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Complete List of Authors:	Apea, Vanessa; Queen Mary University of London Wan, Yize; Queen Mary University of London, Dhairyawan, Rageshri; Queen Mary University of London Puthucheary, Zudin; Barts and The London School of Medicine and Dentistry William Harvey Research Institute; Royal London Hospital, Adult Critical Care Unit Pearse, Rupert; Queen Mary University of London, Barts and the London School of Medicine & Dentistry Orkin, Chloe; Queen Mary University of London Prowle, John; Queen Mary University of London, Barts and the London School of Medicine & Dentistry
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Ethnicity and outcomes in patients hospitalised with COVID-19 infection in East London: an observational cohort study

V. J. Apea[1‡], Y. I. Wan[2‡], R. Dhairyawan[3], Z. A. Puthucheary[4], R. M. Pearse[5], C. M. Orkin[6*], J. R. Prowle[7*]
‡Joint first authors
*Joint senior authors

1. A. Consultant Physician in Sexual Health and HIV Medicine, Sexual Health Clinical Lead, Barts Health NHS Trust, London, E1 1BB, UK
B. Honorary Senior Lecturer, Blizard Institute, Queen Mary University of London, E1 2AT, UK
v.apea@nhs.net

2. A. NIHR Clinical Lecturer, William Harvey Research Institute, Queen Mary University of London, EC1M 6BQ, UK
B. Specialty Registrar in Intensive Care Medicine & Anaesthesia, Barts Health NHS Trust, London, E1 1BB, UK yize.wan@qmul.ac.uk

3. A. Consultant Physician in Sexual Health and HIV Medicine, Barts Health NHS Trust, London, E1 1BB, UK
B. Honorary Senior Lecturer, Blizard Institute, Queen Mary University of London, E1 2AT, UK
rageshri.dhairyawan@nhs.net

4. A. Clinical Senior Lecturer, William Harvey Research Institute, Queen Mary University of London, EC1M 6BQ, UK
B. Honorary Consultant Physician in Intensive Care, Barts Health NHS Trust, London, E1 1BB, UK
z.puthucheary@qmul.ac.uk

5. A. NIHR Research Professor, William Harvey Research Institute, Queen Mary University of London, EC1M 6BQ, UK
B. Consultant Physician in Intensive Care Medicine and Clinical Director for Research & Development, Barts Health NHS Trust, London, E1 1BB, UK r.pearse@qmul.ac.uk

6. A. Professor of HIV Medicine, Blizard Institute, Queen Mary University of London, E1 2AT, UK
B. Clinical lead for HIV and HIV/Hep C Research, Barts Health NHS Trust, London, E1 1BB, UK
c.m.orkin@qmul.ac.uk

7. A. Senior Clinical Lecturer in Intensive Care Medicine, William Harvey Research Institute, Queen Mary University of London, EC1M 6BQ, UK
B. Consultant in Intensive Care and Renal Medicine, Barts Health NHS Trust, London, E1 1BB, UK
j.prowle@qmul.ac.uk

Corresponding author:
John Prowle, MD
Adult Critical Care Unit,
The Royal London Hospital,
London E1 1BB
Email: j.prowle@qmul.ac.uk
Tel: +44 20 3594 40346

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What is known
Asian and Black ethnicity patients are at increased risk of COVID-19 infection, hospital admission, intensive care admission and death from COVID-19 infection, compared with White ethnicity patients. This appears to be only partially attributable to social deprivation and comorbidity. There remains a need to explore this association in more detail, adjusting for broader clinical and laboratory prognostic factors.

What this study adds
Ethnicity is a predictor of poor outcomes for COVID-19 patients at and beyond, 30 days. Those of Asian and Black ethnicities were consistently found to have an increased risk of 30 and 90 day mortality and an increased risk of requiring mechanical ventilation as compared to those of White ethnicity.

Age, sex, deprivation, smoking status, BMI, comorbidities and frailty do not fully account for this association.

The peak CRP and D-dimer levels in those of Black ethnicity were significantly higher than those of other ethnicities suggesting that these biological differences may accompany greater disease severity and increased risk of adverse outcomes.

Abstract

Objective
To describe outcomes within different ethnic groups of a cohort of hospitalised patients with confirmed COVID-19 infection. To quantify and describe the impact of a number of prognostic factors, including frailty and inflammatory markers.

Setting
Five acute NHS Hospitals in east London.

Design
Prospectively defined observational study using registry data.

Participants
1737 patients aged 16 years or over admitted to hospital with confirmed COVID-19 infection between 1st March and 13th May 2020.

Main outcome measures
The primary outcome was 30-day mortality from time of first hospital admission with COVID-19 diagnosis during or prior to admission. Secondary outcomes were 90-day mortality, intensive care unit (ICU) admission, ICU and hospital length of stay, and type and duration of organ support. Multivariable survival analyses were adjusted for potential confounders.

Results
1737 were included in our analysis of whom 511 had died by day 30 (29%). 538 (31%) were from Asian, 340 (20%) Black and 707 (40%) White backgrounds. Compared to White patients, those from minority ethnic backgrounds were younger, with differing comorbidity profiles and less frailty. Asian and Black patients were more likely to be admitted to ICU and to receive invasive ventilation (Odds ratio 1·54, [1·06-2·23]; p=0·023 and 1·80 [1·20-2·71]; p=0·005, respectively). After adjustment for age and sex, patients from Asian (Hazard ratio (HR) 1·49 [1·19-1·86]; p<0·001) and Black (HR 1·30 [1·02-1·65]; p=0·036) backgrounds were more likely to die. These findings persisted across a range of risk-factor adjusted analyses accounting for major comorbidities, obesity, smoking, frailty, and ABO blood group.

Conclusions
Patients from Asian and Black backgrounds had higher mortality from COVID-19 infection despite controlling for all previously identified confounders and frailty. Higher rates of invasive ventilation indicate greater acute disease severity. Our analyses suggest that patients of Asian and Black backgrounds suffered disproportionate rates of premature death from COVID-19.

Strengths and limitations of this study

- This study is both one of the largest and most detailed of studies exploring COVID-19 outcomes in BAME populations so far reported. In contrast to many previous studies, we were able to address the contributions of socio-economic deprivation, comorbid disease, pre-morbid function, lifestyle and demographic factors to ethnic disparities in COVID-19 outcomes, including ICU interventions and inclusion of measures of frailty.
- Importantly, this study was conducted in a single region where COVID-19 has had significant impact and thus is not confounded by differences in incidence of COVID-19 disease across the UK, regional concentration of minority ethnic groups and regional differences in the time-course of the epidemic.
- In addition, we employed a pre-specified statistical analysis plan and performed multiple sensitivity analyses to test the robustness of our findings.
- SARS-CoV-2 testing has an appreciable false negative rate and suspected, but not proven, cases are an important group. In line with the vast majority of published COVID-19 analyses, we only included proven COVID-19 cases. However, suspected diagnoses should be considered in future studies, particularly those occurring outside of hospitals, where not all clinical diagnoses may have been tested.
- Like many datasets, our ethnic categorisations were aggregated and did not reflect the vast heterogeneity within ethnic categories (such as Bangladeshi, Pakistani, Black African or Black Caribbean). Despite its size, our study lacked the power to assess a more detailed ethnicity breakdown.

Introduction

The novel *Severe Acute Respiratory Syndrome Coronavirus*-2 (SARS-CoV-2) which manifests as coronavirus disease 2019 (COVID-19) has led to a global pandemic(1). Older age, male sex, obesity and pre-existing health conditions such as diabetes and hypertension have all been identified as risk factors for poor outcomes(2-4). A disproportionate impact of disease severity and death on people from Black, Asian and minority ethnic (BAME) backgrounds has been reported, though not consistently. The UK Intensive Care National Audit and Research Centre (ICNARC) noted that whilst BAME groups only make up 14% of the UK population, they comprised 33% of COVID-19 patients on intensive care units(5). The degree of this excess risk also appears to differ across, and within, these heterogeneous ethnic groups. In the UK, recent analyses of data from the Office of National Statistics and NHS England described 2.5-4.3 fold greater COVID-19 mortality rates, compared to White groups, across a range of Black and South Asian ethnic groups(6). Whether this adverse association is driven by underlying comorbid disease, socio-economic inequality, genetic factors or a complex interplay of them all is unclear(7). Current data are limited in either number of COVID-19 patients, ethnic diversity or event rates with limited adjustment for known risk factors and potential predictors(8-12). There is an urgent need for the detailed characterisation of ethnic differences in COVID-19 outcomes and associated risk factors, within diverse populations, to inform practice and policy. Identifying and responding to these ethnic inequalities will be key to mitigating the disproportionate impact of COVID-19 on BAME patients.

Barts Health NHS Trust is the largest NHS trust in the UK, comprising six hospitals; The Royal London Hospital, Newham General Hospital, Whipps Cross Hospital, Mile End Hospital (Non-acute), St Bartholomew's Hospital and the London NHS Nightingale Hospital, a purposely built COVID-19 hospital. The hospitals serve the ethnically diverse and socially deprived communities of over 2.6 million people in east London including the London Borough of Newham which experienced 144.3 COVID-19 related deaths per 100,000 population(13), the highest mortality in the UK and Tower Hamlets which has the largest Bangladeshi population in England(14). This large, regional dataset afforded extensive analyses of COVID-19 patients of a higher acuity than other studies. We aimed to examine the demographic, socio-economic, behavioural, biochemical and clinical risk factors associated with outcomes within different ethnic groups of hospitalised COVID-19 patients, using multivariable survival analyses.

Methods

Study population

We considered all patients with confirmed SARS-CoV-2 infection and admitted to the five acute hospitals within Barts Health NHS Trust between 1st January and 13th May 2020. Diagnosis was made using one or more real-time RT-PCR. Those under 16 years were excluded. The first emergency admission encompassing the first positive SARS-CoV-2 test, or the first emergency admission within two weeks of positive outpatient testing was defined as the index admission, community diagnoses without an associated emergency hospital admission were excluded. Patients with unknown or undisclosed ethnicity status were collected for comparison but were not included in our primary ethnicity analysis.

Data collection

Clinical and demographic data, blood results and coding data from current and prior clinical encounters, were collated from the Barts Health Cerner Millennium Electronic Medical Record (EMR) data warehouse and locally held ICNARC databases by members of the direct clinical care team. Mortality data was available to 20th May 2020.

Definition of key variables

Ethnicity was defined using the NHS ethnic category codes and based on five high-level groups: White, Asian or Asian British, Black or Black British, Mixed and Other; to preserve statistical power the Mixed and Other categories were merged. Relative measures of socioeconomic deprivation were assessed using the English Indices of Deprivation 2020 by matching patient postcode to national index of multiple deprivation (IMD) quintiles using the Office of National Statistics Postcode Directory(15, 16). Baseline comorbid diseases and Hospital Frailty Risk Score (HFRS) were identified by mapping to ICD-10 coding(17). Body mass index (BMI) was calculated by height and weight measurements taken at or during the immediately preceding admission episode. Rockwood Clinical Frailty Scoring (RFS) was assessed by the admitting medical team and recorded in the EMR(18). Secondary haemophagocytic lymphohistiocytosis (sHLH) risk score was calculated from peak values of blood results(19). Full definitions are detailed in supplementary materials. National early warning score (NEWS) was recorded in the emergency room and general wards by clinical teams in the EMR and is presented as the total score from 6 physiological parameters(20).

Outcomes

The primary outcome was 30-day mortality from time of index COVID-19 hospital admission. Secondary endpoints were 90-day mortality, ICU admission, ICU length of stay, duration of organ support on ICU, need for mechanical ventilation, hospital length of stay, and discharge destination if discharged alive from hospital.

Statistical analyses

A prospective statistical analysis plan was developed(21). Baseline characteristics are presented as mean and standard deviation, median and interquartile range, or number and percentage, as appropriate. We compared proportions using Pearson's Chi-square test or Fisher's exact test and continuous variables using 2-sample t-test or Wilcoxon rank-sum test, as appropriate. Time-to-event analysis was undertaken with follow-up censored at 30 days, survivors with less than 30 days follow-up were censored at time of maximal follow-up. A Cox proportional hazards model was used to assess survival adjusted for age and sex. A further multivariable Cox model was developed to assess the effect of pre-defined risk factors described as associated with adverse outcomes in COVID19: IMD quintile, smoking status, body mass index, diabetes, hypertension, and chronic kidney disease (CKD). The proportional-hazard assumption was assessed by inspection of scaled Schoenfeld residual plots and investigated by stratification(22). Logistic regression modelling of ethnicity on ICU treatment using mechanical ventilation was carried out. Effect measures are presented as hazard ratios (HR) or odds ratios (OR) with 95% confidence intervals (CI). All analyses were performed using R version 3.6.3 (R Core Team 2020).

Sensitivity analyses

To assess the effect of including patients with incomplete clinical data, missing data for baseline risk variables included in the multivariable Cox model was imputed using Multivariate Imputation by Chained Equations(23). Additional multivariable models were also carried out using aggregate Charlson comorbidity index (CCI) as a measure of total comorbid disease burden, and HFRS or RFS collected at hospital admission and ABO blood group. Longer-term survival to 90 days was assessed using Cox proportional hazards modelling adjusted for age and sex.

Results

A total of 1996 patients, aged 16 years and older, with a confirmed SARS-CoV-2 test result with an acute Barts Health admission on or before 13th May 2020 were included in this study [Figure S1]. The recruitment window encompassed the peak time period of COVID-19 diagnoses [Figure S2]. The majority of patients were classified as being in the two most deprived socio-economic quintiles in England. The ethnic distribution was White (n=703, 35·2%), Asian or Asian British (n=538, 27·0%), Black or Black British (n=340, 17·0%), Mixed and Other (n=156, 7·8%) and unknown or undisclosed (n=259, 13·0%).

Population Characteristics

Baseline characteristics, interventions and outcomes across ethnic groups are shown in Table 1. Black and Asian ethnicity patients were significantly younger with a median age of 59 years (Asian) and 64 years (Black), compared to 73 years in the White group (p<0·001). Comorbidity data was available in 1700 (85.2%) of patients.

Burden of comorbid disease varied between ethnic groups in prevalence, type and age-distribution. Overall distribution of COVID risk factors varied with age and ethnicity with diabetes and CKD more prevalent at an earlier age in Asian and Black patients and frailty and dementia more prevalent in older White patients [Figure 1].

Around one in four patients developed early acute kidney injury (AKI) within seven days of hospital admission, rates of AKI were highest in the Black group (34·7%). Patients in the Black group had higher levels of inflammation CRP (median CRP 181·5 mg/L) and fibrinolysis (median D-dimer 2·5 mg/L) compared to other ethnicities. As a measure of extent of early physiological derangement UK National Early Warning Score (NEWS) was available in 1443 patients, in comparison to White patients first NEWS was modestly higher in Asian patients (mean 4.2 vs. 3.6), p=0.001, but not in Black patients (mean 3.7 vs 3.6).

Age and sex adjusted 30-day mortality

We included 1737 Asian, Black and White patients in the primary outcome analysis. Total mortality to 20th May 2020 was 28·7% (n=573). Based on the raw data, a greater proportion of White patients died (32·7%) compared to Asian (21·1%) and Black (29·7%) patients. The majority of deaths (93·7%) occurred within 30 days of hospital admission. However, after adjustment for the between-group differences in age and sex, patients from Asian and Black ethnic groups were at significantly higher risk of death within 30 days compared to White patients (Asian ethnicity (HR 1·49, CI 1·19-1·86, p<0·001); Black patients (HR 1·30, CI 1·02-1·63, p=0·036). No association was observed in the smaller Mixed and Other Ethnicity group (HR1·08, CI 0·75-1·57, p=0·682) [Table 2]. There was some evidence of non-proportionality for the association between ethnicity and risk of death over time [Figure S16], consequently these HRs should be interpreted as a weighted average over the 30-day follow up period. To investigate change in risk over time we developed an ethnicity-stratified Cox-model, this supported the findings of the unstratified model, but suggested that Black ethnicity might be associated with a higher early rate of death [Figure S17].

Multivariable survival modelling

After inclusion of IMD quintile, smoking history, BMI ≥30 kg/m^2, diabetes, hypertension, and CKD in a multivariable survival analysis, the association with increased rate of death persisted in Asian patients (HR 1·48, CI 1·09-2·01, p=0·011; n=1006). In Black patients, the magnitude of the mortality trend was unchanged, however was outside the limits of standard statistical significance (HR 1·32, CI 0·96-1·84, p=0·090; n=1006), potentially due to the smaller sample size. In this model older age, male sex, smoking, BMI ≥30 kg/m2 and CKD were statistically associated with risk of death [Table 3] and there was no statistical evidence that ethnicity violated the proportional hazards assumption. The associations were broadly unchanged when the model was re-fitted after multiple imputation of missing values [Table S5].

Sensitivity analyses for further multivariable survival models were developed to examine the influence of total comorbidity burden, as assessed by CCI [Table S7], and measures of frailty, the RCFS or HFRS [Tables S8, S9] as well as ABO blood group. In all these analyses the association between Black and Asian ethnicity and 30-day mortality remained significant. Adjusting for RCFS raised the odds of 30-day mortality to a HR of 1·98 (CI 1·37-2·86; p<0.001) in Asian groups and to a HR of 1·67 (CI 1·14-2·45; p=0.009) in Black groups, with similar effect size in analysis adjusted for the HFRS [Tables S8, S9]. After inclusion of ABO blood grouping in and age and sex adjusted multivariable model risks of death in Asian, Black, and Mixed and Other ethnic groups was increased [Table S6]. Asian ethnicity also continued to be associated with greater risks of death through to 90 days follow-up (HR 1·46, CI 1·18-1·81, p<0·001; n=1737) [Table S10].

Critical Care related outcomes

In the White group, 11·0% of patients were admitted to ICU compared to 20·1% of the Asian group and 18·5% of the Black group (p<0.001). In those admitted to ICU, rates of mechanical ventilation requiring intubation did not differ significantly by ethnicity at 76·6% in the White group, 72·2% in the Asian group and 79·4% in the Black group. Similarly, while rates of ICU admission differed significantly between ethnic groups, time from hospital to ICU admission and length of ICU stay did not. Across the entire hospitalised cohort Asian (OR 1·54, CI 1·06-2·23, p=0·023; n=1737) and Black (OR 1·80, CI 1·20-2·71, p=0·005; n=1737) ethnicities were associated with increased age and sex adjusted-risk of receiving invasive mechanical ventilation in ICU [Table S4]. There was a trend toward increased renal replacement therapy use in Black patients (41.3%) admitted to ICU compared to 20-25% across other ethnic groups (p=0.09).

Discussion

We report on treatment and outcomes in COVID-19 patients hospitalised in East London throughout the peak of the UK pandemic, a population with the UK's highest COVID-19 mortality. To our knowledge this is one of the largest UK hospital COVID-19 cohorts reported, and certainly the most diverse, with only 35.2% of 1996 patients identified as White ethnicity. We found those of Asian ethnicity to be at the highest risk of death within 30 days (HR 1·49, CI 1·19-1·86, p<0·001), a finding that persisted at 90 days. Risk of death in Black patients was also greater than those of White ethnicity (HR 1·30, CI 1·02-1·63, p=0·036). This disparity extended to need for ICU care with Asian and Black patients experiencing a 50-80% increased risk of receiving mechanical ventilation in ICU compared to White patients of a similar age.

Strengths and Limitations

We believe this study is both one of the largest and most detailed of studies exploring COVID-19 outcomes in BAME populations so far reported. In contrast to many previous studies examining ethnicity and COVID-19 outcomes we were able to address the contributions of socio-economic deprivation, comorbid disease, pre-morbid function, lifestyle and demographic factors to ethnic disparities in COVID-19 outcomes, including ICU interventions. Our analysis was strengthened by the inclusion of measures of frailty which is a critical determinant of outcomes in acute disease as well as a potential driver of clinician decision-making. It should be acknowledged, however, that frailty has social and biological dimensions and measures have not been extensively validated in BAME groups.

Importantly, this study was conducted in a single region where COVID-19 has had significant impact and thus is not confounded by differences in incidence of COVID-19 disease across the UK, regional concentration of minority ethnic groups and regional differences in the time-course of the epidemic. In addition, we employed a pre-specified statistical analysis plan and performed multiple sensitivity analyses to test the robustness of our findings.

Limitations in our analyses must also be considered. Importantly, SARS-CoV-2 testing has an appreciable false negative rate and suspected, but not proven, cases are an important group. Nevertheless, given that clinical suspicion varied both between cases and across the time-course of the epidemic with coding of suspected cases being inconsistent, in line with the vast majority of published COVID-19 analyses, we only included proven COVID-19 cases. Testing was available for all hospitalised patients with suspected COVID-19 disease, so availability of testing was not a bias. However, suspected diagnoses should be considered in future studies, particularly those occurring outside of hospitals, where not all clinical diagnoses may have been tested.

Similar to many hospital datasets there were missing data for a proportion of co-variates(8, 9), however 85% of patients had coding data for assessment of comorbidity and 63% measured height and weight data, providing a large sample with detailed data for analysis. We also imputed missing data and performed sensitivity analyses on our multivariable comorbidity models. This reinforced the observed ethnic differences, providing further confidence that our findings were not affected by missing data.

Like many datasets, our ethnic categorisations were aggregated and did not reflect the vast heterogeneity within ethnic categories (such as Bangladeshi, Pakistani, Black African or Black Caribbean). Indeed, the descriptive term "BAME" itself is particularly crude and we recognise its limitation. Despite its size, our study lacked the power to assess a more detailed ethnicity breakdown. In addition, our observations in those of Asian ethnicity are likely skewed by our large Bangladeshi community, which has specific socio-economic and healthcare inequalities. It is therefore important that, suitably powered, analyses are conducted to expose differences between sub-ethnic categories. Similarly, whilst we have explored socio-economic factors, our analysis does not allow us to contextualise a number of potential socio-spatial factors including household composition, environmental factors and occupation. These should be considered in future research.

Comparison with other studies

Our findings differ from predominant reports in the UK and US in which Black ethnicity has been consistently associated with greater COVID-related mortality(6, 24). Preliminary analyses of the UK ICNARC report on COVID-19 in critical care highlighted Black ethnicity with the highest likelihood of being admitted to intensive care compared to a matched population (10.7% versus 6.5%)(25). Similarly, in a large UK primary care linked cohort, Black patients were also to found to be at highest risk of COVID-related death(9). In a US study, the composite relative risk of COVID-related death compared to White ethnicity was 3.57 in Black populations, and 1.88 for Latinos(24). Our findings suggest specific South Asian communities may have at least the same or higher risk in COVID-19 as those of Black background. This may reflect characteristics of the large South Asian, and specifically Bangladeshi, community in East London, poorly represented in other studies. Recently the *ISARIC CCP-UK* investigators have described association of ethnicity and outcome in a very large cohort of UK patients, finding Asian, but not Black background was associated with increased risk of death in confirmed or suspected COVID-19(26). While this study documented up to 40% of UK COVID cases, it represented a selection from the total COVID population from across the UK, and, at least in terms of ICU cases, ethnic minorities were significantly under-represented compared to the English ICU COVID population. In contrast while smaller, this study focused on an unbiased population comprising all hospitalised patients in a single geographical area with a much higher level of ethnic diversity. Consequently, we feel our analysis complements ISARIC CCP-UK and provides greater clinical detail in a regionally homogenous population.

Potential confounding associations with risk of death in COVID-19

Older age has been significantly associated with increased COVID-19 mortality across a range of studies(2-4). In our cohort, patients from Asian and Black backgrounds were strikingly younger than White patients. However, despite the expected protective factor of younger age, when this was accounted for, those from Black and Asian backgrounds were more likely to die. The prevalence of comorbid disease has been well described as a risk factor for COVID-19 disease and death(3, 4). We found different ethnic groups had differing age-distribution of baseline comorbidities such as hypertension, diabetes, chronic obstructive pulmonary disease and dementia. Despite accounting for these and other described predictors of poor outcomes, increased risk of death in Asian and Black populations was not attenuated, suggesting comorbidities are not the sole drivers of ethnicity-associated risk.

ABO blood group has recently been suggested to affect the risk of symptomatic COVID-19 and need for respiratory support with supplemental oxygen(12, 27). In these analyses blood group O was associated with less disease acquisition than group A. As there are well-described differences in blood group distribution with ethnicity (in particular, prevalence of blood group B in Asian and to a lesser extent Black populations), in a post-hoc analysis we assessed the association between ABO group and risk of death in 875 patients with blood group data. In contrast to studies focused on risk of COVID-19 acquisition in our cohort of hospitalised COVID diagnoses, blood group O was associated with higher risk of death and blood group B the lowest. Accordingly, when we included ABO blood group in a multivariable survival analysis with age, sex the association between Black and Asian background and increased risk of death was not attenuated but magnified. This suggests ethnic imbalances in blood group distribution did not explain the mortality associations observed in our population.

Patients identified as frail have been predicted to have worse COVID-19 related health outcomes(28), and lower likelihood of benefiting from complex acute interventions, including critical care. In this study White patients, in addition to being notably older than other ethnicities, had higher degrees of frailty. Accounting for measures of frailty magnified the association seen between Asian and Black ethnicity and death. This suggests that whilst in White patients COVID-19 related death may have occurred in already frail and functionally vulnerable patients, in both Asian and Black patients, COVID-19 related deaths are likely to be occurring prematurely, in younger, fitter individuals with less functional vulnerability.

In our cohort, all ethnic groups experienced high levels of deprivation, however, worse deprivation was not associated with higher likelihood of mortality, suggesting ethnicity may affect outcomes independent of purely geographical and socio-economic factors(29).

We found evidence for worse disease severity in Black and Asian groups as evidenced by higher rates of ICU admission and higher rates of AKI, and high levels of D-dimers and CRP in Black patients. High CRP and D-dimer levels have been identified as important inflammatory markers which strongly correlate with COVID-19 disease severity and prognosis(30). Our data suggest potential biological differences in host-response to COVID-19 may occur between ethnicities, however, causative associations in determining COVID-19-related mortality have not been demonstrated.

Finally, although COVID-19 has cast the effects of ethnic inequalities on health outcomes into sharp focus, these inequalities are not new. Health inequalities within and between ethnic minority groups are widely documented and the effects of structural racism are transmitted across generations(31). The risk factors already discussed such comorbidity and obesity are speculated to intersect and be inextricably linked with wider social determinants such as poor living conditions, key worker roles and language barriers which impede the adoption of preventative measures(29, 32, 33). Some researchers have postulated that ethnic inequalities may be associated with decreased symptom recognition and poor engagement with health services(34). However, while frequency of ICU admission, AKI and need for mechanical ventilation suggests more severe peak-disease in minority ethnic groups, time to ICU admission did not differ and differences in first total NEWS were at most modest, suggesting against a large effect from delayed presentation.

Conclusion

In this analysis of a large, ethnically diverse and socio-economically challenged cohort, hospitalised patients of Asian and Black background with COVID-19 were at increased risk of premature death, independent of frailty, comorbidities and social deprivation. Failure to robustly respond to the ethnic disparities so conspicuously unmasked during the COVID-19 pandemic can only further entrench and inflict them on future generations.

Data sharing agreement

The statistical analysis plan can be accessed online. The authors will be happy to consider additional analyses of the anonymised dataset on request. The need for stringent measures to prevent re-identification of individuals within a discrete geographical location and limited time-period however preclude sharing of patient level dataset in a GDPR compliant form.

Author contribution

V Apea developed the study concept, designed the study, wrote the study protocol, submitted the ethics application, provided critical review of the findings and wrote the manuscript. Y Wan wrote the statistical analysis plan, performed data extraction, performed statistical analysis, provided critical review of the findings and wrote the manuscript. R Dhairyawan developed the study concept, designed the study, provided critical review of the findings and wrote the manuscript. Z Puthucheary provided critical review of the findings and wrote the manuscript. R Pearse developed the study concept, designed the study, provided critical review of the findings and wrote the manuscript. C Orkin developed the study concept, designed the study, provided critical review of the findings and wrote the manuscript. J Prowle developed the study concept, designed the study, wrote the study protocol, submitted the ethics application, performed data extraction, performed statistical analysis, provided critical review of the findings and wrote the manuscript. All authors approved the final version of the manuscript. The data was collated and analysed on behalf of all clinicians at Barts Health.

Study Concept and Design	VJA CMO RD JRP RMP
Ethics application and Approvals	VJA JRP
Study protocol and analysis plan	VJA YIW JRP
Data Extraction	YIW JRP
Data Analysis	YIW JRP
Critical review of finding	All authors
Manuscript writing	VJA CMO YIW RD ZAP RP JRP
Review of final submission	All authors

Public and Patient Involvement statement

COVID-19 has presented unique challenges and warranted a unique response in research. This protocol has been swiftly developed in response to concerning data suggesting poorer outcomes of patients with confirmed COVID-19 from a BAME background. This data has led the general public, via social media and community influencers, to call for governmental and health bodies to urgently review patient outcomes to explore this emerging inequality and respond appropriately to mitigate further deaths and inequity. Whilst no direct public and patient involvement has taken place, the research team believe the study in line with current public and patient mandate.

Ethics approval
This study was approved by HRA and Yorkshire & The Humber - Bradford Leeds Research Ethics Committee (Ethics reference **20/YH/0159**). The study was sponsored by Barts Health NHS Trust.

Transparency declaration
J Prowle (the manuscript's guarantor) affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned and registered have been explained.

Role of the funding source
No external funding. The corresponding author had full access to all the data and had final responsibility for the decision to submit for publication**.**

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Conflict of Interest
All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and declare: no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

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Tables

Table 1. Study population baseline characteristics stratified by ethnic group, n (%) unless otherwise stated. Total n=1996 unless otherwise stated. P values based on Chi-square (for categorical) or Kruskal-Wallis test (for continuous). SD: standard deviation, IQR: interquartile range, IMD: index of multiple deprivation, BMI: body mass index, TIA: transient ischaemic accident, HTN: hypertension, CKD: chronic kidney disease, sHLH: secondary haemophagocytic lymphohistiocytosis (without known underlying immunosuppression and bone marrow aspirate data), CRP: C-reactive protein, NEWS: national early warning score, ICU: intensive care unit, RRT: renal replacement therapy.

	Stratified by ethnic group					
	Asian or Asian British	**Black or Black British**	**Mixed and Other Ethnic Groups**	**White**	**Unknown and Undisclosed**	p value
n	538	340	156	703	259	
Age (years) Mean (SD)	57·8 (18·5)	64·2 (16·9)	59·5 (17·2)	69·4 (17·7)	59·8 (16·5)	<0·001
Age (years) Median (IQR)	59·0 (44·0-71·0)	64·0 (53·0-79·0)	59·0 (47·8-72·3)	73·0 (58·0-84·0)	61·0 (50·0-71·5)	<0·001
Male	332 (61·7)	193 (56·8)	103 (66·0)	404 (57·5)	178 (68·7)	0·01
IMD quintile [n=1980]						<0·001
1 (most deprived)	139 (26·0)	124 (36·7)	50 (32·9)	183 (26·2)	66 (25·7)	
2	291 (54·5)	165 (48·8)	72 (47·4)	269 (38·5)	124 (48·2)	
3	49 (9·2)	34 (10·1)	20 (13·2)	99 (14·2)	44 (17·1)	
4	35 (6·6)	9 (2·7)	7 (4·6)	86 (12·3)	18 (7·0)	
5 (least deprived)	20 (3·7)	6 (1·8)	3 (2·0)	62 (8·9)	5 (1·9)	
Smoking [n=1700]	30 (6·6)	21 (7·1)	10 (8·3)	91 (14·8)	21 (9·8)	<0·001
BMI [n=1248]						
Median (IQR)	26·9 (24·1-31·1)	28·2 (24·6-31·8)	25·9 (23·1-29·0)	26·3 (22·5-31·6)	26·3 (22·5-30·8)	0·04
By category						0·04
<18·5 kg/m^2	9 (2·8)	8 (3·6)	1 (1·3)	34 (6·9)	11 (8·5)	
18·5 - <25 kg/m^2	101 (31·2)	57 (25·3)	31 (40·3)	160 (32·5)	43 (33·1)	
25 - <30 kg/m^2	114 (35·2)	83 (36·9)	27 (35·1)	145 (29·5)	40 (30·8)	
30 - <40 kg/m^2	87 (26·9)	65 (28·9)	17 (22·1)	126 (25·6)	28 (21·5)	
≥40 kg/m^2	13 (4·0)	12 (5·3)	1 (1·3)	27 (5·5)	8 (6·2)	
Co-morbidity [n=1700]						
Obesity	108 (23·6)	82 (27·9)	18 (14·9)	161 (26·2)	40 (18·7)	0·01
Ischaemic heart disease	102 (22·3)	62 (21·1)	12 (9·9)	149 (24·3)	21 (9·8)	<0·001
Myocardial infarction	55 (12·0)	23 (7·8)	6 (5·0)	83 (13·5)	14 (6·5)	0·002
Congestive heart failure	67 (14·7)	54 (18·4)	8 (6·6)	114 (18·6)	17 (7·9)	<0·001

Peripheral vascular disease	33 (7·2)	35 (11·9)	7 (5·8)	67 (10·9)	16 (7·5)	0·06
Cerebral vascular accident or TIA	54 (11·8)	54 (18·4)	11 (9·1)	157 (25·6)	16 (7·5)	<0·001
Dementia	25 (5·5)	27 (9·2)	5 (4·1)	103 (16·8)	7 (3·3)	<0·001
Chronic obstructive pulmonary disease	119 (26·0)	45 (15·3)	18 (14·9)	181 (29·5)	34 (15·9)	<0·001
Diabetes	220 (48·1)	157 (53·4)	49 (40·5)	179 (29·2)	59 (27·6)	<0·001
HTN	261 (57·1)	212 (72·1)	64 (52·9)	376 (61·2)	96 (44·9)	<0·001
Moderate to severe CKD	92 (20·1)	93 (31·6)	16 (13·2)	145 (23·6)	17 (7·9)	<0·001
End-stage renal disease	39 (8·5)	36 (12·2)	7 (5·8)	27 (4·4)	4 (1·9)	<0·001
Liver disease	49 (9·1)	24 (7·1)	12 (7·7)	58 (8·3)	12 (4·6)	0·25
Cancer	30 (6·6)	26 (8·8)	8 (6·6)	68 (11·1)	12 (5·6)	0·04
Cancer with metastases	8 (1·8)	5 (1·7)	1 (0·8)	22 (3·6)	6 (2·8)	0·18
Acquired immunodeficiency syndrome	0 (0·0)	5 (1·7)	0 (0·0)	1 (0·2)	0 (0·0)	0·001
Charlson comorbidity index [n=1700]						<0·001
0	131 (28·7)	66 (22·4)	42 (34·7)	143 (23·3)	91 (42·5)	
1-2	178 (38·9)	100 (34·0)	50 (41·3)	203 (33·1)	88 (41·1)	
3-4	70 (15·3)	52 (17·7)	16 (13·2)	146 (23·8)	20 (9·3)	
≥5	78 (17·1)	76 (25·9)	13 (10·7)	122 (19·9)	15 (7·0)	
Rockwood frailty Score [n=831]						<0·001
1-2 (very fit, well)	31 (15·9)	6 (4·3)	7 (14·9)	36 (9·7)	15 (18·8)	
3-4 (managing well, vulnerable)	87 (44·6)	51 (36·7)	17 (36·2)	118 (31·9)	32 (40·0)	
5-6 (mildly to severely frail)	65 (33·3)	73 (52·5)	18 (38·3)	174 (47·0)	29 (36·2)	
8-9 (very severely frail, terminally ill)	12 (6·2)	9 (6·5)	5 (10·6)	42 (11·4)	4 (5·0)	
Hospital frailty Risk Score [n=1700]						<0·001
<5 (low risk)	240 (52·5)	123 (41·8)	66 (54·5)	197 (32·1)	117 (54·7)	
5-15 (intermediate risk)	132 (28·9)	87 (29·6)	38 (31·4)	150 (24·4)	73 (34·1)	
≥15 (high risk)	85 (18·6)	84 (28·6)	17 (14·0)	267 (43·5)	24 (11·2)	
Baseline eGFR ml/min/1·72m² [n=1525]						
Median (IQR)	72·8 (53·3-92·7)	56·4 (36·2-80·2)	75·6 (54·2-91·4)	64·1 (46·2-82·0)	78·2 (61·5-88·7)	<0·001
eGFR <60	130 (29·6)	135 (48·6)	26 (26·0)	239 (40·5)	29 (24·6)	<0·001
Acute kidney injury first 7 days [n=1673]	98 (22·2)	101 (34·7)	32 (24·6)	151 (24·4)	48 (25·0)	0·003
Blood results during admission						

Highest creatinine µmol/L [n=1691]						<0·001
Median (IQR)	91·0 (72·0-157·0)	119·0 (80·0-260·0)	88·0 (71·8-120·3)	98·0 (76·0-147·0)	94·0 (75·0-132·0)	
Highest CRP [n=1761]						<0·001
Median (IQR)	146·0 (72·0-287·8)	181·5 (99·3-289·8)	132·0 (66·0-226·0)	136·0 (68·0-237·0)	156·0 (75·5-272·5)	
Highest D-dimer mg/L [n=968]						<0·001
Median (IQR)	1·0 (0·5-3·5)	2·5 (0·9-10·3)	1·1 (0·5-2·7)	1·4 (0·6-3·4)	1·5 (0·7-6·3)	
Highest sHLH score [n=1881] Mean (SD)	31·1 (27·1)	30·0 (27·9)	27·6 (28·3)	26·4 (24·8)	32·1 (26·7)	0·01
Blood Group [n=875]						<0·001
A	67 (28·4)	37 (23·3)	15 (35·7)	150 (42·1)	36 (43·9)	
AB	14 (5·9)	11 (6·9)	0 (0·0)	12 (3·4)	6 (7·3)	
B	78 (33·1)	37 (23·3)	13 (31·0)	32 (9·0)	8 (9·8)	
O	77 (32·6)	74 (46·5)	14 (33·3)	162 (45·5)	32 (39·0)	
NEWS (first available) [n=1443] Mean (SD)	4·2 (2·6)	3·7 (2·2)	4·0 (2·3)	3·6 (2·5)	3·8 (2·6)	0·001
Intensive care unit (ICU)						
ICU admission	108 (20·1)	63 (18·5)	28 (17·9)	77 (11·0)	85 (32·8)	<0·001
Days in hospital before ICU Mean (SD)	2·3 (5·2)	2·9 (5·1)	1·1 (1·8)	2·3 (11·4)	1·8 (4·2)	0·75
ICU length of stay Median (IQR)	8·0 (3·0-15·2)	8·1 (3·5-14·1)	8·5 (5·0-13·1)	8·0 (3·9-12·0)	10·0 (6·0-16·0)	0·30
Mechanical ventilation within ICU admission	78 (72·2)	50 (79·4)	23 (82·1)	59 (76·6)	71 (83·5)	0·40
RRT within ICU admission	28 (25·9)	26 (41·3)	7 (25·0)	20 (26·0)	18 (21·2)	0·09
Days on organ support						
Advanced respiratory Mean (SD)	11·0 (10·8)	9·4 (8·8)	8·2 (7·1)	7·8 (7·8)	10·3 (8·0)	0·14
Total respiratory Mean (SD)	13·1 (10·4)	11·9 (8·9)	9·8 (7·0)	9·6 (7·7)	11·9 (7·6)	0·08
Cardiovascular system Mean (SD)	13·4 (10·9)	11·5 (8·6)	9·9 (7·2)	9·8 (8·3)	11·8 (7·5)	0·07
Renal Mean (SD)	2·4 (5·5)	4·4 (6·6)	2·1 (4·7)	2·7 (5·7)	1·5 (3·8)	0·03
Total number of organ systems						0·15
0	1 (0·9)	0 (0·0)	0 (0·0)	1 (1·3)	1 (1·2)	
1	3 (2·8)	4 (6·3)	1 (3·6)	5 (6·5)	0 (0·0)	
2	76 (70·4)	33 (52·4)	20 (71·4)	52 (67·5)	66 (77·6)	
3	28 (25·9)	26 (41·3)	7 (25·0)	19 (24·7)	18 (21·2)	
Outcomes						
Died	146 (27·1)	101 (29·7)	34 (21·8)	230 (32·7)	62 (23·9)	0·01

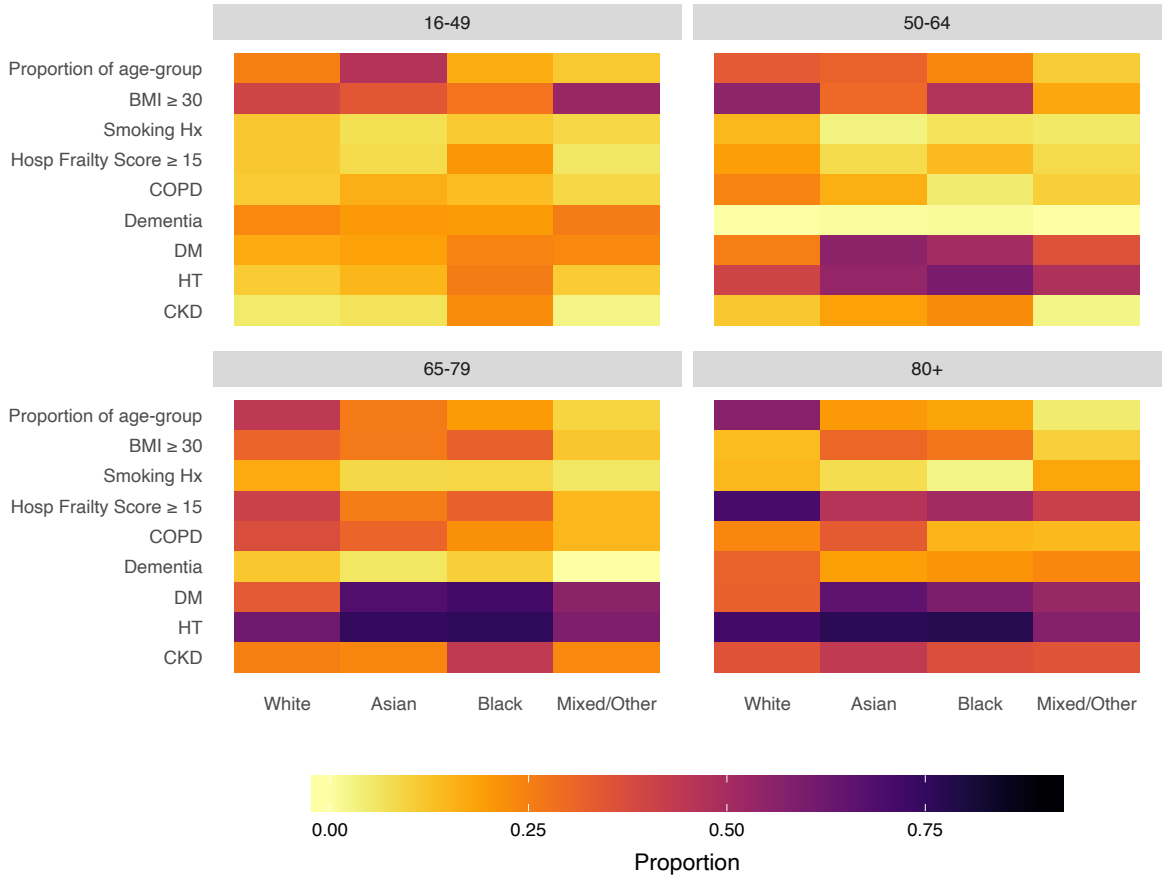
Days to death Mean (SD)	9·7 (10·0)	9·1 (11·0)	11·0 (9·8)	12·9 (13·6)	12·7 (10·0)	0·02
Days to death Median (IQR)	6·0 (3·0-12·0)	5·0 (3·0-11·0)	10·5 (4·3-14·0)	9·0 (4·0-16·0)	10 (6·0-17·0)	<0·001
Died within 30 days	138 (25·7)	97 (28·5)	33 (21·2)	210 (29·9)	58 (22·4)	0·05
Died within 90 days	146 (27·1)	101 (29·7)	34 (21·8)	229 (32·6)	62 (23·9)	0·01
Still in hospital	7 (1·3)	6 (1·8)	3 (1·9)	6 (0·9)	5 (1·9)	0·60
Hospital length of stay Median (IQR)	5·0 (3·0-10·0)	7·0 (4·0-12·0)	5·0 (3·0-11·0)	8·0 (4·0-15·0)	8·0 (4·0-15·0)	<0·001
Discharged Hospital alive	402 (74·7)	241 (70·9)	122 (78·2)	487 (69·3)	200 (77·2)	0·03
Discharge destination						<0·001
Care home or equivalent	7 (1·8)	5 (2·1)	0 (0·0)	40 (8·3)	8 (4·0)	
Health-related institution	7 (1·8)	10 (4·3)	8 (6·7)	23 (4·8)	37 (18·7)	
Usual place of residence	373 (94·4)	216 (91·9)	110 (91·7)	403 (83·8)	152 (76·8)	
Hospice or equivalent	1 (0·3)	0 (0·0)	0 (0·0)	2 (0·4)	1 (0·5)	
Temporary place of residence	7 (1·8)	4 (1·7)	2 (1·7)	13 (2·7)	0 (0·0)	

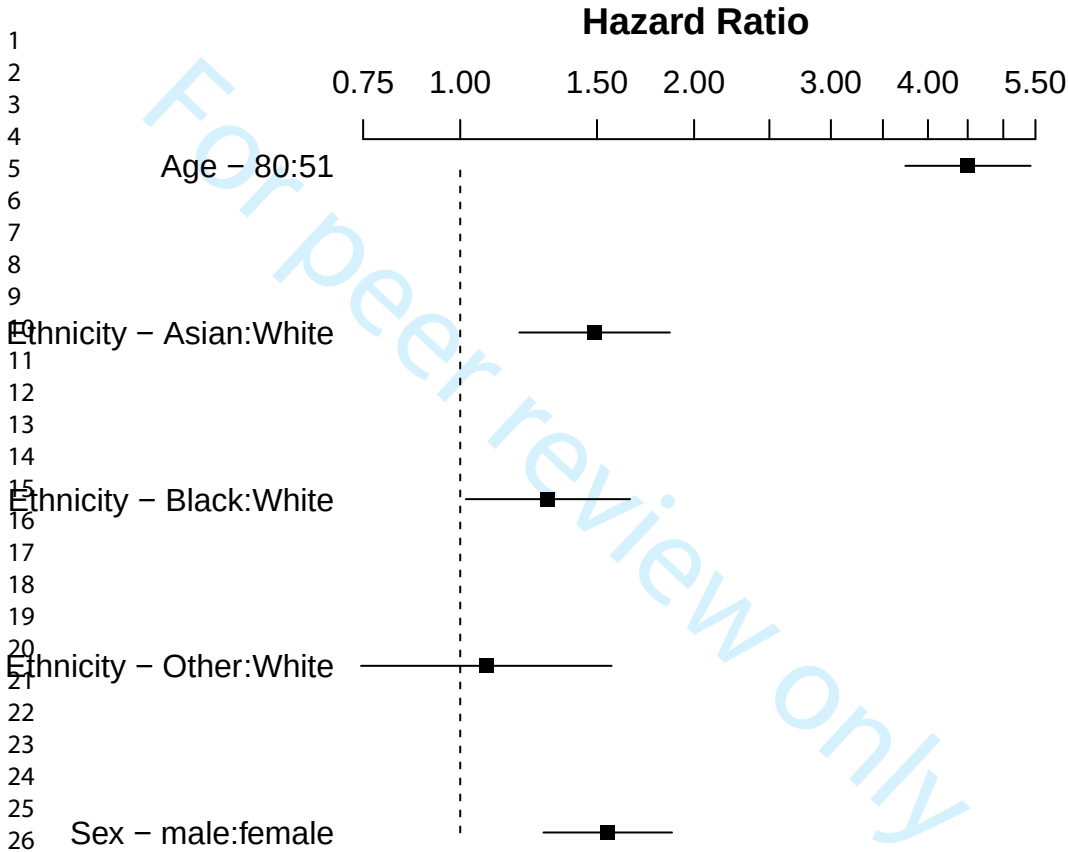
Table 2. Association of ethnic group with mortality to 30 days using Cox proportional hazards modelling, age and sex corrected. Censored to 30 days follow up, observations 1737, events 478.

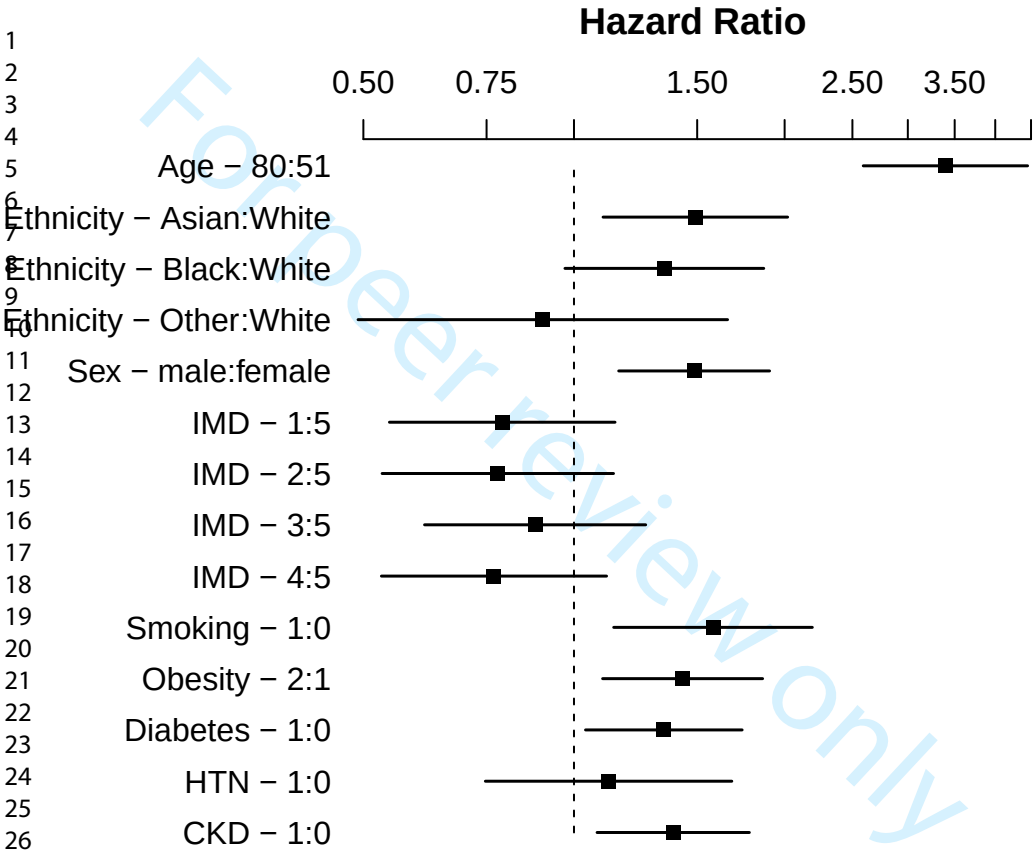
	n		Unadjusted	
	Total	**Events**	**Hazard ratio (95% CI)**	**p value**
Age (25th vs 75th centile)	-	-	4·50 (3·74-5·42)	<0·0001
Sex (Male)	-	-	1·55 (1·28-1·87)	<0·0001
Ethnic group				
Asian or Asian British	521	134	1·49 (1·19-1·86)	<0·001
Black or Black British	331	94	1·30 (1.02-1·65)	0·036
Mixed and Other ethnic groups	150	34	1·08 (0·75-1·57)	0·682
White	674	206	Reference	-

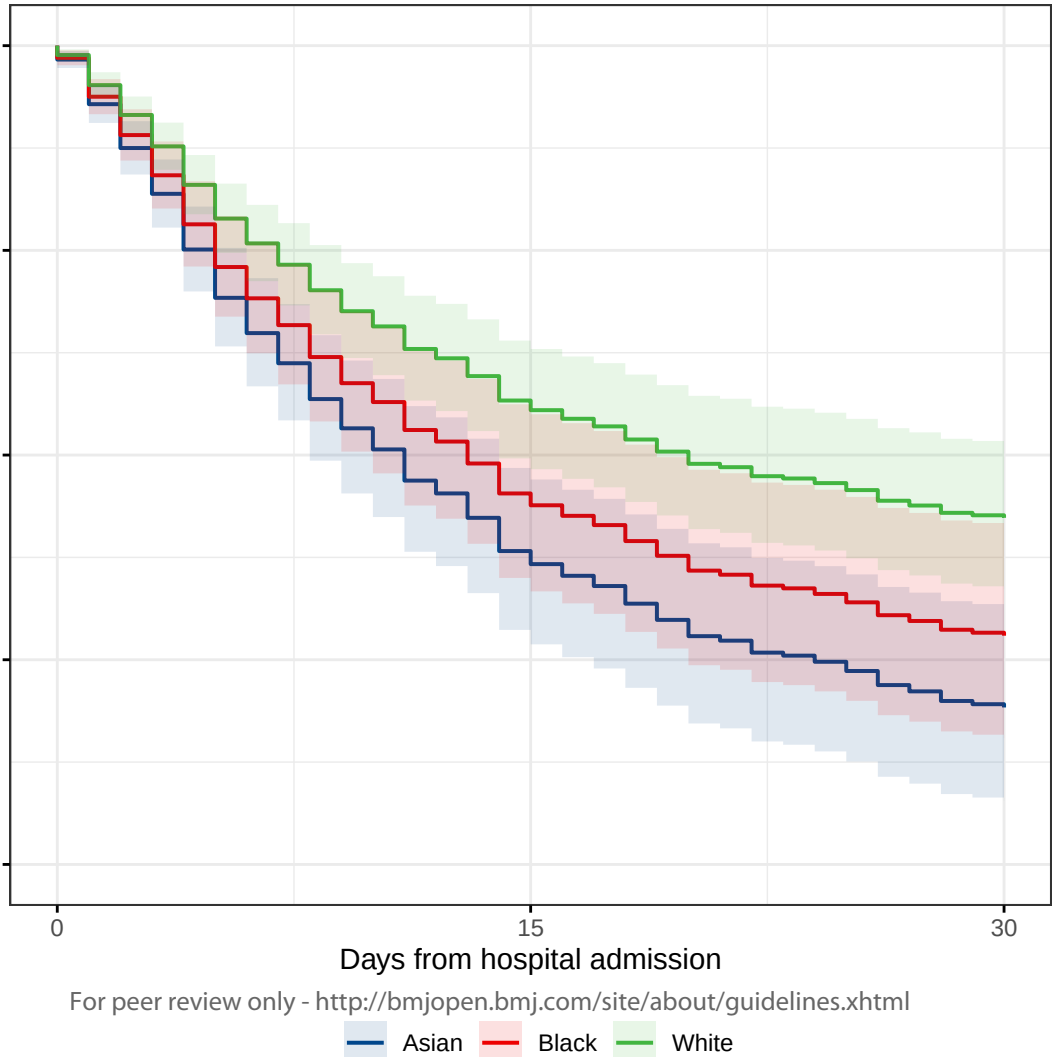
Table 3. Multivariable analysis of mortality to 30 days using Cox proportional hazards modelling, age and sex corrected. Variables included IMD quintile, smoking, BMI ≥30 kg/m^2, diabetes, HTN: hypertension, CKD: chronic kidney disease. Censored to 30 days follow up, observations 1006, events 281.

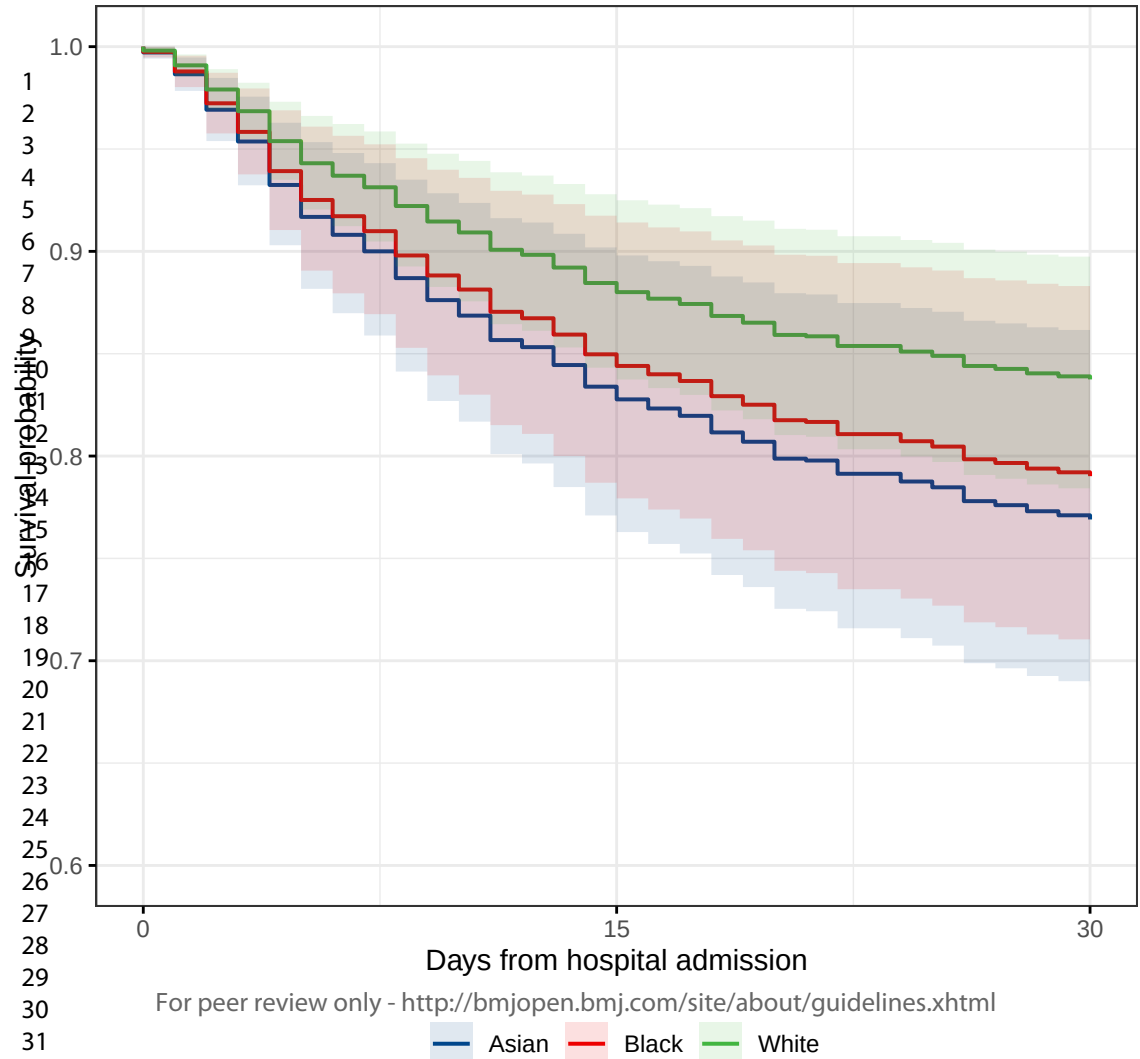
	Adjusted	
	Hazard ratio (95% CI)	**p value**
Age (25th vs 75th centile)	3·24 (2·46-4·26)	<0·0001
Sex (Male)	1·47 (1·15-1·88)	0·002
Ethnic group		
Asian or Asian British	1·48 (1·09-2·01)	0·011
Black or Black British	1·32 (0·96-1·84)	0·090
Mixed and Other ethnic groups	0·90 (0·49-1·65)	0·733
White	Reference	-
IMD quintile		
1 (most deprived)	0·79 (0·55-1·14)	0·213
2	0·79 (0·54-1·15)	0·218
3	0·88 (0·61-1·27)	0·503
4	0·77 (0·53-1·12)	0·176
5 (least deprived)	Reference	-
Smoking	1·56 (1·13-2·17)	0·008
BMI ≥30 kg/m^2	1·42 (1·09-1·85)	0·009
Diabetes	1·29 (1·00-1·67)	0·055
HTN	1·32 (0·92-1·89)	0·131
CKD	1·34 (1·04-1·73)	0·023


16-49
50-64
65-79
80+
Proportion of age-group
BMI ≥ 30
Smoking Hx
Hosp Frailty Score ≥ 15
COPD
Dementia
DM
HT
CKD
White
Asian
Black
Mixed/Other
0.00
0.25
0.50
0.75
Proportion









Supplementary material

Contents

1. Supplemental methods

a. Approvals

The study was reviewed by the Yorkshire & The Humber - Bradford Leeds Research Ethics Committee and approved as anonymised analysis of routinely collected patient data without need for consent by NHS England Health Research Authority (IRAS Project ID 283512).

b. COVID-19 testing

COVID-19 testing was performed by RdRp gene assay test on upper respiratory swab samples (nasopharyngeal, oral or endotracheal aspirate) sent to Barts Health NHS Trust Diagnostic Virology Laboratories and analysed either on-site or at Public Health England (PHE) Colindale facility.

c. Definition of key varaibles

Ethnicity
We defined ethnic groups using the 16+1 categories defined in the 2001 census which form the UK national mandatory standard for the collection and analysis of ethnicity in the NHS data dictionary. Importantly, in the UK 'Asian' ethnic category refers predominantly to those of a South Asian background (including Indian, Pakistani and Bangladeshi), while patients of a Chinese background are placed in the 'Other Ethnic Groups' category.

White	A British B Irish C Any other White background
Mixed	D White and Black Caribbean E White and Black African F White and Asian G Any other mixed background
Asian or Asian British	H Indian J Pakistani K Bangladeshi L Any other Asian background
Black or Black British	M Caribbean N African P Any other Black background
Other Ethnic Groups	R Chinese S Any other ethnic group
+1 category	Z Not stated (Reserved for cases where patients declined to provide information)

In order to preserve statistical power to detect differences between groups, pre-specified analysis was carried out between ethnicity defined by the 5-high level groups White, Mixed, Asian or Asian British, Black or Black British and Other with merging of the "Mixed" and "Other" categories. Category Z was excluded from our primary analysis as were cases where no ethnicity data was recorded (Unknown).

Index of Multiple Deprivation
Index of Multiple Deprivation (IMD) was defined from patient home address postcode using UK government statistics (https://www.gov.uk/government/statistics/english-indices-of-deprivation-2019). Matching of Lower-layer Super Output Areas (LSOAs) was undertaken against the Office of National Statistics Postcode Directory (ONSPD) February 2020 datafile (https://geoportal.statistics.gov.uk/datasets/ons-postcode-directory-february-2020: accessed on 1st May 2020). IMD was presented as quintiles within England using raw scores for descriptive results and quintiles within the study cohort in multivariable analysis.

Smoking
History of tobacco use was defined by presence of the WHO ICD-10 codes F17·1-F17·2, Z72·0, Z87·8, Z71·6 and T65·2.

Ischaemic heart disease
Ischaemic heart disease (IHD) was defined by the presence of the ICD-10 codes I23·4-I23·5, I24, I24·8-I24·9, I25, I25·3-I25·6, I25·8-I25·9, I34·1, I46·1, I51·8-I51·9, and I52.
Wu et al Mapping ICD-10 and ICD-10-CM Codes to Phecodes: Workflow Development and Initial Evaluation JMIR Med Inform 2019;7(4):e14325

End stage Renal disease
End stage Renal disease (ESRD) was defined by the presence of the ICD10 codes I77·0, N16·5, N18·5, T82·4, T86·1, Y60·2, Y61·2, and Y62·2, Y84·1, Z49·0-Z49·2, Z94·0, Z99·2.
Crellin E, et al. Clinical Code List - ICD-10 - End-Stage Renal Disease. [Data Collection]. London School of Hygiene & Tropical Medicine. 2017: https://doi.org/10.17037/DATA.241.

Comorbidity
Diagnosis of co-morbidities and assignment of Charlson Comorbidity Index was based on mapping from ICD-10 coding from previous admissions using the mapping of Quan H, et al.
Quan H, et al. Coding algorithms for defining comorbidities in ICD-9-CM and ICD-10 administrative data. Med Care 2005;43(11):1130-9.
Diagnosis of Hypertension was based on mapping ICD-10 codes to the Elixhauser comorbidity index.
Elixhauser A, et al. Comorbidity measures for use with administrative data. Med Care 1998;36:8-27.

Hospital frailty risk score
Hospital frailty risk score was calculated from mapping ICD-10 coding of hospital attendances.
Gilbert T, et al. Development and validation of a Hospital Frailty Risk Score focusing on older people in acute care settings using electronic hospital records: an observational study. Lancet 2018;391(10132):1775-1782.

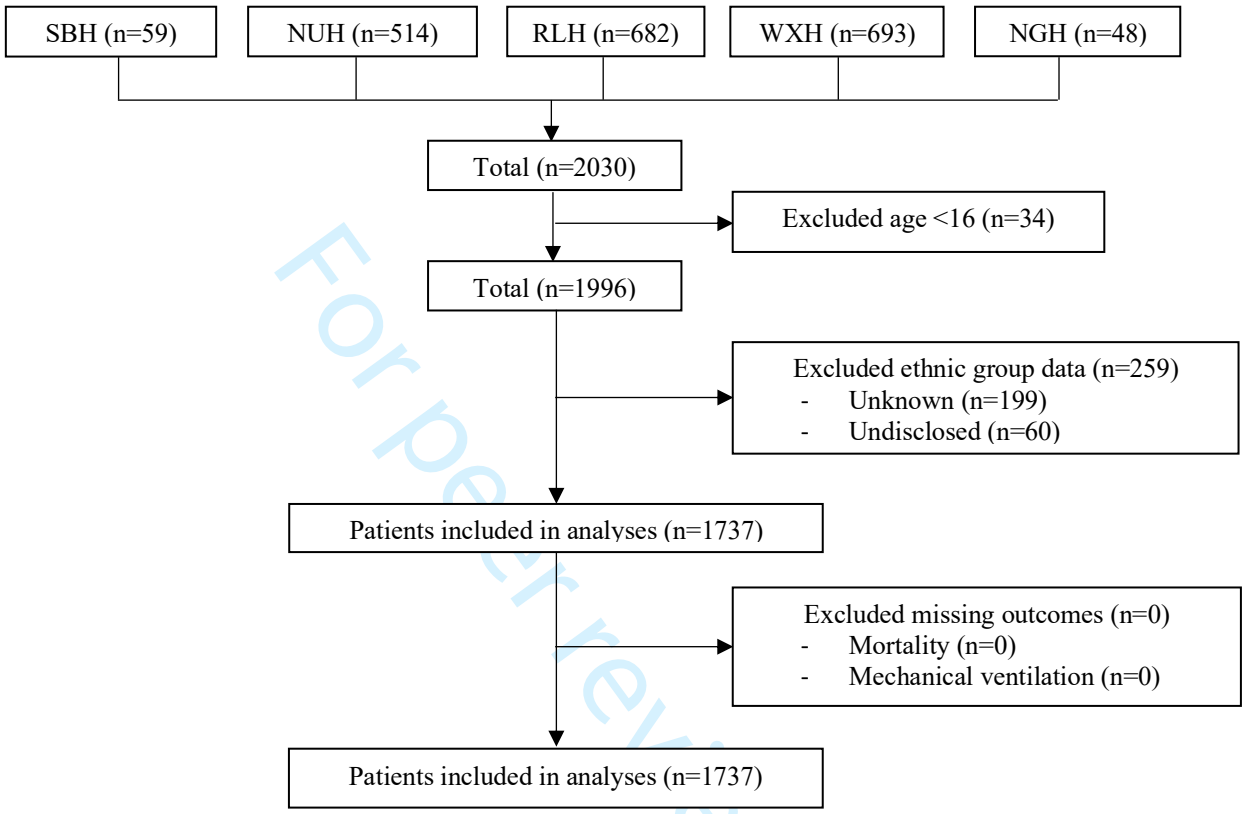
Acute Kidney injury
Acute kidney injury (AKI) within first 7 days of admission was defined using the KDIGO 2012 creatinine criteria either a 1·5-fold rise over baseline within 7 days or 26 μmol rise within 48 hours. Baseline creatinine will be the median value in the 7 to 365 days before hospitalisation. Absent baseline creatinine was determined based on an eGFR of 75 ml/min/1·72m^2 using the CKDepi formula or the admission value whichever was lower.

Chronic kidney disease
History of chronic kidney disease (CKD) using baseline eGFR was calculated using last creatinine value available from results earlier than 7 days before hospitalisation. CKD was defined as baseline eGFR below 60 ml/min/1·72m^2.

Secondary haemophagocytic lymphohistiocytosis
Secondary haemophagocytic lymphohistiocytosis (sHLH) risk scores were calculated using highest values during admission of temperature, haemoglobin, white cell count, platelet count, triglycerides, fibrinogen, ferritin, and aspartate aminotransferase (AST). Total scores did not include haemophagocytosis on bone marrow aspirate or known immunosuppression due to lack of available data leaving a maximum score of 284.
Mehta P, et al. COVID-19: consider cytokine storm syndromes and immunosuppression. Lancet 2020;395(10229):1033-1034.

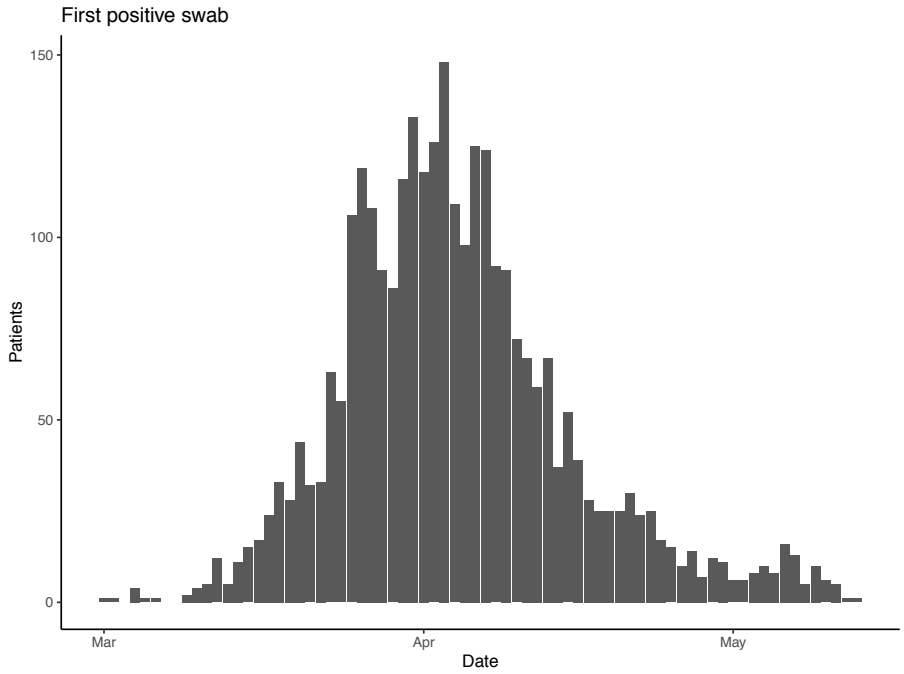
2. STROBE diagram

Figure S1. STROBE flow diagram of study populations. Hospital indicates first admission site and patients admitted to Nightingale hospital who had not been previously admitted to Barts Health hospital: St. Barts Hospital (SBH), Newham University Hospital (NUH), Royal London Hospital (RLH), Whipps Cross Hospital (WXH), Nightingale Hospital (NGH).



3. Inclusion time period by SARS-CoV-2 cases

Figure S2. Timeline of patients with positive SARS-CoV-2 swab tests at Barts Health.



4. Distribution of ethnicity categories within study cohort

Table S1. Distribution of study cohort by 16+1 ethnic data categories.

High-level group	Ethnic data category	n
White	A British	526
	B Irish	11
	C Any other White background	166
Mixed	D White and Black Caribbean	3
	E White and Black African	4
	F White and Asian	1
	G Any other mixed background	8
Asian or Asian British	H Indian	104
	J Pakistani	116
	K Bangladeshi	191
	L Any other Asian background	127
Black or Black British	M Caribbean	118
	N African	168
	P Any other Black background	54
Other Ethnic Groups	R Chinese	23
	S Any other ethnic group	117
	Z Not stated	60
No ethnicity data recorded		199

5. Baseline characteristics comparing died or survived at 30 days

Table S2. Study population baseline characteristics stratified by died or survived at 30 days, n (%) unless otherwise stated. Total n=1996 unless otherwise stated. P values based on Chi-square (for categorical) or Kruskal-Wallis test (for continuous). SD: standard deviation, IQR: interquartile range, IMD: index of multiple deprivation, BMI: body mass index, TIA: transient ischaemic accident, HTN: hypertension, CKD: chronic kidney disease, sHLH: secondary haemophagocytic lymphohistiocytosis (without known underlying immunosuppression and bone marrow aspirate data), CRP: C-reactive protein, NEWS: national early warning score, ICU: intensive care unit, RRT: renal replacement therapy.

	Stratified by survival at 30 days		
	Died	**Survived**	p value
n	536	1460	
Ethnicity			0·05
Asian or Asian British	138 (25·7)	400 (27·4)	
Black or Black British	97 (18·1)	243 (16·6)	
Mixed and Other Ethnic Groups	33 (6·2)	123 (8·4)	
White	210 (39·2)	493 (33·8)	
Unknown and Undsisclosed	58 (10·8)	201 (13·8)	
Age (years)			
Mean (SD)	74·8 (12·6)	59·2 (18·2)	<0·001
Median (IQR)	77·0 (66·0-84·0)	59·0 (46·0-73·0)	<0·001
Male	351 (65·5)	859 (58·8)	0·01
IMD quintile [n=1980]			0·003
1 (most deprived)	155 (29·1)	407 (28·1)	
2	223 (41·9)	698 (48·2)	
3	62 (11·7)	184 (12·7)	
4	56 (10·5)	99 (6·8)	
5 (least deprived)	36 (6·8)	60 (4·1)	
Smoking [n=1700]	57 (11·8)	116 (9·5)	0·19
BMI [n=1248]			
Median (IQR)	26·5 (22·7-31·6)	26·9 (23·6-31·2)	0·43
By category			0·80
<18·5 kg/m^2	20 (6·4)	43 (4·6)	
18·5 - <25 kg/m^2	97 (31·0)	295 (31·6)	
25 - <30 kg/m^2	100 (31·9)	309 (33·0)	
30 - <40 kg/m^2	80 (25·6)	243 (26·0)	
≥40 kg/m^2	16 (5·1)	45 (4·8)	
Co-morbidity using ICD-10 [n=1700]			
Obesity	123 (25·5)	286 (23·5)	0·411
Ischaemic heart disease	149 (30·9)	197 (16·2)	<0·001
Myocardial infarction	73 (15·1)	108 (8·9)	<0·001
Congestive heart failure	120 (24·9)	140 (11·5)	<0·001
Peripheral vascular disease	74 (15·4)	84 (6·9)	<0·001
Cerebral vascular accident or TIA	133 (27·6)	159 (13·1)	<0·001
Dementia	89 (18·5)	78 (6·4)	<0·001
Chronic obstructive pulmonary disease	145 (30·1)	252 (20·7)	<0·001
Diabetes	242 (50·2)	422 (32·6)	<0·001
HTN	372 (77·2)	637 (52·3)	<0·001
Moderate to severe CKD	159 (33·0)	204 (16·7)	<0·001
End-stage renal disease	39 (8·1)	74 (6·1)	0·163

Liver disease	45 (8·4)	110 (7·5)	0·587
Cancer	62 (12·9)	82 (6·7)	<0·001
Cancer with metastases	18 (3·7)	24 (2·0)	0·053
Acquired immunodeficiency syndrome	1 (0·2)	5 (0·4)	0·855
Charlson comorbidity index [n=1700]			<0·001
0	45 (9·3)	428 (35·1)	
1-2	170 (35·3)	449 (36·9)	
3-4	130 (27·0)	174 (14·3)	
≥5	137 (28·4)	167 (13·7)	
Rockwood frailty score [n=831]			<0·001
1-2 (very fit, well)	20 (6·3)	75 (14·5)	
3-4 (managing well, vulnerable)	106 (33·7)	199 (38·6)	
5-6 (mildly to severely frail)	144 (45·7)	215 (41·7)	
8-9 (very severely frail, terminally ill)	45 (14·3)	27 (5·2)	
Hospital frailty risk score [n=1700]			<0·001
<5 (low risk)	88 (18·3)	655 (53·8)	
5-15 (intermediate risk)	187 (38·8)	293 (24·1)	
≥15 (high risk)	207 (42·9)	270 (22·2)	
Baseline eGFR ml/min/1·72m2 [n=1525]			
Median (IQR)	57·3 (38·7-76·2)	72·4 (51·2-90·8)	<0·001
eGFR <60	236 (52·2)	323 (30·1)	<0·001
Acute kidney injury first 7 days [n=1673]	204 (47·0)	226 (18·2)	<0·001
Blood results during admission			
Highest creatinine µmol/L [n=1691]			<0·001
Median (IQR)	168·0 (102·0-326·0)	87·0 (71·0-120·0)	
Highest CRP [n=1761]			<0·001
Median (IQR)	241·5 (149·8-344·0)	120·0 (59·0-218·0)	
Highest D-dimer mg/L [n=968]			<0·001
Median (IQR)	3·1 (1·2-17·7)	1·1 (0·6-3·3)	
Highest sHLH score [n=1881]			
Mean (SD)	34·6 (27·9)	26·9 (25·7)	<0·001
Blood Group [n=875]			0·004
A	109 (36·0)	196 (34·3)	
AB	11 (3·6)	32 (5·6)	
B	49 (16·2)	119 (20·8)	
O	134 (44·2)	225 (39·3)	
NEWS on admission [n=1443]	4·7 (2·9)	3·5 (2.2)	<0·001
Intensive care unit (ICU)			
ICU admission	151 (28·2)	210 (14·4)	<0·001
ICU length of stay			
Median (IQR)	9·0 (5·9-15·0)	8·0 (3·0-15·0)	0·06
Mechanical ventilation within ICU admissions	135 (89·4)	146 (69·5)	<0·001
Days on organ support			
Advanced respiratory Mean (SD)	9·3 (6·2)	9·9 (10·6)	0·49
Total respiratory Mean (SD)	10·4 (6·2)	12·5 (10·2)	0·03
Cardiovascular system Mean (SD)	10·3 (6·3)	12·6 (10·5)	0·02
Renal Mean (SD)	2·5 (4·1)	2·7 (6·2)	0·76
Total number of organ systems			<0·001
0	0 (0·0)	3 (1·4)	

1	1 (0·7)	12 (5·7)	
2	93 (61·6)	154 (73·3)	
3	57 (37·7)	41 (19·5)	
Hospital length of stay			
Median (IQR)	7·0 (4·0-13·0)	7·0 (3·0-12·0)	0·98

6. Completeness of follow-up

Table S3. Numbers at risk and number of deaths (in parenthesis) over five day intervals up to 30 days by ethnic group in primary survival analysis.

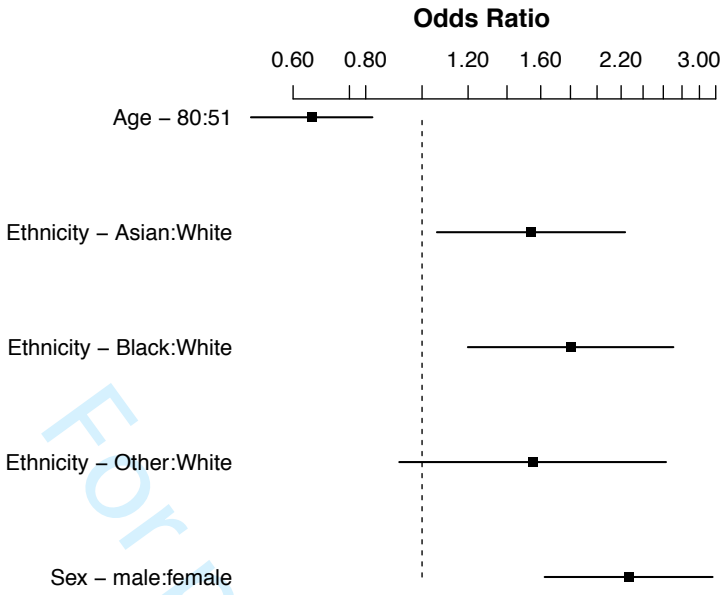
Ethnic group	Days from hospital admission						
	0	**5**	**10**	**15**	**20**	**25**	**30**
Asian or Asian British	538 (3)	488 (60)	446 (96)	421 (115)	402 (124)	389 (131)	365 (138)
Black or Black British	340 (4)	301 (50)	273 (70)	258 (80)	248 (88)	240 (94)	229 (97)
Mixed and Other ethnic groups	156 (1)	147 (12)	140 (17)	127 (26)	122 (32)	117 (33)	113 (33)
White	703 (3)	644 (71)	583 (120)	534 (162)	502 (188)	472 (197)	436 (210)

7. Secondary outcome mechanical ventilation

Table S4. Association of ethnic group with mechanical ventilation using logistic regression modelling, age and sex corrected. Observations 1737, events 210.

	Unadjusted	
	Odds ratio (95% CI)	**p value**
Age (25^{th} vs 75^{th} centile)	0·65 (0·51-0·82)	<0·001
Sex (Male)	2·27 (1·63-3·16)	<0·0001
Ethnic group		
Asian or Asian British	1·54 (1·06-2·23)	0·023
Black or Black British	1·80 (1·20-2·71)	0·005
Mixed and Other ethnic groups	1·55 (0·91-2·63)	0·104
White	Reference	-

Figure S3. Forest plot showing log odds ratios of mechanical ventilation comparing ethnic groups, age and sex corrected.



8. Sensitivity analyses

a. Multivariable imputation

Missing data for baseline risk variables included in the multivariable Cox model was imputed using Multivariate Imputation by Chained Equations based on age, sex, and comorbidity. Five separate imputed datasets were simulated, and a pooled result of multivariable Cox models presented.
Van Buuren S, Groothuis-Oudshoorn K. mice: Multivariate Imputation by Chained Equations in R. J Stat Softw 2011;45(3): https://www.jstatsoft.org/v045/i03.

Figure S4. Patterns of missingness in baseline risk variables. ID: patient identifier, IMD: index of multiple deprivation, DM: diabetes mellitus, HTN: hypertension, CKD: chronic kidney disease, BMI: body mass index.

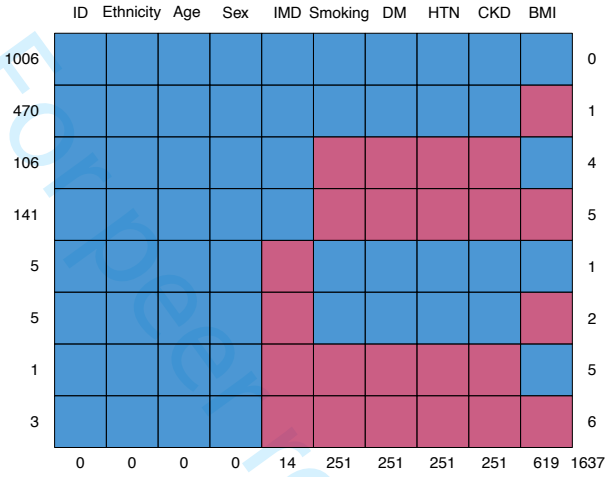
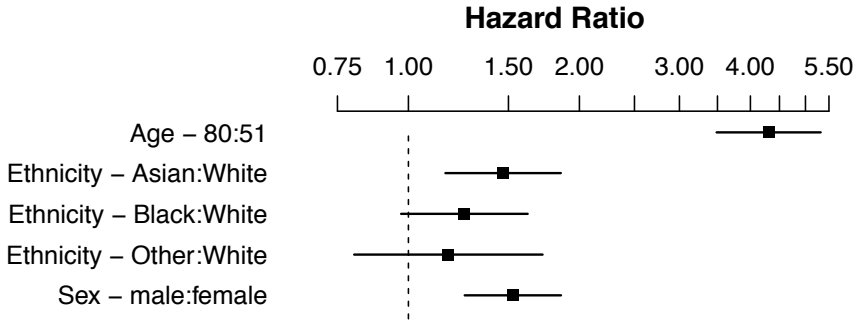


Table S5. Multivariable analysis using imputed dataset of mortality to 30 days using Cox proportional hazards modelling. Missing data imputed for smoking, BMI ≥30 kg/m^2, diabetes, HTN, CKD. Censored to 30 days follow up, observation 1737, events 478.

	n		Unadjusted	
	Total	**Events**	**Hazard ratio (95% CI)**	**P value**
Age (25th vs 75th centile)	-	-	4·31 (3·49-5·32)	<0·0001
Sex (Male)	-	-	1·53 (1·26-1·86)	<0·0001
Ethnic group				
Asian or Asian British	521	134	1·47 (1·16-1·85)	0·001
Black or Black British	331	94	1·25 (0·97-1·62)	0·083
Mixed and Other ethnic groups	150	34	1·18 (0·80-1·72)	0·406
White	674	206	Reference	-

Figure S5. Forest plot showing log hazards ratios of mortality to 30 days using the imputed dataset.



a. ABO blood group

Table S6. Multivariable analysis of mortality to 30 days using cox proportional hazards modelling. Variables included age, sex, and ABO blood group. Censored to 30 days follow up, observations 793, events 281.

	Adjusted	
	Hazard ratio (95% CI)	**P value**
Age (25th vs 75th centile)	3·26 (2·58-4·13)	<0·0001
Sex (Male)	1·67 (1·30-2·13)	<0·0001
Ethnic group		
Asian or Asian British	1·82 (1·35-2·46)	<0·0001
Black or Black British	1·63 (1·17-2·27)	0·004
Mixed and Other ethnic groups	1·62 (0·98-2·68)	0·059
White	Reference	-
ABO blood group		
A	0·81 (0·62-1·05)	0.112
AB	0·65 (0·33-1·28)	0·214
B	0·66 (0·47-0·92)	0·016
O	Reference	-

Figure S6. Forest plot showing log hazards ratios of mortality to 30 days comparing multiple variables including ABO blood group.

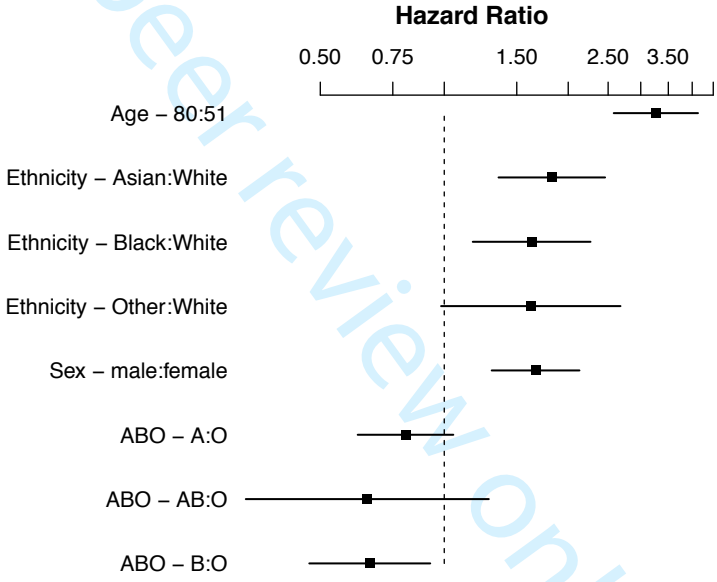
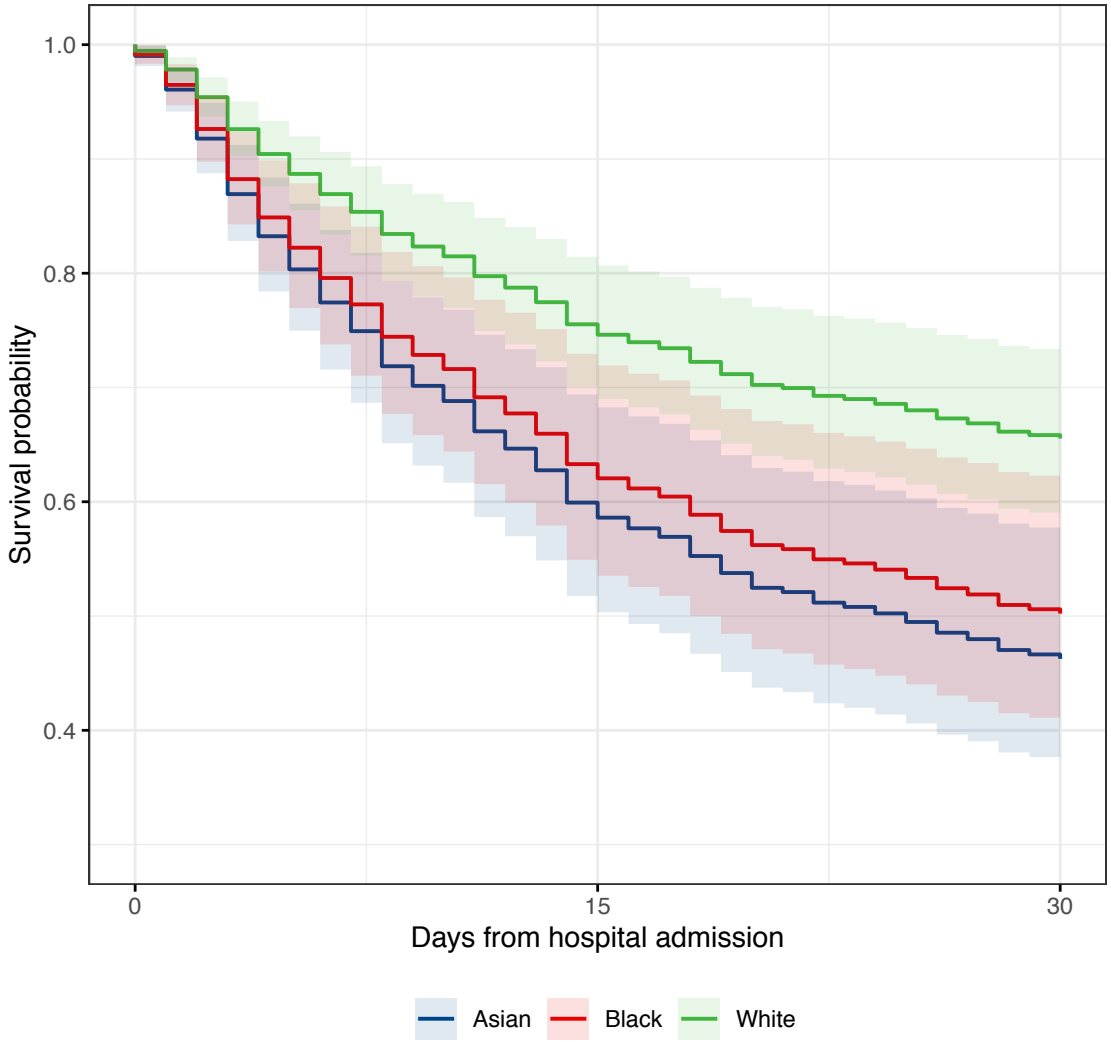


Figure S7. Survival curve to 30 days from multivariable analysis comparing Asian, Black, and White ethnic groups. Survival modelled for median age 65 years and male sex, ABO bloog group O.



b. Charlson comorbidity index

Table S7. Multivariable analysis of mortality to 30 days using cox proportional hazards modelling. Variables included age, sex, IMD quintile, smoking, BMI ≥30 kg/m^2, and Charlson comorbidity index. Censored to 30 days follow up, observations 1006, events 281.

	Adjusted	
	Hazard ratio (95% CI)	**P value**
Age (25th vs 75th centile)	2·90 (2·22-3·79)	<0·0001
Sex (Male)	1·48 (1·16-1·90)	0·002
Ethnic group		
Asian or Asian British	1·54 (1·15-2·08)	0·004
Black or Black British	1·39 (1·01-1·92)	0·044
Mixed and Other ethnic groups	1·02 (0·56-1·88)	0·939
White	Reference	-
IMD quintile		
1 (most deprived)	0·83 (0·57-1·20)	0·316
2	0·81 (0·55-1·18)	0·268
3	0·94 (0·66-1·36)	0·759
4	0·82 (0·57-1·20)	0·311
5 (least deprived)	Reference	-
Smoking	1·36 (0·98-1·89)	0·067
BMI ≥30 kg/m^2	1·48 (1·14-1·92)	0·003
Charlson comorbidity index		
0	Reference	-
1-2	2·00 (1·17-3·41)	0·012
3-4	3·43 (2·00-5·89)	<0·0001
≥5	4·10 (2·42-6·94)	<0·0001

Figure S8. Forest plot showing log hazards ratios of mortality to 30 days comparing multiple variables including CCI: Charlson comorbidity index. IMD: index of multiple deprivation, Obesity defined as BMI ≥30 kg/m^2.

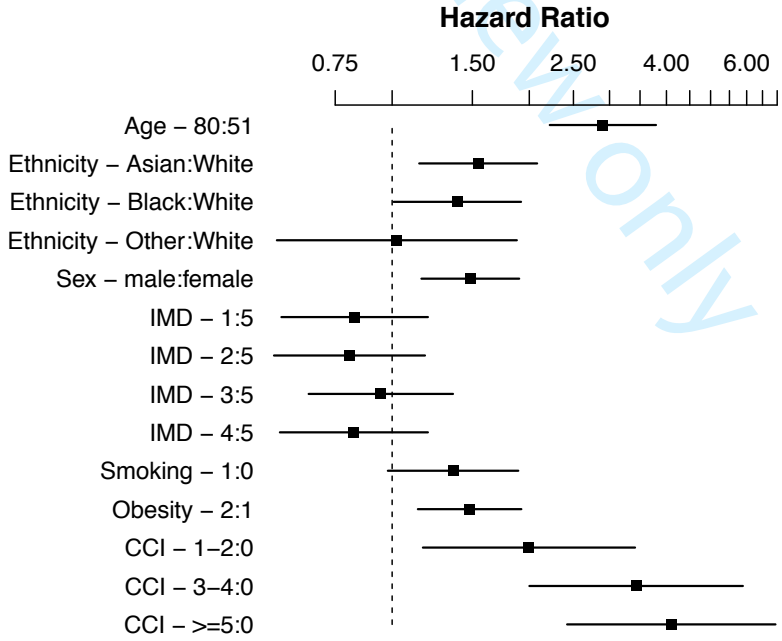
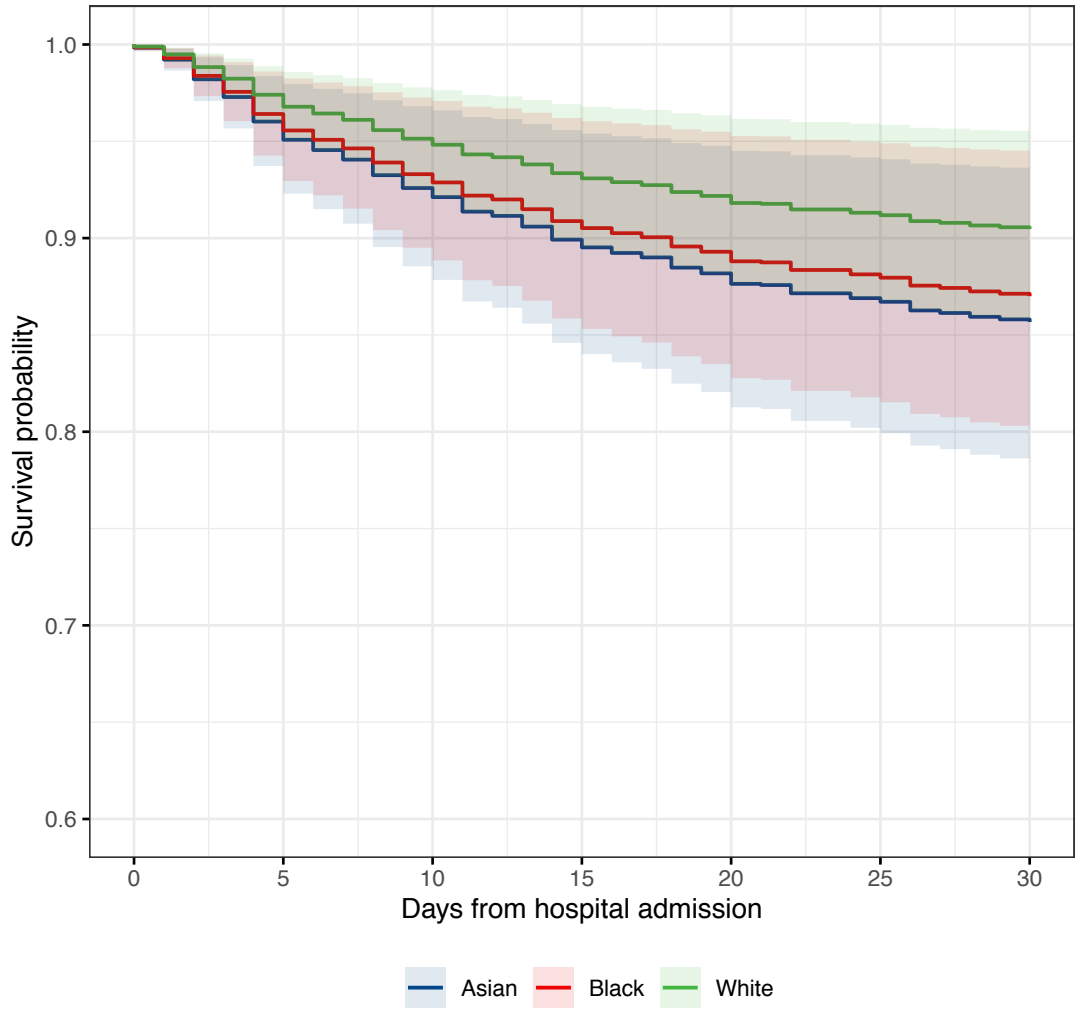


Figure S9. Survival curve to 30 days from multivariable analysis comparing Asian, Black, and White ethnic groups. Survival modelled for median age 65 years and male sex, index of multiple deprivation (IMD) least deprived quintile, no baseline risk factors defined as non-smoking, BMI <30 kg/m^2 and Charlson comorbidity index 0.



c. Rockwood frailty score

Table S8. Multivariable analysis of mortality to 30 days using cox proportional hazards modelling. Variables included age, sex, index of multiple deprivation (IMD) quintile, smoking, BMI ≥30 kg/m^2, and Rockwood frailty score (RFS). Censored to 30 days follow up, observations observations 552, events 199.

	Adjusted	
	Hazard ratio (95% CI)	**P value**
Age (25th vs 75th centile)	2·42 (1·56-3·75)	<0·0001
Sex (Male)	1·61 (1·19-2·16)	0·002
Ethnic group		
Asian or Asian British	1·98 (1·37-2·86)	<0·001
Black or Black British	1·67 (1·14-2·45)	0·009
Mixed and Other ethnic groups	1·27 (0·62-2·56)	0·513
White	Reference	-
IMD quintile		
1 (most deprived)	0·61 (0·38-0·98)	0·040
2	0·79 (0·50-1·22)	0·283
3	0·82 (0·53-1·25)	0·348
4	0·77 (0·51-1·18)	0·234
5 (least deprived)	Reference	-
Smoking	1·38 (0·94-2·03)	0·102
BMI ≥30 kg/m^2	1·39 (1·01-1·91)	0·045
Rockwood frailty score		
1-2 (very fit, well)	Reference	-
3-4 (managing well, vulnerable)	1·61 (0·82-3·16)	0·164
5-6 (mildly to severely frail)	1·84 (0·93-3·64)	0·078
8-9 (very severely frail, terminally ill)	3·25 (1·49-7·06)	0·003

Figure S10. Forest plot showing log hazards ratios of mortality to 30 days comparing multiple variables including RFS: Rockwood frailty score. IMD: index of multiple deprivation, Obesity defined as BMI ≥30 kg/m^2.

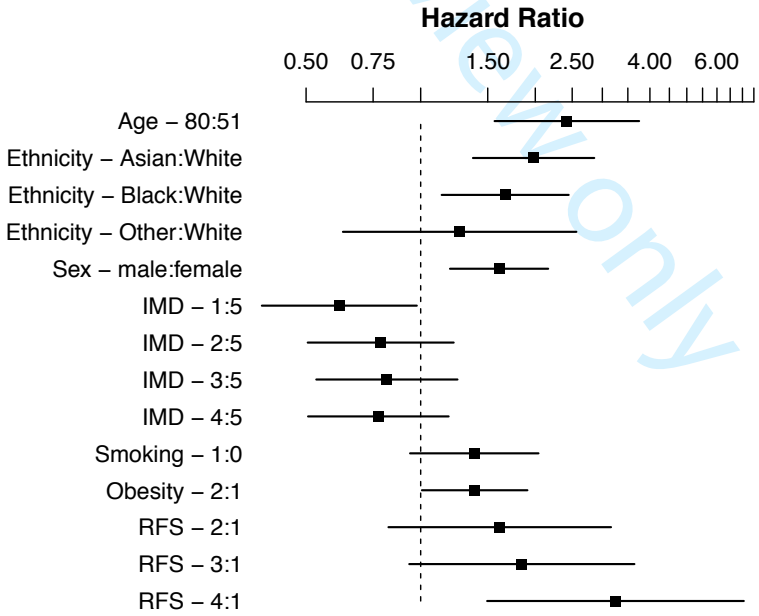
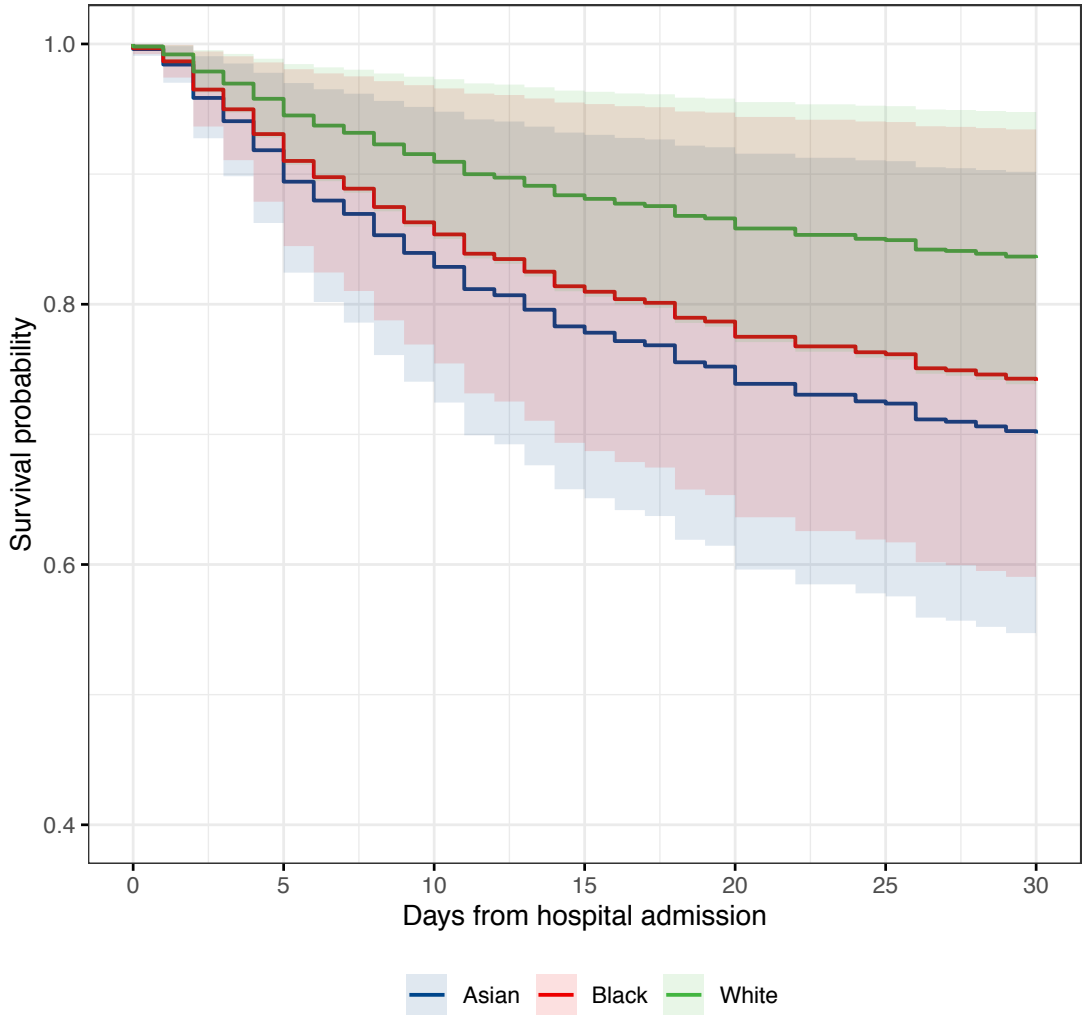


Figure S11. Survival curve to 30 days from multivariable analysis comparing Asian, Black, and White ethnic groups. Survival modelled for median age 65 years and male sex, index of multiple deprivation (IMD) least deprived quintile, no baseline risk factors defined as non-smoking, BMI <30 kg/m^2 and Rockwood frailty score lowest risk group.



d. Hospital frailty risk score

Table S9. Multivariable analysis of mortality to 30 days using cox proportional hazards modelling. Variables included age, sex, index of multiple deprivation (IMD) quintile, smoking, BMI ≥30 kg/m^2, and Hospital frailty risk score (HFRS). Censored to 30 days follow up, observations 1006, events 281.

	Adjusted	
	Hazard ratio (95% CI)	**P value**
Age (25th vs 75th centile)	2·84 (2·17-3·71)	<0·0001
Sex (Male)	1·58 (1·24-2·03)	<0·001
Ethnic group		
Asian or Asian British	1·78 (1·32-2·41)	<0·001
Black or Black British	1·57 (1·13-2·17)	0·007
Mixed and Other ethnic groups	1·10 (0·60-2·04)	0·751
White	Reference	-
IMD quintile		
1 (most deprived)	0·85 (0·59-1·24)	0·404
2	0·83 (0·57-1·22)	0·341
3	0·89 (0·62-1·29)	0·541
4	0·83 (0·57-1·20)	0·310
5 (least deprived)	Reference	-
Smoking	1·42 (1·01-1·96)	0·044
BMI ≥30 kg/m^2	1·57 (1·21-2·05)	<0·001
Hospital frailty risk score		
<5 (low risk)	Reference	-
5-15 (intermediate risk)	2·44 (1·68-3·54)	<0·0001
≥15 (high risk)	2·76 (1·89-4·04)	<0·0001

Figure S12. Forest plot showing log hazards ratios of mortality to 30 days comparing multiple variables including HFRS: Hospital frailty risk score. IMD: index of multiple deprivation, Obesity defined as BMI ≥30 kg/m^2.

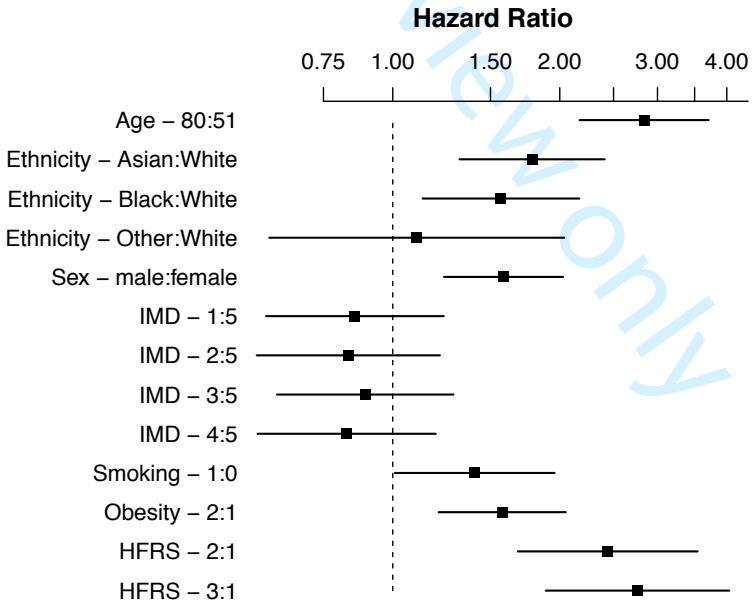
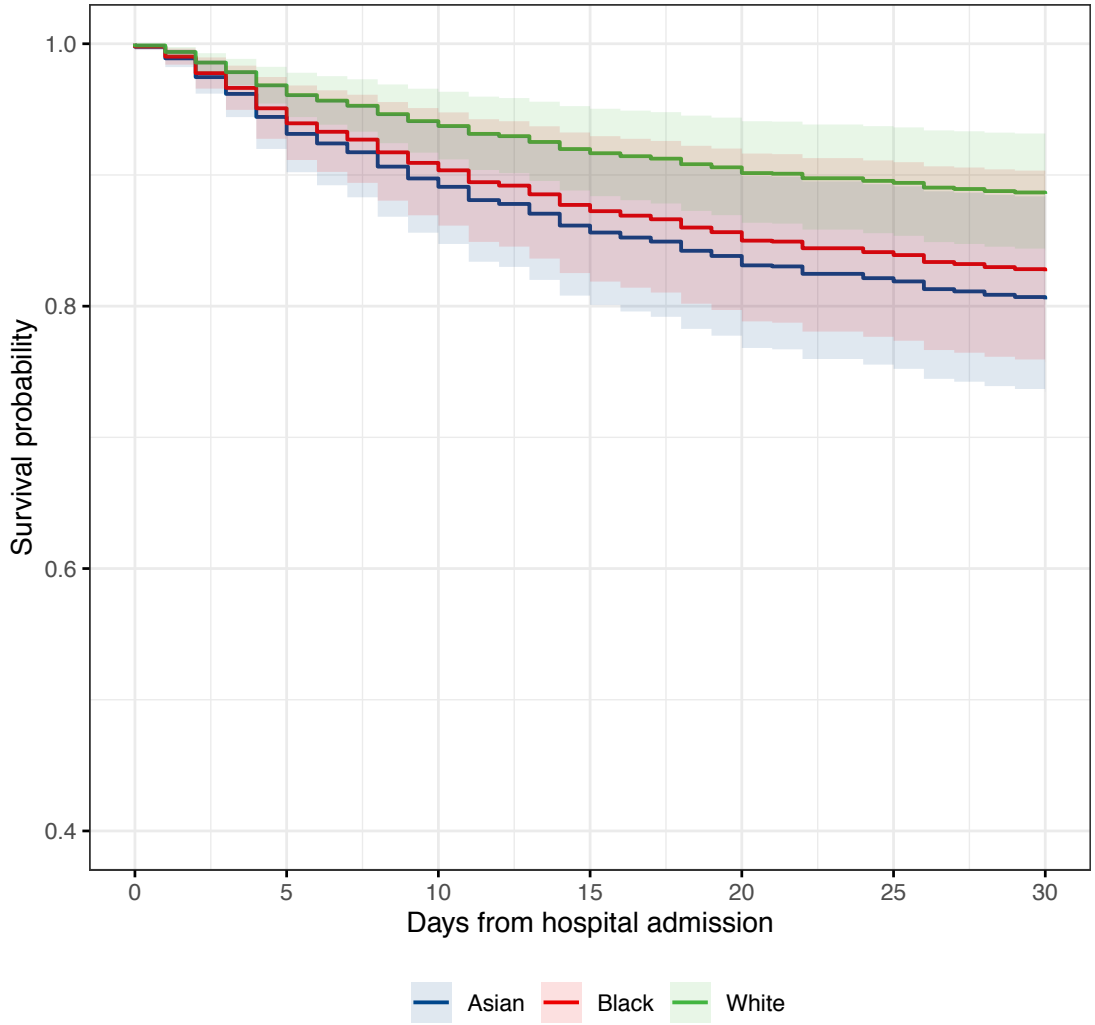


Figure S13. Survival curve to 30 days from multivariable analysis comparing Asian, Black, and White ethnic groups, age and sex corrected. Survival modelled for median age 65 years and male sex, inde of multiple deprivation (IMD) least deprived quintile, no history of baseline risk factors defined as smoking, BMI ≥30 kg/m^2, Hospital frailty risk score lowest risk group.



e. 90 day mortality

Table S10. Association of ethnic group with mortality to 90 days using cox proportional hazards modelling, age and sex corrected. Censored to 90 days follow up, observations 1737, events 510.

	n		Unadjusted	
	Total	**Events**	**Hazard ratio (95% CI)**	**P value**
Age (25^{th} vs 75^{th} centile)	-	-	4·48 (3·74-5·35)	<0·0001
Sex (Male)	-	-	1·52 (1·27-1·83)	<0·0001
Ethnic group				
Asian or Asian British	497	106	1·46 (1·18-1·81)	<0·001
Black or Black British	342	83	1·26 (0·99-1·59)	0·058
Mixed and Other ethnic groups	142	30	1·02 (0·71-1·46)	0·934
White	651	182	Reference	-

Figure S14. Forest plot showing log hazards ratios of mortality to 90 days comparing ethnic groups, age and sex.

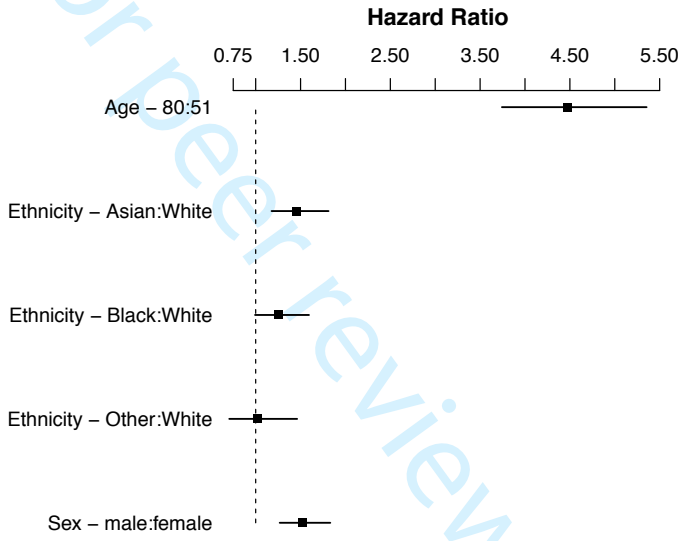
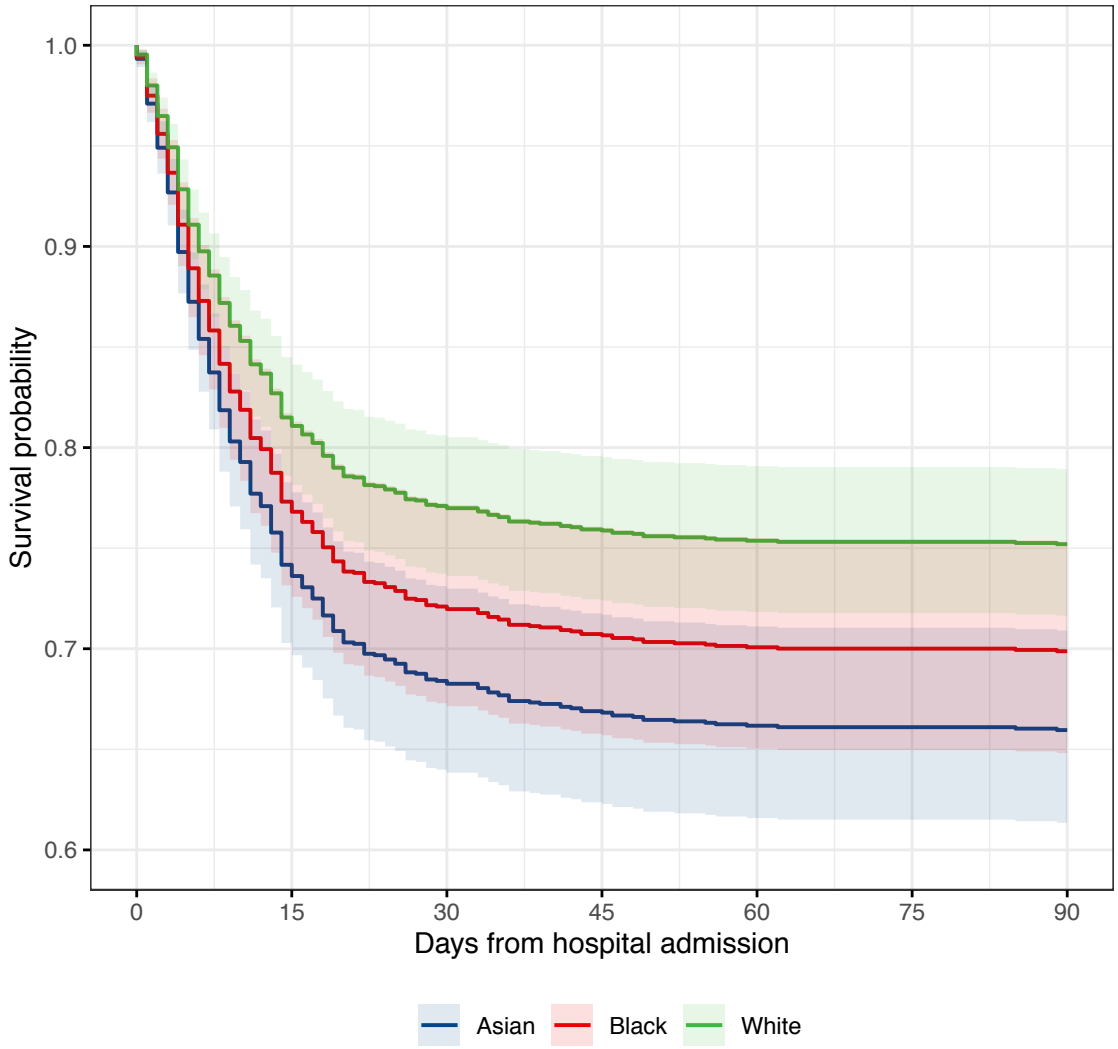


Figure S15. Survival curve to 90 days from univariate analysis comparing Asian, Black, and White ethnic groups, age and sex. Survival modelled for median age 65 years and male sex.



9. Cox proportional hazards testing

We assessed proportional-hazards assumption for ethnicity and adjusted variables by inspection of scaled Schoenfeld residual plots. There was some evidence of non-proportionality for Black ethnicity at later time points in the primary age and sex adjusted analysis. However, the unstratified and ethnicity-stratified survival curves for the age and sex adjusted 30-day survival were similar suggesting minimal impact of non-proportionality.

Figure S16. Scaled Schoenfeld residual plots for ethnicity, age, and sex.

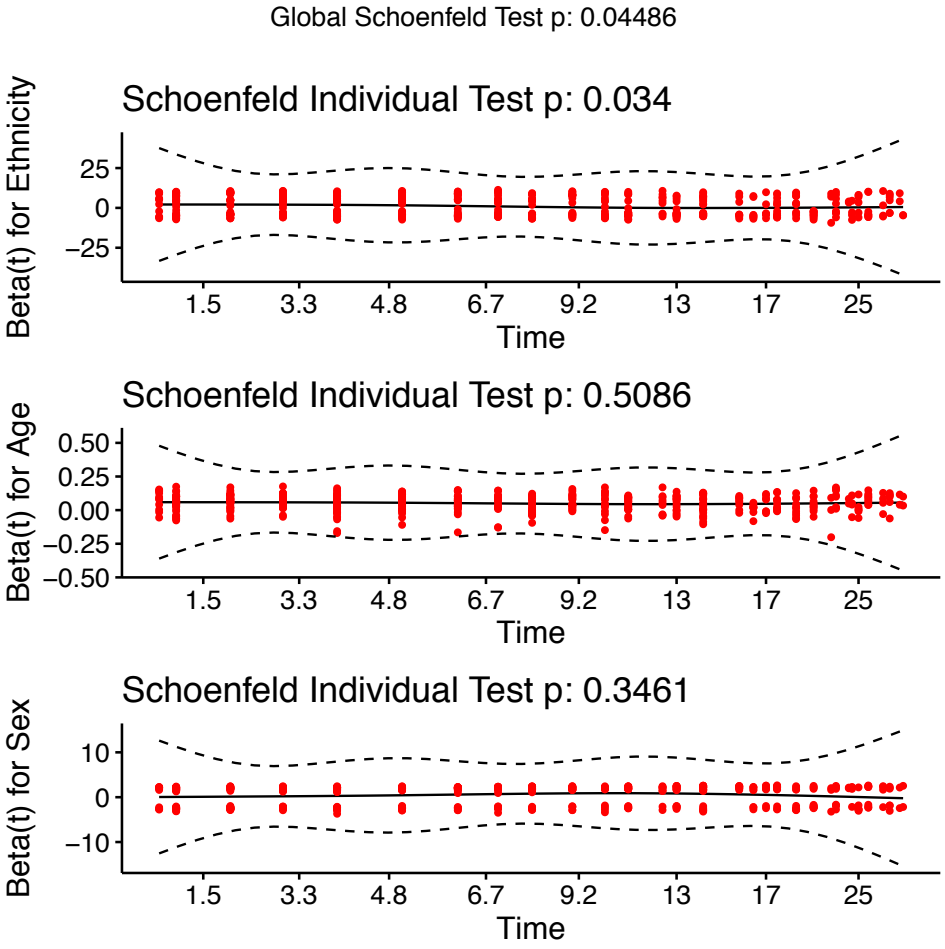
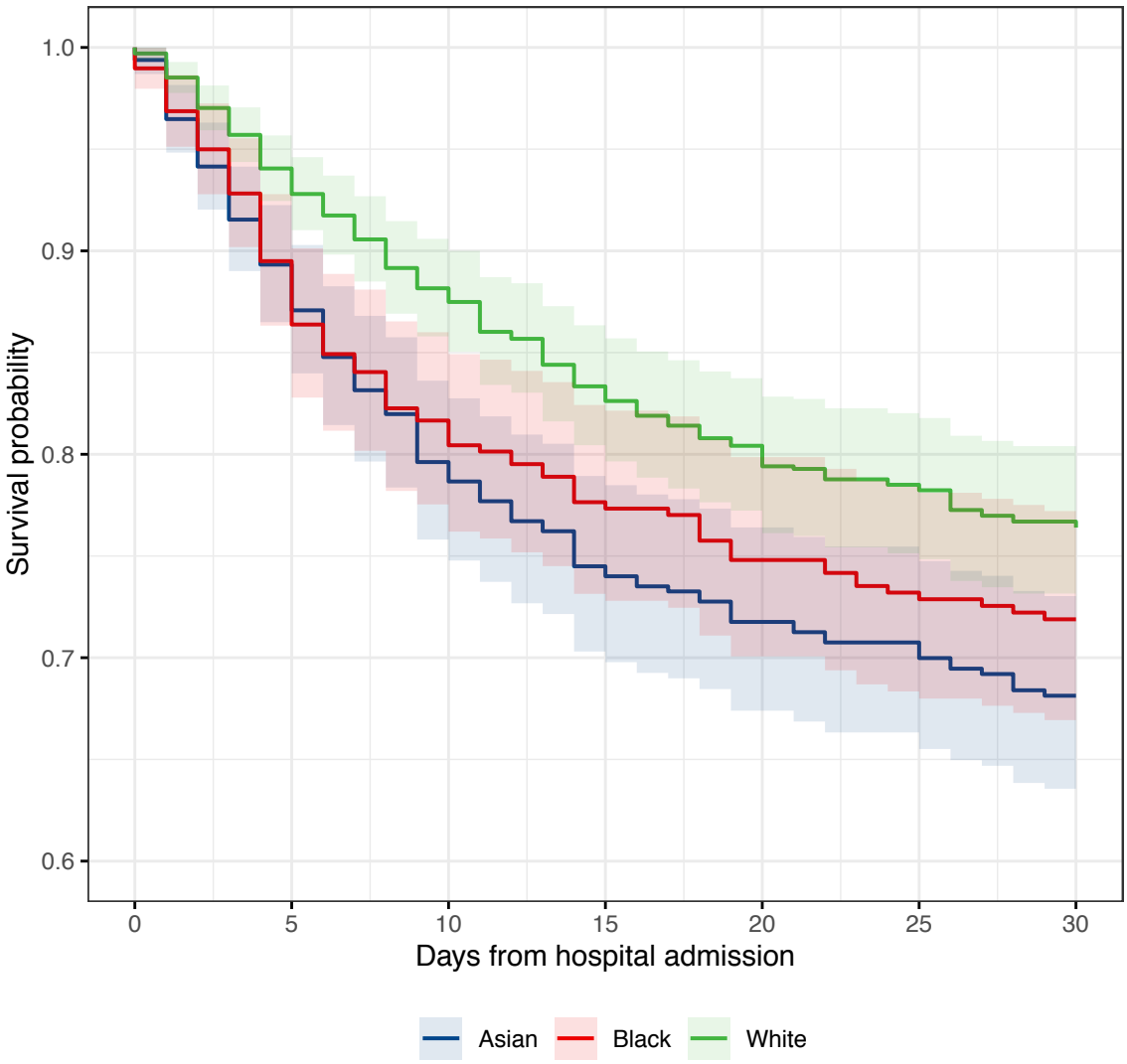


Figure S17. Ethnicity-stratified Cox survival model to 30 days based on age and sex. Survival modelled for median age 65 years and male sex. Survival over 30 days is comparable the unstratified model [Figure 4], however early mortality was greater in patients with Black ethnicity.



STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cohort studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	2, 4
Objectives	3	State specific objectives, including any prespecified hypotheses	2, 4
Methods			
Study design	4	Present key elements of study design early in the paper	4, 5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	4
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	N/A
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4, 5
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	4, 5
Bias	9	Describe any efforts to address potential sources of bias	5
Study size	10	Explain how the study size was arrived at	4
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	4, 5
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	5
		(*b*) Describe any methods used to examine subgroups and interactions	5
		(*c*) Explain how missing data were addressed	5
		(*d*) If applicable, explain how loss to follow-up was addressed	4, 5
		(*e*) Describe any sensitivity analyses	5
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	6, supplement
		(b) Give reasons for non-participation at each stage	supplement
		(c) Consider use of a flow diagram	supplement
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	6, table 1
		(b) Indicate number of participants with missing data for each variable of interest	6, table 1
		(c) Summarise follow-up time (eg, average and total amount)	6
Outcome data	15*	Report numbers of outcome events or summary measures over time	6, supplement
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	6, table 2, table 3, supplement
		(*b*) Report category boundaries when continuous variables were categorized	N/A
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	6
Discussion			
Key results	18	Summarise key results with reference to study objectives	7
Limitations			
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	3, 7
Generalisability	21	Discuss the generalisability (external validity) of the study results	7, 8
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	N/A

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Ethnicity and outcomes in patients hospitalised with COVID-19 infection in East London: an observational cohort study

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Ethnicity and outcomes in patients hospitalised with COVID-19 infection in East London: an observational cohort study

V. J. Apea[1‡], Y. I. Wan[2‡], R. Dhairyawan[3], Z. A. Puthucheary[4], R. M. Pearse[5], C. M. Orkin[6*], J. R. Prowle[7*]
‡Joint first authors
*Joint senior authors

1. A. Consultant Physician in Sexual Health and HIV Medicine, Sexual Health Clinical Lead, Barts Health NHS Trust, London, E1 1BB, UK
B. Honorary Senior Lecturer, Blizard Institute, Queen Mary University of London, E1 2AT, UK
v.apea@nhs.net

2. A. NIHR Clinical Lecturer, William Harvey Research Institute, Queen Mary University of London, EC1M 6BQ, UK
B. Specialty Registrar in Intensive Care Medicine & Anaesthesia, Barts Health NHS Trust, London, E1 1BB, UK yize.wan@qmul.ac.uk

3. A. Consultant Physician in Sexual Health and HIV Medicine, Barts Health NHS Trust, London, E1 1BB, UK
B. Honorary Senior Lecturer, Blizard Institute, Queen Mary University of London, E1 2AT, UK
rageshri.dhairyawan@nhs.net

4. A. Clinical Senior Lecturer, William Harvey Research Institute, Queen Mary University of London, EC1M 6BQ, UK
B. Honorary Consultant Physician in Intensive Care, Barts Health NHS Trust, London, E1 1BB, UK
z.puthucheary@qmul.ac.uk

5. A. NIHR Research Professor, William Harvey Research Institute, Queen Mary University of London, EC1M 6BQ, UK
B. Consultant Physician in Intensive Care Medicine and Clinical Director for Research & Development, Barts Health NHS Trust, London, E1 1BB, UK r.pearse@qmul.ac.uk

6. A. Professor of HIV Medicine, Blizard Institute, Queen Mary University of London, E1 2AT, UK
B. Clinical lead for HIV and HIV/Hep C Research, Barts Health NHS Trust, London, E1 1BB, UK
c.m.orkin@qmul.ac.uk

7. A. Senior Clinical Lecturer in Intensive Care Medicine, William Harvey Research Institute, Queen Mary University of London, EC1M 6BQ, UK
B. Consultant in Intensive Care and Renal Medicine, Barts Health NHS Trust, London, E1 1BB, UK
j.prowle@qmul.ac.uk

Corresponding author:
Yize I Wan, PhD
Adult Critical Care Unit,
The Royal London Hospital,
London E1 1BB
Email: yize.wan@qmul.ac.uk
Tel: +44 20 3594 40352

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Figures	5
References	34
Supplementary File	S1-S9

Keywords:
Ethnicity; COVID-19

Abstract

Objective
To describe outcomes within different ethnic groups of a cohort of hospitalised patients with confirmed COVID-19 infection. To quantify and describe the impact of a number of prognostic factors, including frailty and inflammatory markers.

Setting
Five acute NHS Hospitals in east London.

Design
Prospectively defined observational study using registry data.

Participants
1737 patients aged 16 years or over admitted to hospital with confirmed COVID-19 infection between 1st January and 13th May 2020.

Main outcome measures
The primary outcome was 30-day mortality from time of first hospital admission with COVID-19 diagnosis during or prior to admission. Secondary outcomes were 90-day mortality, intensive care unit (ICU) admission, ICU and hospital length of stay, and type and duration of organ support. Multivariable survival analyses were adjusted for potential confounders.

Results
1737 were included in our analysis of whom 511 had died by day 30 (29%). 538 (31%) were from Asian, 340 (20%) Black and 707 (40%) White backgrounds. Compared to White patients, those from minority ethnic backgrounds were younger, with differing comorbidity profiles and less frailty. Asian and Black patients were more likely to be admitted to ICU and to receive invasive ventilation (Odds ratio 1·54, [1·06-2·23]; p=0·023 and 1·80 [1·20-2·71]; p=0·005, respectively). After adjustment for age and sex, patients from Asian (Hazard ratio (HR) 1·49 [1·19-1·86]; p<0·001) and Black (HR 1·30 [1·02-1·65]; p=0·036) backgrounds were more likely to die. These findings persisted across a range of risk-factor adjusted analyses accounting for major comorbidities, obesity, smoking, frailty, and ABO blood group.

Conclusions
Patients from Asian and Black backgrounds had higher mortality from COVID-19 infection despite controlling for all previously identified confounders and frailty. Higher rates of invasive ventilation indicate greater acute disease severity. Our analyses suggest that patients of Asian and Black backgrounds suffered disproportionate rates of premature death from COVID-19.

Strengths and limitations of this study

- This study is one of the most comprehensive studies exploring COVID-19 outcomes in BAME populations so far reported including evaluation of linked comorbid and socioeconomic risk factors.
- This study was conducted in a single region where COVID-19 has had significant impact and thus not confounded by differences in incidence of COVID-19 disease across the UK, regional concentration of minority ethnic groups and regional differences in the time-course of the epidemic.
- In addition, we employed a pre-specified statistical analysis plan and performed multiple sensitivity analyses to test the robustness of our findings.
- In line with the vast majority of published COVID-19 analyses, we only included proven COVID-19 cases therefore suspected diagnoses should be considered in future studies, particularly those occurring outside of hospitals.
- Despite its size, our study lacked the power to assess a more detailed ethnicity breakdown and like many datasets, may not reflect the vast heterogeneity within ethnic categories (such as Bangladeshi, Pakistani, Black African or Black Caribbean).

Introduction

The novel *Severe Acute Respiratory Syndrome Coronavirus*-2 (SARS-CoV-2) which manifests as coronavirus disease 2019 (COVID-19) has led to a global pandemic(1). Older age, male sex, obesity and pre-existing health conditions such as diabetes and hypertension have all been identified as risk factors for poor outcomes(2-4). A disproportionate impact of disease severity and death on people from Black, Asian and minority ethnic (BAME) backgrounds has been reported, though not consistently. The UK Intensive Care National Audit and Research Centre (ICNARC) noted that whilst BAME groups only make up 14% of the UK population, they comprised 33% of COVID-19 patients on intensive care units(5). The degree of this excess risk also appears to differ across, and within, these heterogeneous ethnic groups. In the UK, recent analyses of data from the Office of National Statistics and NHS England described 2.5-4.3 fold greater COVID-19 mortality rates, compared to White groups, across a range of Black and South Asian ethnic groups(6). Whether this adverse association is driven by underlying comorbid disease, socio-economic inequality, genetic factors or a complex interplay of them all is unclear(7). Current data are limited in either number of COVID-19 patients, ethnic diversity or event rates with limited adjustment for known risk factors and potential predictors(8-12). There is an urgent need for the detailed characterisation of ethnic differences in COVID-19 outcomes and associated risk factors, within diverse populations, to inform practice and policy. Identifying and responding to these ethnic inequalities will be key to mitigating the disproportionate impact of COVID-19 on BAME patients.

Barts Health NHS Trust is the largest NHS trust in the UK, comprising six hospitals; The Royal London Hospital, Newham General Hospital, Whipps Cross Hospital, Mile End Hospital (Non-acute), St Bartholomew's Hospital and the London NHS Nightingale Hospital, a purposely built COVID-19 hospital. The hospitals serve the ethnically diverse and socially deprived communities of over 2.6 million people in east London including the London Borough of Newham which experienced 144.3 COVID-19 related deaths per 100,000 population(13), the highest mortality in the UK and Tower Hamlets which has the largest Bangladeshi population in England(14). This large, regional dataset afforded extensive analyses of COVID-19 patients of a higher acuity than other studies. We aimed to examine the demographic, socio-economic, behavioural, biochemical and clinical risk factors associated with outcomes within different ethnic groups of hospitalised COVID-19 patients, using multivariable survival analyses.

Methods

Study population

We considered all patients with confirmed SARS-CoV-2 infection and admitted to the five acute hospitals within Barts Health NHS Trust between 1st January and 13th May 2020. Diagnosis was made using one or more real-time RT-PCR. Those under 16 years were excluded. The first emergency admission encompassing the first positive SARS-CoV-2 test, or the first emergency admission within two weeks of positive outpatient testing was defined as the index admission, community diagnoses without an associated emergency hospital admission were excluded. Patients with unknown or undisclosed ethnicity status were collected for comparison but were not included in our primary ethnicity analysis.

Data collection

Clinical and demographic data, blood results and coding data from current and prior clinical encounters, were collated from the Barts Health Cerner Millennium Electronic Medical Record (EMR) data warehouse and locally held ICNARC databases by members of the direct clinical care team. Mortality data was available to 20th May 2020.

Definition of key variables

Ethnicity was defined using the NHS ethnic category codes and based on five high-level groups: White, Asian or Asian British, Black or Black British, Mixed and Other; to preserve statistical power the Mixed and Other categories were merged. Relative measures of socioeconomic deprivation were assessed using the English Indices of Deprivation 2020 by matching patient postcode to national index of multiple deprivation (IMD) quintiles using the Office of National Statistics Postcode Directory(15, 16). Baseline comorbid diseases and Hospital Frailty Risk Score (HFRS) were identified by mapping to ICD-10 coding(17). Body mass index (BMI) was calculated by height and weight measurements taken at or during the immediately preceding admission episode. Rockwood Clinical Frailty Scoring (RFS) was assessed by the admitting medical team and recorded in the EMR(18). Secondary haemophagocytic lymphohistiocytosis (sHLH) risk score was calculated from peak values of blood results(19). Full definitions are detailed in supplementary materials. National early warning score (NEWS) was recorded in the emergency room and general wards by clinical teams in the EMR and is presented as the total score from 6 physiological parameters(20).

Outcomes

The primary outcome was 30-day mortality from time of index COVID-19 hospital admission. Secondary endpoints were 90-day mortality, ICU admission, ICU length of stay, duration of organ support on ICU, need for mechanical ventilation, hospital length of stay, and discharge destination if discharged alive from hospital.

Statistical analyses

A prospective statistical analysis plan was developed(21). Baseline characteristics are presented as mean and standard deviation, median and interquartile range, or number and percentage, as appropriate. We compared proportions using Pearson's Chi-square test or Fisher's exact test and continuous variables using 2-sample t-test or Wilcoxon rank-sum test, as appropriate. Time-to-event analysis was undertaken with follow-up censored at 30 days, survivors with less than 30 days follow-up were censored at time of maximal follow-up. A Cox proportional hazards model was used to assess survival adjusted for age and sex. Age was the only continuous variable. A further multivariable Cox model was developed to assess the effect of pre-defined risk factors described as associated with adverse outcomes in COVID19: IMD quintile, smoking status, body mass index, diabetes, hypertension, and chronic kidney disease (CKD). The proportional-hazard assumption was assessed by inspection of scaled Schoenfeld residual plots and investigated by stratification(22). Logistic regression modelling of ethnicity on ICU treatment using mechanical ventilation was carried out. Effect measures are presented as hazard ratios (HR) or odds ratios (OR) with 95% confidence intervals (CI). All analyses were performed using R version 3.6.3 (R Core Team 2020).

Sensitivity analyses

To assess the effect of including patients with incomplete clinical data, missing data for baseline risk variables included in the multivariable Cox model was imputed using Multivariate Imputation by Chained Equations(23). Additional multivariable models were also carried out using aggregate Charlson comorbidity index (CCI) as a measure of total comorbid disease burden, and HFRS or RFS collected at hospital admission and ABO blood group. Longer-term survival to 90 days was assessed using Cox proportional hazards modelling adjusted for age and sex censored at time of maximal follow-up if survivors had less than 90 days follow-up.

Results

A total of 1996 patients, aged 16 years and older, with a confirmed SARS-CoV-2 test result with an acute Barts Health admission on or before 13th May 2020 were included in this study [Figure S1]. The recruitment window encompassed the peak time period of COVID-19 diagnoses [Figure S2]. The majority of patients were classified as being in the two most deprived socio-economic quintiles in England. The ethnic distribution was White (n=703, 35·2%), Asian or Asian British (n=538, 27·0%), Black or Black British (n=340, 17·0%), Mixed and Other (n=156, 7·8%) and unknown or undisclosed (n=259, 13·0%). Supporting results are detailed in supplementary file sections S1-S9 [Tables S1-S10, Figures S1-S17].

Population Characteristics

Baseline characteristics, interventions and outcomes across ethnic groups are shown in Table 1. Black and Asian ethnicity patients were significantly younger with a median age of 59 years (Asian) and 64 years (Black), compared to 73 years in the White group (p<0·001). Comorbidity data was available in 1700 (85.2%) of patients.

Burden of comorbid disease varied between ethnic groups in prevalence, type and age-distribution. Overall distribution of COVID risk factors varied with age and ethnicity with diabetes and CKD more prevalent at an earlier age in Asian and Black patients and frailty and dementia more prevalent in older White patients [Figure 1].

Around one in four patients developed early acute kidney injury (AKI) within seven days of hospital admission, rates of AKI were highest in the Black group (34·7%). Patients in the Black group had higher levels of inflammation CRP (median CRP 181·5 mg/L) and fibrinolysis (median D-dimer 2·5 mg/L) compared to other ethnicities. As a measure of extent of early physiological derangement UK National Early Warning Score (NEWS) was available in 1443 patients, in comparison to White patients first NEWS was modestly higher in Asian patients (mean 4.2 vs. 3.6), p=0.001, but not in Black patients (mean 3.7 vs 3.6).

Age and sex adjusted 30-day mortality

We included 1737 Asian, Black and White patients in the primary outcome analysis. Total mortality to 20th May 2020 was 28·7% (n=573). Based on the raw data, a greater proportion of White patients died (32·7%) compared to Asian (21·1%) and Black (29·7%) patients. The majority of deaths (93·7%) occurred within 30 days of hospital admission. However, after adjustment for the between-group differences in age and sex, patients from Asian and Black ethnic groups were at significantly higher risk of death within 30 days compared to White patients (Asian ethnicity (HR 1·49, CI 1·19-1·86, p<0·001); Black patients (HR 1·30, CI 1·02-1·63, p=0·036). No association was observed in the smaller Mixed and Other Ethnicity group (HR 1·08, CI 0·75-1·57, p=0·682) [Table 2, Figures 2 and 3]. There was some evidence of non-proportionality for the association between ethnicity and risk of death over time [Figure S16], consequently these HRs should be interpreted as a weighted average over the 30-day follow up period. To investigate change in risk over time we developed an ethnicity-stratified Cox-model, this supported the findings of the unstratified model, but suggested that Black ethnicity might be associated with a higher early rate of death [Figure S17].

Multivariable survival modelling

After inclusion of IMD quintile, smoking history, BMI ≥30 kg/m^2, diabetes, hypertension, and CKD in a multivariable survival analysis, the association with increased rate of death persisted in Asian patients (HR 1·48, CI 1·09-2·01, p=0·011; n=1006). In Black patients, the magnitude of the mortality trend was unchanged, however was outside the limits of standard statistical significance (HR 1·32, CI 0·96-1·84, p=0·090; n=1006), potentially due to the smaller sample size. In this model older age, male sex, smoking, BMI ≥30 kg/m2 and CKD were statistically associated with risk of death [Table 3, Figures 4 and 5] and there was no statistical evidence that ethnicity violated the proportional hazards assumption. The associations were broadly unchanged when the model was re-fitted after multiple imputation of missing values [Table S4].

Sensitivity analyses for further multivariable survival models were developed to examine the influence of total comorbidity burden, as assessed by CCI [Table S5], and measures of frailty, the RFS or HFRS [Tables S6, S7] as well as ABO blood group [Table S8]. In all these analyses the association between Black and Asian ethnicity and 30-day mortality remained significant. Adjusting for RFS raised the odds of 30-day mortality to a HR of 1·98 (CI 1·37-2·86; p<0.001) in Asian groups and to a HR of 1·67 (CI 1·14-2·45; p=0.009) in Black groups, with similar effect size in analysis adjusted for the HFRS. After inclusion of ABO blood grouping in and age and sex adjusted multivariable model risks of death in Asian, Black, and Mixed and Other ethnic groups was increased. Asian ethnicity also continued to be associated with greater risks of death through to 90 days follow-up (HR 1·46, CI 1·18-1·81, p<0·001; n=1737) [Table S9].

Critical Care related outcomes

In the White group, 11·0% of patients were admitted to ICU compared to 20·1% of the Asian group and 18·5% of the Black group (p<0.001). In those admitted to ICU, rates of mechanical ventilation requiring intubation did not differ significantly by ethnicity at 76·6% in the White group, 72·2% in the Asian group and 79·4% in the Black group. Similarly, while rates of ICU admission differed significantly between ethnic groups, time from hospital to ICU admission and length of ICU stay did not. Across the entire hospitalised cohort Asian (OR 1·54, CI 1·06-2·23, p=0·023; n=1737) and Black (OR 1·80, CI 1·20-2·71, p=0·005; n=1737) ethnicities were associated with increased age and sex adjusted-risk of receiving invasive mechanical ventilation in ICU [Table S10]. There was a trend toward increased renal replacement therapy use in Black patients (41.3%) admitted to ICU compared to 20-25% across other ethnic groups (p=0.09).

Discussion

We report on treatment and outcomes in COVID-19 patients hospitalised in East London throughout the peak of the UK pandemic, a population with the UK's highest COVID-19 mortality. To our knowledge this is one of the largest UK hospital COVID-19 cohorts reported, and certainly the most diverse, with only 35.2% of 1996 patients identified as White ethnicity. We found those of Asian ethnicity to be at the highest risk of death within 30 days (HR 1·49, CI 1·19-1·86, p<0·001), a finding that persisted at 90 days. Risk of death in Black patients was also greater than those of White ethnicity (HR 1·30, CI 1·02-1·63, p=0·036). This disparity extended to need for ICU care with Asian and Black patients experiencing a 50-80% increased risk of receiving mechanical ventilation in ICU compared to White patients of a similar age.

Strengths and Limitations

We believe this study is both one of the largest and most detailed of studies exploring COVID-19 outcomes in BAME populations so far reported. In contrast to many previous studies examining ethnicity and COVID-19 outcomes we were able to address the contributions of socio-economic deprivation, comorbid disease, pre-morbid function, lifestyle and demographic factors to ethnic disparities in COVID-19 outcomes, including ICU interventions. Our analysis was strengthened by the inclusion of measures of frailty which is a critical determinant of outcomes in acute disease as well as a potential driver of clinician decision-making. It should be acknowledged, however, that frailty has social and biological dimensions and measures have not been extensively validated in BAME groups.

Importantly, this study was conducted in a single region where COVID-19 has had significant impact and thus is not confounded by differences in incidence of COVID-19 disease across the UK, regional concentration of minority ethnic groups and regional differences in the time-course of the epidemic. In addition, we employed a pre-specified statistical analysis plan and performed multiple sensitivity analyses to test the robustness of our findings.

Limitations in our analyses must also be considered. Importantly, SARS-CoV-2 testing has an appreciable false negative rate and suspected, but not proven, cases are an important group. Nevertheless, given that clinical suspicion varied both between cases and across the time-course of the epidemic with coding of suspected cases being inconsistent, in line with the vast majority of published COVID-19 analyses, we only included proven COVID-19 cases. Testing was available for all hospitalised patients with suspected COVID-19 disease, so availability of testing was not a bias. However, suspected diagnoses should be considered in future studies, particularly those occurring outside of hospitals, where not all clinical diagnoses may have been tested.

Similar to many hospital datasets there were missing data for a proportion of co-variates(8, 9), however 85% of patients had coding data for assessment of comorbidity and 63% measured height and weight data, providing a large sample with detailed data for analysis. We also imputed missing data and performed sensitivity analyses on our multivariable comorbidity models. This reinforced the observed ethnic differences, providing further confidence that our findings were not affected by missing data.

Like many datasets, our ethnic categorisations were aggregated and did not reflect the vast heterogeneity within ethnic categories (such as Bangladeshi, Pakistani, Black African or Black Caribbean). Indeed, the descriptive term "BAME" itself is particularly crude and we recognise its limitation. Despite its size, our study lacked the power to assess a more detailed ethnicity breakdown. In addition, our observations in those of Asian ethnicity are likely skewed by our large Bangladeshi community, which has specific socio-economic and healthcare inequalities. It is therefore important that, suitably powered, analyses are conducted to expose differences between sub-ethnic categories. Similarly, whilst we have explored socio-economic factors, our analysis does not allow us to

contextualise a number of potential socio-spatial factors including household composition, environmental factors and occupation. These should be considered in future research.

Comparison with other studies

Our findings differ from predominant reports in the UK and US in which Black ethnicity has been consistently associated with greater COVID-related mortality(6, 24). Preliminary analyses of the UK ICNARC report on COVID-19 in critical care highlighted Black ethnicity with the highest likelihood of being admitted to intensive care compared to a matched population (10.7% versus 6.5%)(25). Similarly, in a large UK primary care linked cohort, Black patients were also to found to be at highest risk of COVID-related death(9). In a US study, the composite relative risk of COVID-related death compared to White ethnicity was 3.57 in Black populations, and 1.88 for Latinos(24). Our findings suggest specific South Asian communities may have at least the same or higher risk in COVID-19 as those of Black background. This may reflect characteristics of the large South Asian, and specifically Bangladeshi, community in East London, poorly represented in other studies. Recently the *ISARIC CCP-UK* investigators have described association of ethnicity and outcome in a very large cohort of UK patients, finding Asian, but not Black background was associated with increased risk of death in confirmed or suspected COVID-19(26). While this study documented up to 40% of UK COVID cases, it represented a selection from the total COVID population from across the UK, and, at least in terms of ICU cases, ethnic minorities were significantly under-represented compared to the English ICU COVID population. In contrast while smaller, this study focused on an unbiased population comprising all hospitalised patients in a single geographical area with a much higher level of ethnic diversity. Consequently, we feel our analysis complements ISARIC CCP-UK and provides greater clinical detail in a regionally homogenous population.

Potential confounding associations with risk of death in COVID-19

Older age has been significantly associated with increased COVID-19 mortality across a range of studies(2-4). In our cohort, patients from Asian and Black backgrounds were strikingly younger than White patients. However, despite the expected protective factor of younger age, when this was accounted for, those from Black and Asian backgrounds were more likely to die. The prevalence of comorbid disease has been well described as a risk factor for COVID-19 disease and death(3, 4). We found different ethnic groups had differing age-distribution of baseline comorbidities such as hypertension, diabetes, chronic obstructive pulmonary disease and dementia. Despite accounting for these and other described predictors of poor outcomes, increased risk of death in Asian and Black populations was not attenuated, suggesting comorbidities are not the sole drivers of ethnicity-associated risk.

ABO blood group has recently been suggested to affect the risk of symptomatic COVID-19 and need for respiratory support with supplemental oxygen(12, 27). In these analyses blood group O was associated with less disease acquisition than group A. As there are well-described differences in blood group distribution with ethnicity (in particular, prevalence of blood group B in Asian and to a lesser extent Black populations), in a post-hoc analysis we assessed the association between ABO group and risk of death in 875 patients with blood group data. In contrast to studies focused on risk of COVID-19 acquisition in our cohort of hospitalised COVID diagnoses, blood group O was associated with higher risk of death and blood group B the lowest. Accordingly, when we included ABO blood group in a multivariable survival analysis with age, sex the association between Black and Asian background and increased risk of death was not attenuated but magnified. This suggests ethnic imbalances in blood group distribution did not explain the mortality associations observed in our population.

Patients identified as frail have been predicted to have worse COVID-19 related health outcomes(28), and lower likelihood of benefiting from complex acute interventions, including critical care. In this study White patients, in addition to being notably older than other ethnicities, had higher degrees of frailty. Accounting for measures of frailty magnified the association seen between Asian and Black ethnicity and death. This suggests that whilst in White patients COVID-19 related death may have occurred in already frail and functionally vulnerable patients, in both Asian and Black patients, COVID-19 related deaths are likely to be occurring prematurely, in younger, fitter individuals with less functional vulnerability.

In our cohort, all ethnic groups experienced high levels of deprivation, however, worse deprivation was not associated with higher likelihood of mortality, suggesting ethnicity may affect outcomes independent of purely geographical and socio-economic factors(29).

We found evidence for worse disease severity in Black and Asian groups as evidenced by higher rates of ICU admission and higher rates of AKI, and high levels of D-dimers and CRP in Black patients. High CRP and D-dimer levels have been identified as important inflammatory markers which strongly correlate with COVID-19 disease severity and prognosis(30). Our data suggest potential biological differences in host-response to COVID-19 may occur between ethnicities, however, causative associations in determining COVID-19-related mortality have not been demonstrated.

Finally, although COVID-19 has cast the effects of ethnic inequalities on health outcomes into sharp focus, these inequalities are not new. Health inequalities within and between ethnic minority groups are widely documented and the effects of structural racism are transmitted across generations(31). The risk factors already discussed such comorbidity and obesity are speculated to intersect and be inextricably linked with wider social determinants such as poor living conditions, key worker roles and language barriers which impede the adoption of preventative measures(29, 32, 33). Some researchers have postulated that ethnic inequalities may be associated with decreased symptom recognition and poor engagement with health services(34). However, while frequency of ICU admission, AKI and need for mechanical ventilation suggests more severe peak-disease in minority ethnic groups, time to ICU admission did not differ and differences in first total NEWS were at most modest, suggesting against a large effect from delayed presentation.

Conclusion
In this analysis of a large, ethnically diverse and socio-economically challenged cohort, hospitalised patients of Asian and Black background with COVID-19 were at increased risk of premature death, independent of frailty, comorbidities and social deprivation. Failure to robustly respond to the ethnic disparities so conspicuously unmasked during the COVID-19 pandemic can only further entrench and inflict them on future generations.

Data sharing agreement
The statistical analysis plan can be accessed online. The authors will be happy to consider additional analyses of the anonymised dataset on request. The need for stringent measures to prevent re-identification of individuals within a discrete geographical location and limited time-period however preclude sharing of patient level dataset in a GDPR compliant form.

Author contribution
V Apea developed the study concept, designed the study, wrote the study protocol, submitted the ethics application, provided critical review of the findings and wrote the manuscript. Y Wan wrote the statistical analysis plan, performed data extraction, performed statistical analysis, provided critical review of the findings and wrote the manuscript. R Dhairyawan developed the study concept, designed the study, provided critical review of the findings and wrote the manuscript. Z Puthucheary provided critical review of the findings and wrote the manuscript. R Pearse developed the study concept, designed the study, provided critical review of the findings and wrote the manuscript. C Orkin developed the study concept, designed the study, provided critical review of the findings and wrote the manuscript. J Prowle developed the study concept, designed the study, wrote the study protocol, submitted the ethics application, performed data extraction, performed statistical analysis, provided critical review of the findings and wrote the manuscript. All authors approved the final version of the manuscript. The data was collated and analysed on behalf of all clinicians at Barts Health.

Study Concept and Design	VJA CMO RD JRP RMP
Ethics application and Approvals	VJA JRP
Study protocol and analysis plan	VJA YIW JRP
Data Extraction	YIW JRP
Data Analysis	YIW JRP
Critical review of finding	All authors
Manuscript writing	VJA CMO YIW RD ZAP RP JRP
Review of final submission	All authors

Public and Patient Involvement statement
COVID-19 has presented unique challenges and warranted a unique response in research. This protocol has been swiftly developed in response to concerning data suggesting poorer outcomes of patients with confirmed COVID-19 from a BAME background. This data has led the general public, via social media and community influencers, to call for governmental and health bodies to urgently review patient outcomes to explore this emerging inequality and respond appropriately to mitigate further deaths and inequity. Whilst no direct public and patient involvement has taken place, the research team believe the study in line with current public and patient mandate.

Ethics approval
This study was approved by HRA and Yorkshire & The Humber - Bradford Leeds Research Ethics Committee (Ethics reference **20/YH/0159**). The study was sponsored by Barts Health NHS Trust.

Transparency declaration
J Prowle (the manuscript's guarantor) affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned and registered have been explained.

Role of the funding source
No external funding. The corresponding author had full access to all the data and had final responsibility for the decision to submit for publication**.**

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Conflict of Interest
All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and declare: no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

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Figure legends

Figure 1. Heat map of prognostic factors in COVID-19 hospital admissions by age and ethnic background showing proportions within each ethnic group for each age group. Asian and Black patients differed from those of white background in the presence of risk factors and their age distribution however differences were also apparent between different Black and Minority Ethnic groups at different ages. Proportions are of those with data (see Table 1). BMI: body mass index, COPD: chronic obstructive pulmonary disease, DM: diabetes mellitus, HT: hypertension, CKD: chronic kidney disease.

Figure 2. Forest plot showing hazards ratios of mortality to 30 days comparing ethnic groups, age and sex corrected, on log scale.

Figure 3. Survival curve to 30 days comparing predicted survival of Asian, Black, and White ethnic groups (Mixed and Other group omitted for clarity), in an age and sex adjusted Cox-hazard analysis. Survival curves adjusted to median age 65 years and male sex.

Figure 4. Forest plot showing hazards ratios of mortality to 30 days comparing ethnic groups, age and sex corrected, on log scale. Additional variables included index of multiple deprivation (IMD) quintile (5 least deprived), smoking, BMI ≥30 kg/m^2, diabetes, HTN: hypertension, CKD: chronic kidney disease.

Figure 5. Survival curve to 30 days from multivariable analysis comparing Asian, Black, and White ethnic groups. Survival modelled for median age 65 years and male sex, index of multiple deprivation (IMD) least deprived quintile, no history of baseline risk factors defined as Non-smoking, BMI <30 kg/m^2 and No diabetes, hypertension or chronic kidney disease. Statistically significant difference in survival between Asian group and White group persists after adjustment for age, sex, social deprivation and major COVID-19 risk factors.

Tables

Table 1. Study population baseline characteristics stratified by ethnic group, n (%) unless otherwise stated. Total n=1996 unless otherwise stated. P values based on Chi-square (for categorical) or Kruskal-Wallis test (for continuous). SD: standard deviation, IQR: interquartile range, IMD: index of multiple deprivation, BMI: body mass index, TIA: transient ischaemic accident, HTN: hypertension, CKD: chronic kidney disease, sHLH: secondary haemophagocytic lymphohistiocytosis (without known underlying immunosuppression and bone marrow aspirate data), CRP: C-reactive protein, NEWS: national early warning score, ICU: intensive care unit, RRT: renal replacement therapy.

	Stratified by ethnic group					
	Asian or Asian British	**Black or Black British**	**Mixed and Other Ethnic Groups**	**White**	**Unknown and Undisclosed**	p value
n	538	340	156	703	259	
Age (years) Mean (SD)	57·8 (18·5)	64·2 (16·9)	59·5 (17·2)	69·4 (17·7)	59·8 (16·5)	<0·001
Age (years) Median (IQR)	59·0 (44·0-71·0)	64·0 (53·0-79·0)	59·0 (47·8-72·3)	73·0 (58·0-84·0)	61·0 (50·0-71·5)	<0·001
Male	332 (61·7)	193 (56·8)	103 (66·0)	404 (57·5)	178 (68·7)	0·01
IMD quintile [n=1980]						<0·001
1 (most deprived)	139 (26·0)	124 (36·7)	50 (32·9)	183 (26·2)	66 (25·7)	
2	291 (54·5)	165 (48·8)	72 (47·4)	269 (38·5)	124 (48·2)	
3	49 (9·2)	34 (10·1)	20 (13·2)	99 (14·2)	44 (17·1)	
4	35 (6·6)	9 (2·7)	7 (4·6)	86 (12·3)	18 (7·0)	
5 (least deprived)	20 (3·7)	6 (1·8)	3 (2·0)	62 (8·9)	5 (1·9)	
Smoking [n=1700]	30 (6·6)	21 (7·1)	10 (8·3)	91 (14·8)	21 (9·8)	<0·001
BMI [n=1248]						
Median (IQR)	26·9 (24·1-31·1)	28·2 (24·6-31·8)	25·9 (23·1-29·0)	26·3 (22·5-31·6)	26·3 (22·5-30·8)	0·04
By category						0·04
<18·5 kg/m^2	9 (2·8)	8 (3·6)	1 (1·3)	34 (6·9)	11 (8·5)	
18·5 - <25 kg/m^2	101 (31·2)	57 (25·3)	31 (40·3)	160 (32·5)	43 (33·1)	
25 - <30 kg/m^2	114 (35·2)	83 (36·9)	27 (35·1)	145 (29·5)	40 (30·8)	
30 - <40 kg/m^2	87 (26·9)	65 (28·9)	17 (22·1)	126 (25·6)	28 (21·5)	
≥40 kg/m^2	13 (4·0)	12 (5·3)	1 (1·3)	27 (5·5)	8 (6·2)	
Co-morbidity [n=1700]						
Obesity	108 (23·6)	82 (27·9)	18 (14·9)	161 (26·2)	40 (18·7)	0·01
Ischaemic heart disease	102 (22·3)	62 (21·1)	12 (9·9)	149 (24·3)	21 (9·8)	<0·001
Myocardial infarction	55 (12·0)	23 (7·8)	6 (5·0)	83 (13·5)	14 (6·5)	0·002
Congestive heart failure	67 (14·7)	54 (18·4)	8 (6·6)	114 (18·6)	17 (7·9)	<0·001

Peripheral vascular disease	33 (7·2)	35 (11·9)	7 (5·8)	67 (10·9)	16 (7·5)	0·06
Cerebral vascular accident or TIA	54 (11·8)	54 (18·4)	11 (9·1)	157 (25·6)	16 (7·5)	<0·001
Dementia	25 (5·5)	27 (9·2)	5 (4·1)	103 (16·8)	7 (3·3)	<0·001
Chronic obstructive pulmonary disease	119 (26·0)	45 (15·3)	18 (14·9)	181 (29·5)	34 (15·9)	<0·001
Diabetes	220 (48·1)	157 (53·4)	49 (40·5)	179 (29·2)	59 (27·6)	<0·001
HTN	261 (57·1)	212 (72·1)	64 (52·9)	376 (61·2)	96 (44·9)	<0·001
Moderate to severe CKD	92 (20·1)	93 (31·6)	16 (13·2)	145 (23·6)	17 (7·9)	<0·001
End-stage renal disease	39 (8·5)	36 (12·2)	7 (5·8)	27 (4·4)	4 (1·9)	<0·001
Liver disease	49 (9·1)	24 (7·1)	12 (7·7)	58 (8·3)	12 (4·6)	0·25
Cancer	30 (6·6)	26 (8·8)	8 (6·6)	68 (11·1)	12 (5·6)	0·04
Cancer with metastases	8 (1·8)	5 (1·7)	1 (0·8)	22 (3·6)	6 (2·8)	0·18
Acquired immunodeficiency syndrome	0 (0·0)	5 (1·7)	0 (0·0)	1 (0·2)	0 (0·0)	0·001
Charlson comorbidity index [n=1700]						<0·001
0	131 (28·7)	66 (22·4)	42 (34·7)	143 (23·3)	91 (42·5)	
1-2	178 (38·9)	100 (34·0)	50 (41·3)	203 (33·1)	88 (41·1)	
3-4	70 (15·3)	52 (17·7)	16 (13·2)	146 (23·8)	20 (9·3)	
≥5	78 (17·1)	76 (25·9)	13 (10·7)	122 (19·9)	15 (7·0)	
Rockwood frailty Score [n=831]						<0·001
1-2 (very fit, well)	31 (15·9)	6 (4·3)	7 (14·9)	36 (9·7)	15 (18·8)	
3-4 (managing well, vulnerable)	87 (44·6)	51 (36·7)	17 (36·2)	118 (31·9)	32 (40·0)	
5-6 (mildly to severely frail)	65 (33·3)	73 (52·5)	18 (38·3)	174 (47·0)	29 (36·2)	
8-9 (very severely frail, terminally ill)	12 (6·2)	9 (6·5)	5 (10·6)	42 (11·4)	4 (5·0)	
Hospital frailty Risk Score [n=1700]						<0·001
<5 (low risk)	240 (52·5)	123 (41·8)	66 (54·5)	197 (32·1)	117 (54·7)	
5-15 (intermediate risk)	132 (28·9)	87 (29·6)	38 (31·4)	150 (24·4)	73 (34·1)	
≥15 (high risk)	85 (18·6)	84 (28·6)	17 (14·0)	267 (43·5)	24 (11·2)	
Baseline eGFR ml/min/1·72m² [n=1525]						
Median (IQR)	72·8 (53·3-92·7)	56·4 (36·2-80·2)	75·6 (54·2-91·4)	64·1 (46·2-82·0)	78·2 (61·5-88·7)	<0·001
eGFR <60	130 (29·6)	135 (48·6)	26 (26·0)	239 (40·5)	29 (24·6)	<0·001
Acute kidney injury first 7 days [n=1673]	98 (22·2)	101 (34·7)	32 (24·6)	151 (24·4)	48 (25·0)	0·003
Blood results during admission						

Highest creatinine µmol/L [n=1691]						<0·001
Median (IQR)	91·0 (72·0-157·0)	119·0 (80·0-260·0)	88·0 (71·8-120·3)	98·0 (76·0-147·0)	94·0 (75·0-132·0)	
Highest CRP [n=1761]						<0·001
Median (IQR)	146·0 (72·0-287·8)	181·5 (99·3-289·8)	132·0 (66·0-226·0)	136·0 (68·0-237·0)	156·0 (75·5-272·5)	
Highest D-dimer mg/L [n=968]						<0·001
Median (IQR)	1·0 (0·5-3·5)	2·5 (0·9-10·3)	1·1 (0·5-2·7)	1·4 (0·6-3·4)	1·5 (0·7-6·3)	
Highest sHLH score [n=1881] Mean (SD)	31·1 (27·1)	30·0 (27·9)	27·6 (28·3)	26·4 (24·8)	32·1 (26·7)	0·01
Blood Group [n=875]						<0·001
A	67 (28·4)	37 (23·3)	15 (35·7)	150 (42·1)	36 (43·9)	
AB	14 (5·9)	11 (6·9)	0 (0·0)	12 (3·4)	6 (7·3)	
B	78 (33·1)	37 (23·3)	13 (31·0)	32 (9·0)	8 (9·8)	
O	77 (32·6)	74 (46·5)	14 (33·3)	162 (45·5)	32 (39·0)	
NEWS (first available) [n=1443] Mean (SD)	4·2 (2·6)	3·7 (2·2)	4·0 (2·3)	3·6 (2·5)	3·8 (2·6)	0·001
Intensive care unit (ICU)						
ICU admission	108 (20·1)	63 (18·5)	28 (17·9)	77 (11·0)	85 (32·8)	<0·001
Days in hospital before ICU Mean (SD)	2·3 (5·2)	2·9 (5·1)	1·1 (1·8)	2·3 (11·4)	1·8 (4·2)	0·75
ICU length of stay Median (IQR)	8·0 (3·0-15·2)	8·1 (3·5-14·1)	8·5 (5·0-13·1)	8·0 (3·9-12·0)	10·0 (6·0-16·0)	0·30
Mechanical ventilation within ICU admission	78 (72·2)	50 (79·4)	23 (82·1)	59 (76·6)	71 (83·5)	0·40
RRT within ICU admission	28 (25·9)	26 (41·3)	7 (25·0)	20 (26·0)	18 (21·2)	0·09
Days on organ support						
Advanced respiratory Mean (SD)	11·0 (10·8)	9·4 (8·8)	8·2 (7·1)	7·8 (7·8)	10·3 (8·0)	0·14
Total respiratory Mean (SD)	13·1 (10·4)	11·9 (8·9)	9·8 (7·0)	9·6 (7·7)	11·9 (7·6)	0·08
Cardiovascular system Mean (SD)	13·4 (10·9)	11·5 (8·6)	9·9 (7·2)	9·8 (8·3)	11·8 (7·5)	0·07
Renal Mean (SD)	2·4 (5·5)	4·4 (6·6)	2·1 (4·7)	2·7 (5·7)	1·5 (3·8)	0·03
Total number of organ systems						0·15
0	1 (0·9)	0 (0·0)	0 (0·0)	1 (1·3)	1 (1·2)	
1	3 (2·8)	4 (6·3)	1 (3·6)	5 (6·5)	0 (0·0)	
2	76 (70·4)	33 (52·4)	20 (71·4)	52 (67·5)	66 (77·6)	
3	28 (25·9)	26 (41·3)	7 (25·0)	19 (24·7)	18 (21·2)	
Outcomes						
Died	146 (27·1)	101 (29·7)	34 (21·8)	230 (32·7)	62 (23·9)	0·01

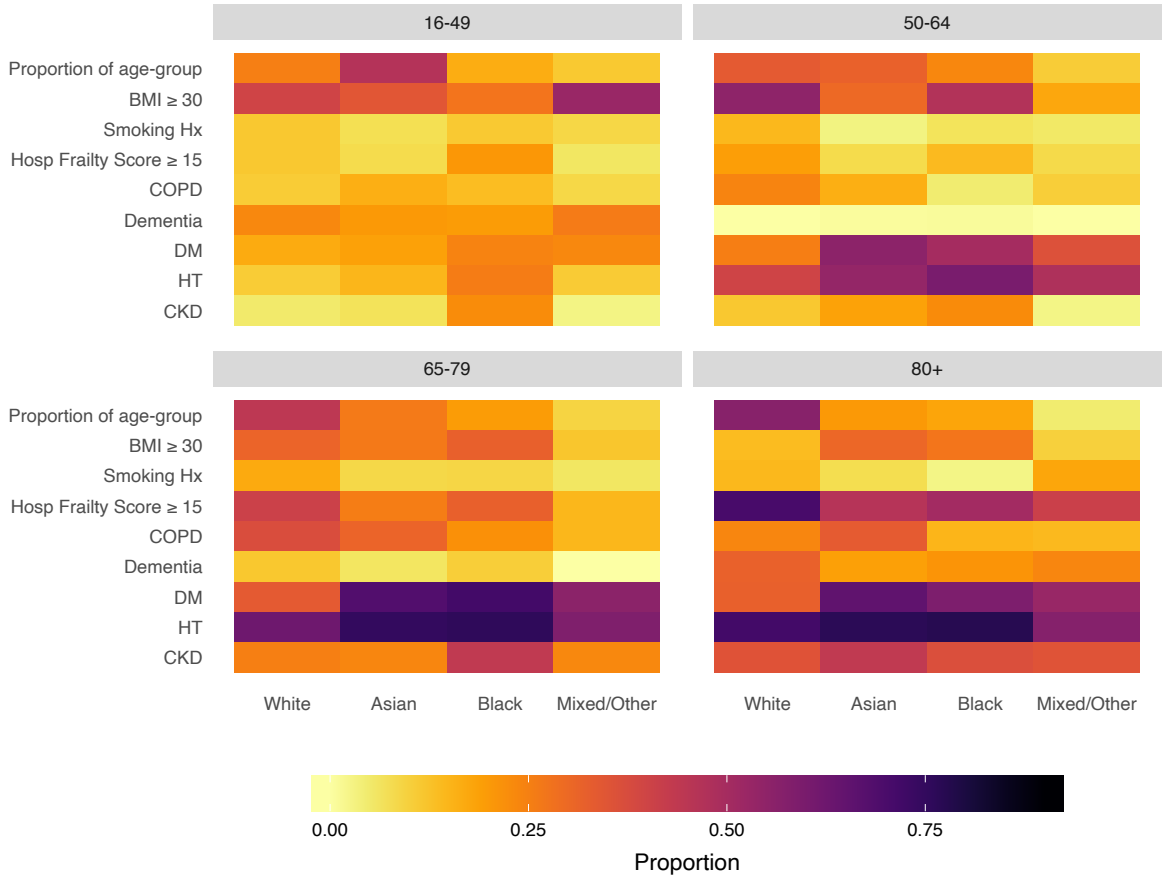
Days to death Mean (SD)	9·7 (10·0)	9·1 (11·0)	11·0 (9·8)	12·9 (13·6)	12·7 (10·0)	0·02
Days to death Median (IQR)	6·0 (3·0-12·0)	5·0 (3·0-11·0)	10·5 (4·3-14·0)	9·0 (4·0-16·0)	10 (6·0-17·0)	<0·001
Died within 30 days	138 (25·7)	97 (28·5)	33 (21·2)	210 (29·9)	58 (22·4)	0·05
Died within 90 days	146 (27·1)	101 (29·7)	34 (21·8)	229 (32·6)	62 (23·9)	0·01
Still in hospital	7 (1·3)	6 (1·8)	3 (1·9)	6 (0·9)	5 (1·9)	0·60
Hospital length of stay Median (IQR)	5·0 (3·0-10·0)	7·0 (4·0-12·0)	5·0 (3·0-11·0)	8·0 (4·0-15·0)	8·0 (4·0-15·0)	<0·001
Discharged Hospital alive	402 (74·7)	241 (70·9)	122 (78·2)	487 (69·3)	200 (77·2)	0·03
Discharge destination [n=1429]						<0·001
Care home or equivalent	7 (1·8)	5 (2·1)	0 (0·0)	40 (8·3)	8 (4·0)	
Health-related institution	7 (1·8)	10 (4·3)	8 (6·7)	23 (4·8)	37 (18·7)	
Usual place of residence	373 (94·4)	216 (91·9)	110 (91·7)	403 (83·8)	152 (76·8)	
Hospice or equivalent	1 (0·3)	0 (0·0)	0 (0·0)	2 (0·4)	1 (0·5)	
Temporary place of residence	7 (1·8)	4 (1·7)	2 (1·7)	13 (2·7)	0 (0·0)	

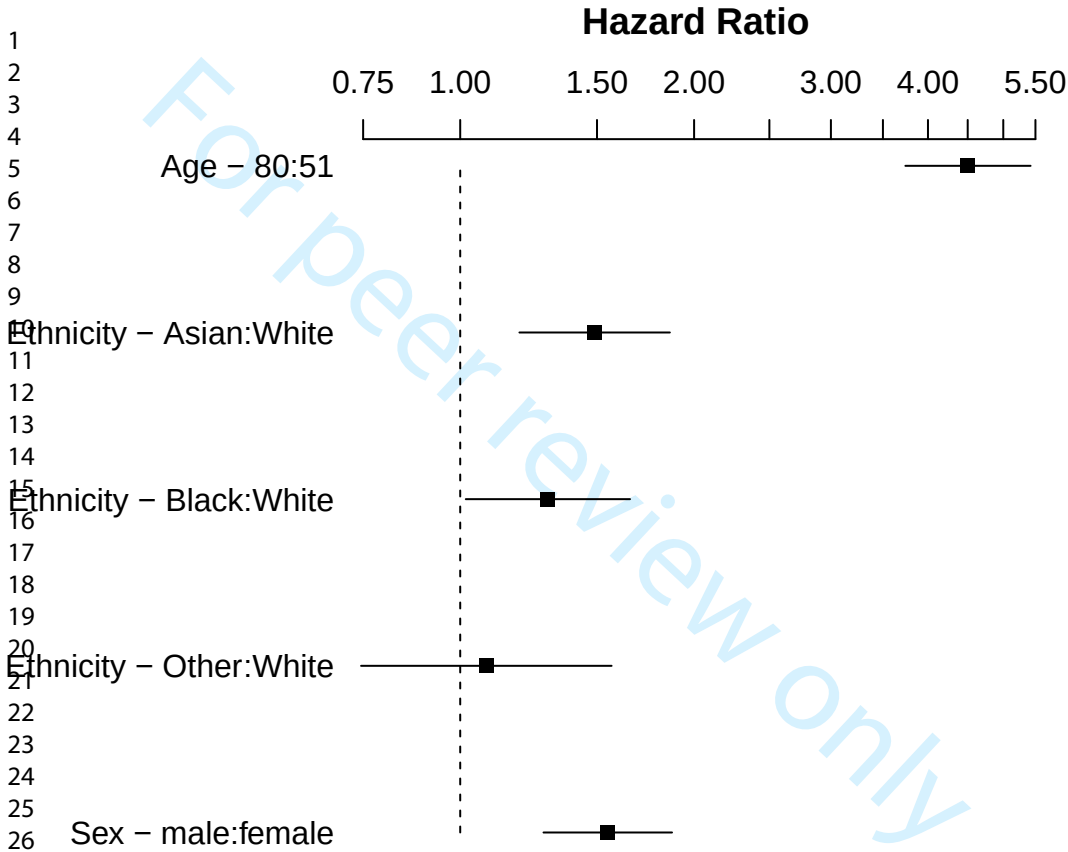
Table 2. Association of ethnic group with mortality to 30 days using Cox proportional hazards modelling, age and sex corrected. Censored to 30 days follow up, observations 1737, events 478.

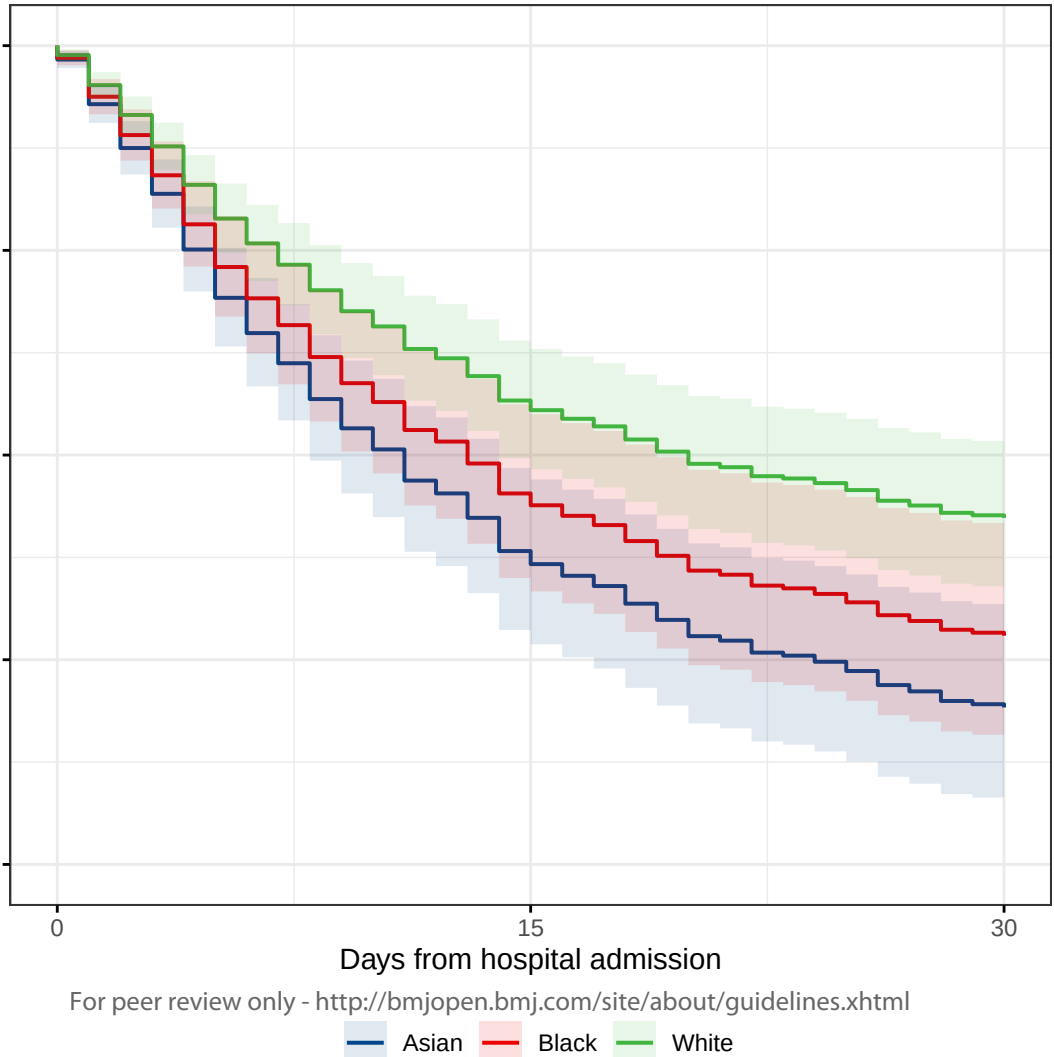
	n		Unadjusted	
	Total	**Events**	**Hazard ratio (95% CI)**	**p value**
Age (25th vs 75th centile)	-	-	4·50 (3·74-5·42)	<0·0001
Sex (Male)	-	-	1·55 (1·28-1·87)	<0·0001
Ethnic group				
Asian or Asian British	521	134	1·49 (1·19-1·86)	<0·001
Black or Black British	331	94	1·30 (1.02-1·65)	0·036
Mixed and Other ethnic groups	150	34	1·08 (0·75-1·57)	0·682
White	674	206	Reference	-

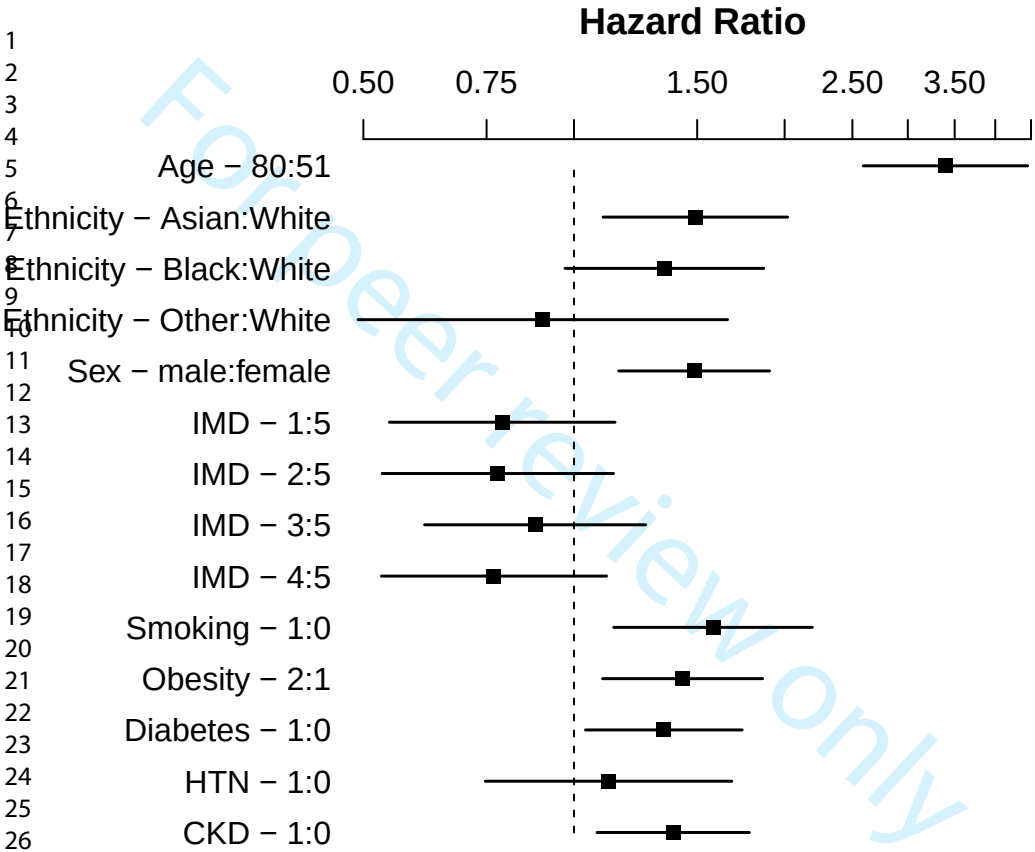
Table 3. Multivariable analysis of mortality to 30 days using Cox proportional hazards modelling, age and sex corrected. Variables included IMD quintile, smoking, BMI ≥30 kg/m^2, diabetes, HTN: hypertension, CKD: chronic kidney disease. Censored to 30 days follow up, observations 1006, events 281.

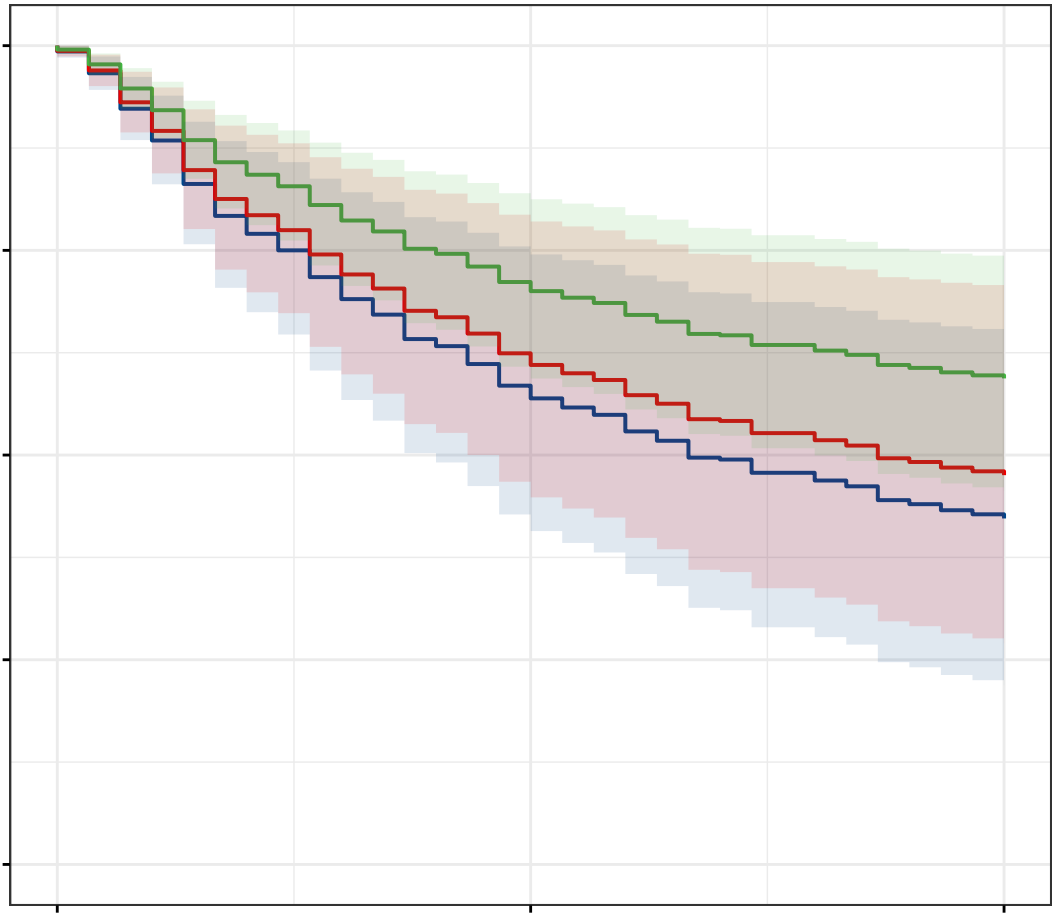
	Adjusted	
	Hazard ratio (95% CI)	**p value**
Age (25th vs 75th centile)	3·24 (2·46-4·26)	<0·0001
Sex (Male)	1·47 (1·15-1·88)	0·002
Ethnic group		
Asian or Asian British	1·48 (1·09-2·01)	0·011
Black or Black British	1·32 (0·96-1·84)	0·090
Mixed and Other ethnic groups	0·90 (0·49-1·65)	0·733
White	Reference	-
IMD quintile		
1 (most deprived)	0·79 (0·55-1·14)	0·213
2	0·79 (0·54-1·15)	0·218
3	0·88 (0·61-1·27)	0·503
4	0·77 (0·53-1·12)	0·176
5 (least deprived)	Reference	-
Smoking	1·56 (1·13-2·17)	0·008
BMI ≥30 kg/m^2	1·42 (1·09-1·85)	0·009
Diabetes	1·29 (1·00-1·67)	0·055
HTN	1·32 (0·92-1·89)	0·131
CKD	1·34 (1·04-1·73)	0·023


16-49
50-64
65-79
80+
Proportion of age-group
BMI ≥ 30
Smoking Hx
Hosp Frailty Score ≥ 15
COPD
Dementia
DM
HT
CKD
White
Asian
Black
Mixed/Other
0.00
0.25
0.50
0.75
Proportion









Supplementary material

Contents

1. Supplemental methods

a. Approvals

The study was reviewed by the Yorkshire & The Humber - Bradford Leeds Research Ethics Committee and approved as anonymised analysis of routinely collected patient data without need for consent by NHS England Health Research Authority (IRAS Project ID 283512).

b. COVID-19 testing

COVID-19 testing was performed by RdRp gene assay test on upper respiratory swab samples (nasopharyngeal, oral or endotracheal aspirate) sent to Barts Health NHS Trust Diagnostic Virology Laboratories and analysed either on-site or at Public Health England (PHE) Colindale facility.

c. Definition of key varaibles

Ethnicity
We defined ethnic groups using the 16+1 categories defined in the 2001 census which form the UK national mandatory standard for the collection and analysis of ethnicity in the NHS data dictionary. Importantly, in the UK 'Asian' ethnic category refers predominantly to those of a South Asian background (including Indian, Pakistani and Bangladeshi), while patients of a Chinese background are placed in the 'Other Ethnic Groups' category.

White	A British B Irish C Any other White background
Mixed	D White and Black Caribbean E White and Black African F White and Asian G Any other mixed background
Asian or Asian British	H Indian J Pakistani K Bangladeshi L Any other Asian background
Black or Black British	M Caribbean N African P Any other Black background
Other Ethnic Groups	R Chinese S Any other ethnic group
+1 category	Z Not stated (Reserved for cases where patients declined to provide information)

In order to preserve statistical power to detect differences between groups, pre-specified analysis was carried out between ethnicity defined by the 5-high level groups White, Mixed, Asian or Asian British, Black or Black British and Other with merging of the "Mixed" and "Other" categories. Category Z was excluded from our primary analysis as were cases where no ethnicity data was recorded (Unknown).

Index of Multiple Deprivation
Index of Multiple Deprivation (IMD) was defined from patient home address postcode using UK government statistics (https://www.gov.uk/government/statistics/english-indices-of-deprivation-2019). Matching of Lower-layer Super Output Areas (LSOAs) was undertaken against the Office of National Statistics Postcode Directory (ONSPD) February 2020 datafile (https://geoportal.statistics.gov.uk/datasets/ons-postcode-directory-february-2020: accessed on 1st May 2020). IMD was presented as quintiles within England using raw scores for descriptive results and quintiles within the study cohort in multivariable analysis.

Smoking
History of tobacco use was defined by presence of the WHO ICD-10 codes F17·1-F17·2, Z72·0, Z87·8, Z71·6 and T65·2.

Ischaemic heart disease
Ischaemic heart disease (IHD) was defined by the presence of the ICD-10 codes I23·4-I23·5, I24, I24·8-I24·9, I25, I25·3-I25·6, I25·8-I25·9, I34·1, I46·1, I51·8-I51·9, and I52.
Wu et al Mapping ICD-10 and ICD-10-CM Codes to Phecodes: Workflow Development and Initial Evaluation JMIR Med Inform 2019;7(4):e14325

End stage Renal disease
End stage Renal disease (ESRD) was defined by the presence of the ICD10 codes I77·0, N16·5, N18·5, T82·4, T86·1, Y60·2, Y61·2, and Y62·2, Y84·1, Z49·0-Z49·2, Z94·0, Z99·2.
Crellin E, et al. Clinical Code List - ICD-10 - End-Stage Renal Disease. [Data Collection]. London School of Hygiene & Tropical Medicine. 2017: https://doi.org/10.17037/DATA.241.

Comorbidity
Diagnosis of co-morbidities and assignment of Charlson Comorbidity Index was based on mapping from ICD-10 coding from previous admissions using the mapping of Quan H, et al.
Quan H, et al. Coding algorithms for defining comorbidities in ICD-9-CM and ICD-10 administrative data. Med Care 2005;43(11):1130-9.
Diagnosis of Hypertension was based on mapping ICD-10 codes to the Elixhauser comorbidity index.
Elixhauser A, et al. Comorbidity measures for use with administrative data. Med Care 1998;36:8-27.

Hospital frailty risk score
Hospital frailty risk score was calculated from mapping ICD-10 coding of hospital attendances.
Gilbert T, et al. Development and validation of a Hospital Frailty Risk Score focusing on older people in acute care settings using electronic hospital records: an observational study. Lancet 2018;391(10132):1775-1782.

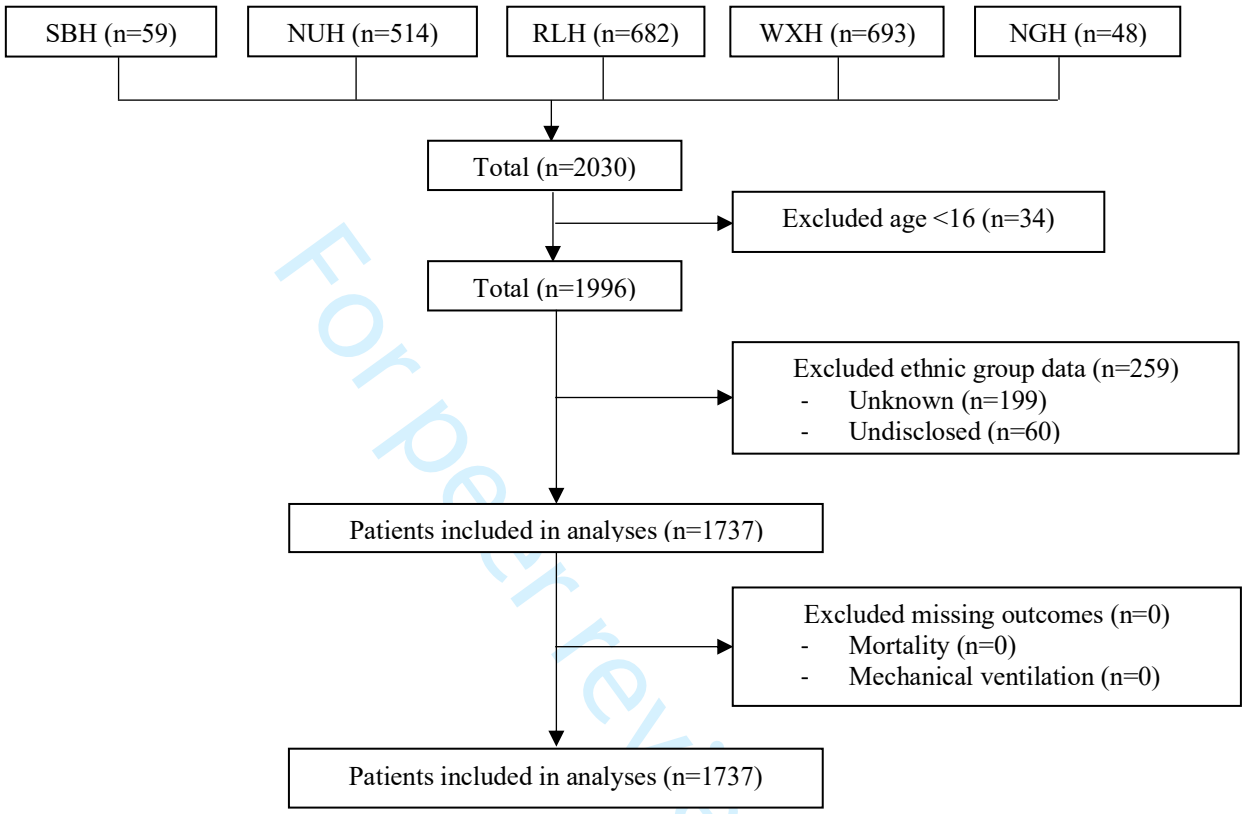
Acute Kidney injury
Acute kidney injury (AKI) within first 7 days of admission was defined using the KDIGO 2012 creatinine criteria either a 1·5-fold rise over baseline within 7 days or 26 μmol rise within 48 hours. Baseline creatinine will be the median value in the 7 to 365 days before hospitalisation. Absent baseline creatinine was determined based on an eGFR of 75 ml/min/1·72m^2 using the CKDepi formula or the admission value whichever was lower.

Chronic kidney disease
History of chronic kidney disease (CKD) using baseline eGFR was calculated using last creatinine value available from results earlier than 7 days before hospitalisation. CKD was defined as baseline eGFR below 60 ml/min/1·72m^2.

Secondary haemophagocytic lymphohistiocytosis
Secondary haemophagocytic lymphohistiocytosis (sHLH) risk scores were calculated using highest values during admission of temperature, haemoglobin, white cell count, platelet count, triglycerides, fibrinogen, ferritin, and aspartate aminotransferase (AST). Total scores did not include haemophagocytosis on bone marrow aspirate or known immunosuppression due to lack of available data leaving a maximum score of 284.
Mehta P, et al. COVID-19: consider cytokine storm syndromes and immunosuppression. Lancet 2020;395(10229):1033-1034.

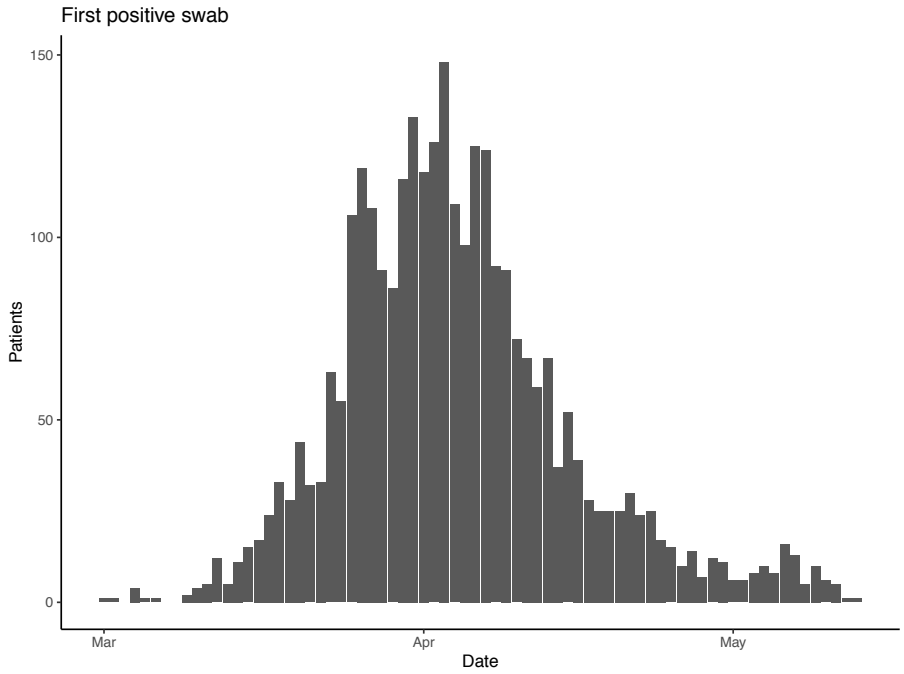
2. STROBE diagram

Figure S1. STROBE flow diagram of study populations. Hospital indicates first admission site and patients admitted to Nightingale hospital who had not been previously admitted to Barts Health hospital: St. Barts Hospital (SBH), Newham University Hospital (NUH), Royal London Hospital (RLH), Whipps Cross Hospital (WXH), Nightingale Hospital (NGH).



3. Inclusion time period by SARS-CoV-2 cases

Figure S2. Timeline of patients with positive SARS-CoV-2 swab tests at Barts Health.



4. Distribution of ethnicity categories within study cohort

Table S1. Distribution of study cohort by 16+1 ethnic data categories.

High-level group	Ethnic data category	n
White	A British	526
	B Irish	11
	C Any other White background	166
Mixed	D White and Black Caribbean	3
	E White and Black African	4
	F White and Asian	1
	G Any other mixed background	8
Asian or Asian British	H Indian	104
	J Pakistani	116
	K Bangladeshi	191
	L Any other Asian background	127
Black or Black British	M Caribbean	118
	N African	168
	P Any other Black background	54
Other Ethnic Groups	R Chinese	23
	S Any other ethnic group	117
	Z Not stated	60
No ethnicity data recorded		199

5. Baseline characteristics comparing died or survived at 30 days

Table S2. Study population baseline characteristics stratified by died or survived at 30 days, n (%) unless otherwise stated. Total n=1996 unless otherwise stated. P values based on Chi-square (for categorical) or Kruskal-Wallis test (for continuous). SD: standard deviation, IQR: interquartile range, IMD: index of multiple deprivation, BMI: body mass index, TIA: transient ischaemic accident, HTN: hypertension, CKD: chronic kidney disease, sHLH: secondary haemophagocytic lymphohistiocytosis (without known underlying immunosuppression and bone marrow aspirate data), CRP: C-reactive protein, NEWS: national early warning score, ICU: intensive care unit, RRT: renal replacement therapy.

	Stratified by survival at 30 days		
	Died	**Survived**	p value
n	536	1460	
Ethnicity			0·05
Asian or Asian British	138 (25·7)	400 (27·4)	
Black or Black British	97 (18·1)	243 (16·6)	
Mixed and Other Ethnic Groups	33 (6·2)	123 (8·4)	
White	210 (39·2)	493 (33·8)	
Unknown and Undsisclosed	58 (10·8)	201 (13·8)	
Age (years)			
Mean (SD)	74·8 (12·6)	59·2 (18·2)	<0·001
Median (IQR)	77·0 (66·0-84·0)	59·0 (46·0-73·0)	<0·001
Male	351 (65·5)	859 (58·8)	0·01
IMD quintile [n=1980]			0·003
1 (most deprived)	155 (29·1)	407 (28·1)	
2	223 (41·9)	698 (48·2)	
3	62 (11·7)	184 (12·7)	
4	56 (10·5)	99 (6·8)	
5 (least deprived)	36 (6·8)	60 (4·1)	
Smoking [n=1700]	57 (11·8)	116 (9·5)	0·19
BMI [n=1248]			
Median (IQR)	26·5 (22·7-31·6)	26·9 (23·6-31·2)	0·43
By category			0·80
<18·5 kg/m^2	20 (6·4)	43 (4·6)	
18·5 - <25 kg/m^2	97 (31·0)	295 (31·6)	
25 - <30 kg/m^2	100 (31·9)	309 (33·0)	
30 - <40 kg/m^2	80 (25·6)	243 (26·0)	
≥40 kg/m^2	16 (5·1)	45 (4·8)	
Co-morbidity using ICD-10 [n=1700]			
Obesity	123 (25·5)	286 (23·5)	0·411
Ischaemic heart disease	149 (30·9)	197 (16·2)	<0·001
Myocardial infarction	73 (15·1)	108 (8·9)	<0·001
Congestive heart failure	120 (24·9)	140 (11·5)	<0·001
Peripheral vascular disease	74 (15·4)	84 (6·9)	<0·001
Cerebral vascular accident or TIA	133 (27·6)	159 (13·1)	<0·001
Dementia	89 (18·5)	78 (6·4)	<0·001
Chronic obstructive pulmonary disease	145 (30·1)	252 (20·7)	<0·001
Diabetes	242 (50·2)	422 (32·6)	<0·001
HTN	372 (77·2)	637 (52·3)	<0·001
Moderate to severe CKD	159 (33·0)	204 (16·7)	<0·001
End-stage renal disease	39 (8·1)	74 (6·1)	0·163

Liver disease	45 (8·4)	110 (7·5)	0·587
Cancer	62 (12·9)	82 (6·7)	<0·001
Cancer with metastases	18 (3·7)	24 (2·0)	0·053
Acquired immunodeficiency syndrome	1 (0·2)	5 (0·4)	0·855
Charlson comorbidity index [n=1700]			<0·001
0	45 (9·3)	428 (35·1)	
1-2	170 (35·3)	449 (36·9)	
3-4	130 (27·0)	174 (14·3)	
≥5	137 (28·4)	167 (13·7)	
Rockwood frailty score [n=831]			<0·001
1-2 (very fit, well)	20 (6·3)	75 (14·5)	
3-4 (managing well, vulnerable)	106 (33·7)	199 (38·6)	
5-6 (mildly to severely frail)	144 (45·7)	215 (41·7)	
8-9 (very severely frail, terminally ill)	45 (14·3)	27 (5·2)	
Hospital frailty risk score [n=1700]			<0·001
<5 (low risk)	88 (18·3)	655 (53·8)	
5-15 (intermediate risk)	187 (38·8)	293 (24·1)	
≥15 (high risk)	207 (42·9)	270 (22·2)	
Baseline eGFR ml/min/1·72m2 [n=1525]			
Median (IQR)	57·3 (38·7-76·2)	72·4 (51·2-90·8)	<0·001
eGFR <60	236 (52·2)	323 (30·1)	<0·001
Acute kidney injury first 7 days [n=1673]	204 (47·0)	226 (18·2)	<0·001
Blood results during admission			
Highest creatinine µmol/L [n=1691]			<0·001
Median (IQR)	168·0 (102·0-326·0)	87·0 (71·0-120·0)	
Highest CRP [n=1761]			<0·001
Median (IQR)	241·5 (149·8-344·0)	120·0 (59·0-218·0)	
Highest D-dimer mg/L [n=968]			<0·001
Median (IQR)	3·1 (1·2-17·7)	1·1 (0·6-3·3)	
Highest sHLH score [n=1881]			
Mean (SD)	34·6 (27·9)	26·9 (25·7)	<0·001
Blood Group [n=875]			0·004
A	109 (36·0)	196 (34·3)	
AB	11 (3·6)	32 (5·6)	
B	49 (16·2)	119 (20·8)	
O	134 (44·2)	225 (39·3)	
NEWS on admission [n=1443]	4·7 (2·9)	3·5 (2.2)	<0·001
Intensive care unit (ICU)			
ICU admission	151 (28·2)	210 (14·4)	<0·001
ICU length of stay			
Median (IQR)	9·0 (5·9-15·0)	8·0 (3·0-15·0)	0·06
Mechanical ventilation within ICU admissions	135 (89·4)	146 (69·5)	<0·001
Days on organ support			
Advanced respiratory Mean (SD)	9·3 (6·2)	9·9 (10·6)	0·49
Total respiratory Mean (SD)	10·4 (6·2)	12·5 (10·2)	0·03
Cardiovascular system Mean (SD)	10·3 (6·3)	12·6 (10·5)	0·02
Renal Mean (SD)	2·5 (4·1)	2·7 (6·2)	0·76
Total number of organ systems			<0·001
0	0 (0·0)	3 (1·4)	

1	1 (0·7)	12 (5·7)	
2	93 (61·6)	154 (73·3)	
3	57 (37·7)	41 (19·5)	
Hospital length of stay			
Median (IQR)	7·0 (4·0-13·0)	7·0 (3·0-12·0)	0·98

6. Completeness of follow-up

Table S3. Numbers at risk and number of deaths (in parenthesis) over five day intervals up to 30 days by ethnic group in primary survival analysis.

Ethnic group	Days from hospital admission						
	0	**5**	**10**	**15**	**20**	**25**	**30**
Asian or Asian British	538 (3)	488 (60)	446 (96)	421 (115)	402 (124)	389 (131)	365 (138)
Black or Black British	340 (4)	301 (50)	273 (70)	258 (80)	248 (88)	240 (94)	229 (97)
Mixed and Other ethnic groups	156 (1)	147 (12)	140 (17)	127 (26)	122 (32)	117 (33)	113 (33)
White	703 (3)	644 (71)	583 (120)	534 (162)	502 (188)	472 (197)	436 (210)

7. Sensitivity analyses

a. Multivariable imputation

Missing data for baseline risk variables included in the multivariable Cox model was imputed using Multivariate Imputation by Chained Equations based on age, sex, and comorbidity. Five separate imputed datasets were simulated, and a pooled result of multivariable Cox models presented.
Van Buuren S, Groothuis-Oudshoorn K. mice: Multivariate Imputation by Chained Equations in R. J Stat Softw 2011;45(3): https://www.jstatsoft.org/v045/i03.

Figure S3. Patterns of missingness in baseline risk variables. ID: patient identifier, IMD: index of multiple deprivation, DM: diabetes mellitus, HTN: hypertension, CKD: chronic kidney disease, BMI: body mass index. Blue indicate complete and pink indicate missing data. Numbers on the left side of the grid represent n records with this pattern, numbers on the right side represent n missing variables, numbers on the bottom represent n records missing this variable. For example, n=1006 records were complete, n=470 were missing 1 variable (BMI), n=14 records were missing IMD data.

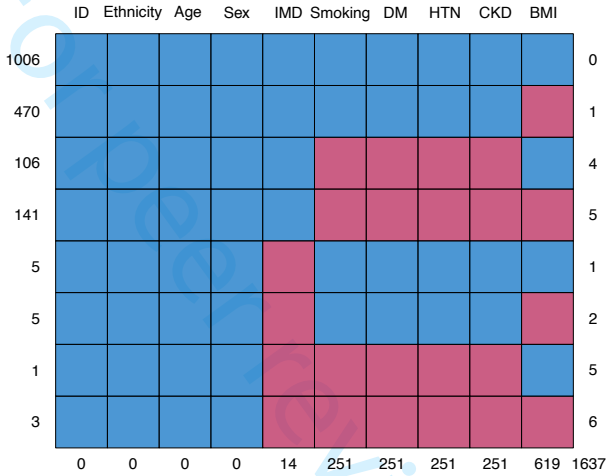
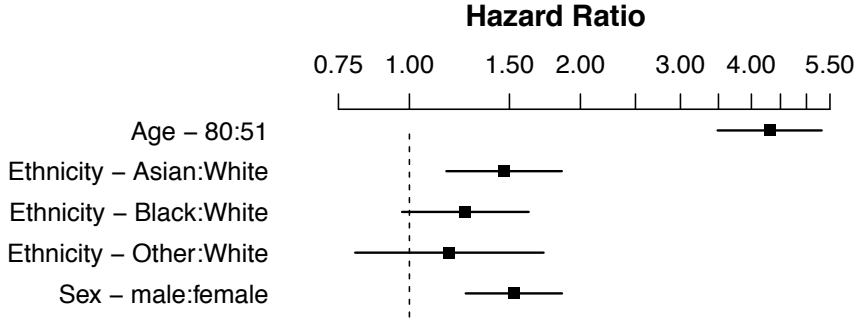


Table S4. Multivariable analysis using imputed dataset of mortality to 30 days using Cox proportional hazards modelling. Missing data imputed for smoking, BMI ≥30 kg/m^2, diabetes, HTN, CKD. Censored to 30 days follow up, observation 1737, events 478.

	n		Unadjusted	
	Total	**Events**	**Hazard ratio (95% CI)**	**P value**
Age (25th vs 75th centile)	-	-	4·31 (3·49-5·32)	<0·0001
Sex (Male)	-	-	1·53 (1·26-1·86)	<0·0001
Ethnic group				
Asian or Asian British	521	134	1·47 (1·16-1·85)	0·001
Black or Black British	331	94	1·25 (0·97-1·62)	0·083
Mixed and Other ethnic groups	150	34	1·18 (0·80-1·72)	0·406
White	674	206	Reference	-

Figure S4. Forest plot showing hazards ratios of mortality to 30 days using the imputed dataset, on log scale.



b. Charlson comorbidity index

Table S5. Multivariable analysis of mortality to 30 days using cox proportional hazards modelling. Variables included age, sex, IMD quintile, smoking, BMI ≥30 kg/m^2, and Charlson comorbidity index. Censored to 30 days follow up, observations 1006, events 281.

	Adjusted	
	Hazard ratio (95% CI)	**P value**
Age (25th vs 75th centile)	2·90 (2·22-3·79)	<0·0001
Sex (Male)	1·48 (1·16-1·90)	0·002
Ethnic group		
Asian or Asian British	1·54 (1·15-2·08)	0·004
Black or Black British	1·39 (1·01-1·92)	0·044
Mixed and Other ethnic groups	1·02 (0·56-1·88)	0·939
White	Reference	-
IMD quintile		
1 (most deprived)	0·83 (0·57-1·20)	0·316
2	0·81 (0·55-1·18)	0·268
3	0·94 (0·66-1·36)	0·759
4	0·82 (0·57-1·20)	0·311
5 (least deprived)	Reference	-
Smoking	1·36 (0·98-1·89)	0·067
BMI ≥30 kg/m^2	1·48 (1·14-1·92)	0·003
Charlson comorbidity index		
0	Reference	-
1-2	2·00 (1·17-3·41)	0·012
3-4	3·43 (2·00-5·89)	<0·0001
≥5	4·10 (2·42-6·94)	<0·0001

Figure S5. Forest plot showing hazards ratios of mortality to 30 days comparing multiple variables including CCI: Charlson comorbidity index. IMD: index of multiple deprivation, Obesity defined as BMI ≥30 kg/m^2, on log scale.

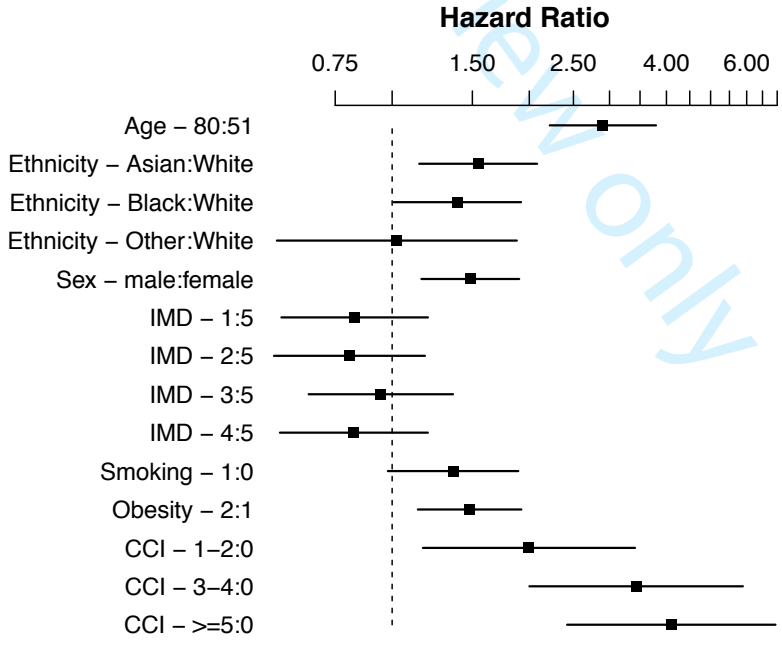
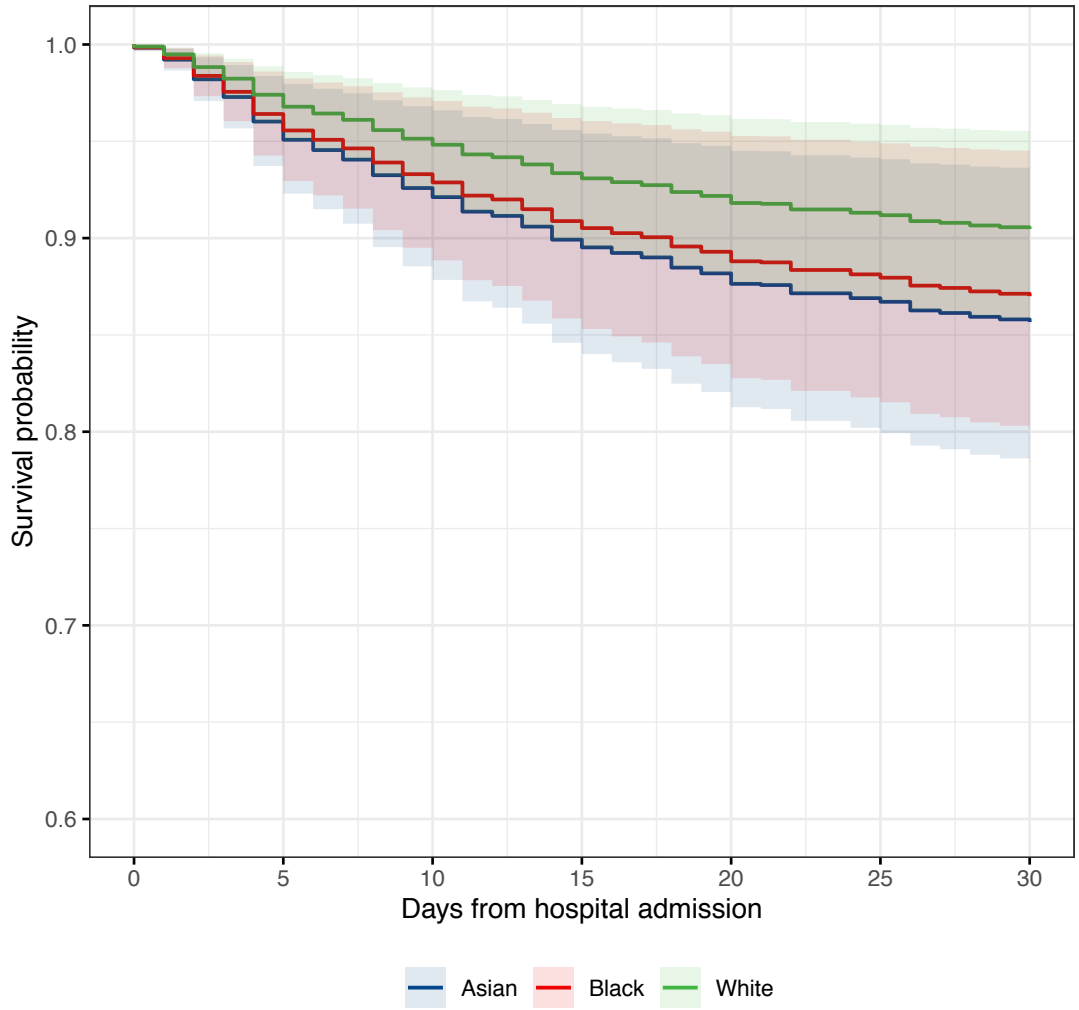


Figure S6. Survival curve to 30 days from multivariable analysis comparing Asian, Black, and White ethnic groups. Survival modelled for median age 65 years and male sex, index of multiple deprivation (IMD) least deprived quintile, no baseline risk factors defined as non-smoking, BMI <30 kg/m^2 and Charlson comorbidity index 0.



c. Rockwood frailty score

Table S6. Multivariable analysis of mortality to 30 days using cox proportional hazards modelling. Variables included age, sex, index of multiple deprivation (IMD) quintile, smoking, BMI ≥30 kg/m^2, and Rockwood frailty score (RFS). Censored to 30 days follow up, observations observations 552, events 199.

	Adjusted	
	Hazard ratio (95% CI)	**P value**
Age (25th vs 75th centile)	2·42 (1·56-3·75)	<0·0001
Sex (Male)	1·61 (1·19-2·16)	0·002
Ethnic group		
Asian or Asian British	1·98 (1·37-2·86)	<0·001
Black or Black British	1·67 (1·14-2·45)	0·009
Mixed and Other ethnic groups	1·27 (0·62-2·56)	0·513
White	Reference	-
IMD quintile		
1 (most deprived)	0·61 (0·38-0·98)	0·040
2	0·79 (0·50-1·22)	0·283
3	0·82 (0·53-1·25)	0·348
4	0·77 (0·51-1·18)	0·234
5 (least deprived)	Reference	-
Smoking	1·38 (0·94-2·03)	0·102
BMI ≥30 kg/m^2	1·39 (1·01-1·91)	0·045
Rockwood frailty score		
1-2 (very fit, well)	Reference	-
3-4 (managing well, vulnerable)	1·61 (0·82-3·16)	0·164
5-6 (mildly to severely frail)	1·84 (0·93-3·64)	0·078
8-9 (very severely frail, terminally ill)	3·25 (1·49-7·06)	0·003

Figure S7. Forest plot showing hazards ratios of mortality to 30 days comparing multiple variables including RFS: Rockwood frailty score. IMD: index of multiple deprivation, Obesity defined as BMI ≥30 kg/m^2, on log scale.

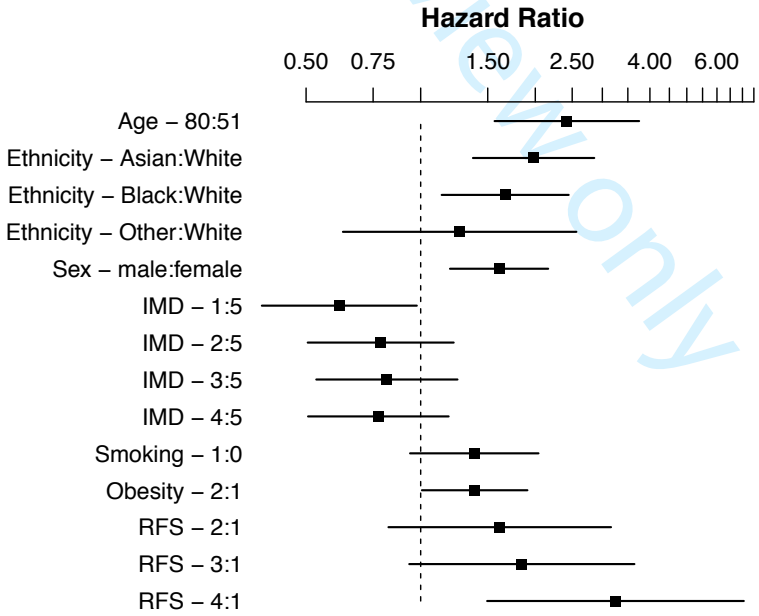
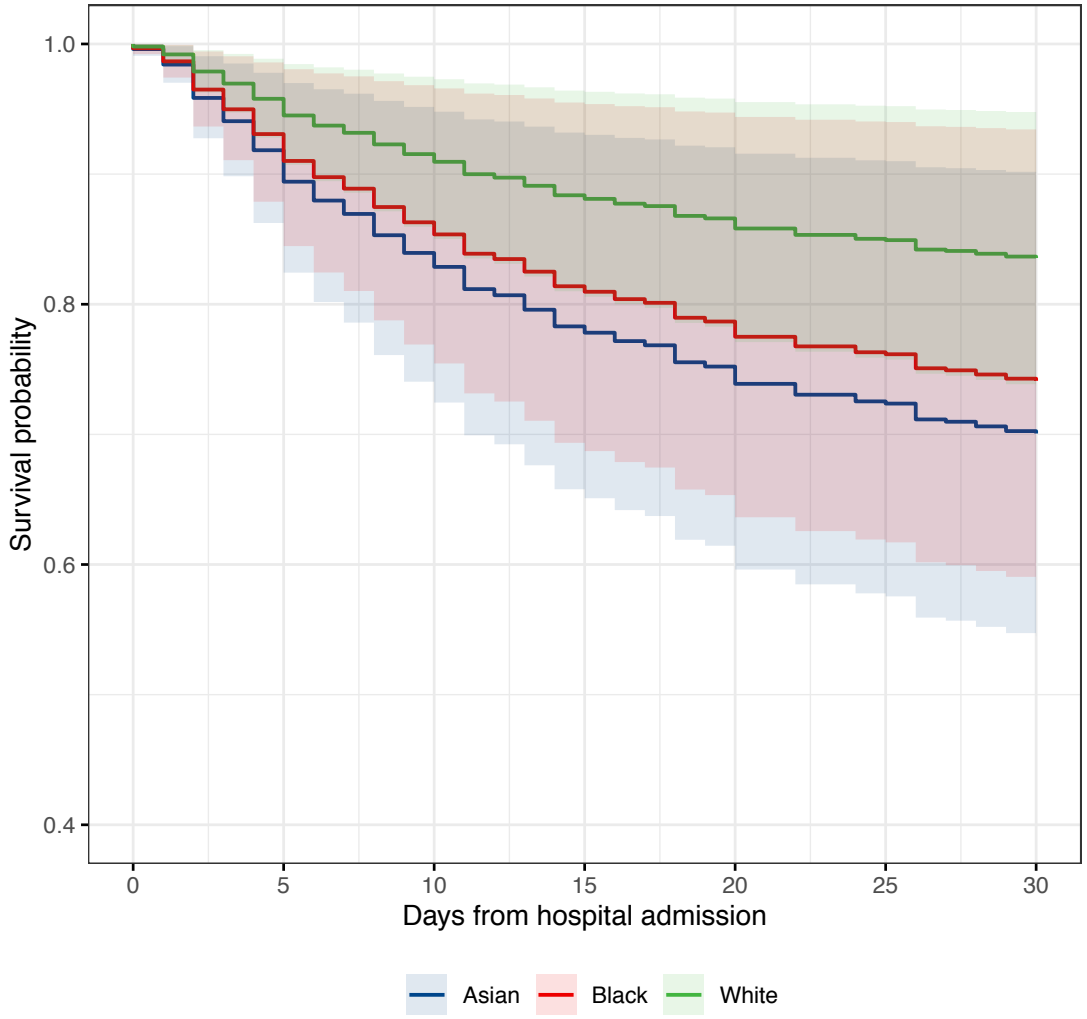


Figure S8. Survival curve to 30 days from multivariable analysis comparing Asian, Black, and White ethnic groups. Survival modelled for median age 65 years and male sex, index of multiple deprivation (IMD) least deprived quintile, no baseline risk factors defined as non-smoking, BMI <30 kg/m^2 and Rockwood frailty score lowest risk group.



d. Hospital frailty risk score

Table S7. Multivariable analysis of mortality to 30 days using cox proportional hazards modelling. Variables included age, sex, index of multiple deprivation (IMD) quintile, smoking, BMI ≥30 kg/m^2, and Hospital frailty risk score (HFRS). Censored to 30 days follow up, observations 1006, events 281.

	Adjusted	
	Hazard ratio (95% CI)	**P value**
Age (25th vs 75th centile)	2·84 (2·17-3·71)	<0·0001
Sex (Male)	1·58 (1·24-2·03)	<0·001
Ethnic group		
Asian or Asian British	1·78 (1·32-2·41)	<0·001
Black or Black British	1·57 (1·13-2·17)	0·007
Mixed and Other ethnic groups	1·10 (0·60-2·04)	0·751
White	Reference	-
IMD quintile		
1 (most deprived)	0·85 (0·59-1·24)	0·404
2	0·83 (0·57-1·22)	0·341
3	0·89 (0·62-1·29)	0·541
4	0·83 (0·57-1·20)	0·310
5 (least deprived)	Reference	-
Smoking	1·42 (1·01-1·96)	0·044
BMI ≥30 kg/m^2	1·57 (1·21-2·05)	<0·001
Hospital frailty risk score		
<5 (low risk)	Reference	-
5-15 (intermediate risk)	2·44 (1·68-3·54)	<0·0001
≥15 (high risk)	2·76 (1·89-4·04)	<0·0001

Figure S9. Forest plot showing hazards ratios of mortality to 30 days comparing multiple variables including HFRS: Hospital frailty risk score. IMD: index of multiple deprivation, Obesity defined as BMI ≥30 kg/m^2, on log scale.

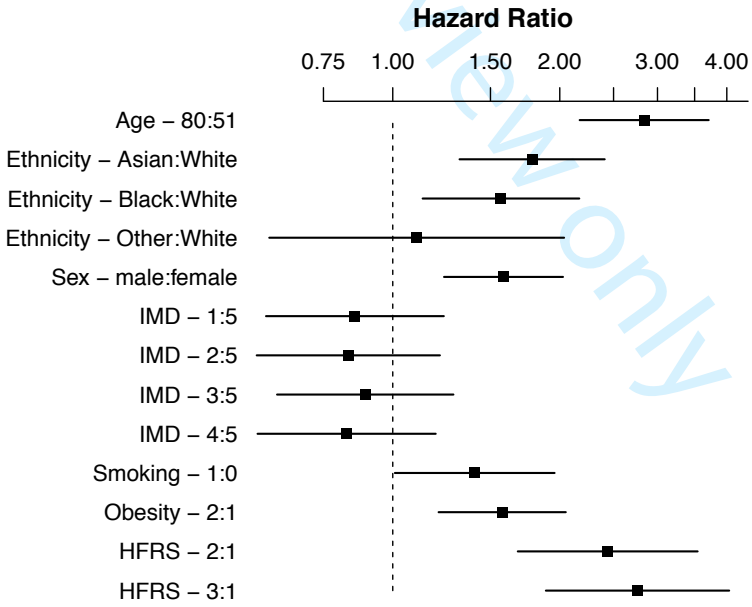
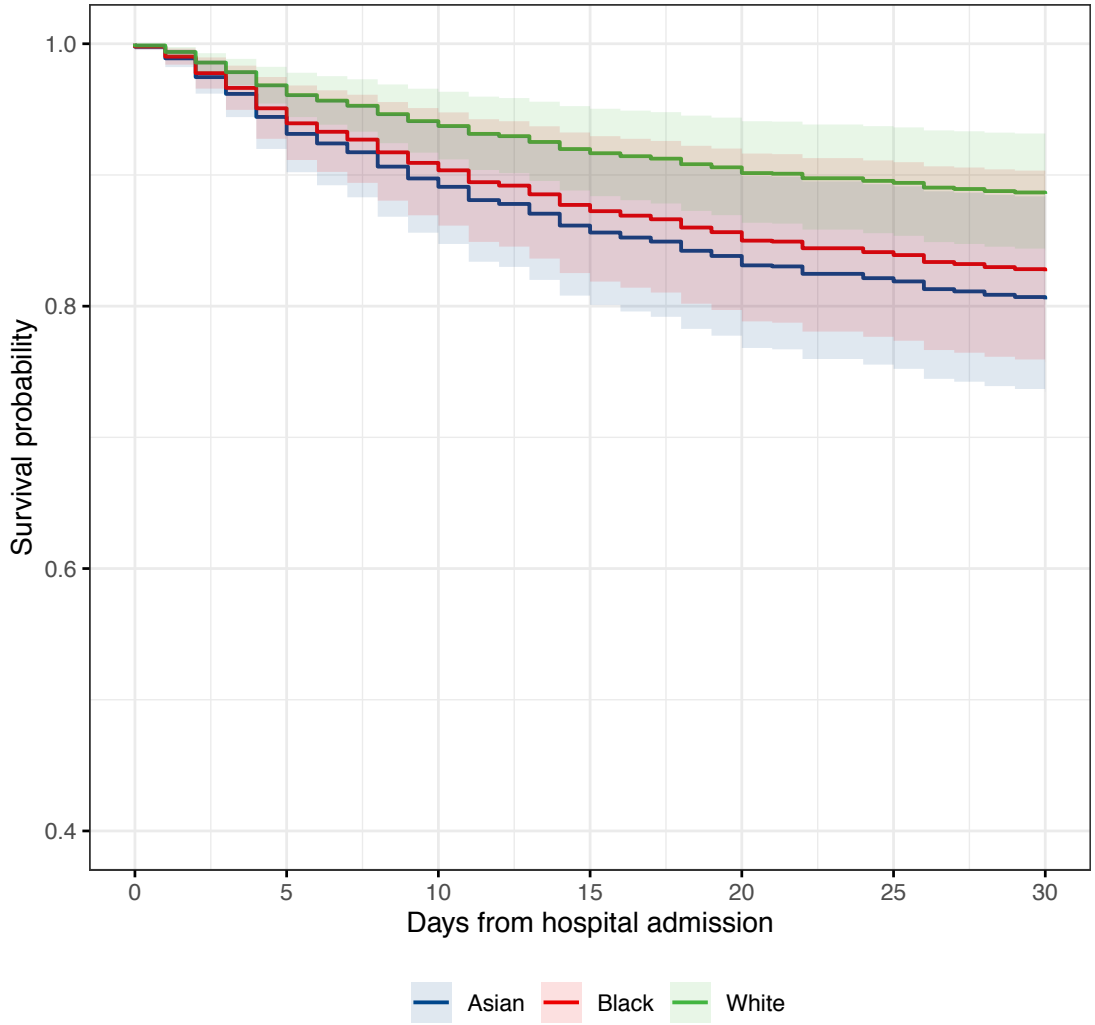


Figure S10. Survival curve to 30 days from multivariable analysis comparing Asian, Black, and White ethnic groups, age and sex corrected. Survival modelled for median age 65 years and male sex, inde of multiple deprivation (IMD) least deprived quintile, no history of baseline risk factors defined as smoking, BMI ≥30 kg/m^2, Hospital frailty risk score lowest risk group.



e. ABO blood group

Table S8. Multivariable analysis of mortality to 30 days using cox proportional hazards modelling. Variables included age, sex, and ABO blood group. Censored to 30 days follow up, observations 793, events 281.

	Adjusted	
	Hazard ratio (95% CI)	**P value**
Age (25th vs 75th centile)	3·26 (2·58-4·13)	<0·0001
Sex (Male)	1·67 (1·30-2·13)	<0·0001
Ethnic group		
Asian or Asian British	1·82 (1·35-2·46)	<0·0001
Black or Black British	1·63 (1·17-2·27)	0·004
Mixed and Other ethnic groups	1·62 (0·98-2·68)	0·059
White	Reference	-
ABO blood group		
A	0·81 (0·62-1·05)	0.112
AB	0·65 (0·33-1·28)	0·214
B	0·66 (0·47-0·92)	0·016
O	Reference	-

Figure S11. Forest plot showing hazards ratios of mortality to 30 days comparing multiple variables including ABO blood group, on log scale.

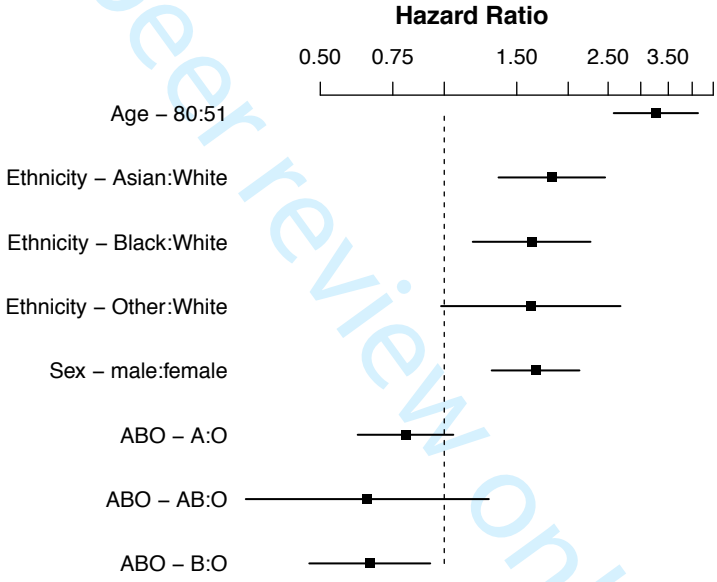
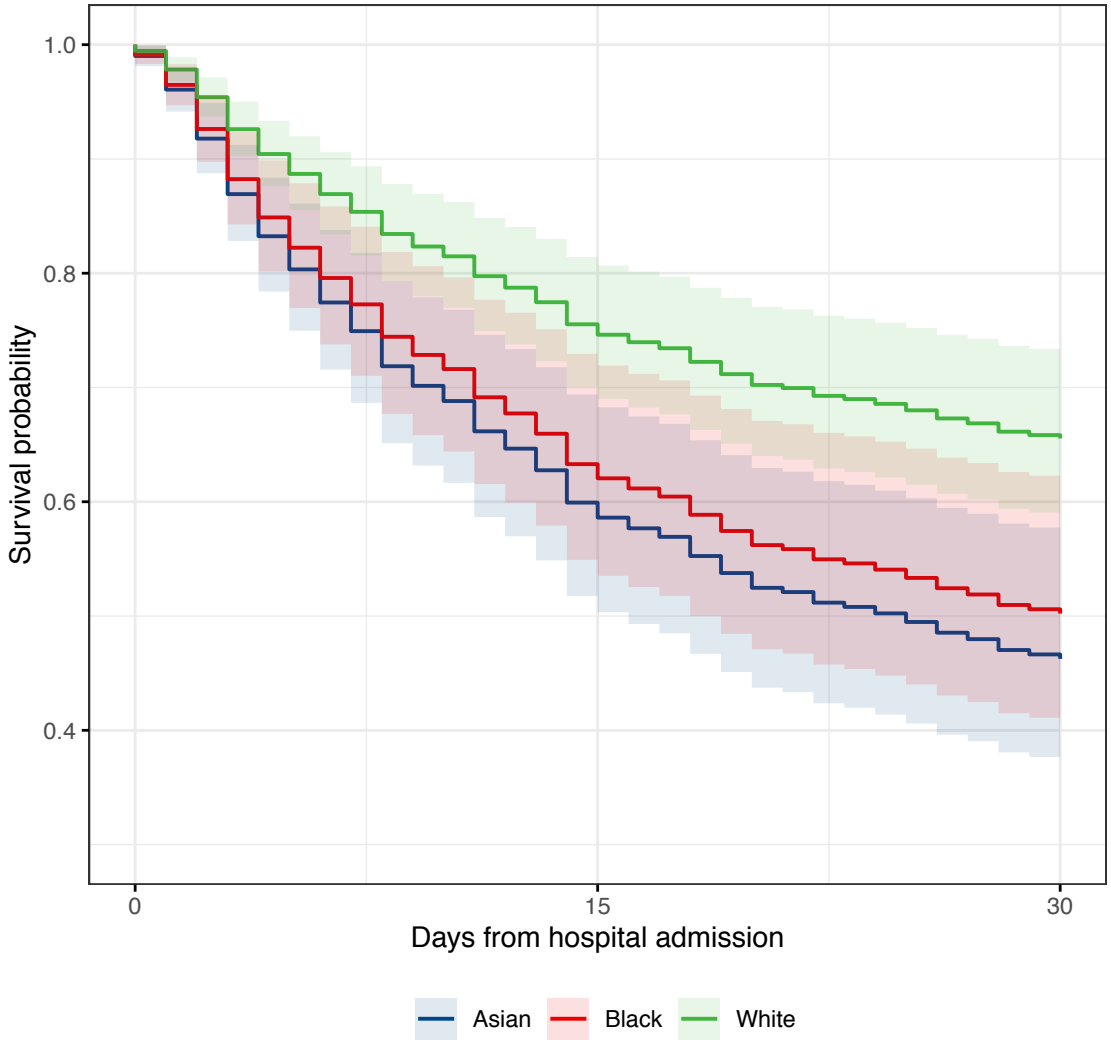


Figure S12. Survival curve to 30 days from multivariable analysis comparing Asian, Black, and White ethnic groups. Survival modelled for median age 65 years and male sex, ABO bloog group O.



f. 90 day mortality

Table S9. Association of ethnic group with mortality to 90 days using cox proportional hazards modelling, age and sex corrected. Censored to 90 days follow up, observations 1737, events 510.

	n		Unadjusted	
	Total	**Events**	**Hazard ratio (95% CI)**	**P value**
Age (25^{th} vs 75^{th} centile)	-	-	4·48 (3·74-5·35)	<0·0001
Sex (Male)	-	-	1·52 (1·27-1·83)	<0·0001
Ethnic group				
Asian or Asian British	497	106	1·46 (1·18-1·81)	<0·001
Black or Black British	342	83	1·26 (0·99-1·59)	0·058
Mixed and Other ethnic groups	142	30	1·02 (0·71-1·46)	0·934
White	651	182	Reference	-

Figure S13. Forest plot showing hazards ratios of mortality to 90 days comparing ethnic groups, age and sex, on log scale.

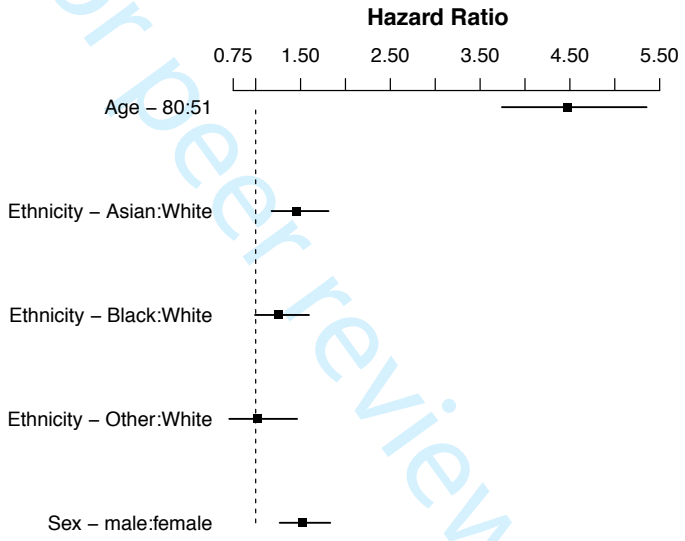
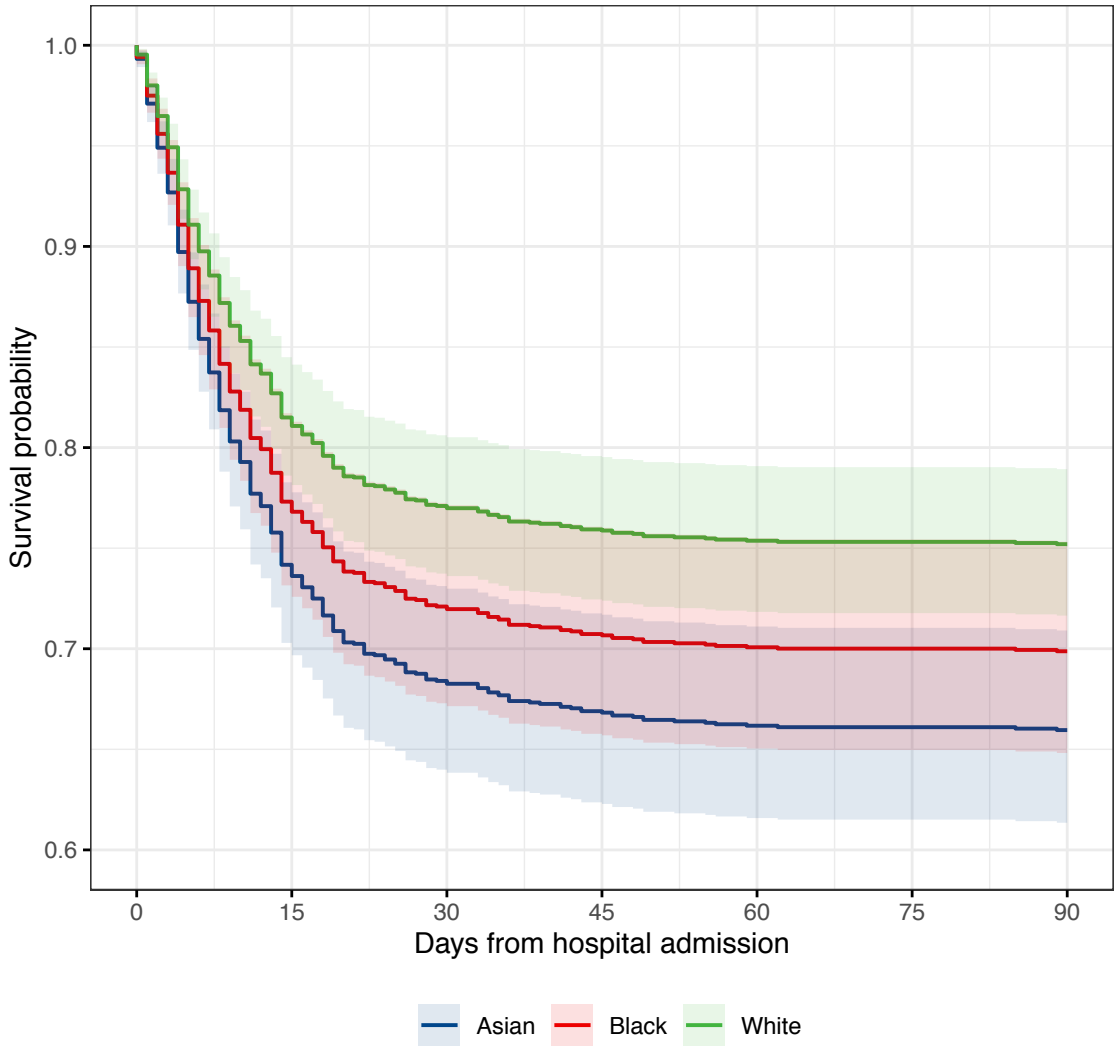


Figure S14. Survival curve to 90 days from univariate analysis comparing Asian, Black, and White ethnic groups, age and sex. Survival modelled for median age 65 years and male sex.

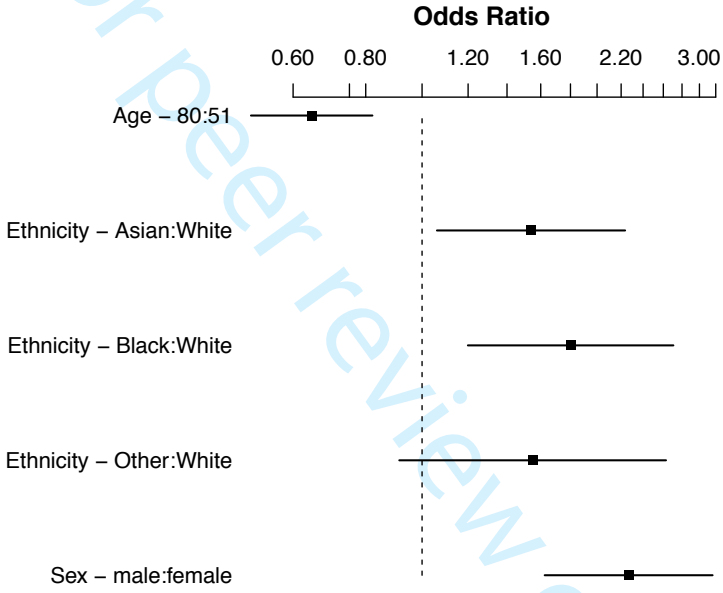


8. Secondary outcome mechanical ventilation

Table S10. Association of ethnic group with mechanical ventilation using logistic regression modelling, age and sex corrected. Observations 1737, events 210.

	Unadjusted	
	Odds ratio (95% CI)	**p value**
Age (25th vs 75th centile)	0·65 (0·51-0·82)	<0·001
Sex (Male)	2·27 (1·63-3·16)	<0·0001
Ethnic group		
Asian or Asian British	1·54 (1·06-2·23)	0·023
Black or Black British	1·80 (1·20-2·71)	0·005
Mixed and Other ethnic groups	1·55 (0·91-2·63)	0·104
White	Reference	-

Figure S15. Forest plot showing odds ratios of mechanical ventilation comparing ethnic groups, age and sex corrected, on log scale.



9. Cox proportional hazards testing

We assessed proportional-hazards assumption for ethnicity and adjusted variables by inspection of scaled Schoenfeld residual plots. There was some evidence of non-proportionality for Black ethnicity at later time points in the primary age and sex adjusted analysis. However, the unstratified and ethnicity-stratified survival curves for the age and sex adjusted 30-day survival were similar suggesting minimal impact of non-proportionality.

Figure S16. Scaled Schoenfeld residual plots for ethnicity, age, and sex.

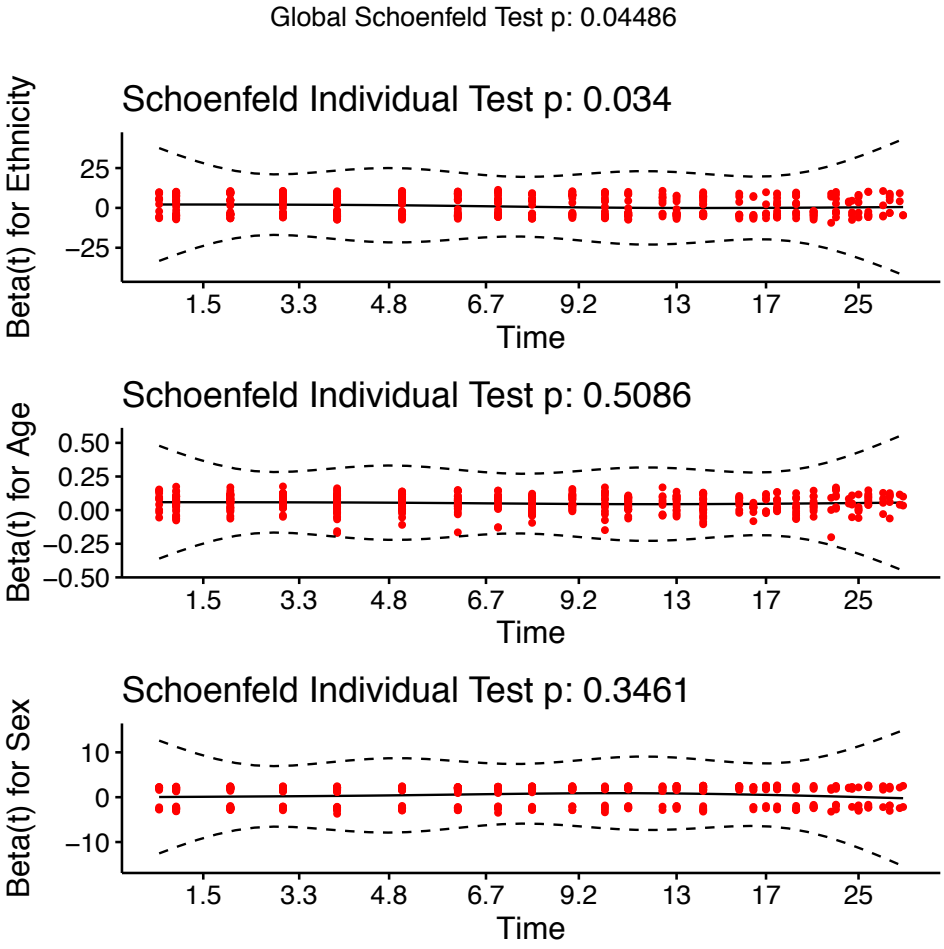
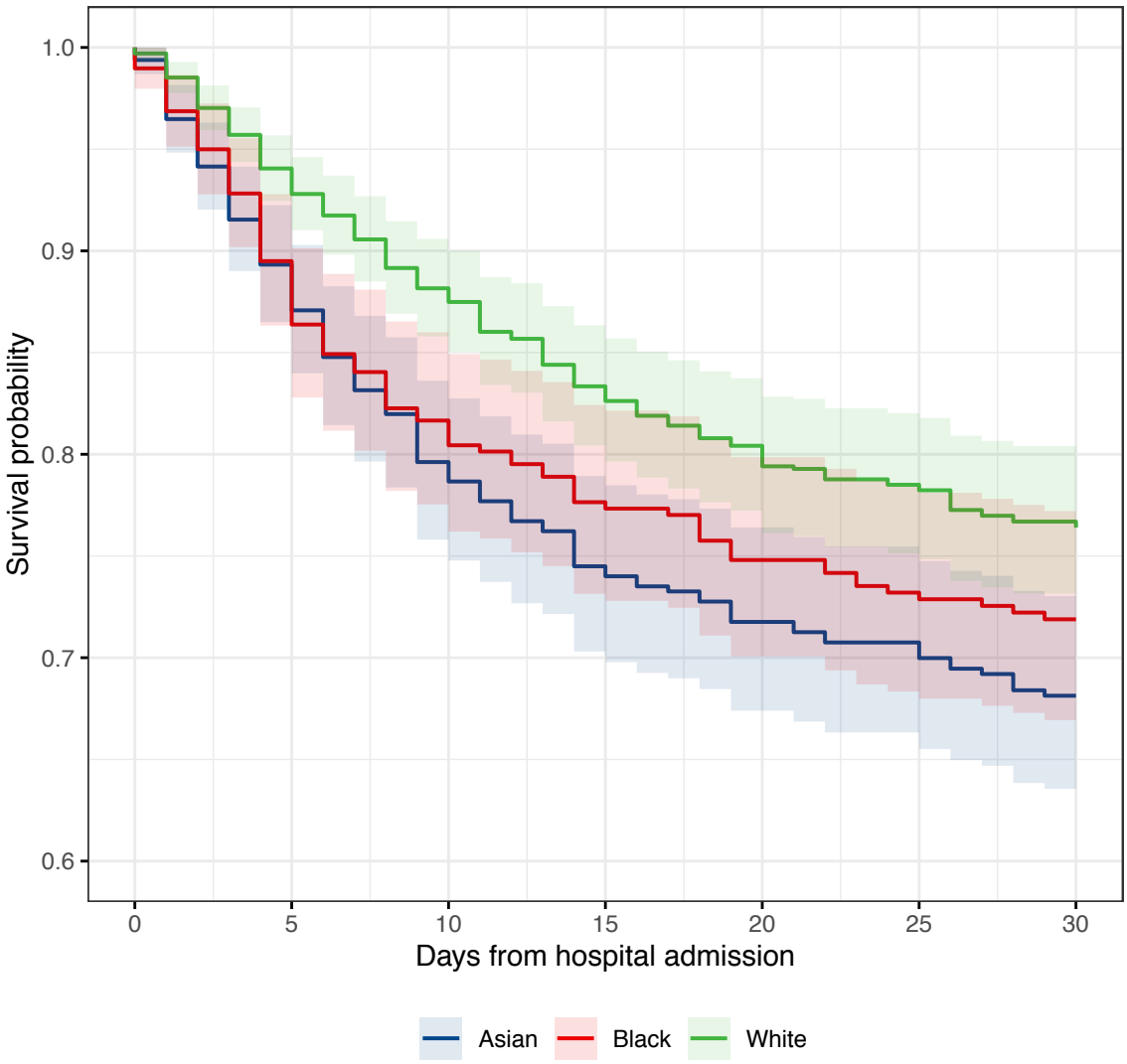


Figure S17. Ethnicity-stratified Cox survival model to 30 days based on age and sex. Survival modelled for median age 65 years and male sex. Survival over 30 days is comparable the unstratified model [Figure 3], however early mortality was greater in patients with Black ethnicity.



STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cohort studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	2, 4
Objectives	3	State specific objectives, including any prespecified hypotheses	2, 4
Methods			
Study design	4	Present key elements of study design early in the paper	4, 5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	4
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	N/A
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4, 5
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	4, 5
Bias	9	Describe any efforts to address potential sources of bias	5
Study size	10	Explain how the study size was arrived at	4
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	4, 5
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	5
		(*b*) Describe any methods used to examine subgroups and interactions	5
		(*c*) Explain how missing data were addressed	5
		(*d*) If applicable, explain how loss to follow-up was addressed	4, 5
		(*e*) Describe any sensitivity analyses	5
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	6, supplement
		(b) Give reasons for non-participation at each stage	supplement
		(c) Consider use of a flow diagram	supplement
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	6, table 1
		(b) Indicate number of participants with missing data for each variable of interest	6, table 1
		(c) Summarise follow-up time (eg, average and total amount)	6
Outcome data	15*	Report numbers of outcome events or summary measures over time	6, supplement
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	6, table 2, table 3, supplement
		(*b*) Report category boundaries when continuous variables were categorized	N/A
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	6
Discussion			
Key results	18	Summarise key results with reference to study objectives	7
Limitations			
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	3, 7
Generalisability	21	Discuss the generalisability (external validity) of the study results	7, 8
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	N/A

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Ethnicity and outcomes in patients hospitalised with COVID-19 infection in East London: an observational cohort study

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Keywords:	Epidemiology < INFECTIOUS DISEASES, Adult intensive & critical care < INTENSIVE & CRITICAL CARE, PUBLIC HEALTH, Respiratory infections < THORACIC MEDICINE

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Ethnicity and outcomes in patients hospitalised with COVID-19 infection in East London: an observational cohort study

V. J. Apea[1‡], Y. I. Wan[2‡], R. Dhairyawan[3], Z. A. Puthucheary[4], R. M. Pearse[5], C. M. Orkin[6*], J. R. Prowle[7*]
‡Joint first authors
*Joint senior authors

1. A. Consultant Physician in Sexual Health and HIV Medicine, Sexual Health Clinical Lead, Barts Health NHS Trust, London, E1 1BB, UK
B. Honorary Senior Lecturer, Blizard Institute, Queen Mary University of London, E1 2AT, UK
v.apea@nhs.net

2. A. NIHR Clinical Lecturer, William Harvey Research Institute, Queen Mary University of London, EC1M 6BQ, UK
B. Specialty Registrar in Intensive Care Medicine & Anaesthesia, Barts Health NHS Trust, London, E1 1BB, UK yize.wan@qmul.ac.uk

3. A. Consultant Physician in Sexual Health and HIV Medicine, Barts Health NHS Trust, London, E1 1BB, UK
B. Honorary Senior Lecturer, Blizard Institute, Queen Mary University of London, E1 2AT, UK
rageshri.dhairyawan@nhs.net

4. A. Clinical Senior Lecturer, William Harvey Research Institute, Queen Mary University of London, EC1M 6BQ, UK
B. Honorary Consultant Physician in Intensive Care, Barts Health NHS Trust, London, E1 1BB, UK
z.puthucheary@qmul.ac.uk

5. A. NIHR Research Professor, William Harvey Research Institute, Queen Mary University of London, EC1M 6BQ, UK
B. Consultant Physician in Intensive Care Medicine and Clinical Director for Research & Development, Barts Health NHS Trust, London, E1 1BB, UK r.pearse@qmul.ac.uk

6. A. Professor of HIV Medicine, Blizard Institute, Queen Mary University of London, E1 2AT, UK
B. Clinical lead for HIV and HIV/Hep C Research, Barts Health NHS Trust, London, E1 1BB, UK
c.m.orkin@qmul.ac.uk

7. A. Senior Clinical Lecturer in Intensive Care Medicine, William Harvey Research Institute, Queen Mary University of London, EC1M 6BQ, UK
B. Consultant in Intensive Care and Renal Medicine, Barts Health NHS Trust, London, E1 1BB, UK
j.prowle@qmul.ac.uk

Corresponding author:
Yize I Wan, PhD
Adult Critical Care Unit,
The Royal London Hospital,
London E1 1BB
Email: yize.wan@qmul.ac.uk
Tel: +44 20 3594 40352

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Abstract

Objective
To describe outcomes within different ethnic groups of a cohort of hospitalised patients with confirmed COVID-19 infection. To quantify and describe the impact of a number of prognostic factors, including frailty and inflammatory markers.

Setting
Five acute NHS Hospitals in east London.

Design
Prospectively defined observational study using registry data.

Participants
1737 patients aged 16 years or over admitted to hospital with confirmed COVID-19 infection between 1st January and 13th May 2020.

Main outcome measures
The primary outcome was 30-day mortality from time of first hospital admission with COVID-19 diagnosis during or prior to admission. Secondary outcomes were 90-day mortality, intensive care unit (ICU) admission, ICU and hospital length of stay, and type and duration of organ support. Multivariable survival analyses were adjusted for potential confounders.

Results
1737 were included in our analysis of whom 511 had died by day 30 (29%). 538 (31%) were from Asian, 340 (20%) Black and 707 (40%) White backgrounds. Compared to White patients, those from minority ethnic backgrounds were younger, with differing comorbidity profiles and less frailty. Asian and Black patients were more likely to be admitted to ICU and to receive invasive ventilation (Odds ratio 1·54, [1·06-2·23]; p=0·023 and 1·80 [1·20-2·71]; p=0·005, respectively). After adjustment for age and sex, patients from Asian (Hazard ratio (HR) 1·49 [1·19-1·86]; p<0·001) and Black (HR 1·30 [1·02-1·65]; p=0·036) backgrounds were more likely to die. These findings persisted across a range of risk-factor adjusted analyses accounting for major comorbidities, obesity, smoking, frailty, and ABO blood group.

Conclusions
Patients from Asian and Black backgrounds had higher mortality from COVID-19 infection despite controlling for all previously identified confounders and frailty. Higher rates of invasive ventilation indicate greater acute disease severity. Our analyses suggest that patients of Asian and Black backgrounds suffered disproportionate rates of premature death from COVID-19.

Strengths and limitations of this study

- This study is one of the most comprehensive studies exploring COVID-19 outcomes in BAME populations so far reported including evaluation of linked comorbid and socioeconomic risk factors.
- This study was conducted in a single region where COVID-19 has had significant impact and thus not confounded by differences in incidence of COVID-19 disease across the UK, regional concentration of minority ethnic groups and regional differences in the time-course of the epidemic.
- In addition, we employed a pre-specified statistical analysis plan and performed multiple sensitivity analyses to test the robustness of our findings.
- In line with the vast majority of published COVID-19 analyses, we only included proven COVID-19 cases therefore suspected diagnoses should be considered in future studies, particularly those occurring outside of hospitals.
- Despite its size, our study lacked the power to assess a more detailed ethnicity breakdown and like many datasets, may not reflect the vast heterogeneity within ethnic categories (such as Bangladeshi, Pakistani, Black African or Black Caribbean).

Introduction

The novel *Severe Acute Respiratory Syndrome Coronavirus*-2 (SARS-CoV-2) which manifests as coronavirus disease 2019 (COVID-19) has led to a global pandemic(1). Older age, male sex, obesity and pre-existing health conditions such as diabetes and hypertension have all been identified as risk factors for poor outcomes(2-4). A disproportionate impact of disease severity and death on people from Black, Asian and minority ethnic (BAME) backgrounds has been reported, though not consistently. The UK Intensive Care National Audit and Research Centre (ICNARC) noted that whilst BAME groups only make up 14% of the UK population, they comprised 33% of COVID-19 patients on intensive care units(5). The degree of this excess risk also appears to differ across, and within, these heterogeneous ethnic groups. In the UK, recent analyses of data from the Office of National Statistics and NHS England described 2.5-4.3 fold greater COVID-19 mortality rates, compared to White groups, across a range of Black and South Asian ethnic groups(6). Whether this adverse association is driven by underlying comorbid disease, socio-economic inequality, genetic factors or a complex interplay of them all is unclear(7). Current data are limited in either number of COVID-19 patients, ethnic diversity or event rates with limited adjustment for known risk factors and potential predictors(8-12). There is an urgent need for the detailed characterisation of ethnic differences in COVID-19 outcomes and associated risk factors, within diverse populations, to inform practice and policy. Identifying and responding to these ethnic inequalities will be key to mitigating the disproportionate impact of COVID-19 on BAME patients.

Barts Health NHS Trust is the largest NHS trust in the UK, comprising six hospitals; The Royal London Hospital, Newham General Hospital, Whipps Cross Hospital, Mile End Hospital (Non-acute), St Bartholomew's Hospital and the London NHS Nightingale Hospital, a purposely built COVID-19 hospital. The hospitals serve the ethnically diverse and socially deprived communities of over 2.6 million people in east London including the London Borough of Newham which experienced 144.3 COVID-19 related deaths per 100,000 population(13), the highest mortality in the UK and Tower Hamlets which has the largest Bangladeshi population in England(14). This large, regional dataset afforded extensive analyses of COVID-19 patients of a higher acuity than other studies. We aimed to examine the demographic, socio-economic, behavioural, biochemical and clinical risk factors associated with outcomes within different ethnic groups of hospitalised COVID-19 patients, using multivariable survival analyses.

Methods

Study population

We considered all patients with confirmed SARS-CoV-2 infection and admitted to the five acute hospitals within Barts Health NHS Trust between 1st January and 13th May 2020. Diagnosis was made using one or more real-time RT-PCR. Those under 16 years were excluded. The first emergency admission encompassing the first positive SARS-CoV-2 test, or the first emergency admission within two weeks of positive outpatient testing was defined as the index admission, community diagnoses without an associated emergency hospital admission were excluded. Patients with unknown or undisclosed ethnicity status were collected for comparison but were not included in our primary ethnicity analysis.

Data collection

Clinical and demographic data, blood results and coding data from current and prior clinical encounters, were collated from the Barts Health Cerner Millennium Electronic Medical Record (EMR) data warehouse and locally held ICNARC databases by members of the direct clinical care team. Mortality data was available to 20th May 2020.

Definition of key variables

Ethnicity was defined using the NHS ethnic category codes and based on five high-level groups: White, Asian or Asian British, Black or Black British, Mixed and Other; to preserve statistical power the Mixed and Other categories were merged. Relative measures of socioeconomic deprivation were assessed using the English Indices of Deprivation 2020 by matching patient postcode to national index of multiple deprivation (IMD) quintiles using the Office of National Statistics Postcode Directory(15, 16). Baseline comorbid diseases and Hospital Frailty Risk Score (HFRS) were identified by mapping to ICD-10 coding(17). Body mass index (BMI) was calculated by height and weight measurements taken at or during the immediately preceding admission episode. Rockwood Clinical Frailty Scoring (RFS) was assessed by the admitting medical team and recorded in the EMR(18). Secondary haemophagocytic lymphohistiocytosis (sHLH) risk score was calculated from peak values of blood results(19). Full definitions are detailed in supplementary materials. National early warning score (NEWS) was recorded in the emergency room and general wards by clinical teams in the EMR and is presented as the total score from 6 physiological parameters(20).

Outcomes

The primary outcome was 30-day mortality from time of index COVID-19 hospital admission. Secondary endpoints were 90-day mortality, ICU admission, ICU length of stay, duration of organ support on ICU, need for mechanical ventilation, hospital length of stay, and discharge destination if discharged alive from hospital.

Statistical analyses

A prospective statistical analysis plan was developed(21). Baseline characteristics are presented as mean and standard deviation, median and interquartile range, or number and percentage, as appropriate. We compared proportions using Pearson's Chi-square test or Fisher's exact test and continuous variables using 2-sample t-test or Wilcoxon rank-sum test, as appropriate. Time-to-event analysis was undertaken with follow-up censored at 30 days, survivors with less than 30 days follow-up were censored at time of maximal follow-up. A Cox proportional hazards model was used to assess survival adjusted for age and sex. Age was the only continuous variable. A further multivariable Cox model was developed to assess the effect of pre-defined risk factors described as associated with adverse outcomes in COVID19: IMD quintile, smoking status, body mass index, diabetes, hypertension, and chronic kidney disease (CKD). The proportional-hazard assumption was assessed by inspection of scaled Schoenfeld residual plots and investigated by stratification(22). Logistic regression modelling of ethnicity on ICU treatment using mechanical ventilation was carried out. Effect measures are presented as hazard ratios (HR) or odds ratios (OR) with 95% confidence intervals (CI). All analyses were performed using R version 3.6.3 (R Core Team 2020).

Sensitivity analyses

To assess the effect of including patients with incomplete clinical data, missing data for baseline risk variables included in the multivariable Cox model was imputed using Multivariate Imputation by Chained Equations(23). Additional multivariable models were also carried out using aggregate Charlson comorbidity index (CCI) as a measure of total comorbid disease burden, and HFRS or RFS collected at hospital admission and ABO blood group. Longer-term survival to 90 days was assessed using Cox proportional hazards modelling adjusted for age and sex censored at time of maximal follow-up if survivors had less than 90 days follow-up.

Results

A total of 1996 patients, aged 16 years and older, with a confirmed SARS-CoV-2 test result with an acute Barts Health admission on or before 13th May 2020 were included in this study [Figure S1]. The recruitment window encompassed the peak time period of COVID-19 diagnoses [Figure S2]. The majority of patients were classified as being in the two most deprived socio-economic quintiles in England. The ethnic distribution was White (n=703, 35·2%), Asian or Asian British (n=538, 27·0%), Black or Black British (n=340, 17·0%), Mixed and Other (n=156, 7·8%) and unknown or undisclosed (n=259, 13·0%). Supporting results are detailed in supplementary file sections S1-S9 [Tables S1-S10, Figures S1-S17].

Population Characteristics

Baseline characteristics, interventions and outcomes across ethnic groups are shown in Table 1. Black and Asian ethnicity patients were significantly younger with a median age of 59 years (Asian) and 64 years (Black), compared to 73 years in the White group (p<0·001). Comorbidity data was available in 1700 (85.2%) of patients.

Burden of comorbid disease varied between ethnic groups in prevalence, type and age-distribution. Overall distribution of COVID risk factors varied with age and ethnicity with diabetes and CKD more prevalent at an earlier age in Asian and Black patients and frailty and dementia more prevalent in older White patients [Figure 1].

Around one in four patients developed early acute kidney injury (AKI) within seven days of hospital admission, rates of AKI were highest in the Black group (34·7%). Patients in the Black group had higher levels of inflammation CRP (median CRP 181·5 mg/L) and fibrinolysis (median D-dimer 2·5 mg/L) compared to other ethnicities. As a measure of extent of early physiological derangement UK National Early Warning Score (NEWS) was available in 1443 patients, in comparison to White patients first NEWS was modestly higher in Asian patients (mean 4.2 vs. 3.6), p=0.001, but not in Black patients (mean 3.7 vs 3.6).

Age and sex adjusted 30-day mortality

We included 1737 Asian, Black and White patients in the primary outcome analysis. Total mortality to 20th May 2020 was 28·7% (n=573). Based on the raw data, a greater proportion of White patients died (32·7%) compared to Asian (21·1%) and Black (29·7%) patients. The majority of deaths (93·7%) occurred within 30 days of hospital admission. However, after adjustment for the between-group differences in age and sex, patients from Asian and Black ethnic groups were at significantly higher risk of death within 30 days compared to White patients (Asian ethnicity (HR 1·49, CI 1·19-1·86, p<0·001); Black patients (HR 1·30, CI 1·02-1·63, p=0·036). No association was observed in the smaller Mixed and Other Ethnicity group (HR 1·08, CI 0·75-1·57, p=0·682) [Table 2, Figures 2 and 3]. There was some evidence of non-proportionality for the association between ethnicity and risk of death over time [Figure S16], consequently these HRs should be interpreted as a weighted average over the 30-day follow up period. To investigate change in risk over time we developed an ethnicity-stratified Cox-model, this supported the findings of the unstratified model, but suggested that Black ethnicity might be associated with a higher early rate of death [Figure S17].

Multivariable survival modelling

After inclusion of IMD quintile, smoking history, BMI ≥30 kg/m^2, diabetes, hypertension, and CKD in a multivariable survival analysis, the association with increased rate of death persisted in Asian patients (HR 1·48, CI 1·09-2·01, p=0·011; n=1006). In Black patients, the magnitude of the mortality trend was unchanged, however was outside the limits of standard statistical significance (HR 1·32, CI 0·96-1·84, p=0·090; n=1006), potentially due to the smaller sample size. In this model older age, male sex, smoking, BMI ≥30 kg/m2 and CKD were statistically associated with risk of death [Table 3, Figures 4 and 5] and there was no statistical evidence that ethnicity violated the proportional hazards assumption. The associations were broadly unchanged when the model was re-fitted after multiple imputation of missing values [Table S4].

Sensitivity analyses for further multivariable survival models were developed to examine the influence of total comorbidity burden, as assessed by CCI [Table S5], and measures of frailty, the RFS or HFRS [Tables S6, S7] as well as ABO blood group [Table S8]. In all these analyses the association between Black and Asian ethnicity and 30-day mortality remained significant. Adjusting for RFS raised the odds of 30-day mortality to a HR of 1·98 (CI 1·37-2·86; p<0.001) in Asian groups and to a HR of 1·67 (CI 1·14-2·45; p=0.009) in Black groups, with similar effect size in analysis adjusted for the HFRS. After inclusion of ABO blood grouping in and age and sex adjusted multivariable model risks of death in Asian, Black, and Mixed and Other ethnic groups was increased. Asian ethnicity also continued to be associated with greater risks of death through to 90 days follow-up (HR 1·46, CI 1·18-1·81, p<0·001; n=1737) [Table S9].

Critical Care related outcomes

In the White group, 11·0% of patients were admitted to ICU compared to 20·1% of the Asian group and 18·5% of the Black group (p<0.001). In those admitted to ICU, rates of mechanical ventilation requiring intubation did not differ significantly by ethnicity at 76·6% in the White group, 72·2% in the Asian group and 79·4% in the Black group. Similarly, while rates of ICU admission differed significantly between ethnic groups, time from hospital to ICU admission and length of ICU stay did not. Across the entire hospitalised cohort Asian (OR 1·54, CI 1·06-2·23, p=0·023; n=1737) and Black (OR 1·80, CI 1·20-2·71, p=0·005; n=1737) ethnicities were associated with increased age and sex adjusted-risk of receiving invasive mechanical ventilation in ICU [Table S10]. There was a trend toward increased renal replacement therapy use in Black patients (41.3%) admitted to ICU compared to 20-25% across other ethnic groups (p=0.09).

Discussion

We report on treatment and outcomes in COVID-19 patients hospitalised in East London throughout the peak of the UK pandemic, a population with the UK's highest COVID-19 mortality. To our knowledge this is one of the largest UK hospital COVID-19 cohorts reported, and certainly the most diverse, with only 35.2% of 1996 patients identified as White ethnicity. We found those of Asian ethnicity to be at the highest risk of death within 30 days (HR 1·49, CI 1·19-1·86, p<0·001), a finding that persisted at 90 days. Risk of death in Black patients was also greater than those of White ethnicity (HR 1·30, CI 1·02-1·63, p=0·036). This disparity extended to need for ICU care with Asian and Black patients experiencing a 50-80% increased risk of receiving mechanical ventilation in ICU compared to White patients of a similar age.

Strengths and Limitations

We believe this study is both one of the largest and most detailed of studies exploring COVID-19 outcomes in BAME populations so far reported. In contrast to many previous studies examining ethnicity and COVID-19 outcomes we were able to address the contributions of socio-economic deprivation, comorbid disease, pre-morbid function, lifestyle and demographic factors to ethnic disparities in COVID-19 outcomes, including ICU interventions. Our analysis was strengthened by the inclusion of measures of frailty which is a critical determinant of outcomes in acute disease as well as a potential driver of clinician decision-making. It should be acknowledged, however, that frailty has social and biological dimensions and measures have not been extensively validated in BAME groups.

Importantly, this study was conducted in a single region where COVID-19 has had significant impact and thus is not confounded by differences in incidence of COVID-19 disease across the UK, regional concentration of minority ethnic groups and regional differences in the time-course of the epidemic. In addition, we employed a pre-specified statistical analysis plan and performed multiple sensitivity analyses to test the robustness of our findings.

Limitations in our analyses must also be considered. Importantly, SARS-CoV-2 testing has an appreciable false negative rate and suspected, but not proven, cases are an important group. Nevertheless, given that clinical suspicion varied both between cases and across the time-course of the epidemic with coding of suspected cases being inconsistent, in line with the vast majority of published COVID-19 analyses, we only included proven COVID-19 cases. Testing was available for all hospitalised patients with suspected COVID-19 disease, so availability of testing was not a bias. However, suspected diagnoses should be considered in future studies, particularly those occurring outside of hospitals, where not all clinical diagnoses may have been tested.

Similar to many hospital datasets there were missing data for a proportion of co-variates(8, 9), however 85% of patients had coding data for assessment of comorbidity and 63% measured height and weight data, providing a large sample with detailed data for analysis. We also imputed missing data and performed sensitivity analyses on our multivariable comorbidity models. This reinforced the observed ethnic differences, providing further confidence that our findings were not affected by missing data.

Like many datasets, our ethnic categorisations were aggregated and did not reflect the vast heterogeneity within ethnic categories (such as Bangladeshi, Pakistani, Black African or Black Caribbean). Indeed, the descriptive term "BAME" itself is particularly crude and we recognise its limitation. Despite its size, our study lacked the power to assess a more detailed ethnicity breakdown. In addition, our observations in those of Asian ethnicity are likely skewed by our large Bangladeshi community, which has specific socio-economic and healthcare inequalities. It is therefore important that, suitably powered, analyses are conducted to expose differences between sub-ethnic categories. Similarly, whilst we have explored socio-economic factors, our analysis does not allow us to

contextualise a number of potential socio-spatial factors including household composition, environmental factors and occupation. These should be considered in future research.

Comparison with other studies

Our findings differ from predominant reports in the UK and US in which Black ethnicity has been consistently associated with greater COVID-related mortality(6, 24). Preliminary analyses of the UK ICNARC report on COVID-19 in critical care highlighted Black ethnicity with the highest likelihood of being admitted to intensive care compared to a matched population (10.7% versus 6.5%)(25). Similarly, in a large UK primary care linked cohort, Black patients were also to found to be at highest risk of COVID-related death(9). In a US study, the composite relative risk of COVID-related death compared to White ethnicity was 3.57 in Black populations, and 1.88 for Latinos(24). Our findings suggest specific South Asian communities may have at least the same or higher risk in COVID-19 as those of Black background. This may reflect characteristics of the large South Asian, and specifically Bangladeshi, community in East London, poorly represented in other studies. Recently the *ISARIC CCP-UK* investigators have described association of ethnicity and outcome in a very large cohort of UK patients, finding Asian, but not Black background was associated with increased risk of death in confirmed or suspected COVID-19(26). While this study documented up to 40% of UK COVID cases, it represented a selection from the total COVID population from across the UK, and, at least in terms of ICU cases, ethnic minorities were significantly under-represented compared to the English ICU COVID population. In contrast while smaller, this study focused on an unbiased population comprising all hospitalised patients in a single geographical area with a much higher level of ethnic diversity. Consequently, we feel our analysis complements ISARIC CCP-UK and provides greater clinical detail in a regionally homogenous population.

Potential confounding associations with risk of death in COVID-19

Older age has been significantly associated with increased COVID-19 mortality across a range of studies(2-4). In our cohort, patients from Asian and Black backgrounds were strikingly younger than White patients. However, despite the expected protective factor of younger age, when this was accounted for, those from Black and Asian backgrounds were more likely to die. The prevalence of comorbid disease has been well described as a risk factor for COVID-19 disease and death(3, 4). We found different ethnic groups had differing age-distribution of baseline comorbidities such as hypertension, diabetes, chronic obstructive pulmonary disease and dementia. Despite accounting for these and other described predictors of poor outcomes, increased risk of death in Asian and Black populations was not attenuated, suggesting comorbidities are not the sole drivers of ethnicity-associated risk.

ABO blood group has recently been suggested to affect the risk of symptomatic COVID-19 and need for respiratory support with supplemental oxygen(12, 27). In these analyses blood group O was associated with less disease acquisition than group A. As there are well-described differences in blood group distribution with ethnicity (in particular, prevalence of blood group B in Asian and to a lesser extent Black populations), in a post-hoc analysis we assessed the association between ABO group and risk of death in 875 patients with blood group data. In contrast to studies focused on risk of COVID-19 acquisition in our cohort of hospitalised COVID diagnoses, blood group O was associated with higher risk of death and blood group B the lowest. Accordingly, when we included ABO blood group in a multivariable survival analysis with age, sex the association between Black and Asian background and increased risk of death was not attenuated but magnified. This suggests ethnic imbalances in blood group distribution did not explain the mortality associations observed in our population.

Patients identified as frail have been predicted to have worse COVID-19 related health outcomes(28), and lower likelihood of benefiting from complex acute interventions, including critical care. In this study White patients, in addition to being notably older than other ethnicities, had higher degrees of frailty. Accounting for measures of frailty magnified the association seen between Asian and Black ethnicity and death. This suggests that whilst in White patients COVID-19 related death may have occurred in already frail and functionally vulnerable patients, in both Asian and Black patients, COVID-19 related deaths are likely to be occurring prematurely, in younger, fitter individuals with less functional vulnerability.

In our cohort, all ethnic groups experienced high levels of deprivation, however, worse deprivation was not associated with higher likelihood of mortality, suggesting ethnicity may affect outcomes independent of purely geographical and socio-economic factors(29).

We found evidence for worse disease severity in Black and Asian groups as evidenced by higher rates of ICU admission and higher rates of AKI, and high levels of D-dimers and CRP in Black patients. High CRP and D-dimer levels have been identified as important inflammatory markers which strongly correlate with COVID-19 disease severity and prognosis(30). Our data suggest potential biological differences in host-response to COVID-19 may occur between ethnicities, however, causative associations in determining COVID-19-related mortality have not been demonstrated.

Finally, although COVID-19 has cast the effects of ethnic inequalities on health outcomes into sharp focus, these inequalities are not new. Health inequalities within and between ethnic minority groups are widely documented and the effects of structural racism are transmitted across generations(31). The risk factors already discussed such comorbidity and obesity are speculated to intersect and be inextricably linked with wider social determinants such as poor living conditions, key worker roles and language barriers which impede the adoption of preventative measures(29, 32, 33). Some researchers have postulated that ethnic inequalities may be associated with decreased symptom recognition and poor engagement with health services(34). However, while frequency of ICU admission, AKI and need for mechanical ventilation suggests more severe peak-disease in minority ethnic groups, time to ICU admission did not differ and differences in first total NEWS were at most modest, suggesting against a large effect from delayed presentation.

Conclusion
In this analysis of a large, ethnically diverse and socio-economically challenged cohort, hospitalised patients of Asian and Black background with COVID-19 were at increased risk of premature death, independent of frailty, comorbidities and social deprivation. Failure to robustly respond to the ethnic disparities so conspicuously unmasked during the COVID-19 pandemic can only further entrench and inflict them on future generations.

Public and Patient Involvement statement
COVID-19 has presented unique challenges and warranted a unique response in research. This protocol has been swiftly developed in response to concerning data suggesting poorer outcomes of patients with confirmed COVID-19 from a BAME background. This data has led the general public, via social media and community influencers, to call for governmental and health bodies to urgently review patient outcomes to explore this emerging inequality and respond appropriately to mitigate further deaths and inequity. Whilst no direct public and patient involvement has taken place, the research team believe the study in line with current public and patient mandate.

Ethics approval
This study was approved by HRA and Yorkshire & The Humber - Bradford Leeds Research Ethics Committee (Ethics reference **20/YH/0159**). The study was sponsored by Barts Health NHS Trust.

Transparency declaration
J Prowle (the manuscript's guarantor) affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned and registered have been explained.

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Contributorship statement
V Apea developed the study concept, designed the study, wrote the study protocol, submitted the ethics application, provided critical review of the findings and wrote the manuscript. Y Wan wrote the statistical analysis plan, performed data extraction, performed statistical analysis, provided critical review of the findings and wrote the manuscript. R Dhairyawan developed the study concept, designed the study, provided critical review of the findings and wrote the manuscript. Z Puthucheary provided critical review of the findings and wrote the manuscript. R Pearse developed the study concept, designed the study, provided critical review of the findings and wrote the manuscript. C Orkin developed the study concept, designed the study, provided critical review of

the findings and wrote the manuscript. J Prowle developed the study concept, designed the study, wrote the study protocol, submitted the ethics application, performed data extraction, performed statistical analysis, provided critical review of the findings and wrote the manuscript. All authors approved the final version of the manuscript. The data was collated and analysed on behalf of all clinicians at Barts Health.

Study Concept and Design	VJA CMO RD JRP RMP
Ethics application and Approvals	VJA JRP
Study protocol and analysis plan	VJA YIW JRP
Data Extraction	YIW JRP
Data Analysis	YIW JRP
Critical review of finding	All authors
Manuscript writing	VJA CMO YIW RD ZAP RP JRP
Review of final submission	All authors

Competing interests

All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and declare: no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

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Data sharing statement

The statistical analysis plan can be accessed online. The authors will be happy to consider additional analyses of the anonymised dataset on request. The need for stringent measures to prevent re-identification of individuals within a discrete geographical location and limited time-period however preclude sharing of patient level dataset in a GDPR compliant form.

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Figure legends

Figure 1. Heat map of prognostic factors in COVID-19 hospital admissions by age and ethnic background showing proportions within each ethnic group for each age group. Asian and Black patients differed from those of white background in the presence of risk factors and their age distribution however differences were also apparent between different Black and Minority Ethnic groups at different ages. Proportions are of those with data (see Table 1). BMI: body mass index, COPD: chronic obstructive pulmonary disease, DM: diabetes mellitus, HT: hypertension, CKD: chronic kidney disease.

Figure 2. Forest plot showing hazards ratios of mortality to 30 days comparing ethnic groups, age and sex corrected, on log scale.

Figure 3. Survival curve to 30 days comparing predicted survival of Asian, Black, and White ethnic groups (Mixed and Other group omitted for clarity), in an age and sex adjusted Cox-hazard analysis. Survival curves adjusted to median age 65 years and male sex.

Figure 4. Forest plot showing hazards ratios of mortality to 30 days comparing ethnic groups, age and sex corrected, on log scale. Additional variables included index of multiple deprivation (IMD) quintile (5 least deprived), smoking, BMI ≥30 kg/m^2, diabetes, HTN: hypertension, CKD: chronic kidney disease.

Figure 5. Survival curve to 30 days from multivariable analysis comparing Asian, Black, and White ethnic groups. Survival modelled for median age 65 years and male sex, index of multiple deprivation (IMD) least deprived quintile, no history of baseline risk factors defined as Non-smoking, BMI <30 kg/m^2 and No diabetes, hypertension or chronic kidney disease. Statistically significant difference in survival between Asian group and White group persists after adjustment for age, sex, social deprivation and major COVID-19 risk factors.

Tables

Table 1. Study population baseline characteristics stratified by ethnic group, n (%) unless otherwise stated. Total n=1996 unless otherwise stated. P values based on Chi-square (for categorical) or Kruskal-Wallis test (for continuous). SD: standard deviation, IQR: interquartile range, IMD: index of multiple deprivation, BMI: body mass index, TIA: transient ischaemic accident, HTN: hypertension, CKD: chronic kidney disease, sHLH: secondary haemophagocytic lymphohistiocytosis (without known underlying immunosuppression and bone marrow aspirate data), CRP: C-reactive protein, NEWS: national early warning score, ICU: intensive care unit, RRT: renal replacement therapy.

	Stratified by ethnic group					
	Asian or Asian British	**Black or Black British**	**Mixed and Other Ethnic Groups**	**White**	**Unknown and Undisclosed**	p value
n	538	340	156	703	259	
Age (years) Mean (SD)	57·8 (18·5)	64·2 (16·9)	59·5 (17·2)	69·4 (17·7)	59·8 (16·5)	<0·001
Age (years) Median (IQR)	59·0 (44·0-71·0)	64·0 (53·0-79·0)	59·0 (47·8-72·3)	73·0 (58·0-84·0)	61·0 (50·0-71·5)	<0·001
Male	332 (61·7)	193 (56·8)	103 (66·0)	404 (57·5)	178 (68·7)	0·01
IMD quintile [n=1980]						<0·001
1 (most deprived)	139 (26·0)	124 (36·7)	50 (32·9)	183 (26·2)	66 (25·7)	
2	291 (54·5)	165 (48·8)	72 (47·4)	269 (38·5)	124 (48·2)	
3	49 (9·2)	34 (10·1)	20 (13·2)	99 (14·2)	44 (17·1)	
4	35 (6·6)	9 (2·7)	7 (4·6)	86 (12·3)	18 (7·0)	
5 (least deprived)	20 (3·7)	6 (1·8)	3 (2·0)	62 (8·9)	5 (1·9)	
Smoking [n=1700]	30 (6·6)	21 (7·1)	10 (8·3)	91 (14·8)	21 (9·8)	<0·001
BMI [n=1248]						
Median (IQR)	26·9 (24·1-31·1)	28·2 (24·6-31·8)	25·9 (23·1-29·0)	26·3 (22·5-31·6)	26·3 (22·5-30·8)	0·04
By category						0·04
<18·5 kg/m^2	9 (2·8)	8 (3·6)	1 (1·3)	34 (6·9)	11 (8·5)	
18·5 - <25 kg/m^2	101 (31·2)	57 (25·3)	31 (40·3)	160 (32·5)	43 (33·1)	
25 - <30 kg/m^2	114 (35·2)	83 (36·9)	27 (35·1)	145 (29·5)	40 (30·8)	
30 - <40 kg/m^2	87 (26·9)	65 (28·9)	17 (22·1)	126 (25·6)	28 (21·5)	
≥40 kg/m^2	13 (4·0)	12 (5·3)	1 (1·3)	27 (5·5)	8 (6·2)	
Co-morbidity [n=1700]						
Obesity	108 (23·6)	82 (27·9)	18 (14·9)	161 (26·2)	40 (18·7)	0·01
Ischaemic heart disease	102 (22·3)	62 (21·1)	12 (9·9)	149 (24·3)	21 (9·8)	<0·001
Myocardial infarction	55 (12·0)	23 (7·8)	6 (5·0)	83 (13·5)	14 (6·5)	0·002
Congestive heart failure	67 (14·7)	54 (18·4)	8 (6·6)	114 (18·6)	17 (7·9)	<0·001

Peripheral vascular disease	33 (7·2)	35 (11·9)	7 (5·8)	67 (10·9)	16 (7·5)	0·06
Cerebral vascular accident or TIA	54 (11·8)	54 (18·4)	11 (9·1)	157 (25·6)	16 (7·5)	<0·001
Dementia	25 (5·5)	27 (9·2)	5 (4·1)	103 (16·8)	7 (3·3)	<0·001
Chronic obstructive pulmonary disease	119 (26·0)	45 (15·3)	18 (14·9)	181 (29·5)	34 (15·9)	<0·001
Diabetes	220 (48·1)	157 (53·4)	49 (40·5)	179 (29·2)	59 (27·6)	<0·001
HTN	261 (57·1)	212 (72·1)	64 (52·9)	376 (61·2)	96 (44·9)	<0·001
Moderate to severe CKD	92 (20·1)	93 (31·6)	16 (13·2)	145 (23·6)	17 (7·9)	<0·001
End-stage renal disease	39 (8·5)	36 (12·2)	7 (5·8)	27 (4·4)	4 (1·9)	<0·001
Liver disease	49 (9·1)	24 (7·1)	12 (7·7)	58 (8·3)	12 (4·6)	0·25
Cancer	30 (6·6)	26 (8·8)	8 (6·6)	68 (11·1)	12 (5·6)	0·04
Cancer with metastases	8 (1·8)	5 (1·7)	1 (0·8)	22 (3·6)	6 (2·8)	0·18
Acquired immunodeficiency syndrome	0 (0·0)	5 (1·7)	0 (0·0)	1 (0·2)	0 (0·0)	0·001
Charlson comorbidity index [n=1700]						<0·001
0	131 (28·7)	66 (22·4)	42 (34·7)	143 (23·3)	91 (42·5)	
1-2	178 (38·9)	100 (34·0)	50 (41·3)	203 (33·1)	88 (41·1)	
3-4	70 (15·3)	52 (17·7)	16 (13·2)	146 (23·8)	20 (9·3)	
≥5	78 (17·1)	76 (25·9)	13 (10·7)	122 (19·9)	15 (7·0)	
Rockwood frailty Score [n=831]						<0·001
1-2 (very fit, well)	31 (15·9)	6 (4·3)	7 (14·9)	36 (9·7)	15 (18·8)	
3-4 (managing well, vulnerable)	87 (44·6)	51 (36·7)	17 (36·2)	118 (31·9)	32 (40·0)	
5-6 (mildly to severely frail)	65 (33·3)	73 (52·5)	18 (38·3)	174 (47·0)	29 (36·2)	
8-9 (very severely frail, terminally ill)	12 (6·2)	9 (6·5)	5 (10·6)	42 (11·4)	4 (5·0)	
Hospital frailty Risk Score [n=1700]						<0·001
<5 (low risk)	240 (52·5)	123 (41·8)	66 (54·5)	197 (32·1)	117 (54·7)	
5-15 (intermediate risk)	132 (28·9)	87 (29·6)	38 (31·4)	150 (24·4)	73 (34·1)	
≥15 (high risk)	85 (18·6)	84 (28·6)	17 (14·0)	267 (43·5)	24 (11·2)	
Baseline eGFR ml/min/1·72m² [n=1525]						
Median (IQR)	72·8 (53·3-92·7)	56·4 (36·2-80·2)	75·6 (54·2-91·4)	64·1 (46·2-82·0)	78·2 (61·5-88·7)	<0·001
eGFR <60	130 (29·6)	135 (48·6)	26 (26·0)	239 (40·5)	29 (24·6)	<0·001
Acute kidney injury first 7 days [n=1673]	98 (22·2)	101 (34·7)	32 (24·6)	151 (24·4)	48 (25·0)	0·003
Blood results during admission						

Highest creatinine µmol/L [n=1691]						<0·001
Median (IQR)	91·0 (72·0-157·0)	119·0 (80·0-260·0)	88·0 (71·8-120·3)	98·0 (76·0-147·0)	94·0 (75·0-132·0)	
Highest CRP [n=1761]						<0·001
Median (IQR)	146·0 (72·0-287·8)	181·5 (99·3-289·8)	132·0 (66·0-226·0)	136·0 (68·0-237·0)	156·0 (75·5-272·5)	
Highest D-dimer mg/L [n=968]						<0·001
Median (IQR)	1·0 (0·5-3·5)	2·5 (0·9-10·3)	1·1 (0·5-2·7)	1·4 (0·6-3·4)	1·5 (0·7-6·3)	
Highest sHLH score [n=1881] Mean (SD)	31·1 (27·1)	30·0 (27·9)	27·6 (28·3)	26·4 (24·8)	32·1 (26·7)	0·01
Blood Group [n=875]						<0·001
A	67 (28·4)	37 (23·3)	15 (35·7)	150 (42·1)	36 (43·9)	
AB	14 (5·9)	11 (6·9)	0 (0·0)	12 (3·4)	6 (7·3)	
B	78 (33·1)	37 (23·3)	13 (31·0)	32 (9·0)	8 (9·8)	
O	77 (32·6)	74 (46·5)	14 (33·3)	162 (45·5)	32 (39·0)	
NEWS (first available) [n=1443] Mean (SD)	4·2 (2·6)	3·7 (2·2)	4·0 (2·3)	3·6 (2·5)	3·8 (2·6)	0·001
Intensive care unit (ICU)						
ICU admission	108 (20·1)	63 (18·5)	28 (17·9)	77 (11·0)	85 (32·8)	<0·001
Days in hospital before ICU Mean (SD)	2·3 (5·2)	2·9 (5·1)	1·1 (1·8)	2·3 (11·4)	1·8 (4·2)	0·75
ICU length of stay Median (IQR)	8·0 (3·0-15·2)	8·1 (3·5-14·1)	8·5 (5·0-13·1)	8·0 (3·9-12·0)	10·0 (6·0-16·0)	0·30
Mechanical ventilation within ICU admission	78 (72·2)	50 (79·4)	23 (82·1)	59 (76·6)	71 (83·5)	0·40
RRT within ICU admission	28 (25·9)	26 (41·3)	7 (25·0)	20 (26·0)	18 (21·2)	0·09
Days on organ support						
Advanced respiratory Mean (SD)	11·0 (10·8)	9·4 (8·8)	8·2 (7·1)	7·8 (7·8)	10·3 (8·0)	0·14
Total respiratory Mean (SD)	13·1 (10·4)	11·9 (8·9)	9·8 (7·0)	9·6 (7·7)	11·9 (7·6)	0·08
Cardiovascular system Mean (SD)	13·4 (10·9)	11·5 (8·6)	9·9 (7·2)	9·8 (8·3)	11·8 (7·5)	0·07
Renal Mean (SD)	2·4 (5·5)	4·4 (6·6)	2·1 (4·7)	2·7 (5·7)	1·5 (3·8)	0·03
Total number of organ systems						0·15
0	1 (0·9)	0 (0·0)	0 (0·0)	1 (1·3)	1 (1·2)	
1	3 (2·8)	4 (6·3)	1 (3·6)	5 (6·5)	0 (0·0)	
2	76 (70·4)	33 (52·4)	20 (71·4)	52 (67·5)	66 (77·6)	
3	28 (25·9)	26 (41·3)	7 (25·0)	19 (24·7)	18 (21·2)	
Outcomes						
Died	146 (27·1)	101 (29·7)	34 (21·8)	230 (32·7)	62 (23·9)	0·01

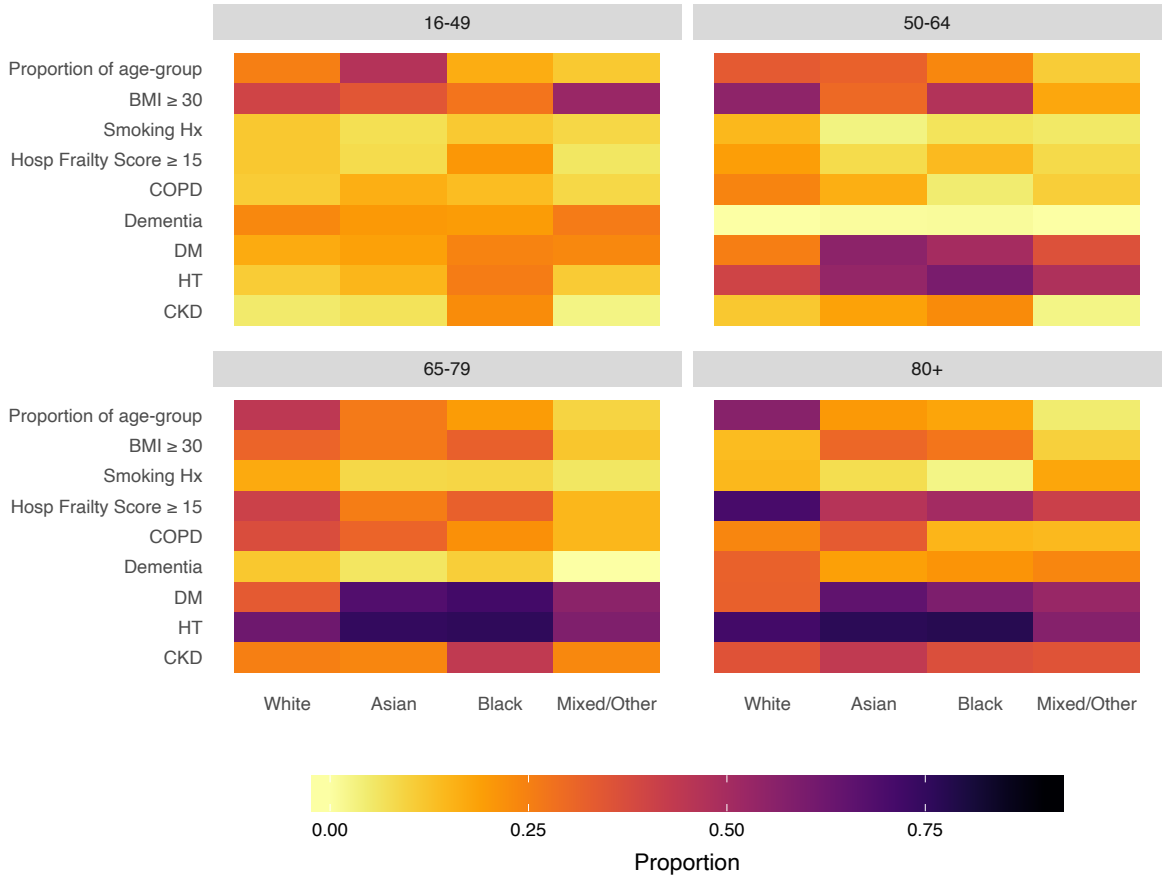
Days to death Mean (SD)	9·7 (10·0)	9·1 (11·0)	11·0 (9·8)	12·9 (13·6)	12·7 (10·0)	0·02
Days to death Median (IQR)	6·0 (3·0-12·0)	5·0 (3·0-11·0)	10·5 (4·3-14·0)	9·0 (4·0-16·0)	10 (6·0-17·0)	<0·001
Died within 30 days	138 (25·7)	97 (28·5)	33 (21·2)	210 (29·9)	58 (22·4)	0·05
Died within 90 days	146 (27·1)	101 (29·7)	34 (21·8)	229 (32·6)	62 (23·9)	0·01
Still in hospital	7 (1·3)	6 (1·8)	3 (1·9)	6 (0·9)	5 (1·9)	0·60
Hospital length of stay Median (IQR)	5·0 (3·0-10·0)	7·0 (4·0-12·0)	5·0 (3·0-11·0)	8·0 (4·0-15·0)	8·0 (4·0-15·0)	<0·001
Discharged Hospital alive	402 (74·7)	241 (70·9)	122 (78·2)	487 (69·3)	200 (77·2)	0·03
Discharge destination [n=1429]						<0·001
Care home or equivalent	7 (1·8)	5 (2·1)	0 (0·0)	40 (8·3)	8 (4·0)	
Health-related institution	7 (1·8)	10 (4·3)	8 (6·7)	23 (4·8)	37 (18·7)	
Usual place of residence	373 (94·4)	216 (91·9)	110 (91·7)	403 (83·8)	152 (76·8)	
Hospice or equivalent	1 (0·3)	0 (0·0)	0 (0·0)	2 (0·4)	1 (0·5)	
Temporary place of residence	7 (1·8)	4 (1·7)	2 (1·7)	13 (2·7)	0 (0·0)	

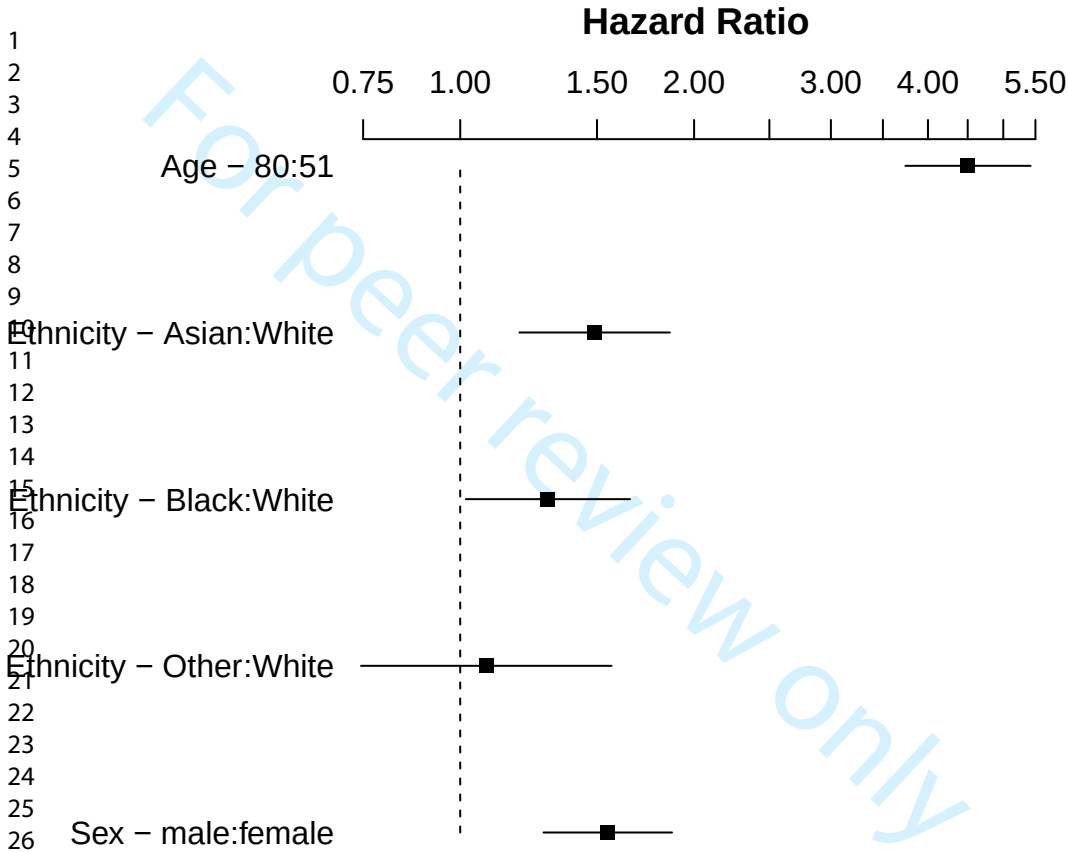
Table 2. Association of ethnic group with mortality to 30 days using Cox proportional hazards modelling, age and sex corrected. Censored to 30 days follow up, observations 1737, events 478.

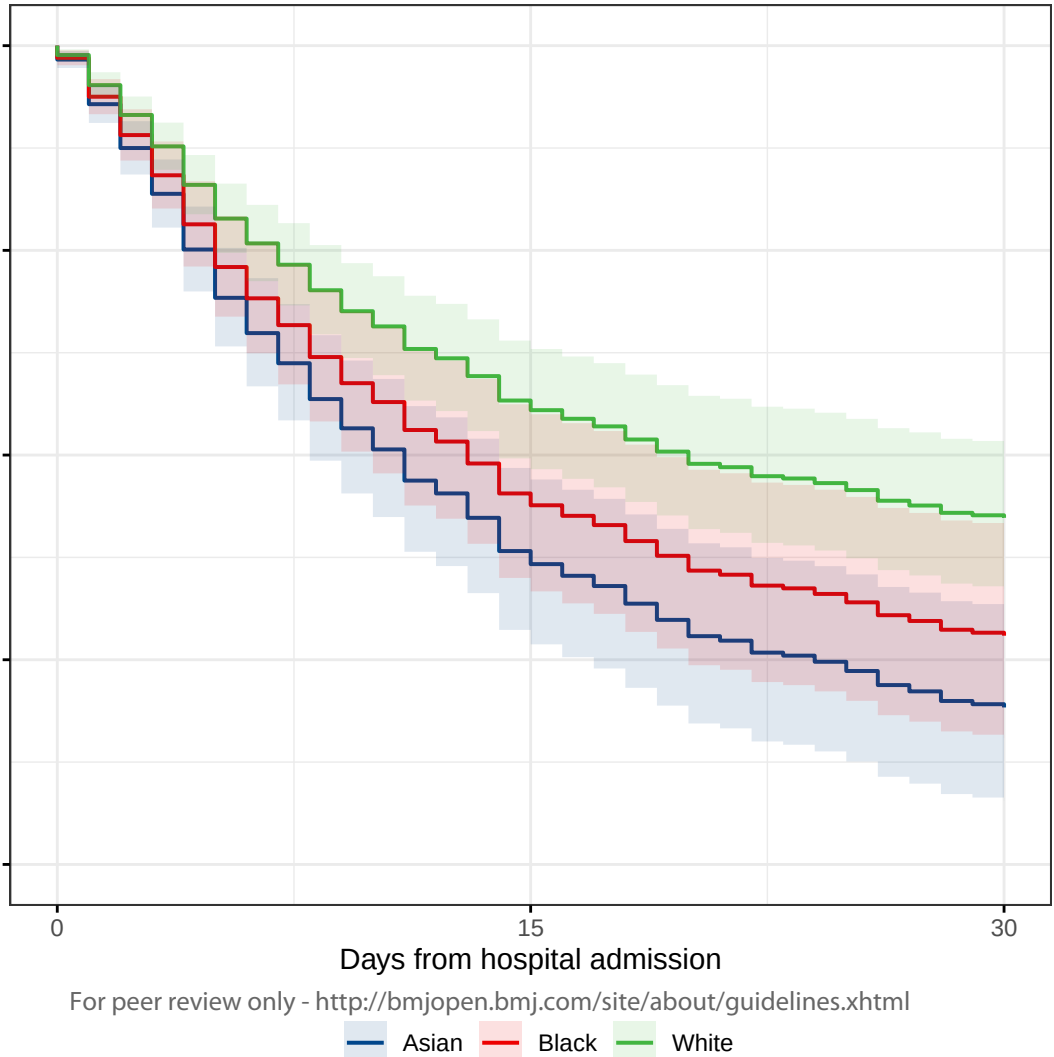
	n		Unadjusted	
	Total	**Events**	**Hazard ratio (95% CI)**	**p value**
Age (25th vs 75th centile)	-	-	4·50 (3·74-5·42)	<0·0001
Sex (Male)	-	-	1·55 (1·28-1·87)	<0·0001
Ethnic group				
Asian or Asian British	521	134	1·49 (1·19-1·86)	<0·001
Black or Black British	331	94	1·30 (1.02-1·65)	0·036
Mixed and Other ethnic groups	150	34	1·08 (0·75-1·57)	0·682
White	674	206	Reference	-

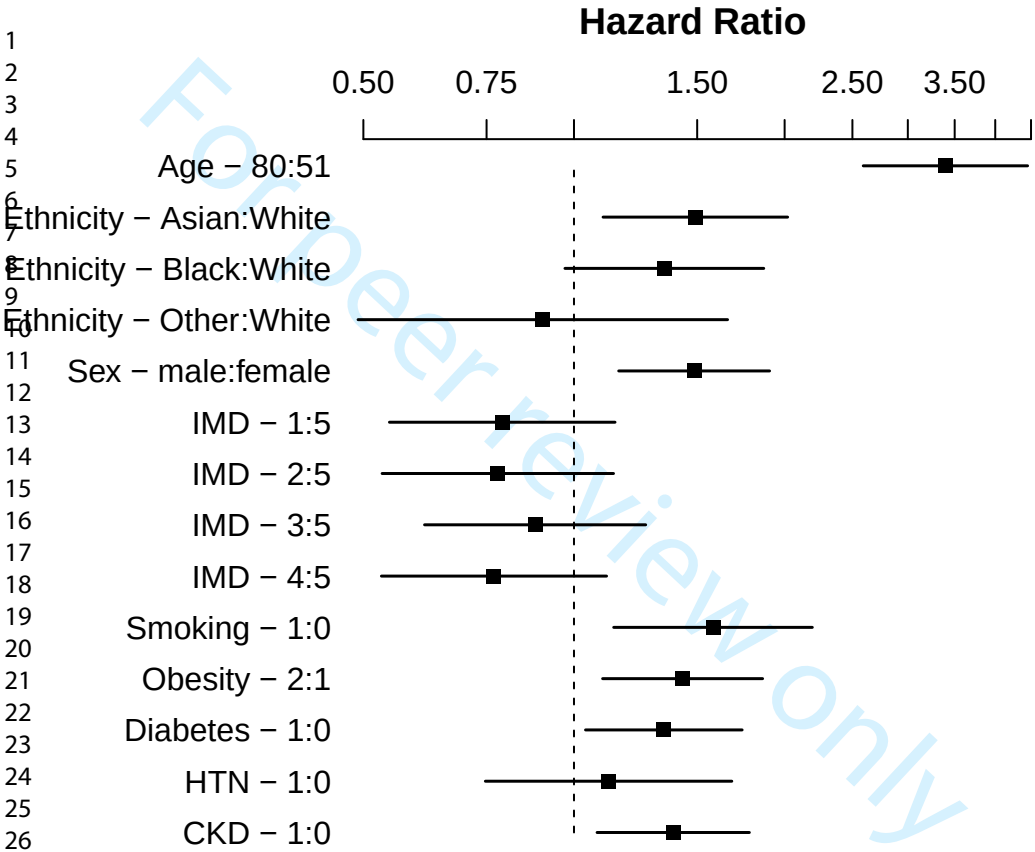
Table 3. Multivariable analysis of mortality to 30 days using Cox proportional hazards modelling, age and sex corrected. Variables included IMD quintile, smoking, BMI ≥30 kg/m^2, diabetes, HTN: hypertension, CKD: chronic kidney disease. Censored to 30 days follow up, observations 1006, events 281.

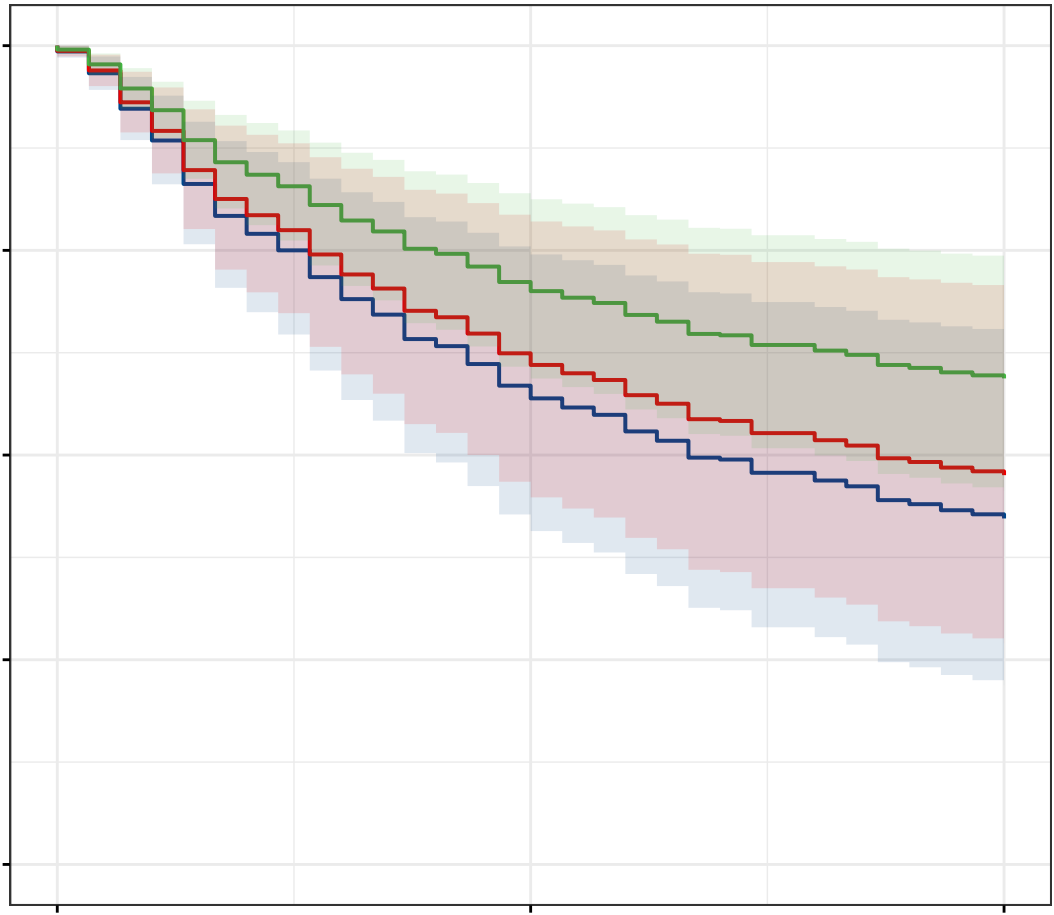
	Adjusted	
	Hazard ratio (95% CI)	**p value**
Age (25th vs 75th centile)	3·24 (2·46-4·26)	<0·0001
Sex (Male)	1·47 (1·15-1·88)	0·002
Ethnic group		
Asian or Asian British	1·48 (1·09-2·01)	0·011
Black or Black British	1·32 (0·96-1·84)	0·090
Mixed and Other ethnic groups	0·90 (0·49-1·65)	0·733
White	Reference	-
IMD quintile		
1 (most deprived)	0·79 (0·55-1·14)	0·213
2	0·79 (0·54-1·15)	0·218
3	0·88 (0·61-1·27)	0·503
4	0·77 (0·53-1·12)	0·176
5 (least deprived)	Reference	-
Smoking	1·56 (1·13-2·17)	0·008
BMI ≥30 kg/m^2	1·42 (1·09-1·85)	0·009
Diabetes	1·29 (1·00-1·67)	0·055
HTN	1·32 (0·92-1·89)	0·131
CKD	1·34 (1·04-1·73)	0·023


16-49
50-64
65-79
80+
Proportion of age-group
BMI ≥ 30
Smoking Hx
Hosp Frailty Score ≥ 15
COPD
Dementia
DM
HT
CKD
White
Asian
Black
Mixed/Other
0.00
0.25
0.50
0.75
Proportion









Supplementary material

Contents

1. Supplemental methods

a. Approvals

The study was reviewed by the Yorkshire & The Humber - Bradford Leeds Research Ethics Committee and approved as anonymised analysis of routinely collected patient data without need for consent by NHS England Health Research Authority (IRAS Project ID 283512).

b. COVID-19 testing

COVID-19 testing was performed by RdRp gene assay test on upper respiratory swab samples (nasopharyngeal, oral or endotracheal aspirate) sent to Barts Health NHS Trust Diagnostic Virology Laboratories and analysed either on-site or at Public Health England (PHE) Colindale facility.

c. Definition of key varaibles

Ethnicity
We defined ethnic groups using the 16+1 categories defined in the 2001 census which form the UK national mandatory standard for the collection and analysis of ethnicity in the NHS data dictionary. Importantly, in the UK 'Asian' ethnic category refers predominantly to those of a South Asian background (including Indian, Pakistani and Bangladeshi), while patients of a Chinese background are placed in the 'Other Ethnic Groups' category.

White	A British B Irish C Any other White background
Mixed	D White and Black Caribbean E White and Black African F White and Asian G Any other mixed background
Asian or Asian British	H Indian J Pakistani K Bangladeshi L Any other Asian background
Black or Black British	M Caribbean N African P Any other Black background
Other Ethnic Groups	R Chinese S Any other ethnic group
+1 category	Z Not stated (Reserved for cases where patients declined to provide information)

In order to preserve statistical power to detect differences between groups, pre-specified analysis was carried out between ethnicity defined by the 5-high level groups White, Mixed, Asian or Asian British, Black or Black British and Other with merging of the "Mixed" and "Other" categories. Category Z was excluded from our primary analysis as were cases where no ethnicity data was recorded (Unknown).

Index of Multiple Deprivation
Index of Multiple Deprivation (IMD) was defined from patient home address postcode using UK government statistics (https://www.gov.uk/government/statistics/english-indices-of-deprivation-2019). Matching of Lower-layer Super Output Areas (LSOAs) was undertaken against the Office of National Statistics Postcode Directory (ONSPD) February 2020 datafile (https://geoportal.statistics.gov.uk/datasets/ons-postcode-directory-february-2020: accessed on 1st May 2020). IMD was presented as quintiles within England using raw scores for descriptive results and quintiles within the study cohort in multivariable analysis.

Smoking
History of tobacco use was defined by presence of the WHO ICD-10 codes F17·1-F17·2, Z72·0, Z87·8, Z71·6 and T65·2.

Ischaemic heart disease
Ischaemic heart disease (IHD) was defined by the presence of the ICD-10 codes I23·4-I23·5, I24, I24·8-I24·9, I25, I25·3-I25·6, I25·8-I25·9, I34·1, I46·1, I51·8-I51·9, and I52.
Wu et al Mapping ICD-10 and ICD-10-CM Codes to Phecodes: Workflow Development and Initial Evaluation JMIR Med Inform 2019;7(4):e14325

End stage Renal disease
End stage Renal disease (ESRD) was defined by the presence of the ICD10 codes I77·0, N16·5, N18·5, T82·4, T86·1, Y60·2, Y61·2, and Y62·2, Y84·1, Z49·0-Z49·2, Z94·0, Z99·2.
Crellin E, et al. Clinical Code List - ICD-10 - End-Stage Renal Disease. [Data Collection]. London School of Hygiene & Tropical Medicine. 2017: https://doi.org/10.17037/DATA.241.

Comorbidity
Diagnosis of co-morbidities and assignment of Charlson Comorbidity Index was based on mapping from ICD-10 coding from previous admissions using the mapping of Quan H, et al.
Quan H, et al. Coding algorithms for defining comorbidities in ICD-9-CM and ICD-10 administrative data. Med Care 2005;43(11):1130-9.
Diagnosis of Hypertension was based on mapping ICD-10 codes to the Elixhauser comorbidity index.
Elixhauser A, et al. Comorbidity measures for use with administrative data. Med Care 1998;36:8-27.

Hospital frailty risk score
Hospital frailty risk score was calculated from mapping ICD-10 coding of hospital attendances.
Gilbert T, et al. Development and validation of a Hospital Frailty Risk Score focusing on older people in acute care settings using electronic hospital records: an observational study. Lancet 2018;391(10132):1775-1782.

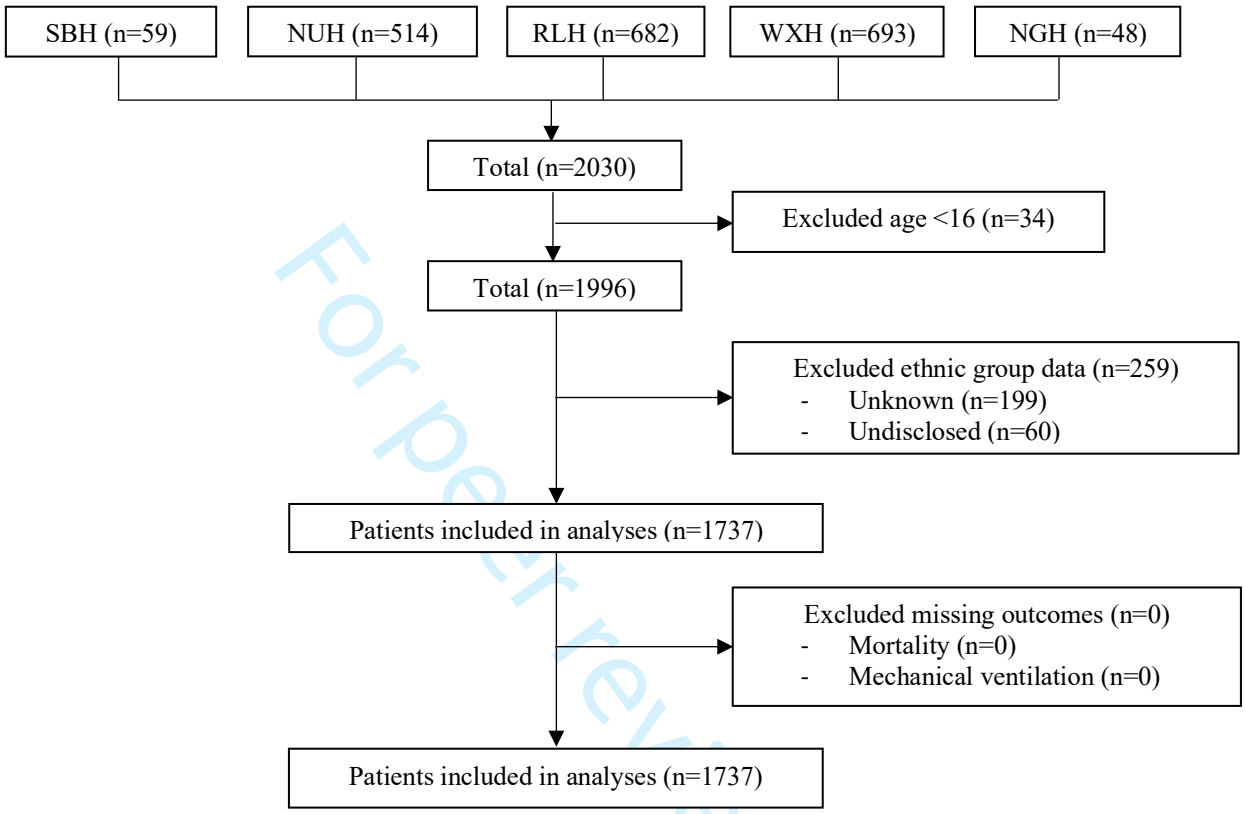
Acute Kidney injury
Acute kidney injury (AKI) within first 7 days of admission was defined using the KDIGO 2012 creatinine criteria either a 1·5-fold rise over baseline within 7 days or 26 μmol rise within 48 hours. Baseline creatinine will be the median value in the 7 to 365 days before hospitalisation. Absent baseline creatinine was determined based on an eGFR of 75 ml/min/1·72m^2 using the CKDepi formula or the admission value whichever was lower.

Chronic kidney disease
History of chronic kidney disease (CKD) using baseline eGFR was calculated using last creatinine value available from results earlier than 7 days before hospitalisation. CKD was defined as baseline eGFR below 60 ml/min/1·72m^2.

Secondary haemophagocytic lymphohistiocytosis
Secondary haemophagocytic lymphohistiocytosis (sHLH) risk scores were calculated using highest values during admission of temperature, haemoglobin, white cell count, platelet count, triglycerides, fibrinogen, ferritin, and aspartate aminotransferase (AST). Total scores did not include haemophagocytosis on bone marrow aspirate or known immunosuppression due to lack of available data leaving a maximum score of 284.
Mehta P, et al. COVID-19: consider cytokine storm syndromes and immunosuppression. Lancet 2020;395(10229):1033-1034.

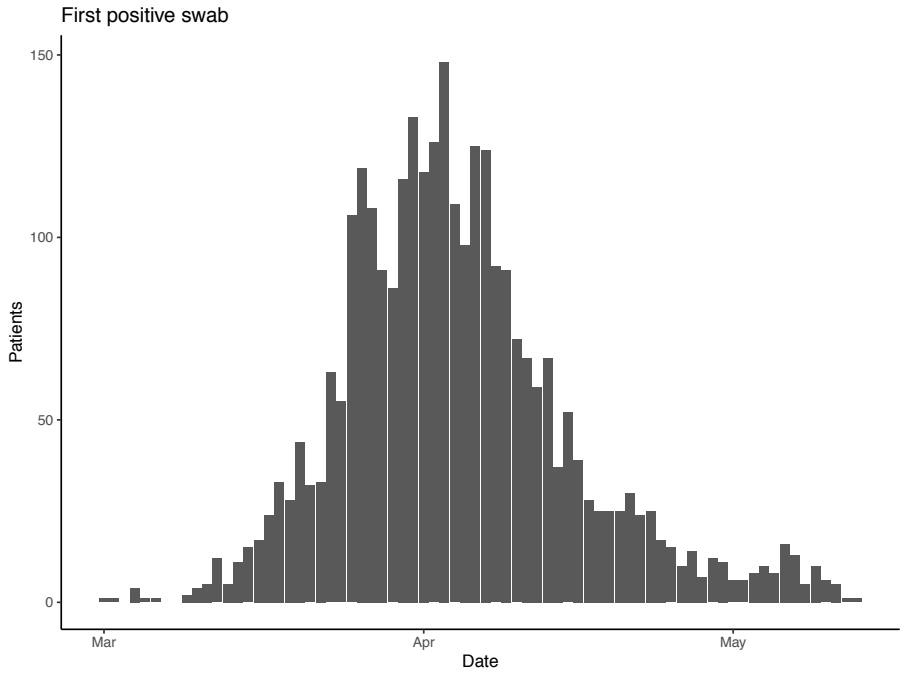
2. STROBE diagram

Figure S1. STROBE flow diagram of study populations. Hospital indicates first admission site and patients admitted to Nightingale hospital who had not been previously admitted to Barts Health hospital: St. Barts Hospital (SBH), Newham University Hospital (NUH), Royal London Hospital (RLH), Whipps Cross Hospital (WXH), Nightingale Hospital (NGH).



3. Inclusion time period by SARS-CoV-2 cases

Figure S2. Timeline of patients with positive SARS-CoV-2 swab tests at Barts Health.



4. Distribution of ethnicity categories within study cohort

Table S1. Distribution of study cohort by 16+1 ethnic data categories.

High-level group	Ethnic data category	n
White	A British	526
	B Irish	11
	C Any other White background	166
Mixed	D White and Black Caribbean	3
	E White and Black African	4
	F White and Asian	1
	G Any other mixed background	8
Asian or Asian British	H Indian	104
	J Pakistani	116
	K Bangladeshi	191
	L Any other Asian background	127
Black or Black British	M Caribbean	118
	N African	168
	P Any other Black background	54
Other Ethnic Groups	R Chinese	23
	S Any other ethnic group	117
	Z Not stated	60
No ethnicity data recorded		199

5. Baseline characteristics comparing died or survived at 30 days

Table S2. Study population baseline characteristics stratified by died or survived at 30 days, n (%) unless otherwise stated. Total n=1996 unless otherwise stated. P values based on Chi-square (for categorical) or Kruskal-Wallis test (for continuous). SD: standard deviation, IQR: interquartile range, IMD: index of multiple deprivation, BMI: body mass index, TIA: transient ischaemic accident, HTN: hypertension, CKD: chronic kidney disease, sHLH: secondary haemophagocytic lymphohistiocytosis (without known underlying immunosuppression and bone marrow aspirate data), CRP: C-reactive protein, NEWS: national early warning score, ICU: intensive care unit, RRT: renal replacement therapy.

	Stratified by survival at 30 days		
	Died	**Survived**	p value
n	536	1460	
Ethnicity			0·05
Asian or Asian British	138 (25·7)	400 (27·4)	
Black or Black British	97 (18·1)	243 (16·6)	
Mixed and Other Ethnic Groups	33 (6·2)	123 (8·4)	
White	210 (39·2)	493 (33·8)	
Unknown and Undsisclosed	58 (10·8)	201 (13·8)	
Age (years)			
Mean (SD)	74·8 (12·6)	59·2 (18·2)	<0·001
Median (IQR)	77·0 (66·0-84·0)	59·0 (46·0-73·0)	<0·001
Male	351 (65·5)	859 (58·8)	0·01
IMD quintile [n=1980]			0·003
1 (most deprived)	155 (29·1)	407 (28·1)	
2	223 (41·9)	698 (48·2)	
3	62 (11·7)	184 (12·7)	
4	56 (10·5)	99 (6·8)	
5 (least deprived)	36 (6·8)	60 (4·1)	
Smoking [n=1700]	57 (11·8)	116 (9·5)	0·19
BMI [n=1248]			
Median (IQR)	26·5 (22·7-31·6)	26·9 (23·6-31·2)	0·43
By category			0·80
<18·5 kg/m^2	20 (6·4)	43 (4·6)	
18·5 - <25 kg/m^2	97 (31·0)	295 (31·6)	
25 - <30 kg/m^2	100 (31·9)	309 (33·0)	
30 - <40 kg/m^2	80 (25·6)	243 (26·0)	
≥40 kg/m^2	16 (5·1)	45 (4·8)	
Co-morbidity using ICD-10 [n=1700]			
Obesity	123 (25·5)	286 (23·5)	0·411
Ischaemic heart disease	149 (30·9)	197 (16·2)	<0·001
Myocardial infarction	73 (15·1)	108 (8·9)	<0·001
Congestive heart failure	120 (24·9)	140 (11·5)	<0·001
Peripheral vascular disease	74 (15·4)	84 (6·9)	<0·001
Cerebral vascular accident or TIA	133 (27·6)	159 (13·1)	<0·001
Dementia	89 (18·5)	78 (6·4)	<0·001
Chronic obstructive pulmonary disease	145 (30·1)	252 (20·7)	<0·001
Diabetes	242 (50·2)	422 (32·6)	<0·001
HTN	372 (77·2)	637 (52·3)	<0·001
Moderate to severe CKD	159 (33·0)	204 (16·7)	<0·001
End-stage renal disease	39 (8·1)	74 (6·1)	0·163

Liver disease	45 (8·4)	110 (7·5)	0·587
Cancer	62 (12·9)	82 (6·7)	<0·001
Cancer with metastases	18 (3·7)	24 (2·0)	0·053
Acquired immunodeficiency syndrome	1 (0·2)	5 (0·4)	0·855
Charlson comorbidity index [n=1700]			<0·001
0	45 (9·3)	428 (35·1)	
1-2	170 (35·3)	449 (36·9)	
3-4	130 (27·0)	174 (14·3)	
≥5	137 (28·4)	167 (13·7)	
Rockwood frailty score [n=831]			<0·001
1-2 (very fit, well)	20 (6·3)	75 (14·5)	
3-4 (managing well, vulnerable)	106 (33·7)	199 (38·6)	
5-6 (mildly to severely frail)	144 (45·7)	215 (41·7)	
8-9 (very severely frail, terminally ill)	45 (14·3)	27 (5·2)	
Hospital frailty risk score [n=1700]			<0·001
<5 (low risk)	88 (18·3)	655 (53·8)	
5-15 (intermediate risk)	187 (38·8)	293 (24·1)	
≥15 (high risk)	207 (42·9)	270 (22·2)	
Baseline eGFR ml/min/1·72m2 [n=1525]			
Median (IQR)	57·3 (38·7-76·2)	72·4 (51·2-90·8)	<0·001
eGFR <60	236 (52·2)	323 (30·1)	<0·001
Acute kidney injury first 7 days [n=1673]	204 (47·0)	226 (18·2)	<0·001
Blood results during admission			
Highest creatinine µmol/L [n=1691]			<0·001
Median (IQR)	168·0 (102·0-326·0)	87·0 (71·0-120·0)	
Highest CRP [n=1761]			<0·001
Median (IQR)	241·5 (149·8-344·0)	120·0 (59·0-218·0)	
Highest D-dimer mg/L [n=968]			<0·001
Median (IQR)	3·1 (1·2-17·7)	1·1 (0·6-3·3)	
Highest sHLH score [n=1881]			
Mean (SD)	34·6 (27·9)	26·9 (25·7)	<0·001
Blood Group [n=875]			0·004
A	109 (36·0)	196 (34·3)	
AB	11 (3·6)	32 (5·6)	
B	49 (16·2)	119 (20·8)	
O	134 (44·2)	225 (39·3)	
NEWS on admission [n=1443]	4·7 (2·9)	3·5 (2.2)	<0·001
Intensive care unit (ICU)			
ICU admission	151 (28·2)	210 (14·4)	<0·001
ICU length of stay			
Median (IQR)	9·0 (5·9-15·0)	8·0 (3·0-15·0)	0·06
Mechanical ventilation within ICU admissions	135 (89·4)	146 (69·5)	<0·001
Days on organ support			
Advanced respiratory Mean (SD)	9·3 (6·2)	9·9 (10·6)	0·49
Total respiratory Mean (SD)	10·4 (6·2)	12·5 (10·2)	0·03
Cardiovascular system Mean (SD)	10·3 (6·3)	12·6 (10·5)	0·02
Renal Mean (SD)	2·5 (4·1)	2·7 (6·2)	0·76
Total number of organ systems			<0·001
0	0 (0·0)	3 (1·4)	

1	1 (0·7)	12 (5·7)	
2	93 (61·6)	154 (73·3)	
3	57 (37·7)	41 (19·5)	
Hospital length of stay			
Median (IQR)	7·0 (4·0-13·0)	7·0 (3·0-12·0)	0·98

6. Completeness of follow-up

Table S3. Numbers at risk and number of deaths (in parenthesis) over five day intervals up to 30 days by ethnic group in primary survival analysis.

Ethnic group	Days from hospital admission						
	0	**5**	**10**	**15**	**20**	**25**	**30**
Asian or Asian British	538 (3)	488 (60)	446 (96)	421 (115)	402 (124)	389 (131)	365 (138)
Black or Black British	340 (4)	301 (50)	273 (70)	258 (80)	248 (88)	240 (94)	229 (97)
Mixed and Other ethnic groups	156 (1)	147 (12)	140 (17)	127 (26)	122 (32)	117 (33)	113 (33)
White	703 (3)	644 (71)	583 (120)	534 (162)	502 (188)	472 (197)	436 (210)

7. Sensitivity analyses

a. Multivariable imputation

Missing data for baseline risk variables included in the multivariable Cox model was imputed using Multivariate Imputation by Chained Equations based on age, sex, and comorbidity. Five separate imputed datasets were simulated, and a pooled result of multivariable Cox models presented.
Van Buuren S, Groothuis-Oudshoorn K. mice: Multivariate Imputation by Chained Equations in R. J Stat Softw 2011;45(3): https://www.jstatsoft.org/v045/i03.

Figure S3. Patterns of missingness in baseline risk variables. ID: patient identifier, IMD: index of multiple deprivation, DM: diabetes mellitus, HTN: hypertension, CKD: chronic kidney disease, BMI: body mass index. Blue indicate complete and pink indicate missing data. Numbers on the left side of the grid represent n records with this pattern, numbers on the right side represent n missing variables, numbers on the bottom represent n records missing this variable. For example, n=1006 records were complete, n=470 were missing 1 variable (BMI), n=14 records were missing IMD data.

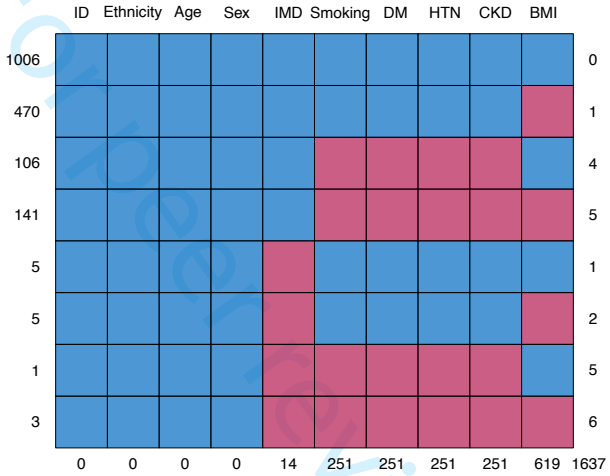
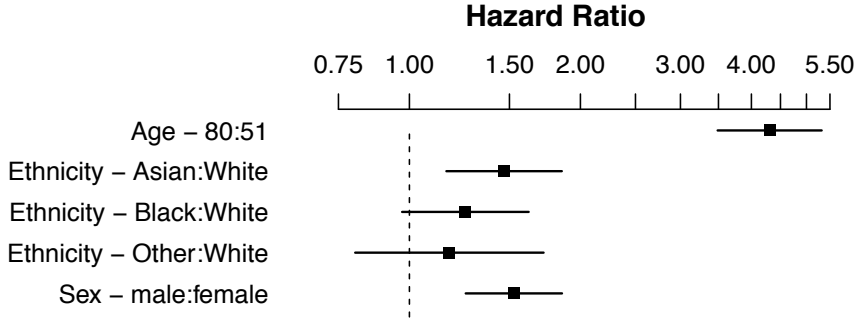


Table S4. Multivariable analysis using imputed dataset of mortality to 30 days using Cox proportional hazards modelling. Missing data imputed for smoking, BMI ≥30 kg/m^2, diabetes, HTN, CKD. Censored to 30 days follow up, observation 1737, events 478.

	n		Unadjusted	
	Total	**Events**	**Hazard ratio (95% CI)**	**P value**
Age (25th vs 75th centile)	-	-	4·31 (3·49-5·32)	<0·0001
Sex (Male)	-	-	1·53 (1·26-1·86)	<0·0001
Ethnic group				
Asian or Asian British	521	134	1·47 (1·16-1·85)	0·001
Black or Black British	331	94	1·25 (0·97-1·62)	0·083
Mixed and Other ethnic groups	150	34	1·18 (0·80-1·72)	0·406
White	674	206	Reference	-

Figure S4. Forest plot showing hazards ratios of mortality to 30 days using the imputed dataset, on log scale.



b. Charlson comorbidity index

Table S5. Multivariable analysis of mortality to 30 days using cox proportional hazards modelling. Variables included age, sex, IMD quintile, smoking, BMI ≥30 kg/m^2, and Charlson comorbidity index. Censored to 30 days follow up, observations 1006, events 281.

	Adjusted	
	Hazard ratio (95% CI)	**P value**
Age (25th vs 75th centile)	2·90 (2·22-3·79)	<0·0001
Sex (Male)	1·48 (1·16-1·90)	0·002
Ethnic group		
Asian or Asian British	1·54 (1·15-2·08)	0·004
Black or Black British	1·39 (1·01-1·92)	0·044
Mixed and Other ethnic groups	1·02 (0·56-1·88)	0·939
White	Reference	-
IMD quintile		
1 (most deprived)	0·83 (0·57-1·20)	0·316
2	0·81 (0·55-1·18)	0·268
3	0·94 (0·66-1·36)	0·759
4	0·82 (0·57-1·20)	0·311
5 (least deprived)	Reference	-
Smoking	1·36 (0·98-1·89)	0·067
BMI ≥30 kg/m^2	1·48 (1·14-1·92)	0·003
Charlson comorbidity index		
0	Reference	-
1-2	2·00 (1·17-3·41)	0·012
3-4	3·43 (2·00-5·89)	<0·0001
≥5	4·10 (2·42-6·94)	<0·0001

Figure S5. Forest plot showing hazards ratios of mortality to 30 days comparing multiple variables including CCI: Charlson comorbidity index. IMD: index of multiple deprivation, Obesity defined as BMI ≥30 kg/m^2, on log scale.

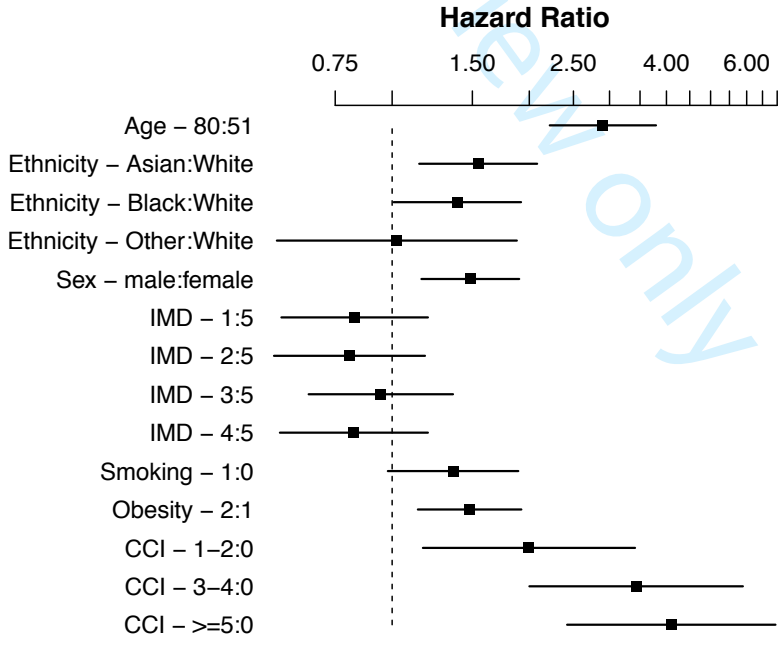
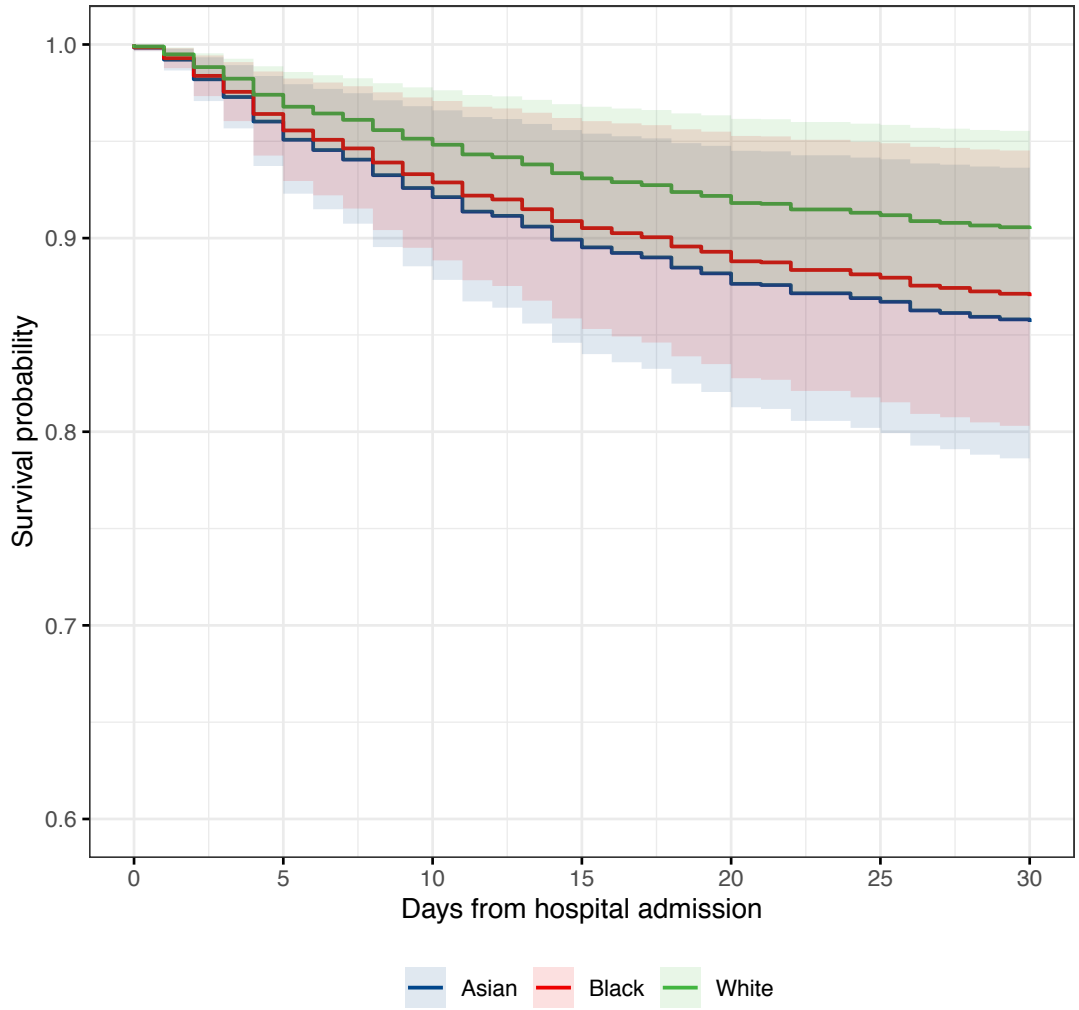


Figure S6. Survival curve to 30 days from multivariable analysis comparing Asian, Black, and White ethnic groups. Survival modelled for median age 65 years and male sex, index of multiple deprivation (IMD) least deprived quintile, no baseline risk factors defined as non-smoking, BMI <30 kg/m^2 and Charlson comorbidity index 0.



c. Rockwood frailty score

Table S6. Multivariable analysis of mortality to 30 days using cox proportional hazards modelling. Variables included age, sex, index of multiple deprivation (IMD) quintile, smoking, BMI ≥30 kg/m^2, and Rockwood frailty score (RFS). Censored to 30 days follow up, observations observations 552, events 199.

	Adjusted	
	Hazard ratio (95% CI)	**P value**
Age (25th vs 75th centile)	2·42 (1·56-3·75)	<0·0001
Sex (Male)	1·61 (1·19-2·16)	0·002
Ethnic group		
Asian or Asian British	1·98 (1·37-2·86)	<0·001
Black or Black British	1·67 (1·14-2·45)	0·009
Mixed and Other ethnic groups	1·27 (0·62-2·56)	0·513
White	Reference	-
IMD quintile		
1 (most deprived)	0·61 (0·38-0·98)	0·040
2	0·79 (0·50-1·22)	0·283
3	0·82 (0·53-1·25)	0·348
4	0·77 (0·51-1·18)	0·234
5 (least deprived)	Reference	-
Smoking	1·38 (0·94-2·03)	0·102
BMI ≥30 kg/m^2	1·39 (1·01-1·91)	0·045
Rockwood frailty score		
1-2 (very fit, well)	Reference	-
3-4 (managing well, vulnerable)	1·61 (0·82-3·16)	0·164
5-6 (mildly to severely frail)	1·84 (0·93-3·64)	0·078
8-9 (very severely frail, terminally ill)	3·25 (1·49-7·06)	0·003

Figure S7. Forest plot showing hazards ratios of mortality to 30 days comparing multiple variables including RFS: Rockwood frailty score. IMD: index of multiple deprivation, Obesity defined as BMI ≥30 kg/m^2, on log scale.

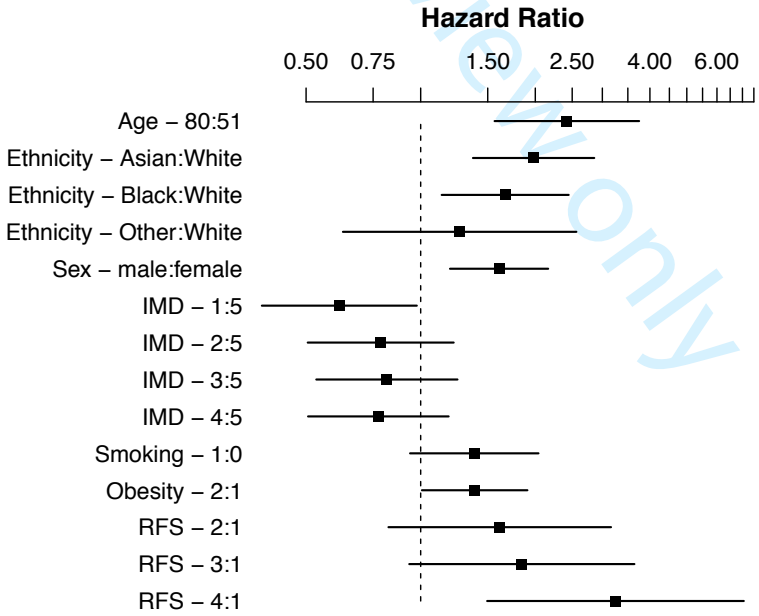
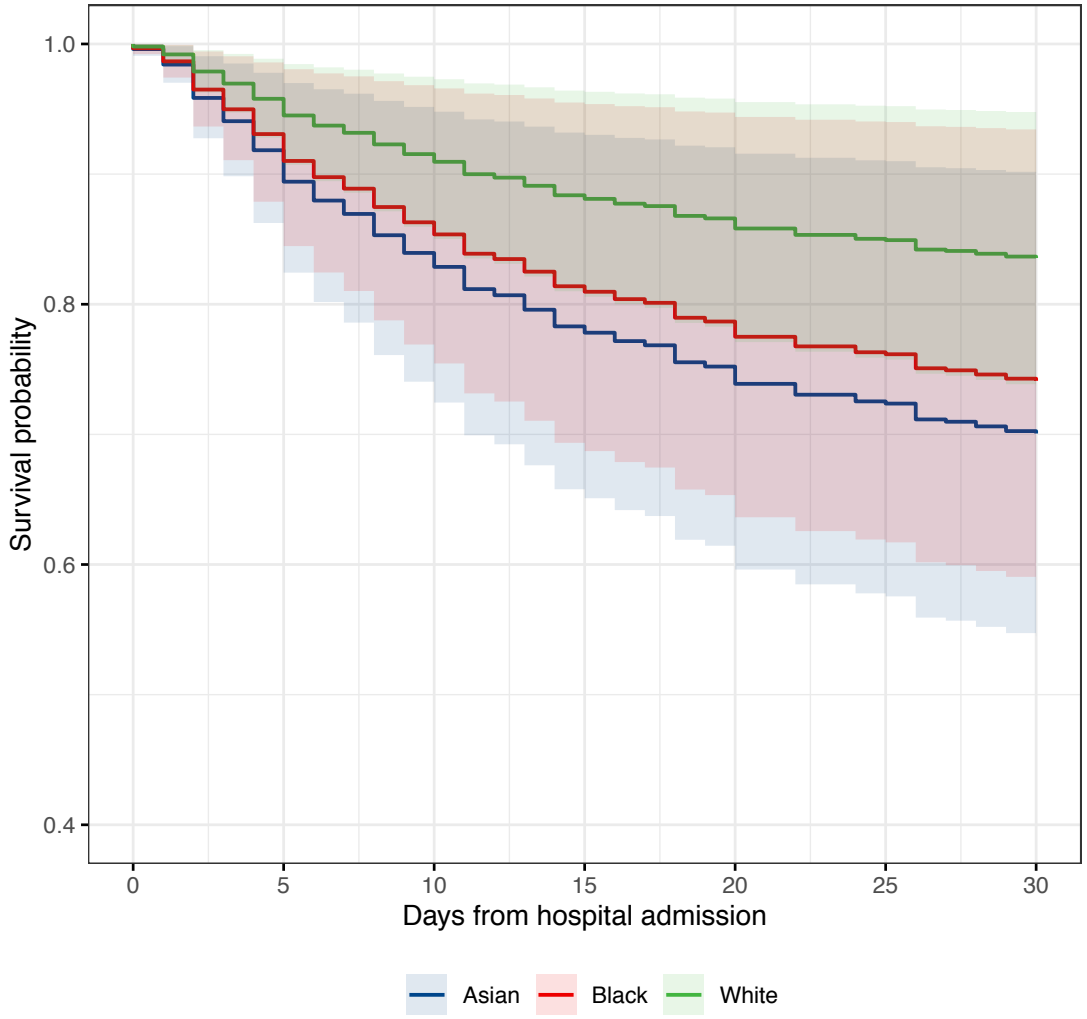


Figure S8. Survival curve to 30 days from multivariable analysis comparing Asian, Black, and White ethnic groups. Survival modelled for median age 65 years and male sex, index of multiple deprivation (IMD) least deprived quintile, no baseline risk factors defined as non-smoking, BMI <30 kg/m^2 and Rockwood frailty score lowest risk group.



d. Hospital frailty risk score

Table S7. Multivariable analysis of mortality to 30 days using cox proportional hazards modelling. Variables included age, sex, index of multiple deprivation (IMD) quintile, smoking, BMI ≥30 kg/m^2, and Hospital frailty risk score (HFRS). Censored to 30 days follow up, observations 1006, events 281.

	Adjusted	
	Hazard ratio (95% CI)	**P value**
Age (25th vs 75th centile)	2·84 (2·17-3·71)	<0·0001
Sex (Male)	1·58 (1·24-2·03)	<0·001
Ethnic group		
Asian or Asian British	1·78 (1·32-2·41)	<0·001
Black or Black British	1·57 (1·13-2·17)	0·007
Mixed and Other ethnic groups	1·10 (0·60-2·04)	0·751
White	Reference	-
IMD quintile		
1 (most deprived)	0·85 (0·59-1·24)	0·404
2	0·83 (0·57-1·22)	0·341
3	0·89 (0·62-1·29)	0·541
4	0·83 (0·57-1·20)	0·310
5 (least deprived)	Reference	-
Smoking	1·42 (1·01-1·96)	0·044
BMI ≥30 kg/m^2	1·57 (1·21-2·05)	<0·001
Hospital frailty risk score		
<5 (low risk)	Reference	-
5-15 (intermediate risk)	2·44 (1·68-3·54)	<0·0001
≥15 (high risk)	2·76 (1·89-4·04)	<0·0001

Figure S9. Forest plot showing hazards ratios of mortality to 30 days comparing multiple variables including HFRS: Hospital frailty risk score. IMD: index of multiple deprivation, Obesity defined as BMI ≥30 kg/m^2, on log scale.

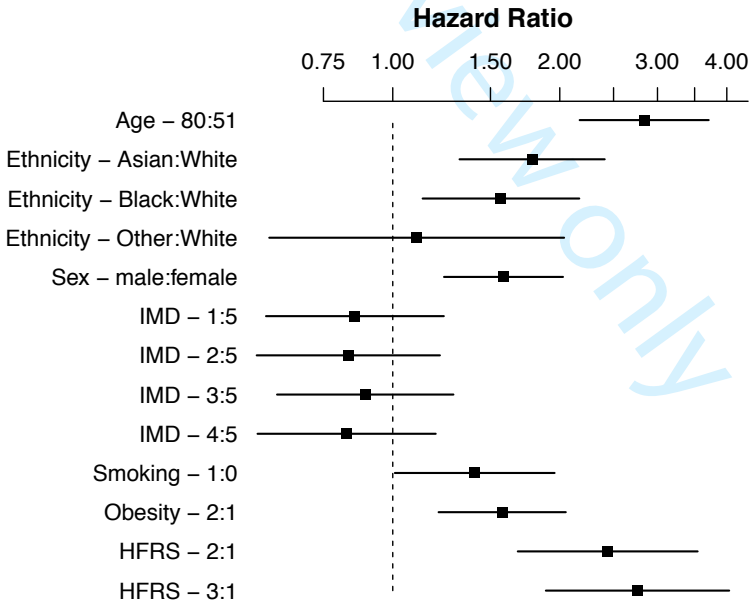
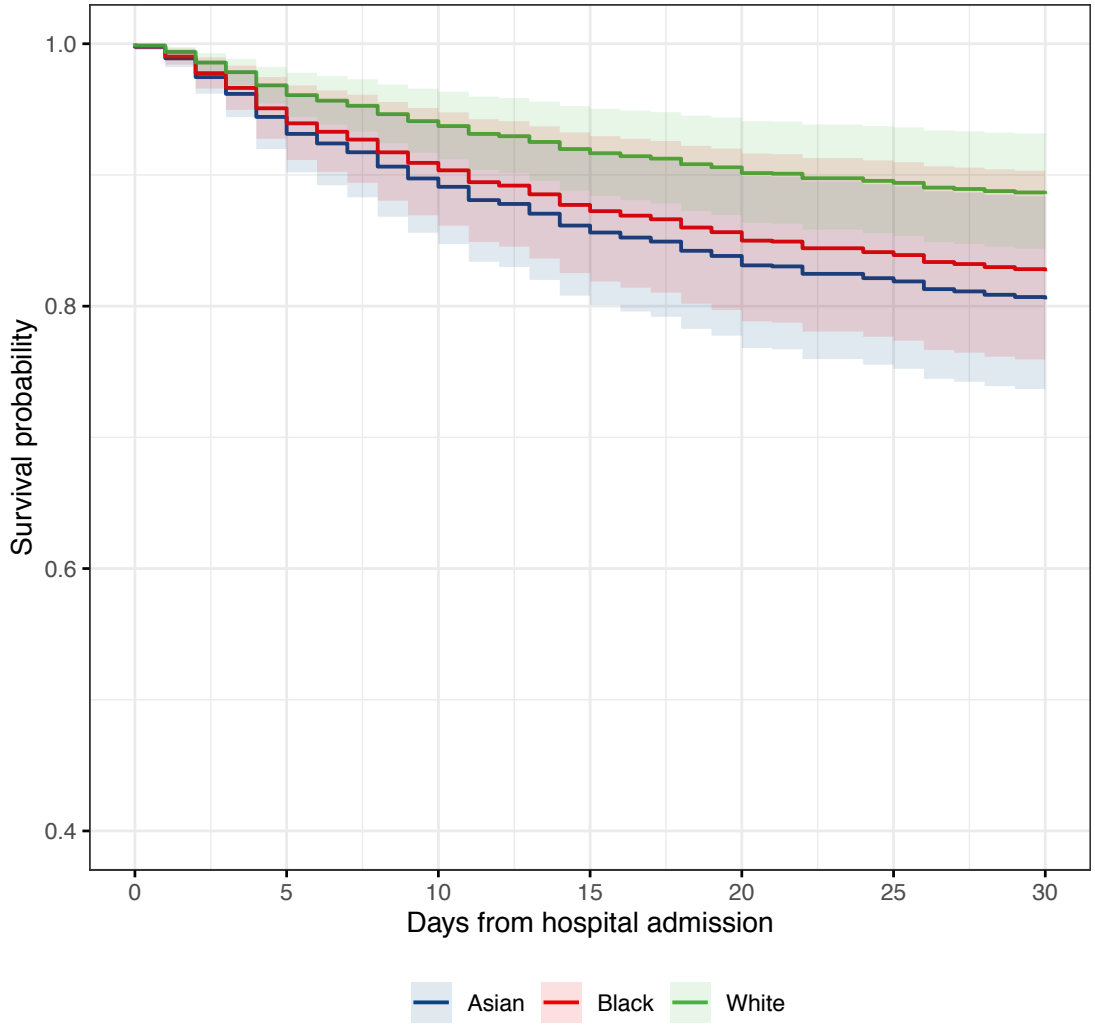


Figure S10. Survival curve to 30 days from multivariable analysis comparing Asian, Black, and White ethnic groups, age and sex corrected. Survival modelled for median age 65 years and male sex, inde of multiple deprivation (IMD) least deprived quintile, no history of baseline risk factors defined as smoking, BMI ≥30 kg/m^2, Hospital frailty risk score lowest risk group.



e. ABO blood group

Table S8. Multivariable analysis of mortality to 30 days using cox proportional hazards modelling. Variables included age, sex, and ABO blood group. Censored to 30 days follow up, observations 793, events 281.

	Adjusted	
	Hazard ratio (95% CI)	**P value**
Age (25th vs 75th centile)	3·26 (2·58-4·13)	<0·0001
Sex (Male)	1·67 (1·30-2·13)	<0·0001
Ethnic group		
Asian or Asian British	1·82 (1·35-2·46)	<0·0001
Black or Black British	1·63 (1·17-2·27)	0·004
Mixed and Other ethnic groups	1·62 (0·98-2·68)	0·059
White	Reference	-
ABO blood group		
A	0·81 (0·62-1·05)	0.112
AB	0·65 (0·33-1·28)	0·214
B	0·66 (0·47-0·92)	0·016
O	Reference	-

Figure S11. Forest plot showing hazards ratios of mortality to 30 days comparing multiple variables including ABO blood group, on log scale.

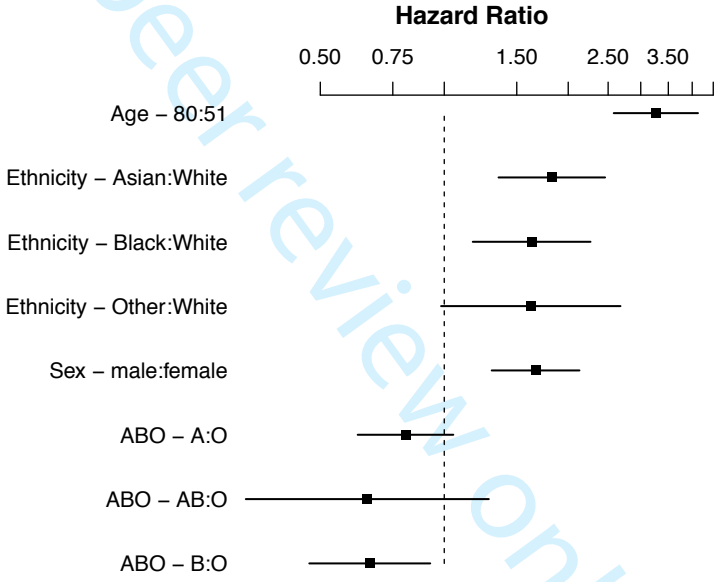
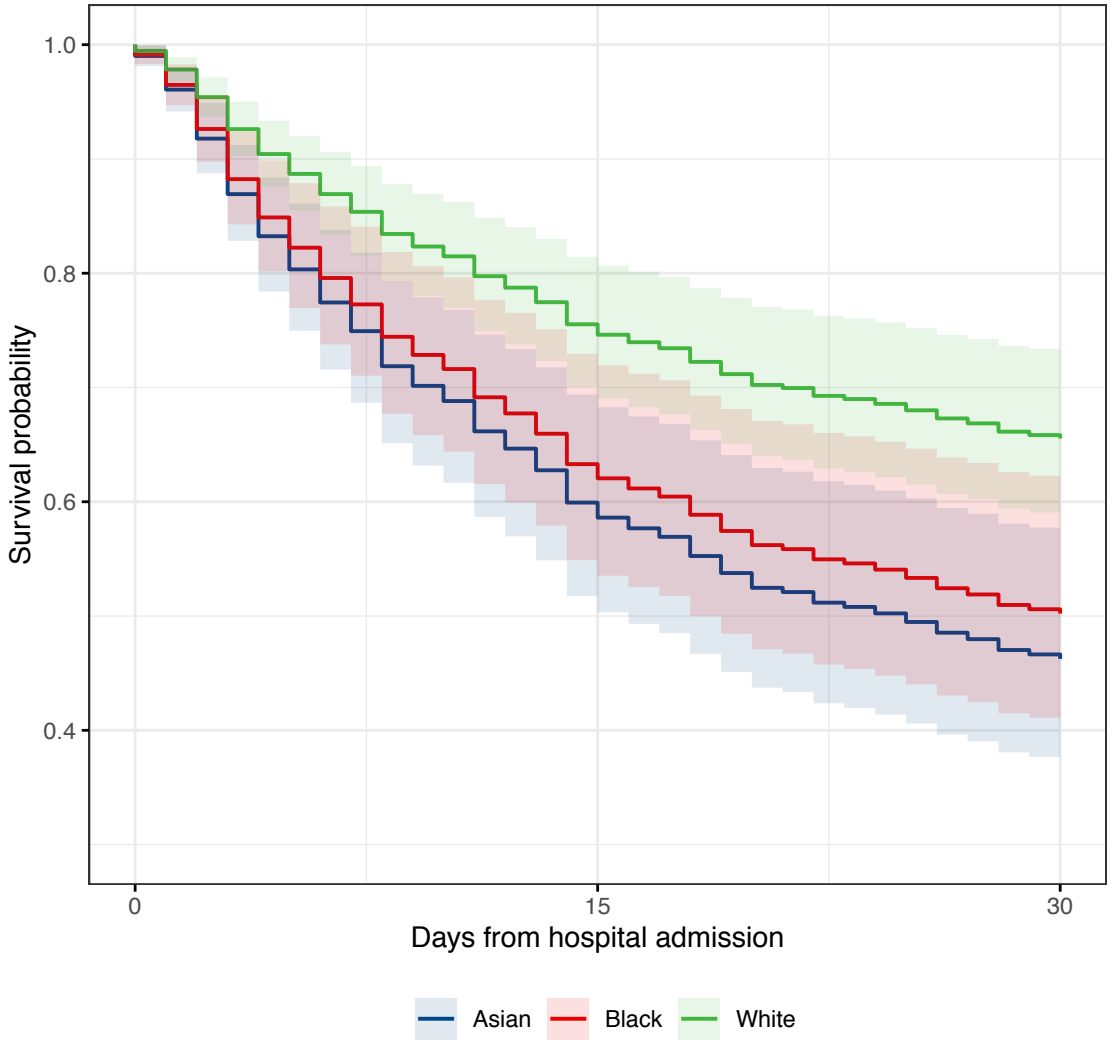


Figure S12. Survival curve to 30 days from multivariable analysis comparing Asian, Black, and White ethnic groups. Survival modelled for median age 65 years and male sex, ABO bloog group O.



f. 90 day mortality

Table S9. Association of ethnic group with mortality to 90 days using cox proportional hazards modelling, age and sex corrected. Censored to 90 days follow up, observations 1737, events 510.

	n		Unadjusted	
	Total	**Events**	**Hazard ratio (95% CI)**	**P value**
Age (25^{th} vs 75^{th} centile)	-	-	4·48 (3·74-5·35)	<0·0001
Sex (Male)	-	-	1·52 (1·27-1·83)	<0·0001
Ethnic group				
Asian or Asian British	497	106	1·46 (1·18-1·81)	<0·001
Black or Black British	342	83	1·26 (0·99-1·59)	0·058
Mixed and Other ethnic groups	142	30	1·02 (0·71-1·46)	0·934
White	651	182	Reference	-

Figure S13. Forest plot showing hazards ratios of mortality to 90 days comparing ethnic groups, age and sex, on log scale.

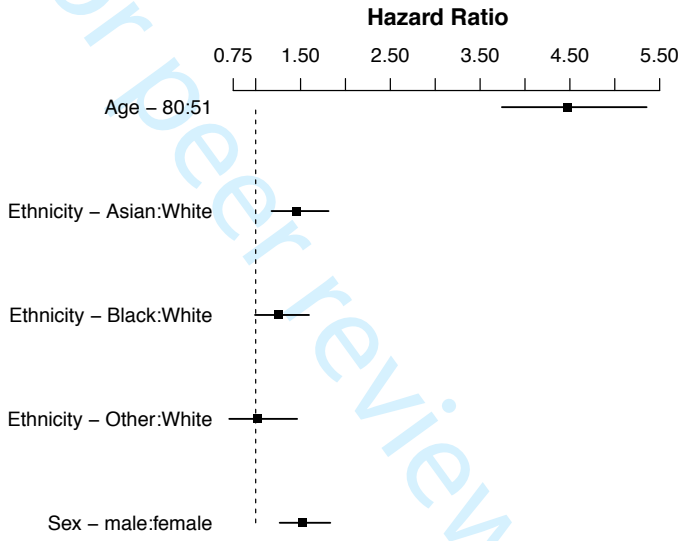
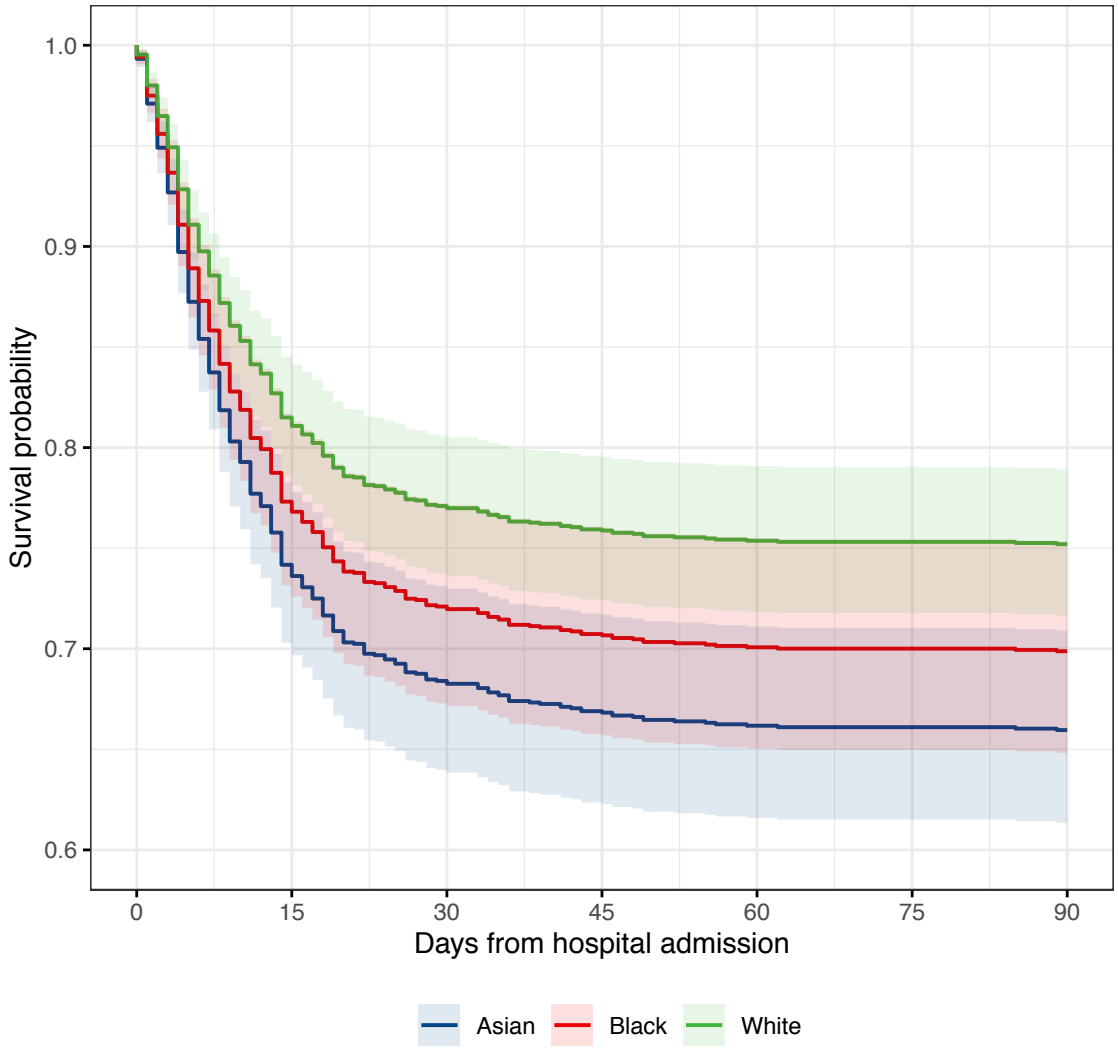


Figure S14. Survival curve to 90 days from univariate analysis comparing Asian, Black, and White ethnic groups, age and sex. Survival modelled for median age 65 years and male sex.

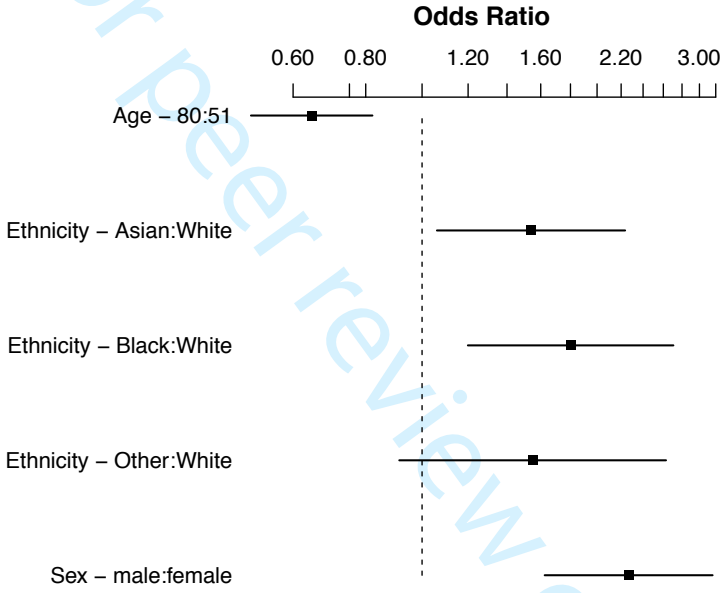


8. Secondary outcome mechanical ventilation

Table S10. Association of ethnic group with mechanical ventilation using logistic regression modelling, age and sex corrected. Observations 1737, events 210.

	Unadjusted	
	Odds ratio (95% CI)	**p value**
Age (25th vs 75th centile)	0·65 (0·51-0·82)	<0·001
Sex (Male)	2·27 (1·63-3·16)	<0·0001
Ethnic group		
Asian or Asian British	1·54 (1·06-2·23)	0·023
Black or Black British	1·80 (1·20-2·71)	0·005
Mixed and Other ethnic groups	1·55 (0·91-2·63)	0·104
White	Reference	-

Figure S15. Forest plot showing odds ratios of mechanical ventilation comparing ethnic groups, age and sex corrected, on log scale.



9. Cox proportional hazards testing

We assessed proportional-hazards assumption for ethnicity and adjusted variables by inspection of scaled Schoenfeld residual plots. There was some evidence of non-proportionality for Black ethnicity at later time points in the primary age and sex adjusted analysis. However, the unstratified and ethnicity-stratified survival curves for the age and sex adjusted 30-day survival were similar suggesting minimal impact of non-proportionality.

Figure S16. Scaled Schoenfeld residual plots for ethnicity, age, and sex.

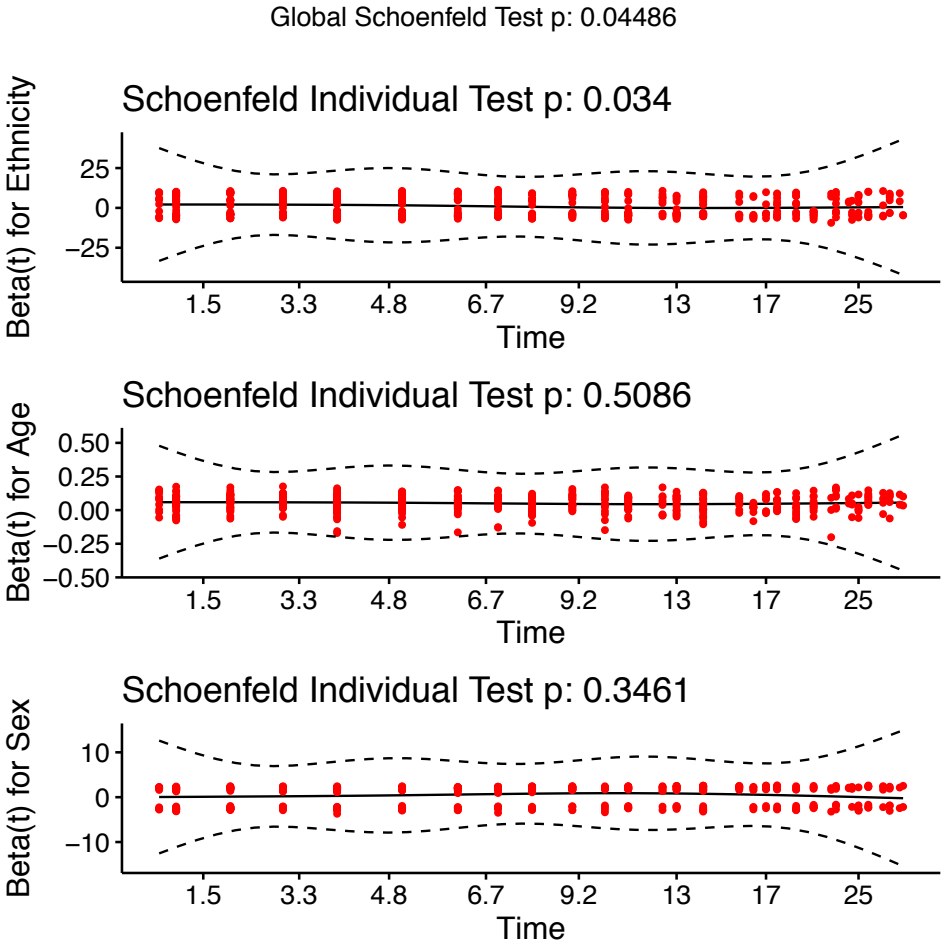
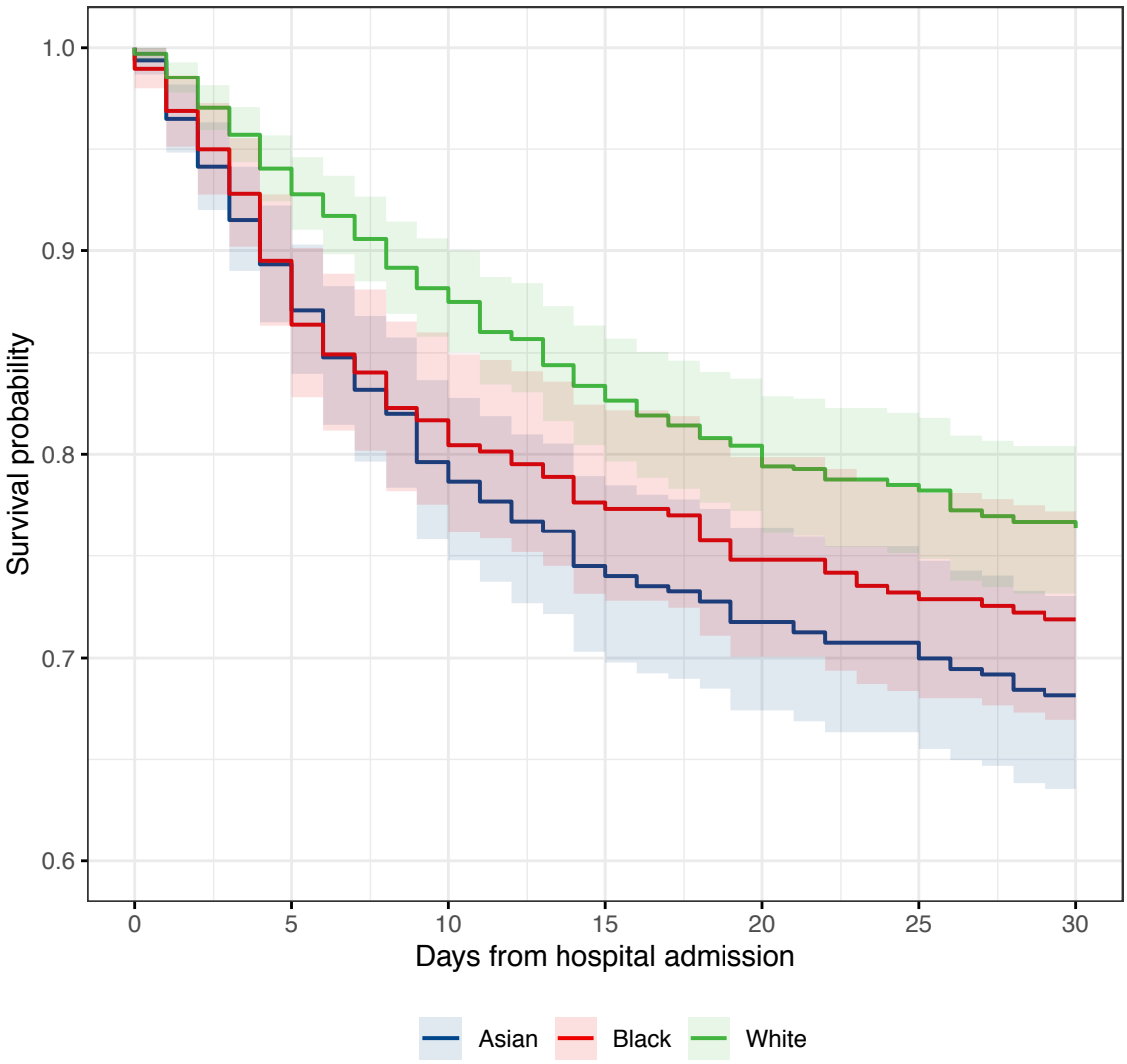


Figure S17. Ethnicity-stratified Cox survival model to 30 days based on age and sex. Survival modelled for median age 65 years and male sex. Survival over 30 days is comparable the unstratified model [Figure 3], however early mortality was greater in patients with Black ethnicity.



STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cohort studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	2, 4
Objectives	3	State specific objectives, including any prespecified hypotheses	2, 4
Methods			
Study design	4	Present key elements of study design early in the paper	4, 5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	4
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	N/A
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4, 5
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	4, 5
Bias	9	Describe any efforts to address potential sources of bias	5
Study size	10	Explain how the study size was arrived at	4
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	4, 5
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	5
		(*b*) Describe any methods used to examine subgroups and interactions	5
		(*c*) Explain how missing data were addressed	5
		(*d*) If applicable, explain how loss to follow-up was addressed	4, 5
		(*e*) Describe any sensitivity analyses	5
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	6, supplement
		(b) Give reasons for non-participation at each stage	supplement
		(c) Consider use of a flow diagram	supplement
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	6, table 1
		(b) Indicate number of participants with missing data for each variable of interest	6, table 1
		(c) Summarise follow-up time (eg, average and total amount)	6
Outcome data	15*	Report numbers of outcome events or summary measures over time	6, supplement
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	6, table 2, table 3, supplement
		(*b*) Report category boundaries when continuous variables were categorized	N/A
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	6
Discussion			
Key results	18	Summarise key results with reference to study objectives	7
Limitations			
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	3, 7
Generalisability	21	Discuss the generalisability (external validity) of the study results	7, 8
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	N/A

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.