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the infectious period is long and cases can be isolated 2–5 days after symptom onset. Furthermore, Bi and colleagues show that contact-based interventions are more efficient than case-based interventions to reduce transmission, since infected contacts are typically isolated earlier in their infection history than index cases. This worthwhile modelling exercise highlights the urgent need for more information about the infectious period of SARS-CoV-2.

However, there is an important caveat in this modelling work: the potential for pre-symptomatic and asymptomatic transmission is not considered. As a result, the conclusion that case-based or contact-based interventions alone could bring the epidemic under control for longer durations of the infectious period is optimistic, and contrasts with previous simulation studies.<sup>6</sup> Viral shedding studies and epidemiological investigations suggest that in the household, around 40% of transmission occurs before symptom onset, the live virus is shed for at least 1 week after symptom onset, and there is high shedding in asymptomatic individuals.<sup>7–9</sup> Crucially, the effectiveness of case isolation and contact tracing will depend on the fraction of transmission originating from asymptomatic and pre-symptomatic individuals.<sup>9</sup>

As we look towards post-lockdown strategies, we should examine the experience of countries that have successfully controlled SARS-CoV2 transmission or have low mortality (eg, China, Singapore, Taiwan, South Korea, Germany, and Iceland). Successful strategies include ample testing and contact tracing, supplemented by moderate forms of social distancing.<sup>10</sup> Contact tracing on the scale that is needed for the SARS-CoV-2 response is labour intensive, and imperfect if done manually. Hence new technology-based approaches are greatly needed

to assist in identification of contacts, especially if case detection is aggressive.<sup>9</sup> Building on the SARS-CoV-2 experience in Shenzhen and other settings, we contend that enhanced case finding and contact tracing should be part of the long-term response to this pandemic—this can get us most of the way towards control.<sup>9</sup>

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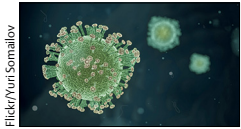
## Importance of precise data on SARS-CoV-2 transmission dynamics control

In December, 2019, COVID-19 was recognised as a novel respiratory disease in Wuhan, China,<sup>1</sup> caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).<sup>2</sup> Accurate and reliable data on SARS-CoV-2 incubation time, secondary attack rate, and transmission dynamics are key to successful containment. In late January, 2020,

infection with SARS-CoV-2 was detected in Germany for the first time. By rapid response, the public health authorities identified a business meeting in a Bavarian company as the primary transmission site and a participating Chinese employee who had travelled from Shanghai to Munich as the index patient.<sup>3</sup> Subsequently,



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the rigorous investigation of contacts led to detection of 16 people infected with SARS-CoV-2 and to successful containment of this outbreak. This well defined event with limited extent of transmission enabled Merle Böhmer and colleagues to provide a meticulous description of SARS-CoV-2 transmission dynamics in an Article published in *The Lancet Infectious Diseases*.<sup>4</sup> The authors did standard and in-depth interviews with case patients and household members to determine the characteristics and the onset of symptoms. Data were used for calculation of SARS-CoV-2 secondary attack rates, defined as the probability that an infection occurs among susceptible people within the incubation period.<sup>5</sup> In addition, whole genome sequencing of virus isolates was done in 15 of the 16 cases. As a result, Böhmer and colleagues report a detailed transmission network of the outbreak, which is accurately displayed in the main figure of the Article.<sup>4</sup>

What are the main lessons to be learned from the analysis of this outbreak? First, the study allows some conclusions on the infectivity of the virus in relation to the intensity of contacts. While 11 out of 217 individuals (secondary attack rate of 5.1%, 95% CI 2.6–8.9) with high-risk non-household contact (defined as cumulative face-to-face contact to a laboratory-confirmed case for  $\geq 15$  min, direct contact with secretions or body fluids of a patient with confirmed COVID-19, or, in the case of health-care workers, had worked within 2 m of a patient with confirmed COVID-19 without personal protective equipment) got infected, none of the low-risk contacts tested positive for SARS-CoV-2. This observation underlines the value of current recommendations of physical distancing as a cornerstone of infection control in this pandemic. However, the intriguing case of a transmission event in two people sitting back to back in a canteen, who only had a very short face-to-face contact while exchanging a salt shaker, shows that the categorisation of high-risk and low-risk contacts has its limitations, too.

Second, SARS-CoV-2 could readily be isolated from throat swabs in all but one patient, who exhibited two negative tests initially. This is in line with the observation that viral replication occurs in the oropharynx in early phases of the disease, when patients still have no clinical signs of pneumonia.<sup>6</sup> But it has also been described in other cases that pharyngeal swabs can convert to negative in later phases, while

lung secretions yield positive results.<sup>6</sup> Thus, for clinicians it is important to know when to use which diagnostic procedure, especially when initial results come back negative.

Third, SARS-CoV-2 can be transmitted very early in the course of the disease, when patients have only mild or even no symptoms. Böhmer and colleagues describe one presymptomatic transmission, four transmissions at the day of onset of symptoms, and up to two transmissions during the prodromal phase of the illness.<sup>4</sup> This is in line with the results of others, who estimate the frequency of presymptomatic transmission to occur in up to a half of all infection events.<sup>7</sup> This is one of the most serious obstacles to controlling the pandemic. While traditional tracing methods might be efficacious in controlling small events such as the Bavarian outbreak, they are clearly insufficient to control an epidemic at its peak. Therefore, novel technologies such as contact tracing applications are urgently needed to effectively control the pandemic.<sup>8</sup> In the Bavarian cohort, only one infected individual was asymptomatic. However, it is likely that mild symptoms were reported only in the setting of such an investigation using standardised interviews. Under usual conditions, unspecific symptoms such as headache, fatigue, or a blocked nose might be not taken seriously enough by many people to isolate themselves.

In conclusion, Böhmer and colleagues' study elegantly shows that a thorough description and analysis of early outbreak events of COVID-19 can be very valuable to improve understanding of transmission dynamics and for applying appropriate infection control measures.

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## Understanding spending trends for tuberculosis

As the tuberculosis community strives to work towards tuberculosis elimination goals, financing and spending continue to be crucial issues.<sup>1</sup> Tuberculosis usually affects the most poor and vulnerable populations and resources have always been few and strained.<sup>2</sup> Year after year, reports from WHO, STOP TB, and other advocacy groups show that tuberculosis spending is inadequate to diagnose and treat existing cases, and recent meetings such as the 2018 UN high-level meeting on tuberculosis have elicited pledges to improve resources and finances available in the fight against tuberculosis.<sup>3,4</sup> Such pledges might become even more crucial as resources, funding, and manpower initially dedicated towards tuberculosis control efforts are redirected to support efforts to fight the coronavirus disease 2019 (COVID-19) pandemic, which is now affecting many, if not all, high tuberculosis burden countries.

Modelling analyses, such as the one published in *The Lancet Infectious Diseases* by Yangfang Su and colleagues,<sup>5</sup> provide useful information to assess and monitor total tuberculosis spending across low-income and middle-income countries. In their study, Su and colleagues used modelling techniques from the Global Burden of Diseases study to generate comprehensive estimates of total tuberculosis spending from all sources across 135 low-income and middle-income countries between 2000 and 2017, allowing for comparisons across countries and over time. The authors estimate total spending for both notified and non-notified cases. These data can be helpful in understanding financial contributions from different sources including government, pre-paid private spending, out-of-pocket medical expenses, and development assistance for health funding, and in capturing the burden experienced by households and communities not typically captured by more traditional reports focused only on notified cases and government and donor spending. They also disaggregated spending estimates by function (eg, outpatient visits, pre-diagnosis visits, private drug spending).

Su and colleagues found that total tuberculosis spending increased for 2000–17, driven primarily by government and national tuberculosis programme spending on notified cases, and that spending on non-notified cases also increased. Total out-of-pocket spending decreased over the same period; however, although the authors captured direct out-of-pocket spending on medical expenses, they did not include non-medical costs including loss of income, transport, and indirect economic costs due to tuberculosis (many of which are now being collected through WHO patient cost surveys) in their analysis. The authors' findings show that three countries with strong private sectors—Democratic Republic of the Congo, Nigeria, and Pakistan—have out-of-pocket medical expenses as the primary source of tuberculosis spending.

Prepaid private and out-of-pocket spending contributions were found to be relatively small and that many governments in low-income and middle-income countries finance most national spending on tuberculosis. Several, but not all, high tuberculosis burden countries were middle-income countries and cost data is often skewed, driven by increased costs in these countries—eg, average outpatient visits were estimated to cost US\$35.92 per visit, while the median cost was only \$4.24 per visit, meaning that in half of the countries the cost per visit was lower than \$4.24.

Conversely many high tuberculosis burden low-income countries are still heavily reliant on development assistance for health spending. Notably, the authors present mean values weighted by population size or number of incident cases for the region, which is in line with the larger global burden of disease approach; however, such presentation requires careful interpretation. For instance, when looking at data for a specific country, the average total spend per incident case might be driven up by a few key countries in that region with large populations or numbers of incident cases, or both.



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