The value of early transmission dynamic studies in emerging infectious diseases

The world is braced for a public health emergency of international concern caused by a novel emerging infectious disease, a coronavirus with similarities to severe acute respiratory syndrome coronavirus (SARS-CoV). Person-to-person transmission of SARS-CoV-2, the causative agent of coronavirus disease 2019 (COVID-19), started in December, 2019, in Wuhan, China and has spread to become a global pandemic, with, as of Feb 26, 2020, community transmission in Italy, Iran, and South Korea.

Modelling studies have aided understanding of COVID-19 dynamics from the first announcement of the epidemic and publication of the genetic sequence of the causative virus. Initial phylogenetic analysis of closely related viruses suggested highly linked person-to-person spread of SARS-CoV-2 originating from mid-November to early December, 2019.[1,2] Following this, modellers provided simple calculations that identified a mismatch between reported cases in China and reported importations of cases from travellers. Based on travel volumes, modellers inferred[3] that cases in Wuhan were underestimated by a factor of 40—a crucially important finding. Further calculations, again based on travel volumes, suggested that some countries would be expected to have many more travel-related cases than had been notified,[4] drawing attention to the possibility of undetected cases and community transmission in several countries.

Transmission dynamic models are a necessary first step in understanding the pandemic potential of an emerging infectious disease, including estimating the reproduction number—the number of new cases arising from a typical infected case. The first published transmission dynamic study of COVID-19 was rapid and uncomplicated, estimating the basic reproduction number as time-invariant[5] without exploring some of the major underlying assumptions, such as lack of infectiousness during the incubation period. Since this early publication, many estimates for the reproduction rate have appeared, ranging from around 2 to more than 6.[6]

In *The Lancet Infectious Diseases*, the study by Adam Kucharski and colleagues[7] addresses many of the assumptions of earlier works. The report contributes a time-varying reproduction number, showing the effect of the massive public health interventions put in place by China from Jan 23, 2020. By using additional datasets of travel-related exported cases, Kucharski and colleagues do not rely entirely on notified cases in Wuhan, which are likely to bias estimates caused by changes in case detection over time. The authors show that the reproduction number fell almost to the threshold value of 1 during the unprecedented public health restrictions in China.[7]

Kucharski and colleagues[7] suggest that chains of transmission might not take off initially and might require up to four imported cases to establish transmission. This estimate assumes that SARS-CoV-2 has heterogeneity of infectiousness similar to SARS, which was characterised by a number of super-spreaders with most cases infecting no other people. If SARS-CoV-2 has a more homogenous infectiousness profile (to which emerging evidence is pointing) in which most people infect two to three others, the risk of established local transmission with a single imported case is considerably higher.

This study answers—at least in one location over a restricted time—a critical question regarding this emerging pandemic, its reproduction number.[7] This crucial number began at 2·35 and declined to 1·05 over the course of December, 2019, and January, 2020. Many questions remain unanswered and should be addressed with urgency, including the infectiousness of cases over the duration of their illness—particularly how much transmission could occur from people who are unaware that they have illness, including asymptomatic and mildly symptomatic people. Initial reports suggest that live virus can be recovered from asymptomatic or mildly symptomatic people,[3] which is of great concern as it will make disease much harder to detect and therefore control. However, what contribution such people make to the overall epidemic is unknown. Additionally, the infection severity, including the infection-fatality rate across different ages and risk groups, must be established. Early reports provide estimates of case fatality of 2·3% within China.[8] However, it is notoriously
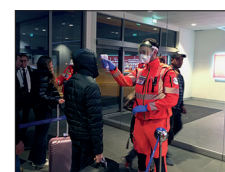
difficult to make such estimates early in an outbreak,[9] and it is clear that not all infections become cases and studies of many tiers of severity (deaths measured as a proportion of hospitalisations, notified cases and syndromic surveillance, and even potentially serosurveillance testing when available) will be needed to establish infection-fatality rates.

Ongoing modelling and surveillance should continue at the epicentre of the pandemic in mainland China to assess the effect of public health measures. However, attention must also move to the emerging foci outside of China, including Italy, Iran, and South Korea, to determine if the reproduction ratio might vary in different climates and sociological contexts. New foci of infection across different continents change the risk to global communities, as this coronavirus becomes a pandemic.

I declare no competing interests.

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1   Lu R, Zhao X, Li J, et al. Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. *Lancet* 2020; **395:** 565–74.

2   GISAID: Genomic epidemiology of BetaCoV 2019–2020. https://www.gisaid.org/epiflu-applications/next-sars-cov2-app/ (accessed Feb 26, 2020).

3   Rothe C, Schunk M, Sothmann P, et al. Transmission of 2019-nCoV infection from an asymptomatic contact in Germany. *N Engl J Med* 2020; published online Jan 30. DOI:10.1056/NEJMc2001468.

4   De Salazar PM, Niehus R, Taylor A, Buckee CO, Lipsitch M. Using predicted imports of 2019-nCoV cases to determine locations that may not be identifying all imported cases. *medRxiv* 2020; published online Feb 11. DOI:10.1101/2020.02.04.20020495 (preprint).

5   Wu JT, Leung K, Leung GM. Nowcasting and forecasting the potential domestic and international spread of the 2019-nCoV outbreak originating in Wuhan, China: a modelling study. *Lancet* 2020; published online Jan 31. https://doi.org/10.1016/S0140-6736(20)30260-9.

6   Liu Y, Gayle AA, Wilder-Smith A, Rocklöv J. The reproductive number of COVID-19 is higher compared to SARS coronavirus. *J Travel Med* 2020; published online Feb 13. DOI: 10.1093/jtm/taaa021.

7   Kucharski AJ, Russell TW, Diamond C, et al. Early dynamics of transmission and control of COVID-19: a mathematical modelling study. *Lancet Infect Dis* 2020; published online March 11. https://doi.org/10.1016/S1473-3099(20)30144-4.

8   WHO. Coronavirus disease 2019 (COVID-19) situation report—29. Feb 19, 2020. https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200218-sitrep-29-covid-19.pdf?sfvrsn=6262de9e_2 (accessed Feb 26, 2020).

9   Ghani AC, Donnelly CA, Cox DR, et al. Methods for estimating the case fatality ratio for a novel, emerging infectious disease. *Am J Epidemiol* 2005; **162:** 479–86.