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.

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Applying prospective genomic surveillance to support investigation of hospital-onset COVID-19

Here, we provide an update on our previous Article,[1] which described the use of rapid SARS-CoV-2 genome sequencing to investigate hospital-acquired infections (HAIs) at Cambridge University Hospitals NHS Foundation Trust (CUH), Cambridge, UK. CUH experienced a substantial second wave of COVID-19 (figure). Between Nov 2, 2020, and Feb 7, 2021, 162 (14%) of 1178 patients with COVID-19 at CUH had a suspected or definite HAI (as previously defined[1]), and 465 infected health-care workers (HCWs) were identified via the staff screening programme.[2] Nanopore sequencing was attempted for 513 (44%) of 1178 patients, prioritising those with hospital-onset infections, and 324 (70%) of 465 HCWs; 252 (21%) of 1178 patients and 317 (68%) of 465 HCWs had SARS-CoV-2 genomes available after quality control filtering (as previously described[1]). Patient coverage was lower than in our previous study[1] and for HCWs, reflecting different diagnostic testing methods and limitations on sequencing capacity. The frequency of the B.1.1.7 PANGO-lineage[3] increased from 8% (nine of 109) in November, 2020, to 83% (257 of 311) in January, 2021.

As in the first wave, outbreaks of hospital-onset COVID-19 occurred on wards intended for patients without COVID-19, termed green wards. Where genomics were available, cases on these wards were often phylogenetically clustered (virus genomes with zero to one single nucleotide polymorphism differences), consistent with ward-based transmission.[1] This transmission occurred despite substantial efforts to reduce HAIs, including universal surgical mask wearing by staff, SARS-CoV-2 screening of all patients at hospital admission and regularly thereafter, cohorting of patients to green, amber, and red wards, and a comprehensive staff screening programme. Continued hospital-based transmission despite these efforts emphasises how challenging it is to limit SARS-CoV-2 transmission in hospitals with limited side-room capacity, given the high infectivity of SARS-CoV-2 and potential for asymptomatic transmission. Genomic data were presented at seven of 11 clinical HAI review meetings and at infection-control meetings, informing decision-making. Staff vaccinations began in January, 2021, and have already had a substantial impact on reducing COVID-19 incidence.[4]

Our experience from the first and second epidemic waves of COVID-19 at CUH identified several challenges to applying prospective genomic surveillance to infection control. First, close and efficient working between clinical, infection-control, sequencing, and bioinformatic-analysis teams is crucial. Second, changes in SARS-CoV-2 diagnostic methods resulted in technical difficulties in obtaining sufficient good-quality genetic material for sequencing. Third, the speed from sampling to sequencing to analysis is crucial; for maximum impact, genomic data should be available to inform real-time decision-making. Finally, sustained funding and human resource capacity are essential for consistent service delivery. Nevertheless, we have shown that introducing rapid genomic sequencing and data analysis into hospital outbreak investigations is both feasible and beneficial; the challenge is to translate this from an emergency response into routine clinical practice.

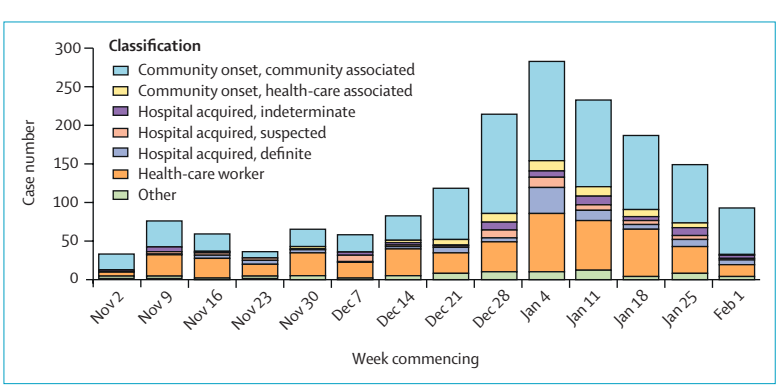

***Figure*: Hospital-acquired SARS-CoV-2 infections in Cambridge University Hospitals during the second wave**

Epidemic curve showing weekly case numbers for new diagnoses of COVID-19 at Cambridge University Hospitals (positive SARS-CoV-2 PCR tests) from Nov 2, 2020, to Feb 7, 2021, coloured by infection classification (appendix).

See **Online** for appendix

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