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First and second SARS-CoV-2 waves in inner London: A comparison of admission characteristics and the impact of the B.1.1.7 variant.

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1 **Ethics**

2 Ethical approval for data informatics was granted by The London Bromley Research Ethics Committee
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4 collect clinically relevant data points from patient's electronic health records.

5
6 Whole genome sequencing of residual viral isolates was conducted under the COVID-19 Genomics UK
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Abstract

Introduction A second wave of SARS-CoV-2 infection spread across the UK in 2020 linked with emergence of the more transmissible B.1.1.7 variant. The emergence of new variants, particularly during relaxation of social distancing policies and implementation of mass vaccination, highlights the need for real-time integration of detailed patient clinical data alongside pathogen genomic data. We linked clinical data with viral genome sequence data to compare cases admitted during the first and second waves of SARS-CoV-2 infection.

Methods Clinical, laboratory and demographic data from five electronic health record (EHR) systems was collected for all cases with a positive SARS-CoV-2 RNA test between March 13th 2020 and February 17th 2021. SARS-CoV-2 viral sequencing was performed using Oxford Nanopore Technology. Descriptive data are presented comparing cases between waves, and between cases of B.1.1.7 and non-B.1.1.7 variants.

Results There were 5810 SARS-CoV-2 RNA positive cases comprising inpatients (n=2341), healthcare workers (n=1549), outpatients (n=874), emergency department (ED) attenders not subsequently admitted (n=532), inter-hospital transfers (n=281) and nosocomial cases (n=233). There were two dominant waves of hospital admissions, with wave one starting from March 13th (n=838) and wave two from October 20th (n=1503), both with a temporally aligned rise in nosocomial cases (n=96 in wave one, n=137 in wave two). 1470 SARS-CoV-2 isolates were successfully sequenced, including 216/838 (26%) admitted cases from wave one, 472/1503 (31%) admitted cases in wave two and 121/233 (52%) nosocomial cases. The first B.1.1.7 variant was identified on 15th November 2020 and increased rapidly such that it comprised 400/472 (85%) of sequenced isolates from admitted cases in wave two. Females made up a larger proportion of admitted cases in wave two (47.3% vs 41.8%, p=0.011), and in those infected with the B.1.1.7 variant compared to non-B.1.1.7 variants (48.0% vs 41.8%, p=0.042). A diagnosis of frailty was less common in wave two (11.5% v 22.8%, p<0.001) and in the group infected with B.1.1.7 (14.5% v 22.4%, p=0.001). There was no difference in severity on admission between waves, as measured by hypoxia at admission (wave one: 64.3% vs wave two: 65.5%, p=0.67). However, a higher proportion of cases infected with the B.1.1.7 variant were hypoxic on admission compared to other variants (70.0% vs 62.5%, p=0.029).

58 **Conclusions** Automated EHR data extraction linked with SARS-CoV-2 genome sequence data provides
59 valuable insight into the evolving characteristics of cases admitted to hospital with COVID-19. The proportion
60 of cases with hypoxia on admission was greater in those infected with the B.1.1.7 variant, which supports
61 evidence the B.1.1.7 variant is associated with more severe disease. The number of nosocomial cases was
62 similar in both waves despite introduction of many infection control interventions before wave two, an
63 observation requiring further investigation.

64

Background

SARS-CoV-2 infection has led to the death of over 1 million individuals worldwide since its emergence in China during December 2019, with over 100,000 deaths reported in the UK. SARS-CoV-2 incidence shows a highly dynamic course often described in waves. The first wave involved community and nosocomial transmission following the introduction of SARS-CoV-2 into a non-immune population. In London, the estimated incidence in the first wave peaked around March 23rd at 2.2% [1] and then rapidly declined following 2 weeks of social distancing and restrictions. Hospital admissions peaked about 1 week later [2] reflecting the median period of symptoms before hospital presentation.

Incidence of SARS-CoV-2 remained low during the summer months in the UK before a “second wave” of infections, starting in London around the beginning of October [3]. The second wave occurred in a very different environment. Many public health interventions had been introduced such as universal mask use in hospitals [4] and many indoor settings [5]. There was better understanding of risk factors for severe disease [6,7], which prompted vulnerable and elderly people to shield. People were urged to work from home when possible [8]. Schools reopened in September and students returned to University probably representing the largest population movement around the country preceding the second wave [9]. There was also rapid scale up of community testing with contact tracing and isolation. Genome sequencing identified new variants, including the B.1.1.7 variant which was first identified around the South East of England and spread rapidly as part of the emerging second wave. [10] The B.1.1.7 variant has been associated with increased transmissibility in community studies [11] [12] [13], and there is evidence from community studies that it may also confer increased mortality [14] [15] [16] [17]. Finally, vaccination is being rolled out at pace prioritising high risk groups and healthcare workers (HCW), with over 25% of the adult population receiving the first dose by mid February 2021 [18]

These many changes have potential to affect the burden on healthcare systems, and modify the characteristics of cases presenting to hospital including the demographics, co-morbidities and severity of disease associated with SARS-CoV-2 infection. For instance, a report from Japan suggests cases admitted during the second wave are younger, with fewer co-morbidities and with lower markers of disease severity [19]. It is important to understand these changes in real time, to help assess the impact of public health

95 interventions and predict the potential burden on the healthcare system to plan resourcing and potentially
96 modify community interventions.

97
98 Currently data are collected in routine clinical systems, alongside which ISARIC WHO CCP-UK collects data
99 as a large prospective cohort study of COVID-19 patients [20] and COG-UK [21] supports collection of isolates
100 for genome sequencing. As SARS-CoV-2 prevalence falls to potentially become endemic, informatics teams
101 would benefit from an automated mechanism to iteratively extract and link patient and SARS-CoV-2 genomic
102 data for local healthcare planning and to support national and international research studies. We therefore
103 established a dataset integrating multiple health record systems and linked with local SARS-CoV-2 variant
104 analysis to compare admission characteristics of hospitalised cases during the two dominant waves of
105 infection.

106

107 **Methods**

108 **Population of interest and setting**

109 Guy's and St Thomas' NHS Foundation Trust (GSTT) is a multi-site inner-city healthcare institution providing
110 general and emergency services predominantly to the South London boroughs of Lambeth and Southwark.
111 The acute-admitting site (St Thomas' Hospital) has an adult emergency department, with a large critical care
112 service including one of the UK's eight nationally commissioned ECMO centres for severe respiratory failure.
113 A second site (Guy's Hospital) provides elective surgery, cancer care and other specialist services. A
114 paediatric hospital (Evelina London) and several satellite sites for specialist services like dialysis,
115 rehabilitation and long term care are also part of the Trust. COVID-19 cases are admitted through different
116 pathways comprising emergency department (ED), tertiary referrals to the severe respiratory failure service
117 (ECMO), through specialist referral pathways and clinics (eg haemato-oncology and renal transplantation),
118 and from regional hospitals predominantly to critical care through 'mutual aid' scheme.
119

120 **SARS-CoV-2 laboratory testing**

121 GSTT has an on-site laboratory providing SARS-CoV-2 testing to all patients and HCW. The policies and
122 technologies employed for SARS-CoV-2 testing changed over time based on national and local screening
123 guidance and improvements in diagnostics. Our laboratory began testing on 13th March 2020 with initial
124 capacity for around 150 tests per day, before increasing to around 500 tests per day in late April during wave
125 one, and up to 1000 tests per day during wave two (Supplementary Figure 1)
126

127 Assays used for the detection of SARS-CoV-2 RNA include PCR testing using Aus Diagnostics or by the
128 Hologic Aptima SARS-CoV-2 Assay. Nucleic acid was first extracted using the QIAGEN QIA Symphony SP
129 system and a QIA Symphony DSP Virus/Pathogen Mini Kit (catalogue No: 937036) with the off-board lysis
130 protocol. This method utilises 200µl respiratory specimen with a 60µl elution volume. Testing commenced
131 during the first wave on 13th March 2020 limited to cases requiring admission or inpatients who had symptoms
132 of fever or cough, as per national recommendation; guidance suggested cases who did not require admission
133 should not be tested. For wave two, all cases admitted to hospital were screened and underwent universal
134 interval screening at varying time points. Staff testing for symptomatic healthcare workers was also introduced
135 towards the end of wave one. Comparative analysis was therefore restricted to SARS-CoV-2 RNA positive
136 cases requiring admission. Cases without laboratory confirmation of SARS-CoV-2 infection were not
137 included.

138

139 **Definitions**

140 Cases were identified by first positive SARS-CoV-2 RNA test. Cases were placed in mutually exclusive
141 categories with the following definitions: 1) outpatients 2) testing through occupational health 3) emergency
142 department attenders not subsequently admitted within 14 days 4) patients admitted within 14 days of a
143 positive test 5) nosocomial cases, defined based on ECDC definitions, as those having a first positive test on
144 day 8 or later after admission to hospital where COVID-19 was not suspected on admission [22] and 6)
145 interhospital transfers. For the purpose of comparison only the inpatient group, admitted within 14 days
146 following a positive test, were taken forward for onward comparison. A composite datapoint for 'hypoxia' was
147 created, with cases taken to be hypoxic if on admission they had oxygen saturations of <94%, if they were
148 recorded as requiring supplemental oxygen, or if the fraction of inspired oxygen was recorded as being
149 greater than 0.21.

150

151 **Determination of SARS-CoV-2 lineage**

152 Whole genome sequencing of residual samples from SARS-CoV-2 cases was performed using GridION
153 (Oxford Nanopore Technology), using version 3 of the ARTIC protocol [23] and bioinformatics pipeline [24].
154 Samples were selected for sequencing if the corrected CT value was 33 or below, or the Hologic Aptima
155 assay was above 1000 RLU. During the first wave sequencing occurred between March 1st - 31st, whilst
156 sequencing in the second wave restarted in November 2020 and is ongoing. Lineage determination was
157 performed using updated versions of pangolin 2.0 [25]. Samples were regarded as successfully sequenced
158 if over 50% of the genome was recovered and if lineage assignment by pangolin was given with at least 50%
159 confidence.

160

161 **Data sources, extraction and integration**

162 Clinical, laboratory and demographic data for all cases with a laboratory reported SARS-CoV-2 PCR RNA
163 test on nose and throat swabs or lower respiratory tract specimens were extracted from hospital electronic
164 health record (EHR) data sources using records closest to the test date (DXC Technology's i.CM EPR, Philips
165 IntelliVue Clinical Information Portfolio (ICIP) Critical Care, DXC Technology's MedChart, e-Noting and Citrix
166 Remote PACS - Sectra). Data was linked to the Index of Multiple Deprivation (IMD), with 1 denoting the least
167 deprived areas, and 5 the most deprived ones. Age and sex were extracted from EPR. Self-reported ethnicity
168 of cases were stratified according to the 18 ONS categories of White (British, Irish, Gypsy and White-Other),

169 Black (African, Caribbean, and Black-Other), Asian (Bangladeshi, Chinese, Indian, Pakistan, and Asian-
170 Other), and Mixed/Other, with cases from Black ethnicities further separated into Black-Caribbean and Black-
171 African.

172 Comorbidities and medication history were extracted from the EPR and e-Noting using natural language
173 processing (NLP). Comorbidities were extracted from any of the databases covering the pathway of the cases
174 from arrival in accident and emergency through inpatient general ward and critical care unit, where applicable,
175 to hospital discharge or death. If a comorbidity was not recorded we assume that it was not present. Cases
176 were characterised as having/not having a past medical history of hypertension, cardiovascular disease
177 (stroke, transient ischaemic attack, atrial fibrillation, congestive heart failure, ischaemic heart disease,
178 peripheral artery disease or atherosclerotic disease), diabetes mellitus, chronic kidney disease, chronic
179 respiratory disease (chronic obstructive pulmonary disease, asthma, bronchiectasis or pulmonary fibrosis)
180 and neoplastic disease (solid tumours, haematological neoplasias or metastatic disease). Obesity was
181 defined as either morbid obesity present in the notes, or recorded Body Mass Index (BMI) ≥ 30 kg/m².

182 Data management was performed using SQL databases, with analysis carried out on the secure King's Health
183 Partners (KHP) Rosalind high-performance computer infrastructure [26] running Jupyter Notebook 6.0.3, R
184 3.6.3 and Python 3.7.6. Medicines data were extracted using both structured queries and natural language
185 processing tools with medical and drug dictionaries. Additionally, checks on free text data were performed by
186 a cardiovascular clinician to ensure the information was accurate.

187 **Statistical analysis**

188 The statistical analysis in the paper is mainly descriptive. The general statistics were summarised with mean
189 and standard deviation (SD) for continuous variables if the distribution is normal and median and interquartile
190 range (IQR) if the distribution is non-normal. Count and percentages were used for categorical variables. For
191 the comparisons between wave one and two variables, Kruskal-Wallis test was used for continuous variables
192 and Chi-squared test for categorical variables. The reference significant level was set to be $p=0.05$.

193

194

Results

General epidemiology and results of viral sequencing.

Figure 1 shows the incidence of SARS-CoV-2 cases, SARS-CoV-2 admissions, and nosocomial cases since March 13th 2020. In total 5810 individuals had a positive SARS-CoV-2 PCR test up until the data extraction date of 17th February 2021. Two “waves” are evident with July 25th taken as an arbitrary separation date between waves, at which point a minimum of 12 wave one cases remained in hospital. Wave one comprised 1528 unique cases (26.3%) from when laboratory testing commenced on March 13th to peak rapidly between the 1st and 8th April 2020 with 57 new cases, before falling to a baseline by May 12th 2020. 1391/1528 (91%) of all cases in wave one occurred during these 60 days. Wave two comprised 4282 unique cases (73.7%), with incidence first increasing gradually from the beginning of October. There was then a period of rapidly escalating incidence from about 10th December, peaking on 28th December 2020 139 cases were diagnosed. 3446/4282 (80%) of wave two cases detected during a comparable 60 day period ending 8th February 2021. The number of cases admitted, the primary focus of this report, and the number of nosocomial cases are highlighted in Figure 1. In both waves nosocomial cases peaked early increasing along with admissions but then fell while the number of community admissions continued at peak levels.

Individuals with a positive test were placed into six categories (Figure 2). Some observed differences between wave one and two reflected the increased availability of testing particularly for outpatients (208;13.6% v 666;15.6%), people sent home from ED (111;7.3% v 421; 9.8%) and healthcare workers (171;11.2% v 1378;32.2%). There were also more interhospital transfers of known COVID-19 cases in wave two (177;4.1% v 104;6.8% in wave one). In wave two, the number of admissions increased (1503; 35.1% v 838; 54.8%) along with nosocomial cases (137;3.2% v 96;6.3%) compared with wave one.

Figure 3 shows the number of successfully sequenced SARS-CoV-2 isolates over time, with 382 from wave one and 1088 from wave two. The proportion of B.1.1.7 variant increased rapidly after the first B.1.1.7 isolate was identified on 15th November 2020, accounting for approximately two thirds within 3 weeks, and almost 100% (600/617 isolates, 97%) in January 2021. In the second wave, the B.1.1.7 variant made up 83% (908/1088) of all sequenced isolates, 85% (400/472) of sequenced isolates from admitted cases, and 88% (51/59) of sequenced isolates from nosocomial cases. In addition, two cases of the B.1.351 variant of concern were also detected in the wave two admission cohort.

Comparison of characteristics of admitted cases between wave one and two

226 General statistics of cases admitted during wave one (n=838) and wave two (n=1503) were compared (Table
227 1). There was only a small difference in mean age (62yrs in wave one v 60yrs in wave two, p=0.019), however
228 admitted cases were more likely to be female in wave two (47.3% v 41.8%, p=0.011). Comparison of
229 comorbidities showed those in wave two were less likely to have a diagnosis of frailty (11.5% v 22.8%,
230 p<0.001), history of stroke (4.3% v 8.6%, p<0.001) or cancer (4.8% v 7.2%, p=0.022). A larger proportion of
231 admitted cases in wave two were obese (29.1% v 24.6%, p=0.02). There was no significant difference in
232 proportion with known comorbidities of diabetes, kidney disease, hypertension, cardiovascular disease or
233 respiratory disease.

234
235 There were no significant differences between waves in the proportion with severe SARS-CoV-2 disease
236 upon admission as judged by hypoxia (64.3% in wave one vs 65.5% in wave two, p=0.67) or tachypnoea
237 (respiratory rate>20) (23.9% vs 24.3%, p=0.86). There were small differences in other physiological
238 parameters on admission, some of which reached statistical significance but differences were not clinically
239 relevant.

240
241 Laboratory markers were compared between waves (Table 1). There were small but significant differences,
242 such as lower CRP (median 51.0 mg/dL (IQR: 18.0-103.8) v 74.5 mg/dL (IQR: 26.0-148.0), p<0.001) and
243 lower ferritin (699.0 [IQR: 342.0-1359.0] v 855.0 [IQR: 394.0-1533.5], p=0.05) in wave two. There were other
244 small statistically significant differences without clear clinical significance, such as a lower D-Dimer in wave
245 two (0.9 mg/L FEU [IQR: 0.5-2.2] v 1.1 mg/L FEU [IQR:0.6-3.0], p=0.001) and lower estimated GFR (69.0
246 ml/min [IQR: 48.0-89.0] v 73.0 ml/min [IQR: 48.0-98.0], p=0.001), lower urea (6.0 mmol/L [IQR: 4.3-9.3] v 7.0
247 mmol/L [IQR: 4.6-12.2], p=0.001) and higher albumin (38.0 g/L [IQR: 34.0-41.0 g/L] vs 37.0 g/L [IQR: 32.0-
248 40.0], p<0.001). There was no significant difference with neutrophils, lymphocytes, neutrophils and
249 lymphocytes ratio (NLR), creatinine and glucose.

251 **Comparison of characteristics of admitted cases infected with B.1.1.7 and non-B.1.1.7 variants**

252 Given the reported association between increased disease severity and transmission with the B.1.1.7 variant,
253 we compared demographic, physiological and laboratory parameters between admitted cases with infection
254 caused by B.1.1.7 variant (n=400) compared with non-B.1.1.7 (n=910) variants (Table 2). We considered all
255 cases in wave one to be non-B.1.1.7, as wave one took place prior to emergence of the B.1.1.7 variant and
256 before B.1.1.7 variant was first identified in our population in November 2021.

257

258 Groups with non-B.1.1.7 and B.1.1.7 variant were not significantly different in mean age (62yrs vs 64yrs,
259 $p=0.22$) or ethnicity. The proportion of admissions who were female was larger in the group infected with the
260 B.1.1.7 variant compared to those infected by non-B.1.1.7 variants (48.0% vs 41.8%, $p=0.01$).

261

262 Cases infected with the B.1.1.7 variant were less likely to be frail (14.5% vs 22.4% $p=0.001$). A higher
263 proportion of those in the B.1.1.7 group were obese (30.2% v 24.8%, $p=0.048$). Other minor differences in
264 comorbidities between groups are shown in Table 2, but did not reach statistical significance.

265

266 On admission a higher proportion of those infected with B.1.1.7 were hypoxic (70.0% vs 62.5%, $p=0.029$),
267 the main indicator of severe disease. CRP on admission was lower in the B.1.1.7 group (54 mg/L IQR: 24.0-
268 102.0) compared to those infected with non-B.1.1.7 variants (70 mg/L, IQR: 25.0-142.0 $p<0.001$). Differences
269 in other laboratory parameters did not meet either statistical or clinical significance.

Discussion

Current hospital-based data collection methods predominantly rely on manual data extraction or linkage of multiple electronic records, which is resource intensive. Here we investigated the utility of automated data extraction from electronic health records as applied to investigation of changes during the second wave linked with emergence of a dominant new variant (B.1.1.7). Our data from a large healthcare institution in one of the worst affected regions internationally provides a large dataset for in-depth comparison; for instance we report a similar number of cases as reported from a national observational cohort study from Japan [19].

There were threefold more SARS-CoV-2 RNA positive cases reported by the hospital laboratory in wave two. The interpretation of this increase must recognise the many changes in testing guidelines and testing capacity between the two waves. Testing capacity increased substantially throughout 2020 both in hospital and in the community. Partly due to these capacity limits, during wave one it was not local policy to offer testing to outpatients and those not requiring admission, instead relying on clinical diagnosis. Healthcare workers were not offered occupational health testing until the end of wave one. We therefore restricted comparison to admitted and nosocomial cases.

There were almost twice as many admitted cases in wave two compared with wave one (1503 v 838). This is consistent with a higher local community incidence as reported by the ONS infection survey with 3.5% of individuals in London infected in January 2021 [27], compared with 2.2% of individuals in London at the peak of wave one [1]. The increase in peak hospital occupancy in wave two has also been reported nationally [28].

A major contributor to this increase in hospital admissions is likely to be the emergence of the B.1.1.7 variant, which is reported to be more transmissible and more virulent [14] [15] [16] [17]. However, the published studies thus far are largely based on mortality in community populations, and data on hospitalised cohorts is lacking. Our finding that those admitted with infection by the B.1.1.7 variant are more likely to be hypoxic on admission, a key marker of severe disease, is consistent with increased virulence of the B.1.1.7 variant as reported in these studies.

There was also an increase in the proportion of females in the admitted cohort of wave two, and those infected with B.1.1.7, accounting for an extra 5% of admissions with SARS-CoV-2 infection. Unpublished data referenced by NERVTAG [29] suggests hospitalised females infected with the B.1.1.7 variant may be more

301 likely to die or require ICU care. Our data, showing an increase in the proportion of females in the admission
302 cohort is consistent with the finding that B.1.1.7 may show increased virulence in females. Further analysis
303 is required to determine whether this effect is attenuated when adjusted for age and other variables.

304
305 Admitted cases in the wave two were also around half as likely to have a diagnosis of frailty, which may be
306 due to fewer admissions from care homes during wave two, which has been reported both nationally [30]
307 and internationally [31]. Additionally, admitted cases were around a third less likely to have cancer in wave
308 two. Both of these reductions may also be as a result of individuals shielding, and therefore at reduced risk
309 for acquiring SARS-CoV-2 infection. Other differences in comorbidities between waves were small and of
310 unclear clinical significance. Those admitted with B.1.1.7 infection were also less likely to be frail, however
311 no other clinically significant difference in co-morbidities was found.

312
313 Our findings contrast to those seen in other areas where differences between waves have been compared.
314 For instance, in Japan the second wave had fewer cases, which were younger and less comorbid [19]. Our
315 results differ, showing a similar age distribution between waves, similar to what has been reported
316 internationally [31] [32].

317
318 One additional striking observation was the similarity in number of nosocomial cases in wave one (n=96) and
319 wave two (n=137). Interestingly, nosocomial cases in wave one increased and started to fall before impact of
320 the main infection control interventions of banning hospital visitors (March 25th), introducing universal surgical
321 mask wearing (28th March 2020) and universal regular inpatient screening (after the first wave). In
322 comparison, all these measures were in place prior to the second wave. The increased number of cases in
323 wave two may in part be due to increased inpatient screening, which would identify asymptomatic cases, or
324 introduction of the more transmissible B.1.1.7 variant which made up the vast majority of our sequenced
325 nosocomial cases.

326
327 In both waves the incidence of nosocomial cases rose temporally aligned with increasing community
328 incidence and hospital admissions, and then started to fall while new admissions continued to increase. This
329 is not consistent with the predominant mode by which nosocomial cases acquire infection being via
330 transmission from admitted cases. It seems more likely that incidence in the community and in nosocomial

331 cases are mechanistically linked and therefore follow the same course, peaking prior to hospitalisations of
332 cases.

333
334 Some healthcare institutions report far fewer nosocomial acquisitions; for instance an academic hospital in
335 Boston, USA reported only 2 nosocomial cases in over 9000 admissions [33]. This could be due to greater
336 availability of side rooms for isolation or their use of N95 masks by HCWs, which may decrease transmission
337 between HCWs and patients. In contrast, current UK public health policy recommends surgical facemasks
338 for patient interactions unless performing aerosol generating procedures [34]. This incidence of nosocomial
339 infection is a major challenge for UK healthcare institutions, with associated crude mortality at around 30%
340 during the first wave [35,36]. For this reason it will be important to further investigate the factors involved in
341 nosocomial acquisition in both waves.

342 343 **Limitations**

344 Our study population comes from a single inner-city healthcare institution and therefore needs to be compared
345 with findings from other centres. Our dataset included cases identified by SARS-CoV-2 RNA testing in our
346 laboratory, so some cases diagnosed by external laboratories prior to admission may not be represented
347 unless subsequently testing positive in our laboratory. The impact of differences in testing strategy and
348 capacity during both waves needs further investigation, particularly the impact of the increase in
349 asymptomatic cases in wave two. Finally, the analysis of clinical characteristics in this study was restricted
350 to those recorded on admission to hospital. A follow-up study will include outcome data, when the wave two
351 cohort has completed hospital stay, alongside other unstructured data points such as radiology or genome
352 sequence results in clinical or external reports, to facilitate linkage with national and international research
353 studies.

354 355 **Conclusion**

356 Our data extraction method is able to iteratively extract clinical information from multiple clinical systems and
357 integrate into a clinical dataset of SARS-CoV-2 cases. This compares to the more labour intensive
358 prospective data collection by research staff conducting manual data collection. The study also highlights the
359 benefits of being able to integrate detailed clinical data with genome sequence to obtain rapid insight into
360 genotype/phenotype differences. The number of cases diagnosed, admissions and nosocomial cases were
361 higher in wave two than wave one, likely due to the increased incidence caused by the more transmissible

362 B.1.1.7 variant. A larger proportion of admitted cases in wave two and in those infected by B.1.1.7 were
363 female. B.1.1.7 was associated with higher proportion being hypoxic on admission, which may reflect
364 increased virulence of B.1.1.7.

365

Figures and Tables.

Figure 1: Distribution of laboratory confirmed SARS-CoV-2 cases over time. Daily incidence of new cases (beige), newly admitted cases (orange) and nosocomial acquisitions (green) over time.

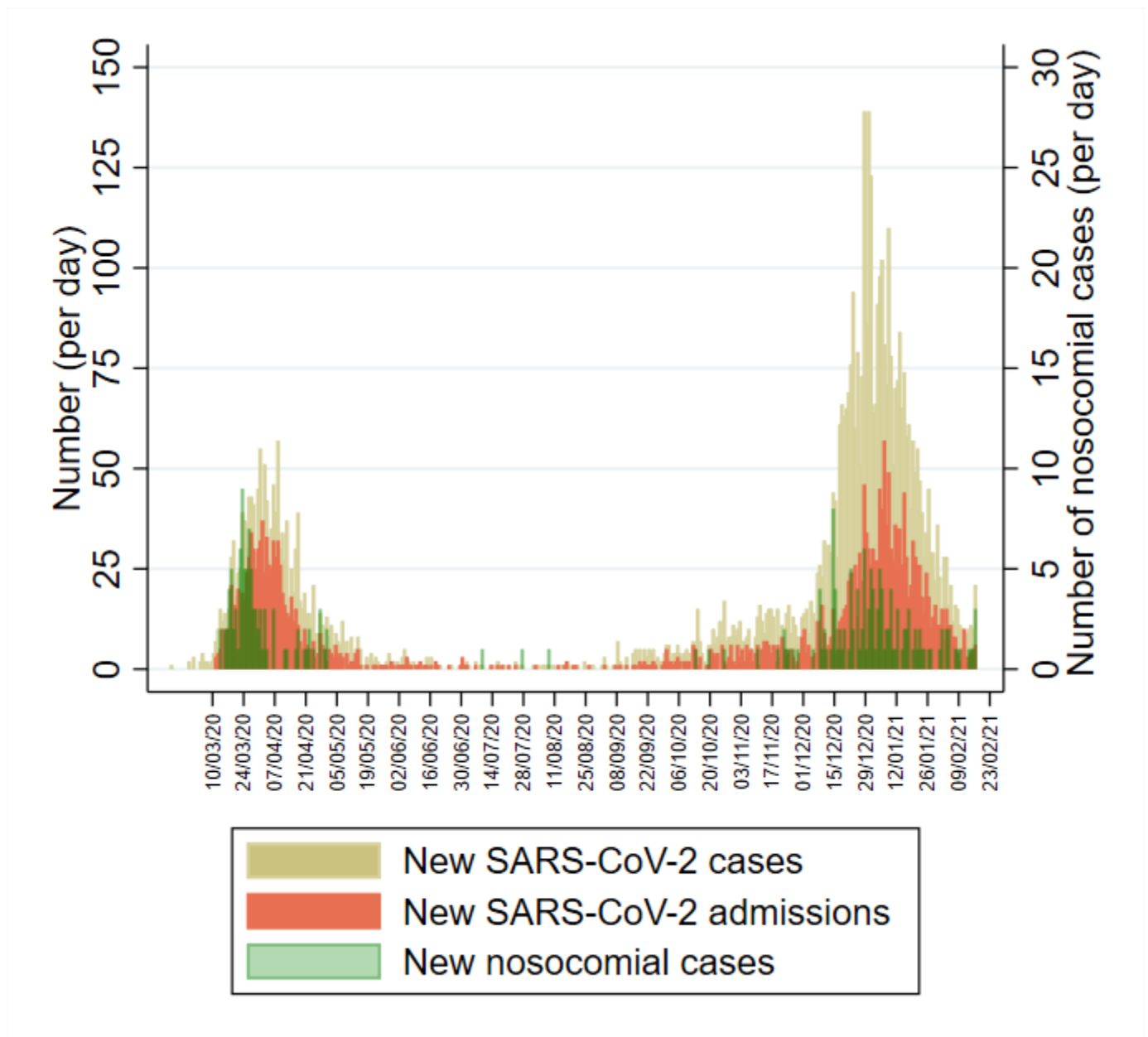
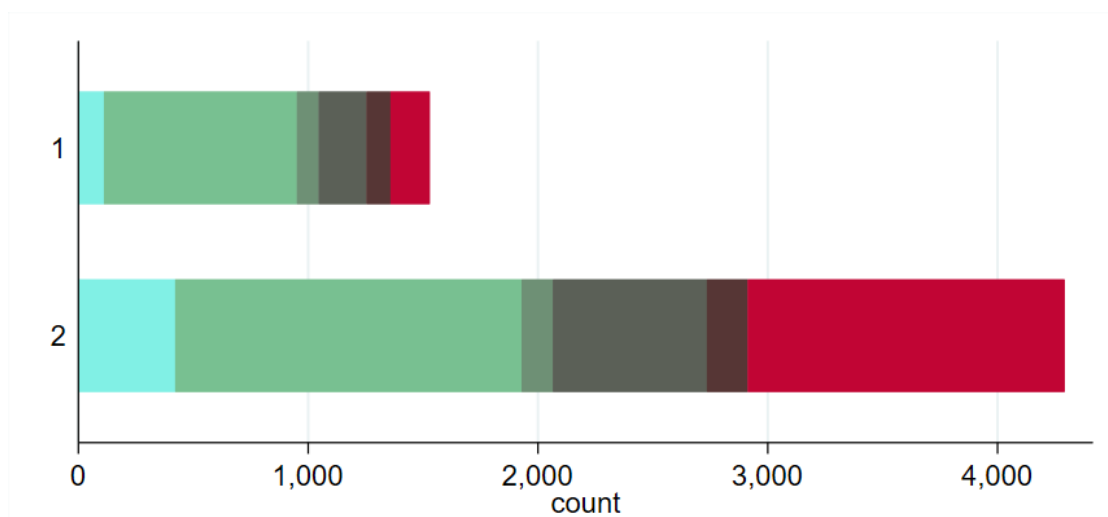


Figure 2 (A) Absolute number of cases within the different hospital cohorts during wave one (upper) and wave two (lower). **(B)** Proportion of cases within the different hospital cohorts during wave one (upper) and wave two (lower).

A



B

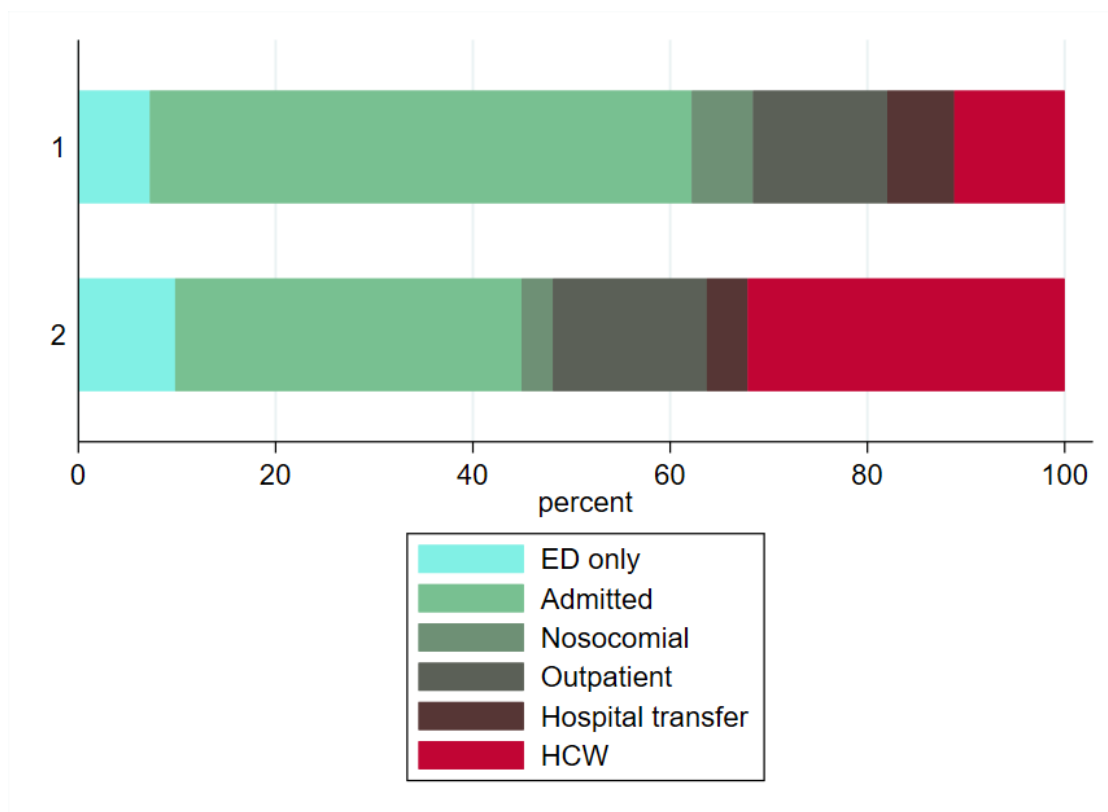


Figure 3 Number of cases with sequenced SARS-CoV-2 isolates by epi-week (bar) and the proportion of which were made up of the variant B.1.1.7 (red line)

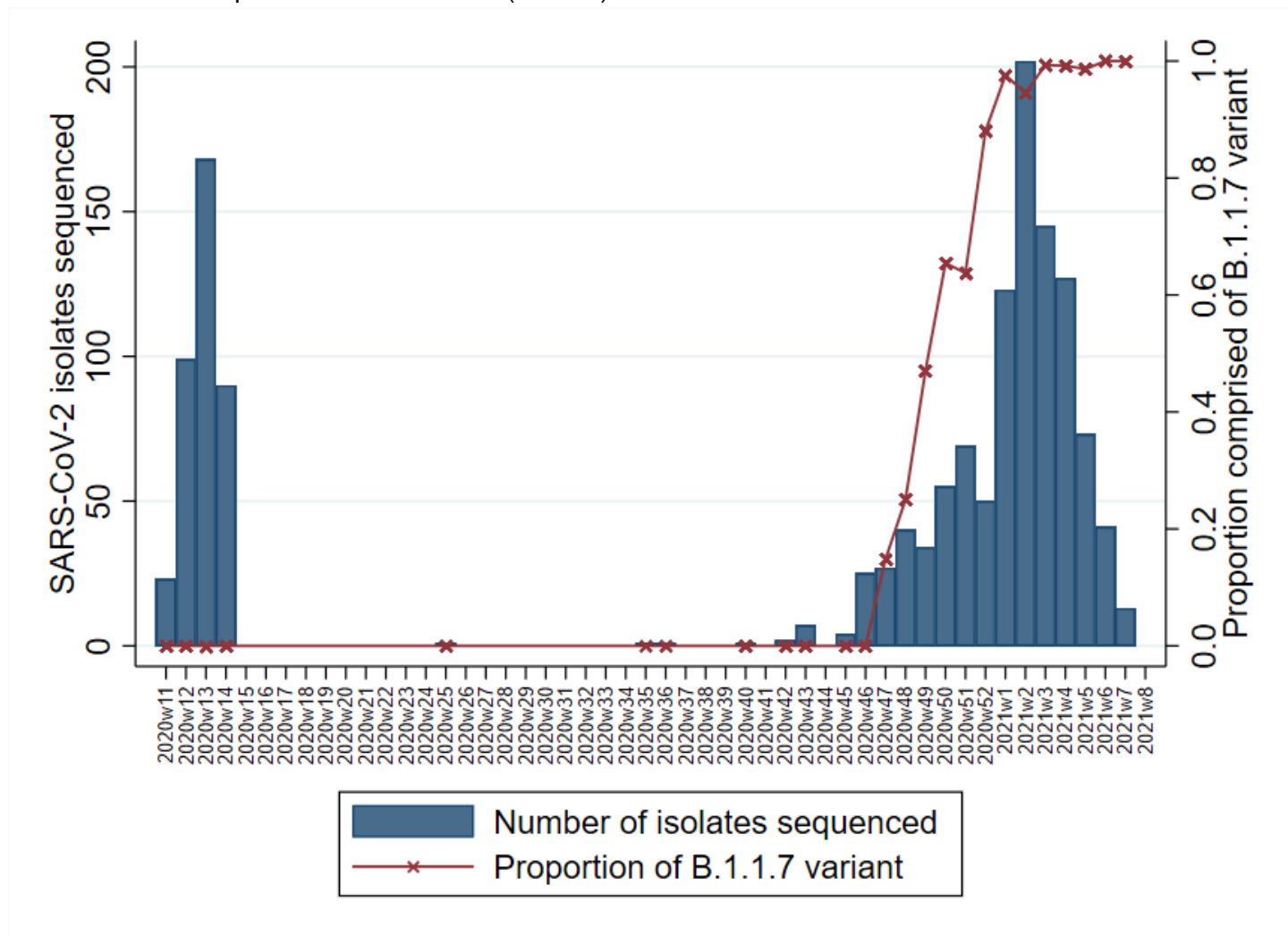


Table 1, General statistics of the cohort for wave one and two admissions

	Missing	Wave one admissions n (%) / value [IQR]	Wave two admissions n (%) / value [IQR]	P-Value
n		838	1503	
Demographics				
Age	0	62.0 [49.0,78.0]	60.0 [47.0,74.0]	0.019
Male	0	488 (58.2)	792 (52.7)	0.011
Ethnicity	0			0.013
White		331 (39.5)	598 (39.8)	
Asian		64 (7.6)	121 (8.1)	
Black-African		177 (21.1)	262 (17.4)	
Black-Caribbean		73 (8.7)	98 (6.5)	
Mixed		15 (1.8)	18 (1.2)	
Other		45 (5.4)	107 (7.1)	
Unknown		133 (15.9)	299 (19.9)	
BMI	577	27.0 [23.8,31.7]	27.7 [24.0,32.9]	0.022
BMI>30		206 (24.6)	438 (29.1)	0.02
BMI>40		34 (4.1)	86 (5.7)	0.098
Physiological parameters				
Heart Rate	360	84.0 [75.0,94.0]	81.0 [72.0,91.0]	<0.001
Heart Rate>100		105 (12.5)	142 (9.4)	0.02
Blood pressure				
Systolic	369	125.0 [113.0,139.0]	127.0 [115.0,141.0]	0.013
Diastolic	369	73.0 [65.0,80.0]	75.0 [68.0,82.0]	<0.001
MAP	369	90.7 [82.2,99.0]	92.3 [84.7,101.3]	<0.001
Respiratory Rate	359	19.0 [18.0,22.0]	19.0 [18.0,22.0]	0.764
Respiratory Rate>20		200 (23.9)	365 (24.3)	0.86
Hypoxia	658	370 (64.3)	726 (65.5)	0.67
Temperature	361	36.9 [36.4,37.5]	36.6 [36.2,37.2]	<0.001
NEWS2	405			0.86
0		95 (11.3)	173 (11.5)	
1		108 (12.9)	192 (12.8)	
2		117 (14.0)	188 (12.5)	

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2+		371 (44.3)	692 (46.0)	
Laboratory parameters				
Neutrophils	8	4.9 [3.4,7.6]	5.0 [3.3,7.5]	0.724
Lymphocytes	7	0.9 [0.6,1.3]	0.9 [0.6,1.4]	0.741
NLR	8	5.4 [3.1,9.9]	5.4 [3.2,9.8]	0.951
Creatinine	43	83.0 [64.0,115.0]	86.0 [68.0,117.0]	0.065
Urea	855	7.0 [4.6,12.2]	6.0 [4.3,9.9]	0.001
Estimated GFR	114	73.0 [48.0,98.0]	69.0 [48.0,89.0]	0.001
Albumin	185	37.0 [32.0,40.0]	38.0 [34.0,41.0]	<0.001
CRP	61	74.5 [26.0,148.0]	51.0 [18.0,103.8]	<0.001
DDimer	1297	1.1 [0.6,3.0]	0.9 [0.5,2.2]	0.001
Ferritin	905	855.0 [394.0,1533.5]	699.0 [342.0,1359.0]	0.05
Co-morbidities				
Stroke	0	72 (8.6)	64 (4.3)	<0.001
TIA	0	9 (1.1)	20 (1.3)	0.731
Hypertension	0	288 (34.4)	464 (30.9)	0.091
Diabetes	0	246 (29.4)	384 (25.5)	0.052
AF	0	63 (7.5)	115 (7.7)	0.972
IHD	0	146 (17.4)	244 (16.2)	0.495
Heart Failure	0	54 (6.4)	105 (7.0)	0.679
COPD	0	64 (7.6)	109 (7.3)	0.796
Asthma	0	74 (8.8)	138 (9.2)	0.835
Cancer	0	60 (7.2)	72 (4.8)	0.022
Kidney disease	0	112 (13.4)	181 (12.0)	0.389
HIV	0	21 (2.5)	36 (2.4)	0.979
Solid organ Transplant	0	24 (2.9)	49 (3.3)	0.686
Frailty	0	191 (22.8)	173 (11.5)	<0.001

Note: p-value was from Kruskal-Wallis test for continuous variables and Chi-squared test for categorical variables.

Abbreviations: BMI: Body Mass Index, TIA: Transient Ischaemic Attack, IHD: Ischemic Heart Disease, COPD: Chronic Obstructive Pulmonary Disease, HIV: Human Immunodeficiency Virus, MAP: Mean Arterial Pressure, SPO2: Oxygen Saturation, GFR: Glomerular Filtration Rate, CRP: C-Reactive Protein, NLR: Neutrophils and Lymphocytes Ratio, NEWS2: National Early Warning Score 2.

Table 2, General statistics of the cohort for non B.1.1.7 variant and B.1.1.7 variant admissions

	Missing	Non B.1.1.7 variant n (%) / value [IQR]	B.1.1.7 variant n (%) / value [IQR]	P-Value
n		910	400	
Demographics				
Age	0	62.0 [49.0,78.0]	64.0 [52.0,78.0]	0.22
Male		530 (58.2)	208 (52.0)	0.042
Ethnicity	0			0.402
White		358 (39.3)	164 (41.0)	
Asian		71 (7.8)	38 (9.5)	
Black-African		191 (21.0)	67 (16.8)	
Black-Caribbean		78 (8.6)	27 (6.8)	
Mixed		16 (1.8)	6 (1.5)	
Other		50 (5.5)	23 (5.8)	
Unknown		146 (16.0)	75 (18.8)	
BMI	334	27.1 [23.8,31.7]	28.1 [24.0,34.2]	0.036
BMI>30		226 (24.8)	121 (30.2)	0.048
BMI>40		36 (4.0)	26 (6.5)	0.063
Physiological parameters				
Heart Rate	198	84.0 [74.0,94.0]	80.0 [72.0,90.0]	0.001
Heart Rate>100		118 (13.0)	36 (9.0)	0.05
Blood pressure				
Systolic	201	125.0 [113.0,139.5]	127.0 [115.0,142.0]	0.138
Diastolic	201	73.0 [65.0,80.0]	75.0 [67.0,83.0]	0.01
MAP	201	90.7 [82.3,99.2]	92.7 [84.0,101.7]	0.022
Respiratory Rate	194	19.0 [18.0,21.0]	19.0 [18.0,22.0]	0.591
Respiratory Rate>20		209 (23.0)	96 (24.0)	0.737
Hypoxia	0	392 (62.5)	217 (70.0)	0.029
Temperature	199	36.9 [36.4,37.5]	36.6 [36.2,37.1]	<0.001
NEWS2	0			0.038
0		107 (11.8)	43 (10.8)	
1		125 (13.7)	39 (9.8)	
2		127 (14.0)	53 (13.2)	

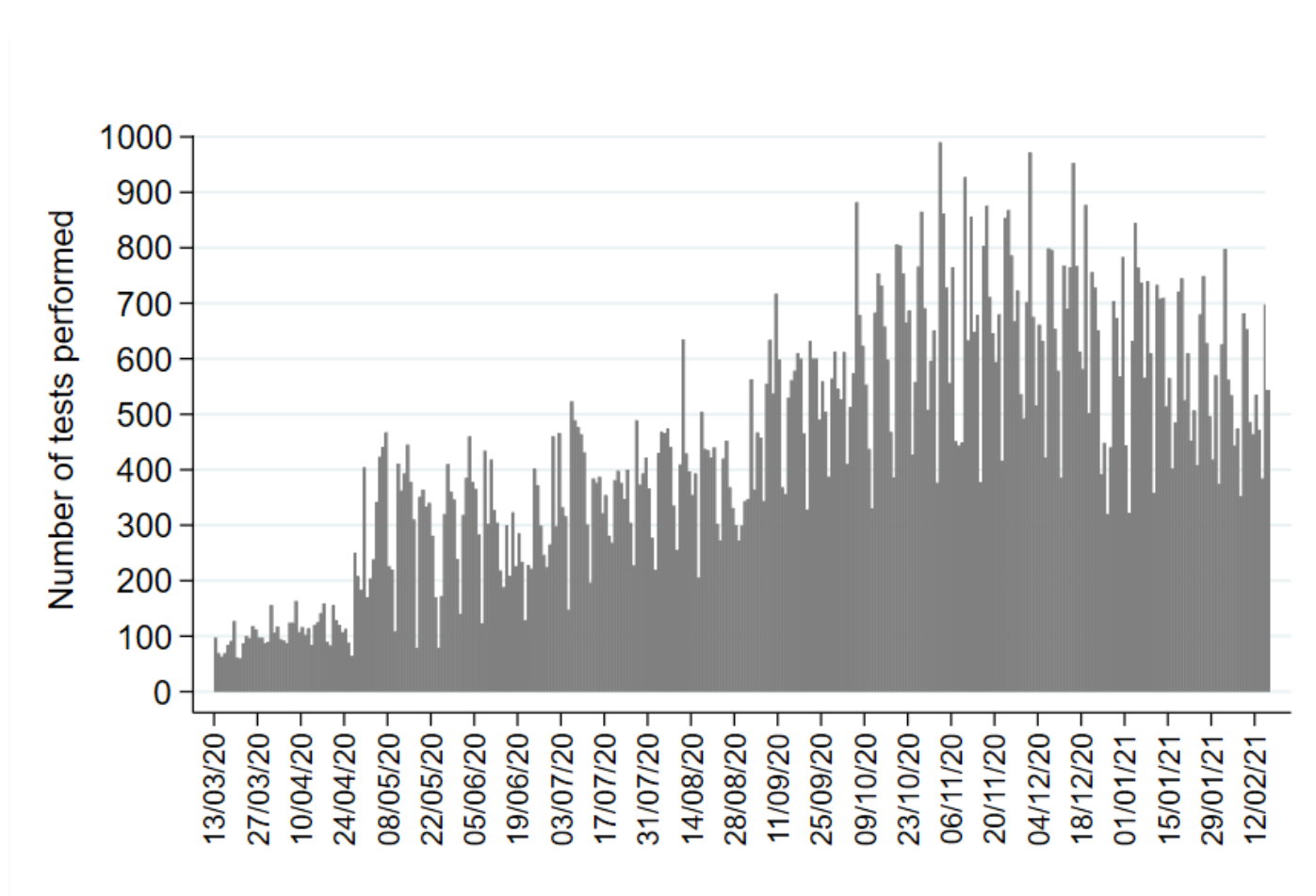
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2+		391 (43.0)	207 (51.7)	
nan		160 (17.6)	58 (14.5)	
Laboratory parameters				
Neutrophils	2	4.9 [3.4,7.6]	4.8 [3.3,6.9]	0.479
Lymphocytes	1	0.9 [0.6,1.3]	0.8 [0.5,1.2]	0.005
NLR	2	5.4 [3.1,9.9]	5.8 [3.5,10.2]	0.195
Creatinine	16	83.0 [64.0,115.0]	92.0 [74.0,126.0]	<0.001
Urea	536	6.8 [4.3,12.0]	6.6 [4.4,10.6]	0.573
Estimated GFR	43	73.0 [48.5,97.0]	63.5 [44.0,81.0]	<0.001
Albumin	107	37.0 [33.0,41.0]	38.0 [34.0,41.0]	0.009
CRP	21	70.0 [25.0,142.0]	54.0 [24.0,102.0]	<0.001
DDimer	727	1.1 [0.6,2.8]	0.9 [0.5,1.9]	0.019
Ferritin	501	815.0 [366.2,1499.0]	712.0 [357.5,1294.0]	0.341
Co-morbidities				
Stroke	0	74 (8.1)	22 (5.5)	0.117
TIA	0	12 (1.3)	5 (1.2)	0.87
Hypertension	0	315 (34.6)	144 (36.0)	0.674
Diabetes	0	267 (29.3)	106 (26.5)	0.326
AF	0	72 (7.9)	42 (10.5)	0.154
IHD	0	162 (17.8)	78 (19.5)	0.513
Heart Failure	0	61 (6.7)	34 (8.5)	0.299
COPD	0	74 (8.1)	32 (8.0)	0.977
Asthma	0	84 (9.2)	39 (9.8)	0.846
Cancer	0	64 (7.0)	21 (5.2)	0.278
Kidney disease	0	122 (13.4)	62 (15.5)	0.359
HIV	0	22 (2.4)	10 (2.5)	0.916
Solid organ transplant	0	25 (2.7)	19 (4.8)	0.092
Frailty	0	204 (22.4)	58 (14.5)	0.001

Note: p-value was from Kruskal-Wallis test for continuous variables and Chi-squared test for categorical variables.

Abbreviations: BMI: Body Mass Index, TIA: Transient Ischaemic Attack, IHD: Ischemic Heart Disease, COPD: Chronic Obstructive Pulmonary Disease, HIV: Human Immunodeficiency Virus, MAP: Mean Arterial Pressure, SPO2: Oxygen Saturation, GFR: Glomerular Filtration Rate, CRP: C-Reactive Protein, NLR: Neutrophils and Lymphocytes Ratio, NEWS2: National Early Warning Score 2.

Supplementary Figure 1: Daily number of SARS-CoV-2 tests performed in our laboratory between 13th March 2021, when testing was introduced, until 17th February 2021.



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