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

Nathan J Brendisha,b\*, Stephen Poolea,b,c, Vasanth V Naidub, Christopher T Mansbridgeb, Nicholas Nortonb, Florina Borcac,d, Hang TT Phanc,d, Helen Wheelerc, Matthew Harveyc, Laura Preslandc and Tristan W Clarka,b,c,e

a. School of Clinical and Experimental Sciences, Faculty of Medicine, University of Southampton, Southampton, UK

b. Department of Infection, University Hospital Southampton NHS Foundation Trust,

Southampton, UK

c. NIHR Southampton Biomedical Research Centre, University Hospital Southampton NHS

Foundation Trust, Southampton, UK

d. Clinical Informatics Research Unit, Faculty of Medicine, University of Southampton,

Southampton, UK

e. NIHR Post Doctoral Fellowship Programme, UK

\* Corresponding author:

Dr Nathan J Brendish BSc MBBS MRCP DMCC PhD, NIHR Clinical Lecturer in Infectious Diseases and General Internal Medicine. LF81, South Academic Block, University of Southampton, Southampton General Hospital, Tremona Road, Southampton SO16 6YD, UK. n.brendish@soton.ac.uk 0044(0)2381208560

Running title: Features of 1054 hospitalised adults tested for COVID-19

# Abstract

## 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.

Keywords:

COVID-19, SARS-CoV-2, clinical characteristics, symptoms, cohort, outcomes, healthcare workers, smokers, COPD.

# 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 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 (130mmHg [120 to 146] vs 135mmHg [120 to 154], difference of -5mmHg [-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 x109/L [0.63 to 1.3] vs 1.2 x109/L [0.8 to 1.8], and lower neutrophil count (5.6 x109/L [4.1 to 8.3] vs 8.0 x109/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 negative 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.

## 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 hours [9.0 to 67.0] versus 9.8 hours [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 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 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.

# Declaration of Competing Interests

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.

# Funding

The CoV-19POC trial was funded by University of Southampton and University Hospital Southampton NHS Foundation Trust. NJB is supported by a National Institute of Health Research (NIHR) Clinical Lecturer post. TWC is supported by a NIHR Fellowship (PDF 2016-09-061). The views expressed in this publication are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health and Social Care.

# Acknowledgements

We thank all the patients who kindly participated in this study and all the clinical staff at Southampton General Hospital who cared for them. The CoV-19POC study was supported by the NIHR Southampton Clinical Research Facility and NIHR Southampton Biomedical Research Centre, both are partnerships between University Hospital Southampton NHS Foundation Trust and the University of Southampton.

# 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.

# References

[1] World Health Organisation, Coronavirus disease (COVID-19) Situation Report – 209 16 August 2020. https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200709-covid-19-sitrep-171.pdf [Last accessed 17 August 2020].

[2] UK Government: <https://coronavirus.data.gov.uk/> [Last accessed 17 August 2020].

[3] Docherty AB, Harrison EM, Green CA, Hardwick HE, Pius R, Norman L, *et al*. Features of 20 133 UK patients in hospital with covid-19 using the ISARIC WHO Clinical Characterisation Protocol: prospective observational cohort study. BMJ 2020; 369:m1985.

[4] Suleyman G, Fadel RA, Malette KM, Hammond C, Abdulla H, Entz A et al. Clinical Characteristics and Morbidity Associated With Coronavirus Disease 2019 in a Series of Patients in Metropolitan Detroit. Jama Netw Open 2020; 3:e2012270.

[5] Petrilli CM, Jones SA, Yang J, Rajagopalan H, O’Donnell L, Chernyak Y, et al. Factors associated with hospital admission and critical illness among 5279 people with coronavirus disease 2019 in New York City: prospective cohort study. BMJ 2020; 369:m1966.

[6] Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet2020; 395:497-506.

[7] Argenziano MG, Bruce SL, Slater CL, Tiao JR, Baldwin MR, Barr RG, et al. Characterization and clinical course of 1000 patients with coronavirus disease 2019 in New York: retrospective case series. BMJ 2020; 369:m1996.

[8] Berenguer J, Ryan P, Rodríguez-Baño J, Jarrín I, Carratalà J, Pachón J, et al. Characteristics and predictors of death among 4,035 consecutively hospitalized patients with COVID-19 in Spain. Clin Microbiol Infect2020; S1198-743X30431-6.

[9] Wang X, Fang J, Zhu Y, Chen L, Ding F, Zhou R, Ge L, et al. Clinical characteristics of non-critically ill patients with novel coronavirus infection (COVID-19) in a Fangcang Hospital. Clin Microbiol Infect2020; 26(8):1063-1068.

[10] Clark TW, Brendish NJ, Poole S, Naidu VV, Mansbridge CT, Norton N et al. Clinical impact of molecular point-of-care testing for suspected COVID-19 in hospital: A prospective, interventional, non-randomised, controlled study (COV-19POC). Lancet Respir Med 2020. (in press)

[11] Clark TW, Brendish NJ. Evaluating the clinical impact of routine molecular point-of-care testing for COVID-19 in adults presenting to hospital: A prospective, interventional, non-randomised, controlled study (CoV-19POC) [Protocol] https://eprints.soton.ac.uk/439309/2/CoV\_19POC\_Protocol\_v2\_0\_eprints.pdf. [Last accessed 17 August 2020].

[12] Visseaux B, Hingrat Q, Collin G, Bouzid D, Lebourgeois S, Pluart D, et al. Evaluation of the QIAstat-Dx Respiratory SARS-CoV-2 Panel, the first rapid multiplex PCR commercial assay for SARS-CoV-2 detection. J Clin Microbiol. 2020; 58:e00630-20.

[13] Boers SA, Melchers WJG, Peters CJA, Toonen M, McHugh MP, Templeton KE, et al. Multicenter evaluation of the QIAstat-Dx® Respiratory Panel V2 for the detection of viral and bacterial respiratory pathogens. JClinMicrobiol. 2020; 58:e01793-19.

[14] Nguyen LH, Drew DA, Graham MS, Joshi AD, Guo C-G, Ma W, et al. Risk of COVID-19 among front-line health-care workers and the general community: a prospective cohort study. Lancet Public Health2020; S2468-2667 30164-X.

[15] Grasselli G, Zangrillo A, Zanella A, Antonelli M, Cabrini L, Castelli A, et al. Baseline Characteristics and Outcomes of 1591 Patients Infected With SARS-CoV-2 Admitted to ICUs of the Lombardy Region, Italy. JAMA2020; 323:1574-1581.

[16] Zheng Z, Peng F, Xu B, Zhao J, Liu H, Peng J, et al. Risk factors of critical & mortal COVID-19 cases: A systematic literature review and meta-analysis. J Infect 2020; 81:e16-e25.

[17] Clark TW, Medina M-J, Batham S, Curran MD, Parmar S, Nicholson KG. C-reactive protein level and microbial aetiology in patients hospitalised with acute exacerbation of COPD. Eur Respir J 2015; 45:76-86.

[18] Clark TW, Medina M-J, Batham S, Curran MD, Parmar S, Nicholson KG. Adults hospitalised with acute respiratory illness rarely have detectable bacteria in the absence of COPD or pneumonia; viral infection predominates in a large prospective UK sample. J Infect2014; 69:507-515.

[19] Pan D, Sze S, Minhas JS, Bangash MN, Pareek N, Divall P, et al. The impact of ethnicity on clinical outcomes in COVID-19: A systematic review. EClinicalMedicine2020; 23:100404.

[20] Aldridge RW, Lewer D, Katikireddi SV, Mathur R, Pathak N, Burns R, et al. Black, Asian and Minority Ethnic groups in England are at increased risk of death from COVID-19: indirect standardisation of NHS mortality data. Wellcome Open Res2020; 5:88.

[21] Brendish NJ, Malachira AK, Armstrong L, Houghton R, Aitken S, Nyimbili E, et al. Routine molecular point-of-care testing for respiratory viruses in adults presenting to hospital with acute respiratory illness (ResPOC): a pragmatic, open-label, randomised controlled trial. Lancet Respir Med 2017;5(5):401–11.

[22] Patel P, Hiam L, Sowemimo A, Devakumar D, McKee M. Ethnicity and covid-19. BMJ 2020; 369:m2282.

[23] Guan W-J, Ni Z-Y, Hu Y, Liang W-H, Ou C-Q, He J-X et al. Clinical Characteristics of Coronavirus Disease 2019 in China. N Engl J Med 2020; 382:1708-1720.

[24] Bartoletti M, Giannella M, Scudeller L, Tedeschi S, Rinaldi M, Bussini L, et al. Development and validation of a prediction model for severe respiratory failure in hospitalized patients with SARS-Cov-2 infection: a multicenter cohort study (PREDI-CO study). Clin Microbiol Infect2020; S1198-743X(20)30479-1.

[25] Ellul MA, Benjamin L, Singh B, Lant S, Michael BD, Easton A, et al. Neurological associations of COVID-19. Lancet Neurol 2020; S1474-442230221-0.

[26] Lechien JR, Chiesa-Estomba CM, Hans S, Barillari MR, Jouffe L, Saussez S. Loss of Smell and Taste in 2013 European Patients With Mild to Moderate COVID-19. Ann Intern Med2020; 10.7326/M20-2428.

[27] UK Government. COVID-19: investigation and initial clinical management of possible cases https://www.gov.uk/government/publications/wuhan-novel-coronavirus-initial-investigation-of-possible-cases/investigation-and-initial-clinical-management-of-possible-cases-of-wuhan-novel-coronavirus-wn-cov-infection. [Last accessed 17 August 2020].

[28] Lansbury L, Lim B, Baskaran V, Lim WS. Co-infections in people with COVID-19: a systematic review and meta-analysis. J Infect 2020; 81:266-275.

[29] Nickbakhsh S, Mair C, Matthews L, Reeve R, Johnson PCD, Thorburn F, et al. Virus-virus interactions impact the population dynamics of influenza and the common cold. P Natl Acad Sci Usa 2019; 116:27142-27150.

[30] Essaidi-Laziosi M, Geiser J, Huang S, Constant S, Kaiser L, Tapparel C. Interferon-Dependent and Respiratory Virus-Specific Interference in Dual Infections of Airway Epithelia. Sci Rep 2020;10:10246.

[31] Woloshin S, Patel N, Kesselheim AS. False Negative Tests for SARS-CoV-2 Infection - Challenges and Implications. N Engl J Med. 2020;383:e38.[32] Clark TW, Brendish NJ, Poole S, Naidu VV, Mansbridge C, Norton N, et al. Diagnostic accuracy of the FebriDx host response point-of-care test in patients hospitalised with suspected COVID-19. J Infect 2020; S0163-4453(20)30432-1.

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

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **COVID-19 positive** | **COVID-19 negative** | **Difference** | **p value** |
|   | **(n=352)** | **(n=702)** |  **(95% CI)** |   |
| ***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 (109/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 (109/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 & 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 x 109/L; neutrophil count upper limit of normal is 8 x 109/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** | **COVID-19 negative** | **Difference** | **p value** |
|   | **(n=352)** | **(n=702)** | **(95% CI)** |   |
| ***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 |

# 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** |
|   | **Yes : No** | **Yes %** | **Median (IQR) days** | **Yes : No** | **Yes %** | **Median (IQR) days** | **Difference in proportion (95% CI)** | **p value** | **in duration (95% CI)** | **p value** |
| 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. |

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

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **COVID-19 positive** | **COVID-19 negative** | **Difference** | **p value** |
|   | **(n=197)** | **(n=302)** | **(95% CI)** |  |
| *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** | **COVID-19 negative** | **Difference** | **p value** |
|   | **(n=352)** | **(n=702)** | **(95% CI)** |   |
| 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 O2 (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.

O2, oxygen; NIV, non-invasive ventilation; I+V, intubation and ventilation; ICU, intensive care unit.

# Supplementary Table 1 (S1): Smoking status of patients testing positive and negative for COVID-19

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **COVID-19 positive** | **COVID-19 negative** | **Difference** | **p value** |
|   | **(n=352)** | **(n=702)** | **(95% CI)** |   |
| Current smoker | 20 (5.7%) | 116 (16.5%) | -10.8% (-7.0% to -14.4%) | **0.0001** |
| Ex-smoker | 80 (22.7%) | 193 (27.5%) | -4.8% (-10.1% to -0.9%) | 0.1013 |
| Never smoked | 189 (53.7%) | 252 (35.9%) | 17.8% (11.4% to 24.0%) | **<0.0001** |
| Unknown smoking status | 63 (17.9%) | 141 (20.1%) | -2.2% (-7.0% to -3.0%) | 0.4098 |