.* **18**, e248–e258 (2018).
71. Shammi, M., Bodrud-Doza, M., Towfiqul Islam, A. R. M. & Rahman, M. M. COVID-19 pandemic, socioeconomic crisis and human stress in resource-limited settings: a case from Bangladesh. *Heliyon* **6**, e04063 (2020).
72. Bossuyt, P. M. et al. STARD 2015: an updated list of essential items for reporting diagnostic accuracy studies. *Radiology* **277**, 826–832 (2015).
73. World Health Organization. Technical guidance series (TGS) for WHO prequalification – diagnostic assessment panels for quality assurance and quality control of in vitro diagnostic medical devices. in Technical Guidance vol. 6. https://www.who.int/diagnostics_laboratory/guidance/technical_guidance_series/en/ (2017).
74. World Health Organization. Technical guidance series (TGS) for WHO prequalification – designing instructions for use for in vitro diagnostic medical devices. in Technical Guidance vol. 5. https://www.who.int/diagnostics_laboratory/guidance/technical_guidance_series/en/ (2017).
75. Guest, J. L., Del Rio, C. & Sanchez, T. The three steps needed to end the COVID-19 pandemic: bold public health leadership, rapid innovations, and courageous political will. *JMIR Public Health Surveill.* **6**, e19043 (2020).
76. Linton, T. & Vakil, B. Coronavirus is proving we need more resilient supply chains. *Harvard Business Review* https://hbr.org/2020/03/coronavirus-is-proving-that-we-need-more-resilient-supply-chains (2020).

77. Ivanov, D. Predicting the impacts of epidemic outbreaks on global supply chains: a simulation-based analysis on the coronavirus outbreak (COVID-19/SARS-CoV-2) case. *Transp. Res. E Logist. Transp. Rev.* **136**, 101922 (2020).
78. Lamprou, D. A. Emerging technologies for diagnostics and drug delivery in the fight against COVID-19 and other pandemics. *Expert Rev. Med. Devices* **17**, 1–6 (2020).
79. Cundell, T., Guilfoyle, D., Kreil, T. R. & Sawant, A. Controls to minimize disruption of the pharmaceutical supply chain during the COVID-19 pandemic. *PDA J. Pharm. Sci. Technol.* **74**, 468–494 (2020).
80. Mascuch, S. J. et al. Buzz about RT-qPCR: An RT-qPCR formulation for SARS-CoV-2 detection using reagents produced at Georgia Institute of Technology. Preprint at *medRxiv* https://doi.org/10.1101/2020.07.29.20163949 (2020).
81. Beetz, C. et al. Rapid large-scale COVID-19 testing during shortages. *Diagnostics* **10**, E464 (2020).
82. Silverman, E. Roche backpedals and agrees to provide a solution for Covid-19 tests in the Netherlands. *STAT News Agency* https://www.statnews.com/pharmalot/2020/03/27/roche-covid19-coronavirus-netherlands/ (2020).
83. Clark, A. E., Levy, J. & Lee, F. M. Laboratory-developed test regulation and the immunocompromised patient: uncertainty ahead. *Curr. Opin. Infect. Dis.* **33**, 304–311 (2020).
84. Seric, A. & Hauge, J. COVID-19 and the global contraction in FDI. United Nations Industrial Development Organization (UNIDO) Industrial Analytics Platform. https://iap.unido.org/articles/covid-19-and-global-contraction-fdi (2020).
85. López-Gómez, C., Corsini, L., Leal-Ayala, D. & Fokeer, S. COVID-19 critical supplies: the manufacturing repurposing challenge. United Nations Industrial Development Organization (UNIDO) Industrial Analytics Platform. https://www.unido.org/news/covid-19-critical-supplies-manufacturing-repurposing-challenge (2020).
86. Jin, Y. H. et al. A rapid advice guideline for the diagnosis and treatment of 2019 novel coronavirus (2019-nCoV) infected pneumonia. *Mil. Med. Res.* **7**, 4 (2020).
87. Yan, Y., Chang, L. & Wang, L. Laboratory testing of SARS-CoV, MERS-CoV, and SARS-CoV-2 (2019-nCoV): current status, challenges, and countermeasures. *Rev. Med. Virol.* **30**, e2106 (2020).
88. Choi, T. M. Innovative "bring-service-near-your-home" operations under corona-virus (COVID-19/SARS-CoV-2) outbreak: can logistics become the messiah? *Transp. Res. E Logist. Transp. Rev.* **140**, 101961 (2020).
89. Kim, S., Ramkumar, M. & Subramanian, N. Logistics service provider selection for disaster preparation: a socio-technical systems perspective. *Ann. Oper. Res.* **283**, 1259–1282 (2019).
90. Liu, Y., Cui, N. & Zhang, J. Integrated temporary facility location and casualty allocation planning for post-disaster humanitarian medical service. *Transp. Res. E Logist. Transp. Rev.* **128**, 1–16 (2019).
91. Mukwege, D., Cadière, G. B. & Vandenberg, O. COVID-19 response in sub-Saharan low-resource setting: healthcare soldiers need bullets. *Am. J. Trop. Med. Hyg* https://doi.org/10.4269/ajtmh.20-0543 (2020).
92. Kavanagh, M. M. et al. Access to lifesaving medical resources for African countries: COVID-19 testing and response, ethics, and politics. *Lancet* **395**, 1735–1738 (2020).
93. Patriquin, G. et al. Exploring alternative swabs for use in SARS-CoV-2 detection from the oropharynx and anterior nares. *J. Virol. Methods* **285**, 113948 (2020).
94. Callahan, C. J. et al. Open development and clinical validation of multiple 3D-printed sample-collection swabs: rapid resolution of a critical COVID-19 testing bottleneck. Preprint at *medRxiv* https://doi.org/10.1101/2020.04.14.20065094 (2020).
95. Condo, J., Uwizihiwe, J. P. & Nsanzimana, S. Learn from Rwanda's success in tackling COVID-19. *Nature* **581**, 384 (2020).
96. Nkengasong, J. Let Africa into the market for COVID-19 diagnostics. *Nature* **580**, 565 (2020).
97. Miles, D., Stedman, M. & Heald, A. H. "Stay at Home, Protect the National Health Service, Save Lives": a cost benefit analysis of the lockdown in the United Kingdom. *Int. J. Clin. Pract.* https://doi.org/10.1111/ijcp.13674 (2020).
98. Chen, J. et al. Medical costs of keeping the US economy open during COVID-19. Preprint at *medRxiv* https://doi.org/10.1101/2020.07.17.20156232 (2020).
99. Kirigia, J. M. & Muthuri, R. N. D. K. The fiscal value of human lives lost from coronavirus disease (COVID-19) in China. *BMC Res. Notes* **13**, 198 (2020).
100. Banatvala, J. COVID-19 testing delays and pathology services in the UK. *Lancet* **395**, 1831 (2020).
101. Kluge, S. et al. German recommendations for critically ill patients with COVID-19. *Med. Klin. Intensivmed. Notfmed.* **14**, 1–4 (2020).
102. Vandenberg, O. et al. Consolidation of clinical microbiology laboratories and introduction of transformative technologies. *Clin. Microbiol. Rev.* **33**, e00057–e00119 (2020).
103. COVID-19 Genomics UK (COG-UK) consortium. An integrated national scale SARS-CoV-2 genomic surveillance network. *Lancet Microbe* https://doi.org/10.1016/S2666-5247(20)30054-9 (2020).
104. Blomberg, N. & Lauer, K. B. Connecting data, tools and people across Europe: ELIXIR's response to the COVID-19 pandemic. Version 2. *Eur. J. Hum. Genet.* **28**, 719–723 (2020).
105. World Health Organization. COVID-19 Public Health Emergency of International Concern (PHEIC) global research and innovation forum. https://www.who.int/publications/m/item/covid-19-public-health-emergency-of-international-concern-(pheic)-global-research-and-innovation-forum (2020).
106. Thai, P. Q. et al. Factors associated with the duration of hospitalisation among COVID-19 patients in Vietnam: a survival analysis. *Epidemiol. Infect.* **148**, e114 (2020).
107. Cruz, C. H. B. Social distancing in São Paulo State: demonstrating the reduction in cases using time series analysis of deaths due to COVID-19. *Rev. Bras. Epidemiol.* **23**, e200056 (2020).
108. Abdullahi, I. N. et al. Roles and challenges of coordinated public health laboratory response against COVID-19 pandemic in Africa. *J. Infect. Dev. Ctries* **14**, 691–695 (2020).
109. Rouzier, V., Liautaud, B. & Deschamps, M. M. Facing the monster in Haiti. *N. Engl. J. Med.* **383**, e4 (2020).
110. Ahmed, S. et al. Protecting children in low-income and middle-income countries from COVID-19. *BMJ Glob. Health* **5**, e002844 (2020).
111. Venkatesan, P. COVID-19 diagnostics — not at the expense of other diseases. *Lancet Microbe* **1**, E64 (2020).
112. London, A. J. & Kimmelman, J. Against pandemic research exceptionalism. *Science* **368**, 476–477 (2020).
113. Jacobs, J. et al. Diagnostic bacteriology in district hospitals in sub-Saharan Africa: at the forefront of the containment of antimicrobial resistance. *Front. Med.* **6**, 205 (2019).
114. Crick COVID-19 Consortium. Scalable and robust SARS-CoV-2 testing in an academic center. *Nat. Biotechnol.* **38**, 927–931 (2020).
115. Pettit, S. D. et al. 'All In': a pragmatic framework for COVID-19 testing and action on a global scale. *EMBO Mol. Med.* **12**, 12634 (2020).
116. Morlacchi, L. C. et al. COVID-19 in lung transplant recipients: a case series from Milan, Italy. *Transpl. Infect. Dis.* https://doi.org/10.1111/tid.13356 (2020).
117. Schmitz, J. E. & Tang, Y. W. The GenMark ePlex®: another weapon in the syndromic arsenal for infection diagnosis. *Future Microbiol.* **13**, 1697–1708 (2018).
118. Li, J. et al. Rapid detection of respiratory organisms with the FilmArray respiratory panel in a large children's hospital in China. *BMC Infect. Dis.* **18**, 510 (2018).
119. World Health Organization. Clinical management of severe acute respiratory infection when novel coronavirus (2019-nCoV) infection is suspected: interim guidance. https://apps.who.int/iris/handle/10665/330893 (2020).
120. Lansbury, L., Lim, B., Baskaran, V. & Lim, W. S. Co-infections in people with COVID-19: a systematic review and meta-analysis. *J. Infect.* **81**, 266–275 (2020).
121. Koehler, P. et al. COVID-19 associated pulmonary aspergillosis. *Mycoses* **63**, 528–534 (2020).
122. Togun, T., Kampmann, B., Stoker, N. G. & Lipman, M. Anticipating the impact of the COVID-19 pandemic on TB patients and TB control programmes. *Ann. Clin. Microbiol. Antimicrob.* **19**, 21 (2020).
123. Wehrhahn, M. C. et al. Self-collection: an appropriate alternative during the SARS-CoV-2 pandemic. *J. Clin. Virol.* **128**, 104417 (2020).
124. Hopman, J., Allegranzi, B. & Mehtar, S. Managing COVID-19 in low- and middle-income countries. *JAMA* **323**, 1549–1550 (2020).
125. Le Page, M. Home testing is no quick fix. *New Sci.* **245**, 11 (2020).
126. Williams, E., Bond, K., Zhang, B., Putland, M. & Williamson, D. A. Saliva as a non-invasive specimen for detection of SARS-CoV-2. *J. Clin. Microbiol.* **58**, e00776-20 (2020).
127. Scott, B. K. et al. Advanced digital health technologies for COVID-19 and future emergencies. *Telemed. J. E Health* https://doi.org/10.1089/tmj.2020.0140 (2020).
128. Addeo, A. & Friedlaender, A. Cancer and COVID-19: unmasking their ties. *Cancer Treat. Rev.* **88**, 102041 (2020).
129. Fuellen, G. et al. The preventive strategy for pandemics in the elderly is to collect in advance samples & data to counteract chronic inflammation (inflammaging). *Ageing Res. Rev.* **62**, 101091 (2020).
130. Shi, F. et al. Review of artificial intelligence techniques in imaging data acquisition, segmentation and diagnosis for COVID-19. *IEEE Rev. Biomed. Eng.* https://doi.org/10.1109/RBME.2020.2987975 (2020).
131. Smith, K. P. et al. Application of artificial intelligence in clinical microbiology diagnostic testing. *Clin. Microbiol. Newsletter.* **42**, 61–70 (2020).
132. Noh, J. et al. Prediction of the mortality risk in peritoneal dialysis patients using machine learning models: a nation-wide prospective cohort in Korea. *Sci. Rep.* **10**, 7470 (2020).
133. Cánovas-Segura, B. et al. Development of a clinical decision support system for antibiotic management in a hospital environment. *Prog. Artif. Intell.* **5**, 181–197 (2016).
134. Peiffer-Smadja, N. et al. Machine learning in the clinical microbiology laboratory: has the time come for routine practice? *Clin. Microbiol. Infect.* https://doi.org/10.1016/j.cmi.2020.02.006 (2020).
135. Chowdhury, A. S., Lofgren, E. T., Moehring, R. W. & Broschat, S. L. Identifying predictors of antimicrobial exposure in hospitalized patients using a machine learning approach. *J. Appl. Microbiol.* **128**, 688–696 (2020).
136. Reeves, J. J. et al. Rapid response to COVID-19: health informatics support for outbreak management in an academic health system. *J. Am. Med. Inform. Assoc.* **27**, 853–859 (2020).
137. Luo, L. et al. Contact settings and risk for transmission in 3410 close contacts of patients with COVID-19 in Guangzhou, China: a prospective cohort study. *Ann. Intern. Med.* https://doi.org/10.7326/M20-2671 (2020).
138. Ayouba, A. et al. New technologies for controlling emerging infectious diseases in Guinea and the Democratic Republic of the Congo: their role in response to the Ebola epidemic. *Med. Sante Trop.* **29**, 362–365 (2019).
139. Amid, C. et al. The COMPARE data hubs. *Database* **2019**, baz136 (2019).
140. Lau, H. et al. The positive impact of lockdown in Wuhan on containing the COVID-19 outbreak in China. *J. Travel. Med.* **27**, taaa037 (2020).
141. Larremore, D. B. et al. Test sensitivity is secondary to frequency and turnaround time for COVID-19 surveillance. Preprint at *medRxiv* https://doi.org/10.1101/2020.06.22.20136309 (2020).
142. Sirijatuphat, R., Pongsuttiyakorn, S., Supapueng, O., Kiratisin, P. & Thamlikitkul, V. Implementation of global antimicrobial resistance surveillance system (GLASS) in patients with bacteriuria. *J. Glob. Antimicrob. Resist.* **20**, 60–67 (2020).
143. Morley, J., Cowls, J., Taddeo, M. & Floridi, L. Ethical guidelines for COVID-19 tracing apps. *Nature* **582**, 29–31 (2020).
144. Matheeussen, V. et al. Preparedness of European diagnostic microbiology labs for detection of SARS-CoV-2, March 2020. *J. Clin. Virol.* **128**, 104432 (2020).
145. Holub, P. et al. BBMRI-ERIC's contributions to research and knowledge exchange on COVID-19. *Eur. J. Hum. Genet.* **28**, 728–731 (2020).
146. Huang, S. F. et al. Rapid establishment of a COVID-19 biobank in NHRI by National Biobank Consortium of Taiwan. *Biomed. J.* https://doi.org/10.1016/j.bj.2020.05.018 (2020).
147. Adepoju, P. Africa's first biobank start-up receives seed funding. *Lancet* **394**, 108 (2019).
148. Peeling, R. W., Boeras, D., Wilder-Smith, A., Sall, A. & Nkengasong, J. Need for sustainable biobanking networks for COVID-19 and other diseases of epidemic potential. *Lancet Infect. Dis.* https://doi.org/10.1016/S1473-3099(20)30461-8 (2020).
149. Kozlakidis, Z. & Nigam, A. Ten minutes with Zisis Kozlakidis, Head of Laboratory Services and Biobanking at the International Agency for Research

on Cancer, World Health Organization. *BMJ Leader* https://doi.org/10.1136/leader-2020-000282 (2020).
150. Fernando, B., King, M. & Sumathipala, A. Advancing good governance in data sharing and biobanking - international aspects. *Wellcome Open Res.* **4**, 184 (2019).
151. Yates, T. et al. Obesity and risk of COVID-19: analysis of UK biobank. *Prim. Care Diab.* https://www.primary-care-diabetes.com/article/S1751-9918(20)30196-0/pdf (2020).
152. Hastie, C. E. et al. Vitamin D concentrations and COVID-19 infection in UK Biobank. *Diabetes Metab. Syndr.* **14**, 561–565 (2020).
153. Hofman, P. et al. Possible consequences of the COVID-19 pandemic on the use of biospecimens from cancer biobanks for research in academia and bioindustry. *Nat. Med.* **26**, 809–810 (2020).
154. Van Boheemen, S. et al. Retrospective validation of a metagenomic sequencing protocol for combined detection of RNA and DNA viruses using respiratory samples from pediatric patients. *J. Mol. Diagn.* **22**, 196–207 (2020).
155. Holmes, E. C. Reagent contamination in viromics: all that glitters is not gold. *Clin. Microbiol. Infect.* **25**, 1167–1168 (2019).
156. Asplund, M. et al. Contaminating viral sequences in high-throughput sequencing viromics: a linkage study of 700 sequencing libraries. *Clin. Microbiol. Infect.* **25**, 1277–1285 (2019).
157. Roser, M., Ritchie, H., Ortiz-Ospina, E. & Hasell, J. Coronavirus Pandemic (COVID-19). https://ourworldindata.org/coronavirus (2020).
158. Pereira, E. M. et al. COVID-19's impact on genetics at one medical center in New York. *Genet. Med.* https://doi.org/10.1038/s41436-020-0857-7 (2020).
159. Rajan, N. & Joshi, G. P. COVID-19: Role of ambulatory surgery facilities in this global pandemic. *Anesth. Analg.* **131**, 31–36 (2020).
160. Søreide, K. et al. Immediate and long-term impact of the COVID-19 pandemic on delivery of surgical services. *Br. J. Surg.* https://doi.org/10.1002/bjs.11670 (2020).
161. Grimm, C. A. Hospital experiences responding to the COVID-19 pandemic: results of a national pulse survey march 23–27, 2020. https://www.oig.hhs.gov/oei/reports/oei-06-20-00300.pdf (U.S. Department of Health and Human Services, Office of Inspector General, 2020).
162. Alfaro, L., Chari, A., Greenland, A. N., & Schott, P. K. Aggregate and firm-level stock returns during pandemics, in real time (No. w26950). (National Bureau of Economic Research, 2020).
163. Tartari, F., Guglielmo, A., Fuligni, F. & Pileri, A. Changes in emergency service access after spread of COVID19 across Italy. *J. Eur. Acad. Dermatol. Venereol.* https://doi.org/10.1111/jdv.16553. (2020).
164. KPMG International. The healthcare diagnostics value game: The challenges of delivering and demonstrating value in under-pressure markets. Realizing value series. https://assets.kpmg/content/dam/kpmg/xx/pdf/2018/07/the-healthcare-diagnostics-value-game.pdf (2018).
165. Bartsch, S. M. et al. The potential health care costs and resource use associated with COVID-19 In the United States. *Health Aff.* **39**, 927–935 (2020).
166. Bayham, J. & Fenichel, E. P. Impact of school closures for COVID-19 on the US health-care workforce and net mortality: a modelling study. *Lancet Public Health* **5**, e271–e278 (2020).
167. Kliff, S. Most Coronavirus tests cost about $100. Why did one cost $2,315? *New York Times*, 16 June (New York Times, 2020).
168. Adams, M. L., Katz, D. L. & Grandpre, J. Population-based estimates of chronic conditions affecting risk for complications from coronavirus disease, United States. *Emerg. Infect. Dis.* **26**, 1831–1833 (2020).
169. Krech, R., Kickbusch, I., Franz, C. & Wells, N. Banking for health: the role of financial sector actors in investing in global health. *BMJ Glob. Health* **3**, e000597 (2018).
170. Prakash, J., Chatterjee, K. & Srivastava, K. Industrial impact of COVID-19 pandemic: mental health perspective. *Ind. Psychiatry J.* [Epub ahead of print] http://www.industrialpsychiatry.org/preprintarticle.asp?id=283541 (2020).
171. Wynants, L. et al. Prediction models for diagnosis and prognosis of covid-19 infection: systematic review and critical appraisal. *BMJ* **369**, m1328 (2020).
172. Naluyima, P. et al. The joint mobile emerging disease clinical capability (JMEDICC) laboratory approach: capabilities for high-consequence pathogen clinical research. *PLoS Negl. Trop. Dis.* **13**, e0007787 (2019).
173. Li, X. et al. Quality of primary health care in China: challenges and recommendations. *Lancet* **395**, 1802–1812 (2020).
174. Meinert, E., Milne-Ives, M., Surodina, S. & Lam, C. Agile requirements engineering and software planning for a digital health platform to engage the effects of isolation caused by social distancing: case study. *JMIR Public Health Surveill.* **6**, 19297 (2019).
175. Jung, G., Lee, H., Kim, A. & Lee, U. Too much information: assessing privacy risks of contact trace data disclosure on people with COVID-19 in South Korea. *Front. Public Health* https://doi.org/10.3389/fpubh.2020.00305 (2020).
176. Rocher, L., Hendrickx, J. M. & de Montjoye, Y. A. Estimating the success of re-identifications in incomplete datasets using generative models. *Nat. Commun.* **10**, 3069 (2019).

Acknowledgements
The authors gratefully acknowledge the help of all those involved in the development of the Laboratoire Hospitalier Universitaire de Bruxelles — Universitair Laboratorium Brussel. They also thank M. Goldman for help in the design of Fig. 1.

Author contributions
The authors contributed equally to all aspects of the article.

Competing interests
A.v.B. and O.R. are employees of bioMérieux, a company designing, developing and selling diagnostic tests for infectious diseases. bioMérieux had no part in the design and writing of this work. Where an author is identified as a member of the personnel of the International Agency for Research on Cancer, WHO, the authors alone are responsible for the views expressed in this article and the views do not necessarily represent the decisions, policy or views of the International Agency for Research on Cancer, WHO. O.V., D.M. and Z.K. declare no competing interests.

Peer review information
Nature Reviews Microbiology thanks G. Greub, J. Moran-Gilad, who co-reviewed with H. Craddock, and R. Sampath for their contribution to the peer review of this work.

Supplementary information
Supplementary information is available for this paper at https://doi.org/10.1038/s41579-020-00461-z.

RELATED LINKS
bioRxiv: www.biorxiv.org
CDC test protocol: https://www.businessinsider.com/us-coronavirus-testing-problems-timeline-2020-3
COMBACTE: https://www.combacte.com
European Centre for Disease Prevention and Control: https://www.ecdc.europa.eu/en/publications-data/covid-19-testing
Foundation for Innovative New Diagnostics (FIND): https://www.finddx.org/
In Vitro Diagnostics EUAs: https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/vitro-diagnostics-euas#individual-molecular
Innovative Medicines Initiative: https://www.imi.europa.eu
International Society for Biological and Environmental Repositories town hall meeting "The COVID-19 impact part 1: preparedness and response across Indo-Pacific rim and China": https://youtu.be/KT5tlOwWnD0
medRxiv: www.medrxiv.org
SKUP: https://skup.org
VALUE-Dx: www.value-dx.eu
WHO ASSURED: https://www.who.int/bulletin/volumes/95/9/16-187468/
WHO Coronavirus Disease (COVID-19) Dashboard: https://covid19.who.int/?gclid=EAIaIQobChMIsKr314Xo6wIVjuJ3Ch129AWHEAAYASAAEgJePvD_BwE