

Report 17: Clinical characteristics and predictors of outcomes of hospitalised patients with COVID-19 in a London NHS Trust: a retrospective cohort study

Pablo N Perez-Guzman, Anna Daunt*, Sujit Mukherjee*, Peter Crook, Roberta Forlano, Mara D Kont, Alessandra Løchen, Michaela Vollmer, Paul Middleton, Rebekah Judge, Chris Harlow, Anet Soubieres, Graham Cooke, Peter J White, Timothy B Hallett, Paul Aylin, Neil Ferguson*, Katharina Hauck*, Mark Thursz*, Shevanthi Nayagam^a

WHO Collaborating Centre for Infectious Disease Modelling

MRC Centre for Global Infectious Disease Analysis

Abdul Latif Jameel Institute for Disease and Emergency Analytics (J-IDEA)

Division of Digestive Diseases, Department of Metabolism Digestion and Reproduction

Department of Infectious Diseases

Department of Primary Care and Public Health

NIHR Imperial Biomedical Research Centre

Imperial College Healthcare NHS Trust

Imperial College London

*contributed equally

^aCorresponding author: s.nayagam01@imperial.ac.uk

SUGGESTED CITATION

Pablo N Perez-Guzman, Anna Daunt, Sujit Mukherjee *et al.* Clinical characteristics and predictors of outcomes of hospitalised patients with COVID-19 in a London NHS Trust: a retrospective cohort study (29-04-2020), doi: <https://doi.org/10.25561/78613>.



This work is licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License.

Summary

Clinical characteristics and determinants of outcomes for hospitalised COVID-19 patients in the UK are important to guide the national response to this current pandemic and emerging evidence suggests ethnic minorities might be disproportionately affected. We describe the characteristics and outcomes of patients hospitalised for COVID-19 in three large London hospitals with a multi-ethnic catchment population.

We performed a retrospective cohort study on all patients hospitalised with laboratory-confirmed SARS-CoV-2 infection at Imperial College Healthcare NHS Trust between February 25 and April 5, 2020. Outcomes were recorded as of April 19, 2020. Logistic regression models, survival analyses and cumulative competing risk analyses were performed to evaluate factors associated with COVID-19 hospital mortality.

Of 520 patients in this cohort (median age 67 years, (IQR 26) and 62% male), 302 (68%) had been discharged alive, 144 (32%) died and 74 (14%) were still hospitalised at the time of censoring. Increasing age (adjusted odds ratio [aOR] 2.16, 95%CI 1.50-3.12), severe hypoxia (aOR 3.75, 95%CI 1.80-7.80), low platelets (increase in aOR 1.54, 95%CI 1.18, 2.04, for every $\times 10^9/L$), reduced estimated glomerular filtration rate (aOR 4.11, 95%CI 1.58-10.69), bilirubin >21mmol/L (aOR 2.32, 95%CI 1.05-5.14) and low albumin (increase in aOR 1.30, 95%CI 0.99, 1.69, for every g/L) were associated with increased risk of in-hospital mortality. Individual comorbidities were not independently associated with risk of death. Regarding ethnicity, 209 (40%) were from a black and Asian minority, for 115 (22%) ethnicity was unknown and 196 (38%) patients were white. Compared to the latter, black patients were significantly younger and had fewer comorbidities. Whilst the crude OR of death of black compared to white patients was not significant (1.14, 95%CI 0.69-1.88, $p=0.62$), adjusting for age and comorbidity showed a trend towards significance (aOR 1.72, 95%CI 0.98-3.02, $p=0.06$) and further accounting for admission severity (Early Warning Score) showed a significant difference (aOR 1.83 95% CI 1.02-3.30, $p=0.04$).

In one of the first studies to describe the characteristics and predictors of outcome for hospitalised COVID-19 patients in the UK, we find that older age, male sex and admission hypoxia, thrombocytopenia, renal failure, hypoalbuminaemia and raised bilirubin are associated with increased odds of death. Ethnic minority groups were over-represented in our cohort and, compared to whites, people of black ethnicity may be at increased odds of mortality. Further research is urgently needed to investigate these associations on a larger scale.

1. Introduction

The United Kingdom (UK) reported its first cases of SARS-CoV-2 infection, the causative agent of COVID-19 disease, in late January 2020 and is now the 5th worst affected country in the world, with a reported death toll of 20,732 as of the 26th April 2020.¹ More than half of the reported deaths in the UK have occurred in London,² a densely populated, multicultural capital city of nearly 9 million inhabitants where over 40% of residents are identified as belonging to a black, Asian or other ethnic minority (BAME) group.³

Previously published studies in China, Italy and USA have suggested that age, gender, and co-morbidities including cardiovascular disease are associated with poorer outcomes of COVID-19 disease.⁴⁻⁷ However, whether these COVID-19 patient-level characteristics and outcomes in the UK mirror those reported elsewhere needs more research. An improved understanding of local drivers of outcomes and predictors of clinical deterioration is vital from both clinical and public health perspectives. Such information can allow frontline clinicians to tailor their management decisions and hospital policymakers to plan their strategic response to COVID-19 more efficiently.⁸

Data from the Intensive Care National Audit and Research Centre in the UK on over 6,000 COVID-19-positive patients admitted to the intensive treatment units (ITU) suggests that BAME groups are disproportionately represented amongst critical care admissions, compared with historic ITU admissions (2017/19) due to viral pneumonia.⁹ With mounting pressure from the British Medical Association and other groups, on the 17th April the UK government agreed to launch formal review to investigate the reported disproportionate impact of COVID-19 on people from BAME backgrounds.¹⁰

Imperial College Healthcare NHS Trust (ICHNT), which is comprised of three hospitals, is one of the largest NHS Trusts in England, serving a diverse population of over 600,000 people in North West London with 40% of non-white ethnicity.¹¹ This study aims to:

1. Describe baseline characteristics and outcomes for patients hospitalised with laboratory-confirmed SARS-CoV-2 infection in a large London hospital trust since the start of the pandemic,
2. Evaluate demographic and clinical factors associated with outcomes, and
3. Evaluate the proportion of patients hospitalised at ICHNT for COVID-19 who are from BAME groups and evaluate whether ethnicity is associated with different outcomes.

Such data are urgently needed and will inform national policy planning to reduce health inequalities and target prevention and treatment interventions for those at the greatest risk of mortality.

2. Methods

Study Setting

We performed a retrospective observational study at ICHNT, a large tertiary level London Trust consisting of three acute hospital; St Mary's, Charing Cross and Hammersmith Hospitals. We included all consecutive patients with reverse transcription polymerase chain reaction (RT-PCR) swab-positive SARS-CoV-2 infection requiring hospitalisation between February 25th and April 5th, 2020. The cohort opened at the time of admission and censoring was done as of April 19th, 2020, thus including at least two weeks past the date of admission for all patients.

We excluded from analyses those who did not initially present with symptoms suggestive of COVID-19, those with clinical suspicion of COVID-19 but negative RT-PCR, those who did not require hospitalisation and transfers into ICHNT from other NHS Trusts. Where a patient had two or more COVID-19 RT-PCRs performed we only included the first positive swab episode that required hospitalisation.

Ethics

The study was approved by the ICHNT clinical governance team. As we report on routinely collected non-identifiable clinical audit data, no ethical approval was required under the UK policy framework for health and social care.

Data Collection

Individual patient electronic medical records (Cerner Hospital and Healthcare Systems and ITU computer records systems) were used to extract demographic, clinical, laboratory, radiological, comorbidity and outcome data including need for ITU admission and invasive ventilation, using a standardised data template. Demographic characteristics included patients' sex, age, ethnicity, whether they were a health worker and known pre-existing medical conditions. Chronic comorbidities were recorded individually and used to calculate the Elixhauser comorbidity score, a points system validated in hospital administrative datasets in the UK to evaluate risk of hospital mortality.^{12,13} Ethnicity is normally registered on initial presentation to the Emergency department for all patients at ICHNT. Given the challenges with capacity and infection control at ICHNT during the present epidemic, this variable was often recorded as 'other-ethnicity' as a default. For completeness, these entries were checked against London Ambulance Service records, previous clinic letters and GP referral letters and reclassified as appropriate. Where ethnicity was still unable to be confirmed, we report this as unknown.

We recorded clinical observations at the time of initial presentation to hospital, including early warning score (EWS), respiratory rate, mean arterial blood pressure, temperature, oxygen saturations (SaO₂) and oxygen requirements. SARS-CoV-2 testing was performed by RT-PCR of specimens collected by nasopharyngeal swabs. Blood test results included those that were routinely collected as part of clinical care. Laboratory results of serum creatinine, urea, glucose and lactate were only included if the blood test was performed within 4 hours of admission. All other blood tests and chest radiography were included if performed within 24 hours of admission. After 25th March 2020, the standardised COVID-19 investigations bundle across ICHNT also included the serum D-dimer, lactate dehydrogenase (LDH), creatine kinase, cortisol and troponin.

Chest radiography findings were included as reported by a radiologist, as per recommendations by the British Society of Thoracic Imaging Guidelines.¹⁴ This information includes (i) radiological findings (CVCX0 = Normal, CVCX1 = Classic, CVCX2 = Indeterminate, CVCX3 = Non-COVID-19) and (ii) quantification of radiographic disease severity (mild, moderate, severe). As CT scans were not systematically performed for all COVID-19 patients in this clinical setting, they were excluded from this analysis.

Outcomes of interest and statistical analysis

The primary outcome measure was whether the patient was discharged alive or died in hospital. An intermediate outcome measure of clinical deterioration was also investigated, defined here as either requiring a 60% or greater concentration of supplementary oxygen to maintain SaO₂ > 94%, invasive ventilation or admission to ITU.

We used standard chi squared, t-student or Wilcoxon rank sum tests, as appropriate, to describe the prevalence of covariates at admission among patients with a completed outcome. We further used adjusted and unadjusted logistic regression to assess a) predictors of COVID-19 hospital mortality and b) differences in mortality by ethnicity. Numeric variables (e.g. age, haemoglobin, creatinine, etc.) were treated as continuous if their density distribution plot showed a normal distribution in either the natural or logarithmic scale, else they were coded into categorical. Variables with a *p*-value below 0.157 in unadjusted regression were selected for adjusted regression, as per the Akaike Information Criterion.¹⁵ In the adjusted regression models, variables were considered statistically significant with a *p*-value <0.05 and thus kept as final candidates in the prediction model. Variables with more than 20% missing values were excluded from regression analysis.

We evaluated time from hospital admission to clinical deterioration and final outcome accounting for competing risks and right-censored data (i.e. patients still in hospital at the time of censoring) using the Nelson-Aalen and Kaplan-Meier estimators, respectively (Equation 1a and 1b, Supplement). The effect of selected covariates on the hazard of clinical deterioration and death was assessed using Cox Proportional-Hazard models. The proportional hazards assumptions were evaluated using Schoenfeld's residuals.¹⁶

3. Results

Description of cohort

689 patients had a positive SARS-CoV-2 nasopharyngeal swab and were hospitalised at ICHNT between 25th February 2020 and 5th April 2020. One hundred and sixty-nine patients were excluded from analyses, as their index presentation was for other medical non-COVID-19 conditions, but subsequently tested positive for SARS-CoV-2 during hospitalisation. Out of the 520 patients included in analyses, 445 had completed outcomes and 74 (14%) were still hospitalised at the date of the last recorded follow-up, on April 19th, 2020 (Figure 1). Amongst this cohort of 520 patients, the median age was 67 years (IQR 26), 322 (62%) were male and 22 patients (4%) were healthcare workers (Table 1). Regarding ethnic background, 196 (38%) patients were white, 209 (40%) were from a BAME group and for 115 (22%) the ethnic background was unknown.

The mean time from symptom onset to hospital admission was 7.12 days (SD 5.64). The prevalence of cough, fever and shortness of breath at presentation were high and 165 (32%) had gastrointestinal symptoms. On initial clinical assessment, 166 patients (32%) had an EWS score ≥ 7 , with 71% having a SaO₂ <94% on room air or requiring supplemental oxygen to maintain normal SaO₂. Haematological investigations revealed that 224 (44%) patients had anaemia <130g/L, 332 (65%) patients had lymphopenia <1.1 x 10⁹/L and 78 (15%) had thrombocytopenia <130 x 10⁹/L (77%). Biochemical and inflammatory marker abnormalities were also found to be abnormal in a high proportion of patients, most notably a reduced glomerular filtration rate (eGFR) and a raised C-reactive protein (CRP) >100mg/L in 268 (54%) patients (Table 1). D-Dimer, LDH, troponin and B-type natriuretic peptide (BNP) were raised in 89%, 93%, 31% and 19% of patients, respectively, albeit there was significant under-recording of these parameters in the study population (Table 1).

Nearly half of the patients ($n=252$) received at least 60% oxygen during their admission and 73 (14%) received invasive ventilation. Of patients with completed outcomes, 302 (68%) were discharged alive and 144 (32%) patients died in hospital. The median length of hospital stay, accounting for patients with pending outcomes, was 7 days (IQR 6-8) and the median time to clinical deterioration was 9 days (IQR 6-17) (Figure 2A).

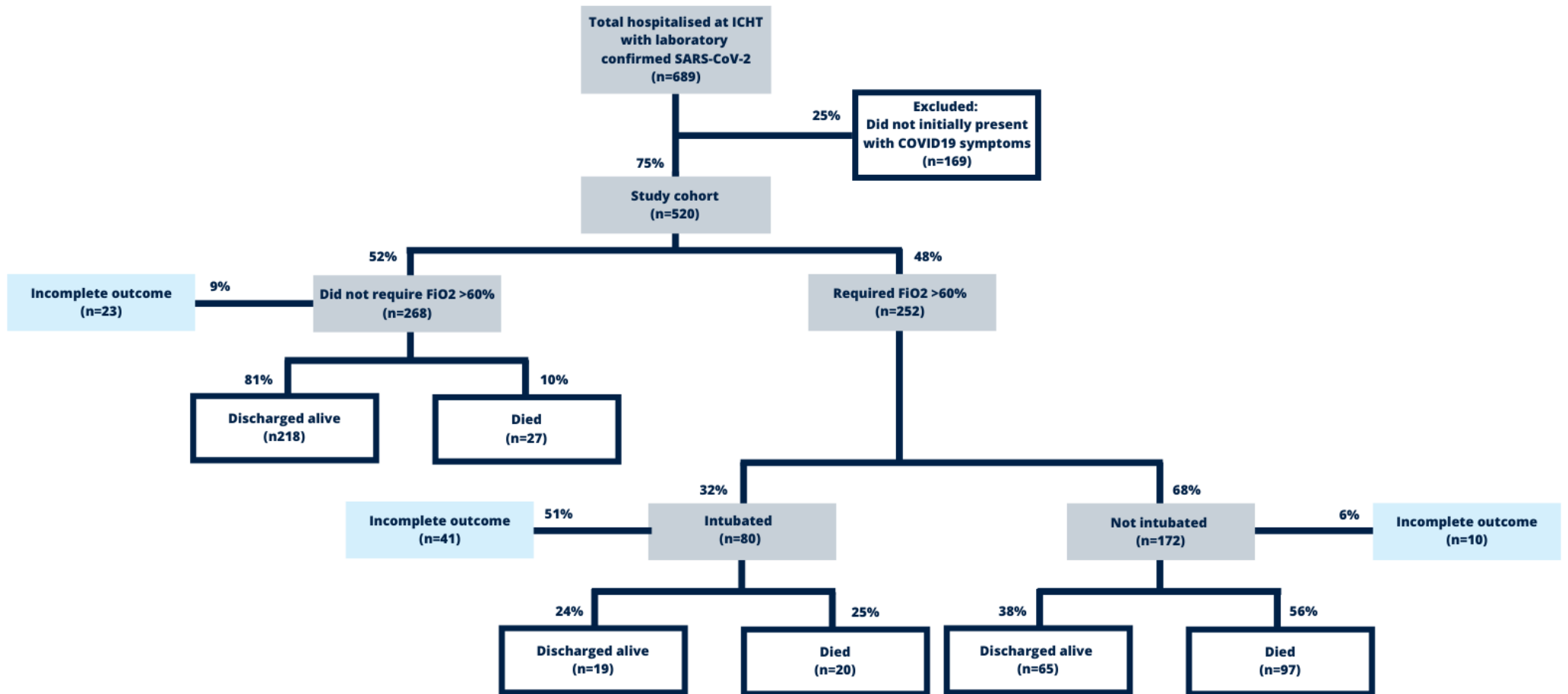


Figure 1: Overview of cohort and patient pathways. Last included patients as of the 5th of April and last recorded outcomes as of the 19th of April, 2020

Predictors of mortality

Out of those with completed outcomes ($n=302$ patients), the median age, sex and comorbidity profiles were significantly different between those who died and those who were discharged alive (Table 1). In unadjusted logistic regression, male sex (OR 1.72, 95% CI 1.13-2.62) and age (OR 1.06, 95% CI 1.04-10.07) were strongly associated with increased odds of hospital mortality (Table 2 and Figure 2B). Other patient characteristics on admission with a significant increase in odds of mortality were having an EWS ≥ 7 (OR 3.33, 95% CI 2.02-5.57), body temperature $>38^{\circ}\text{C}$ (OR 1.92, 95% CI 1.24-2.99) and either SaO₂ $<94\%$ despite supplementary oxygen (OR 3.28, 95% CI 1.44-7.43) or any SaO₂ measurement whilst on high-flow oxygen above 60% FiO₂ (OR 4.53, 95% CI 2.51-8.33).

The admission blood tests associated with poor outcomes in unadjusted logistic regression included thrombocytopenia $<100 \times 10^9/\text{L}$ (OR 3.28, 95% CI 1.40-7.93), lymphopenia $<0.5 \times 10^9/\text{L}$ (OR 3.06, 95% CI 1.47-6.39), white cell count $\geq 10.6 \times 10^9/\text{L}$ (OR 1.74, 95% CI 1.01-2.98), eGFR $<30\text{mL}/\text{min}/1.73\text{m}^2$ (OR 10.05, 95% CI 4.92-21.74) and albumin $<25\text{g}/\text{L}$ (OR 2.62, 95% CI 1.21-5.72). Although raised troponin, BNP and D-dimer appeared to be associated with increased odds of mortality, missingness of data greater than 20% meant these observations could not be conclusively interpreted in logistic regression.

Individual comorbidities significantly associated with increased odds of mortality included hypertension (OR 1.92, 95% CI 1.28-2.88), ischaemic heart disease (OR 2.54, 95% CI 1.30-4.98), chronic heart failure (OR 2.42, 95% CI 1.00-5.83), atrial fibrillation (OR 2.00, 95% CI 1.13-3.53), chronic kidney disease (OR 2.40, 95% CI 1.39-4.13) and dementia (OR 5.25, 95% CI 2.33-11.85). However, when adjusted for age, no individual comorbidities remained statistically significant.

In adjusted logistic regression, clinical and laboratory observations with an increased odds ratio of mortality that remained statistically significant were having a SaO₂ $<94\%$ whilst on supplementary oxygen or if more than 60% FiO₂ was administered on admission, decreasing platelet count (continuous), bilirubin $>21\text{mmol}/\text{L}$, albumin (continuous) and a reduced eGFR (Table 2), even after adjusting for age and pre-existing chronic kidney disease (goodness-of-fit <0.01).

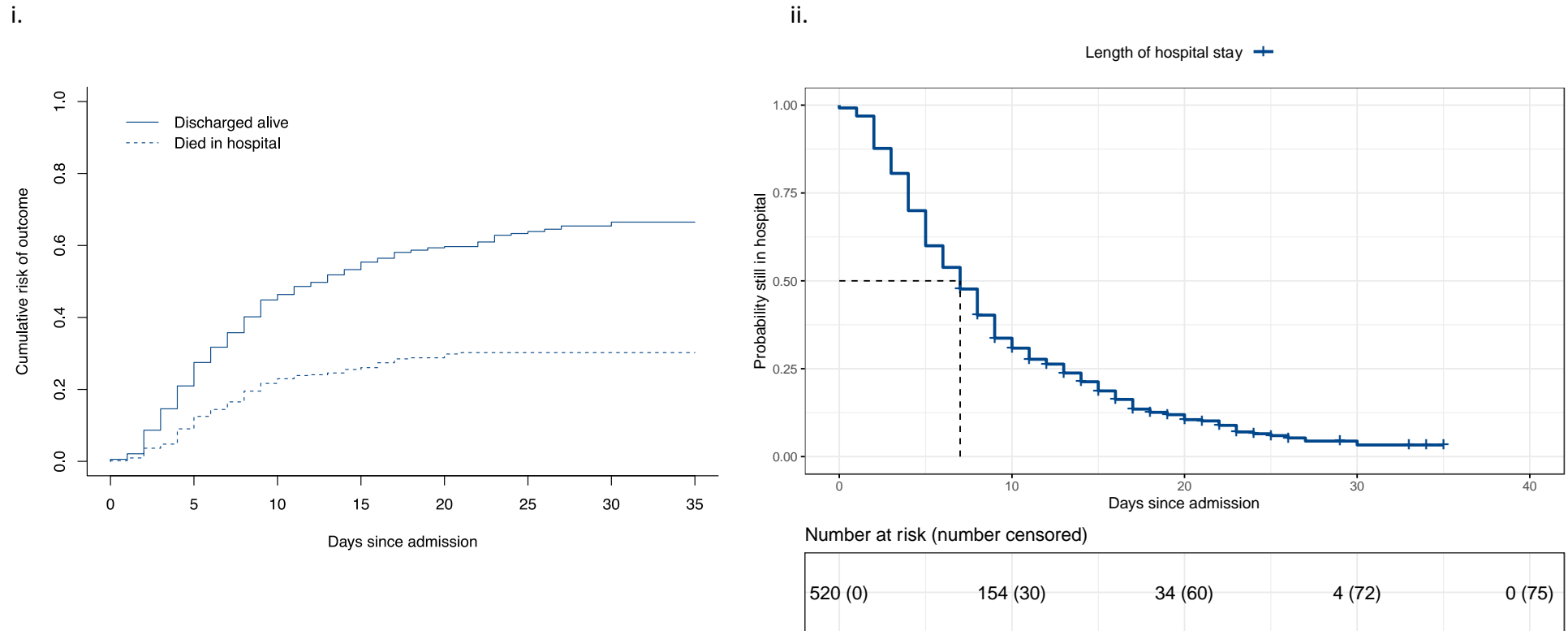


Figure 2(A) i. Cumulative incidence function for final outcomes ii. Cumulative survival function for length of hospital stay

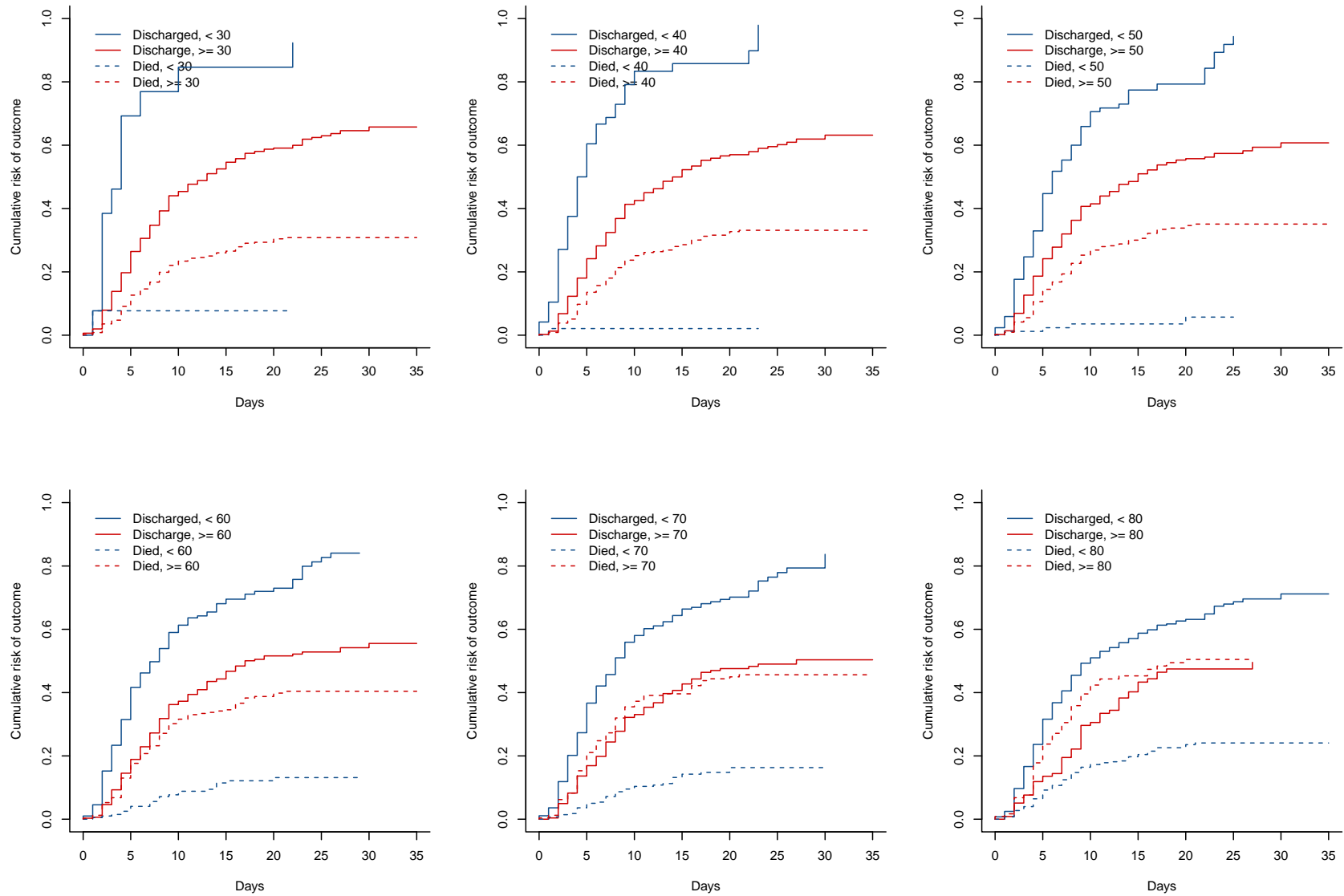


Figure 2(B): Cumulative incidence function for death vs discharged alive by age

Outcomes by ethnic minority groups

The ethnic breakdown of the cohort of COVID-19 patients hospitalised at ICHNT was: 196 (38%) white, 116 (22%) black, 78 (15%) Asian, 15 (3%) 'other' and 115 (22%) with unknown ethnicity. The mean age of BAME groups was significantly different to those of white ethnicity (Figure 3A and Table 3), at 62.8 years for black, 66.1 Asian and 55.1 for 'other' ethnic groups compared with 69.5 years for white ($p < 0.01$). The burden of comorbidities was also significantly different across ethnic groups, with whites and Asians having higher Elixhauser scores than those of black and 'other' ethnic backgrounds ($p < 0.01$). In particular, the prevalence of diabetes ($p < 0.01$), chronic kidney disease ($p < 0.01$), dementia ($p < 0.01$) and atrial fibrillation ($p < 0.05$) were different between groups.

Despite the overall younger age composition and lower Elixhauser score of BAME groups compared with whites, the severity of disease on presentation (EWS) was similar across ethnic groups ($p = 0.15$). In unadjusted logistic regression, neither the intermediate (requirement of $\text{FiO}_2 \geq 60\%$ or invasive ventilation) nor final outcomes (death or discharged alive) were significantly different between ethnic groups. Similarly, when adjusting for age and comorbidities, there remained no significant difference between the ethnic groups. Whilst the crude OR of death of black compared to white patients was not significant (1.14, 95%CI 0.69-1.88, $p = 0.62$), adjusting for age and comorbidity showed a trend towards significance (aOR 1.72, 95%CI 0.98-3.02, $p = 0.06$) and further accounting for admission severity (Early Warning Score) was significant (aOR 1.83 95% CI 1.02-3.30, $p = 0.04$, goodness-of-fit < 0.01). (Table 3).

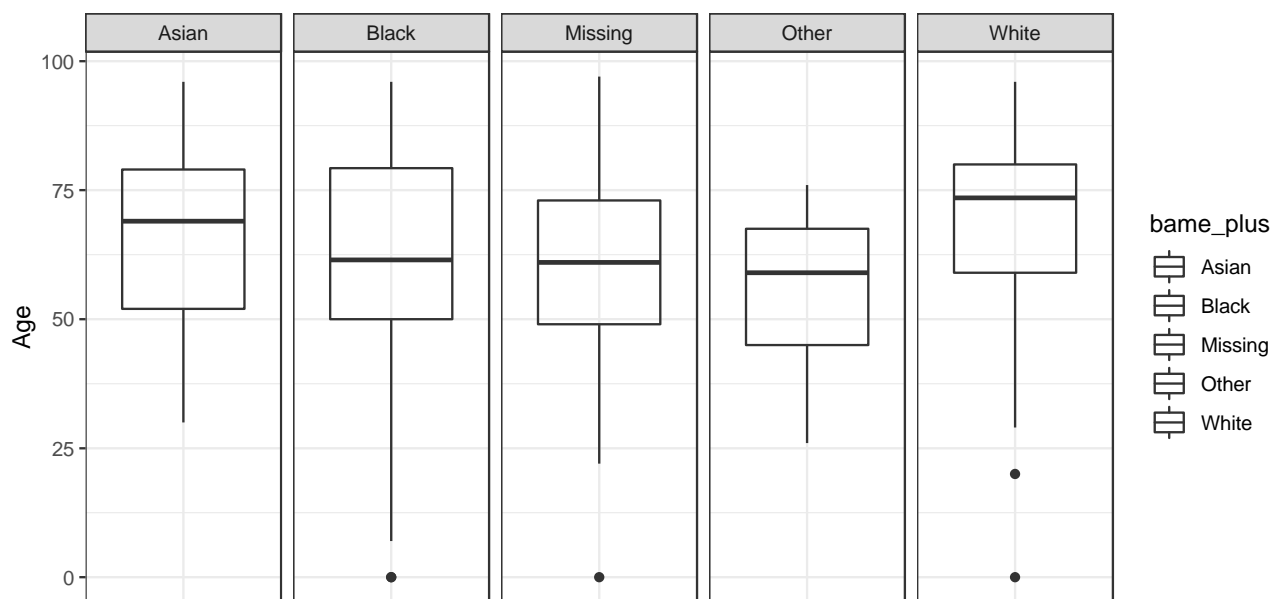


Figure 3(A): Overall age profile of hospitalised patients by ethnic group

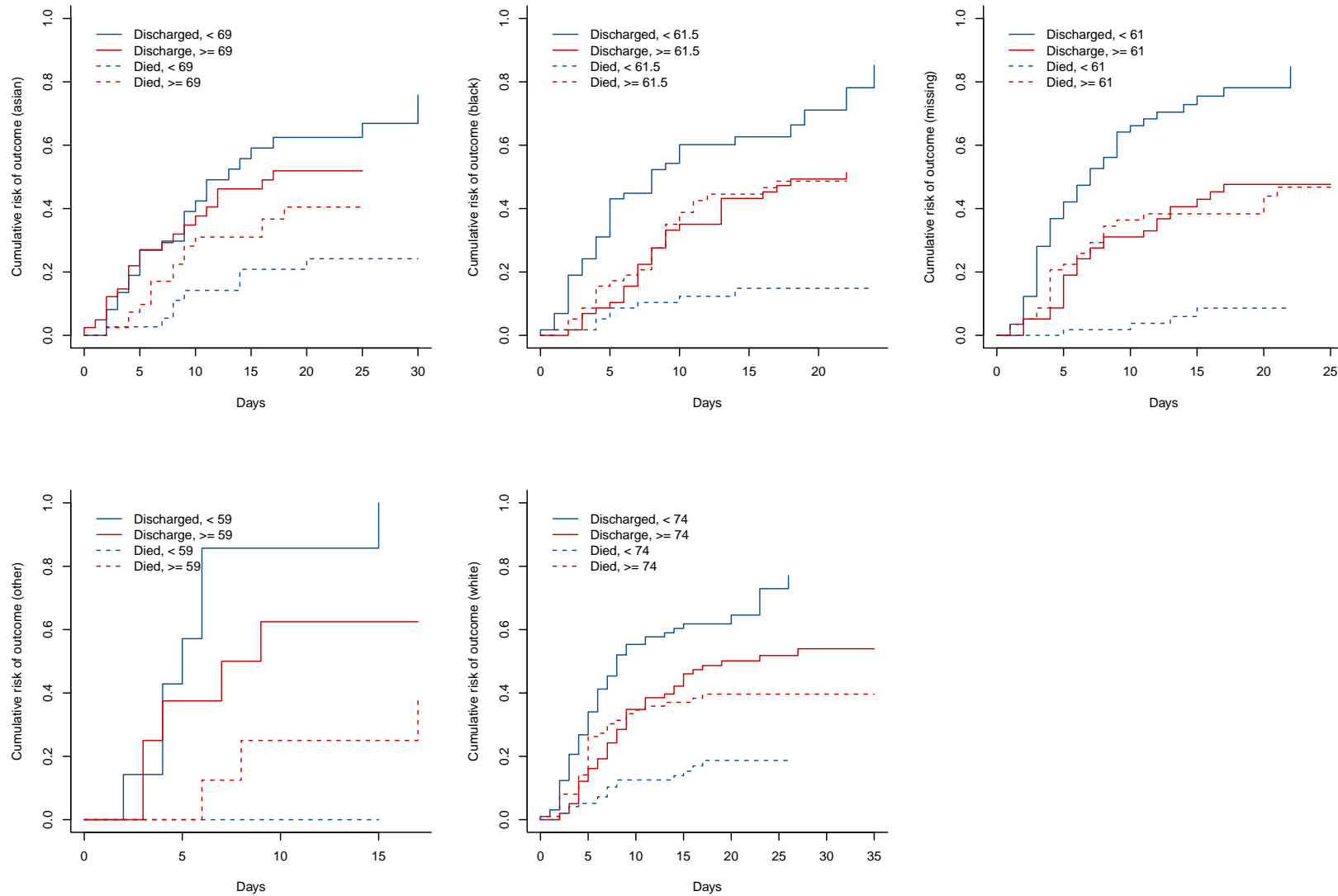


Figure 3(B): Cumulative incidence function of death vs discharged alive by ethnic group and corresponding median age

4. Discussion

This study presents comprehensive demographic, clinical and outcome data for 520 laboratory-confirmed SARS-CoV-2 cases at a large London NHS Trust. To our knowledge, this is one of the first such studies in the United Kingdom to include all hospitalised patients, including critical care patients. We find that increasing age, male sex and a high burden of comorbidities are associated with poorer outcomes in patients with COVID-19, which is consistent with literature emerging from other settings like China, Italy and USA.^{4-6,17-19} These findings are also consistent with emerging data on characteristics of patients in the UK.²⁰ However, we find that when adjusted for age, the association of these main comorbidities (i.e. dementia, CKD, IHD, CCF and hypertension) no longer remains statistically significant. In our study population, the admission characteristics associated with increased odds of hospital mortality on multiple regression included severe hypoxia, low platelet count, elevated bilirubin and reduced eGFR.

Our study is the first to investigate the clinical association between ethnicity and patient outcomes during the COVID-19 epidemic in the UK, a current topic of high national priority. Our results suggest BAME groups are over-represented amongst those hospitalised at ICHNT for COVID-19, particularly black and Asian populations, when compared with historic emergency admissions across ICHNT in 2018-2019 (45% white, 11% black, 9% Asian, 17% other and 17% unknown - see Supplement). This disproportionate ethnic composition of COVID-19 patients of BAME groups in the UK has also been suggested amongst critical care admissions.⁹ Whether this difference is related to biological characteristics or sociodemographic factors associated with increased transmission remains unknown. However, the underlying profiles of the different ethnic groups was shown to significantly vary in our study population, with black and 'other' ethnic minority groups being younger, and Asian and white groups having a higher burden of pre-existing comorbidities. Previous studies have suggested a high burden of undiagnosed comorbidities amongst those from ethnic minority groups, however, the significance of this in the current pandemic is not yet known.²¹ Finally, whilst in the unadjusted regression there seemed to be no difference in COVID-19 mortality by ethnic background, when adjusting for age, Elixhauser comorbidity score and severity of disease on admission, we observed higher odds of death for those from black ethnic background compared with whites. However, this finding merits further investigation given its borderline statistical significance.

The symptom profile of patients in our study are largely consistent with other descriptive studies of COVID-19 disease.^{4-6,20} However, a much higher proportion of our hospitalised cohort reported shortness of breath compared with that reported on a meta-analysis of Chinese studies (67% versus 25%).²² Furthermore, a higher proportion of our cohort showed abnormal blood test results, including raised inflammatory markers, D-dimer and thrombocytopenia. These discrepant findings are likely to reflect differing thresholds and criteria for hospitalisation between the two countries, with China also extending hospitalisation as a method of curbing transmission. Outside China, Grasselli *et al.*²³ reported outcomes of nearly 1,600 patients admitted to ITUs in Italy, which showed a mortality of 26%, with the majority of intubated patients remaining in ITU at the time of their study's censoring date. A subsequent study in the USA described a case series of 5,700 patients hospitalised in 12 centres in New York with a much higher mortality of 88% for those requiring mechanical ventilation.⁶ In our study, only 39 out of 80 intubated patients had completed outcomes, of which 50% have died. The outcomes of the remaining 41 patients of this intubated cohort who remain mechanically ventilated will determine the true mortality rate in our cohort.

A key strength of our study is that we have systematically attempted to identify factors associated with outcomes in a large cohort of over 500 patients through multiple logistic regression. The majority of previously published studies have focused on descriptive statistics, with few studies attempting to correct for age and comorbidity in their evaluation of patient outcomes. A study in China found that older age, high D-dimer ($> 1,000\text{ng/mL}$) and high admission SOFA score were associated with higher odds of mortality.⁴ However, this early study reported only on 191 patients with completed outcomes and excluded over 600 patients who were still hospitalised at the time of publication. Another non-peer reviewed study of over 4,000 cases in New York City found age, high CRP, hypoxia as risk factors for critical illness. Interestingly the odds ratio comparing African-American ethnicity to whites for critical illness in their study was 0.58 (95% CI 0.39-0.87).¹⁷ The comparability of their results to ours might be limited, given differences in the approach for selection of variables and aims of adjusted regression models.

Our study presents interim analyses of outcomes on all admissions up to 5th April 2020, with at least 2 weeks of follow-up for all patients in our study population. Although 14% of our cohort were still hospitalised at the end of the reporting period, the methodology we adopted of cumulative hazards of death and discharge took into account censoring. However, the most uncertain outcomes are likely to be amongst those who are currently still requiring mechanical ventilation.

There are some limitations of our study. First, although we attempted to be as comprehensive as possible, the retrospective nature of this study limited the availability of data. There are missing data for certain variables including ethnicity, BMI and many of the novel laboratory biomarkers now systematically being collected for patients with COVID-19, including D-dimer. In the case of ethnicity, 22% of patients had been classified as 'other' ethnicity upon admission. Due to pressures on the system and infection control measures at ICHNT, hospital receptionists were not directly seeing patients and therefore the ethnicity of patients arriving by ambulance is often unknown. We attempted to overcome this limitation by searching other databases for ethnicity information and only classified patients as 'other' ethnic minority if this was explicitly documented, else we classified them as unknown. This did not limit the conclusions reached in our logistic regression analysis, as these patients were explicitly coded as being of unknown ethnicity. For similar reasons, 50% of admissions had BMI data missing, which could be possibly related to the severity of disease on admission and thus the lack of association seen between increasing BMI and mortality in our study. Many of the non-routine laboratory tests (including D-dimer, BNP and troponin) were only introduced systematically at ICHNT a couple of weeks into the pandemic. Although descriptive statistics suggest there are differences in the prevalence of these variables by patient outcomes, they were excluded from the multiple logistic regression given incomplete recording.

Finally, this study did not consider the characteristics and outcomes of those hospitalised with clinical features of COVID-19 but were RT-PCR swab-negative and those who might have had hospital-acquired SARS-CoV-2 infection. The profiles of these patients and whether their outcomes are different to the patients presented here requires further research.²⁴ Furthermore, we could not quantify the impact of changes in clinical practise over the time of our study. However, only a few patients were enrolled in clinical trials early in the pandemic so changing clinical practices are unlikely to impact on our study findings.

5. Conclusions

This is one of the first studies describing a UK cohort of patients hospitalised with COVID-19 disease which also includes patients outside of the ITU setting and uses robust methodology to account for the effect of patients with uncompleted outcomes. The admission characteristics with the strongest association with increased odds of death were severe hypoxia, low platelet count, elevated bilirubin and a reduced eGFR. BAME groups were overrepresented in our study population, compared with patients historically admitted to our hospitals. Although there is no crude difference in mortality between the different ethnic groups, after accounting for age, comorbidity profile and disease severity on admission, patients of black ethnic background do appear to have increased odds of hospital mortality compared with those of white ethnicity. Further research is urgently needed to investigate whether such an association exists on a national scale and if so, to understand the sociodemographic and biologic factors underpinning it. Linking clinical data from hospitals to that from COVID-19 cases in the community will be crucial to identify patterns of disease transmission. As the SARS-CoV-2 epidemic continues in the UK and other countries, continuous monitoring of clinical data such as those in this study is paramount. These analyses will be vital to inform potential changes in clinical practice locally and could also be considered useful for other clinical settings treating COVID-19 patients in the UK and abroad.

6. References

- 1 UK Government. Number of coronavirus (COVID-19) cases and risk in the UK. Number of coronavirus (COVID-19) cases and risk in the UK. 2020; published online April 27. <https://www.gov.uk/guidance/coronavirus-covid-19-information-for-the-public> (accessed April 27, 2020).
- 2 Office for National Statistics. Deaths registered weekly in England and Wales, provisional: week ending 10 April 2020. Deaths registered weekly in England and Wales, provisional: week ending 10 April 2020. 2020; published online April 21. <https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/deaths/bulletins/deathsregisteredweeklyinenglandandwalesprovisional/weekending10april2020> (accessed April 27, 2020).
- 3 UK Government. Regional ethnic diversity. 2018; published online Aug 1. <https://www.ethnicity-facts-figures.service.gov.uk/uk-population-by-ethnicity/national-and-regional-populations/regional-ethnic-diversity/latest> (accessed April 27, 2020).
- 4 Zhou F, Yu T, Du R, *et al.* Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *The Lancet* 2020; **395**: 1054–62.
- 5 Porcheddu R, Serra C, Kelvin D, Kelvin N, Rubino S. Similarity in Case Fatality Rates (CFR) of COVID-19/SARS-COV-2 in Italy and China. *J Infect Dev Ctries* 2020; **14**: 125–8.
- 6 Richardson S, Hirsch JS, Narasimhan M, *et al.* Presenting Characteristics, Comorbidities, and Outcomes Among 5700 Patients Hospitalized With COVID-19 in the New York City Area. *JAMA* 2020; published online April 22. DOI:10.1001/jama.2020.6775.

- 7 Du R-H, Liang L-R, Yang C-Q, *et al.* Predictors of Mortality for Patients with COVID-19 Pneumonia Caused by SARS-CoV-2: A Prospective Cohort Study. *Eur Respir J* 2020; : 2000524.
- 8 Vincent J-L, Taccone FS. Understanding pathways to death in patients with COVID-19. *The Lancet Respiratory Medicine* 2020; : S221326002030165X.
- 9 Intensive Care National Audit & Research Centre. ICNARC report on COVID-19 in critical care. 2020.
- 10 British Medical Association. Review into COVID-19 impact on BAME communities must be backed by real-time data and include measures to address problem now, says BMA. 2020; published online April 17. <https://www.bma.org.uk/news-and-opinion/review-into-covid-19-impact-on-bame-communities-must-be-backed-by-real-time-data-and-include-measures-to-address-problem-now-says-bma>.
- 11 Imperial College Healthcare. Imperial NHS Trust. 2019; published online Oct 1. <https://www.imperial.nhs.uk/about-us/who-we-are> (accessed April 27, 2020).
- 12 Bottle A, Aylin P. Comorbidity scores for administrative data benefited from adaptation to local coding and diagnostic practices. *Journal of Clinical Epidemiology* 2011; **64**: 1426–33.
- 13 Sharabiani MTA, Aylin P, Bottle A. Systematic Review of Comorbidity Indices for Administrative Data: *Medical Care* 2012; **50**: 1109–18.
- 14 British Society of Thoracic Imaging. Thoracic Imaging in COVID-19 Infection. 2020.
- 15 Terasvirta T, Mellin I. Model Selection Criteria and Model Selection Tests in Regression Models. 1986; : 14.
- 16 Schoenfeld D. Partial Residuals for The Proportional Hazards Regression Model. 1982; : 4.
- 17 Petrilli CM, Jones SA, Yang J, *et al.* Factors associated with hospitalization and critical illness among 4,103 patients with COVID-19 disease in New York City. *Intensive Care and Critical Care Medicine*, 2020 DOI:10.1101/2020.04.08.20057794.
- 18 Deng Y, Liu W, Liu K, *et al.* Clinical characteristics of fatal and recovered cases of coronavirus disease 2019 (COVID-19) in Wuhan, China: a retrospective study. *Chinese Medical Journal* 2020; : 1.
- 19 Rodriguez-Morales AJ, Cardona-Ospina JA, Gutiérrez-Ocampo E, *et al.* Clinical, laboratory and imaging features of COVID-19: A systematic review and meta-analysis. *Travel Medicine and Infectious Disease* 2020; : 101623.
- 20 Docherty AB, Harrison EM, Green CA, *et al.* Features of 16,749 hospitalised UK patients with COVID-19 using the ISARIC WHO Clinical Characterisation Protocol. *Infectious Diseases (except HIV/AIDS)*, 2020 DOI:10.1101/2020.04.23.20076042.
- 21 Moody A, Cowley G, Ng Fat L, Mindell JS. Social inequalities in prevalence of diagnosed and undiagnosed diabetes and impaired glucose regulation in participants in the Health Surveys for England series. *BMJ Open* 2016; **6**: e010155.
- 22 Fu L, Wang B, Yuan T, *et al.* Clinical characteristics of coronavirus disease 2019 (COVID-19) in China: A systematic review and meta-analysis. *Journal of Infection* 2020; : S0163445320301705.

23 Grasselli G, Pesenti A, Cecconi M. Critical Care Utilization for the COVID-19 Outbreak in Lombardy, Italy: Early Experience and Forecast During an Emergency Response. *JAMA* 2020; published online March 13. DOI:10.1001/jama.2020.4031.

24 West CP, Montori VM, Sampathkumar P. COVID-19 Testing: The Threat of False-Negative Results. *Mayo Clinic Proceedings* 2020; : S0025619620303657.

7. Tables

Table 1: Description of clinical characteristics

*Chest radiograph classification as per the British Society of Thoracic Imaging, whereby 0 = normal, 1 = classic COVID-19 findings, 2= abnormal findings indeterminate for COVID-19, and 3 = non-COVID-19 findings

Abbreviations: ALP, alkaline phosphatase; AST, aspartate aminotransferase; BMI, body mass index; BP, blood pressure; CK, creatine kinase; CRP, C-reactive protein; EWS, early warning score; eGFR, estimated glomerular filtration rate; FiO₂, inspiratory fraction of oxygen; HDU/ITU, high dependency unit / intensive treatment unit; IU, international units; IQR, interquartile range; LDH, lactate dehydrogenase; MDRD, modification of diet in renal disease; PT, prothrombin time; SD, standard deviation; WCC, white cell count

	All (n = 520)	Died (n = 144)	Discharged alive (n = 302)	p-value
Demography				
Male, n (%)	322 (62%)	100 (69%)	172 (57%)	<0.05
Median age in years (IQR)	67 (26)	77 (16)	60 (26)	<0.01
BMI	28.92 (7.37)	29.7 (8.43)	28.81 (7.1)	0.42
Median Elixhauser (IQR)	0 (7)	5 (11)	0 (5)	<0.01
Ethnicity				
White (%)	196 (38%)	54 (38%)	111 (37%)	0.96
Black (%)	116 (22%)	35 (24%)	67 (22%)	0.71
Asian (%)	78 (15%)	23 (16%)	43 (14%)	0.73
Other (%)	15 (3%)	3 (2%)	12 (4%)	0.45
Missing (%)	115 (22%)	29 (20%)	69 (23%)	0.60
Healthcare worker, n (%)	22 (4%)	3 (2%)	15 (5%)	0.23
Symptoms				
Mean days prior to admission (SD)	7 (6)	6 (6)	8 (6)	<0.01
Cough, n (%)	397 (76%)	101 (70%)	236 (78%)	0.09
Fever, n (%)	430 (83%)	120 (83%)	249 (82%)	0.92
Shortness of breath, n (%)	347 (67%)	104 (72%)	193 (64%)	0.10
Gastrointestinal, n (%)	165 (32%)	34 (24%)	112 (37%)	<0.01
Other, n (%)	342 (66%)	81 (56%)	215 (71%)	<0.01
Outcomes				
Received >60% FiO ₂ (%)	252 (48%)	117 (81%)	84 (28%)	<0.01
Admitted to HDU/ITU (%)	80 (15%)	20 (14%)	19 (6%)	<0.05
Received invasive ventilation (%)	73 (14%)	16 (11%)	17 (6%)	0.06
Median length of hospital stay (IQR)	7 (6-8)	6 (5-7)	8 (7-9)	<0.01
Median time to clinical deterioration (IQR)	9 (6-17)	NA	3 (1-4)	<0.01

		All (n = 520)	Died (n = 144)	Discharged alive (n = 302)	p-value
Clinical observations on admission					
Fever $\geq 38^{\circ}\text{C}$ (%)		135/513 (26%)	47/143 (33%)	64/299 (21%)	<0.05
Respiratory rate	< 20	144/504 (29%)	37/142 (26%)	91/292 (31%)	0.33
	20 - 29	257/504 (51%)	72/142 (51%)	153/292 (52%)	1.00
	≥ 30	103/504 (20%)	33/142 (23%)	48/292 (16%)	0.12
SaO ₂	$\geq 95\%$ on	151 (29%)	23 (16%)	106 (35%)	<0.01
	< 95% and/or	369 (71%)	121 (84%)	196 (65%)	<0.01
Mean arterial pressure	≥ 100	186/512 (36%)	52/143 (36%)	102/297 (34%)	0.76
	70 - 99	298/512 (58%)	79/143 (55%)	181/297 (61%)	0.30
	< 90	28/512 (5%)	12/143 (8%)	14/297 (5%)	0.19
Pulse	≥ 100	199/515 (39%)	49/143 (34%)	117/300 (39%)	0.39
	60 - 99	308/515 (60%)	92/143 (64%)	177/300 (59%)	0.27
	< 60	8/515 (2%)	2/143 (1%)	6/300 (2%)	0.95
EWS	≥ 7	166/516 (32%)	66 (46%)	69/300 (23%)	<0.01
	5 - 6	115/516 (22%)	30 (21%)	75/300 (25%)	0.40
	< 5	235/516 (46%)	48 (33%)	156/300 (52%)	<0.01
Bloods					
Haemoglobin g/L	≥ 130	288/512 (56%)	70/140 (50%)	173/299 (58%)	0.15
	100 - 129	190/512 (37%)	54/140 (39%)	111/299 (37%)	0.85
	< 100	34/512 (7%)	16/140 (11%)	15/299 (5%)	<0.05
WCC 10 ⁹ L	≥ 10.6	85/512 (17%)	28/140 (20%)	39/299 (13%)	0.08
	4.2 - 10.5	381/512 (74%)	98/140 (70%)	236/299 (79%)	<0.05
	< 4.2	46/512 (9%)	15/140 (11%)	25/299 (8%)	0.54
Lymphocytes 10 ⁹ L	≥ 3.6	8/511 (2%)	2/140 (1%)	3/298 (1%)	1.00
	1.1 - 3.5	171/511 (33%)	36/140 (26%)	116/298 (39%)	<0.01
	0.5 - 1.0	288/511 (56%)	83/140 (59%)	159/298 (53%)	0.29
	< 0.5	44/511 (7%)	19/140 (14%)	20/298 (7%)	<0.05
Platelets 10 ⁹ L	≥ 370	28/511 (5%)	6/139 (4%)	17/299 (6%)	0.71
	130 - 369	416/511 (81%)	99/139 (71%)	250/299 (84%)	<0.01
	< 130	78/511 (15%)	34/139 (24%)	32/299 (11%)	<0.01
Creatinine mmol/L	≥ 125	134/508 (26%)	59/139 (42%)	56/296 (19%)	<0.01
	< 125	374/508 (74%)	80/139 (58%)	240/296 (81%)	<0.01
Urea mmol/L	≥ 7.8	182/506 (36%)	74/138 (54%)	86/296 (29%)	<0.01
	< 7.8	324/506 (64%)	64/138 (46%)	210/296 (71%)	<0.01
eGFR MDRD mL/min/1.73m ²	≥ 90	135/505 (27%)	13/139 (9%)	102/293 (35%)	<0.01
	60 - 89	173/505 (34%)	45/139 (32%)	101/293 (34%)	0.90
	30 - 59	115/505 (23%)	40/139 (29%)	58/293 (20%)	<0.05
	< 30	82/505 (16%)	41/139 (30%)	32/293 (11%)	<0.01
Albumin g/L	≥ 35	108/459 (24%)	22/120 (18%)	77/269 (29%)	<0.05
	25 - 34	301/459 (66%)	80/120 (67%)	168/269 (62%)	0.18
	< 25	50/459 (11%)	18/120 (15%)	24/269 (9%)	0.11
ALT IU/L	$\geq 3x$ ULN	17/450 (4%)	5/118 (4%)	11/261 (4%)	1.00
	1 - 2.9x ULN	110/450 (24%)	19/118 (16%)	68/261 (26%)	<0.05
	< 1x ULN	323/450 (72%)	94/118 (80%)	182/261 (70%)	0.06
Bilirubin mmol/L	≥ 21	57/440 (13%)	20/114 (18%)	26/256 (10%)	0.07
	< 21	383/440 (87%)	94/114 (82%)	230/256 (90%)	0.07

		All (n = 520)	Died (n = 144)	Discharged alive (n = 302)	p-value
Bloods (continued)					
ALPh IU/L	≥ 130	66/466 (14%)	27/124 (22%)	31/272 (11%)	<0.05
	< 130	400/466 (86%)	97/124 (78%)	241/272 (89%)	<0.05
PT sec	≥ 17.4	37/382 (10%)	16/98 (16%)	14/221 (6%)	<0.01
	< 17.4	345/382 (90%)	82/98 (84%)	207/221 (94%)	<0.01
Lactate mmol/L	≥ 2	102/411 (25%)	38/115 (33%)	48/236 (20%)	<0.05
	< 2	309/411 (75%)	77/115 (67%)	188/236 (80%)	<0.05
Glucose mmol/L	≥ 5.2	385/423 (91%)	108/120	221/242 (91%)	0.83
	3.7 - 5.1	185/423 (44%)	10/120 (8%)	21/242 (9%)	1.00
	< 3.7	4/423 (1%)	2/120 (2%)	1/242 (0%)	0.53
CRP mg/L	≥ 100	268/497 (54%)	83/134 (62%)	132/292 (45%)	<0.01
	10 - 99	196/497 (39%)	48/134 (36%)	132/292 (45%)	0.09
	< 10	33/497 (7%)	3/134 (2%)	28/292 (10%)	<0.05
D-dimer ng/mL	≥ 3000	48/258 (19%)	15/70 (21%)	22/142 (15%)	0.38
	2000 - 2999	32/258 (12%)	15/70 (21%)	14/142 (10%)	<0.05
	1000 - 1999	78/258 (30%)	18/70 (26%)	44/142 (31%)	0.53
	500 - 999	71/258 (28%)	16/70 (23%)	41/142 (29%)	0.45
	< 500	29/258 (11%)	6/70 (9%)	21/142 (15%)	0.29
LDH IU/L	≥ 243	191/206 (93%)	49/54 (91%)	104/112 (93%)	0.87
	< 243	15/206 (7%)	5/54 (9%)	8/112 (7%)	0.87
Troponin ng/L	≥ 34	104/341 (31%)	51/95 (54%)	37/190 (19%)	<0.01
	5 - 34	236/341 (69%)	44/95 (46%)	152/190 (80%)	<0.01
CK U/L	≥ 320	73/240 (30%)	26/66 (39%)	31/130 (24%)	<0.05
	< 320	167/240 (70%)	40/66 (61%)	99/130 (76%)	<0.05
BNP pg/mL	≥ 150	42/219 (19%)	20/56 (36%)	17/128 (13%)	<0.01
	< 150	177/219 (81%)	36/56 (64%)	111/128 (87%)	<0.01
Ferritin ng/mL	≥ 5000	14/297 (5%)	4/81 (5%)	8/162 (5%)	1.00
	1000 - 4999	114/297 (38%)	28/81 (35%)	59/162 (36%)	0.89
	500 - 999	83/297 (28%)	24/81 (30%)	45/162 (28%)	0.88
	300 - 499	43/297 (14%)	10/81 (12%)	27/162 (17%)	0.49
	< 300	43/297 (14%)	15/81 (19%)	23/162 (14%)	0.49
Cortisol nmol/L	≥ 550	114/164 (70%)	32/44 (73%)	60/90 (67%)	0.61
	< 550	50/164 (30%)	12/44 (27%)	30/90 (33%)	0.61
Chest Radiograph*					
0		67/427 (16%)	12/119 (10%)	50/250 (20%)	<0.05
1	Mild	25/516 (5%)	3 (2%)	17/298 (6%)	0.14
	Moderate	104/512 (20%)	28/142 (20%)	65/297 (22%)	0.69
	Severe	94/514 (18%)	23/141 (16%)	48/301 (16%)	1.00
2	Mild	40/516 (8%)	9 (6%)	27/298 (9%)	0.41
	Moderate	63/512 (12%)	26/142 (18%)	27/297 (9%)	<0.01
	Severe	11/514 (2%)	7/141 (5%)	4/301 (1%)	<0.05
3		23/427 (5%)	11/119 (9%)	12/250 (5%)	0.16

Table 2: Logistic regression for clinical and laboratory predictors of hospital death

*Adjusted regression values are presented for variables that remained statistically significant through to the final prediction model. For full adjusted model selection process see Table S3 (supplement). Final model misclassification error was 24.1%, goodness-of-fit p -value <0.01

**Variables with greater than 20% missing values were excluded from adjusted regression analysis

***The increased odds of death for individual comorbidities was not statistically significant after adjusting for age

¹For clarity, platelets and albumin are presented as categorical in the unadjusted regression; however, they were handled as numeric in adjusted regression given normal distribution

²Pre-final model was adjusted for pre-existing CKD, with eGFR remaining the strongest predictor of death

Abbreviations: 95%CI, 95% confidence interval; BMI, body mass index; BNP, brain natriuretic peptide; BP, blood pressure; CK, creatine kinase; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; CRP, C-reactive protein; DVT/PE, deep vein thrombosis / pulmonary embolism; EWS, early warning score; eGFR, estimated glomerular filtration rate; FiO₂, inspiratory fraction of oxygen; IU, international units; LDH, lactate dehydrogenase; MDRD, modification of diet in renal disease; OR, odds ratio; SaO₂, oxygen saturation; WCC, white cell count

Variable	Unadjusted regression		Adjusted regression*	
	OR (95%CI)	p-value	OR (95%CI)	p-value
Demography				
Male sex	1.72 (1.13, 2.62)	0.01		
Age*	1.06 (1.04, 1.07)	<0.01	2.16 (1.50, 3.12)	<0.01
Elixhauser score	1.07 (1.04, 1.11)	<0.01		
BMI**	18 - 24.9 (intercept)			
	< 18	1.24 (0.15, 8.04)	0.82	
	25 - 29.9	0.95 (0.46, 1.97)	0.89	
	30 - 34.9	1.01 (0.47, 2.14)	0.98	
	35 - 39.9	1.49 (0.50, 4.33)	0.46	
	≥ 40	1.86 (0.61, 5.74)	0.27	
	Missing	0.72 (0.40, 1.32)	0.28	
Ethnic background	White (intercept)			
	Black	1.07 (0.63, 1.81)	0.79	
	Asian	1.10 (0.60, 2.00)	0.76	
	Other	0.51 (0.11, 1.70)	0.32	
	Missing	0.86 (0.50, 1.48)	0.60	
Comorbidities***				
Any comorbidity	2.07 (1.35, 3.17)	<0.01		
Diabetes	1.44 (0.93, 2.21)	0.10		
Ischaemic heart	2.54 (1.30, 4.98)	0.01		
Hypertension	1.92 (1.28, 2.88)	<0.01		
Hyperlipidaemia	1.03 (0.61, 1.76)	0.91		
Chronic heart failure	2.42 (1.00, 5.83)	0.04		
Stroke	1.43 (0.67, 3.06)	0.35		

Variable	Unadjusted regression		Adjusted regression*	
	OR (95%CI)	p-value	OR (95%CI)	p-value
Comorbidities*** (continued)				
Asthma	0.62 (0.26, 1.48)	0.28		
COPD	1.92 (0.72, 5.07)	0.18		
Dementia	5.25 (2.33, 11.85)	< 0.01		
CKD	2.40 (1.39, 4.13)	0.01		
Solid tumour	2.39 (1.19, 4.80)	0.01		
Liver non-cirrhotic	0.74 (0.34, 1.63)	0.45		
Liver cirrhotic	3.24 (0.90, 11.66)	0.06		
Atrial fibrillation	2.00 (1.13, 3.53)	0.02		
DVT/PE	2.85 (0.63, 12.89)	0.16*		
Clinical observations on admission				
Days to admission	0.93 (0.89, 0.97)	< 0.01		
	60-90 (intercept)			
Pulse	< 60	0.64 (0.09, 2.85)	0.59	
	≥ 100	0.81 (0.53, 1.22)	0.31	
	<20 (intercept)			
Respiratory rate	20-29	1.16 (0.72, 1.87)	0.55	
	≥ 30	1.69 (0.94, 3.04)	0.08	
Clinical observations on admission (continued)				
	36.1-38 (intercept)			
Temperature	< 36.1	1.79 (0.85, 3.67)	0.12	
	≥ 38	1.92 (1.24, 2.99)	< 0.01	
	> 94% on room air			
	< 94% on room air	1.99 (0.97, 4.05)	0.06	1.42 (0.60, 3.37) 0.42
SaO2*	> 94% on O2	1.97 (1.13, 3.47)	0.02	1.37 (0.68, 2.74) 0.32
	< 94% on O2	3.28 (1.44, 7.43)	< 0.01	2.82 (0.97, 8.18) 0.03
	FI02 > 0.6	4.53 (2.51, 8.33)	< 0.01	3.75 (1.80, 7.80) <0.01
	70 - 99 (intercept)			
Mean arterial BP	< 70	1.96 (0.86, 4.44)	0.1	
	≥ 100	1.17 (0.76, 1.79)	1.79	
EWS	< 4 (intercept)			
	4 - 6	1.38 (0.82, 2.31)	0.23	
	≥ 7	3.33 (2.02, 5.57)	< 0.01	
Bloods				
Haemoglobin g/L	≥ 130 (intercept)			
	100-129	1.20 (0.78, 1.84)	0.4	
	<100	2.19 (1.01, 4.81)	0.5	
WCC 10 ⁹ L	4.2 - 10.5 (intercept)			
	< 4.2	1.45 (0.72, 2.85)	0.28	
	≥ 10.6	1.74 (1.01, 2.98)	0.04	

Variable	Unadjusted regression		Adjusted regression*	
	OR (95%CI)	p-value	OR (95%CI)	p-value
Bloods (continued)				
Lymphocytes 10⁹L	1.1-3.5 (intercept)			
	< 0.5	3.06 (1.47, 6.39)	< 0.01	
	0.5 - 1.0	1.68 (1.07, 2.68)	0.03	
	≥ 3.6	2.15 (0.27, 13.45)	0.41	
Platelets*¹ 10⁹L	130 - 369 (intercept)		1.54 (1.18, 2.04)	<0.01
	< 100	3.28 (1.40, 7.93)	0.01	
	100 - 130	2.41 (1.26, 4.59)	0.01	
	≥ 370	0.89 (0.31, 2.21)	0.81	
eGFR (MDRD)*	> 90 (intercept)			
	60 - 89	3.50 (1.82, 7.11)	< 0.01	2.20 (0.93, 5.18) 0.06
	30 - 59	5.41 (2.74, 11.29)	< 0.01	2.15 (0.83, 5.56) 0.09
	< 30	10.05 (4.92, 21.74)	< 0.01	4.11 ² (1.58, 10.69) <0.01
Albumin*¹ g/L	≥ 35 (intercept)		1.30 (0.99-1.69)	<0.05
	25 - 34	1.67 (0.98, 2.92)	0.07	
	< 25	2.62 (1.21, 5.72)	0.01	
	Missing	2.55 (1.26, 5.21)	0.01	
Bilirubin* mmol/L	≥ 21 (intercept)		2.32 (1.05, 5.14)	<0.05
	< 21	1.88 (0.99, 3.53)	<0.05	
	Missing	1.60 (0.94, 2.67)	0.08	
Lactate** mmol/L	< 2.0 (intercept)			
	≥ 2.0	1.93 (1.17, 3.19)	<0.01	
	Missing	1.07 (0.64, 1.78)	0.79	
Glucose mmol/L	3.7 - 5.1 (intercept)			
	< 3.7	4.00 (0.34, 92.39)	0.28	
	≥ 5.2	0.98 (0.45, 2.24)	0.95	
	Missing	0.80 (0.33, 2.01)	0.62	
D-Dimer** ng/mL	< 500 (intercept)			
	500 - 1000	1.37 (0.48, 4.27)	0.57	
	1000 - 2000	1.43 (0.51, 4.42)	0.51	
	2000 - 3000	3.75 (1.21, 12.76)	0.03	
	≥ 3000	2.39 (0.81, 7.77)	0.13	
	Missing	1.62 (0.66, 4.56)	0.32	
LDH** IU/L	< 243 (intercept)			
	≥ 243	0.75 (0.24, 2.60)	0.64	
	Missing	0.76 (0.25, 2.57)	0.64	
BNP** pg/mL	< 150 (intercept)			
	≥ 150	3.63 (1.72, 7.75)	<0.01	
	Missing	1.56 (1.00, 2.48)	0.06	

Variable	Unadjusted regression		Adjusted regression*	
	OR (95%CI)	p-value	OR (95%CI)	p-value
Bloods (continued)				
Troponin** ng/mL	< 34 (intercept)			
	≥ 34	4.79 (2.81, 8.29)		<0.01
	Missing	1.52 (0.95, 2.45)		0.08
CK** IU/L	< 320 (intercept)			
	≥ 320	0.74 (0.26, 2.31)		0.59
	Missing	0.68 (0.24, 2.09)		0.48
Ferritin** ng/mL	< 300 (intercept)			
	300 - 499	0.57 (0.21, 1.49)		0.2
	500 - 999	0.82 (0.36, 1.87)		0.26
	1000 - 5000	0.73 (0.33, 1.62)		0.63
	≥ 5000	0.77 (0.18, 2.90)		0.7
	Missing	0.69 (0.34, 1.43)		0.31
Cortisol** nmol/L	< 550 (intercept)			
	≥ 550	1.33 (0.61, 3.03)		0.48
	Missing	1.18 (0.59, 2.48)		0.65
Abnormal X-ray		2.23 (1.14, 4.37)		0.02

Table 3: Clinical characteristics by ethnicity and logistic regression of odds of death

*Adjusted logistic regression for age, Elixhauser and EWS differences of ethnic groups

**Additional logistic regression models adjusted for individual comorbidities that had statistically significant variation across ethnic groups, but were inferior predictors compared to the selected model with Elixhauser score. CKD, cirrhotic liver disease and HIV/AIDS were not used in logistic regression models, as they had low n values for ethnic groups

Abbreviations: COPD, chronic obstructive pulmonary disease; DVT/PE, deep vein thrombosis / pulmonary embolism; HDU/ITU, high dependency unit / intensive treatment unit; HIV/AIDS, human immunodeficiency virus / acquired immunodeficiency syndrome; IVS, invasive ventilation support; SD, standard deviation

	White (n = 196)	Black (n = 116)	Asian (n = 78)	Other (n = 15)	NA (n = 115)	p-value
Male, n (%)	119 (61%)	66 (57%)	51 (65%)	10 (67%)	76 (66%)	0.60
Mean age (SD)	69.94 (15.6)	62.8 (19.53)	66.05 (15.45)	55.07 (16.01)	59.67 (17.91)	<0.01
Mean days to admission (SD)	6.78 (5.76)	7.3 (6.12)	5.87 (4.84)	7.47 (6.8)	8.34 (5.09)	0.28
Mean Elixhauser score (SD)	4.89 (6.81)	3.63 (5.84)	4.96 (6.66)	2.47 (4.53)	2.38 (4.72)	<0.01
Mean EWS score (SD)	5.01 (3.26)	4.98 (3.11)	4.53 (3.29)	5.47 (2.75)	5.53 (2.76)	0.15
Outcomes						
FiO2 >=60%, n (%)	88 (45%)	54 (47%)	38 (49%)	5 (33%)	67 (58%)	0.14
Admitted HDU/ITU, n (%)	22 (11%)	18 (16%)	12 (15%)	2 (13%)	26 (23%)	0.12
Received IVS, n (%)	21 (11%)	16 (14%)	11 (14%)	2 (13%)	23 (20%)	0.27
Died in hospital, n (%)	54 (28%)	35 (30%)	23 (29%)	3 (20%)	29 (25%)	0.86
Discharged alive, n (%)	111 (57%)	67 (58%)	43 (55%)	12 (80%)	69 (60%)	0.46
Pending outcome, n (%)	31 (16%)	14 (12%)	12 (15%)	0 (0%)	17 (15%)	0.49
Comorbidities						
Ischaemic heart disease, n (%)	18 (9%)	9 (8%)	10 (13%)	0 (0%)	6 (5%)	0.27
Chronic heart failure, n (%)	10 (5%)	6 (5%)	0 (0%)	0 (0%)	5 (4%)	0.30
Hypertension, n (%)	68 (35%)	45 (39%)	27 (35%)	5 (33%)	42 (37%)	0.96
Hyperlipidaemia, n (%)	32 (16%)	13 (11%)	18 (23%)	1 (7%)	18 (16%)	0.20
Diabetes**, n (%)	36 (18%)	39 (34%)	31 (40%)	3 (20%)	29 (25%)	<0.01
Chronic kidney disease**, n (%)	31 (16%)	12 (10%)	19 (24%)	0 (0%)	8 (7%)	<0.01
Peripheral vascular disease, n (%)	7 (4%)	2 (2%)	0 (0%)	0 (0%)	2 (2%)	0.38
Stroke, n (%)	17 (9%)	9 (8%)	6 (8%)	0 (0%)	2 (2%)	0.12
Atrial fibrillation**, n (%)	33 (17%)	10 (9%)	9 (12%)	2 (13%)	7 (6%)	<0.05
DVT/PE history, n (%)	4 (2%)	2 (2%)	0 (0%)	0 (0%)	1 (1%)	0.68
Hemiplegia, n (%)	3 (2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0.29
Dementia**, n (%)	23 (12%)	5 (4%)	4 (5%)	0 (0%)	3 (3%)	<0.01
Asthma, n (%)	9 (5%)	11 (9%)	5 (6%)	3 (20%)	9 (8%)	0.15
COPD**, n (%)	15 (8%)	2 (2%)	2 (3%)	0 (0%)	1 (1%)	<0.01
Connective tissue disease, n (%)	1 (1%)	1 (1%)	0 (0%)	0 (0%)	1 (1%)	0.93
Peptic ulcer, n (%)	5 (3%)	2 (2%)	1 (1%)	0 (0%)	2 (2%)	0.92
Liver (non-cirrhotic), n (%)	12 (6%)	9 (8%)	7 (9%)	3 (20%)	5 (4%)	0.20
Liver (cirrhotic)**, n (%)	2 (1%)	2 (2%)	5 (6%)	0 (0%)	1 (1%)	<0.05
Solid tumour, n (%)	23 (12%)	6 (5%)	4 (5%)	1 (7%)	7 (6%)	0.16
Haematologic tumour, n (%)	2 (1%)	1 (1%)	0 (0%)	0 (0%)	2 (2%)	0.80
HIV/AIDS**, n (%)	1 (1%)	5 (4%)	0 (0%)	0 (0%)	0 (0%)	0.01

	White (n = 196)	Black (n = 116)	Asian (n = 78)	Other (n = 15)	NA (n = 115)	p-value
Logistic regression of odds of death by ethnicity						
Unadjusted OR (95%CI)	Intercept	1.14 (0.69, 1.88)	1.10 (0.62, 1.96)	0.66 (0.18, 2.42)	0.89 (0.52, 1.50)	---
Adjusted OR (95%CI) *	Intercept	1.86 (1.03, 3.35)	1.74 (0.90, 3.36)	1.72 (0.42, 7.01)	1.73 (0.94, 3.18)	---

8. Supplementary Appendix

Equation 1. Cumulative transition hazard and survival function defined by the Nelson-Aeler (a) and Kaplan-Meier (b) estimators.

$$a) \text{ Cumulative transition hazard } (t) = \sum_{k=1}^K \frac{\text{number observed} \rightarrow \text{transitions at } t_k}{\text{numer at risk just prior to } t_k}$$

$$b) \text{ Survival } (t) = \prod_{t_i \leq t} \left(1 - \frac{d_i}{n_i}\right)$$

Supplementary Table S1: Comorbidities and outcomes by age

Abbreviations: 95% CI, 95% confidence interval; COPD, chronic obstructive pulmonary disease; DVT/PE, deep vein thrombosis / pulmonary embolism; HIV/AIDS, human immunodeficiency virus / acquired immunodeficiency syndrome; HDU/ITU, high dependency unit / intensive treatment unit; OR, odds ratio

	< 18	18-29	30-39	40-49	50-59	60-69	70-79	80+
Comorbidities (%)								
Any comorbidity	0 (0%)	3 (33%)	11 (31%)	18 (49%)	67 (60%)	42 (52%)	85 (69%)	84 (71%)
Hypertension	0 (0%)	0 (0%)	3 (9%)	8 (22%)	34 (30%)	28 (35%)	52 (42%)	62 (53%)
Diabetes	0 (0%)	0 (0%)	5 (14%)	8 (22%)	33 (30%)	24 (30%)	36 (29%)	32 (27%)
Ischaemic heart disease	0 (0%)	0 (0%)	0 (0%)	0 (0%)	5 (5%)	5 (6%)	12 (10%)	21 (18%)
Chronic heart failure	0 (0%)	0 (0%)	0 (0%)	1 (3%)	0 (0%)	4 (5%)	7 (6%)	9 (8%)
Stroke	0 (0%)	0 (0%)	0 (0%)	2 (5%)	5 (5%)	4 (5%)	10 (8%)	13 (11%)
Chronic kidney disease	0 (0%)	0 (0%)	2 (6%)	5 (14%)	11 (10%)	6 (7%)	19 (1%)	27 (23%)
Dementia	0 (0%)	0 (0%)	0 (0-0%)	0 (0%)	1 (1%)	2 (3%)	9 (7%)	23 (20%)
DVT/PE (previous)	0 (0%)	0 (0%)	0 (0-0%)	0 (0%)	1 (1%)	3 (4%)	2 (2%)	1 (1%)
Atrial fibrillation	0 (0%)	0 (0%)	1 (3%)	1 (3%)	12 (11%)	6 (7%)	17 (14%)	24 (20%)
COPD	0 (0%)	0 (0%)	0 (0-0%)	0 (0%)	2 (2%)	4 (5%)	8 (7%)	6 (5%)
Asthma	0 (0%)	2 (22%)	2 (6%)	5 (14%)	7 (6%)	3 (4%)	6 (5%)	12 (10%)
Liver disease (non-	0 (0%)	1 (11%)	3 (9%)	2 (5%)	11 (10%)	5 (6%)	9 (7%)	5 (4%)
Liver disease (cirrhotic)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	5 (5%)	0 (0%)	3 (2%)	2 (2%)
Solid malignant tumour	0 (0%)	0 (0%)	0 (0%)	0 (0%)	4 (4%)	4 (5%)	15 (12%)	18 (15%)
Haematologic	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	2 (3%)	2 (2%)	1 (1%)
HIV/AIDS	0 (0%)	0 (0%)	1 (3%)	1 (3%)	2 (2%)	2 (3%)	0 (0%)	0 (0%)
Outcomes (%)								
Required FiO2 > 0.6	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Admitted to HDU/ITU	0 (0%)	0 (0%)	8 (23%)	12 (32%)	30 (27%)	19 (24%)	9 (7%)	2 (2%)
Received IVS	0 (0%)	0 (0%)	8 (23%)	11 (30%)	28 (25%)	17 (21%)	8 (7%)	1 (1%)
Died in hospital	0 (0%)	1 (11%)	0 (0%)	3 (8%)	19 (17%)	16 (20%)	48 (39%)	57 (48%)

Supplementary Table S2: Logistic regression of odds of death given pre-existing comorbidities
 *** $p < 0.001$; ** $p < 0.01$; * $p < 0.05$

	Unadjusted	Adjusted for age
Any comorbidity	1.98** [1.29, 3.03]	1.43 [0.90, 2.27]
Ischaemic heart disease	2.54** [1.30, 4.98]	1.46 [0.72, 2.97]
Chronic heart failure	2.42* [1.00, 5.83]	1.51 [0.60, 3.80]
Atrial fibrillation	2.00* [1.13, 3.53]	1.51 [0.83, 2.76]
Hypertension	1.92** [1.28, 2.88]	1.25 [0.80, 1.95]
Diabetes	1.44 [0.93, 2.21]	1.36 [0.86, 2.16]
COPD	1.92 [0.72, 5.07]	1.39 [0.51, 3.81]
Chronic kidney disease	2.40** [1.39, 4.13]	1.78 [0.99, 3.19]
Dementia	5.25*** [2.33, 11.85]	2.35 [1.00, 5.54]

Supplementary Table S3: Ethnicity breakdown compared to previous emergency admissions at ICHNT

Ethnicity	Emergency admissions of >18 years (%)	
	COVID-19 ICHNT 2020	ICHNT 2018/2019
White	196 (38%)	21,236 (45%)
Asian or Asian British	78 (15%)	4,182 (9%)
Black or Black British	116 (22%)	5,130 (11%)
Other*	15 (5%)	7,936 (17.2%)*
Unknown	115 (22%)	8,019 (17.4%)

Supplementary Table S4: Adjusted model selection for odds of death by ethnicity

*** p < 0.001; ** p < 0.01; * p < 0.05

Abbreviations: AF, atrial fibrillation; AIC, Akaike information criterion; BIC, Bayesian information criterion; CKD, chronic kidney disease; EWS, early warning score

	Model 1	Model 2	Model 3	Model 4	Model 5	Model 6	Model 7	Model 8	Model 9	Model 10	Model 11	Model 12
White (Intercept)	0.38 ***	0.24 ***	0.23 ***	0.19 ***	0.40 **	0.32 ***	0.36 **	0.42 *	0.41 **	0.30 ***	0.31 ***	0.39 *
	[0.28, 0.52]	[0.16, 0.34]	[0.16, 0.33]	[0.13, 0.29]	[0.22, 0.73]	[0.19, 0.53]	[0.20, 0.66]	[0.20, 0.92]	[0.22, 0.75]	[0.18, 0.51]	[0.17, 0.58]	[0.17, 0.86]
Asian	1.10	1.41	1.42	1.74	1.33	1.31	1.48	1.48	1.59	1.54	1.75	1.75
	[0.62, 1.96]	[0.76, 2.63]	[0.76, 2.66]	[0.90, 3.36]	[0.71, 2.50]	[0.70, 2.46]	[0.79, 2.76]	[0.79, 2.77]	[0.82, 3.05]	[0.80, 2.95]	[0.92, 3.35]	[0.91, 3.35]
Black	1.14	1.64	1.72	1.86 *	1.69	1.53	1.72	1.71	1.78	1.56	1.78	1.77
	[0.69, 1.88]	[0.94, 2.85]	[0.98, 3.02]	[1.03, 3.35]	[0.97, 2.96]	[0.87, 2.68]	[0.98, 3.00]	[0.98, 3.00]	[0.99, 3.20]	[0.87, 2.79]	[1.00, 3.19]	[0.99, 3.17]
Missing	0.89	1.53	1.69	1.73	1.62	1.49	1.61	1.61	1.62	1.44	1.57	1.56
	[0.52, 1.50]	[0.86, 2.74]	[0.94, 3.06]	[0.94, 3.18]	[0.90, 2.91]	[0.83, 2.66]	[0.90, 2.90]	[0.90, 2.89]	[0.89, 2.94]	[0.80, 2.61]	[0.86, 2.86]	[0.86, 2.84]
Mixed - Other	0.66	1.51	1.62	1.72	1.67	1.46	1.54	1.60	1.74	1.49	1.57	1.62
	[0.18, 2.42]	[0.38, 6.04]	[0.40, 6.52]	[0.42, 7.01]	[0.42, 6.68]	[0.36, 5.89]	[0.39, 6.11]	[0.40, 6.39]	[0.43, 7.13]	[0.36, 6.11]	[0.39, 6.36]	[0.40, 6.59]
Adjusted for age		2.84 ***	2.65 ***	2.88 ***	2.76 ***	2.84 ***	2.79 ***	2.69 ***	3.01 ***	3.12 ***	3.05 ***	2.93 ***
		[2.16, 3.73]	[2.01, 3.49]	[2.15, 3.86]	[2.10, 3.63]	[2.16, 3.73]	[2.12, 3.66]	[2.04, 3.55]	[2.26, 4.02]	[2.33, 4.17]	[2.29, 4.08]	[2.18, 3.93]
Adjusted for Elixhauser			1.35 **	1.48 ***								
			[1.10, 1.65]	[1.19, 1.83]								
Adjusted for NEWS-2				1.87 ***					1.83 ***	1.79 ***	1.76 ***	1.77 ***
				[1.49, 2.35]					[1.46, 2.29]	[1.43, 2.24]	[1.41, 2.20]	[1.42, 2.21]
Adjusted for CKD					0.53 *				0.45 **			
					[0.30, 0.94]				[0.25, 0.81]			
Adjusted for diabetes						0.69				0.64		
						[0.44, 1.09]				[0.40, 1.03]		
Adjusted for AF							0.59				0.61	
							[0.33, 1.06]				[0.33, 1.12]	
Adjusted for dementia								0.52				0.51
								[0.24, 1.12]				[0.23, 1.12]
N	520	520	520	520	520	520	520	520	520	520	520	520
AIC	622.32	550.92	544.23	514.89	548.31	550.47	549.90	550.07	520.97	524.55	525.45	525.04
BIC	643.59	576.44	574.00	548.92	578.09	580.24	579.67	579.85	555.00	558.58	559.48	559.08
Pseudo R2	0.00	0.19	0.21	0.29	0.20	0.20	0.20	0.20	0.27	0.26	0.26	0.26