PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Ethnicity and outcomes in patients hospitalised with COVID-19 infection in East London: an observational cohort study
AUTHORS	Apea, Vanessa; Wan, Yize; Dhairyawan, Rageshri; Puthucheary, Zudin; Pearse, Rupert; Orkin, Chloe; Prowle, John

VERSION 1 – REVIEW

REVIEWER	Francisco Caramelo Faculty of Medicine, University of Coimbra, Portugal
REVIEW RETURNED	21-Jul-2020

GENERAL COMMENTS	The manuscript presents a study on the influence of ethnicity on the survival rate of COVID-19 patients as well as other risk factors. The authors also addressed additional outcomes such as intensive care unit (ICU) admission, hospital and ICU length stay and, type and duration of organ support. The manuscript is clear, the statistical analysis is well conducted and, its results support the conclusions. I have only a few minor remarks that can be easily corrected or answered. It seems that the age variable was transformed into an ordinal variable and entered in the Cox regression that way. This is not well explained in the text, and in my opinion using age as a quantitative variable in Cox regression would be a superior alternative. Please, explain better how age entered in the analysis and the reason(s) behind that. Table 1 shows the median days to death, which refers to the median days to the death of individuals who died after hospitalization. It is not incorrect, but in the context of time to event analysis (survival analysis), the median is generally accepted considering the events and censored data together. Please, provide a clarification of the meaning of the median value. The same table shows the number of patients that died within 90 days. Data collection was performed between 1st March and 13th May and the mortality data until the 20th of May (line 44, page 5), which gives a maximum number of days of 81. Please, clarify this point. Also in table 1, the sum of the discharge destinations is slightly different from the number of patients alive discharged from the hospital. Please, clarify this point. Figures of pages 20, 21, 22, 23 and 24 are not labelled and do not have caption. The captions of the forest plots in supplementary material mention "log hazard ratios" but the charts show hazard ratios instead. Please, correct this aspect. Finally, the caption of figure S4 only refers to the variables depicted in the image, but no explanation for the values at the

	margins. Please, provide a more comprehensive explanation of the picture.

REVIEWER	Amer Harky UK
REVIEW RETURNED	25-Aug-2020

GENERAL COMMENTS	I must comment the authors on this excellent work and study, we all are in agreement that there is significant racial and ethnic disparities when it comes to COVID-19 related outcomes. The government needs to take such studies into serious consideration and plan further actions toward BAME communities. Although your results have been reported over and over again in many other studies, I think it will add significant values to this. Can I suggest you to discuss below articles in your study and cite them where appropriate. 1. Zaim S, Chong JH, Sankaranarayanan V, et al.. COVID-19 and Multiorgan Response. Curr Probl Cardiol. 2020;45(8):100618. doi:10.1016/j.cpcardiol.2020.100618 2. Abuelgasim E, Saw LJ, Shirke M, Zeinah M, Harky A. COVID-19: Unique public health issues facing Black, Asian and minority ethnic communities. Curr Probl Cardiol. 2020;45(8):100621. doi:10.1016/j.cpcardiol.2020.100621

VERSION 1 – AUTHOR RESPONSE

Reviewer(s)' Comments to Author:

Reviewer: 1

Reviewer Name

Francisco Caramelo

Institution and Country

Faculty of Medicine, University of Coimbra, Portugal&#a0;

Please state any competing interests or state 'None declared':
None declared

Please leave your comments for the authors below
The manuscript presents a study on the influence of ethnicity on the survival rate of COVID-19 patients as well as other risk factors. The authors also addressed additional outcomes such as intensive care unit (ICU) admission, hospital and ICU length stay and, type and duration of organ support. The manuscript is clear, the statistical analysis is well conducted and, its results support the conclusions. I have only a few minor remarks that can be easily corrected or answered.
It seems that the age variable was transformed into an ordinal variable and entered in the Cox regression that way. This is not well explained in the text, and in my opinion using age as a quantitative variable in Cox regression would be a superior alternative. Please, explain better how age entered in the analysis and the reason(s) behind that.

Response: Age was included as a continuous variable. It was not transformed. A note on the interpretation of the hazard ratio in the results tables was added to state 25th compared to the 75th centile. To clarify this point, we have now included in the statistical analysis section of methods:

Age was the only continuous variable. (page 6, line 14)

Table 1 shows the median days to death, which refers to the median days to the death of individuals who died after hospitalization. It is not incorrect, but in the context of time to event analysis (survival analysis), the median is generally accepted considering the events and censored data together. Please, provide a clarification of the meaning of the median value.

Response: The median value refers to the median days to death of individuals who died after hospitalization. We have chosen to use this definition in the baseline tables to aid this interpretation rather than give a measure duration of follow-up in the context of the time to event analysis.

The same table shows the number of patients that died within 90 days. Data collection was performed between 1st March and 13th May and the mortality data until the 20th of May (line 44, page 5), which gives a maximum number of days of 81. Please, clarify this point.

Response: Thank you for highlighting this point. This was an error in the abstract. Data collection was carried out to include all patients admitted between 1st January and 13th May. This is stated in the methods in the main text and the abstract has now been corrected to state:

1737 patients aged 16 years or over admitted to hospital with confirmed COVID-19 infection between 1st January and 13th May 2020. (page 3, line 17)

Also in table 1, the sum of the discharge destinations is slightly different from the number of patients alive discharged from the hospital. Please, clarify this point.

Response: Thank you for pointing this out. This is because n=23 were missing discharge destination data. We had edited the table to make this clear and included total n for this variable [n=1429].

Figures of pages 20, 21, 22, 23 and 24 are not labelled and do not have caption.

Response: Thank you for pointing this out. The figure legends were uploaded alongside the figures on the submission portal. Apologies if these have not been transferred to the version given to the reviewers. We have now included the figure legends to the end of the manuscript. The captions are:

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

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

Figure 3. Forest plot showing hazards ratios of mortality to 30 days comparing ethnic groups, age and sex corrected, on log scale. Additional variables included index of multiple deprivation (IMD) quintile (5 least deprived), smoking, BMI ≥30 kg/m^2, diabetes, HTN: hypertension, CKD: chronic kidney disease.

Figure 4. Survival curve to 30 days comparing predicted survival of Asian, Black, and White ethnic groups (Mixed and Other group omitted for clarity), in an age and sex adjusted Cox-hazard analysis. Survival curves adjusted to median age 65 years and male sex.

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

The captions of the forest plots in supplementary material mention "log hazard ratios" but the charts show hazard ratios instead. Please, correct this aspect.

Response: Thank you for pointing this out. The charts do show hazard ratios. Only the scale is log transformed. We have corrected this to state 'hazard ratios' and added 'on log scale'.

Finally, the caption of figure S4 only refers to the variables depicted in the image, but no explanation for the values at the margins. Please, provide a more comprehensive explanation of the picture.

Response: Thank you for this suggestion. We have revised the figure legend to include the additional explanation below:

Figure S4. Patterns of missingness in baseline risk variables. ID: patient identifier, IMD: index of multiple deprivation, DM: diabetes mellitus, HTN: hypertension, CKD: chronic kidney disease, BMI: body mass index. Blue indicate complete and pink indicate missing data. Numbers on the left side of the grid represent n records with this pattern, numbers on the right side represent n missing variables, numbers on the bottom represent n records missing this variable. For example, n=1006 records were complete, n=470 were missing 1 variable (BMI), n=14 records were missing IMD data.

Reviewer: 2

Reviewer Name

Amer Harky

Institution and Country

University of Liverpool, UK

Please state any competing interests or state 'None declared':
None

Please leave your comments for the authors below
I must comment the authors on this excellent work and study, we all are in agreement that there is significant racial and ethnic disparities when it comes to COVID-19 related outcomes. The government needs to take such studies into serious consideration and plan further actions toward

BAME communities. Although your results have been reported over and over again in many other studies, I think it will add significant values to this. Can I suggest you to discuss below articles in your study and cite them where appropriate.

1. Zaim S, Chong JH, Sankaranarayanan V, et al.. COVID-19 and Multiorgan Response. Curr Probl Cardiol. 2020;45(8):100618. doi:10.1016/j.cpcardiol.2020.100618

2. Abuelgasim E, Saw LJ, Shirke M, Zeinah M, Harky A. COVID-19: Unique public health issues facing Black, Asian and minority ethnic communities. Curr Probl Cardiol. 2020;45(8):100621. doi:10.1016/j.cpcardiol.2020.100621

Response: Thank you for your comment. However, there are a substantial number of discussion articles on this topic in the literature and as such we have focused on references to include primary research articles only.

VERSION 2 – REVIEW

REVIEWER	Francisco Caramelo Faculty of Medicine, University of Coimbra, Portugal
REVIEW RETURNED	22-Oct-2020

GENERAL COMMENTS	The authors improved the manuscript, corrected all aspects mentioned, and answered all the questions referred to in the first round of review.

REVIEWER	Amer Harky Liverpool
REVIEW RETURNED	07-Oct-2020

GENERAL COMMENTS	Thanks for the revised work, although you have included data from a large centre in UK, however the major limitation from your work comes from your included data which is ending till 13th May 2020 (which is < 2 month worth of data since the lockdown in UK) and considering that we are now in October and within the second wave of COVID-19, it will be more robust, appropriate and valid if you include data on your patients at least till end of first wave (end of July). This will make it more feasible for your conclusions and the readership of the journal to understand the impact of COVID-19 on BAME.

VERSION 2 – AUTHOR RESPONSE

Response to reviewer 2:
We thank the reviewer for their comment. As demonstrated by Figure S2 showing the inclusion time period by cases admitted to Barts Health, the recruitment window encompassed the peak and vast majority of the first wave of COVID-19 disease in East London. The analysis was completed shortly after the follow-up date and we submitted this manuscript in June. Given that the second wave is here, the impact of the findings from this analysis are important in informing our evolving clinical management and minimising the impact of COVID-19 upon the BAME community. Any further delay in publication would not be warranted.