# Ethnicity and outcomes from COVID-19 in UK hospital patients using the ISARIC WHO Clinical Characterisation Protocol: prospective observational cohort study

Ewen Harrison, Annemarie Docherty, Calum Semple, CO-CIN, ISARIC4C investigators.

## Abstract

Background

COVID-19 outcomes may differ by ethnicity, but reports are conflicting. We investigated ethnic variations in the risks of critical care admission, invasive mechanical ventilation (IMV), and in-hospital mortality, among hospitalised patients with COVID-19.

Methods

A network of research nurses and students in 208 Acute Care Trusts/Health Boards entered data contemporaneously and from records between 6th February and 8th May 2020 with follow-up until 22nd May 2020. Analysis used hierarchical regression models accounting for competing risks and the geographical clustering of patients. Potential mediators for death were explored with a three-way decomposition mediation analysis.

Findings

Of 34,986 patients enrolled, 30,693 (88%) had ethnicity recorded: South Asian (1,388, 5%), East Asian (266, 1%), Black (1,094, 4%), Other Ethnic Minority (2,398, 8%) (collectively Ethnic Minorities), and White (25,547, 83%). Ethnic Minorities were younger and more likely to have diabetes but had fewer other comorbidities such as chronic heart disease and dementia than the White group. No difference was seen between ethnic groups in the time from symptom onset to hospital admission, nor in illness severity at admission.

Critical care admission was more common in South Asian (odds ratio 1.28, 95% confidence interval 1.09 to 1.52), Black (1.36, 95% CI 1.14 to 1.62), and Other Ethnic Minority (1.29, 95% CI 1.13 to 1.47) groups compared to White, after adjusting for age, sex and location. This was broadly unchanged after adjustment for deprivation and comorbidities. Patterns were similar for IMV.

Higher adjusted mortality was seen in the South Asian group (hazard ratio 1.19, 95% CI 1.05 to 1.36), but not East Asian (1.00, 95% CI 0.74 to 1.35), Black (1.05, 95% CI 0.91 to 1.26) or Other Ethnic Minority (0.99, 95% CI 0.89 to 1.10) groups, compared to the White group. Of the apparent excess mortality in the South Asian group, 17.8% (95% CI 9.1% to 56.4%, P = 0.002) was mediated by pre-existing diabetes.

Interpretation

Ethnic Minorities in hospital with COVID-19 were more likely to be admitted to critical care and receive IMV than White patients, despite similar disease severity on admission and duration of symptoms. South Asian patients were at greater risk of dying, at least partly due to higher rates of pre-existing diabetes.

Funding

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## Research in Context

### Evidence before this study:

Evidence is emerging of an association between ethnicity and increased mortality in patients with COVID-19. In a cohort study on the relative risk of COVID-19 infection by ethnic group, linked UK Biobank data was used to show that Black (relative risk 4.01, 95% CI 2.92 to 5.12), South Asian (2.11, 95% CI 1.43 to 3.10) and White Irish (1.60, 95% CI 1.08 to 2.38) people were more likely to have confirmed infection and were more likely to be hospitalised compared to White British people. This relationship persisted after controlling for socioeconomic deprivation. In a different study, actual vs. expected hospital deaths were compared and all ethnic groups other than White British and White Irish were found to have an age adjusted excess mortality.
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### Added value of this study

This is the largest prospective study of patients in hospital with COVID-19. We provide granular data on the stark differences in age and levels of comorbidity between White and Ethnic Minority people in hospital with COVID-19. We show high levels of use of critical care and invasive ventilation in Ethnic Minorities compared with White people, even after adjustment for age, sex, deprivation, and comorbidities. We find a higher likelihood of death in South Asian people, and for the first time show that a significant proportion of that effect appears to be due to a higher prevalence of diabetes in the South Asian group.

### Implications of all the available evidence

These findings have important implications for policy. South Asian people are over-represented in frontline key worker occupations, and policies should consider shielding advice regarding at-risk patients. Work is on-going to devise risk assessment tools to help mitigate the likelihood of coronavirus infection and manage the easing of lockdown restrictions. Careful consideration needs to be given in these tools to the weighting of ethnicity and mediators of risk such as diabetes. Further research integrating primary and secondary care data is key to improving the understanding of the other drivers of poor outcomes in Ethnic Minority patients.

## Introduction

The novel severe acute respiratory syndrome coronavirus SARS-CoV-2 has caused a pandemic, with 5.5 million reported as infected and 350,000 reported as having died across the world. Studies from China, Italy and the UK consistently report that age, comorbidity, and male sex are associated with increased mortality.[1,2]

COVID-19 deaths appear to disproportionately affect people from South Asian and Black ethnic backgrounds, but it is unclear if the incidence of infection is greater, the prognosis is worse once infected, or both.[3,4] Patients from Asian, Black and Minority ethnic backgrounds are reported to have accounted for 34% of COVID-19 admissions to intensive care (ICU) in England, Wales and Northern Ireland, compared with only 12% for viral pneumonia (2017-2019), and a higher than expected proportion have required organ support and have died.[5] Of 119 NHS staff known to have died with COVID-19, 64% were from an ethnic minority background.[6] In the USA, the mortality rate for Black African Americans is quoted as 2.7 times higher than the rate for White Americans.[7] However, differences in socioeconomic circumstances or pre-existing conditions may account for some or all such differences in risk.

Ethnicity and socioeconomic position were associated with poor health outcomes during previous pandemics.[8] People living in more deprived areas in the UK have experienced COVID-19 mortality rates more than double those living in less deprived areas.[9] Ethnic minority groups may be at greater risk of infection, severe disease, and poor outcomes for multiple reasons. These include socioeconomic conditions that increase risk of transmission and vulnerability, such as overcrowded housing,[10] employment in essential occupations,[16] poverty, healthcare seeking behaviours,[11] and reliance on public transport.

Theoretical biological mechanisms include susceptibility due to common comorbid illnesses such as diabetes and cardiovascular disease,[14,15] or genetic factors associated with susceptibility or disease progression. Susceptibility to infectious disease,[PMID: 3347221] including influenza[PMID: 23841736] and viral pneumonia,[PMID: 26524966] is strongly heritable, and early reports have suggested this is also true for COVID-19.[ https://www.medrxiv.org/content/10.1101/2020.04.22.20072124v2] Genetic variation in factors affecting the host immune response,[12] or viral entry,[13] may lead to differential susceptibility according to genetic heritage.

In the wake of the A/H1N1pdm2009 influenza pandemic, the Clinical Characterisation Protocol (CCP) for Severe Emerging Infection was developed by the International Severe Acute Respiratory and emerging Infections Consortium (ISARIC). As the pandemic potential of SARS-CoV-2 became apparent, CCP-UK was activated on 17th January 2020, in time to recruit the early patients of COVID-19 admitted to hospitals in the UK.

Our aim was to assess how prognosis in relation to critical care admission, use of invasive mechanical ventilation, and in-hospital mortality differs by ethnicity in the CCP-UK cohort of hospitalised patients with COVID-19.

## Methods

### *Study design and setting*

ISARIC CCP-UK is an ongoing prospective cohort study in 208 hospitals in England, Scotland, and Wales (table E1). The protocol, revision history, case report form, information leaflets and consent forms and detail of the Independent Data and Material Access Committee (IDAMAC) are available at https://isaric4c.net. The study was approved by the South Central - Oxford C Research Ethics Committee in England (Ref: 13/SC/0149), and by the Scotland A Research Ethics Committee (Ref: 20/SS/0028). The STROBE guidelines were used when reporting.

### *Participants*

Inclusion criteria were people of all ages who were admitted to hospital in England, Scotland and Wales, with proven or high likelihood of infection with SARS-CoV-2 leading to COVID-19 disease. Reverse transcriptase-PCR was the only mode of testing available during the period of study. The decision to test was at the discretion of the clinician attending the patient, and not defined by protocol. The enrolment criterion "high likelihood of infection" reflected that a preparedness protocol cannot assume that a diagnostic test will be available for an emergent pathogen.

### *Data collection*

Data were entered contemporaneously and extracted from the routine healthcare record by research nurses, administrators and medical students, into case report forms on a REDCap database (Research Electronic Data Capture, https://projectredcap.org). With consent, additional biological samples were collected for research purposes. Data regarding illness progression and severity, including location within the hospital (ward vs. critical care) were collected on Day 1 (admission/diagnosis), Day 3, Day 6, Day 9, and discharge/death, with further daily data collected on consented patients.

Self-reported ethnicity was transcribed from the healthcare record, where it had been recorded/checked along with other demographics and religion on admission. The care report form used an internationally applicable ethnicity definition with East Asian, South Asian, West Asian, Black, White, Latin American, Aboriginal/First Nations and Other. For the purposes of this analysis, these are collapsed into South Asian, East Asian, Black, Other Ethnic Minority (West Asian, Arab, Latin American, Aboriginal/First Nations, Other) and White, based on frequency (table E2).

Recorded comorbidities were asthma, diabetes, chronic cardiac disease (excluding hypertension), chronic haematologic disease, chronic kidney disease, chronic neurological disorder, chronic pulmonary disease, dementia, HIV/AIDS, malignancy, malnutrition, mild liver disease, moderate/severe liver disease, obesity (defined in records typically as body mass index > 30), rheumatologic disorder, and smoking. As the home address was not available, the Index of Multiple Deprivation (IMD) was used to create a hospital weighted average based on the admission population. Definitions varied on a pragmatic basis between devolved nations. For patients admitted in England, a weighted deprivation measure was aggregated by hospital provider catchment (defined by the Lower Layer Super Output Areas (LSOAs)). All admissions for that provider in 2018 were determined from the Hospital Episode Statistics dataset and the IMD weighted by the relative contribution of each LSOA. For Wales, an average Welsh Index of Multiple Deprivation (WIMD) was constructed for each hospital by averaging the 2019 version of the WIMD from all admissions to hospital with a pneumonia or flu diagnosis in 2019 (ICD10: J09-J18). For Scotland, a weighted average of the Scottish Index of Multiple Deprivation (2018 mid-year datazone estimates) was made at the hospital level and weighted for all non-elective admissions. To account for differences in the construction of these indices across the devolved nations, measures were centred, standardised, and incorporated with a random gradient into models.

### *Outcomes*

The main outcomes were admission to critical care, use of invasive mechanical ventilation (IMV), and in-hospital mortality. To avoid bias in the assessment of outcomes where the sickest patients have the longest hospital stays, patients admitted to hospital in the most recent two weeks were excluded from all outcome analyses. A sensitivity analysis excluding patients admitted in the most recent four weeks was performed.

### *Statistical analyses*

Continuous data are presented as mean (standard deviation), or median (interquartile range) if non-normally distributed. Binary data are presented as frequency (%). Binomial confidence intervals for proportions were calculated using the method of Wilson (REF). For univariable comparisons, we used Welch's t, ANOVA, Mann–Whitney U, or Kruskal–Wallis tests according to data distribution. Categorical data were compared using chi-squared tests.

Our modelling strategy was informed by a directed acyclic graph (DAG) (figure E1). Critical care admission and IMV use were modelled using hierarchical logistic regression models, adjusting for patient characteristics at level 1 and hospital of treatment at level 2. Baseline models included an adjustment for age, sex, and location. Index of multiple deprivation was aggregated at hospital level, centred, and standardised, and allowed to vary as a random gradient by devolved nation (level 3).

Survival was modelled using Cox Proportional Hazards regression, with alternative methods used for sensitivity analyses. Symptom onset was considered time zero. In the primary approach, discharge from hospital as an "absorbing state" – once discharged, patients were considered no longer at risk of death. Discharged patients were not censored and included in the risk set until the end of follow-up, thus discharge did not compete death. Sensitivity analyses with the Fine and Gray approach was included. Hierarchical Cox proportional hazards approaches included hospital as a random intercept and incorporated deprivation gradients varying by devolved nation. A parsimonious criterion-based model building approach was used based on the following principles: relevant explanatory variables were identified via a DAG *a priori* for exploration; age, sex, and hospital (random effect) were incorporated in baseline models; interactions were checked at first order level; final model selection was informed by the Akaike Information Criterion (AIC) and c-statistic for logistic regression models and c-statistic for survival models, with appropriate assumptions checked including the distribution of residuals and requirement for proportional hazards.

A classical approach to mediation analysis in survival models was taken, extending into a three-way decomposition of total effect into direct, pure indirect, and mediated interactive effects. Associations between exposure and outcome, mediators and exposure, and mediator and outcome were explored. Logistic regression models were fitted for mediators and Cox proportional survival models for outcomes, which were then combined. Bootstrapping of estimates was performed to provide 95% confidence intervals, together with a bootstrapped estimate of the mediated proportion of the total effect. All mediation models included age and sex as covariates.

### *Missing data*

There were substantial levels of missing data due to the overwhelming recruitment in the early growth phase of the epidemic. Missing data are reported, and patterns of missing data explored (appendix). Multiple imputation of missing values was performed using chained equations. Ten sets, each with ten iterations, were imputed using available explanatory variables and mortality. Missing ethnicity data was not imputed, but ethnicity was used in models for imputation. Graphical checks were performed, and imputed sets combined using Rubin's rules. Multiple imputation sets were used for sensitivity analyses.

Data were analysed using R (R Core Team v.3.6.3, Vienna, Austria) with packages including tidyverse, finalfit, survival, cmprsk, coxme and regmedint.

## Results

Between 6th February and 8th May 2020, we enrolled 34,986 patients admitted to 208 Acute Care Trusts / Health Boards with COVID-19 in England, Scotland, and Wales. This is estimated to represent 40.4% of all people admitted to hospital with COVID-19 in England, Scotland, and Wales.

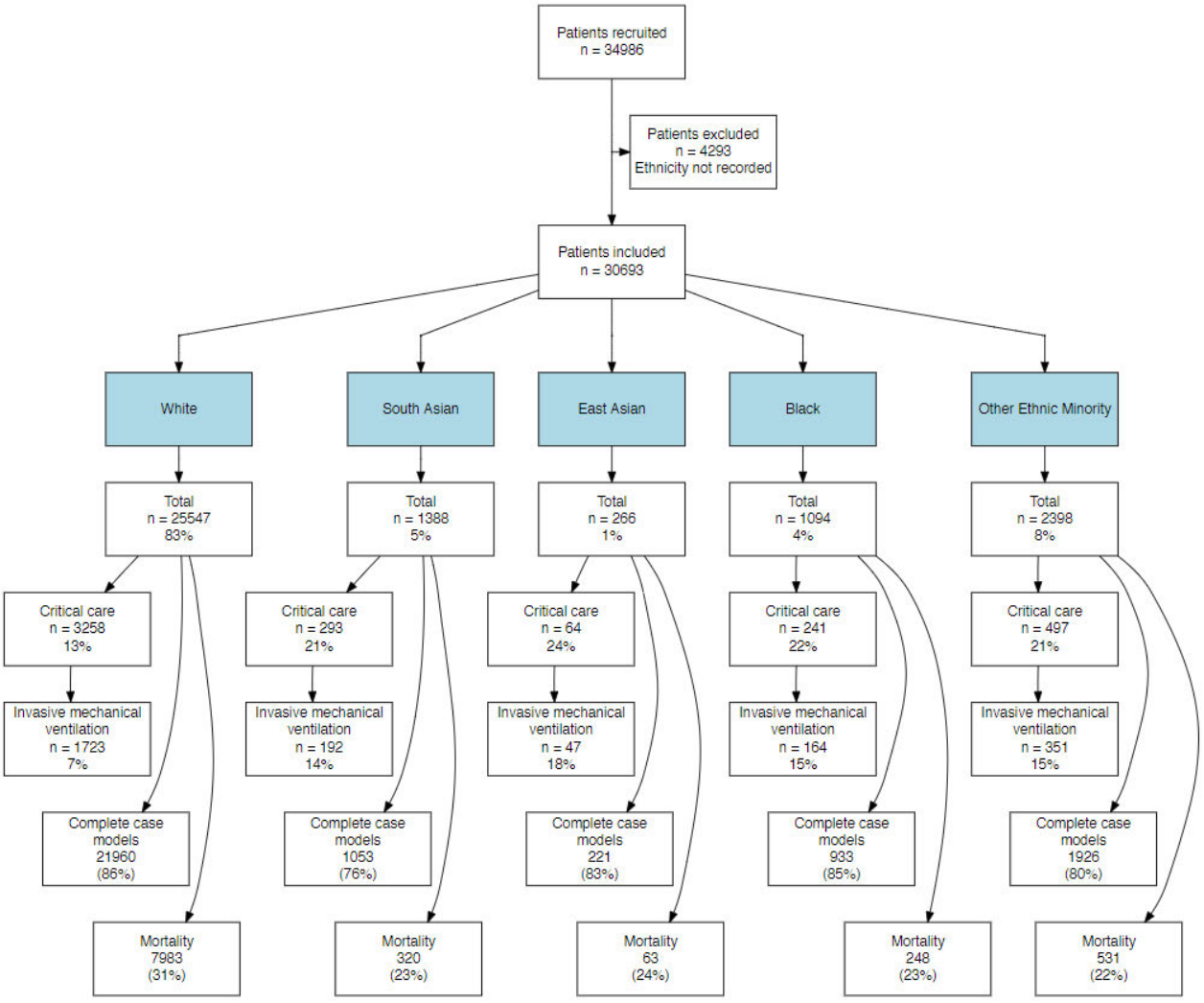


Figure 1. Patient inclusion stratified by ethnicity. Critical care use, invasive mechanical ventilation, and mortality in complete cohort.

Table 1. Characteristics of patients admitted to hospital with COVID-19 during between 6th February 2020 and 8th May 2020 by ethnic group. P-value is for a comparison across ethnic groups excluding missing data and is a chi-squared test for categorical variables and an F-test for continuous variables. Data n (%) unless otherwise stated. IMD, index of multiple deprivation. 4,293 missing ethnicity (see table E9).

| Ethnicity | | White | South Asian | East Asian | Black | Other Ethnic Minority | p |
|---|---|---|---|---|---|---|---|
| Total N (%) | | 25547 (83.2) | 1388 (4.5) | 266 (0.9) | 1094 (3.6) | 2398 (7.8) | |
| Age on admission (years) | Mean (SD) | 72.3 (15.6) | 59.8 (17.4) | 60.3 (17.3) | 61.4 (17.3) | 62.4 (17.8) | <0.001 |
| | 18-39 | 1025 (4.0) | 180 (13.0) | 32 (12.0) | 126 (11.5) | 275 (11.5) | |
| | 40-49 | 1308 (5.1) | 243 (17.5) | 43 (16.2) | 140 (12.8) | 336 (14.0) | |
| | 50-59 | 2962 (11.6) | 248 (17.9) | 57 (21.4) | 273 (25.0) | 432 (18.0) | |
| | 60-69 | 3928 (15.4) | 286 (20.6) | 43 (16.2) | 197 (18.0) | 431 (18.0) | |
| | 70-79 | 6319 (24.7) | 222 (16.0) | 46 (17.3) | 143 (13.1) | 430 (17.9) | |
| | 80+ | 10005 (39.2) | 209 (15.1) | 45 (16.9) | 215 (19.7) | 494 (20.6) | |
| Sex at Birth | Male | 14684 (57.5) | 887 (63.9) | 174 (65.4) | 602 (55.0) | 1426 (59.5) | <0.001 |
| | Female | 10778 (42.2) | 500 (36.0) | 91 (34.2) | 490 (44.8) | 964 (40.2) | |
| | (Missing) | 85 (0.3) | 1 (0.1) | 1 (0.4) | 2 (0.2) | 8 (0.3) | |
| Diabetes | No | 17447 (74.9) | 679 (60.6) | 169 (70.4) | 606 (61.2) | 1435 (69.3) | <0.001 |
| | Yes | 5838 (25.1) | 441 (39.4) | 71 (29.6) | 384 (38.8) | 636 (30.7) | |
| Obesity | No | 18952 (74.2) | 910 (65.6) | 207 (77.8) | 804 (73.5) | 1718 (71.6) | 0.201 |
| | Yes | 2382 (9.3) | 114 (8.2) | 19 (7.1) | 123 (11.2) | 210 (8.8) | |
| | (Missing) | 4213 (16.5) | 364 (26.2) | 40 (15.0) | 167 (15.3) | 470 (19.6) | |
| Chronic cardiac disease | No | 15403 (60.3) | 867 (62.5) | 195 (73.3) | 841 (76.9) | 1629 (67.9) | <0.001 |
| | Yes | 8228 (32.2) | 266 (19.2) | 47 (17.7) | 162 (14.8) | 467 (19.5) | |
| | (Missing) | 1916 (7.5) | 255 (18.4) | 24 (9.0) | 91 (8.3) | 302 (12.6) | |
| Chronic pulmonary disease | No | 18821 (73.7) | 1043 (75.1) | 223 (83.8) | 929 (84.9) | 1857 (77.4) | <0.001 |
| | Yes | 4751 (18.6) | 86 (6.2) | 18 (6.8) | 73 (6.7) | 218 (9.1) | |
| | (Missing) | 1975 (7.7) | 259 (18.7) | 25 (9.4) | 92 (8.4) | 323 (13.5) | |
| Asthma | No | 20079 (78.6) | 945 (68.1) | 207 (77.8) | 870 (79.5) | 1803 (75.2) | 0.108 |
| | Yes | 3358 (13.1) | 188 (13.5) | 34 (12.8) | 129 (11.8) | 281 (11.7) | |
| | (Missing) | 2110 (8.3) | 255 (18.4) | 25 (9.4) | 95 (8.7) | 314 (13.1) | |
| Chronic kidney disease | No | 19201 (75.2) | 931 (67.1) | 218 (82.0) | 831 (76.0) | 1796 (74.9) | <0.001 |
| | Yes | 4208 (16.5) | 193 (13.9) | 26 (9.8) | 170 (15.5) | 286 (11.9) | |
| | (Missing) | 2138 (8.4) | 264 (19.0) | 22 (8.3) | 93 (8.5) | 316 (13.2) | |
| Moderate/severe liver disease | No | 22739 (89.0) | 1102 (79.4) | 237 (89.1) | 976 (89.2) | 2012 (83.9) | 0.221 |
| | Yes | 460 (1.8) | 13 (0.9) | 2 (0.8) | 17 (1.6) | 37 (1.5) | |
| | (Missing) | 2348 (9.2) | 273 (19.7) | 27 (10.2) | 101 (9.2) | 349 (14.6) | |
| Mild Liver disease | No | 22798 (89.2) | 1096 (79.0) | 233 (87.6) | 979 (89.5) | 2006 (83.7) | 0.719 |
| | Yes | 344 (1.3) | 18 (1.3) | 6 (2.3) | 13 (1.2) | 32 (1.3) | |
| | (Missing) | 2405 (9.4) | 274 (19.7) | 27 (10.2) | 102 (9.3) | 360 (15.0) | |
| Chronic neurological disorder | No | 20243 (79.2) | 1045 (75.3) | 221 (83.1) | 928 (84.8) | 1870 (78.0) | <0.001 |
| | Yes | 3032 (11.9) | 78 (5.6) | 21 (7.9) | 68 (6.2) | 183 (7.6) | |
| | (Missing) | 2272 (8.9) | 265 (19.1) | 24 (9.0) | 98 (9.0) | 345 (14.4) | |
| Malignancy | No | 20665 (80.9) | 1072 (77.2) | 229 (86.1) | 915 (83.6) | 1910 (79.6) | <0.001 |
| | Yes | 2530 (9.9) | 48 (3.5) | 9 (3.4) | 85 (7.8) | 144 (6.0) | |
| | (Missing) | 2352 (9.2) | 268 (19.3) | 28 (10.5) | 94 (8.6) | 344 (14.3) | |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Chronic hematologic disease | No | 22195 (86.9) | 1085 (78.2) | 232 (87.2) | 922 (84.3) | 1971 (82.2) | <0.001 |
| | Yes | 975 (3.8) | 33 (2.4) | 8 (3.0) | 76 (6.9) | 80 (3.3) | |
| | (Missing) | 2377 (9.3) | 270 (19.5) | 26 (9.8) | 96 (8.8) | 347 (14.5) | |
| AIDS/HIV | No | 22931 (89.8) | 1092 (78.7) | 239 (89.8) | 947 (86.6) | 2020 (84.2) | <0.001 |
| | Yes | 74 (0.3) | 4 (0.3) | 1 (0.4) | 34 (3.1) | 9 (0.4) | |
| | (Missing) | 2542 (10.0) | 292 (21.0) | 26 (9.8) | 113 (10.3) | 369 (15.4) | |
| Rheumatologic disorder | No | 20412 (79.9) | 1042 (75.1) | 230 (86.5) | 936 (85.6) | 1899 (79.2) | <0.001 |
| | Yes | 2717 (10.6) | 67 (4.8) | 8 (3.0) | 62 (5.7) | 141 (5.9) | |
| | (Missing) | 2418 (9.5) | 279 (20.1) | 28 (10.5) | 96 (8.8) | 358 (14.9) | |
| Dementia | No | 19252 (75.4) | 1055 (76.0) | 220 (82.7) | 933 (85.3) | 1872 (78.1) | <0.001 |
| | Yes | 4106 (16.1) | 60 (4.3) | 19 (7.1) | 74 (6.8) | 193 (8.0) | |
| | (Missing) | 2189 (8.6) | 273 (19.7) | 27 (10.2) | 87 (8.0) | 333 (13.9) | |
| Malnutrition | No | 21456 (84.0) | 1050 (75.6) | 225 (84.6) | 948 (86.7) | 1922 (80.2) | 0.031 |
| | Yes | 607 (2.4) | 20 (1.4) | 5 (1.9) | 13 (1.2) | 46 (1.9) | |
| | (Missing) | 3484 (13.6) | 318 (22.9) | 36 (13.5) | 133 (12.2) | 430 (17.9) | |
| Smoking | Yes | 1266 (5.0) | 34 (2.4) | 9 (3.4) | 27 (2.5) | 95 (4.0) | <0.001 |
| | Never Smoked | 9271 (36.3) | 744 (53.6) | 142 (53.4) | 609 (55.7) | 1133 (47.2) | |
| | Former Smoker | 6310 (24.7) | 126 (9.1) | 34 (12.8) | 114 (10.4) | 332 (13.8) | |
| | (Missing) | 8700 (34.1) | 484 (34.9) | 81 (30.5) | 344 (31.4) | 838 (34.9) | |
| Prior immunosuppression | No | 20734 (81.2) | 1027 (74.0) | 216 (81.2) | 907 (82.9) | 1906 (79.5) | 0.003 |
| | Yes | 2329 (9.1) | 88 (6.3) | 15 (5.6) | 86 (7.9) | 173 (7.2) | |
| | (Missing) | 2484 (9.7) | 273 (19.7) | 35 (13.2) | 101 (9.2) | 319 (13.3) | |
| Prior infection treatment | No | 18342 (71.8) | 892 (64.3) | 187 (70.3) | 817 (74.7) | 1672 (69.7) | 0.193 |
| | Yes | 4659 (18.2) | 216 (15.6) | 44 (16.5) | 176 (16.1) | 389 (16.2) | |
| | (Missing) | 2546 (10.0) | 280 (20.2) | 35 (13.2) | 101 (9.2) | 337 (14.1) | |
| Deprivation (IMD) | Mean (SD) | 0.1 (0.8) | 0.1 (0.8) | 0.2 (0.8) | 0.1 (0.7) | 0.3 (0.7) | <0.001 |

## Presentation at hospital

30,693 (88%) had ethnicity data recorded and were considered in the following groups: South Asian (n=1,388, 5%), East Asian (266, 1%), Black (1,094, 4%), Other Ethnic Minority (2,398, 8%) (collectively Ethnic Minorities), and White (25,547, 83%) (Figure 1).

Ethnic Minorities were younger (White, mean 72 y (standard deviation 16); South Asian 60 y (17); East Asian 60 y (17); Black 61 y (17); Other Ethnic Minority 62 y (18)) and more likely to have diabetes (South Asian n=441 (39.4%); East Asian 71 (29.6%); Black 384 (38.8%); Other Ethnic Minority 636 (30.7%)) compared to the White group (5838 (25.1%)) (Table 1).

In unadjusted analysis, the White group was more likely than Ethnic Minority groups to have other comorbidities such as chronic cardiac disease (White n=8228 (32.2%); South Asian 266 (19.2%); East Asian 47 (17.7%); Black 162 (14.8%); Other Ethnic Minority 467 (19.5%), chronic pulmonary disease (White 4751 (18.6%); South Asian 86 (6.2%); East Asian 18 (6.8%); Black 73 (6.7%); Other Ethnic Minority 218 (9.1%)), and dementia (White 4106 (16.1%); South Asian 60 (4.3%); East Asian 19 (7.1%); Black 74 (6.8%); Other Ethnic Minority 193 (8.0%)).

With age and sex adjustment, ethnic differences in comorbidity persisted with all Ethnic Minorities more likely to have diabetes and less likely to have chronic pulmonary disease and obesity than the White group (Figure 2). No difference in the likelihood of chronic cardiac disease was seen between the South Asian and the White group.

No significant differences were seen in the distribution of severity scores (national early warning score 2 (NEWS2)) at admission between ethnic groups (figure 3A and figure 3C). In patients presenting to hospital with COVID-19, no differences were seen in the time from symptom onset to admission between ethnic groups (figure 3B) when modelled using Cox proportion hazards methods for the relative hazard of admission (figure 3D).

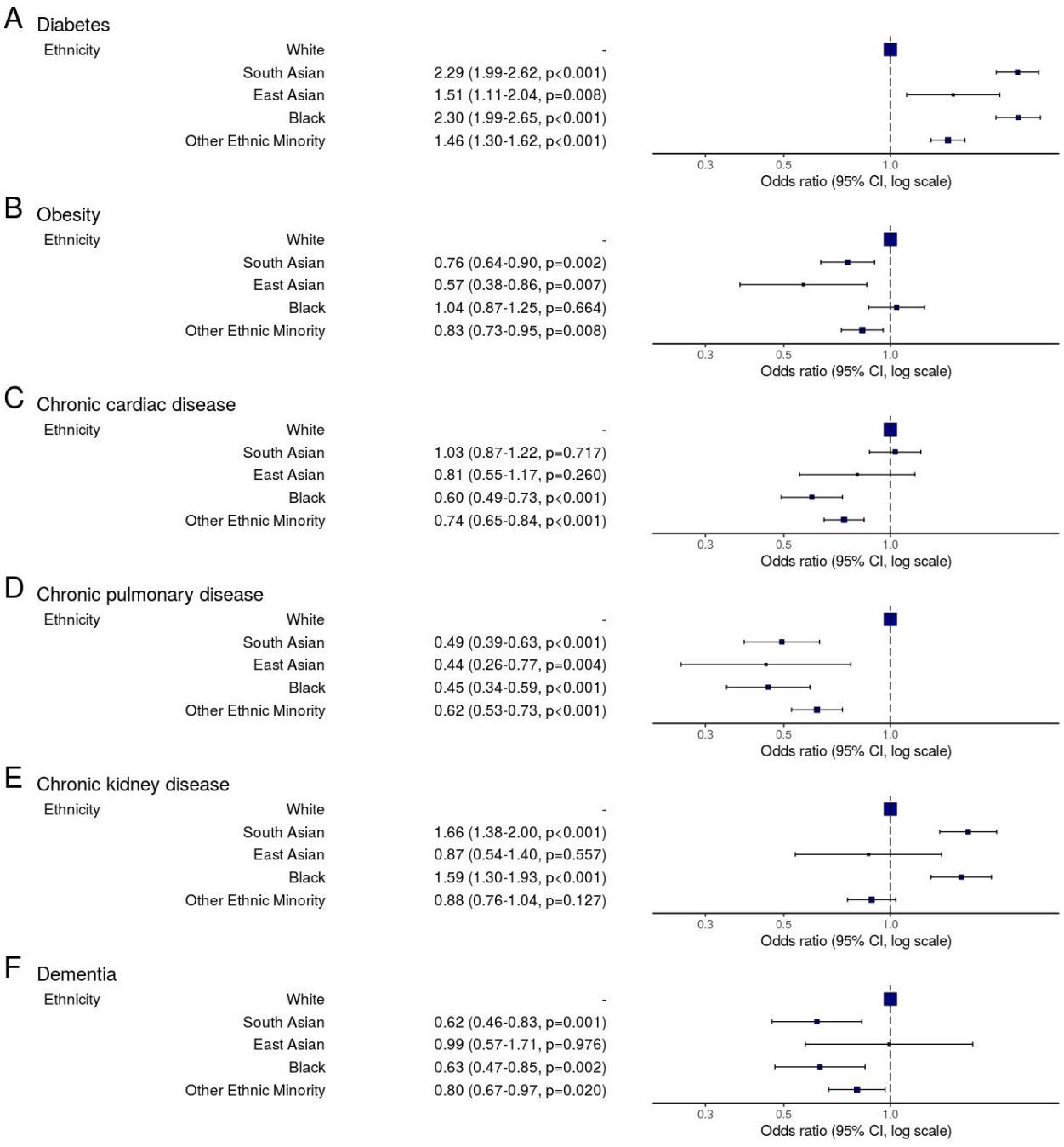


Figure 2. Age and sex adjusted association between ethnicity and comorbidity for patients in hospital with COVID-19. Hierarchical logistic regression models of complete data. Data are odds ratios (95% confidence interval, P-value).

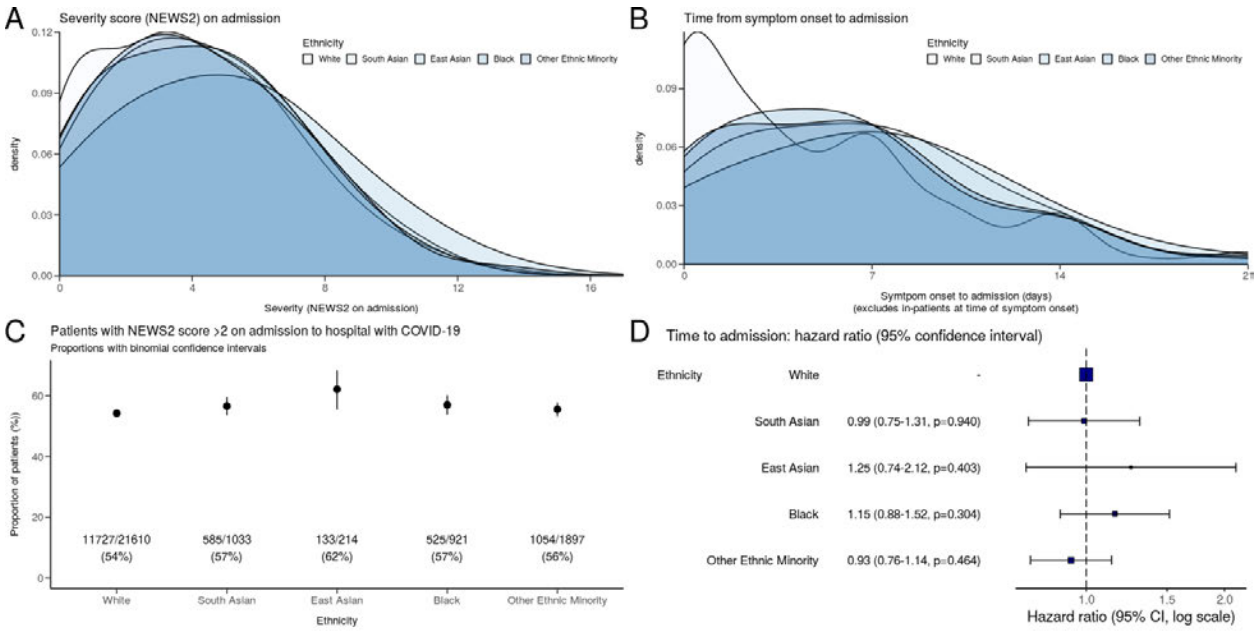


Figure 3. Severity score at admission and time from symptom onset to admission by ethnicity. National early warning score 2 (NEWS2) distribution (A) and proportion with NEWS2 >2 (C) by ethnicity. In patients presenting to hospital with COVID-19, distribution of time from symptom onset to admission (B) and Cox proportion hazards model of time to admission showing relative hazard for admission (D) by ethnicity.

## Ethnicity, critical care admission and invasive mechanical ventilation

Overall, 4,353 patients (14%) were admitted to a critical care facility (figure 3A). On crude analysis, the White ethnic group (n=3,258, 13%) was less likely to be admitted to critical care compared to the South Asian (293, 21%), East Asian (64, 24%), Black (241, 22%), or Other Ethnic Minority (497, 21%) groups.

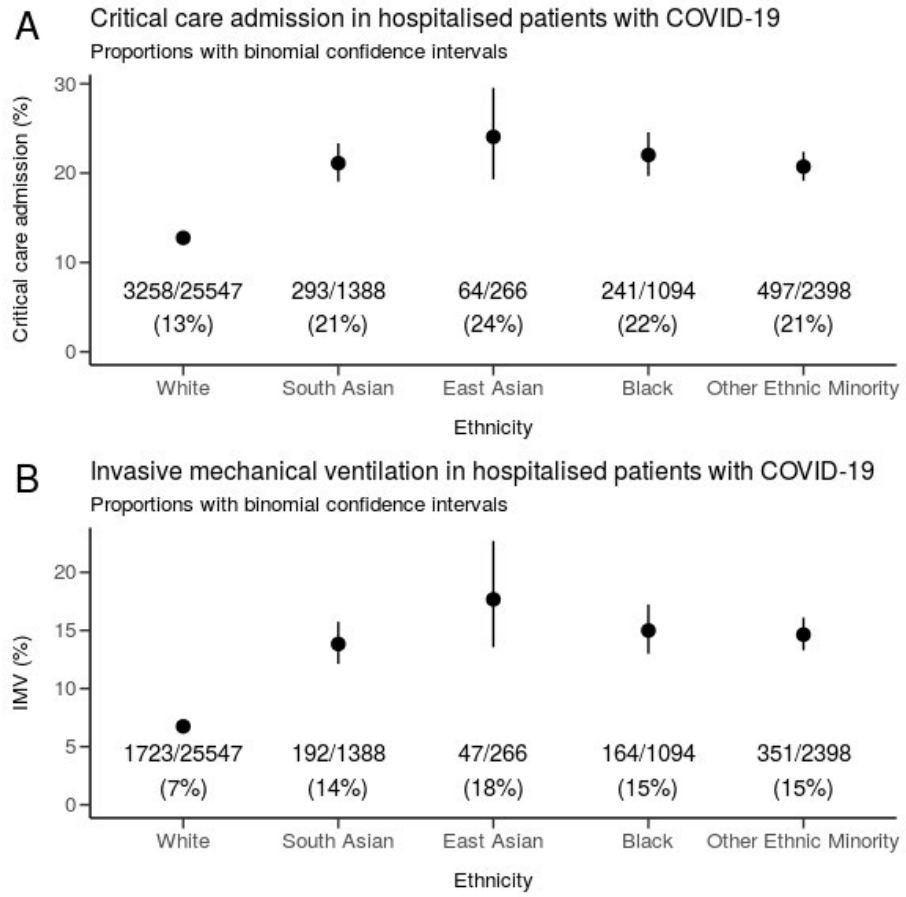


Figure 4. Unadjusted critical care admission (A) and use of invasive mechanical ventilation (B) in hospitalised patients with COVID-19 by self-defined ethnicity. Binomial confidence intervals. Numbers are patient counts per group / total cohort (%).

In models accounting for age, sex, and location (figure 5B), these associations persisted in the South Asian (odds ratio 1.28, 95% confidence interval 1.09 to 1.59), Black (1.36, 1.14 to 1.62), and Other Ethnic Minority (1.29, 95% CI 1.13 to 1.47) groups (table E3). No meaningful change in these estimates was seen with the sequential introduction of potential mediators including deprivation and comorbidities (diabetes, obesity, chronic cardiac disease, chronic pulmonary disease, chronic kidney disease, and dementia) (figure 5C).

Similar findings were found in analyses of invasive mechanical ventilation (Figure E2, table E3).

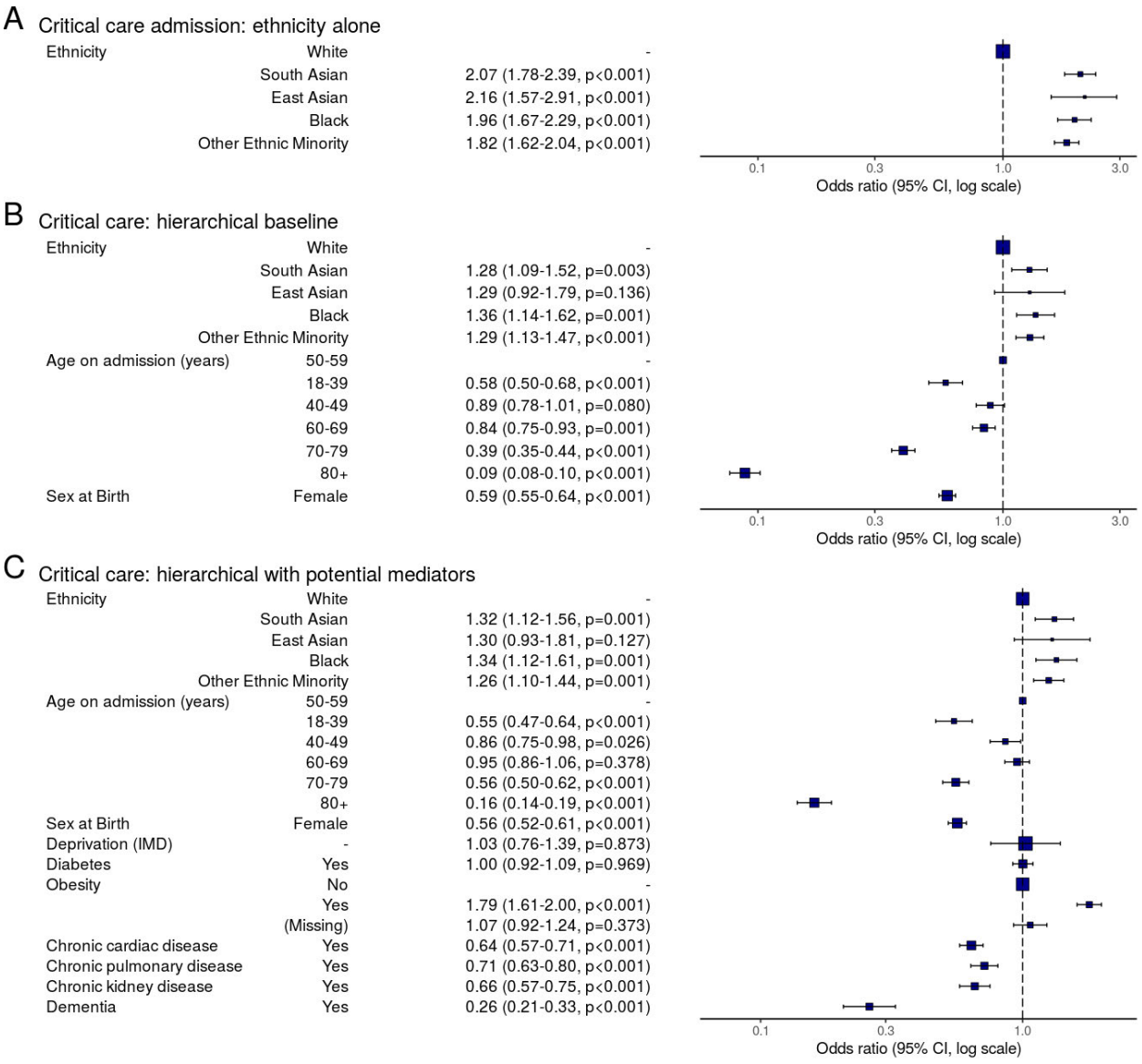


Figure 5. Critical care admission by ethnic group. (A) Univariable logistic regression model of ethnicity alone. (B) Hierarchical logistic regression model adjusting for age, sex and accounting for clustering in hospitals. (C) Hierarchical logistic regression models with adjustment for factors potentially mediating critical care admission were explored sequentially. Full model presented here accepting potential bias in comorbidity estimates. Complete case data. See table E3 for full models. IMD, index of multiple deprivation (centred and standardised).

## Ethnicity and survival from COVID-19

In analyses not accounting for age and sex differences between ethnic groups, in-hospital mortality occurred more frequently in the White group compared to the Ethnic Minorities (figure 6).

However, in models accounting for age, sex, and location, evidence of higher mortality was seen in the South Asian group (hazard ratio 1.19, 95% CI 1.05 to 1.36), but not the East Asian (1.00, 95% CI 0.74 to 1.35), Black (1.05, 95% CI 0.91 to 1.21) or Other Ethnic Minority group (0.99, 95% CI 0.89-1.10), compared to the White group (figure 7B; table E5). Similar results were seen in alternative models of competing risks (table E10) and in models replaced in the ten multiple imputation sets (figure E3).

Comorbidities were explored as potential mediators of the apparent association between South Asian ethnicity and an increased hazard of death. Comorbities associated with death in age and sex adjusted analysis were explored (table E11 to E15). Of these, diabetes (hazard ratio 2.29, 95% CI 1.99 to 2.62, $P < 0.001$) and chronic kidney disease (1.66, 95% CI 1.38 to 2.00 $P < 0.001$) had strong positive associations with South Asian ethnicity (figure 2).

A significant mediation effect (total natural indirect) of diabetes was found (hazard ratio 1.03, 95% CI 1.02 to 1.04, $P < 0.001$; table E16) representing 17.8% (95% CI 8.9% to 65.7%, $P = 0.009$; table E17) of the total effect of South Asian ethnicity on mortality (figure 8). Chronic kidney disease did not contribute significantly in addition to diabetes. No significant interaction effect was found with either diabetes or chronic kidney disease.

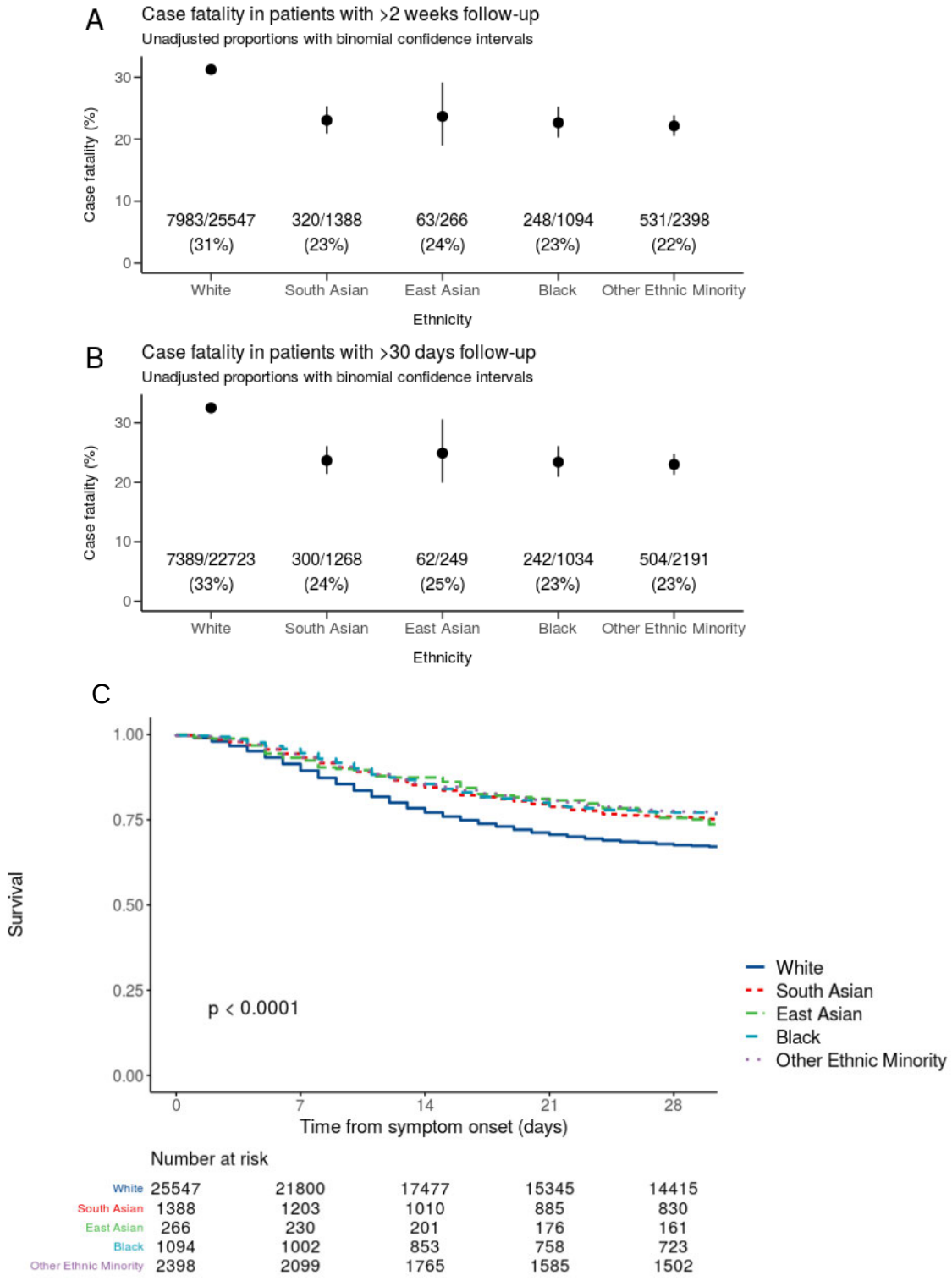


Figure 6. In-hospital case fatality by ethnicity. (A) Case fatality in patients with at least 2 weeks follow-up. (B) Case-fatality in patients with at least 4 weeks follow-up. (C) Kaplan-Meier survival curves stratified by ethnicity.

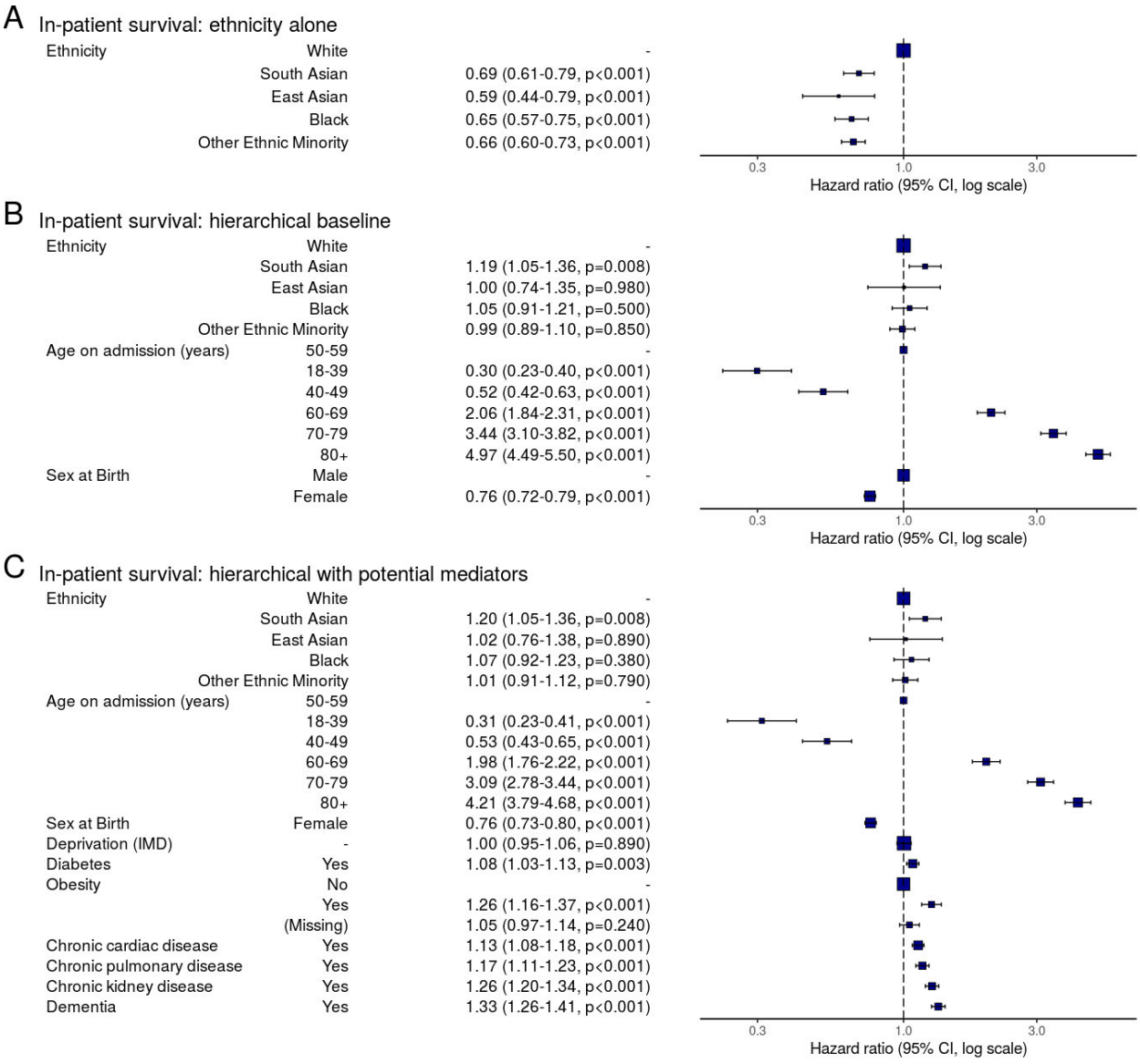


Figure 7. In-hospital survival by ethnic group. Estimates are hazard ratio (95% confidence interval, P-value). (A) Univariable Cox proportional hazards regression model of ethnicity alone. (B) Hierarchical Cox proportional hazards regression model adjusting for age, sex and deprivation, accounting for clustering within hospital. (C) Hierarchical Cox proportional hazards regression models with adjustment for factors potentially mediating survival by ethnic group were explored sequentially. accounting for clustering. Full model presented here accepting potential bias in comorbidity estimates. Complete case data. CI, confidence interval; IMD, index of multiple deprivation (centred and standardised).

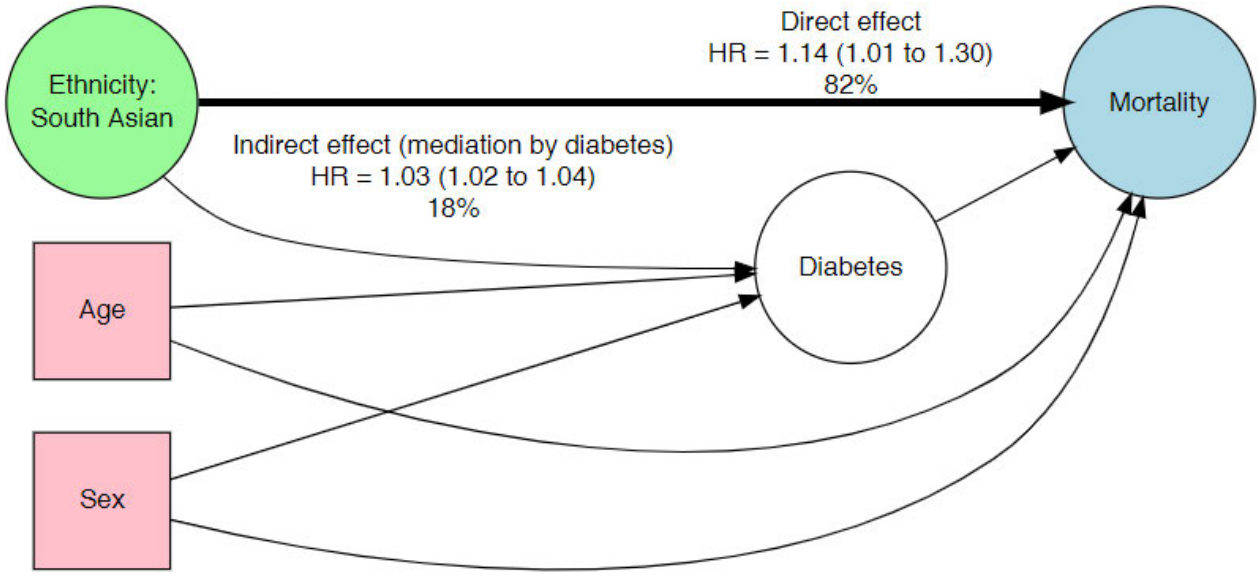


Figure 8. Mediation of apparent excess hazard of death in South Asian group by diabetes. Three-way decomposition mediation analysis was performed for comorbidities associated with ethnicity (figure 2; table E11 to E15) and outcome (figure 7). All models included age and sex as covariates. The proportion of the total effect mediated by diabetes for mortality in South Asian patients with bootstrapped 95% CI intervals was determined.

## Discussion

In this UK prospective cohort of 34,986 patients in hospital with COVID-19, Ethnic Minority people were more likely to be admitted to critical care and to undergo invasive mechanical ventilation (IMV) than White people, despite there being no difference in disease severity at presentation nor duration of symptoms. South Asian people in hospital with COVID-19 appeared 20% more likely to die than White people, and 18% of this increased risk seemed to be mediated by higher levels of diabetes.

The ISARIC WHO CCP is the largest prospective observational cohort study of in-hospital patients with COVID-19 to date, accounting for 40% of patients admitted to hospitals in the UK. It is the first study to look at in-hospital trajectories between different ethnic groups. We analysed the data with several separate approaches and our findings remained consistent. Our study has demonstrated the vital importance of forward planning and investment in preparedness studies: we were able to collect granular patient data in near-real time, and undertake analyses during the growth part of the pandemic in the UK, without the delay associated with routine healthcare data linkages. Analyses have been performed in depth taking a number of different approaches, all with consistent results.

This was a cohort of patients already admitted to hospital, and we were unable to assess the risk of hospital admission or out-of-hospital mortality, leading to a potential risk of selection/collider bias when assessing mediators. We were unable to take community factors into account such as population infection rates, and differential rates between different ethnic groups. Higher infection rates may be the result of bigger families, multi-generational households, more likely to be living in urban areas, more likely to be in a public facing occupation. There were limitations in the measurement of some key concepts: we did not have individual measures of socioeconomic position and had limited information on health behaviours such as smoking.

While we recruited 40% of patients admitted to hospital with COIVD-19, the results may reflect the differential risk in the whole hospital COVID-19 population, however we have no information on the 60% of patients that were not recruited. Our ethnicity definitions were broad, and we were unable to explore these in greater depth, meaning that we may have missed differences within groups. The Other Ethnic Minority group in particular was unlikely to be homogeneous. Obesity was recorded as present or absent, rather than BMI, which may underrepresent obesity in Asian population where obesity is defined as BMI greater than 27.5. There were significant missing data given the nature of collecting prospective data during a pandemic, but analyses of imputed datasets broadly reflect those of the complete case analysis.

Characteristics of ethnic groups going into hospital were different: patients from non-White groups were younger, with more diabetes, compared with the White group who were older and had more cardiorespiratory disease. Variation in healthcare seeking behaviours and access to healthcare amongst more disadvantaged groups could also contribute to differences in the consequences of COVID-19,[17] however, we found no significant difference between ethnic groups in duration or severity of symptoms to hospital presentation in patients who were admitted.

Although the age-adjusted proportions of patients admitted to critical care was higher in the Ethnic Minority group, a large majority of patients admitted to critical care were White (White 75%, South Asian 6.7%, East Asian 1.5%, Black 5.5%, Other Ethnic Minority 11.4%). This is a higher proportion compared with the latest ICNARC report which found a third of patients admitted to critical care were from non-White groups.[20] This may represent a selection bias in our cohort, or differences in definitions of critical care.

Extreme elderly age and the presence of comorbidities were associated with a lower likelihood of critical care admission, suggesting advanced care planning decisions on the ward. While this may have disproportionately affected patients in the White group who were significantly older with more

cardiorespiratory disease, the increased likelihood of critical care admission and IMV in Ethnic Minorities persisted after adjustment. This may reflect an increased severity of disease in Ethnic Minority populations.

Our finding of increased mortality in the South Asian group reflects several recent reports which found that people from Asian and Black ethnic groups were at increased risk of in-hospital death from COVID-19, and that this was only partially attributable to pre-existing clinical risk factors or deprivation.[17,18,21] We add an important and detailed picture of differences in characteristics of ethnic groups in hospital. Why is it that Ethnic Minority groups are significantly younger than the White group? The prevalence of diabetes is also striking at around 40% in South Asian and Black patients. The mediation of part of the mortality effect by diabetes is important. This appeared independent of chronic cardiac disease and chronic kidney disease and is presumably due to the multitude of other negative associations carried by the condition. What of the 80% effect left unexplained? Our models did not account well for wide socioeconomic determinants of outcome, as well nuance in the comorbidity data. Local authorities with a greater proportion of residents from non-White groups had higher COVID19 mortality rates, as did local authorities with a greater proportion of residents experiencing deprivation from low income.[19] This may lead to higher infection rates as a result of bigger families, multi-generational households, more likely to be living in urban areas, or more likely to be in public facing occupations. We did not find that deprivation at the level of the hospital was significant for hospital admission or severity of illness in hospital, however aggregation of deprivation at hospital level will mask individual socioeconomic effects. Accounting for this will be essential for future studies. Finally, why have we not shown an excess in mortality in Black people, as others have reported? (REF). It seems unlikely that this group are dying disproportionately more often in the community rather than in hospital, so any effect would be expected to be seen in this cohort. It may be selection bias, and our on-going work includes linking our dataset widely to better understand the place of the in-hospital stay as part of the full patient journey.

Our findings have important implications. People of South Asian ethnicity are over-represented in front-line key worker occupations, and policies should consider shielding advice regarding at risk patients. On-going work to devise risk assessment tools to help mitigate the likelihood of coronavirus infection and manage the easing of lockdown restrictions need to consider the effects of ethnicity on outcomes. Careful consideration needs to be given in these tools to the weighting of mediators of risk such as diabetes. Further research integrating primary and secondary care data is key to improving the understanding of other drivers of poor outcomes in Ethnic Minority patients.

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## Online supplement

Figure E1. Directed acyclic graph for total effects mortality model. Green, exposure; blue, outcome; pink boxes, adjusted in analysis; white circles, not adjusted in analysis.

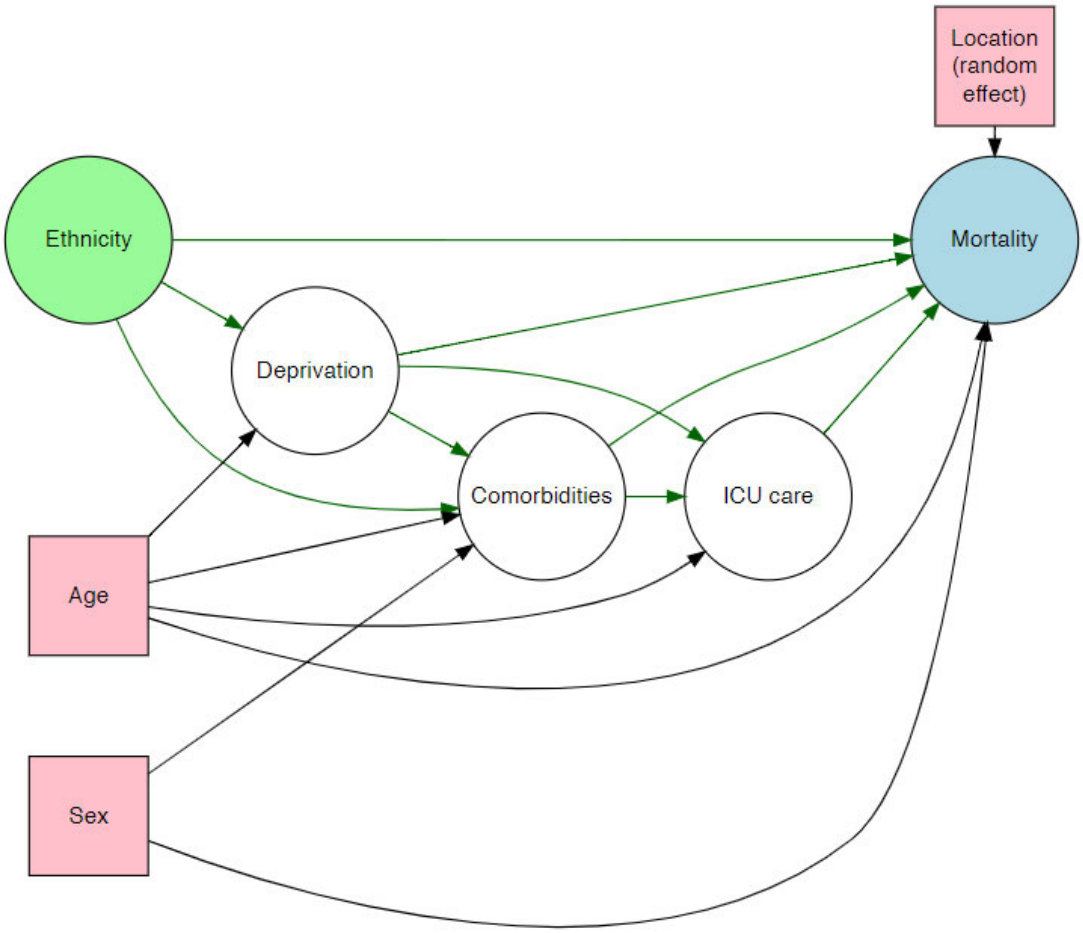

Table E1. Distribution of patients by ethnicity and devolved nation.

| | | England | Scotland | Wales |
|---|---|---|---|---|
| Total N | | 28617 | 1488 | 588 |
| Ethnicity | White | 23589 (82.4) | 1420 (95.4) | 538 (91.5) |
| | South Asian | 1355 (4.7) | 16 (1.1) | 17 (2.9) |
| | East Asian | 258 (0.9) | 8 (0.5) | 0 (0.0) |
| | Black | 1082 (3.8) | 10 (0.7) | 2 (0.3) |
| | Other Ethnic Minority | 2333 (8.2) | 34 (2.3) | 31 (5.3) |

Table E2. Classification of ethnicity.

| Ethnicity | | White | South Asian | East Asian | Black | Other Ethnic Minority |
|---|---|---|---|---|---|---|
| Total N (%) | | 25547 (83.2) | 1388 (4.5) | 266 (0.9) | 1094 (3.6) | 2398 (7.8) |
| Ethnicity | Aboriginal/First Nations | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 8 (0.3) |
| | Arab | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 144 (6.0) |
| | Black | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1094 (100.0) | 0 (0.0) |
| | East Asian | 0 (0.0) | 0 (0.0) | 266 (100.0) | 0 (0.0) | 0 (0.0) |
| | Latin American | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 51 (2.1) |
| | Other | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 2085 (86.9) |
| | South Asian | 0 (0.0) | 1388 (100.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| | West Asian | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 110 (4.6) |
| | White | 25547 (100.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) |

Table E3. Admission to Critical care in hospitalised patients with COVID-19. Univariable, multivariable baseline and multivariable with mediators hierarchical logistic regression models. Complete case data. OR, odds ratio. Data are n (%) and odds ratio (95% confidence interval, P-value).

| Critical care admission | | No | Yes | OR (univariable) | OR (baseline) | OR (with mediators) |
|---|---|---|---|---|---|---|
| Ethnicity | White | 22289 (84.6) | 3258 (74.8) | - | - | - |
| | South Asian | 1095 (4.2) | 293 (6.7) | 1.83 (1.60-2.09, p<0.001) | 1.28 (1.09-1.52, p=0.003) | 1.32 (1.12-1.56, p=0.001) |
| | East Asian | 202 (0.8) | 64 (1.5) | 2.17 (1.62-2.86, p<0.001) | 1.29 (0.92-1.79, p=0.136) | 1.30 (0.93-1.81, p=0.127) |
| | Black | 853 (3.2) | 241 (5.5) | 1.93 (1.66-2.24, p<0.001) | 1.36 (1.14-1.62, p=0.001) | 1.34 (1.12-1.61, p=0.001) |
| | Other Ethnic Minority | 1901 (7.2) | 497 (11.4) | 1.79 (1.61-1.99, p<0.001) | 1.29 (1.13-1.47, p<0.001) | 1.26 (1.10-1.44, p=0.001) |
| Age on admission (years) | 50-59 | 3364 (11.2) | 1256 (25.2) | - | - | - |
| | 18-39 | 1581 (5.3) | 352 (7.0) | 0.60 (0.52-0.68, p<0.001) | 0.58 (0.50-0.68, p<0.001) | 0.55 (0.47-0.64, p<0.001) |
| | 40-49 | 1868 (6.2) | 638 (12.8) | 0.91 (0.82-1.02, p=0.115) | 0.89 (0.78-1.01, p=0.080) | 0.86 (0.75-0.98, p=0.026) |
| | 60-69 | 4254 (14.2) | 1339 (26.8) | 0.84 (0.77-0.92, p<0.001) | 0.84 (0.75-0.93, p=0.001) | 0.95 (0.86-1.06, p=0.378) |
| | 70-79 | 7038 (23.5) | 1027 (20.6) | 0.39 (0.36-0.43, p<0.001) | 0.39 (0.35-0.44, p<0.001) | 0.56 (0.50-0.62, p<0.001) |
| | 80+ | 11887 (39.6) | 382 (7.6) | 0.09 (0.08-0.10, p<0.001) | 0.09 (0.08-0.10, p<0.001) | 0.16 (0.14-0.19, p<0.001) |
| Sex at Birth | Male | 16859 (56.4) | 3504 (70.4) | - | - | - |
| | Female | 13032 (43.6) | 1474 (29.6) | 0.54 (0.51-0.58, p<0.001) | 0.59 (0.55-0.64, p<0.001) | 0.56 (0.52-0.61, p<0.001) |
| Deprivation (IMD) | Mean (SD) | 0.1 (0.8) | 0.1 (0.8) | 1.10 (1.06-1.15, p<0.001) | - | 1.03 (0.76-1.39, p=0.873) |
| Obesity | No | 21794 (72.7) | 3450 (69.1) | - | - | - |
| | Yes | 2305 (7.7) | 867 (17.4) | 2.38 (2.18-2.59, p<0.001) | - | 1.79 (1.61-2.00, p<0.001) |
| | (Missing) | 5893 (19.6) | 677 (13.6) | 0.73 (0.66-0.79, p<0.001) | - | 1.07 (0.92-1.24, p=0.373) |
| Diabetes | No | 19427 (73.7) | 3420 (73.7) | - | - | - |
| | Yes | 6945 (26.3) | 1223 (26.3) | 1.00 (0.93-1.07, p=0.993) | - | 1.00 (0.92-1.09, p=0.969) |
| Chronic cardiac disease | No | 17557 (65.4) | 3871 (83.0) | - | - | - |
| | Yes | 9276 (34.6) | 791 (17.0) | 0.39 (0.36-0.42, p<0.001) | - | 0.64 (0.57-0.71, p<0.001) |
| Chronic pulmonary disease | No | 21606 (80.8) | 4138 (89.2) | - | - | - |
| | Yes | 5142 (19.2) | 503 (10.8) | 0.51 (0.46-0.56, p<0.001) | - | 0.71 (0.63-0.80, p<0.001) |
| Asthma | No | 22988 (86.5) | 3851 (82.7) | - | - | - |
| | Yes | 3597 (13.5) | 804 (17.3) | 1.33 (1.23-1.45, p<0.001) | - | - |
| Chronic kidney disease | No | 21637 (81.4) | 4225 (91.1) | - | - | - |
| | Yes | 4943 (18.6) | 415 (8.9) | 0.43 (0.39-0.48, p<0.001) | - | 0.66 (0.57-0.75, p<0.001) |
| Moderate/severe liver disease | No | 25782 (98.0) | 4549 (98.8) | - | - | - |
| | Yes | 519 (2.0) | 57 (1.2) | 0.62 (0.47-0.81, p=0.001) | - | - |
| Mild Liver disease | No | 25824 (98.5) | 4536 (98.8) | - | - | - |
| | Yes | 406 (1.5) | 57 (1.2) | 0.80 (0.60-1.05, p=0.116) | - | - |
| Chronic neurological disorder | No | 22899 (86.8) | 4364 (94.5) | - | - | - |
| | Yes | 3491 (13.2) | 254 (5.5) | 0.38 (0.33-0.43, p<0.001) | - | - |
| Malignancy | No | 23460 (89.1) | 4352 (94.4) | - | - | - |
| | Yes | 2857 (10.9) | 259 (5.6) | 0.49 (0.43-0.56, p<0.001) | - | - |
| Chronic hematologic disease | No | 25126 (95.6) | 4468 (97.0) | - | - | - |
| | Yes | 1161 (4.4) | 139 (3.0) | 0.67 (0.56-0.80, p<0.001) | - | - |
| AIDS/HIV | No | 25990 (99.6) | 4520 (99.3) | - | - | - |
| | Yes | 104 (0.4) | 31 (0.7) | 1.71 (1.13-2.53, p=0.009) | - | - |

| | | | | | | |
|---|---|---|---|---|---|---|
| Rheumatologic disorder | No | 23262 (88.8) | 4272 (92.9) | - | - | - |
| | Yes | 2938 (11.2) | 328 (7.1) | 0.61 (0.54-0.68, p<0.001) | - | - |
| Dementia | No | 21681 (81.9) | 4528 (97.8) | - | - | - |
| | Yes | 4791 (18.1) | 103 (2.2) | 0.10 (0.08-0.12, p<0.001) | - | 0.26 (0.21-0.33, p<0.001) |
| Malnutrition | No | 24189 (97.2) | 4450 (98.8) | - | - | - |
| | Yes | 698 (2.8) | 54 (1.2) | 0.42 (0.31-0.55, p<0.001) | - | - |
| Prior immunosuppression | No | 23583 (90.3) | 4140 (90.7) | - | - | - |
| | Yes | 2537 (9.7) | 425 (9.3) | 0.95 (0.86-1.06, p=0.395) | - | - |
| Prior infection treatment | No | 20836 (80.0) | 3643 (80.0) | - | - | - |
| | Yes | 5202 (20.0) | 911 (20.0) | 1.00 (0.93-1.08, p=0.968) | - | - |

Table E4. Invasive mechanical ventilation in hospitalised patients with COVID-19. Univariable, multivariable baseline and multivariable with mediators hierarchical logistic regression models. Complete case data. OR, odds ratio. Data are n (%) and odds ratio (95% confidence interval, P-value).

| IMV | | No | Yes | OR (univariable) | OR (baseline) | OR (with mediators) |
|---|---|---|---|---|---|---|
| Ethnicity | White | 23824 (84.4) | 1723 (69.6) | - | - | - |
| | South Asian | 1196 (4.2) | 192 (7.8) | 2.22 (1.89-2.60, p<0.001) | 1.44 (1.19-1.75, p<0.001) | 1.52 (1.25-1.84, p<0.001) |
| | East Asian | 219 (0.8) | 47 (1.9) | 2.97 (2.13-4.04, p<0.001) | 1.45 (1.00-2.11, p=0.049) | 1.44 (0.99-2.10, p=0.056) |
| | Black | 930 (3.3) | 164 (6.6) | 2.44 (2.04-2.89, p<0.001) | 1.53 (1.24-1.88, p<0.001) | 1.55 (1.26-1.90, p<0.001) |
| | Other Ethnic Minority | 2047 (7.3) | 351 (14.2) | 2.37 (2.09-2.68, p<0.001) | 1.53 (1.31-1.78, p<0.001) | 1.48 (1.27-1.73, p<0.001) |
| Age on admission (years) | 50-59 | 3832 (11.9) | 788 (27.1) | - | - | - |
| | 18-39 | 1733 (5.4) | 200 (6.9) | 0.56 (0.47-0.66, p<0.001) | 0.51 (0.42-0.62, p<0.001) | 0.47 (0.38-0.57, p<0.001) |
| | 40-49 | 2107 (6.6) | 399 (13.7) | 0.92 (0.81-1.05, p=0.220) | 0.86 (0.74-1.01, p=0.066) | 0.82 (0.70-0.97, p=0.017) |
| | 60-69 | 4727 (14.7) | 866 (29.8) | 0.89 (0.80-0.99, p=0.032) | 0.89 (0.79-1.01, p=0.077) | 1.05 (0.93-1.19, p=0.440) |
| | 70-79 | 7519 (23.4) | 546 (18.8) | 0.35 (0.31-0.40, p<0.001) | 0.39 (0.34-0.44, p<0.001) | 0.59 (0.51-0.68, p<0.001) |
| | 80+ | 12159 (37.9) | 110 (3.8) | 0.04 (0.04-0.05, p<0.001) | 0.05 (0.04-0.06, p<0.001) | 0.10 (0.08-0.12, p<0.001) |
| Sex at Birth | Male | 18250 (57.1) | 2113 (72.9) | - | - | - |
| | Female | 13720 (42.9) | 786 (27.1) | 0.49 (0.45-0.54, p<0.001) | 0.55 (0.50-0.61, p<0.001) | 0.52 (0.47-0.57, p<0.001) |
| Deprivation (IMD) | Mean (SD) | 0.1 (0.8) | 0.1 (0.8) | 1.08 (1.03-1.13, p=0.003) | - | 1.16 (0.84-1.59, p=0.376) |
| Obesity | No | 23230 (72.4) | 2014 (69.2) | - | - | - |
| | Yes | 2624 (8.2) | 548 (18.8) | 2.41 (2.17-2.67, p<0.001) | - | 1.82 (1.60-2.07, p<0.001) |
| | (Missing) | 6223 (19.4) | 347 (11.9) | 0.64 (0.57-0.72, p<0.001) | - | 1.06 (0.88-1.28, p=0.551) |
| Diabetes | No | 20834 (73.7) | 2013 (73.6) | - | - | - |
| | Yes | 7446 (26.3) | 722 (26.4) | 1.00 (0.92-1.10, p=0.938) | - | 0.95 (0.85-1.06, p=0.342) |
| Chronic cardiac disease | No | 19077 (66.3) | 2351 (85.7) | - | - | - |
| | Yes | 9676 (33.7) | 391 (14.3) | 0.33 (0.29-0.37, p<0.001) | - | 0.63 (0.55-0.72, p<0.001) |
| Chronic pulmonary disease | No | 23228 (81.0) | 2516 (92.3) | - | - | - |
| | Yes | 5436 (19.0) | 209 (7.7) | 0.35 (0.31-0.41, p<0.001) | - | 0.53 (0.45-0.63, p<0.001) |
| Asthma | No | 24547 (86.1) | 2292 (83.8) | - | - | - |
| | Yes | 3957 (13.9) | 444 (16.2) | 1.20 (1.08-1.34, p=0.001) | - | - |
| Chronic kidney disease | No | 23335 (81.9) | 2527 (93.0) | - | - | - |
| | Yes | 5168 (18.1) | 190 (7.0) | 0.34 (0.29-0.39, p<0.001) | - | 0.54 (0.45-0.66, p<0.001) |
| Moderate/severe liver disease | No | 27652 (98.1) | 2679 (99.0) | - | - | - |
| | Yes | 549 (1.9) | 27 (1.0) | 0.51 (0.34-0.73, p=0.001) | - | - |
| Mild Liver disease | No | 27694 (98.5) | 2666 (98.9) | - | - | - |
| | Yes | 434 (1.5) | 29 (1.1) | 0.69 (0.47-0.99, p=0.058) | - | - |
| Chronic neurological disorder | No | 24674 (87.2) | 2589 (95.5) | - | - | - |
| | Yes | 3622 (12.8) | 123 (4.5) | 0.32 (0.27-0.39, p<0.001) | - | - |
| Malignancy | No | 25241 (89.4) | 2571 (95.2) | - | - | - |
| | Yes | 2985 (10.6) | 131 (4.8) | 0.43 (0.36-0.51, p<0.001) | - | - |
| Chronic hematologic disease | No | 26969 (95.7) | 2625 (97.1) | - | - | - |
| | Yes | 1221 (4.3) | 79 (2.9) | 0.66 (0.52-0.83, p=0.001) | - | - |
| AIDS/HIV | No | 27837 (99.6) | 2673 (99.6) | - | - | - |
| | Yes | 125 (0.4) | 10 (0.4) | 0.83 (0.41-1.51, p=0.579) | - | - |
| Rheumatologic disorder | No | 24998 (89.0) | 2536 (93.6) | - | - | - |

| | | | | | | |
|---|---|---|---|---|---|---|
| | Yes | 3094 (11.0) | 172 (6.4) | 0.55 (0.47-0.64, p<0.001) | - | - |
| Dementia | No | 23519 (82.9) | 2690 (98.9) | - | - | - |
| | Yes | 4863 (17.1) | 31 (1.1) | 0.06 (0.04-0.08, p<0.001) | - | 0.19 (0.13-0.28, p<0.001) |
| Malnutrition | No | 25998 (97.3) | 2641 (99.2) | - | - | - |
| | Yes | 732 (2.7) | 20 (0.8) | 0.27 (0.17-0.41, p<0.001) | - | - |
| Prior immunosuppression | No | 25278 (90.2) | 2445 (91.7) | - | - | - |
| | Yes | 2740 (9.8) | 222 (8.3) | 0.84 (0.72-0.96, p=0.015) | - | - |
| Prior infection treatment | No | 22364 (80.1) | 2115 (79.3) | - | - | - |
| | Yes | 5561 (19.9) | 552 (20.7) | 1.05 (0.95-1.16, p=0.334) | - | - |

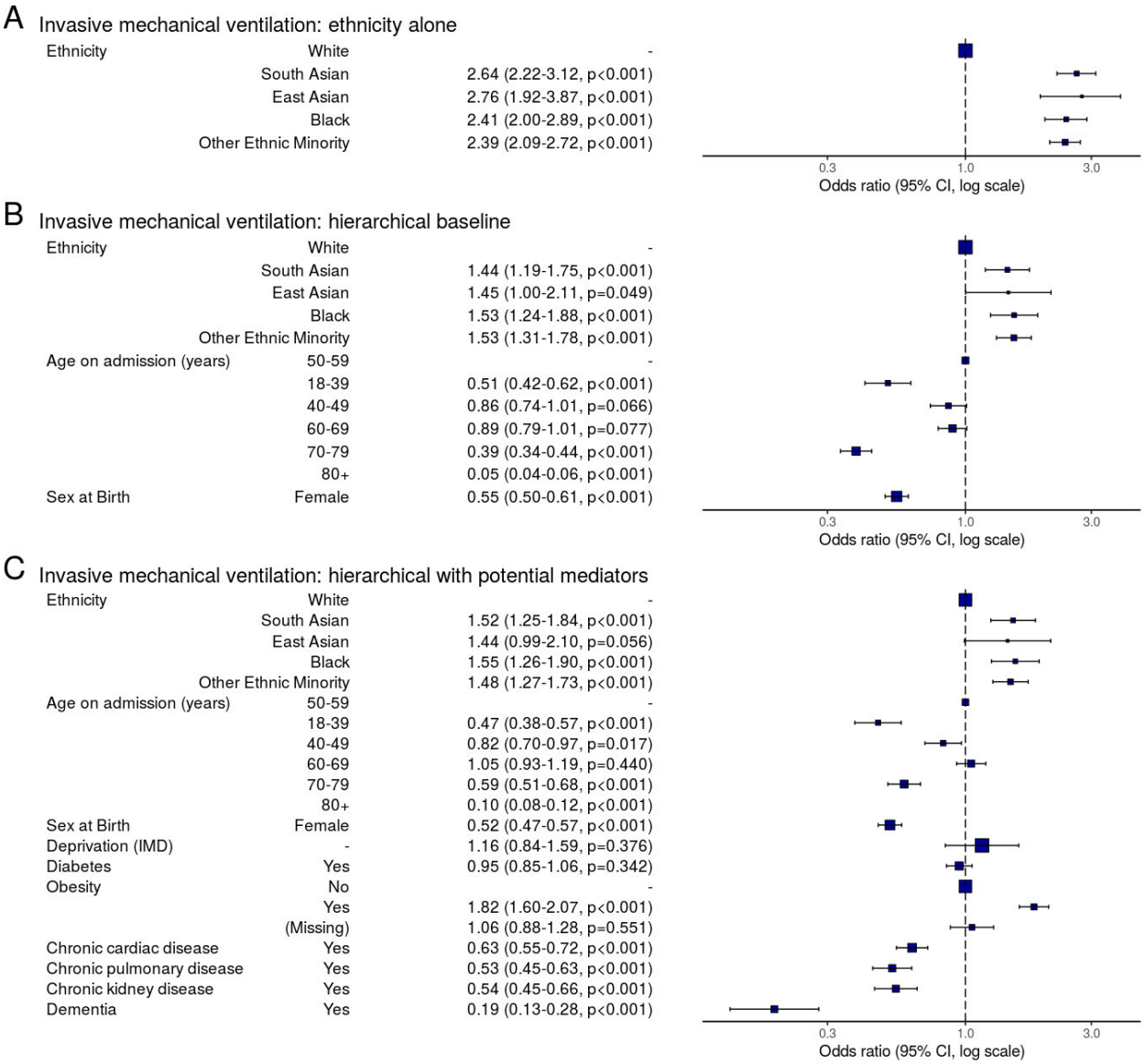


Figure E2. Invasive mechanical ventilation by ethnic group. (A) Univariable logistic regression model of ethnicity alone. (B) Hierarchical total effects logistic regression model adjusting for age, sex and accounting for clustering within CCG/HB. (C) Hierarchical logistic regression model with adjustment for factors potentially mediating ventilation by ethnic group, accounting for clustering within CCG/HB. IMD, index of multiple deprivation (centred and standardised).

Table E5. In-hospital mortality in hospitalised patients with COVID-19. Univariable, multivariable baseline, hierarchical baseline, and hierarchical with mediators Cox Proportional Hazards models. Complete case data. OR, odds ratio. Data are n (%) and hazard ratio (95% confidence interval, P-value).

| Surv(time, status) | | all | HR (univariable) | HR (baseline) | HR (hierarchical baseline) | HR (hierarchical with mediators) |
|---|---|---|---|---|---|---|
| Ethnicity | White | 21960 (84.2) | - | - | - | - |
| | South Asian | 1053 (4.0) | 0.69 (0.61-0.79, p<0.001) | 1.18 (1.04-1.34, p=0.010) | 1.19 (1.05-1.36, p=0.008) | 1.20 (1.05-1.36, p=0.008) |
| | East Asian | 221 (0.8) | 0.59 (0.44-0.79, p<0.001) | 1.00 (0.75-1.35, p=0.982) | 1.00 (0.74-1.35, p=0.980) | 1.02 (0.76-1.38, p=0.890) |
| | Black | 933 (3.6) | 0.65 (0.57-0.75, p<0.001) | 1.04 (0.91-1.20, p=0.534) | 1.05 (0.91-1.21, p=0.500) | 1.07 (0.92-1.23, p=0.380) |
| | Other Ethnic Minority | 1926 (7.4) | 0.66 (0.60-0.73, p<0.001) | 0.97 (0.88-1.07, p=0.575) | 0.99 (0.89-1.10, p=0.850) | 1.01 (0.91-1.12, p=0.790) |
| Age on admission (years) | 50-59 | 3458 (13.3) | - | - | - | - |
| | 18-39 | 1431 (5.5) | 0.29 (0.22-0.39, p<0.001) | 0.30 (0.23-0.40, p<0.001) | 0.30 (0.23-0.40, p<0.001) | 0.31 (0.23-0.41, p<0.001) |
| | 40-49 | 1832 (7.0) | 0.52 (0.42-0.63, p<0.001) | 0.51 (0.42-0.63, p<0.001) | 0.52 (0.42-0.63, p<0.001) | 0.53 (0.43-0.65, p<0.001) |
| | 60-69 | 4197 (16.1) | 2.06 (1.84-2.31, p<0.001) | 2.06 (1.84-2.30, p<0.001) | 2.06 (1.84-2.31, p<0.001) | 1.98 (1.76-2.22, p<0.001) |
| | 70-79 | 6035 (23.1) | 3.44 (3.10-3.82, p<0.001) | 3.47 (3.13-3.86, p<0.001) | 3.44 (3.10-3.82, p<0.001) | 3.09 (2.78-3.44, p<0.001) |
| | 80+ | 9140 (35.0) | 4.86 (4.40-5.37, p<0.001) | 5.05 (4.57-5.58, p<0.001) | 4.97 (4.49-5.50, p<0.001) | 4.21 (3.79-4.68, p<0.001) |
| Sex at Birth | Male | 15117 (57.9) | - | - | - | - |
| | Female | 10976 (42.1) | 0.81 (0.78-0.85, p<0.001) | 0.76 (0.73-0.80, p<0.001) | 0.76 (0.72-0.79, p<0.001) | 0.76 (0.73-0.80, p<0.001) |
| Deprivation (IMD) | Mean (SD) | 0.1 (0.8) | 0.98 (0.95-1.01, p=0.156) | - | - | 1.00 (0.95-1.06, p=0.890) |
| Obesity | No | 21354 (81.8) | - | - | - | - |
| | Yes | 2601 (10.0) | 0.87 (0.80-0.94, p<0.001) | - | - | 1.26 (1.16-1.37, p<0.001) |
| | (Missing) | 2138 (8.2) | 1.15 (1.07-1.24, p<0.001) | - | - | 1.05 (0.97-1.14, p=0.240) |
| Diabetes | No | 19420 (74.4) | - | - | - | - |
| | Yes | 6673 (25.6) | 1.26 (1.20-1.32, p<0.001) | - | - | 1.08 (1.03-1.13, p=0.003) |
| Chronic cardiac disease | No | 18033 (69.1) | - | - | - | - |
| | Yes | 8060 (30.9) | 1.85 (1.77-1.93, p<0.001) | - | - | 1.13 (1.08-1.18, p<0.001) |
| Chronic pulmonary disease | No | 21626 (82.9) | - | - | - | - |
| | Yes | 4467 (17.1) | 1.58 (1.50-1.66, p<0.001) | - | - | 1.17 (1.11-1.23, p<0.001) |

| | | | | | | |
|---|---|---|---|---|---|---|
| Asthma | No | 22474 (86.5) | - | - | - | - |
| | Yes | 3517 (13.5) | 0.77 (0.72-0.83, p<0.001) | - | - | - |
| Chronic kidney disease | No | 21848 (83.7) | - | - | - | - |
| | Yes | 4245 (16.3) | 1.80 (1.71-1.90, p<0.001) | - | - | 1.26 (1.20-1.34, p<0.001) |
| Moderate/severe liver disease | No | 25633 (98.2) | - | - | - | - |
| | Yes | 460 (1.8) | 1.37 (1.18-1.59, p<0.001) | - | - | - |
| Mild Liver disease | No | 25642 (98.6) | - | - | - | - |
| | Yes | 377 (1.4) | 0.80 (0.65-0.99, p=0.036) | - | - | - |
| Chronic neurological disorder | No | 23034 (88.7) | - | - | - | - |
| | Yes | 2934 (11.3) | 1.43 (1.34-1.52, p<0.001) | - | - | - |
| Malignancy | No | 23394 (90.2) | - | - | - | - |
| | Yes | 2532 (9.8) | 1.57 (1.47-1.68, p<0.001) | - | - | - |
| Chronic hematologic disease | No | 24932 (96.0) | - | - | - | - |
| | Yes | 1043 (4.0) | 1.48 (1.34-1.63, p<0.001) | - | - | - |
| AIDS/HIV | No | 25620 (99.6) | - | - | - | - |
| | Yes | 114 (0.4) | 0.87 (0.62-1.24, p=0.446) | - | - | - |
| Rheumatologic disorder | No | 23238 (89.7) | - | - | - | - |
| | Yes | 2659 (10.3) | 1.18 (1.10-1.27, p<0.001) | - | - | - |
| Dementia | No | 22178 (85.0) | - | - | - | - |
| | Yes | 3915 (15.0) | 2.09 (1.99-2.21, p<0.001) | - | - | 1.33 (1.26-1.41, p<0.001) |
| Malnutrition | No | 24273 (97.6) | - | - | - | - |
| | Yes | 595 (2.4) | 1.56 (1.38-1.77, p<0.001) | - | - | - |
| Prior immunosuppression | No | 22477 (90.3) | - | - | - | - |
| | Yes | 2412 (9.7) | 1.13 (1.05-1.22, p=0.001) | - | - | - |
| Prior infection treatment | No | 19882 (80.2) | - | - | - | - |
| | Yes | 4906 (19.8) | 1.15 (1.09-1.22, p<0.001) | - | - | - |

Table E6. Characteristics of patients admitted to critical care, stratified by ethnicity.

| Ethnicity (admitted to critical care) | | White | South Asian | East Asian | Black | Other Ethnic Minority |
|---|---|---|---|---|---|---|
| Total N (%) | | 3258 (74.8) | 293 (6.7) | 64 (1.5) | 241 (5.5) | 497 (11.4) |
| Age on admission (years) | Mean (SD) | 63.0 (13.3) | 55.9 (13.7) | 53.3 (12.1) | 55.5 (12.3) | 55.4 (12.9) |
| | 50-59 | 788 (24.2) | 68 (23.2) | 26 (40.6) | 90 (37.3) | 134 (27.0) |
| | 18-39 | 169 (5.2) | 35 (11.9) | 7 (10.9) | 26 (10.8) | 58 (11.7) |
| | 40-49 | 316 (9.7) | 62 (21.2) | 14 (21.9) | 42 (17.4) | 104 (20.9) |
| | 60-69 | 889 (27.3) | 87 (29.7) | 13 (20.3) | 57 (23.7) | 133 (26.8) |
| | 70-79 | 790 (24.2) | 30 (10.2) | 2 (3.1) | 19 (7.9) | 54 (10.9) |
| | 80+ | 306 (9.4) | 11 (3.8) | 2 (3.1) | 7 (2.9) | 14 (2.8) |
| Sex at Birth | Male | 2281 (70.2) | 221 (75.4) | 44 (69.8) | 157 (65.4) | 346 (69.9) |
| | Female | 969 (29.8) | 72 (24.6) | 19 (30.2) | 83 (34.6) | 149 (30.1) |
| Obesity | No | 2248 (79.2) | 208 (84.2) | 51 (86.4) | 161 (75.2) | 341 (82.4) |
| | Yes | 592 (20.8) | 39 (15.8) | 8 (13.6) | 53 (24.8) | 73 (17.6) |
| Diabetes | No | 2329 (76.1) | 170 (63.7) | 45 (77.6) | 134 (59.3) | 311 (68.7) |
| | Yes | 732 (23.9) | 97 (36.3) | 13 (22.4) | 92 (40.7) | 142 (31.3) |
| Chronic cardiac disease | No | 2477 (80.7) | 227 (85.0) | 58 (95.1) | 212 (92.6) | 399 (87.5) |
| | Yes | 593 (19.3) | 40 (15.0) | 3 (4.9) | 17 (7.4) | 57 (12.5) |
| Chronic pulmonary disease | No | 2650 (86.6) | 252 (94.4) | 59 (95.2) | 214 (93.4) | 422 (94.8) |
| | Yes | 409 (13.4) | 15 (5.6) | 3 (4.8) | 15 (6.6) | 23 (5.2) |
| Asthma | No | 2505 (81.6) | 223 (83.2) | 57 (93.4) | 194 (85.1) | 383 (85.5) |
| | Yes | 566 (18.4) | 45 (16.8) | 4 (6.6) | 34 (14.9) | 65 (14.5) |
| Chronic kidney disease | No | 2785 (91.0) | 239 (89.5) | 58 (95.1) | 197 (86.4) | 411 (92.2) |
| | Yes | 274 (9.0) | 28 (10.5) | 3 (4.9) | 31 (13.6) | 35 (7.8) |
| Moderate/severe liver disease | No | 2995 (98.6) | 261 (98.9) | 59 (98.3) | 227 (99.1) | 432 (98.0) |
| | Yes | 41 (1.4) | 3 (1.1) | 1 (1.7) | 2 (0.9) | 9 (2.0) |
| Mild Liver disease | No | 2988 (98.7) | 263 (99.2) | 59 (98.3) | 224 (99.1) | 436 (99.3) |
| | Yes | 40 (1.3) | 2 (0.8) | 1 (1.7) | 2 (0.9) | 3 (0.7) |
| Chronic neurological disorder | No | 2851 (93.8) | 254 (95.5) | 59 (96.7) | 221 (97.4) | 431 (96.9) |
| | Yes | 188 (6.2) | 12 (4.5) | 2 (3.3) | 6 (2.6) | 14 (3.1) |
| Malignancy | No | 2831 (93.4) | 256 (96.6) | 59 (96.7) | 216 (94.3) | 432 (97.3) |
| | Yes | 201 (6.6) | 9 (3.4) | 2 (3.3) | 13 (5.7) | 12 (2.7) |
| Chronic hematologic disease | No | 2940 (97.0) | 261 (98.1) | 59 (96.7) | 217 (96.0) | 431 (96.9) |
| | Yes | 91 (3.0) | 5 (1.9) | 2 (3.3) | 9 (4.0) | 14 (3.1) |
| AIDS/HIV | No | 2987 (99.6) | 259 (99.6) | 60 (100.0) | 208 (95.4) | 435 (99.3) |
| | Yes | 13 (0.4) | 1 (0.4) | 0 (0.0) | 10 (4.6) | 3 (0.7) |
| Rheumatologic disorder | No | 2786 (91.9) | 249 (94.7) | 61 (100.0) | 213 (93.8) | 423 (95.7) |
| | Yes | 246 (8.1) | 14 (5.3) | 0 (0.0) | 14 (6.2) | 19 (4.3) |
| Dementia | No | 2965 (97.2) | 261 (98.9) | 60 (98.4) | 227 (99.6) | 443 (98.4) |
| | Yes | 86 (2.8) | 3 (1.1) | 1 (1.6) | 1 (0.4) | 7 (1.6) |
| Malnutrition | No | 2921 (98.6) | 254 (99.6) | 61 (100.0) | 219 (99.5) | 432 (98.6) |
| | Yes | 42 (1.4) | 1 (0.4) | 0 (0.0) | 1 (0.5) | 6 (1.4) |
| Smoking | Yes | 156 (6.1) | 6 (2.8) | 2 (4.3) | 6 (3.3) | 24 (6.8) |
| | Never Smoked | 1428 (56.2) | 172 (80.0) | 38 (80.9) | 143 (79.0) | 258 (72.9) |
| | Former Smoker | 959 (37.7) | 37 (17.2) | 7 (14.9) | 32 (17.7) | 72 (20.3) |

| | | | | | | |
|---|---|---|---|---|---|---|
| Prior immunosuppression | No | 2705 (89.6) | 238 (92.6) | 60 (100.0) | 205 (91.5) | 417 (92.1) |
| | Yes | 314 (10.4) | 19 (7.4) | 0 (0.0) | 19 (8.5) | 36 (7.9) |
| Prior infection treatment | No | 2406 (79.9) | 197 (77.9) | 49 (81.7) | 179 (80.3) | 357 (78.6) |
| | Yes | 604 (20.1) | 56 (22.1) | 11 (18.3) | 44 (19.7) | 97 (21.4) |
| Deprivation (IMD) | Mean (SD) | 0.1 (0.8) | 0.2 (0.8) | 0.3 (0.9) | 0.2 (0.7) | 0.3 (0.8) |

Table E7. Characteristics of patients undergoing mechanical ventilation, stratified by ethnicity.

| Ethnicity (receiving invasive mechanical ventilation) | | White | South Asian | East Asian | Black | Other Ethnic Minority |
|---|---|---|---|---|---|---|
| Total N (%) | | 1723 (69.6) | 192 (7.8) | 47 (1.9) | 164 (6.6) | 351 (14.2) |
| Age on admission (years) | Mean (SD) | 61.6 (12.2) | 54.8 (12.4) | 54.4 (10.7) | 56.5 (11.0) | 55.5 (12.5) |
| | 50-59 | 455 (26.4) | 50 (26.0) | 17 (36.2) | 60 (36.6) | 100 (28.5) |
| | 18-39 | 88 (5.1) | 22 (11.5) | 3 (6.4) | 10 (6.1) | 38 (10.8) |
| | 40-49 | 165 (9.6) | 43 (22.4) | 12 (25.5) | 32 (19.5) | 73 (20.8) |
| | 60-69 | 529 (30.7) | 59 (30.7) | 12 (25.5) | 47 (28.7) | 94 (26.8) |
| | 70-79 | 404 (23.4) | 15 (7.8) | 1 (2.1) | 13 (7.9) | 38 (10.8) |
| | 80+ | 82 (4.8) | 3 (1.6) | 2 (4.3) | 2 (1.2) | 8 (2.3) |
| Sex at Birth | Male | 1251 (72.8) | 146 (76.0) | 36 (78.3) | 111 (68.1) | 254 (72.4) |
| | Female | 468 (27.2) | 46 (24.0) | 10 (21.7) | 52 (31.9) | 97 (27.6) |
| Obesity | No | 1194 (77.3) | 150 (86.2) | 34 (82.9) | 107 (75.4) | 237 (81.7) |
| | Yes | 351 (22.7) | 24 (13.8) | 7 (17.1) | 35 (24.6) | 53 (18.3) |
| Diabetes | No | 1263 (77.2) | 121 (65.8) | 32 (78.0) | 94 (61.4) | 217 (67.0) |
| | Yes | 374 (22.8) | 63 (34.2) | 9 (22.0) | 59 (38.6) | 107 (33.0) |
| Chronic cardiac disease | No | 1363 (83.1) | 160 (87.4) | 41 (95.3) | 150 (95.5) | 287 (88.6) |
| | Yes | 278 (16.9) | 23 (12.6) | 2 (4.7) | 7 (4.5) | 37 (11.4) |
| Chronic pulmonary disease | No | 1476 (90.3) | 178 (97.3) | 41 (93.2) | 147 (94.2) | 304 (95.9) |
| | Yes | 159 (9.7) | 5 (2.7) | 3 (6.8) | 9 (5.8) | 13 (4.1) |
| Asthma | No | 1368 (83.1) | 154 (84.2) | 40 (93.0) | 131 (84.5) | 272 (84.7) |
| | Yes | 278 (16.9) | 29 (15.8) | 3 (7.0) | 24 (15.5) | 49 (15.3) |
| Chronic kidney disease | No | 1525 (93.3) | 166 (90.7) | 42 (97.7) | 139 (89.7) | 293 (93.0) |
| | Yes | 109 (6.7) | 17 (9.3) | 1 (2.3) | 16 (10.3) | 22 (7.0) |
| Moderate/severe liver disease | No | 1608 (98.8) | 181 (99.5) | 43 (100.0) | 154 (98.7) | 308 (98.7) |
| | Yes | 19 (1.2) | 1 (0.5) | 0 (0.0) | 2 (1.3) | 4 (1.3) |
| Mild Liver disease | No | 1604 (99.0) | 182 (100.0) | 43 (100.0) | 152 (98.7) | 308 (99.4) |
| | Yes | 17 (1.0) | 0 (0.0) | 0 (0.0) | 2 (1.3) | 2 (0.6) |
| Chronic neurological disorder | No | 1536 (94.6) | 178 (96.7) | 41 (95.3) | 152 (98.1) | 308 (97.2) |
| | Yes | 87 (5.4) | 6 (3.3) | 2 (4.7) | 3 (1.9) | 9 (2.8) |
| Malignancy | No | 1520 (94.0) | 176 (96.7) | 42 (97.7) | 147 (93.6) | 307 (97.5) |
| | Yes | 97 (6.0) | 6 (3.3) | 1 (2.3) | 10 (6.4) | 8 (2.5) |
| Chronic hematologic disease | No | 1572 (97.0) | 180 (98.9) | 42 (97.7) | 149 (96.1) | 307 (97.2) |
| | Yes | 49 (3.0) | 2 (1.1) | 1 (2.3) | 6 (3.9) | 9 (2.8) |
| AIDS/HIV | No | 1610 (99.8) | 179 (100.0) | 43 (100.0) | 144 (97.3) | 312 (99.4) |
| | Yes | 3 (0.2) | 0 (0.0) | 0 (0.0) | 4 (2.7) | 2 (0.6) |
| Rheumatologic disorder | No | 1514 (93.0) | 172 (96.1) | 43 (100.0) | 147 (94.2) | 300 (95.2) |
| | Yes | 114 (7.0) | 7 (3.9) | 0 (0.0) | 9 (5.8) | 15 (4.8) |
| Dementia | No | 1612 (98.7) | 182 (100.0) | 42 (97.7) | 155 (99.4) | 313 (98.1) |
| | Yes | 21 (1.3) | 0 (0.0) | 1 (2.3) | 1 (0.6) | 6 (1.9) |
| Malnutrition | No | 1573 (98.9) | 179 (100.0) | 43 (100.0) | 149 (100.0) | 311 (99.7) |
| | Yes | 17 (1.1) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (0.3) |
| Smoking | Yes | 70 (5.1) | 4 (2.7) | 0 (0.0) | 4 (3.3) | 15 (5.8) |
| | Never Smoked | 797 (58.5) | 122 (81.3) | 29 (85.3) | 92 (76.0) | 189 (73.3) |

| | | | | | | |
|---|---|---|---|---|---|---|
| | Former Smoker | 496 (36.4) | 24 (16.0) | 5 (14.7) | 25 (20.7) | 54 (20.9) |
| Prior immunosuppression | No | 1457 (90.7) | 165 (93.2) | 43 (100.0) | 137 (92.6) | 294 (92.7) |
| | Yes | 149 (9.3) | 12 (6.8) | 0 (0.0) | 11 (7.4) | 23 (7.3) |
| Prior infection treatment | No | 1273 (79.2) | 138 (80.2) | 36 (83.7) | 115 (77.7) | 242 (75.9) |
| | Yes | 335 (20.8) | 34 (19.8) | 7 (16.3) | 33 (22.3) | 77 (24.1) |
| Deprivation (IMD) | Mean (SD) | 0.1 (0.8) | 0.2 (0.7) | 0.2 (0.6) | 0.1 (0.7) | 0.3 (0.7) |

Table E8. Characteristics of patients who died, stratified by ethnicity.

| Ethnicity (patients who died) | | White | South Asian | East Asian | Black | Other Ethnic Minority |
|---|---|---|---|---|---|---|
| Total N (%) | | 7983 (87.3) | 320 (3.5) | 63 (0.7) | 248 (2.7) | 531 (5.8) |
| Age on admission (years) | Mean (SD) | 78.9 (11.1) | 71.5 (14.7) | 71.8 (13.9) | 73.5 (13.7) | 72.8 (14.8) |
| | 50-59 | 357 (4.5) | 38 (11.9) | 8 (12.7) | 40 (16.1) | 52 (9.8) |
| | 18-39 | 35 (0.4) | 8 (2.5) | 1 (1.6) | 2 (0.8) | 18 (3.4) |
| | 40-49 | 92 (1.2) | 16 (5.0) | 4 (6.3) | 8 (3.2) | 26 (4.9) |
| | 60-69 | 926 (11.6) | 74 (23.1) | 12 (19.0) | 50 (20.2) | 80 (15.1) |
| | 70-79 | 2218 (27.8) | 74 (23.1) | 15 (23.8) | 44 (17.7) | 150 (28.2) |
| | 80+ | 4355 (54.6) | 110 (34.4) | 23 (36.5) | 104 (41.9) | 205 (38.6) |
| Sex at Birth | Male | 4921 (61.8) | 213 (66.6) | 43 (69.4) | 159 (64.1) | 340 (64.3) |
| | Female | 3038 (38.2) | 107 (33.4) | 19 (30.6) | 89 (35.9) | 189 (35.7) |
| Obesity | No | 6005 (89.9) | 219 (89.4) | 41 (83.7) | 173 (84.8) | 399 (91.1) |
| | Yes | 673 (10.1) | 26 (10.6) | 8 (16.3) | 31 (15.2) | 39 (8.9) |
| Diabetes | No | 5283 (71.7) | 134 (49.8) | 35 (66.0) | 108 (49.1) | 294 (62.8) |
| | Yes | 2081 (28.3) | 135 (50.2) | 18 (34.0) | 112 (50.9) | 174 (37.2) |
| Chronic cardiac disease | No | 4134 (55.3) | 166 (60.6) | 37 (67.3) | 175 (76.4) | 323 (66.5) |
| | Yes | 3346 (44.7) | 108 (39.4) | 18 (32.7) | 54 (23.6) | 163 (33.5) |
| Chronic pulmonary disease | No | 5552 (74.5) | 240 (88.2) | 43 (76.8) | 205 (89.5) | 397 (83.6) |
| | Yes | 1903 (25.5) | 32 (11.8) | 13 (23.2) | 24 (10.5) | 78 (16.4) |
| Asthma | No | 6522 (88.2) | 221 (80.4) | 46 (83.6) | 194 (85.1) | 414 (87.3) |
| | Yes | 873 (11.8) | 54 (19.6) | 9 (16.4) | 34 (14.9) | 60 (12.7) |
| Chronic kidney disease | No | 5573 (75.2) | 199 (73.4) | 45 (80.4) | 178 (78.1) | 369 (77.2) |
| | Yes | 1839 (24.8) | 72 (26.6) | 11 (19.6) | 50 (21.9) | 109 (22.8) |
| Moderate/severe liver disease | No | 7152 (97.6) | 265 (98.5) | 54 (98.2) | 220 (96.9) | 458 (97.2) |
| | Yes | 179 (2.4) | 4 (1.5) | 1 (1.8) | 7 (3.1) | 13 (2.8) |
| Mild Liver disease | No | 7211 (98.7) | 265 (98.5) | 55 (100.0) | 226 (99.1) | 463 (99.1) |
| | Yes | 96 (1.3) | 4 (1.5) | 0 (0.0) | 2 (0.9) | 4 (0.9) |
| Chronic neurological disorder | No | 6221 (84.5) | 239 (88.8) | 45 (81.8) | 206 (90.0) | 409 (85.9) |
| | Yes | 1139 (15.5) | 30 (11.2) | 10 (18.2) | 23 (10.0) | 67 (14.1) |
| Malignancy | No | 6261 (85.5) | 250 (92.6) | 50 (94.3) | 201 (87.4) | 423 (89.8) |
| | Yes | 1064 (14.5) | 20 (7.4) | 3 (5.7) | 29 (12.6) | 48 (10.2) |
| Chronic hematologic disease | No | 6901 (94.2) | 256 (95.9) | 52 (96.3) | 210 (91.3) | 445 (94.9) |
| | Yes | 423 (5.8) | 11 (4.1) | 2 (3.7) | 20 (8.7) | 24 (5.1) |
| AIDS/HIV | No | 7245 (99.7) | 260 (99.2) | 55 (100.0) | 215 (96.8) | 460 (99.4) |
| | Yes | 23 (0.3) | 2 (0.8) | 0 (0.0) | 7 (3.2) | 3 (0.6) |
| Rheumatologic disorder | No | 6361 (87.1) | 243 (91.7) | 53 (96.4) | 215 (94.7) | 427 (92.0) |
| | Yes | 942 (12.9) | 22 (8.3) | 2 (3.6) | 12 (5.3) | 37 (8.0) |
| Dementia | No | 5529 (74.6) | 232 (87.2) | 45 (83.3) | 197 (84.5) | 397 (83.8) |
| | Yes | 1880 (25.4) | 34 (12.8) | 9 (16.7) | 36 (15.5) | 77 (16.2) |
| Malnutrition | No | 6640 (96.4) | 232 (95.9) | 49 (96.1) | 211 (98.1) | 420 (95.9) |
| | Yes | 249 (3.6) | 10 (4.1) | 2 (3.9) | 4 (1.9) | 18 (4.1) |
| Smoking | Yes | 342 (6.7) | 6 (2.9) | 1 (2.4) | 6 (3.6) | 13 (4.1) |
| | Never Smoked | 2611 (51.2) | 171 (81.8) | 31 (73.8) | 129 (76.8) | 209 (66.6) |
| | Former Smoker | 2142 (42.0) | 32 (15.3) | 10 (23.8) | 33 (19.6) | 92 (29.3) |
| Prior immunosuppression | No | 6530 (89.3) | 228 (88.0) | 49 (92.5) | 198 (87.6) | 407 (87.2) |

| | | | | | | |
|---|---|---|---|---|---|---|
| | Yes | 784 (10.7) | 31 (12.0) | 4 (7.5) | 28 (12.4) | 60 (12.8) |
| Prior infection treatment | No | 5637 (77.5) | 193 (76.3) | 42 (79.2) | 188 (83.2) | 370 (79.1) |
| | Yes | 1636 (22.5) | 60 (23.7) | 11 (20.8) | 38 (16.8) | 98 (20.9) |
| Deprivation (IMD) | Mean (SD) | 0.1 (0.8) | 0.2 (0.7) | -0.0 (0.8) | 0.0 (0.7) | 0.2 (0.7) |

Table E9. Association of missingness in ethnicity variable with other patient characteristics.

| Missing data analysis: Ethnicity | | Not missing | Missing |
|---|---|---|---|
| Age on admission (years) | Mean (SD) | 70.5 (16.5) | 67.6 (17.2) |
| | 18-39 | 1638 (84.7) | 295 (15.3) |
| | 40-49 | 2070 (82.6) | 436 (17.4) |
| | 50-59 | 3972 (86.0) | 648 (14.0) |
| | 60-69 | 4885 (87.3) | 708 (12.7) |
| | 70-79 | 7160 (88.8) | 905 (11.2) |
| | 80+ | 10968 (89.4) | 1301 (10.6) |
| Sex at Birth | Male | 17773 (87.3) | 2590 (12.7) |
| | Female | 12823 (88.4) | 1683 (11.6) |
| Obesity | No | 22591 (89.5) | 2653 (10.5) |
| | Yes | 2848 (89.8) | 324 (10.2) |
| Diabetes | No | 20336 (89.0) | 2511 (11.0) |
| | Yes | 7370 (90.2) | 798 (9.8) |
| Chronic cardiac disease | No | 18935 (88.4) | 2493 (11.6) |
| | Yes | 9170 (91.1) | 897 (8.9) |
| Chronic pulmonary disease | No | 22873 (88.8) | 2871 (11.2) |
| | Yes | 5146 (91.2) | 499 (8.8) |
| Asthma | No | 23904 (89.1) | 2935 (10.9) |
| | Yes | 3990 (90.7) | 411 (9.3) |
| Chronic kidney disease | No | 22977 (88.8) | 2885 (11.2) |
| | Yes | 4883 (91.1) | 475 (8.9) |
| Moderate/severe liver disease | No | 27066 (89.2) | 3265 (10.8) |
| | Yes | 529 (91.8) | 47 (8.2) |
| Mild Liver disease | No | 27112 (89.3) | 3248 (10.7) |
| | Yes | 413 (89.2) | 50 (10.8) |
| Chronic neurological disorder | No | 24307 (89.2) | 2956 (10.8) |
| | Yes | 3382 (90.3) | 363 (9.7) |
| Malignancy | No | 24791 (89.1) | 3021 (10.9) |
| | Yes | 2816 (90.4) | 300 (9.6) |
| Chronic hematologic disease | No | 26405 (89.2) | 3189 (10.8) |
| | Yes | 1172 (90.2) | 128 (9.8) |
| AIDS/HIV | No | 27229 (89.2) | 3281 (10.8) |
| | Yes | 122 (90.4) | 13 (9.6) |
| Rheumatologic disorder | No | 24519 (89.0) | 3015 (11.0) |
| | Yes | 2995 (91.7) | 271 (8.3) |
| Dementia | No | 23332 (89.0) | 2877 (11.0) |
| | Yes | 4452 (91.0) | 442 (9.0) |
| Malnutrition | No | 25601 (89.4) | 3038 (10.6) |
| | Yes | 691 (91.9) | 61 (8.1) |
| Smoking | Yes | 1431 (88.4) | 187 (11.6) |
| | Never Smoked | 11899 (88.8) | 1506 (11.2) |
| | Former Smoker | 6916 (91.4) | 647 (8.6) |

Table E10. Baseline model for in-hospital mortality using Fine and Gray methods.

| Surv(time, status) | | | HR (univariable) | HR (baseline Fine and Gray) |
|---|---|---|---|---|
| Ethnicity | White | 21960 (84.2) | - | - |
| | South Asian | 1053 (4.0) | 0.69 (0.61-0.79, p<0.001) | 1.18 (1.04-1.33, p=0.009) |
| | East Asian | 221 (0.8) | 0.59 (0.44-0.79, p<0.001) | 1.00 (0.75-1.33, p=0.990) |
| | Black | 933 (3.6) | 0.65 (0.57-0.75, p<0.001) | 1.04 (0.91-1.19, p=0.560) |
| | Other Ethnic Minority | 1926 (7.4) | 0.66 (0.60-0.73, p<0.001) | 0.97 (0.88-1.07, p=0.560) |
| Age on admission (years) | 50-59 | 3458 (13.3) | - | - |
| | 18-39 | 1431 (5.5) | 0.29 (0.22-0.39, p<0.001) | 0.31 (0.23-0.40, p<0.001) |
| | 40-49 | 1832 (7.0) | 0.52 (0.42-0.63, p<0.001) | 0.52 (0.42-0.63, p<0.001) |
| | 60-69 | 4197 (16.1) | 2.06 (1.84-2.31, p<0.001) | 2.05 (1.83-2.29, p<0.001) |
| | 70-79 | 6035 (23.1) | 3.44 (3.10-3.82, p<0.001) | 3.44 (3.11-3.81, p<0.001) |
| | 80+ | 9140 (35.0) | 4.86 (4.40-5.37, p<0.001) | 4.98 (4.51-5.50, p<0.001) |
| Sex at Birth | Male | 15117 (57.9) | - | - |
| | Female | 10976 (42.1) | 0.81 (0.78-0.85, p<0.001) | 0.76 (0.73-0.80, p<0.001) |

Figure E3. Multiple imputation of missing values was performed using chained equations. Ten sets, each with ten iterations, were imputed using available explanatory variables. Graphical checks were performed and imputed sets combined using Rubin's rules.

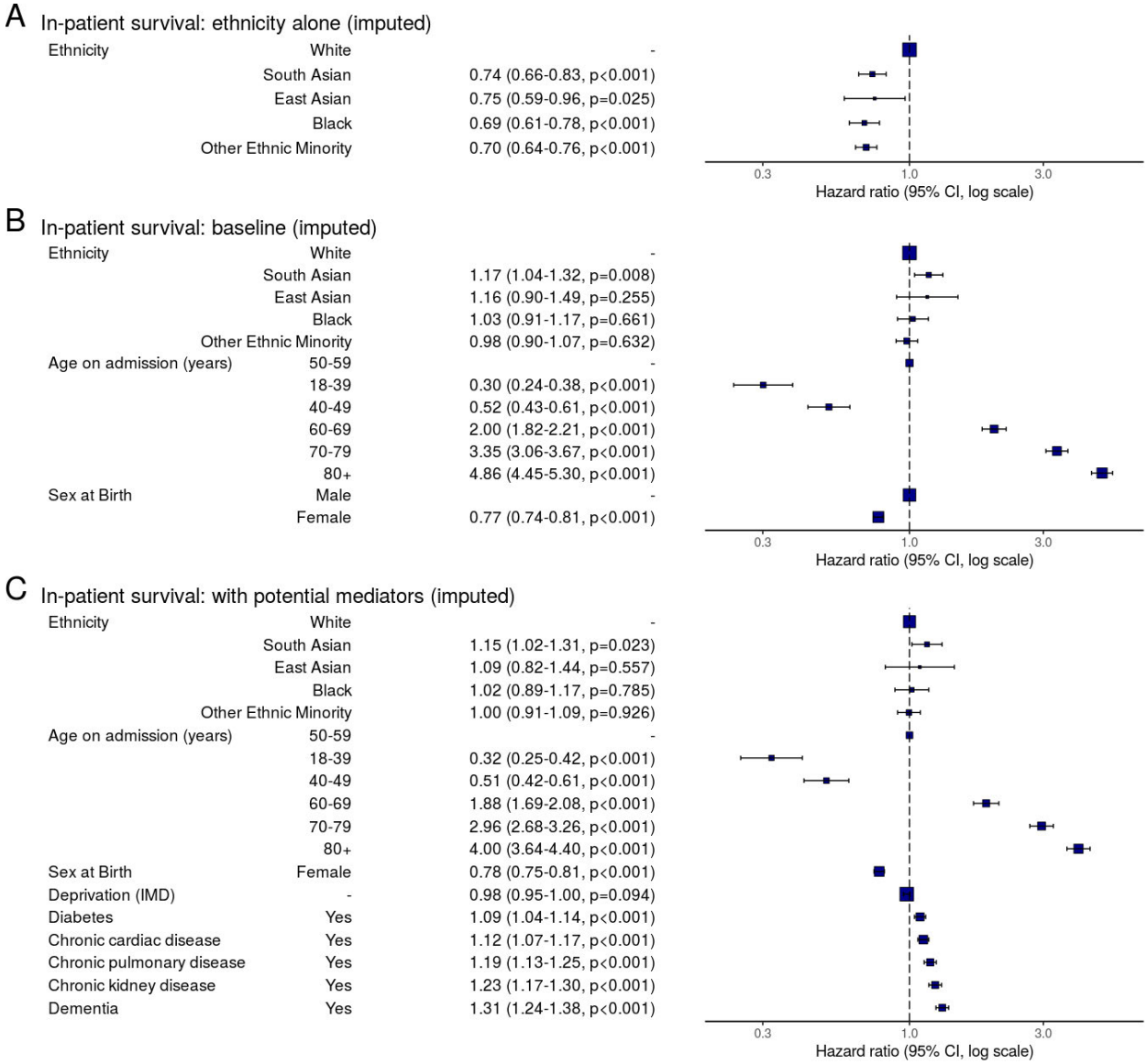

Table E11. Diabetes. Age, sex, and location corrected association with ethnicity. Hierarchical logistic regression analysis. OR, odds ratio.

| Diabetes | | No | Yes | OR (univariable) | OR (multilevel) |
|---|---|---|---|---|---|
| Ethnicity | White | 16650 (75.8) | 5310 (24.2) | - | - |
| | South Asian | 659 (62.6) | 394 (37.4) | 1.87 (1.65-2.13, p<0.001) | 2.29 (1.99-2.62, p<0.001) |
| | East Asian | 159 (71.9) | 62 (28.1) | 1.22 (0.90-1.63, p=0.182) | 1.51 (1.11-2.04, p=0.008) |
| | Black | 582 (62.4) | 351 (37.6) | 1.89 (1.65-2.17, p<0.001) | 2.30 (1.99-2.65, p<0.001) |
| | Other Ethnic Minority | 1370 (71.1) | 556 (28.9) | 1.27 (1.15-1.41, p<0.001) | 1.46 (1.30-1.62, p<0.001) |
| Age on admission (years) | 50-59 | 2632 (76.1) | 826 (23.9) | - | - |
| | 18-39 | 1288 (90.0) | 143 (10.0) | 0.35 (0.29-0.43, p<0.001) | 0.33 (0.27-0.40, p<0.001) |
| | 40-49 | 1521 (83.0) | 311 (17.0) | 0.65 (0.56-0.75, p<0.001) | 0.60 (0.52-0.70, p<0.001) |
| | 60-69 | 2940 (70.1) | 1257 (29.9) | 1.36 (1.23-1.51, p<0.001) | 1.42 (1.28-1.57, p<0.001) |
| | 70-79 | 4197 (69.5) | 1838 (30.5) | 1.40 (1.27-1.54, p<0.001) | 1.54 (1.40-1.70, p<0.001) |
| | 80+ | 6842 (74.9) | 2298 (25.1) | 1.07 (0.98-1.17, p=0.145) | 1.23 (1.12-1.35, p<0.001) |
| Sex at Birth | Male | 10936 (72.3) | 4181 (27.7) | - | - |
| | Female | 8484 (77.3) | 2492 (22.7) | 0.77 (0.73-0.81, p<0.001) | 0.79 (0.74-0.84, p<0.001) |

Table E12. Obesity. Age, sex, and location corrected association with ethnicity. Hierarchical logistic regression analysis. OR, odds ratio.

| Dependent: Obesity | | No | Yes | OR (univariable) | OR (multilevel) |
|---|---|---|---|---|---|
| Ethnicity | White | 17932 (81.7) | 2190 (10.0) | - | - |
| | South Asian | 861 (81.8) | 102 (9.7) | 0.99 (0.84-1.16, p=0.929) | 0.76 (0.64-0.90, p=0.002) |
| | East Asian | 194 (87.8) | 17 (7.7) | 0.62 (0.40-0.91, p=0.020) | 0.57 (0.38-0.86, p=0.007) |
| | Black | 759 (81.4) | 110 (11.8) | 1.02 (0.86-1.20, p=0.812) | 1.04 (0.87-1.25, p=0.664) |
| | Other Ethnic Minority | 1608 (83.5) | 182 (9.4) | 0.88 (0.78-1.00, p=0.046) | 0.83 (0.73-0.95, p=0.008) |
| Age on admission (years) | 50-59 | 2609 (75.4) | 608 (17.6) | - | - |
| | 18-39 | 1105 (77.2) | 254 (17.7) | 0.91 (0.78-1.05, p=0.188) | 0.91 (0.79-1.06, p=0.250) |
| | 40-49 | 1441 (78.7) | 277 (15.1) | 0.83 (0.73-0.95, p=0.009) | 0.84 (0.73-0.97, p=0.016) |
| | 60-69 | 3254 (77.5) | 596 (14.2) | 0.89 (0.80-0.99, p=0.032) | 0.87 (0.78-0.97, p=0.013) |
| | 70-79 | 4950 (82.0) | 544 (9.0) | 0.67 (0.61-0.75, p<0.001) | 0.62 (0.56-0.69, p<0.001) |
| | 80+ | 7995 (87.5) | 322 (3.5) | 0.44 (0.40-0.49, p<0.001) | 0.40 (0.36-0.44, p<0.001) |
| Sex at Birth | Male | 12465 (82.5) | 1396 (9.2) | - | - |
| | Female | 8889 (81.0) | 1205 (11.0) | 1.10 (1.04-1.18, p=0.002) | 1.16 (1.08-1.24, p<0.001) |

Table E13. Chronic cardiac disease. Age, sex, and location corrected association with ethnicity. Hierarchical logistic regression analysis. OR, odds ratio.

| Dependent: Chronic cardiac disease | | No | Yes | OR (univariable) | OR (multilevel) |
|---|---|---|---|---|---|
| Ethnicity | White | 14683 (66.9) | 7277 (33.1) | - | - |
| | South Asian | 825 (78.3) | 228 (21.7) | 0.56 (0.48-0.65, p<0.001) | 1.03 (0.87-1.22, p=0.717) |
| | East Asian | 182 (82.4) | 39 (17.6) | 0.43 (0.30-0.60, p<0.001) | 0.81 (0.55-1.17, p=0.260) |
| | Black | 792 (84.9) | 141 (15.1) | 0.36 (0.30-0.43, p<0.001) | 0.60 (0.49-0.73, p<0.001) |
| | Other Ethnic Minority | 1551 (80.5) | 375 (19.5) | 0.49 (0.43-0.55, p<0.001) | 0.74 (0.65-0.84, p<0.001) |
| Age on admission (years) | 50-59 | 3059 (88.5) | 399 (11.5) | - | - |
| | 18-39 | 1383 (96.6) | 48 (3.4) | 0.27 (0.19-0.36, p<0.001) | 0.29 (0.21-0.39, p<0.001) |
| | 40-49 | 1739 (94.9) | 93 (5.1) | 0.41 (0.32-0.52, p<0.001) | 0.42 (0.33-0.53, p<0.001) |
| | 60-69 | 3235 (77.1) | 962 (22.9) | 2.28 (2.01-2.59, p<0.001) | 2.24 (1.97-2.54, p<0.001) |
| | 70-79 | 3850 (63.8) | 2185 (36.2) | 4.35 (3.88-4.90, p<0.001) | 4.27 (3.79-4.80, p<0.001) |
| | 80+ | 4767 (52.2) | 4373 (47.8) | 7.03 (6.29-7.88, p<0.001) | 7.16 (6.39-8.02, p<0.001) |
| Sex at Birth | Male | 10103 (66.8) | 5014 (33.2) | - | - |
| | Female | 7930 (72.2) | 3046 (27.8) | 0.77 (0.73-0.82, p<0.001) | 0.69 (0.65-0.73, p<0.001) |

Table E14. Chronic pulmonary disease. Age, sex, and location corrected association with ethnicity. Hierarchical logistic regression analysis. OR, odds ratio.

| Dependent: Chronic pulmonary disease | | No | Yes | OR (univariable) | OR (multilevel) |
|---|---|---|---|---|---|
| Ethnicity | White | 17823 (81.2) | 4137 (18.8) | - | - |
| | South Asian | 978 (92.9) | 75 (7.1) | 0.33 (0.26-0.42, p<0.001) | 0.49 (0.39-0.63, p<0.001) |
| | East Asian | 207 (93.7) | 14 (6.3) | 0.29 (0.16-0.48, p<0.001) | 0.44 (0.26-0.77, p=0.004) |
| | Black | 872 (93.5) | 61 (6.5) | 0.30 (0.23-0.39, p<0.001) | 0.45 (0.34-0.59, p<0.001) |
| | Other Ethnic Minority | 1746 (90.7) | 180 (9.3) | 0.44 (0.38-0.52, p<0.001) | 0.62 (0.53-0.73, p<0.001) |
| Age on admission (years) | 50-59 | 3187 (92.2) | 271 (7.8) | - | - |
| | 18-39 | 1403 (98.0) | 28 (2.0) | 0.23 (0.15-0.34, p<0.001) | 0.25 (0.17-0.37, p<0.001) |
| | 40-49 | 1766 (96.4) | 66 (3.6) | 0.44 (0.33-0.57, p<0.001) | 0.47 (0.35-0.62, p<0.001) |
| | 60-69 | 3536 (84.3) | 661 (15.7) | 2.20 (1.90-2.56, p<0.001) | 2.13 (1.83-2.47, p<0.001) |
| | 70-79 | 4490 (74.4) | 1545 (25.6) | 4.05 (3.54-4.65, p<0.001) | 3.79 (3.31-4.36, p<0.001) |
| | 80+ | 7244 (79.3) | 1896 (20.7) | 3.08 (2.70-3.53, p<0.001) | 2.86 (2.50-3.28, p<0.001) |
| Sex at Birth | Male | 12459 (82.4) | 2658 (17.6) | - | - |
| | Female | 9167 (83.5) | 1809 (16.5) | 0.92 (0.87-0.99, p=0.020) | 0.92 (0.86-0.98, p=0.013) |

Table E15. Dementia. Age, sex, and location corrected association with ethnicity. Hierarchical logistic regression analysis. OR, odds ratio.

| Dependent: Dementia | | No | Yes | OR (univariable) | OR (multilevel) |
|---|---|---|---|---|---|
| Ethnicity | White | 18339 (83.5) | 3621 (16.5) | - | - |
| | South Asian | 997 (94.7) | 56 (5.3) | 0.28 (0.21-0.37, p<0.001) | 0.62 (0.46-0.83, p=0.001) |
| | East Asian | 204 (92.3) | 17 (7.7) | 0.42 (0.25-0.67, p=0.001) | 0.99 (0.57-1.71, p=0.976) |
| | Black | 875 (93.8) | 58 (6.2) | 0.34 (0.25-0.43, p<0.001) | 0.63 (0.47-0.85, p=0.002) |
| | Other Ethnic Minority | 1763 (91.5) | 163 (8.5) | 0.47 (0.40-0.55, p<0.001) | 0.80 (0.67-0.97, p=0.020) |
| Age on admission (years) | 50-59 | 3426 (99.1) | 32 (0.9) | - | - |
| | 18-39 | 1427 (99.7) | 4 (0.3) | 0.30 (0.09-0.76, p=0.023) | 0.30 (0.11-0.83, p=0.021) |
| | 40-49 | 1824 (99.6) | 8 (0.4) | 0.47 (0.20-0.97, p=0.056) | 0.48 (0.22-1.04, p=0.064) |
| | 60-69 | 4032 (96.1) | 165 (3.9) | 4.38 (3.04-6.53, p<0.001) | 4.34 (2.97-6.34, p<0.001) |
| | 70-79 | 5173 (85.7) | 862 (14.3) | 17.84 (12.73-25.98, p<0.001) | 17.26 (12.12-24.59, p<0.001) |
| | 80+ | 6296 (68.9) | 2844 (31.1) | 48.36 (34.68-70.13, p<0.001) | 45.62 (32.16-64.71, p<0.001) |
| Sex at Birth | Male | 13106 (86.7) | 2011 (13.3) | - | - |
| | Female | 9072 (82.7) | 1904 (17.3) | 1.37 (1.28-1.46, p<0.001) | 1.22 (1.14-1.32, p<0.001) |

Table E16. Mediation analysis. Decomposition of South Asian ethnicity effect on mortality by potential mediators. Models include all ethnicities and are adjusted for age and sex. Deprivation and location are not incorporated into models. HR, hazard ratio; L95, lower 95% confidence interval; U95, upper 95% confidence interval.

### Diabetes: South Asian

| | Estimate | L95 | U95 | HR | HR (L95) | HR (U95) |
|---|---|---|---|---|---|---|
| Total natural indirect effect | 0.029 | 0.019 | 0.039 | 1.030 | 1.020 | 1.040 |
| Total natural direct effect | 0.134 | 0.011 | 0.257 | 1.144 | 1.011 | 1.294 |
| Total effect | 0.163 | 0.040 | 0.286 | 1.177 | 1.041 | 1.332 |

### Obesity: South Asian

| | Estimate | L95 | U95 | HR | HR (L95) | HR (U95) |
|---|---|---|---|---|---|---|
| Total natural indirect effect | -0.019 | -0.048 | 0.009 | 0.981 | 0.953 | 1.009 |
| Total natural direct effect | 0.191 | 0.060 | 0.321 | 1.210 | 1.062 | 1.379 |
| Total effect | 0.173 | 0.042 | 0.304 | 1.189 | 1.043 | 1.356 |

### Dementia: South Asian

| | Estimate | L95 | U95 | HR | HR (L95) | HR (U95) |
|---|---|---|---|---|---|---|
| Total natural indirect effect | -0.001 | -0.002 | -0.001 | 0.999 | 0.998 | 0.999 |
| Total natural direct effect | 0.158 | 0.035 | 0.281 | 1.171 | 1.035 | 1.325 |
| Total effect | 0.157 | 0.033 | 0.280 | 1.169 | 1.034 | 1.323 |

### Chronic heart disease: South Asian

| | Estimate | L95 | U95 | HR | HR (L95) | HR (U95) |
|---|---|---|---|---|---|---|
| Total natural indirect effect | 0.002 | -0.001 | 0.004 | 1.002 | 0.999 | 1.004 |
| Total natural direct effect | 0.161 | 0.039 | 0.282 | 1.174 | 1.040 | 1.326 |
| Total effect | 0.162 | 0.041 | 0.284 | 1.176 | 1.042 | 1.328 |

### Chronic pulmonary disease: South Asian

| | Estimate | L95 | U95 | HR | HR (L95) | HR (U95) |
|---|---|---|---|---|---|---|
| Total natural indirect effect | -0.013 | -0.017 | -0.008 | 0.988 | 0.983 | 0.992 |
| Total natural direct effect | 0.190 | 0.068 | 0.312 | 1.210 | 1.071 | 1.367 |
| Total effect | 0.178 | 0.056 | 0.300 | 1.195 | 1.057 | 1.350 |

### Chronic kidney disease: South Asian

| | Estimate | L95 | U95 | HR | HR (L95) | HR (U95) |
|---|---|---|---|---|---|---|
| Total natural indirect effect | 0.009 | 0.005 | 0.014 | 1.009 | 1.005 | 1.014 |
| Total natural direct effect | 0.159 | 0.037 | 0.281 | 1.173 | 1.038 | 1.325 |
| Total effect | 0.169 | 0.046 | 0.291 | 1.184 | 1.047 | 1.337 |

### Chronic kidney disease and/or diabetes: South Asian

| | Estimate | L95 | U95 | HR | HR (L95) | HR (U95) |
|---|---|---|---|---|---|---|
| Total natural indirect effect | 0.032 | 0.023 | 0.041 | 1.033 | 1.023 | 1.042 |
| Total natural direct effect | 0.127 | 0.006 | 0.248 | 1.135 | 1.006 | 1.281 |
| Total effect | 0.159 | 0.038 | 0.280 | 1.172 | 1.039 | 1.323 |

Table E17. Mediation analysis. Proportion of total effect mediated by diabetes for mortality in South Asian patients. Bootstrapped intervals (5000 replications). HR, hazard ratio; L95, lower 95% confidence interval; U95, upper 95% confidence interval.

### Diabetes: South Asian

| | Estimate | Proportion (95% CI) | P-value for proportion different to zero (two-sided) |
|---|---|---|---|
| Total natural indirect effect | 0.029 | | |
| Total natural direct effect | 0.134 | | |
| Total effect | 0.163 | | |
| Indirect effect as a proportion of total effect | | 17.8% (8.9% to 65.7%) | P = 0.009 |

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