Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

attributed to a factor that increases transmissibility uniformly across the population (ie, a mutation) or to an increased number of transmission events in a high-risk subset is essential public health information. In addition to the authors' call for improved estimates of R_0, quantifying and understanding the source of potential individual-level heterogeneity is essential to monitoring and characterising the risk of this emerging outbreak.

I declare no competing interests.

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Authors' reply

Concerning the current monkeypox outbreak, we argued[1] that it is irrelevant whether monkeypox mainly spreads in the community of men who have sex with men or whether it spreads in the general population; reducing its reproduction number to less than 1 to control the outbreak is all that is necessary. On the basis of well known results, Jonathan Smith points out the importance of transmission heterogeneity,[2] but ignores the fact that our argument is independent of transmission heterogeneity. As stated in Lloyd-Smith and colleagues,[2] on which Jonathan Smith's Correspondence is based, the central role of R_0 in epidemic analysis is unassailable: the epidemic dies out with certainty if the effective reproduction number R is lower than 1, yet the extinction probability is lower than 1 if R is higher than 1. Transmission heterogeneity increases the extinction probability of an outbreak caused by a single case, but this is no longer of concern in the current outbreak. The panel B of Smith's figure wrongly gives the impression that monkeypox outbreaks of 100 cases or more should be highly unlikely.[2] In any case, these results are irrelevant for the outbreak with currently more than 23 000 confirmed cases.[3] Transmission heterogeneity renders contact tracing more efficient for most cases (who caused few secondary cases), but also much more difficult for a few superspreaders; what eventually counts is the detected overall percentage of secondary cases.

Evidence of accelerated evolution of the virus and human adaptation suggests that R_0 might be larger than in earlier outbreaks.[4] This finding might also be caused by a specific contact behaviour or routes of transmission. Because more than 95% of the cases are in the community of men who have sex with men[3] and more than 90% are associated with sexual contacts,[3] disease transmission during the early phase, during which no characteristic symptoms are visible, seems plausible. The fact that the virus has not found its way into other groups of the population on a large scale gives evidence that infection control works, in line with our original Comment.[1] Although the number of cases seems to slowly decline (except in the Americas), the continued spread in the community of men who have sex with men suggests that contact tracing might still be difficult for the presymptomatic period in this group and that, therefore, a higher vaccination level is needed in this community. The high percentage of individuals who are HIV positive (and hence immunosuppressed) is alarming. In the context of increasing evidence of asymptomatic infections,[5] which lead to silent transmission, more rigid contact tracing and routine tests in risk groups might be necessary in addition to our original suggestions of pre-exposure and ring vaccination.

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Maintaining genomic surveillance using whole-genome sequencing of SARS-CoV-2 from rapid antigen test devices

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Genomic sequencing of SARS-CoV-2 has had a major role in the public health response to the COVID-19 pandemic, enabling mapping of viral transmission at global and local levels, informing infection control measures, and, importantly, identifying and tracking the emergence of new SARS-CoV-2 variants.[1–3] The rapid detection and characterisation of new variants is crucial for informing the potential efficacy of vaccines and

therapeutics. With point-of-care rapid antigen tests replacing PCR as the main diagnostic modality in many settings, opportunities for genomic characterisation of circulating variants are increasingly limited. We describe an approach for whole-genome sequencing of SARS-CoV-2 from rapid antigen test devices and demonstrate the application of this technique to devices collected as part of clinical care (appendix pp 2–8).

See Online for appendix

Residual SARS-CoV-2 PCR diagnostic samples (cryopreserved nasopharyngeal swabs) were diluted in kit-supplied test buffer (Panbio COVID-19 Ag RapidTest Device, Abbott, Abbott Park, IL, USA; and InnoScreen COVID-19 Antigen Rapid Test Device, Innovation Scientific, Mulgrave, VIC, Australia) before being applied to rapid antigen test devices and allowed to dry (appendix p 3). Devices were then opened using a blunt instrument and nucleic acid was extracted from sectioned test strips (appendix p 15). Extracted RNA was used for SARS-CoV-2 PCR amplification and genomic sequencing using a Midnight RT PCR Expansion kit and Rapid Barcoding Kit 96 (both Oxford Nanopore Technologies, Oxford, UK; appendix p 5). Following their application to rapid antigen test devices, complete SARS-CoV-2 genomes were recovered from 42 (65%) of 65 samples; this proportion increased to 42 (89%) of 47 when only considering samples that had a SARS-CoV-2 PCR cycle threshold (Ct) value of less than 35. Of the 45 samples for which lineage could be ascertained, 44 (98%) were assigned a lineage that was identical with and without rapid antigen test application before sequencing (appendix p 14). For the single sample for which lineage designation changed, classification was retained within the same variant of concern status (appendix p 7).

56 rapid antigen test devices that showed positive results for SARS-CoV-2 were collected from staff and patients at the Royal Melbourne Hospital (Melbourne, VIC, Australia). A complete SARS-CoV-2 genome was obtained from 24 (43%) devices overall and from 23 (68%) of 34 samples with a Ct value below 35. Lineage assignment was possible in 25 (45%) samples overall and in 24 (71%) samples with a Ct below 35 (appendix p 14). All SARS-CoV-2 isolates from these samples were identified as omicron subvariants, consistent with known epidemiology during the period of sample collection. Multiplexed PCR with primers designed to detect key lineage-defining mutations was done with clinical samples that had sufficient residual nucleic acid available (n=49), with SARS-CoV-2 variant ascertained in 45 (92%). For the 23 samples that had a Pango lineage assigned and were tested by variant-specific PCR, all had a variant of concern status determined by PCR and were concordant with the whole-genome sequencing result (appendix p 12).

Our data show that whole-genome sequencing of SARS-CoV-2 can be done using material obtained from rapid antigen test devices collected as part of clinical care, with real-world storage and transport conditions. This work builds on smaller proof-of-principle studies,[4,5] and our finding that SARS-CoV-2 genomes were successfully recovered from rapid antigen test devices up to 8 days after initial sample collection provides an important potential opportunity for the inclusion of self-collected positive rapid antigen test devices in genomic surveillance. For example, self-collected devices could be deposited at a pathology collection centre or couriered to a laboratory for subsequent sequencing. In an era in which RT-PCR testing for SARS-CoV-2 RNA is being used less widely, our approach provides an opportunity for ongoing genomic characterisation, particularly in settings where the ability to detect early incursion of emerging variants is useful—eg, in health-care facilities at border interfaces. Our data also have applicability to low-income and middle-income settings, where rapid antigen test devices are widely deployed.

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Variation in reported SARS-CoV-2 cases after testing policy changes

SARS-CoV-2 testing policies in England continually varied up to April 1, 2022, when, as part of