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Clinical characteristics, symptoms and outcomes of 1054 adults presenting to hospital with suspected COVID-19: A comparison of patients with and without SARS-CoV-2 infection

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SUMMARY

Objectives: Most reports describing the characteristics of patients hospitalised with COVID-19 lack a comparator group. We compared clinical characteristics, symptoms, and outcomes of adults presenting to hospital during the pandemic first wave, who tested positive and negative for SARS-CoV-2.

Methods: Detailed patient data was obtained from a large, controlled, non-randomised trial of molecular point-of-care testing versus laboratory RT-PCR for SARS-CoV-2 in adults presenting to a large UK hospital with suspected COVID-19.

Results: 1054 patients were included: 352 (33.4%) tested positive and 702 (66.6%) negative. 13.4% (47/352) COVID-19-positive patients had COPD versus 18.7% (131/702) of COVID-19-negative patients (difference=5.3% [95%CI −9.7% to −0.5%], $p=0.0297$). 5.7% (20/352) of COVID-19-positive patients were smokers versus 16.5% (116/702) of negative patients (difference=−10.8% [−14.4% to −7.0%], $p=0.0001$). 70.5% (248/352) of COVID-19-positive patients were White-British versus 85.5% (600/702) of negative patients (difference=−15.0% [−20.5% to −9.7%], $p<0.0001$). 20.9% (39/187) of COVID-19-positive patients were healthcare workers versus 5.2% (15/287) of negative patients ($p<0.0001$).

Anosmia was reported in 33.1% (47/142) versus 8.8% (19/216) of COVID-19-positive and negative patients respectively ($p<0.0001$). Non-SARS-CoV-2 respiratory viruses or atypical bacteria were detected in 2.5% (5/197) of COVID-19 patients versus 7.9% (24/302) of COVID-19-negative patients ($p=0.0109$).

Hospitalisation duration and 30-day-mortality were higher in COVID-19 patients and invasive ventilation was more frequent (11.1% vs 2.8%, $p<0.0001$), and longer (14.5 vs 4.7 days, $p=0.0015$).

Conclusions: There were substantial differences between patients with and without COVID-19 in terms of ethnicity, healthcare worker-status, comorbidities, symptoms, and outcomes. These data can inform healthcare planning for the next phase of the pandemic.

Introduction

The COVID-19 pandemic caused by SARS-CoV-2 has led to over 21 million cases and over 700,000 deaths worldwide.[1] Over 130,000 patients have been admitted to hospitals in the UK with confirmed COVID-19.[2]

Large cohort studies of patients presenting to hospital with COVID-19 from countries including the USA, China, Spain, and the UK, have improved our understanding of the disease.[3-9] Cohort studies of hospitalised patients have shown that about a quarter of patients with severe COVID-19 die, and that risk factors such as age, obesity, male sex, and comorbidities are associated with adverse outcomes.

However, published cohorts of patients with severe COVID-19 have typically lacked a comparison or control group. This weakness means that clinical guidance, decision making, and pre-test

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risk stratification of patients with suspected COVID-19 is incomplete.

We did a large, non-randomised, controlled trial of molecular point-of-care testing (mPOCT) for SARS-CoV-2 in adults presenting to hospital with suspected COVID-19 (the CoV-19POC trial).[10] Within the CoV-19POC trial is a large cohort of patients: patients who have tested positive and patients who have tested negative for SARS-CoV-2.

The aim of the study presented here was to examine and compare the clinical characteristics, symptoms, and outcomes of adult patients presenting to hospital testing positive and negative for COVID-19, using data collected from a large clinical trial.

Methods

The CoV-19POC trial was a prospective, interventional, non-randomised study of mPOCT implementation. The CoV-19POC trial protocol is freely available.[11] The study reported here is a cohort study including all patients in the analysed in the CoV-19POC trial. The sample size is therefore based on a convenience sample.

The inclusion criteria, in brief, were adults (≥18 years old), presenting to the Emergency Department or Acute Medicine Unit or other admissions area of Southampton General Hospital, UK, with an acute respiratory illness or otherwise clinically suspected of having COVID-19. Patients were tested with the QIAstat-Dx Respiratory SARS-CoV-2 Panel (QIAGEN, Germany) as mPOCT or on-site laboratory testing by RT-PCR using the Public Health England recommended assay. The QIAstat-Dx Respiratory SARS-CoV-2 Panel is a multiplex PCR panel that detects: SARS-CoV-2 (E and Orf1 genes), influenza A (H1N1/2009, H1, H3), influenza B, coronaviruses (229E, HKU1, NL63, and OC43), parainfluenza viruses (1, 2, 3, and 4), adenovirus, respiratory syncytial virus, human metapneumovirus, bocavirus, and rhinovirus/enterovirus plus *Mycoplasma pneumoniae, Legionella pneumophila*, and *Bordetella pertussis*.[12,13]

The study was amended once to update the time period of the control group to be contemporaneous to the intervention group. The study was approved by Regional Ethics Committee South Central – Hampshire A on 16th March 2020 (reference 20/SC/0138), and prospectively registered on an international database (ISRCTN14966673).

Patients who received mPOCT gave fully informed written consent and were asked detailed questions on their symptoms prior to mPOCT result. Questions about anosmia were added five days after the trial started as supporting evidence emerged. Only routinely collected data was used in the RT-PCR group. Retrospective outcomes data collection was completed from electronic medical records. Potential bias was reduced by prospective data collection where possible prior to mPOCT result, and by wide inclusion criteria with minimal exclusion criteria.

Patients with COVID-19, as defined by PCR positivity by either mPOCT or laboratory testing were compared to those without COVID-19. Statistical analyses were done with Prism version 8.2.1 (GraphPad Software, La Jolla, CA, USA). Categorical variables, summarised in counts and percentages, were compared using differences in proportions using Chi-squared or Fisher's exact test. Continuous variables, expressed as medians and interquartile ranges (IQR), were compared using the Mann–Whitney *U* test. Missing data were <2% in all analyses unless stated otherwise. This study is reported according to the STROBE guideline.

Results

Overall

1054 adults presenting to hospital with acute respiratory illness or otherwise suspected of having COVID-19 were tested for SARS-CoV-2 and included in this analysis: 352 (33.4%) tested PCR positive and 702 (66.6%) tested PCR negative for SARS-CoV-2. The patients presented to hospital between 20th March and 29th April 2020, corresponding to the peak of the first wave of the pandemic in the UK.[2]

Demographics, comorbidities, and presenting clinical and laboratory features

The median age of COVID-19 positive patients was 68 years (IQR 50 to 80) versus 69 (52 to 81; difference of −1 [95%CI −3 to 2], $p = 0.4689$). 57.4% (202/352) were male in the COVID-19 positive group versus 51.7% (363/702) in the COVID-19 negative group (difference of 5.7% [95%CI −0.7% to 11.9%], $p = 0.0887$). Fewer patients had COPD in the COVID-19 positive group than negative group (13.4% (47/352) vs 18.7% (131/702), difference of −5.3% [−9.7% to −0.5%], $p = 0.0297$). There were no significant differences in a range of other comorbidities including hypertension, cardiovascular disease, and diabetes (Table 1).

5.7% (20/352) were current smokers in the COVID-19 positive group versus 16.5% (116/702) in the COVID-19 negative group (difference of −10.8% [−7.0% to −14.4%], $p = 0.0001$; Table S1 in Supplementary material). 53.7% (189/352) had never smoked in the COVID-19 positive group compared to 35.9% (252/702) in the COVID-19 negative group (difference of 17.8% [11.4% to 24.0%], $p<0.0001$).

Patients with COVID-19 were more frequently healthcare workers than patients who tested negative for COVID-19 (20.9% (39/187) vs 5.2% (15/287), difference of 15.6% [9.5% to 22.3%], $p<0.0001$).

Fewer patients were of White-British ethnicity in the COVID-19 positive group than in the COVID-19 negative group (70.5% (248/352) vs 85.5%, $p<0.0001$; Table 2). There were proportionally more COVID-19 positive patients of Indian (3.4% (12/352) vs 1.0% (7/702), $p = 0.0115$), non-Indian/Pakistani/Bangladeshi/Chinese Asian (8.0% (28/352) vs 0.7% (5/702), $p<0.0001$), and Black-African or Black-British-African (3.7% (13/352) vs 0.6% (4/702), $p = 0.0003$) backgrounds than patients testing negative for COVID-19.

On the first set of observations (vital signs) at presentation to hospital, patients with COVID-19 had a higher proportion of fever (≥37.8 °C) than patients without COVID-19 (31.8% (112/352) vs 15.4% (108/702); difference 16.4% [10.1% to 22.1%], $p<0.0001$). Patients with COVID-19 also had a higher respiratory rate (24 [20 to 30] vs 21 [18 to 26], difference of 3 [2 to 4], $p<0.0001$) and slightly lower systolic blood pressure (130 mmHg [120 to 146] vs 135 mmHg [120 to 154], difference of −5 mmHg [−7 to 0], $p = 0.0245$) than patients who did not have COVID-19. Patients with COVID-19 were more frequently on supplemental oxygen (38.4% (135/352) vs 22.2% (156/702), difference of 16.1% [10.2% to 22.1%], $p<0.0001$) and had a higher National Early Warning Score 2 (NEWS2: a national severity scoring system; 5 [3 to 7] vs 4 [2 to 6], difference of 1 [1 to 2], $p<0.0001$) than COVID-19 negative patients.

On patients' first blood tests, COVID-19 patients had a higher median C-reactive protein (95 [36 to 158] vs 26 [8 to 101.5], lower lymphocyte count (0.9×10^9/L [0.63 to 1.3] vs 1.2×10^9/L [0.8 to 1.8], and lower neutrophil count (5.6×10^9/L [4.1 to 8.3] vs 8.0 x10^9/L [5.3 to 12.0] compared to COVID-19 negative patients (all $p<0.0001$; Table 1). Patients in the COVID-19 group more frequently had lymphopenia combined with a non-raised neutrophil count (59.7% (184/308) vs 29.0% (176/607), difference of 30.7% [24.0% to 37.1%], $p<0.0001$).

Symptoms

The median duration of symptoms prior to hospital presentation was longer in COVID-19 positive patients than COVID-19 neg-

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Table 1
Demographics, comorbidities, and clinical and laboratory features of patients testing positive and negative for COVID-19.

	COVID-19 positive (n = 352)	COVID-19 negative (n = 702)	Difference (95% CI)	p value
Demographics				
Age (years)	68 (50 to 80)	69 (52 to 81)	−1 (−3 to 2)	0.4689
Male gender	202 (57.4%)	363 (51.7%)	5.7% (−0.7% to 11.9%)	0.0887
Current smoker	20 (5.7%)	116 (16.5%)	−10.8% (−14.4% to −7.0%)	**0.0001**
Pregnant	3 (0.9%)	6 (0.9%)	0.0% (−1.2% to 1.7%)	>0.9999
Healthcare worker	39 (20.9%)[a]	15 (5.2%)[a]	15.6% (9.5% to 22.3%)	**<0.0001**
Comorbidities				
Hypertension	144 (40.9%)	278 (39.6%)	1.3% (−4.9% to 7.6%)	0.6897
Cardiovascular disease	125 (35.5%)	280 (39.9%)	−4.4% (−10.4% to 1.9%)	0.1796
Respiratory disease (any)	86 (24.4%)	202 (28.8%)	−4.3% (−9.8% to 1.4%)	0.1431
Asthma	53 (15.1%)	126 (17.9%)	−2.9% (−7.4% to 2.0%)	0.2587
COPD	47 (13.4%)	131 (18.7%)	−5.3% (−9.7% to −0.5%)	**0.0297**
Chronic kidney disease	41 (11.6%)	82 (11.7%)	0.0% (−4.0% to 4.3%)	>0.9999
Chronic liver disease	17 (4.8%)	50 (7.1%)	−2.3% (−5.1% to 0.9%)	0.1806
Diabetes	91 (25.9%)	152 (21.7%)	4.2% (−1.2% to 9.8%)	0.1407
Active malignancy	18 (5.1%)	58 (8.3%)	−3.1% (−6.1% to 2.1%)	0.0765
Dementia	47 (13.4%)	66 (9.4%)	4.0% (−0.01% to 8.4%)	0.0573
Immunosuppressed	12 (3.4%)	38 (5.4%)	−2.0% (−4.4% to 0.8%)	0.1684
Presentation characteristics				
Heart rate (beats/min)	93 (82 to 106)	94 (79 to 108)	−1 (−2 to 3)	0.5639
Respiratory rate (breaths/min)	24 (20 to 30)	21 (18 to 26)	3 (2 to 4)	**<0.0001**
Systolic blood pressure (mmHg)	130 (120 to 146)	135 (120 to 154)	−5 (−7 to 0)	**0.0245**
Temperature (°C)	37.15 (36.6 to 38.1)	36.7 (36.3 to 37.2)	0.45 (0.3 to 0.6)	**<0.0001**
Temperature ≥37.8 °C	112 (31.8%)	108 (15.4%)	16.4% (10.1% to 22.1%)	**<0.0001**
On supplemental oxygen	135 (38.4%)	156 (22.2%)	16.1% (10.2% to 22.1%)	**<0.0001**
NEWS2 score	5 (3 to 7)	4 (2 to 6)	1 (1 to 2)	**<0.0001**
C reactive protein	95 (36 to 158)	26 (8 to 101.5)	69 (39 to 79)	**<0.0001**
Lymphocyte count (10^9/L)	0.9 (0.63 to 1.3)	1.2 (0.8 to 1.8)	−0.3 (−0.3 to −0.2)	**<0.0001**
Neutrophil count (10^9/L)	5.6 (4.1 to 8.3)	8.0 (5.3 to 12.0)	−2.4 (−2.6 to −1.5)	**<0.0001**
Lymphopenia and non-raised neutrophil count	184 (59.7%)[b]	176 (29.0%)[b]	30.7% (24.0% to 37.1%)	**<0.0001**
Pneumonia on CXR	212 (62.2%)[c]	201 (30.7%)[c]	31.4% (25.0% to 37.5%)	**<0.0001**
Duration of symptoms (days)	5 (2 to 9)	3 (1 to 7)	2 (0 to 2)	**0.0021**

Data are n (%) or median (IQR). [a] n = 187 and [b] 287 respectively. [b] n = 308 and n = 607 respectively. [c] n = 341 and n = 654 respectively. NEWS2, National Early Warning Score 2; COPD, Chronic Obstructive Pulmonary Disease, CXR, Chest X-ray; 95% CI, 95% Confidence Interval. Lymphopenia is defined as lymphocyte count $<1.5 \times 10^9$/L; neutrophil count upper limit of normal is 8×10^9/L. Pneumonia on CXR as reported by study-independent radiologists or reporting radiographers, blinded to COVID-19 status.

Table 2
Ethnicity of patients testing positive and negative for COVID-19.

	COVID-19 positive (n = 352)	COVID-19 negative (n = 702)	Difference (95% CI)	p value
White				
British	248 (70.5%)	600 (85.5%)	−15.0% (−20.5% to −9.7%)	**<0.0001**
Irish	0	4 (0.6%)	−0.6% (−1.5% to 0.6%)	0.3075
Any other White background	13 (3.7%)	25 (3.6%)	0.1% (−2.9% to 2.1%)	>0.9999
Mixed				
White and Black Caribbean	0	2 (0.3%)	−0.3% (−1.0% to 0.8%)	0.5547
White and Black African	0	2 (0.3%)	−0.3% (−1.0% to 0.8%)	0.5547
White and Asian	2 (0.6%)	2 (0.3%)	0.3% (−0.6% to 1.8%)	0.6048
Any other mixed background	0	2 (0.3%)	−0.3% (−1.0% to 0.8%)	0.5547
Asian or Asian British				
Indian	12 (3.4%)	7 (1.0%)	2.4% (0.6% to 4.9%)	**0.0115**
Pakistani	5 (1.4%)	5 (0.7%)	0.7% (−0.5% to 2.6%)	0.3157
Bangladeshi	2 (0.6%)	1 (0.1%)	0.4% (−0.4% to 1.9%)	0.2599
Any other Asian background	28 (8.0%)	5 (0.7%)	7.2% (4.7% to 10.6%)	**<0.0001**
Black or Black British				
Caribbean	2 (0.6%)	2 (0.3%)	0.3% (−0.6% to 1.8%)	0.6048
African	13 (3.7%)	4 (0.6%)	3.1% (1.4% to 5.7%)	**0.0003**
Any other Black background	0	1 (0.1%)	−0.1% (−0.8% to 0.9%)	>0.9999
Other ethnic groups				
Chinese	1 (0.3%)	1 (0.1%)	0.1% (−0.6% to 1.5%)	>0.9999
Any other ethnic group	4 (1.1%)	2 (0.3%)	0.9% (−0.2 to 2.6%)	0.1001
Not stated or unknown	22 (6.3%)	37 (5.3%)	1.0% (−1.9% to 4.3%)	0.5701

ative patients, 5 days (2 to 9) vs 3 days (1 to 7), difference of 2 [0 to 2], p = 0.0021) (Table 1).

Sore throat, cough, sputum, fever, chills, fatigue, reduced appetite, headache, diarrhoea, and anosmia (Table 3) were more frequently reported in COVID-19 positive patients than in negative patients. Anosmia was found in 33.1% (47/142) of COVID-19 positive patients versus 8.8% (19/216) of COVID-19 negative patients (difference of 24.3% [15.8% to 33.0%], p<0.0001). Anosmia was the only symptom with <10% prevalence in COVID-19 negative patients. The pre-hospital duration of reported fever, chills, fatigue, reduced appetite, and headache was longer in COVID-19 positive patients than in COVID-19 negative patients.

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Table 3
Symptoms of patients at presentation to hospital testing positive and negative for COVID-19.

	COVID-19 positive (n = 197)			COVID-19 negative (n = 302)			Difference in proportion (95% CI)	p value	Difference in duration (95% CI)	p value
	Yes: No	Yes%	Median (IQR) days	Yes: No	Yes%	Median (IQR) days				
Sore throat	50: 99	33.6%	5 (3 to 8.5)	45: 191	19.1%	4 (2 to 10)	14.5% (5.5% to 23.6%)	**0.0016**	1 (−1 to 2)	0.6396
Rhinorrhoea	39: 109	26.4%	5 (2 to 7)	54: 181	23.0%	4 (2 to 14)	3.4% (−5.3% to 12.5%)	0.4649	1 (−2 to 1)	0.8566
Wheeze	48: 102	32.0%	5 (2 to 7)	91: 150	37.8%	4.5 (2 to 11.25)	−5.8% (−15.1% to 4.0%)	0.2777	0.5 (−2 to 1)	0.3901
Shortness of breath	130: 38	77.4%	5 (2 to 7)	179: 81	68.8%	4 (2 to 10)	8.5% (−0.2% to 16.7%)	0.0606	1 (−1 to 1)	0.9924
Pleuritic chest pain	43: 107	28.7%	4 (2 to 7)	55: 187	22.7%	3 (2 to 7)	5.9% (−2.8% to 15.0%)	0.1895	1 (−1 to 2)	0.4076
Cough	128: 42	75.3%	6 (3 to 9.5)	124: 131	48.6%	4 (2 to 10)	26.7% (17.4% to 35.1%)	**<0.0001**	2 (0 to 2)	0.1380
Sputum	53: 101	34.4%	5 (3 to 7)	56: 181	23.6%	4 (2 to 14)	10.8% (1.7% to 20.0%)	**0.0215**	1 (−2 to 1)	0.8838
Fever	103: 60	63.2%	7 (4 to 9)	97: 152	39.0%	3 (1 to 7)	24.2% (14.4% to 33.4%)	**<0.0001**	4 (1 to 4)	**0.0009**
Chills	84: 67	55.6%	7 (5 to 9)	83: 156	34.7%	2 (1 to 7)	20.9% (10.8% to 30.5%)	**<0.0001**	5 (1 to 5)	**<0.0001**
Fatigue	117: 33	78.0%	7 (4.75 to 10)	144: 92	61.0%	5 (2 to 14)	17.0% (7.6% to 25.6%)	**0.0005**	2 (0 to 3)	**0.0216**
Reduced appetite	112: 40	73.7%	7 (4.5 to 10)	116: 116	50.0%	5 (2 to 10)	23.7% (13.8% to 32.7%)	**<0.0001**	2 (0 to 3)	**0.0047**
Headache	73: 76	49.0%	7 (4 to 9)	78: 157	33.2%	2 (1 to 7)	15.8% (5.7% to 25.6%)	**0.0026**	5 (1 to 5)	**0.0008**
Myalgia	62: 87	41.6%	7 (4 to 8)	58: 174	25.0%	3.5 (2 to 8.5)	16.6% (7.0% to 26.1%)	**0.001**	3.5 (0 to 3.5)	0.0867
Diarrhoea	57: 96	37.3%	4.5 (2 to 7)	42: 197	17.6%	3 (2 to 7)	19.7% (10.7% to 28.7%)	**<0.0001**	1.5 (0 to 2)	0.2774
Abdominal pain	24: 127	15.9%	4 (3 to 7)	38: 199	16.0%	2.5 (1 to 7)	−0.1% (−7.3% to 7.7%)	>0.9999	1.5 (−1 to 2)	0.2315
Anosmia	47: 95[a]	33.1%	6 (4 to 8)	19: 197[b]	8.8%	7 (3 to 20)	24.3% (15.8% to 33.0%)	**<0.0001**	−1 (−6 to 2)	0.4474

Data from patients tested with mPOCT only.
Data expressed as a ratio of Yes: No. Data is not included where patients were unable to communicate their symptoms to researchers or no other record was made by clinicians.
[a] n = 181 and [b] n = 278, respectively. Anosmia was added to symptom data collection five days after the trial started recruitment.

Other respiratory viruses and atypical bacteria

2.5% (5/197) of COVID-19 positive patients had co-detections with viruses or atypical bacteria alongside SARS-CoV-2 via mPOCT compared with 7.9% (24/302) of COVID-19 negative patients having any pathogen detected via mPOCT (difference of −5.4% [−5.4% (−9.3% to −1.3%)], p = 0.0109; Table 4). COVID-19 positive patients had no detections of rhinovirus compared with 12 detections in COVID-19 negative patients (0/197 vs 4.0% (12/302), difference of −4.0% [−9.3% to −1.3%], p = 0.0045).

Clinical outcomes

Patients with COVID-19 more frequently received antibiotics than patients who did not have COVID-19 (86% (303/352) vs 71.5% (502/702), difference 14.6% [9.4% to 19.3%], p<0.0001; Table 5). COVID-19 positive patients more frequently received supplementary oxygen than COVID-19 negative patients (71.3% (251/352) vs 40.9% (287/702), difference of 30.4% [24.3% to 36.2%], p<0.0001), and patients who received supplementary oxygen had a longer duration of therapy (20.0 h [9.0 to 67.0] versus 9.8 h [3.0 to 30.0], difference of 10.2 [5.8 to 12.5], p<0.0001). Patients with COVID-19 were more likely to receive high flow nasal oxygen or non-invasive ventilation at any time during hospitalisation, and the duration of non-invasive ventilation was longer than patients who did not have COVID-19 (Table 5). COVID-19 patients were more frequently admitted to an intensive care unit than COVID-19 negative patients (17.6% (62/352) vs 6.3% (44/702), difference of 11.3% [7.2% to 15.9%], p<0.0001). 11.1% (39/352) patients in the COVID-19 positive group underwent invasive ventilation compared with 2.8% (20/702) in the COVID-19 negative group (difference of 8.2% [5.0% to 12.1%], p<0.0001) and the duration was longer (14.5 vs 4.7 days, difference of 9.7 days [2.3 to 13.5], p = 0.0015). A higher proportion of patients with COVID-19 died in hospital up to 30 days from presentation compared with COVID-19 negative patients (21.3% (75/352) vs 8.7% (61/702), p<0.0001). Where patient data were available, more patients died within 30 days in any setting, but fewer patients were readmitted to hospital, in the COVID-19 group compared to the COVID-19 negative group. The hospitalisation duration of COVID-19 patients was almost twice that of patients who did not have COVID-19 (7.2 days (3.1 to 12.2) vs 3.7 days (1.1 to 7.8), difference of 3.5 days [1.9 to 3.5], p<0.0001).

Discussion

This large study of adults presenting to hospital with suspected COVID-19 shows that patients with COVID-19 have substantial differences in ethnicity, health care worker status, smoking status, physiological markers including observations and blood tests, symptoms, and outcomes compared with patients who did not have COVID-19. There was no difference in age, gender, and most comorbidities between the two groups.

Over a fifth of COVID-19 patients were healthcare workers compared to less than six percent of COVID-19 negative patients, strengthening the concept that occupational exposure is a major risk factor in COVID-19 acquisition.[14] Most large cohorts of patients hospitalised with COVID-19 have not described the proportion of patients who are healthcare workers,[3–9,15] therefore this is a major finding that impacts upon planning in healthcare systems.

The lower proportion of current smokers, and higher proportion of never smokers, in COVID-19 positive patients compared to COVID-19 negative patients is unexpected. A large UK study of hospitalised patients with COVID-19 found only six-percent of patients were current smokers.[3] The lower proportion of patients with COPD in the COVID-19 positive group may be linked with

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Table 4
Respiratory viruses and atypical bacteria detected by mPOCT in patients testing positive and negative for COVID-19.

	COVID-19 positive (n = 197)	COVID-19 negative (n = 302)	Difference (95% CI)	p value
Mycoplasma pneumoniae	3 (1.5%)	6 (2.0%)	−0.5% (−3.0% to 2.6%)	>0.9999
human Metapneumovirus	0	3 (1.0%)	−1.0% (−2.9% to 1.0%)	0.2818
HCoV-HKU1	1 (0.5%)	0	0.5% (−0.8% to 2.8%)	0.3948
HCoV-OC43	0	3 (1.0%)	−1.0% (−2.9% to 1.0%)	0.2818
HCoV-NL63	0	1 (0.3%)	−0.3% (−1.9% to 1.6%)	>0.9999
Adenovirus	1 (0.5%)	0	0.5% (−0.8% to 2.8%)	0.3948
human Rhinovirus	0	12 (4.0%)	−4.0% (−6.8% to −1.4%)	**0.0045**
Any virus or atypical bacteria detected	*5 (2.5%)*	*24 (7.9%)*	*−5.4% (−9.3% to −1.3%)*	**0.0109**

No other targets on the QIAstat-Dx Respiratory SARS-CoV-2 Panel detected. *Bordatella pertussis* detections excluded as uncertain significance.
One patient in the COVID-19 negative group had both human Rhinovirus & *Mycoplasma pneumoniae* detected.
HCoV, human coronavirus; mPOCT, molecular point-of-care testing.

Table 5
Clinical outcomes in patients testing positive and negative for COVID-19.

	COVID-19 positive (n = 352)	COVID-19 negative (n = 702)	Difference (95% CI)	p value
Antibiotic use at any time	303 (86.1%)	502 (71.5%)	14.6% (9.4% to 19.3%)	**<0.0001**
Received supplemental oxygen	251 (71.3%)	287 (40.9%)	30.4% (24.3% to 36.2%)	**<0.0001**
Duration of received O_2 (hours)	20.0 (9.0 to 67.0)	9.8 (3.0 to 30.0)	10.2 (5.8 to 12.5)	**<0.0001**
Received NIV	56 (15.9%)	24 (3.4%)	12.5% (8.7% to 16.8%)	**<0.0001**
NIV duration (hours)	24.4 (13.8 to 57.0)	8.5 (2.2 to 34.5)	15.9 (3.8 to 23.2)	**0.0064**
Received $I+V$	39 (11.1%)	20 (2.8%)	8.2% (5.0% to 12.1%)	**<0.0001**
$I+V$ duration (days)	14.5 (5.8 to 20.5)	4.7 (1.1 to 11.1)	9.7 (2.3 to 13.5)	**0.0015**
Received high flow nasal oxygen	27 (7.7%)	23 (3.3%)	4.4% (1.6% to 7.8%)	**0.0031**
Admitted to ICU	62 (17.6%)	44 (6.3%)	11.3% (7.2% to 15.9%)	**<0.0001**
Died within 30 days in hospital	75 (21.3%)	61 (8.7%)	12.6% (8.0% to 17.6%)	**<0.0001**
Died within 30 days overall	87 (25.5%)[a]	79 (12.1%)[a]	13.4% (8.3% to 18.8%)	**<0.0001**
Readmitted in 30 days	30 (10.6%)[b]	105 (17.7%)[b]	−7.2% (−11.7% to 2.2%)	**0.0033**
Length of hospital stay (days)	7.2 (3.1 to 12.2)	3.7 (1.1 to 7.8)	3.5 (1.9 to 3.5)	**<0.0001**

Data are n (%) or median (IQR).
[a] n = 341 and n = 654 respectively.
[b] n = 284 and n = 592 respectively.O_2, oxygen; NIV, non-invasive ventilation; $I+V$, intubation and ventilation; ICU, intensive care unit.

smoking status. Conversely, in other studies current smokers appear at higher risk of worse outcomes than non-smokers,[16] and exacerbations of COPD are associated with non-SARS-CoV-2 respiratory virus infections.[17,18]

The notable proportion of non-White-British patients with COVID-19 compared with COVID-19 negative patients found in this study and others warrants urgent investigation.[19,20] The COVID-19 group contains four times the proportion of non-white British people than a similar study in 2015/16 in the same hospital enrolling patients with acute respiratory illness and/or fever.[21] There has been considerable pressure for a wide-reaching investigation into the higher incidence and mortality of COVID-19 in racially minoritised people.[20,22]

Only about one-third of COVID-19 patients had a fever at presentation, reinforcing the finding that temperature screening is not meaningful in this setting.[23] Lymphopenia in the context of a non-raised neutrophil count was found in about 60% of COVID-19 positive patients compared to about a third of COVID-19 negative patients; lymphopenia has been incorporated into outcome prediction models,[24] and lymphopenia with normal neutrophil count may contribute to future prediction tools in COVID-19.

Recently, anosmia has been reported as a symptom of COVID-19 but data in hospitalised patients is limited.[25,26] This study shows that about a third of patients hospitalised with COVID-19 report anosmia, compared to less than 10% of comparable patients without COVID-19. This suggests that the change in UK-national screening policy to include anosmia as symptom of potential COVID-19 is also appropriate in hospitalised adults.[27]

The viral co-infection rate was lower than other studies, although this may reflect the time period of the study in relation to usual seasonal respiratory virus activity locally and therefore lower rates of influenza and other seasonal viruses may be expected.[28] However, the lower rate of respiratory virus infection and the conspicuous absence of rhinovirus infection in COVID-19 positive versus negative patient's requires further investigation. Epidemiological and modelling observations of temporal patterns suggests that a peak in one respiratory virus circulation typically suppresses other respiratory virus circulation, and in vitro innate immune responses to influenza or RSV inhibit replication of rhinovirus; this may be early evidence that SARS-CoV-2 exhibits similar viral interference with rhinovirus and other respiratory viruses.[29,30]

The comprehensively worse outcomes in COVID-19 patients versus comparable non-COVID-19 patients is an important finding, although COVID-19 positive patients had markers suggesting they were marginally more physiologically impaired at presentation to hospital. The duration of invasive ventilation of COVID-19 patients in this cohort was around two weeks, compared to fewer than five days for comparison patients, and hospital admission duration for COVID-19 patients was more than three days longer than comparable patients. Therefore the burden on hospital wards and intensive care units of patient length of stay is significant and future planning must incorporate provision for expanded COVID-19 ward capacity and prolonged-stay intensive care capacity.

The key strength of this analysis of COVID-19 patients is the presence of a comparator group of patients who tested negative for SARS-CoV-2. As we used data from a clinical trial, the detail and fidelity of data is high. We believe our report of both presence and duration of symptoms, including anosmia, with a comparison group in adults presenting to hospital, is novel. The broad inclusion criteria of adults presenting to a large UK teaching hospital with acute respiratory illness or otherwise suspected COVID-19 makes this study highly generalisable. The limitations of this

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study include that it is single-centre. It is possible that some patients categorised as COVID-19 negative may have had COVID-19 as even testing with very accurate RT-PCR assays for SARS-CoV-2 has sub-optimal sensitivity on upper respiratory tract specimens,[31] however RT-PCR currently remains the gold-standard. We do not have individual patient data on experimental trial therapeutic interventions that COVID-19 patients received, which may have influenced clinical outcomes including mortality.

Despite the significant differences found in characteristics and symptoms of adults presenting to hospital with suspected COVID-19 who are positive and negative for the disease, no presenting feature appears to reliably distinguish between which patients have COVID-19 and which do not. The diagnostic uncertainty is compounded by long turnaround times of laboratory RT-PCR for SARS-CoV-2, creating significant challenges in infection control and patient flow in hospitals. These challenges may be addressed by implementing molecular point-of-care testing for SARS-CoV-2.[10] Even faster, finger-prick host response point-of-care testing also has the potential to streamline triage and patient care decisions.[32]

In conclusion, this study of adults presenting to hospital with suspected COVID-19 shows there are significant differences in the clinical characteristics, symptoms, and clinical outcomes of patients testing positive and negative for SARS-CoV-2 infection. These data can be used to inform healthcare planning in preparation for the next phase of the pandemic.

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Author contributions

NJB conceptualised this cohort study with TWC and SP. NJB analysed the data and wrote the first manuscript draft. SP, TWC, and NJB curated the data. NJB, SP, VN, CM, NN, FB, HP, HW, MH and LP recruited patients and/or collected data. TWC was chief investigator of the CoV-19POC trial. All authors have contributed to and approved the final manuscript.

Declaration of Competing Interest

TWC reports non-financial support from QIAGEN in the form of discounted equipment and consumables for this work. He also reports personal fees from BioMerieux and BioFire LLC, non-financial support from BioMerieux and BioFire LLC, personal fees from Synairgen Research Ltd, Roche, Cidara therapeutics, Janssen, Planet Innovation and Randox diagnostics, and grants from NIHR, all outside this work. Other authors report no conflicts of interest.

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