The Alpha variant was not associated with excess nosocomial SARS-CoV-2 infection in a multi-centre UK hospital study

Article  (Published Version)

Boshier, Florencia A T, Venturini, Cristina, Stirrup, Oliver, Guerra-Assunção, José Afonso, Alcolea-Medina, Adela, Becket, Angela H, Byott, Matthew, Charalampous, Themoula, Filipe, Themoula, Frampton, Dan, Glaysher, Sharon, Khan, Tabassum, Kulasegara-Shylini, Tabassum, Kele, Beatrix, Price, Beatrix et al. (2021) The Alpha variant was not associated with excess nosocomial SARS-CoV-2 infection in a multi-centre UK hospital study. Journal of Infection, 83 (6). pp. 693-700. ISSN 0163-4453

This version is available from Sussex Research Online: http://sro.sussex.ac.uk/id/eprint/103890/

This document is made available in accordance with publisher policies and may differ from the published version or from the version of record. If you wish to cite this item you are advised to consult the publisher’s version. Please see the URL above for details on accessing the published version.

Copyright and reuse:
Sussex Research Online is a digital repository of the research output of the University.

Copyright and all moral rights to the version of the paper presented here belong to the individual author(s) and/or other copyright owners. To the extent reasonable and practicable, the material made available in SRO has been checked for eligibility before being made available.

Copies of full text items generally can be reproduced, displayed or performed and given to third parties in any format or medium for personal research or study, educational, or not-for-profit purposes without prior permission or charge, provided that the authors, title and full bibliographic details are credited, a hyperlink and/or URL is given for the original metadata page and the content is not changed in any way.
The Alpha variant was not associated with excess nosocomial SARS-CoV-2 infection in a multi-centre UK hospital study


Department of Infection, Immunity and Inflammation, UCL Great Ormond Street Institute of Child Health, University College London, London, United Kingdom

Institute for Global Health, University College London, London, United Kingdom

Department of Genetics and Genomic Medicine, UCL Great Ormond Street Institute of Child Health, University College London, London, United Kingdom

Centre for Clinical Infection and Diagnostics Research, School of Immunology and Microbial Sciences, King's College London, London, United Kingdom

Infection Sciences, Viapath, London, United Kingdom

Centre for Enzyme Innovation, University of Portsmouth, Portsmouth PO1 2DE, United Kingdom

School of Biological Sciences, University of Portsmouth, Portsmouth PO1 2DY, United Kingdom

Advanced Pathogen Diagnostics Unit, University College London Hospitals NHS Foundation Trust, London, United Kingdom

The Francis Crick Institute, London, United Kingdom

NRC-University of Glasgow Centre for Virus Research, Glasgow, United Kingdom

Division of Infection and Immunity, University College London, London, United Kingdom

Portsmouth Hospitals University NHS Trust, Queen Alexandra Hospital, Portsmouth PO6 3LY, United Kingdom

Division of Infection, The Royal London Hospital, Barts Health, United Kingdom

Institute for Infection and Immunity, St George's University of London, Cranmer Terrace, London SW17 0RE, United Kingdom

Sheffield Bioinformatics Core, The University of Sheffield, Sheffield, United Kingdom

Sheffield Institute for Translational Neuroscience, The University of Sheffield, Sheffield, United Kingdom

Sheffield Biomedical Research Centre, The University of Sheffield, Sheffield, United Kingdom

Southampton Specialist Virology Centre, University Hospital Southampton NHS Foundation Trust, Southampton, United Kingdom

Department of Infection and Immunity, North West London Pathology, London, United Kingdom

Department of Microbiology, South West London Pathology, Jenner Wing, St. George's Hospital, Blackshaw Road, London SW17 0QT, United Kingdom

Department of Virology, Royal Free London NHS Foundation Trust, London, United Kingdom

Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield, United Kingdom

The Florey Institute for Host-Pathogen Interactions and Department of Infection, Immunity and Cardiovascular Disease, Medical School, University of Sheffield, Sheffield, United Kingdom

https://www.cogconsortium.uk, United Kingdom

Institute for Clinical Trials and Methodology, University College London, London, United Kingdom

Institute of Epidemiology and Health Care, University College London, London, United Kingdom

Department of Infectious Disease, Faculty of Medicine, Imperial College London, United Kingdom

Imperial College Healthcare NHS Trust, Hammersmith Hospital, London, United Kingdom

Corresponding author at: Department of Infection, Immunity and Inflammation, UCL Great Ormond Street Institute of Child Health, University College London, London, United Kingdom

E-mail address: j.breuer@ucl.ac.uk (J. Breuer).

These authors contributed equally to this work.

Full list of consortium member’s names and affiliations can be found in the appendix.

https://doi.org/10.1016/j.jinf.2021.09.022

© 2021 The Authors. Published by Elsevier Ltd on behalf of The British Infection Association. This is an open access article under the CC BY license [http://creativecommons.org/licenses/by/4.0/]
ARTICLE INFO

Article history:
Accepted 12 September 2021
Available online 2 October 2021

Keywords:
COVID-19
Transmissibility
Nosocomial outbreaks
Lineage B.1.1.7
Alpha variant
SARS-CoV-2
Variants of concern

SUMMARY

Objectives: Recently emerging SARS-CoV-2 variants have been associated with an increased rate of transmission within the community. We sought to determine whether this also resulted in increased transmission within hospitals.

Methods: We collected viral sequences and epidemiological data of patients with community and healthcare associated SARS-CoV-2 infections, sampled from 16th November 2020 to 10th January 2021, from nine hospitals participating in the COG-UK HOCI study. Outbreaks were identified using ward information, lineage and pairwise genetic differences between viral sequences.

Results: Mixed effects logistic regression analysis of 4184 sequences showed healthcare-associated infections were no more likely to be identified as the Alpha variant than community acquired infections. Nosocomial outbreaks were investigated based on overlapping ward stay and SARS-CoV-2 genome sequence similarity. There was no significant difference in the number of patients involved in outbreaks caused by the Alpha variant compared to outbreaks caused by other lineages.

Conclusions: We find no evidence to support it causing more nosocomial transmission than previous lineages. This suggests that the stringent infection prevention measures already in place in UK hospitals contained the spread of the Alpha variant as effectively as other less transmissible lineages, providing reassurance of their efficacy against emerging variants of concern.

© 2021 The Authors. Published by Elsevier Ltd on behalf of The British Infection Association. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/)

Methods

Sequence and patient meta-data

Data were collected as part of the COG-UK HOCI variant sub-study from nine NHS hospitals across the UK, six of which were within London. The first SARS-CoV-2 positive sample from all inpatients, outpatient, A&E patients and healthcare workers (HCW), tested by hospital laboratories between 16th November 2020 and 10th January 2021, were sequenced. In addition metadata were collected on patient age, sex (f/m/other/unknown), date of hospital admission and ward location. Ethical approval for the HOCI study was provided by REC 20/EE/0118. Additional clinical details and co-morbidities for this dataset are available elsewhere.17

Inpatients were classified into 3 groups: (i) patients admitted with SARS-CoV-2 (community-acquired infections, CAIs), (ii) those without symptoms of COVID 19 on admission, testing negative upon admission but testing positive between 3–7 days following admission (indeterminate healthcare-associated infections, HCAIs) and (iii) those without symptoms of COVID-19 on admission with a positive test ≥≥8 days post-admission (probable/definite HCAIs).18 Sequence data were also available for patients who presented to hospital but were not admitted, hospital outpatients and healthcare workers. The non-inpatients groups are included in the evaluation of Alpha variant prevalence only.

SARS-CoV-2 sequencing

Samples were sequenced by Oxford Nanopore Technologies (ONT)-based or Illumina-based methods as part of the COG-UK consortium.19 To maximise success 3 of 9 labs sequenced only those samples with qPCR cycle thresholds (Ct) values of ≤32
or equivalent, corresponding to 54% of samples (2268/4184). Sequences were assigned to lineages using COG-UK Pangolin (date 2021-04-14).20 The GISAID and/or ENA accession number of 3589 sequences which are publicly available are in supplementary Table 1.

Prevalence in community testing (Pillar 2) from COG-UK

The number of samples in the COG-UK dataset collected between 16th November 2020 and 10th January 2021 from community areas, local to participating hospitals (i.e. shared adm2 designation), was tallied by week.21

Statistical analysis

Differences between patient groups in the prevalence of the Alpha variant among positive samples were evaluated using mixed effects logistic regression,22 CAI or HCAI sex, age and sample week were included as predictive variables. Parameters for sample weeks were fitted separately for London sites compared with other sites grouped, and random intercept terms were included for each hospital and for weekly periods nested within hospitals. This analysis was also repeated including only the London sites.

Outbreak analyses were conducted using sequences with greater than 90% coverage across the SARS-CoV-2 genome (1043 sequences). Sequence diversity was measured by pairwise distance, defined as the number of single nucleotide polymorphisms (SNPs) differences between two sequences (excluding Ns), calculated in the R 'ape' package.23 The summary results were then grouped by lineage. To determine whether sequences were part of a nosocomial outbreak, we only focused on probable/definite HCAIs diagnosed ≥8 days post-admission. Cases occurring on the same wards (excluding known COVID-19 wards), with a pairwise distance of 0 (i.e. identical sequences) and within a time window of ≤7 days were considered linked and part of the same outbreak. We also included, as independent outbreaks, all samples not linked to any other (i.e. one unlinked sample irrespective of time and location will count as an outbreak of size 1). As these patients all acquired the infection in hospital, they are likely to represent nosocomial transmission (for example from other patients or HCWs whose virus was not sequenced or did not achieve adequate coverage).

All analyses were conducted in R version 4.0.2, using tidyverse collection of packages and other statistical packages such as lme4,22 jtools24 and rcompanion.25 All plots were generated using ggplot2.26

Results

Study dataset

Between November 16th 2020 and January 10th 2021 SARS-CoV-2 RNA positive upper respiratory tract samples from 4184 subjects were successfully sequenced, including 2455 inpatients, 450 outpatients, 1166 HCWs and 113 (4.4 %) with unknown status. Of the inpatients, 1666 (64.9 %) were hospitalised with community-acquired infection, 215 (8.4 %) with indeterminate HCAI and 574 (22.4 %) with probable/definite HCAI, (Table 1). In total, 2058 samples were the Alpha variant, 4 samples were the Beta variant (lineage B.1.351) and 2122 were of lineages not designated variants of concern. The two most prominent lineages across the dataset were B.1.1.7 (the Alpha variant) and B.1.177. This was also true when restricting to HCAI samples alone (Supplementary Fig. 1).

Data from laboratories not using Ct or equivalent thresholds confirmed that the proportions of the Alpha variant and non-Alpha variant viruses did not differ in samples with Ct values < =32 (Supplementary Fig. 2, Chi-square test p=0.16).

Prevalence of the Alpha variant

The prevalence of the Alpha variant was highest in London and Hampshire (South of England), but substantially increased at all sites over the study period (Fig. 1). On mixed effects logistic regression analysis of the Alpha variant, using 4165 samples with complete metadata, samples from HCWs (OR 0.78, 95% CI 0.60 to 1.01), indeterminate HCAIs (OR 0.45, 95% CI 0.30 to 0.70) or probable/definite HCAI (0.45, 0.34 to 0.59) were less likely to be identified as the Alpha variant compared to CAIs than non-Alpha variant. Suggesting that the proportion of hospital-acquired infections due to the Alpha variant was lower in any given week than the proportion among those presenting to hospital with community-acquired infection. However, changes in the frequency of the Alpha variant in CAIs correlated with those in HCAIs on a regional basis (Pearson’s correlation coefficient in London 0.90, 95% CI: 0.54-0.98, p-value<0.01, outside London 0.88, 95% CI 0.45-0.98, p-value<0.05) (Supplementary Fig. 3a). This relationship was confirmed also between HCAIs and community data from the general population (Pillar2, Supplementary Fig. 3b). Following the rapid growth of the Alpha variant within the community and hospitals, we observed a decrease of other lineages. In particular, B.1.177, which was the dominant strain in Europe before November 2020,27,28 showed a correlation between CAIs and HCAIs (overall correlation 0.85) and an opposite trend to the Alpha variant with frequencies decreasing overtime (Supplementary Fig. 4).

Pairwise distance in HCAI

To help define outbreaks within hospitals, we used the sequence diversity within outbreaks involving patients with defined probable/definite HCAIs. We first compared the genetic distance among the Alpha variant sequences and separately among non-Alpha variant sequences of the same lineage. We found the mean pairwise distance (measured as number of SNPs difference) was lower between the Alpha variant samples than between samples from other lineages (mean=6.75 SNPs (95% CI 6.74-6.78) vs mean=8.01 SNPs (95% CI 7.95-8.07), Mann-Whitney U test p <0.05, Supplementary Fig. 5). We next considered only viruses from patients who had very likely acquired their infection in hospital (i.e. probable/definite HCAIs). Excluding wards that were used for cohorting COVID-19 patients, the mean pairwise distance between sequences from patients on the same ward was higher for the Alpha variant acquired in hospital than for non-Alpha (mean=1.95 SNPs (95% CI 1.64-2.27) vs mean = 0.71 SNPs (95% CI 0.635-0.78), Mann-Whitney U test p <0.05). However, for both the Alpha variant and non-Alpha variants the pairwise distance between samples in the same ward was low.

Outbreaks

Given the low diversity observed within wards, and in agreement with previous studies,34 a stringent definition was applied to define linked infections. Samples were considered linked, and part of the same outbreak, when the the sequences were completely identical and occurred on the same ward within a period of 7 days. Outbreaks of size one, corresponding to samples not linked to any other sample, were allowed. The 7 day threshold is consistent with evidence that most people become symptomatic 7 days after exposure.29,30 This choice was also inline with previous transmission studies.16 The impact of allowing for multi-ward outbreaks and varying the time period and the pairwise SNP differences defining an outbreak was tested in a sensitivity analysis.

Ward data was available for a total of 497 probable/definite HCAI patients. A total of 83 outbreaks were identified (by the above definition) caused by any lineage across all hospitals, 19 of
which were caused by the Alpha variant. Outbreaks caused by the Alpha variant in hospitals increased with time, associated with the changing prevalence of the Alpha variant within the community (Fig. 2). In contrast outbreaks due to other lineages decreased in line with reduced circulation of those lineages in the community. Whilst this trend is observed both within and outside London, the dominance of the Alpha variant outbreaks occurs earlier within London, reflecting the earlier rise in the community.

The sizes of outbreak clusters within hospitals caused by the Alpha variant and by other lineages were compared. The total number of probable/definite HCAI patients in a single outbreak ranged from 1 to 11. There was no significant difference in the number of patients involved in outbreaks caused by the Alpha variant compared to outbreaks caused by other lineages (global Kruskal-Wallis p-value=0.27, pairwise comparisons non-significant, Fig. 3). The mean size for the Alpha variant outbreaks was 2.22 in London (95% CI 1.22–3.22) and 3.30 in other locations (95% CI 1.39–5.21). Outbreaks of non-B.1.1.7 lineages had a mean size of 3.72 and 2.78 in London and outside respectively (95% CI 2.32–5.13 in London and 95% CI 2.08–3.49 outside). These conclusions were unchanged, by the sensitivity analyses (Supplementary Fig. 6).

Discussion

Nosocomial transmission continues to present a major challenge to the control of SARS-CoV-2 infection. Overall SARS-CoV-2 acquired in hospitals is estimated to have accounted for up to 20% COVID-19 inpatient cases during the first wave. Recent data from Scotland suggest that up to 36% of severe COVID-19 is associated with recent exposure in hospital (from 1 March 2020 to 28 January 2021). This is in line with the proportions identified in our data, with 22.4% of inpatients having probable/definite HCAI and 8.4% having indeterminate HCAI across all sites. The emergence of new variants with evidence of greater transmissibility in the community presents a potentially increased threat of nosocomial transmission leading to calls for better protection for staff and patients.

Using detailed metadata on community and healthcare-acquired infections from 2455 patients in 9 hospitals across the UK linked to genomic data sequenced during the winter of 20/21 as part of COG-UK HOCI study, logistic regression analysis showed that having a healthcare-acquired infection was predictive of non-Alpha variants. This implies that the Alpha variant was not spreading faster within hospitals than in the community (Table 2). This finding was despite a rise in numbers of COVID-19 cases among both inpatients and the community, with an increasing proportion caused by the Alpha variant (Fig. 1). As has been previously reported, the total numbers of HCAIs were closely correlated with the rising numbers of cases in the community and the increase in HCAI infections caused by the Alpha variant also correlated with increasing prevalence of the Alpha variant overall.

We made use of the genomic data and detailed information on hospital acquired infections to better identify and quantify linked hospital infections. The definition of an outbreak was considered carefully. Previous outbreak data suggest that the mutation rate of SARS-CoV-2 is low, with an average of less than one fixed mutation occurring for each transmission. Nonetheless, up to 2 single nucleotide differences have been described in viruses that are known to be part of a single nosocomial outbreak. In our data, we noted very little genetic diversity across the Alpha variant (Supplementary Fig. 5), reflecting the rapid expansion and selective sweep that occurred as the variant rapidly spread. We therefore chose a stringent definition of linked infections, requiring identical sequences and included only patients with a high likelihood of having acquired their infection in hospital (i.e. probable or definite hospital onset SARS-CoV-2 infection). We also restricted putatively linked

Table 1

Proportion of SARS-CoV-2 due to the Alpha variant for all sequenced samples.

<table>
<thead>
<tr>
<th>Age [mean (sd)]</th>
<th>Alpha variant (n=2058)</th>
<th>Non-Alpha variant (n=2126)</th>
<th>Total (n=4184)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Missing</td>
<td>53.4 (21.8)</td>
<td>58 (22.6)</td>
<td>55.7 (22.3)</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>1109 (48.6)</td>
<td>1175 (51.4)</td>
<td>2,284 (100.0)</td>
</tr>
<tr>
<td>Male</td>
<td>938 (49.8)</td>
<td>944 (50.2)</td>
<td>1,882 (100.0)</td>
</tr>
<tr>
<td>Missing</td>
<td>11</td>
<td>7</td>
<td>18</td>
</tr>
<tr>
<td>Week starting:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>16/11/2020</td>
<td>22 (8.5)</td>
<td>238 (91.5)</td>
<td>260 (100.0)</td>
</tr>
<tr>
<td>23/11/2020</td>
<td>50 (15.0)</td>
<td>284 (85.0)</td>
<td>334 (100.0)</td>
</tr>
<tr>
<td>30/11/2020</td>
<td>83 (20.4)</td>
<td>324 (79.6)</td>
<td>407 (100.0)</td>
</tr>
<tr>
<td>07/12/2020</td>
<td>128 (30.0)</td>
<td>299 (70.0)</td>
<td>427 (100.0)</td>
</tr>
<tr>
<td>14/12/2020</td>
<td>312 (45.7)</td>
<td>370 (54.3)</td>
<td>682 (100.0)</td>
</tr>
<tr>
<td>21/12/2020</td>
<td>411 (57.2)</td>
<td>307 (42.8)</td>
<td>718 (100.0)</td>
</tr>
<tr>
<td>28/12/2020</td>
<td>648 (75.2)</td>
<td>214 (24.8)</td>
<td>862 (100.0)</td>
</tr>
<tr>
<td>04/01/2021</td>
<td>404 (81.8)</td>
<td>90 (18.2)</td>
<td>494 (100.0)</td>
</tr>
<tr>
<td>Patient Class</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Outpatients</td>
<td>250 (55.6)</td>
<td>200 (44.4)</td>
<td>450 (100.0)</td>
</tr>
<tr>
<td>Any HCW</td>
<td>559 (47.9)</td>
<td>607 (52.1)</td>
<td>1,166 (100.0)</td>
</tr>
<tr>
<td>Inpatients</td>
<td>1182 (48.1)</td>
<td>1273 (51.9)</td>
<td>2,455 (100.0)</td>
</tr>
<tr>
<td>CAI†</td>
<td>926 (55.6)</td>
<td>740 (44.4)</td>
<td>1,666 (100.0)</td>
</tr>
<tr>
<td>Indeterminate HCAI†</td>
<td>56 (26.0)</td>
<td>159 (74.0)</td>
<td>215 (100.0)</td>
</tr>
<tr>
<td>Probable/definite HCAI†</td>
<td>200 (34.8)</td>
<td>374 (65.2)</td>
<td>574 (100.0)</td>
</tr>
<tr>
<td>Unknown category</td>
<td>67 (59.3)</td>
<td>46 (40.7)</td>
<td>113 (100.0)</td>
</tr>
<tr>
<td>Region</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glasgow</td>
<td>91 (31.6)</td>
<td>197 (68.4)</td>
<td>288 (100.0)</td>
</tr>
<tr>
<td>Hampshire</td>
<td>288 (66.2)</td>
<td>147 (33.8)</td>
<td>435 (100.0)</td>
</tr>
<tr>
<td>London</td>
<td>1480 (65.6)</td>
<td>775 (34.4)</td>
<td>2,255 (100.0)</td>
</tr>
<tr>
<td>South Yorkshire</td>
<td>199 (16.5)</td>
<td>1007 (83.5)</td>
<td>1,206 (100.0)</td>
</tr>
</tbody>
</table>

† Diagnosed at or <2 days from admission.
‡ Diagnosed 3-7 days from admission.
† Diagnosed >8 days from admission. CAI, community-acquired infection; HCAI, healthcare-associated infection; HCW, healthcare worker.

Fig. 1

Boxplot showing the distribution of the date of symptom onset in the community, with bars indicating the 25th and 75th percentiles and the median. The date of admission is also indicated with bars extending from the date of symptom onset. The distribution of onset date in the community is right-skewed, with a median of 33 days (interquartile range 11-69). The distribution of onset date in the hospital is also right-skewed, with a median of 2 days (interquartile range 1-9). This suggests that the proportion of infections acquired in hospitals is higher than in the community.
Fig. 1. Prevalence over time of the Alpha variant in hospitalized patients, healthcare workers (HCWs) and community samples (Pillar 2 data as described in methods) from different geographical regions in the UK. Hospitalized patients are displayed according to community-acquired infection (CAI) (diagnosed at or ≤2 days from admission) or healthcare-associated infection (HCAI) (diagnosed ≥3 days from admission).

Fig. 2. Barplot showing number of HOCI patients involved in outbreaks by week and location, coloured by variant (Alpha vs non-Alpha). Line-chart represents the number of CAI (community-acquired infections, including inpatients, outpatient, A&E patients and healthcare workers) overtime coloured by variant (Alpha variant presence/absence).
cases to those on the same ward and within a time window of 7 days to further increase the specificity of outbreak definition. Within these constraints, the genomic data failed to identify a difference between the size of outbreaks occurring on wards between the Alpha variant and previously circulating lineages.

However, the outbreak definition implemented in our primary analysis is rather stringent. First, as we lack complete records of patients movement, we potentially exclude linked cases in different wards, for example patients who were infected by the same health-care worker or patients who moved before/after diagnosis. Second, our choice of a 7 days window is rather conservative, considering that estimates of the incubation period vary with some outbreak studies opting for a larger period of 14 days. Third, using only identical sequences we could bias against lineages with smaller diversity. To assess the impact of our parameters' choice and the robustness of our results, we carried out a sensitivity analysis varying our parameters to link cases. Allowing for multi-ward outbreaks, increasing the numbers of SNP differences to two and varying the time interval for defining linked cases (0, 7 and 14 days) failed to change the findings.

There are a number of limitations to our work. First, we were not able to sequence all positive cases. Five of nine centres only
sequenced samples with PCR cycle thresholds of 32 and below i.e. higher viral loads. Notably though, sequencing of 694 cases, from three labs not using Ct thresholds with available Ct data, did not find any difference in the distribution of genotypes in samples with Ct values below and above 32 (supplementary Fig. 1). A second limitation of our work is that towards the end of the study all three trusts outside London were using a sequence reporting tool (SRT), as part of the HOCI study,33 rather than phylogenetic analysis alone to help determine whether cases were part of linked outbreaks. It is not known whether the SRT may have limited the extent of outbreaks as data processing and analysis for the HOCI study is still ongoing. Finally, this study was not designed to account for use of personal protective equipment (PPE), aerosol generating procedures (AGP) or ventilation which may also impact transmission.

In summary notwithstanding its greater transmissibility in the community, we find no evidence to support the Alpha variant as having caused more nosocomial transmission than previous variants. This suggests that the stringent infection prevention measures already in place in UK hospitals are similarly effective at containing the spread of SARS-CoV-2 in a healthcare setting irrespective of its transmissibility. This finding implies that ongoing nosocomial spread of SARS-CoV-2 is likely to be influenced by factors such as fixed estate, e.g. building infrastructure, beds in bays, shared facilities and ventilation, which are not readily mitigated by the existing infection prevention and control (IPC) measures. However, there is some reassurance that currently implemented IPC measures are likely to be as effective against more transmissible variants.

**Funding**

COG-UK HOCI funded by COG-UK consortium. The COG-UK consortium is supported by funding from the Medical Research Council (MRC) part of UK Research & Innovation (UKRI), the National Institute of Health Research (NIHR) and Genome Research Limited, operating as the Wellcome Sanger Institute.

**Acknowledgments**

This report was produced by members of the COG-UK HOCI Variant subconsortium. COG-UK HOCI is part of COG-UK. COG-UK is supported by funding from the Medical Research Council (MRC) part of UK Research & Innovation (UKRI), the National Institute of Health Research (NIHR) and Genome Research Limited, operating as the Wellcome Sanger Institute.

**Supplementary materials**


**References**

32. McGeigue PM, McAllister DA, Caldwell D, et al. Relation of severe COVID-19 in Scotland to transmission-related factors and risk conditions eligi-
ble for shielding support: REACT-SCOT case-control study. BMC Medicine 2021;2319(1):149.
