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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 naso-oropharyngeal 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).

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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

the UK Government's Living with COVID-19 strategy, access to free community testing ended for most of the population.[1] These policy changes were reflected in the number of COVID-19 cases reported in England. Cornelia Adlhoch and Helena de Carvalho Gomes[2] discussed how surveillance systems for SARS-CoV-2 need to be representative to ensure the provision of high-quality information to understand the ongoing impact of COVID-19.

Following the changes to testing, we investigated trends and demographics of 10 862 278 COVID-19 cases reported to the UK Health Security Agency between Nov 1, 2021, and June 30, 2022, detected by PCR at National Health Service (NHS) laboratories or in the community. Of the 10 862 278 positive cases that were extracted, 10 356 716 (95·3%) were community cases. Within this group, there was a shift from most reported cases being identified by laboratory-reported PCR to mostly by self-reported lateral flow device (LFD), coinciding with the cessation of PCR confirmatory testing of initial LFD-positive results on Jan 11, 2022.

After stratifying by deprivation quintiles, the trends in community LFD-tested cases initially followed that of NHS-tested cases, with the highest daily incidence rates observed in the most deprived populations and the lowest daily incidence rates observed among the least deprived populations. However, after Jan 11, 2022, this trend reversed, whereby the highest incidence rates of community LFD-tested COVID-19 cases were among the least deprived groups (appendix).

When evaluating by ethnic group, the highest incidence of NHS-tested COVID-19 cases was consistently observed in the Other ethnic groups, with the lowest rates observed among the White ethnic groups (appendix). From Jan 11, 2022, the highest rates of LFD-tested community cases were reported among White ethnic groups, followed by Mixed or multiple ethnic groups (appendix), and lowest among Black or Black British ethnic groups.

These differences between cases tested through the NHS (mostly by PCR) and by LFDs in the community indicate that there are potential inequalities associated with testing and reporting, and that changes to testing policies had varying impacts on surveillance within the population. Throughout the pandemic, case detection within England has never reached 100%,[3] and with the end to widespread testing, this will have decreased further.

More caution is required in interpreting COVID-19 surveillance data with changes to SARS-CoV-2 testing in England. It is important to monitor cases by deprivation and ethnic group using health care-based testing for this aim, to support ongoing work in addressing inequalities. Potential inequalities associated with accessing and reporting testing must be considered in the development of all surveillance systems.

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Uncoupling of all-cause excess mortality from COVID-19 cases in a highly vaccinated state

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Since March, 2020, excess mortality—the number of all-cause deaths exceeding the baseline number of expected deaths—has been observed in waves coinciding with COVID-19 outbreaks in the USA and worldwide.[1,2] However, after February, 2022, the reported number of COVID-19-associated deaths decreased despite a notable spring wave of infections primarily due to omicron subvariants (BA.2, BA.2.12.1, BA.4, BA.5).[3] Until now, it has been unknown whether the spring, 2022, COVID-19 wave in Massachusetts, USA, was associated with all-cause excess mortality.

Accordingly, we assembled population data (2014–19) and weekly mortality data (January, 2015–February, 2020) provided by the Massachusetts Registry of Vital Records and Statistics (MRVRS) and applied seasonal autoregressive integrated moving averages to project the weekly number of expected deaths for the state for the pandemic period (Feb 3, 2020–June 26, 2022). We summed age-specific mortality to create state-level estimates and additionally corrected for the lower-than-expected state population owing to cumulative excess mortality recorded during the pandemic (for a more detailed description, see appendix p 1).[4–6] Weekly observed deaths provided by the MRVRS are more than 99% complete for all study weeks. Case, wastewater, and hospitalisation data were accessed from publicly available databases.[7,8] Analyses were conducted with R (version 4.1.2). The MRVRS deemed the study exempt from institutional review board review.

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In the 18-week period after BA.2, BA.2.12.1, BA.4, and BA.5 subvariants became prevalent (week