and children. The new sensor’s ability to detect pulse signals indicates its malleability and versatility. Another feature of this system is its ability to monitor heart-rate variability, which can be useful in predicting a change in the baby’s clinical status before obvious signs of disease become apparent. Furthermore, the water resistance allows its use in the high-humidity environment of a preterm neonate’s incubator. Additionally, the system-level integration provided by Bluetooth technology could alleviate practicality-of-usage concerns.

It is notable that although the absolute differences between measurements obtained with this sensor and those obtained with standard sensors were within acceptable ranges, differences for certain parameters may have clinical relevance for extremely preterm neonates with relatively low blood pressure and warrant further investigation before implementation of this system in the ICU. Additionally, the current testing was limited to children with relatively normal vital parameters; further testing is also needed in children with abnormal vital signs to ensure that the results remain similar.

Furthermore, a particularly important and challenging consideration for the new biosensors will be their implementation in routine care. As the recommendation for neonatal care is moving more and more to skin-to-skin care and family integration, wireless monitoring is immensely valuable from the perspectives of the psychosocial well-being of the children and their parents, health outcomes, and resource utilization. This technology offers most elements desired by healthcare workers for an intensive care monitoring system, but they will need some further reassurance about perceived barriers, including trust in newer digital technologies. A review of trust in digital health has also identified other barriers—excessive cost, defective technology, and time-consuming troubleshooting—which are probably applicable to this technology and should not be forgotten. Finally, the traditional preference for status quo over innovation and the demands of stricter validation for newer technologies may signal an arduous path ahead from a regulatory-approval perspective. However, the proliferation of digital health technologies at all levels has opened an effective dialog with regulatory agencies, and there is willingness from all parties to push this envelope faster than before, with an understanding of the limitations and process of ongoing evaluation.

Overall, Chung et al. have described a promising technology that can revolutionize monitoring and humanize care. They have undertaken pilot testing of a patient- and parent-friendly monitoring device with improved capabilities for recording more information. It can integrate multiple outputs for machine-learning algorithms to develop prediction models to identify acute deteriorations before they occur.

Thus, this wireless monitoring system demonstrates many hallmarks of a health-technology revolution. However, the path between testing and routine use in both high-resource settings and low-resource settings includes several surmountable challenges. Once these are met, we can easily think that such systems can only lead to improved outcomes and that the ICUs of the coming decade could be more comforting places.

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Competing interests
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INFECTIOUS DISEASE

Emergence of a novel human coronavirus threatening human health

In late December 2019, a cluster of patients with ‘atypical pneumonia’ of unknown etiology was reported in Wuhan, China. A novel human coronavirus, now provisionally called ‘SARS-CoV-2’, was identified as the cause of this disease, now named ‘COVID-19’.

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It is increasingly recognized that coronaviruses can cause major emerging viral disease threats, with the respiratory syndromes SARS and MERS being two recent examples, and two coronaviruses now endemic in humans (229E and OC43) have emerged from animals within the past few hundred years. The outbreak of the coronavirus SARS-CoV-2 started in December 2019. On the 30 January 2020, the World Health Organization declared this event a Public Health Emergency of International Concern. The reported cases and deaths of COVID-19 already exceed those of SARS or MERS. Here we highlight some of the key recent findings related to this global epidemic.

SARS-CoV-2 can be readily cultured from clinical specimens, and viral isolates are now available in mainland China and elsewhere, including in our own laboratory (Fig. 1). SARS-CoV-2 is genetically similar to other coronaviruses in the subgenus Sarbecovirus, a clade of betacoronaviruses formed by the coronavirus that causes SARS (SARS-CoV) and other SARS-CoV-like coronaviruses...
The virus is relatively stable, genetically, a single zoonotic introduction and that of a bat coronavirus detected in 2013 genome of SARS-CoV-2 is highly similar to is believed to be a recombinant between bat coronaviruses are common, and SARS-CoV involved. Identification of the antecedent an intermediate mammalian species was whether the initial zoonotic jump occurred this market5. It is therefore not yet clear with young adults and children having this market2,5 that is known to sell live seafood market2,5 which suggests that the immediate ancestor of SARS-CoV-2 has been circulating in bats for at least several years.

Full genome analyses of the virus2,3 indicate that this epidemic was caused by a single zoonotic introduction and that the virus is relatively stable, genetically, in humans1. The first human case was reported in association with exposure to a seafood market1-3 that is known to sell live wild game animals for consumption. It is possible that the zoonotic transmission of SARS-CoV-2 might involve an intermediate host (or hosts), as was observed in the SARS epidemic. However, some of the earliest cases had no epidemiological exposure to this market1. It is therefore not yet clear whether the initial zoonotic jump occurred directly from bats to humans or whether an intermediate mammalian species was involved. Identification of the antecedent zoonotic source is relevant because further zoonotic transmission events may well occur unless the transmission pathways of the initial zoonotic event are identified and interrupted.

Previous research on several SARS-CoV-like bat coronaviruses demonstrated that some of these viruses can use the human receptor ACE-2 for infection. The SARS-CoV-2 spike protein is predicted to be structurally similar to that of SARS-CoV and, indeed, it can be bound by a monoclonal antibody that is specific for the spike of SARS-CoV. Although variations in key residues that are essential for binding to ACE-2 were found in the spike of SARS-CoV-2, this novel virus is experimentally capable of using human, swine, bat and civet ACE-2, but not mouse ACE-2, for entry1. The spike of SARS-CoV-2 can also theoretically interact with ACE-2 from other animal species.

In initial clinical reports on 99 patients confirmed as being infected with SARS-CoV-2, symptoms of fever and cough were commonly seen (>80%). Shortness of breath (31%) and muscle ache (11%) were also seen in patients5. In contrast to patients infected by human coronaviruses that cause the common cold, runny nose and sore throat were less common (<5%) in hospitalized patients but may be more common in milder illness (discussed below)10,11. In the hospital-based case series, radiological evidence of bilateral (75%) or unilateral (25%) pneumonia was seen, sometimes with evidence of multiple mottling and ground-glass opacities. 17% of the patients developed acute respiratory distress syndrome that sometimes led to multiple organ dysfunction and death. Approximately 75% of the patients required supplemental oxygen, and 13% required mechanical ventilation. The age of affected patients ranged from 21 years to 82 years, with 67% of them being >50 years of age and 51% having underlying co-morbidities. The clinical presentations and progression were broadly similar to those in patients with MERS or SARS.

Recent data from case clusters suggest that the overall clinical spectrum of this disease can be more heterogeneous9,10. Upper respiratory symptoms such as sore throat and nasal congestion, as well as diarrhea, may be seen in milder cases. Radiological evidence of pneumonia may be seen even in asymptomatic infections. These clusters also suggest that older age is associated with more-severe disease, with young adults and children having progressively less-severe disease4. An age-associated increase in disease severity was also observed in SARS.

Lower respiratory specimens (e.g., sputum) appear to have a higher viral load than that of upper respiratory specimens (e.g., throat swab)3, Viral RNA was also detected in blood and stool specimens11,12, but it is not known whether these non-respiratory samples are infectious or not. Given that fecal samples from patients with SARS were infectious in some instances (e.g., the Amoy Gardens incident in Hong Kong), precautions against fecal–oral transmission are advisable.

Apart from the early cases2,5, subsequent human infections were caused by sustainable human-to-human transmission. Using the first 425 confirmed cases in Wuhan, Li et al. estimated that the mean incubation period of infection with SARS-CoV-2 was 5.2 days (95% confidence interval (CI), 4.1–7.0), with about 95% of the cases developing symptoms within 12.5 days of an exposure, justifying the current recommendations of a 14-day period for medical observation or quarantine. The reproductive number ($R_0$, the number of secondary cases expected in a completely susceptible population) and the epidemic doubling time were estimated to be 2.2 (95% CI, 1.4–3.9) and 7.4 days (95% CI, 4.2–14), respectively. Studies from other areas have also led to broadly similar figures11,12. These are comparable to those observed during the SARS epidemic. However, transmission of SARS-CoV-2 can occur from patients with mild disease13,14. Whether transmission can occur during the late incubation period remains unclear if global spread of this disease can now be prevented.

Using data from the numbers of exported cases from Wuhan and data on travel patterns, Wu et al. estimated that there were >75,000 infected people in Wuhan between 1 December 2019 and 25 January 2020 (ref. 13). With the current trends and assuming a reduction in transmissibility due to interventions, they predicted the outbreak in Wuhan will peak in April 2020. They also predicted that this epidemic will continue to grow exponentially outside Wuhan. Their simulations further suggested that a 50% reduction in the transmission of this disease achieved through public-health interventions, but without a reduction in population movement, can dramatically delay the exponential growth of this disease for at least a few months. While implementation of aggressive disease-control measures such as school closure and social distancing may defer the establishment of transmission in countries at risk of disease importation, it is still unclear if global spread of this disease can now be prevented.

Although much has been learned in the past few weeks, a number of crucial knowledge gaps remain. These include the modes of transmission, the stability of the virus in environments, mechanisms of pathogenesis and effective treatments and vaccines. In the current circumstances, the
most important question is that of disease severity. It is relevant to note that in the early stage of the 2009 H1N1 influenza virus pandemic, case-fatality estimates as high as 10% were reported. However, population-based age-stratified sero-epidemiological studies revealed that the true overall case fatality was about 0.001% (ref. 14). Thus, sero-epidemiology is needed for a reliable estimate of true disease severity. Past infection may also translate into population immunity, which are data that need to be accounted for in future transmission models of the virus. It is relevant to note that infection with MERS-CoV or MERS disease does not always lead to detectable antibody responses15. If SARS-CoV-2 infection has antibody-response kinetics similar to those of MERS-CoV infection, this may have implications for sero-epidemiology and the development of herd immunity. Thus, research on both the antibody kinetics and cell-mediated immune-response kinetics of SARS-CoV-2 is a priority.

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Competing interests
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