To what extent are social determinants of health, including household overcrowding, air pollution and housing quality deprivation, modulators of presentation, ITU admission and outcomes among patients with SARS-COV-2 infection in an urban catchment area in Birmingham, United Kingdom?

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Abstract

**Background**: Internationally, researchers have called for evidence to support tackling health inequalities during the Severe acute respiratory syndrome coronavirus 2 (COVID19) pandemic. UK Office for National Statistics data suggests that patients in regions of most deprived overall, generic Index of Multiple Deprivation Score (IMDS) are twice as likely to die of COVID19 than other causes. The Intensive Care National Audit and Research Centre (ICNARC) report that BAME patients account for 34% of critically ill COVID19 patients nationally despite constituting 14% of the population. This paper is the first to explore the roles of social determinants of health, including specific IMDS sub-indices with indicators for household quality deprivation, household overcrowding deprivation and air pollution deprivation, as modulators of presentation, Intensive Care Unit (ITU) admission and outcomes among COVID19 patients of all ethnicities.

**Methods**: An in-depth retrospective cohort study of 408 hospitalised COVID19 patients admitted to the Queen Elizabeth Hospital, Birmingham was conducted. Quantitative data analyses including two-step cluster analyses were applied.

**Results**: Patients admitted from highest living environment (LE) deprivation indices were at increased risk of presenting with multi-lobar pneumonia and, in turn, ITU admission whilst patients admitted from highest Barriers to Housing and Services (BHS) deprivation indices were at increased risk of ITU admission. Admission to ITU significantly increased the risk of death. Black, Asian and Minority Ethnic (BAME) patients were more likely, than white patients, to present with multi-lobar pneumonia, be admitted to ITU and be admitted from highest BHS and LE deprivation indices. Comorbidities and frailty significantly increased the risk of death among COVID19 patients irrespective of deprivation.

**Conclusions**: Air pollution and housing quality deprivation are potential modulators of presentation with multi-lobar pneumonia. Household overcrowding deprivation and presentation with multi-lobar pneumonia are potential modulators of ITU admission. Patients of BAME ethnicity are more likely to be admitted from regions of highest air pollution, housing quality and household overcrowding deprivation; this is likely to contribute an explanation towards the higher ITU admissions reported among COVID19 BAME patients. These findings have urgent implications for supporting front line clinical decisions, disseminating practical advice around applying social distancing messages at the household level and informing wider pandemic strategy.

**Background**

UK data published by the Office for National Statistics suggests that patients in regions of most deprived Index of Multiple Deprivation Score (IMDS) are twice as likely to die of COVID19 than other causes and that patients from the city of Birmingham, UK, are twice as likely to die of COVID than the national average between the 1st of March 2020 and the 17th April 2020 (1). Birmingham is the 2nd largest UK city and the 3rd most deprived UK city with a diverse population, 40.04% BAME, and the full range of deprivation indices (2); studies at the city level exploring the social determinants of health including deprivation with greater granularity are essential in informing the national and international picture.

The IMDS incorporates seven weighted sub-indices of deprivation: crime, education, health and disability, income, employment, barriers to housing and services (BHS) and living environment (LE). Whilst the IMDS may be a helpful broad marker of deprivation, it is of limited value when exploring deprivation as a modulator of presentation, ITU admissions and outcomes among COVID19 positive patients owing to a lack of relevance of some sub-indices, e.g. crime deprivation.

This paper is the first of its kind to explore the roles of social determinants of health, including specific deprivation sub-indices with constituent indicators for household quality deprivation, household overcrowding deprivation and air pollution deprivation, as modulators of presentation, ITU admission and outcomes among COVID19 positive patients of all ethnicities.

The Intensive Care National Audit and Research Centre (ICNARC) has reported that patients of BAME ethnicity account for 34% of critically ill COVID19 nationally patients despite constituting 14% of the population (3). Several potential hypotheses have been cited thus far to explain the presentation and increased admission to ITU among COVID19 positive BAME patients including vitamin D deficiency (4) and genetic predisposition (5) but studies have not explored the potential roles of BHS deprivation, which includes an indicator of household overcrowding, or LE deprivation, which includes indicators for household quality deprivation and air pollution deprivation.

It is already established that exposure to air pollutants (6) and household overcrowding (7) are associated with an increased incidence of community acquired pneumonia in general. Furthermore, studies have reported that the worst air pollution levels are seen in ethnically diverse neighbourhoods with a high population of BAME residents (8). Moreover, UK Government statistics show that BAME households are more overcrowded with 30% of overcrowded households being of Asian ethnicity, 15% of Black ethnicity, 3% of Mixed ethnicity and 2% White ethnicity (9). Reported research has not yet explored these factors in the context of COVID19 positive patients admitted to hospital.

This study explores the roles of social determinants of health (BHS deprivation, LE deprivation, ethnicity, comorbidities and frailty) on modulating: presentation, ITU admissions and outcomes among COVID19 positive patients of BAME and white ethnicities at the city level. A greater understanding of these factors will support front-line clinicians in risk stratifying patients and in identifying the index of suspicion for care as well as informing wider pandemic strategic planning.

**Methods**

**Design and setting**
An in-depth study of patients admitted to the Queen Elizabeth Hospital in Birmingham was performed to explore the role of social determinants of health as modulators of presentation, ITU admissions and outcomes among hospitalised COVID19 positive patients.

**Patient population**

The inclusion criteria for this study was adult patients (>16 years old) admitted to the Queen Elizabeth Hospital, Birmingham, UK with confirmed COVID19 infection from the 1st March 2020 until 13th April 2020. The COVID19 infection diagnosis was based upon PCR analysis of a combined nose and throat swab in accordance with Public Health England guidance. Patients who were not admitted to the Queen Elizabeth Hospital, for example due to attendance as a day case for routine dialysis, were excluded from this study.

Four hundred and eight patients were assessed for eligibility for inclusion into this study. A CONSORT flow diagram of study participants is shown in Figure 1. Forty five patients were excluded on account of either having not met the inclusion criteria (n=36) or clinical records being unavailable (n=9). Patients eligible for inclusion in this study (n=363) were analysed in this paper. A two-step cluster analysis was undertaken to identify homogenous clusters based on BHS deprivation index and completed hospitalised episode outcome (n=344). Patients who did not have a BHS deprivation score attributed to their place of admission (n=7), or who were in hospital for ongoing management (n=12) were not included in this analysis.

**Patient management**

Patients were admitted and treated initially according to British Thoracic Society (BTS) guidelines for COVID19 community acquired pneumonia with antibiotics, fluids and controlled oxygen where appropriate. The hospital's local antibiotic policy uses CURB-65 to risk stratify CAP patients in full. Trust infection prevention measures were followed.

No experimental agents were administered to these patients outside of clinical trials. A limited number of patients were enrolled in the UK RECOVERY trial and a trial of inhaled IFN-beta1a in COVID19 disease. No patients were given corticosteroids unless there was concurrent non-COVID-19-related disease where they were indicated. No patients received ward-based continuous positive airway pressure non-invasive ventilation. Ward based bi-level non-invasive ventilation was only used if patients with pre-existing causes for chronic type-two respiratory failure were admitted with acute respiratory acidosis, with no evidence of infiltrates on their chest x-ray. At the beginning of the pandemic, the trust introduced a rapid review Chest Xray reporting service staffed by Consultant radiologists to ensure Chest X-rays were reported within 12 hours of being undertaken.

All patients were prescribed their regular medications for existing medical conditions whilst in hospital unless a medication was contraindicated for clinical reasons in which case it was paused temporarily until safe to resume. All patients received 40 mg subcutaneous enoxaparin as venous thromboembolic disease prophylaxis daily, unless it was contraindicated, as per our hospital policy.

**Data collection and scoring analysis**

The hospital informatics system records each patient's: demographics (ethnicity, age, place of admission, postcode), medical records (admission review, clinical assessments, escalation decisions, past medical history, comorbidities, management), clinical metrics (blood tests, observation, imaging), information about whether a patient was admitted to ITU and completed hospitalised episode outcomes (discharge or death).

All suspected COVID19 infected patients had a decision about escalation to critical care and discussion in relation to resuscitation status at their first review after admission (typically in less than 4 hours due to the introduction of resident consultants during the pandemic).

Patients who were for critical care escalation were reviewed by the critical care assessment team if they had an altered GCS, persistently low systolic blood pressure (<90mmHg), respiratory acidosis (pH<7.2) or were unable to maintain their target saturations or had a respiratory rate >30 breaths per minute despite receiving a fractional inspired oxygen (FiO\textsubscript{2}) of ≥ 0.5. If deemed appropriate, patients were intubated and transferred to critical care subsequently.

Chest X-Rays were carried out on admission, where clinically indicated, and reported by a radiologist within 4 hours and reviewed again by a Professor of Respiratory Medicine (DT) for the purposes of this study.

**Index of Multiple Deprivation Score (IMDS)**

The English Index of Multiple Deprivation categorises deprivation by postcode on a scale of 1-10. The IMDS incorporates 7 sub-indices of deprivation weighted as indicated: income (22.5%), employment (22.5%), education (13.5%), health (13.5%), crime (9.3%), Barriers to Housing and Services (BHS) (9.3%) and living environment (9.3%). Within the IMDS and within each of the 7 sub-indices of deprivation, a score of one indicates postcodes within the most deprived centile nationally whereas a score of ten includes postcodes within the least deprived centile nationally (10).

The BHS deprivation index is a measure of the physical and financial accessibility of housing and local services incorporating "geographical barriers" and "wider barriers" which includes an indicator for household overcrowding (11). The Living Environment deprivation index is a measure of the quality of the local environment both indoors with respect to housing quality and outdoors including an indicator for air quality (11). Detailed descriptions of the IMDS and its constituent seven sub-indices are published by the UK Ministry of Housing, Communities and Local Government Department (UKMHCG) (11).

The deprivation scores for each patient were computed by inputting the postcode corresponding with each patient's place of admission into the UKMHCG English Indices of Deprivation 2019 postcode lookup tool. Where, the postcode is stored on file, the tool provides a downloadable file with the overall
weighted IMDS and the index for each of the seven sub-indices (11). Seven patients in this study either did not provide a postcode or deprivation metrics were not available for the provided postcode.

Charlson Comorbidity Score
The Charlson Comorbidity Index is a widely validated tool for categorising comorbidities among patients based on the International Classification of Diseases (ICD). The tool is a weighted index that takes into account the number and the seriousness of comorbid disease. The higher the score, the more likely the predicted outcome will result in mortality (12).

Clinical Frailty Scale
NICE guidelines recommend that physicians use the Clinical Frailty Score, as measured by the Clinical frailty Scale, available from the NHS Specialised Clinical Frailty Network, when assessing adults for frailty irrespective of COVID19 status (13). The Clinical Frailty Scale is a globally utilised and validated measure of frailty based on clinical judgement (14).

CURB65
Severity of presentation on admission was assessed using the CURB65 score in accordance with the British Thoracic Society Guidelines (15). The CURB65 score, which is a simple, six point score based on confusion, urea, RR, BP and Age is a validated score for the assessment of the severity of pneumonia on presentation (16).

Data points
This study explored the role of social determinants of health in modulating: presentations, admissions to ITU and completed hospitalised episode outcomes (death or discharge) among COVID19 positive patients.

Statistical Analysis
Baseline characteristics were presented as mean (standard deviation) for continuous variables and proportions were calculated for categorical data. Normality of distributions for quantitative variables was assessed by the Shapiro-Wilk test. Variables, in this paper, did not show parametric distribution (CURB 65 scores, Clinical Frailty Scores, Charlson Comorbidity Scores, IMDS, BHS Deprivation Index, Living Environment Deprivation Index). For categorial variables with non-parametric distribution, Fisher’s exact test for comparison between two groups and Pearson’s Chi-squared test was used for comparisons between more than two groups. For ordinal variables with non-parametric distribution, Mann Whitney U test was used for comparisons between two groups and Kruskall Wallis was used for comparisons between more than two groups. Data is presented as a Median (IQR) for non-parametric data. To quantify an association between two variables with non-parametric distribution, Spearman's correlation was used. Statistical analysis was carried out using IBM SPSS Statistics for MAC V.24 and Prism 8.

Cluster Analyses
Two-step cluster analysis is an exploratory analysis of a sample to identify homogenous groups of cases based on the distribution of the input variables using log-likelihood to model distances between variables. Cluster analysis identifies groupings by running pre-clustering first and then by hierarchical methods. This technique can detect latent relationships within a complex dataset between patients with multiple distinct characteristics. It is appropriate for continuous, ordinal and categorical data sets larger than 200 data points (17) (18). The number of clusters was determined automatically following the Bayesian Information criterion (BIC) using IBM SPSS Statistics for MAC V.24. When clusters had been identified within the samples, group comparisons were performed. Descriptive statistics were used to describe the data by clusters. For categorical and ordinal data, the X^2 and Kruskall Wallis tests respectively were used to examine any significant differences between clusters. The post-hoc Bonferroni correction was applied for multiple group comparisons and all results were considered significant at p<0.05.

Patient and Public involvement
In view of the current stay at home measures implemented by the UK government; there was no explicit patient or public involvement. This study was undertaken in accordance with the Strengthening The Reporting of Observational Studies in Epidemiology (STROBE) guidelines for cohort studies (19).

Ethics statement
Ethics was not required based on the Health Research Authority Decision tool (http://www.hra-decisiontools.org.uk/research/result7.html (20) (Appendix 1)). Local approval was granted from the audit and quality improvement department.

Results

Participant Characteristics
# Population Demographics

|                                   | All COVID19-positive patients | COVID19-positive patients with Radiological Changes of Pneumonia | COVID19-positive patients without Radiological Changes of Pneumonia |
|-----------------------------------|-------------------------------|---------------------------------------------------------------|---------------------------------------------------------------|
| **N**                             | 363                           | 294                                                           | 69                                                            |
| **Age, mean (SD)**                | 66.9 (16.7)                   | 66.8 (15.4)                                                   | 67.0 (21.5)                                                   |
| **Gender, n (% of column total)** |                               |                                                               |                                                               |
| Male                              | 217 (59.8)                    | 185 (62.9)                                                    | 32 (46.4)                                                    |
| Female                            | 146 (40.2)                    | 109 (37.1)                                                    | 37 (53.6)                                                    |
| **Ethnicity, n (% of column total)** |                               |                                                               |                                                               |
| White                             | 231 (63.6)                    | 179 (61.1)                                                    | 52 (75.4)                                                    |
| Asian/Asian British               | 87 (21)                       | 75 (25.6)                                                     | 12 (17.4)                                                    |
| Black/African/Caribbean           | 26 (7.2)                      | 24 (8.2)                                                      | 22 (2.9)                                                     |
| Mixed                             | 1 (0.3)                       | 1 (0.3)                                                       | 0 (0)                                                        |
| Other ethnic groups               | 10 (2.7)                      | 9 (3.1)                                                       | 1 (1.4)                                                      |
| Unknown                           | 7 (1.9)                       | 5 (1.7)                                                       | 2 (2.9)                                                      |
| **Place of admission, n (% of column)** |                               |                                                               |                                                               |
| Nursing/Residential home          | 47 (12.9)                     | 38 (12.9)                                                     | 9 (13.0)                                                     |
| Private Residence                 | 315 (86.8)                    | 255 (86.7)                                                    | 60 (87.0)                                                    |
| **Comorbidity, n (% of column)**  |                               |                                                               |                                                               |
| Chronic kidney Disease            | 105 (28.9)                    | 82 (27.9)                                                     | 23 (33.3)                                                    |
| Hypertension                      | 175 (48.2)                    | 150 (51.0)                                                    | 25 (36.2)                                                    |
| Type 2 Diabetes Mellitus          | 121 (33.3)                    | 102 (34.7)                                                    | 19 (27.5)                                                    |
| Dementia                          | 32 (8.8)                      | 23 (7.8)                                                      | 9 (13.0)                                                     |
| Ischaemic Heart Disease           | 70 (19.3)                     | 55 (19.7)                                                     | 12 (17.4)                                                    |
| **ITU admission, n (% of column)** |                               |                                                               |                                                               |
| ITU admission                     | 64 (17.6)                     | 61 (20.7)                                                     | 3 (4.3)                                                      |
| **Discharge, n (% of column)**    |                               |                                                               |                                                               |
| Discharge                         | 245 (67.5)                    | 190 (64.6)                                                    | 55 (79.7)                                                    |
| **Mortality, n (% of column)**    |                               |                                                               |                                                               |
| Mortality                         | 106 (29.2)                    | 92 (31.3)                                                     | 14 (20.3)                                                    |

Table 1- Population Demographics (Age, Gender and Comorbidities among COVID19 positive patients presenting with and without Radiological Changes within 24 hours of admission

The study population is outlined in table 1 and figure 2. Males (59.8%) were hospitalised more than females (40.2%). The mean age of all patients in this study was 67. Patients of BAME ethnicity were younger (mean-61.85 (14.5)) whilst patients of White ethnicity were older (mean-69.5 (17.3)). Patients of BAME ethnicity constituted 31.2% of admissions whilst patients of white ethnicity constituted 63.6% of admissions. Admissions from IMDS 1 and 2 (52.9%)
were proportionally similar (figure 2a) to the local Birmingham city population where 56.3% of postcodes are within IMDS 1 and 2 (21). Patients admitted from the highest BHS deprivation indices, 1 and 2, constituted 47.4% of all admissions whilst patients admitted from the highest Living Environment deprivation indices, 1 and 2, constituted 42.4% of all admissions (Figure 2e). 60.2% of BAME patients were populated within the highest BHS deprivation indices, 1 and 2, in comparison to 40.9% of White patients. 69.9% of BAME patients were populated within the highest Living Environment deprivation indices, 1 and 2, in comparison to 52.0% of White patients. Patients admitted from nursing homes (n=47) were all admitted from the top five most deprived BHS deprivation indices.

Patients admitted from regions of highest BHS deprivation, indices 1 and 2, were more likely to be admitted to ITU (OR 2.22, 95% CI 1.111-4.469, p=0.030) in comparison with patients admitted from all other BHS deprivation indices. Patients admitted from regions of highest Living Environment deprivation, indices 1 and 2, were more likely to present with radiological multi-lobar pneumonia (OR 1.923, 95% CI 1.195-3.039, p=0.006) in comparison with patients admitted from all other Living Environment deprivation indices. Patients presenting with radiological multi-lobar pneumonia were more likely to be admitted to ITU (OR 3.174, 95% CI 1.250-8.103, p=0.019) and die (OR 2.224, 95% CI 1.296-3.928, p=0.004).

COVID19 positive patients of BAME ethnicity were more likely to be admitted from regions of highest BHS deprivation (OR 2.18, 95% CI 1.410-3.445, p<0.001), admitted from regions of highest Living Environment deprivation (OR 2.30, 95% CI 1.450-3.701, p<0.001), present with radiological pneumonia (OR 2.31 95% CI 1.249-4.394, p=0.008), present with multi-lobar pneumonia (OR 2.480, 95% CI 1.446-4.172, p<0.001) than patients of white ethnicity (figure 3a).

Furthermore, COVID19 positive patients who were admitted to ITU were more likely to: be of BAME ethnicity (OR 3.5 95% CI 2.00-6.06, p<0.001), be admitted from regions of highest BHS deprivation (OR 2.22, 95% CI 1.111-4.469, p=0.030), present with radiological pneumonia (OR 4.880, 95% CI 1.452-16.14, p=0.008) and present with multi-lobar pneumonia (OR 3.174, 95% CI 1.250-8.103, P=0.019) than COVID19 positive patients who were not admitted to ITU (figure 3b).

Moreover, COVID19 positive patients who died were more likely to: be admitted from a nursing/residential home (OR 4.729, 95% CI 2.533 – 8.922, p<0.001), present with radiological pneumonia (OR 4.880, 95% CI 1.452-16.14, p=0.008), present with multi-lobar pneumonia (OR 2.224, 95% CI 1.296-3.928, p=0.004), present with increased severity, present with CURB 65 ≥ 3, (OR 5.32, 95% CI 3.267-8.662, p<0.001), and have been admitted to ITU during the inpatient stay (OR 14.57, 95% CI 5.089-36.85, P<0.001) than patients who were discharged (figure 3c).

Individual comorbidities were significantly associated with increased risk of death among hospitalised COVID19 positive patients: hypertension (OR-1.806, 95% CI 1.129-2.644, p=0.014), ischaemic heart disease (OR-2.096, 95% CI 1.204-3.625, p=0.011), diabetes mellitus (OR 1.67 95%CI 1.046-2.650, p=0.037) dementia (OR-3.375, 95% CI 1.657-7.314, p=0.002) and chronic kidney disease (OR-2.36, 95% CI 1.452-3.841, p=0.001) (figure 4). Charlson Comorbidity Scores were higher among COVID19 positive patients who died (Median 6 (IQR 4)) in comparison with patients who were discharged (Median 3 (IQR 5), p<0.001). Patients with higher Charlson Comorbidity Scores, presented with increased severity, CURB 65, (p<0.001). Charlson Comorbidity Index Scores were higher among patients of white ethnicity in comparison to patients BAME ethnicity (White- median 5 (IQR 5), BAME-median- 3 (IQR 4.75), p=0.002). Patients of White ethnicity were more likely to present with increased severity on admission, CURB65 ≥ 3, (OR 2.15, 95% CI 1.306-3.39, p=0.0023) in comparison to patients of BAME ethnic origin. Charlson Comorbidity Scores were also higher among patients admitted from a private residence (Nursing/Residential home - Median 6 (IQR 3), Private residence- Median 4 (IQR 4), p=0.001). Patients admitted from nursing/residential homes were more likely to present with increased severity on admission, CURB65 ≥ 3, (OR 5.016, 95% CI 2.656-9.385, p<0.001) in comparison to patients admitted from a private residence.

Clinical Frailty Scores were higher among COVID19 positive patients who died (median-6.00 (IQR-3.50) in comparison to COVID19 positive patients who survived (median-3.00 (IQR-3.00), p<0.001). Patients admitted from Nursing/Residential homes had higher Clinical Frailty Scores than patients admitted from a private residence (Nursing/Residential home - Median 7 (IQR 1), Private residence- Median 3 (IQR 3), p<0.001). There is no statistical significance in Clinical Frailty Score between patients of BAME and White ethnic origin (BAME: median-3 (IQR-4), White: median-4 (IQR-4), p=0.188).

Exploring the profiles of social determinants of health among patients clustered by outcome and deprivation (BHS and LE deprivation respectively)

Two two-step cluster analyses were undertaken to identify homogenous clusters based on:
(A) BHS deprivation and completed hospital episode outcome (n=344) and (B) LE deprivation and completed hospital episode outcome (n=344). Within each analysis four distinct clusters emerged reflecting four statistically distinct groups (table 2):

(A) Two step cluster analysis “A” clustering hospitalised COVID19 positive patients by BHS deprivation and completed hospital episode outcome

Cluster A1 is characterised by patients admitted from regions of highest BHS deprivation, indices 1-2, who died. Cluster A2 is characterised by patients admitted from all other BHS deprivation indices who died. Cluster A3 is characterised by patients admitted from regions of highest BHS deprivation, indices 1-2, who were discharged. Cluster A4 is characterised by patients admitted from all other BHS deprivation indices who were discharged.

(B) Two step cluster analysis “B” clustering hospitalised COVID19 positive patients by LE deprivation and completed hospital episode outcome

Cluster B1 is characterised by patients admitted from regions of highest LE deprivation, indices 1-2, who died. Cluster B2 is characterised by patients admitted from all other LE deprivation indices who died. Cluster B3 is characterised by patients admitted from regions of highest LE deprivation, indices 1-2, who were discharged. Cluster B4 is characterised by patients admitted from all other LE deprivation indices who were discharged.

Clusters A1 and B1 had relatively high proportions of: BAME patients, comorbidities among patients (chronic kidney disease, dementia, ischaemic heart disease, hypertension and type 2 diabetes mellitus) and admissions from nursing/residential homes in comparison to the corresponding proportions among
Clusters A2 and B2 had relatively high proportions of: white patients, comorbidities among patients (chronic kidney disease, dementia, ischaemic heart disease, hypertension and type 2 diabetes mellitus) and admissions from nursing/residential homes in comparison to the corresponding proportions among all patients.

Clusters A3 and B3 had a relatively high proportion of BAME patients but relatively lower proportions of: comorbidities among patients (chronic kidney disease, dementia, ischaemic heart disease, hypertension and type 2 diabetes mellitus) and admissions from nursing/residential homes in comparison to the corresponding proportions among all patients.

Clusters A4 and B4 had a relatively high proportion of white patients but relatively lower proportions of: comorbidities among patients (chronic kidney disease, dementia, ischaemic heart disease, hypertension and type 2 diabetes mellitus) and admissions from nursing/residential homes in comparison to the corresponding proportions among all patients.

Table 2 shows the cluster membership profiles in relation to: age, gender, ethnicity, place of admission, comorbidities, Charlson Comorbidity Index and Clinical Frailty Score. Figure 5a shows a graphical representation of individual comorbidity profiles within each of the four emergent clusters from a two-step cluster analysis clustering hospitalised COVID19 positive patients by BHS deprivation and hospitalised episode outcome. Figure 5b shows a graphical representation of individual comorbidity profiles within each of the four emergent clusters from a two-step cluster analysis clustering hospitalised COVID19 positive patients by LE deprivation and hospitalised episode outcome. Group comparisons were performed to examine the profiles of independent comorbidities, Charlson Comorbidity Scores and Clinical Frailty Scores.

Examining comorbidities within clusters

Charlson Comorbidity Index scores for patients who died were above the average for all patients (Median 4.00, IQR 4.00), irrespective of deprivation; this was regardless of whether patients were admitted from indices of highest BHS and LE deprivation respectively (Cluster A1; Median 6.00, IQR 5.00, Cluster B1; Median 6.00, IQR 4.00) or all other BHS and LE deprivation indices respectively (Cluster A2; Median 6.00, IQR 3.00, Cluster B2; Median 6.00, IQR 4.75). Patients who were discharged from hospital had Charlson Comorbidity Index scores around/below the average for all patients in indices of highest BHS and LE deprivation respectively (Cluster A3, Median 2.00, IQR 4.00, Cluster B3, Median 3.00, IQR 4.25) and all other BHS and LE deprivation indices respectively (Cluster A4, Median 4.00, IQR 4.00, Cluster B4, Median 3.00, IQR 4.00). There was a statistically significant difference between the cluster A medians (p<0.001) and the cluster B medians (p<0.001).

Irrespective of BHS deprivation, among patients who died (Clusters A1 and A2), there was no statistically significant difference in comorbidities: chronic kidney disease (p=0.158), dementia (p=0.304), ischaemic heart disease (p=1.000), hypertension (p=0.413), type 2 diabetes mellitus (p=1.000). Furthermore, irrespective of LE deprivation, among patients who died (Clusters B1 and B2), there was no statistically significant difference in comorbidities: chronic kidney disease (p=0.840), dementia (p=0.793), ischaemic heart disease (p=0.376), hypertension (p=0.536), type 2 diabetes mellitus (p=0.411).

Among COVID19 positive patients admitted from the most deprived BHS indices (Cluster A1 and A3), patients who died were more likely to have: chronic kidney disease (OR 2.619, 95% CI 1.180-5.697, p=0.0253), dementia (OR 6.525, 95% CI 2.021-18.16, p=0.001) and ischaemic heart disease (OR 4.950, 95% CI 1.725-13.21, p=0.0042) in comparison to patients who were discharged. Furthermore, among COVID19 positive patients admitted from the most deprived LE indices (Cluster B1 and B3), patients who died were more likely to have: chronic kidney disease (OR 2.408, 95% CI 1.314-4.443, p=0.0063), dementia (OR 4.500, 95% CI 1.725-13.21, p=0.0042) and ischaemic heart disease (OR 3.111, 95% CI 1.505-6.185, p=0.0024) but were not more likely to have hypertension (p>0.05) or type 2 diabetes mellitus (p=0.084) in comparison to patients who were discharged.

Examining frailty within clusters

Clinical Frailty Scores for patients who died were above the average for all patients (Median 4.00, IQR 4.00), irrespective of deprivation; this was regardless of whether patients were admitted from indices of highest BHS and LE deprivation respectively (Cluster A1; Median 6.00, IQR 4.00, Cluster B1; Median 6.00, IQR 3.50) or from all other BHS and LE deprivation indices respectively (Cluster A2; Median 6.00, IQR 3.00, Cluster B2; Median 5.50, IQR 4.00). Patients who were discharged from hospital had Clinical Frailty Scores around/below the average for all patients, irrespective of deprivation, in indices of highest BHS and LE deprivation respectively (Cluster A3, Median 3.00, IQR 3.00; Cluster B3, Median 3.00, IQR 4.00) and all other BHS and LE deprivation indices respectively (Cluster A4, Median 4.00, IQR 4.00, Cluster B4, Median 4.00, IQR 3.00). There was a statistically significant difference between the cluster A medians (p<0.001) and the cluster B medians (p<0.001).
### Table 2: Cluster membership profiles in relation to: age, gender, ethnicity, place of admission, comorbidities, Charlson Comorbidity Index and Clinical Frailty Score. Cluster membership profiles are of the four emergent clusters from two two-step cluster analyses which were carried out clustering hospitalised COVID-19 positive patients by: (a) BHS deprivation and completed hospitalised episode outcomes and (b) LE deprivation and completed hospitalised episode outcome.
among patients who died, there is no statistical significance in the respective comorbidity profiles between patients admitted from indices of highest BHS deprivation and all other BHS deprivation indices.

Among patients admitted from indices of highest BHS deprivation, there is a statistical significance in the respective comorbidity profiles between patients who died and those who were discharged.

among patients who died, there is no statistical significance in the respective comorbidity profiles between patients admitted from indices of highest LE deprivation and all other LE deprivation indices.

among patients admitted from indices of highest LE deprivation, there is a statistical significance in the respective comorbidity profiles between patients who died and those who were discharged.

**Discussion**

In the present study, patients admitted from the highest LE deprivation indices were at increased risk of presenting with multi-lobar pneumonia and, in turn, ITU admission whilst patients admitted from the highest Barriers to Housing and Services (BHS) deprivation indices were at increased risk of ITU admission in comparison with patients admitted from all other deprivation indices. Comorbidities and frailty modulated mortality, irrespective of deprivation.

This study presents novel insights into the reported relatively higher ITU admissions among COVID19 positive BAME patients in this study and more widely. The Intensive Care National Audit and Research Centre (ICNARC) has reported that patients of BAME ethnicity account for 34% of critically ill COVID19 nationally patients despite constituting 14% of the population (3).

It is interesting that despite being younger, presenting with lower Charlson Comorbidity Scores and presenting with lower severity, CURB 65, patients of BAME ethnicity in this study were more likely, than patients of white ethnicity, to present with radiological pneumonia and multi-lobar pneumonia which is associated with increased risk of admission to ITU.

This study finds that COVID19 positive BAME patients were more likely, than patients of White ethnicity to be admitted from regions of: (a) highest Living Environment deprivation, which includes indicators for household quality and air pollution, and from which admissions were associated with increased presentation with multi-lobar pneumonia and, in turn, increased ITU admission and, (b) highest BHS deprivation, which includes an indicator for household overcrowding and from which admissions were associated with increased admission to ITU. These findings have significant implications nationally and internationally especially in the context of data showing increased household overcrowding and air pollution (8) in UK BAME households.

This study finds that air pollution deprivation and housing quality deprivation modulate presentation of COVID19 positive patients with radiological pneumonia and multi-lobar pneumonia. This finding has implications for understanding the varying presentations reported among COVID19 patients and adds to findings from previous studies showing an association between air pollution and the incidence of community acquired pneumonia. Presentation with radiological pneumonia and multi-lobar pneumonia increases the risk of ITU admission among COVID19 positive patients and thus this study highlights the importance of minimising air pollution deprivation inequalities.

Furthermore, this study identifies household overcrowding deprivation as a moderator of ITU admissions among COVID19 positive patients. This finding has implications for the provision of social distancing measures at the level of the household and adds to previous studies showing that household overcrowding is associated increased incidence of community acquired pneumonia. This finding has implications nationally and internationally especially given reported data showing that overcrowding is highest among BAME households (9) and nursing/residential homes. There have been several calls for research exploring explanatory factors for the high proportion of deaths in nursing/residential homes in more detail (22). Between the 10th and 24th April 2020, the Care Quality Commission recorded 4,343 deaths involving COVID19 in nursing/residential homes (23). This study suggests that there are likely to be a number of modulators of outcomes among hospitalised COVID19 positive patients admitted from residential/nursing homes including: BHS deprivation, which includes an indicator for household overcrowding, comorbidities and clinical frailty. COVID19 positive patients admitted from nursing/residential homes were admitted from regions of high BHS deprivation and were more likely to present with higher Charlson comorbidity scores, higher Clinical Frailty Scores and die in comparison with COVID19 positive patients admitted from a private residence. The increased burden of comorbidities among COVID19 positive patients admitted from nursing/residential homes is likely to be a moderator of increased severity, CURB 65, on presentation to hospital. LE deprivation does not appear to play a significant role in modulating outcomes among COVID19 positive patients admitted from nursing/residential homes as residents are potentially less exposed to outdoor deprivation and the CQC plays a role in regulating housing quality which contributes to the indoor deprivation aspect of the LE deprivation score.

In the present study, we believe it to be of interest that, among COVID19 positive patients admitted from regions of highest BHS and LE deprivation, those who died were more likely to have chronic kidney disease, ischaemic heart disease, dementia, higher Charlson Comorbidity Scores and higher Clinical Frailty Scores in comparison to patients who were discharged. This finding suggests that irrespective of deprivation, comorbidities and clinical frailty have a significant role to play in predicting outcomes, death or discharge, among hospitalised COVID19 positive patients. It is of considerable note that comorbidities including ischaemic heart disease, chronic kidney disease, dementia and hypertension significantly increased the risk of death among all COVID19-positive patients. Furthermore, we found it of particular interest that patients presenting with higher Charlson Comorbidity Scores presented with increased severity, CURB 65, which, in turn, increases the risk of mortality. These findings emphasise the modulating role which comorbidities play in predicting outcomes among hospitalised COVID19 positive patients. The UK's Chief Medical Officer has highlighted that comorbidities and the proportion of patients with two or more medical conditions simultaneously, multi-morbidities, is rising presenting a challenge to the entire medical profession including within acute and long term hospital settings (24). Studies have previously explored the independent comorbidity risk factors associated with COVID19 patients (25) but not the role of comorbidities as modulators of outcomes, irrespective of deprivation, among COVID19-positive patients.
The present study explores hospitalised COVID19 positive patients within one Birmingham trust. This study does not explore COVID19 positive patients who were not hospitalised or who died in the community. Future studies need to relate these findings with those of populations from other urban cities and rural regions, focusing on this level of granularity to explore the role of social determinants of health, including BHS deprivation and LE deprivation, as modulators of presentation, ITU admission and outcomes among COVID19 positive patients. Future studies should explore the timing of presentation in relation to the onset of symptoms among COVID19 positive patients of all ethnicities. Furthermore, it is important to note that the current national pneumonia severity score, CURB 65, has not thus far been validated for use among COVID19 positive patients.

Conclusions

Air pollution and housing quality deprivation are potential modulators of presentation with multi-lobar pneumonia among COVID19 positive patients. Household overcrowding deprivation and presentation with multi-lobar pneumonia are potential modulators of ITU admission among COVID19 positive patients. Patents of BAME ethnicity are more likely to be admitted from regions of highest air pollution, housing quality and household overcrowding deprivation; this is likely to contribute an explanation towards the higher ITU admissions reported among COVID19 BAME patients. These findings have urgent implications for supporting front line clinical decisions, disseminating practical advice around applying social distancing messages at the household level and informing wider pandemic strategy. However, irrespective of deprivation, comorbidities increase the risk of death among COVID19 positive patients. Consideration of the Charlson Comorbidity Score and the Clinical Frailty Score on admission supports clinicians in stratifying high risk patients and informing the index of suspicion for care. These findings have urgent implications for: supporting front line clinical decisions, disseminating practical advice around applying social distancing messages effectively at the household level and informing wider pandemic strategy.

Future studies should explore the extent to which household overcrowding deprivation, housing quality deprivation and air pollution deprivation, in private and social residences, modulate outcomes among COVID19 positive patients long term and in different cities as this will further inform pandemic strategic planning. Furthermore, future studies should explore effective and validated tools which healthcare professionals can integrate within consultations to acquire a holistic picture of patients’ deprivation risk factors including housing quality deprivation, household crowding deprivation and air pollution deprivation.

Abbreviations

- COVID19/SARS-COV-2: Severe acute respiratory syndrome coronavirus 2
- BHS: Barriers to Housing and Services deprivation
- BAME: Black, Asian and Minority Ethnic
- IMDS: Index of Multiple Deprivation Score
- ITU: Intensive Care Unit
- UK: United Kingdom

Declarations

Ethics approval and consent to participate and consent for publication

Ethics was deemed not to be required based on the Health Research Authority Decision tool (http://www.hra-decisiontools.org.uk/research/result7.html (20) (Appendix 1)). Local approval was granted from the audit and quality improvement department.

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Authors Contributions

MS collected data, undertook data analyses, designed this study and wrote this paper.

LC, SC collected data for this study. CRM, JV, DD, DT made substantial contributions to the conception, design of the work and supported data interpretation. RM oversaw and quality checked the data collected for this study. FG, DP, DD and DT revised the manuscript. All authors contributed to and approved the final version of the manuscript.

Competing interests

The authors declare that they have no competing interests

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**Authors' Information**

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Appendix

Appendix 1

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Figures
Figure 1

Legend: CONSORT Flow Diagram
Figure 2

Legend: Population Demographics (a) Study population distribution v Birmingham population distribution, (b) Study Population Distribution: Index of Multiple Deprivation and Biological Sex, (c) Study Population Distribution: Index of Multiple Deprivation and Ethnicity, (d) Study Population Distribution: Age and Biological Sex, (e) Study Population Distribution: BHS deprivation and Living Environment Deprivation distributions
Figure 3
Legend: (a) Odds ratios of BAME ethnicity patients: admission from regions of highest BHS deprivation indices, 1 and 2, admission from regions of highest living environment deprivation indices, 1 and 2, presentation with radiological pneumonia, presentation with radiological multi-lobar pneumonia, presentation with a CURB 65 score $\geq 3$. (b) Odds ratios of ITU admission among COVID19 positive patients: BAME ethnicity, admission from regions of highest BHS deprivation indices, 1 and 2, admission from regions of highest living environment deprivation indices, 1 and 2, presentation with radiological pneumonia, presentation with radiological multi-lobar pneumonia, presentation with a CURB 65 score $\geq 3$. (c) Odds ratios of mortality among COVID19 positive patients: BAME ethnicity, admission from the highest BHS deprivation indices, 1 and 2, admission from nursing/residential homes, presentation with radiological pneumonia, presentation with radiological multi-lobar pneumonia, presentation with a CURB 65 score $\geq 3$ and admission to ITU.

Figure 4
Legend: Odds ratio of mortality among hospitalised COVID19 positive patients with the respective comorbidities (hypertension, ischaemic heart disease, diabetes mellitus, dementia, chronic kidney disease)
Figure 5

Legend: (a) A graphical representation of comorbidities within groups of hospitalised COVID19 positive patients clustered by BHS deprivation and completed hospitalised episode outcome: Cluster 1 (patients admitted from indices of highest BHS deprivation who died), Cluster 2 (patients admitted from all other indices of BHS deprivation who died), Cluster 3 (patients admitted from indices of highest BHS deprivation who were discharged), Cluster 4 (patients admitted from all other indices of BHS deprivation who were discharged). (b) A graphical representation of comorbidities within groups of hospitalised COVID19 positive patients clustered by LE deprivation and completed hospitalised episode outcome: Cluster 1 (patients admitted from indices of highest LE deprivation who died), Cluster 2 (patients admitted from all other indices of LE deprivation who died), Cluster 3 (patients admitted from indices of highest LE deprivation who were discharged), Cluster 4 (patients admitted from all other indices of LE deprivation who were discharged).