

Surveillance for the variant era

Adam J Kucharski^{1,2} and Cheryl Cohen³

¹*Centre for Epidemic Preparedness and Response, London School of Hygiene & Tropical Medicine, London, UK*

²*Centre for Mathematical Modelling of Infectious Diseases, London School of Hygiene & Tropical Medicine, London, UK*

³*Centre for Respiratory Diseases and Meningitis, National Institute for Communicable Diseases of the National Health Laboratory Service, Johannesburg, South Africa*

Omicron has put us firmly in the SARS-CoV-2 variant era. After months of Delta dominance, many countries saw their epidemic curves steepen once again as Omicron spread widely and rapidly. In England, the REACT-1 study has been tracking community infection levels since May 2020, routinely collecting samples from hundreds of thousands of randomly selected individuals. On page XXX of this issue, Elliott et al.¹ show a rapid increase of Omicron in REACT-1 data during December 2021, estimating that this variant grew from making up 10% of all infections to 90% in just over a week. In contrast, that leap took around a month for Delta.

Whereas the emergence of Delta was accompanied by scenes of overwhelmed hospitals in India, the initial identification of Omicron in South Africa was not followed by the same severe impact of earlier waves. Faced with a novel variant, it is crucial to understand its ability to spread and cause disease. Early analysis of clinical data in South Africa suggested Omicron was associated with a lower risk of hospitalisation than other circulating SARS-CoV-2 variants, using a surveillance system that links case and hospital records with genome data². Even so, it is increasingly hard to extrapolate conclusions about emerging variants such as Omicron because of variation in prior population immunity through natural infection and vaccination across different countries. Four major variants have now circulated in South Africa, causing large epidemics³, which means there are multiple different combinations of prior infection and vaccination that individuals may have had. In contrast, a larger proportion of immunity in Europe and the United States has been derived from vaccination⁴, further complicating the extent to which researchers can obtain generalisable insights. Moreover, symptom-based surveillance systems – like the ones used to analyse early trends in South Africa – may not reflect mild or symptomless infections in the community. Throughout the pandemic, additional data have been required to understand the true relationship between observed disease and background levels of infection.

Elliott et al. highlight the value of systematic repeated community surveys with testing that samples individuals regardless of symptoms. Their framework of prospective surveys of similar structure allowed comparison to age-specific trends observed in previous waves and prior to availability of vaccination in these age groups. They show that as vaccination coverage increased among adolescents, the burden of infection for Delta shifted to unvaccinated younger age groups, with the booster dose campaign also followed by reduced infection levels among older ages. The approach of randomly sampling from the population is resource intensive as large numbers must be sampled; Elliott et al. invited over 800,000 individuals to participate during late November and early December 2021, with 97,000

samples collected and analysed. However, these efforts allow quantification of community transmission dynamics, including among asymptotically infected individuals. These data are critically important if we are to properly understand the underlying dynamics of SARS-CoV-2, particularly during periods of sudden growth or decline. Such studies will become yet more valuable as the relationship between infection and disease continues to change: countries with growing levels of immunity against SARS-CoV-2 will have an increasing proportion of infections that are vaccine breakthrough or reinfections, with a decreasing fraction of infections having symptoms or severe illness.

Since 2020, there have been several examples of routine testing regardless of symptoms in specific populations, including the SIREN and SAFER studies of UK healthcare workers^{5,6} and the NBA testing program in the US⁷. Such studies can provide valuable epidemiological insights, from viral shedding dynamics to the characteristics of reinfection. However, it is increasingly challenging to generalise results from these subpopulations. The exposure and immunity history of groups such as healthcare workers can be dramatically different to the wider community⁶ and in the UK, SARS-CoV-2 transmission has become increasingly focused in unvaccinated younger age groups, which are not included in workplace cohorts. Community testing studies therefore provide an important complement to other data collection efforts.

Although Elliott et al. provide an overview of early Omicron dynamics in the form of a discrete scientific paper, much of the value of REACT-1 lies in its continuous nature, illustrating the importance of having studies in place proactively to provide data on emerging variants. Relying on reactively implemented research to understand epidemics can lead to delayed – and hence less useful – insights, as has happened during previous health emergencies⁸. For Omicron, comparisons in the UK were also helped by circumstance. Whereas South Africa saw Omicron emerge amid relatively low levels of infection following the mid-2021 Delta wave, the UK was still experiencing a plateauing Delta epidemic in late 2021. This provided a clearer picture of Omicron's ability to replace existing circulating viruses. Given the potential for the emergence of further variants with greater immune escape in future, routine community surveillance will be important to provide fundamental insights into the causes of changing variant dynamics. The population growth rate of a novel variant can be influenced by multiple factors: the inherent ability of the virus to spread between hosts, the social interactions of the groups within which it is spreading, and the extent to which prior vaccination or infection protects against the new variant. Untangling these factors will continue to be essential for effective monitoring of SARS-CoV-2 variants.

Uncertainty about the future evolutionary path of SARS-CoV-2 means it will also be crucial to make use of triangulation when analysing variant characteristics⁹. As well as the REACT-1 infection testing study and REACT-2 antibody study, the UK Office for National Statistics runs a community testing survey and antibody study; there is also routine testing data from symptomatic and hospitalised cases, plus data from contact tracing studies¹⁰. Triangulation using such data can help make sense of epidemiological patterns in real-time. For example, in early May 2021 there was an apparent discrepancy between estimated growth in Delta cases, which suggested substantial spread in the community¹¹, and initial transmission estimates from contact tracing data¹⁰, which did not show Delta having an advantage over Alpha. In REACT-1, however, it was observed that 2 out of 3 sequenced samples in London during early May 2021 were Delta, supporting the hypothesis of extensive community

spread¹². Although there will always be a data gap for the early pandemic in the UK, these community studies have provided a valuable anchoring for scientific understanding of SARS-CoV-2 since spring 2020.

There is also potential for better triangulation with international data sources. In particular, traveller screening has been another major example of routine testing regardless of symptoms¹³. Both for Omicron and earlier variants, such data provided early insights into the geographic distribution of spread, in some instances with imported infections coming from countries yet to report the variant domestically¹⁴. However, efforts to share and combine these datasets globally have been limited to date, reducing the potential for real-time estimation of variant distribution and prevalence globally.

As well as supporting the response to COVID-19 and future pandemics, carefully designed community studies can also help us rethink familiar infections. For example, research involving routine testing has revealed the role of asymptomatic and undetected infections during influenza epidemics¹⁵. As SARS-CoV-2 restrictions are lifted, many countries could see increased circulation of previously suppressed seasonal respiratory viruses such as influenza and respiratory syncytial virus. Expanding testing in platforms such as REACT to include these seasonal viruses would provide a better view of the underlying dynamics of viral transmission, as well as proof of concept for similar potential surveillance programmes in future.

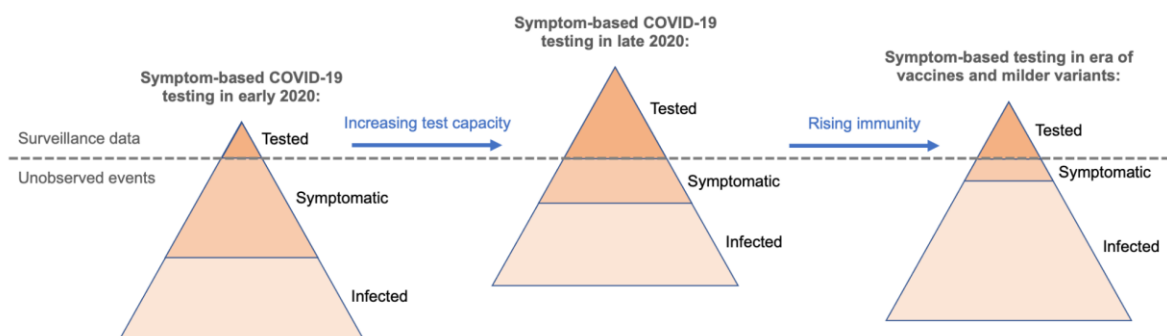


Figure: The relationship between symptom-based testing systems and underlying infection level has changed during the pandemic.

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