PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Ethnic variation in outcome of people hospitalised during the first COVID-19 epidemic wave in Wales (UK): An analysis of national surveillance data using Onomap, a name-based ethnicity classification tool
AUTHORS	Thomas, Daniel; Orife, Oghogho; Plimmer, Amy; Williams, Christopher; Karani, George; Evans, Meirion; Longley, Paul; Janiec, Janusz; Saltus, Roiyah; Shankar, Ananda

VERSION 1 – REVIEW

REVIEWER	Ali, Hamad Dasman Diabetes Institute
REVIEW RETURNED	04-Feb-2021

GENERAL COMMENTS	Emerging indications have suggested a possible implication for ethnicity and race as contributors to the wide disparity in COVID-19 outcomes. It is now well established that differences in COVID-19 related hospitalization and death rates are influenced by ethnicity. In the presented manuscript, authors show that ethnic minorities in Wales are more likely to be admitted to ICU when encountering COVID-19 than those classified as 'white'. However, results showed no significant differences in mortality rates. Limitations: - In term of structure, the introduction is too short must be re written to properly presenting the topic of ethnicity influence on COVID-19 outcomes. - One of the major limitations in the presented work is the lack of data on comorbidity prevalence in the cohort. When adjusted for diabetes, hypertension, obesity, etc. the OR might change. - No age distribution is shown for each ethnic group which might be helpful in results interpretation. - Possible explanations for results obtained are inadequate. - Tables are poorly presented. I think this work requires major revisions and is more suitable for a short report or communication but defiantly not full length research paper.

REVIEWER	Lassale, Camille Institut Hospital del Mar d'Investigacions Mediques
REVIEW RETURNED	25-Feb-2021

GENERAL COMMENTS	Nice concise paper on ethnic disparities of COVID-19 test and in-hospital mortality, with data from Wales. The results on non-British

	whites is novel. The name-based ethnicity classification appears as the major weakness of this study and the results of the validation studies are not particularly encouraging (a specificity of 77% is not considered "high"). Moreover the authors should explain their definition of sensitivity and specificity in greater detail as they are not straightforward. The adjustment is only minimal and is also a problem, although it is already discussed. In some ethnic groups, numbers are very low for the hospitalized patient analysis, and more caution should be given when interpreting these results. In Table 2, why are all cells with number <10 presented as such except Unknown ethnicity? Also, I would suggest dropping the Unknown category which is a mixed bag and is not interpretable as such. The presentation of data is not easy to follow in the text, but the tables and figure are fine. Please consider expanding the text for a clearer message. Abstract line 36-40: I do not understand this sentence. Some references should be added in the Discussion. For example, page 13 line 24-29 this sentence should be supported by references.

REVIEWER	Mathur, Rohini London School of Hygiene and Tropical Medicine, Department of Non-Communicable Disease Epidemiology
REVIEW RETURNED	01-Mar-2021

GENERAL COMMENTS	This study reports on ethnic differences in testing positive for SARS-CoV-2 amongst those tested and ethnic differences in the risk of COVID-19 ICU admission and mortality amongst those hospitalised with COVID-19. The authors report good validity of the ONOMAP tool which reaches 97-99% completeness of ethnicity for the study population.The study highlights important ethnic differences in testing and ICU admissions - with risk of ICU admission particularly high in Bangladeshi groups. Reassuringly, the authors report no ethnic differences in mortality amongst those admitted to hospital with COVID-19. This study adds important evidence to the ethnic patterning of COVID-19 in Wales. I have some concerns over the interpretation of the findings and the appropriateness of the conclusions. I have made some suggestions which I hope are useful to the authors. Abstract: 1. The objective doesn't reflect the design - may be better to state to describe ethnic differences in SARS-CoV-2 testing, ICU admissions, and mortality. Methods: 2. I would strongly suggest removing the analysis comparing white to BAME populations Ethnic minority groups are heterogenous with different lived experiences, migration histories, and health/lifestyle characteristics. Grouping them together implies that these groups

	are interchangeable and defined primarily by their otherness. Scientifically, we would not expect these diverse groups to experience similar risks of SARS-CoV-2 exposure/infection and outcomes. Such perpetuation of simple categories is not useful in progressing our understanding of ethnic disparities in health. For example, previous research in the UK has shown that Chinese ethnic groups experience lower risks of most health outcomes, including COVID-19 - a very large aggregate category erases this important variation and is meaningless to interpret clinically or for public health/policy planning. This recommendation has been highlighted in the media https://www.bbc.co.uk/news/uk-53194376 And in the recent report by the Race Disparities Unit released last week which states “As different ethnic groups experience different outcomes, it is not analytically useful to aggregate all ethnic minority groups under a heading of “BAME” or to draw conclusions about COVID-19 outcomes by looking only at aggregated data for all ethnic minorities. It is vital to understand the differences between ethnic groups and to consider the circumstances that may have contributed to health inequalities from COVID-19.” https://www.gov.uk/government/publications/second-quarterly-report-on-progress-to-address-covid-19-health-inequalities/second-quarterly-report-on-progress-to-address-covid-19-health-inequalities 3. Given that the authors have information on the % tested and % testing positive, I am curious as to why there isn’t a more formal analysis of ethnic differences in odds of being tested or testing positive. This would strengthen the paper and make it more cohesive as the authors could apply the same methodology across all outcomes of interest (ethnic differences in the odds of being tested, testing positive, ICU admission, mortality) 4. Did the authors have access to information on COVID-19 mortality in the general population? Or only those admitted to hospital? This has important implications for interpretation of ethnic differences in the outcome. For example, are there ethnic differences in the odds of COVID-19 mortality outside of hospital (perhaps due to severity of the disease or potential lack of space in hospitals and ICUs)? Discussion: 5. A key factor affecting the interpretation of these findings is selection bias, which is not mentioned in the interpretation of the findings. While the authors do mention that ethnic differences in test positive rates may be due to differences in testing policy, some further interrogation of this would be welcome. For example: Testing during the first wave was not population based. In England testing was prioritized for healthcare workers and those admitted to hospital with COVID. Even now, though testing is much more widely available, it is unclear whether those receiving a test represent the general population. It would be important for the authors to comment on this. Differential access to testing or knowledge about testing availability may explain why fewer tests were conducted in non-white groups than in white groups. Furthermore healthcare workers or those in other

	frontline/person facing occupations may have been receiving more regular testing, and this may differ by ethnicity. 6. Related to this, the statement that the finding of no ethnic differences in mortality being at odds with other data sources would benefit from some more careful interpretation Many other studies reporting excess mortality risks in ethnic minority groups in the UK examined a) ethnic differences in mortality using the general population as a denominator b) mortality both in and out of hospital. The fact that the authors look at in-hospital death amongst those hospitalized may account for some of the differences with other studies. For example, the proportion of people dying without ever being admitted to hospital may differ by ethnic group. It may be that once ethnic disparities may stem from stages along the care pathway prior to hospital admission, and that those not admitted to hospital are different from those who are. 8. Is it possible that there are ethnic differences in COVID-19 deaths amongst those who were never tested for SARS-CoV-2? These people would not meet the definition of death within 28 days of a positive test. 9. The conclusion that 'Primary, secondary, and tertiary prevention should target BAME communities in Wales' is quite vague and doesn't really stem from the findings of this particular study or point to specific recommendations for public health planning or policy. Minor points: The Williamson et al. Publication can now be updated from a MedRxiv preprint to published.

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1
Dr. Hamad Ali, Dasman Diabetes Institute Comments to the Author:
Emerging indications have suggested a possible implication for ethnicity and race as contributors to the wide disparity in COVID-19 outcomes. It is now well established that differences in COVID-19 related hospitalization and death rates are influenced by ethnicity.
In the presented manuscript, authors show that ethnic minorities in Wales are more likely to be admitted to ICU when encountering COVID-19 than those classified as 'white'. However, results showed no significant differences in mortality rates.

Limitations:
- In term of structure, the introduction is too short must be re written to properly presenting the topic of ethnicity influence on COVID-19 outcomes.

We have kept the introduction relatively short, but have expanded and updated the discussion section to take into account new information, including about the second wave and about ethnic variation in vaccination uptake. As the paper presents data from the first wave, we thought it was more logical to present the information as known at the time of the analysis, but to include new understanding later in the paper.

- One of the major limitations in the presented work is the lack of data on comorbidity prevalence in the cohort. When adjusted for diabetes, hypertension, obesity, etc. the OR might change.

We agree with the reviewer on this point. Unfortunately, these data are not available in our routine surveillance. We have listed this up front as a limitation of the study. This is currently being addressed through a further study using data linkage, and a sentence has been added to the discussion to this effect.

- No age distribution is shown for each ethnic group which might be helpful in results interpretation.

In the results section we state that the median age of hospitalised black, Asian and minority ethnicity individuals was 53 years compared to 76 years for White individuals ($p<0.01$; Mann Whitney 2 sample test). We could present these data for each ethnic group but numbers would be small.

- Possible explanations for results obtained are inadequate.

We have expanded an updated the discussion.

- Tables are poorly presented.

We have dropped one table and included a second forest plot.

I think this work requires major revisions and is more suitable for a short report or communication but defiantly not full length research paper.

We have added some new analysis and revised the discussion to take into account new thinking on this topic.

Reviewer: 2
Dr. Camille Lassale, Institut Hospital del Mar d'Investigacions Mediques Comments to the Author:
Nice concise paper on ethnic disparities of COVID-19 test and in-hospital mortality, with data from Wales. The results on non-British whites is novel.

Thank you for this comment. That the White-Other group is at increased risk strengthens the hypothesis that ethnic disparities are socio-economic in basis. We've added something to the discussion to this effect.

The name-based ethnicity classification appears as the major weakness of this study and the results of the validation studies are not particularly encouraging (a specificity of 77% is not considered "high"). Moreover the authors should explain their definition of sensitivity and specificity in greater detail as they are not straightforward.

We agree with the reviewer that using name-based classification is a limitation, albeit that the software that we use has been deployed in at least 30 previous studies in healthcare, public health and epidemiology (and more widely in social equity audits in housing, management and social media). What all of these many published applications have in common is absence of ethnicity recording and our firm view is that ethnicity estimation facilitates scientific investigation with margins of error that are understood. Moreover, many of the existing studies where individual-level ethnicity is available have missing data, and are not without their own classification bias. From anecdotal reports, members of minority ethnic groups are more likely to defer from reporting their ethnicities, and clinician-based recording is often incorrect. The discussion has been expanded to include these

points.

The adjustment is only minimal and is also a problem, although it is already discussed.

In some ethnic groups, numbers are very low for the hospitalized patient analysis, and more caution should be given when interpreting these results.
In Table 2, why are all cells with number <10 presented as such except Unknown ethnicity? Also, I would suggest dropping the Unknown category which is a mixed bag and is not interpretable as such.

We include 'unknown' for completeness, and for the reasons given above. We have changed the tables so all small numbers are presented as <10.

The presentation of data is not easy to follow in the text, but the tables and figure are fine. Please consider expanding the text for a clearer message.
Abstract line 36-40: I do not understand this sentence.

We have read through the results section and simplified where possible. Abstract sentence in lines 36-40 has been simplified.

Some references should be added in the Discussion. For example, page 13 line 24-29 this sentence should be supported by references.

The discussion has been updated and some new references added.

Reviewer: 3
Dr. Rohini Mathur, London School of Hygiene and Tropical Medicine, Queen Mary University of London Comments to the Author:
This study reports on ethnic differences in testing positive for SARS-CoV-2 amongst those tested and ethnic differences in the risk of COVID-19 ICU admission and mortality amongst those hospitalised with COVID-19. The authors report good validity of the ONOMAP tool which reaches 97-99% completeness of ethnicity for the study population. The study highlights important ethnic differences in testing and ICU admissions - with risk of ICU admission particularly high in Bangladeshi groups. Reassuringly, the authors report no ethnic differences in mortality amongst those admitted to hospital with COVID-19. This study adds important evidence to the ethnic patterning of COVID-19 in Wales. I have some concerns over the interpretation of the findings and the appropriateness of the conclusions. I have made some suggestions which I hope are useful to the authors.

Abstract:
1. The objective doesn't reflect the design - may be better to state to describe ethnic differences in SARS-CoV-2 testing, ICU admissions, and mortality.

Thanks, we have changed as suggested.

Methods:
2. I would strongly suggest removing the analysis comparing white to BAME populations Ethnic minority groups are heterogenous with different lived experiences, migration histories, and health/lifestyle characteristics. Grouping them together implies that these groups are interchangeable and defined primarily by their otherness. Scientifically, we would not expect these diverse groups to experience similar risks of SARS-CoV-2 exposure/infection and outcomes. Such perpetuation of simple categories is not useful in progressing our understanding of ethnic disparities in health. For example, previous research in the UK has shown that Chinese ethnic groups experience lower risks of most health outcomes, including COVID-19 - a very large aggregate category erases this important

variation and is meaningless to interpret clinically or for public health/policy planning.

This recommendation has been highlighted in the media
https://scanmail.trustwave.com/?c=261&d=pre_4Njl-WoEjJ_TKRan1YIQ34S695CXQWMfZYyslA&u=https%3a%2f%2fwww%2ebbc%2eco%2euk%2fnews%2fuk-53194376

And in the recent report by the Race Disparities Unit released last week which states “As different ethnic groups experience different outcomes, it is not analytically useful to aggregate all ethnic minority groups under a heading of “BAME” or to draw conclusions about COVID-19 outcomes by looking only at aggregated data for all ethnic minorities. It is vital to understand the differences between ethnic groups and to consider the circumstances that may have contributed to health inequalities from COVID-19.”

https://scanmail.trustwave.com/?c=261&d=pre_4Njl-WoEjJ_TKRan1YIQ34S695CXQTxLYo-skg&u=https%3a%2f%2fwww%2egov%2euk%2fgovernment%2fpublications%2fsecond-quarterly-report-on-progress-to-address-covid-19-health-inequalities%2fsecond-quarterly-report-on-progress-to-address-covid-19-health-inequalities

The reviewer makes a very good point. Since this paper was put together there has been much discussion and debate about this.

Firstly, we have now taken on the recommendation of the Socio-economic sub group of the Welsh Government First Minister’s Group on BAME and COVID-19, that the term ‘BAME’ should no longer be used. Whilst it is clear that the term ‘BAME’ should not be used, what is less clear is how best to refer to ethnic minorities, with some preferring ‘minority ethnic group’, some ‘BME’. In our revised paper we have substituted ‘BAME’ with ‘BME’, largely for technical reasons as ‘White-other’, an important minority group in Wales has been included with ‘White – British’ and ‘White-Irish’ in our analysis (see: Writing about ethnicity - GOV.UK (ethnicity-facts-figures.service.gov.uk). We hope this is acceptable.

The second point, is the one about aggregating minority ethnic groups together. Whilst we as an authorship group completely agree with reviewer 3 that ‘BME’ or ‘BAME’ are highly heterogeneous in their racial backgrounds and lived experiences, what minority ethnic populations have in common is their minoritisation and the impact this has on all facets of their life. Minority status and the host of structural factors underpinning health inequalities can be seen to have an overdetermining impact. Work of the First Ministers Group has identified structural racism as an important factor in COVID-19 epidemiology. This will be experienced to varying degrees by all Black and Asian minority ethnic groups, irrespective of heritage or whether first, second or third generation. Indeed, the situation in Wales is quite complex with a relatively high proportion of people of mixed ethnicity who have lived in Wales for many generations, but are still afforded minority status.

In short, we are keen to keep our epidemiological approach of first comparing BME and White ethnicities, then drilling down in more detail to look at specific ethnicities. We feel we have successfully shown that Bangladeshi and White-other groups are particularly vulnerable to COVID-19. The latter finding is novel.

3. Given that the authors have information on the % tested and % testing positive, I am curious as to why there isn’t a more formal analysis of ethnic differences in odds of being tested or testing positive. This would strengthen the paper and make it more cohesive as the authors could apply the same methodology across all outcomes of interest (ethnic differences in the odds of being tested, testing positive, ICU admission, mortality)

We are grateful for this comment and have carried out some new analysis. Odds of testing positive after adjustment for age, sex and deprivation have been calculated and a forest plot added. We think this additional analysis strengthens the paper.

4. Did the authors have access to information on COVID-19 mortality in the general population? Or only those admitted to hospital? This has important implications for interpretation of ethnic differences in the outcome. For example, are there ethnic differences in the odds of COVID-19 mortality outside of hospital (perhaps due to severity of the disease or potential lack of space in hospitals and ICUs)?

Unfortunately, we only had access to in-hospital deaths. We've added a comment on this in the discussion.

Discussion:
5. A key factor affecting the interpretation of these findings is selection bias, which is not mentioned in the interpretation of the findings. While the authors do mention that ethnic differences in test positive rates may be due to differences in testing policy, some further interrogation of this would be welcome.

For example:
Testing during the first wave was not population based. In England testing was prioritized for healthcare workers and those admitted to hospital with COVID. Even now, though testing is much more widely available, it is unclear whether those receiving a test represent the general population.

It would be important for the authors to comment on this. Differential access to testing or knowledge about testing availability may explain why fewer tests were conducted in non-white groups than in white groups. Furthermore healthcare workers or those in other frontline/person facing occupations may have been receiving more regular testing, and this may differ by ethnicity.

Good points. We have expanded the discussion to include this.

6. Related to this, the statement that the finding of no ethnic differences in mortality being at odds with other data sources would benefit from some more careful interpretation Many other studies reporting excess mortality risks in ethnic minority groups in the UK examined a) ethnic differences in mortality using the general population as a denominator b) mortality both in and out of hospital. The fact that the authors look at in-hospital death amongst those hospitalized may account for some of the differences with other studies. For example, the proportion of people dying without ever being admitted to hospital may differ by ethnic group.
It may be that once ethnic disparities may stem from stages along the care pathway prior to hospital admission, and that those not admitted to hospital are different from those who are.

Thank you for this comment. We've added something to the discussion on this.

8. Is it possible that there are ethnic differences in COVID-19 deaths amongst those who were never tested for SARS-CoV-2? These people would not meet the definition of death within 28 days of a positive test.

Does the reviewer consider that BME people might be more likely to die of COVID-19 without a positive SARS-CoV-2 test? Whilst possible, we are not sure how we could look at this without doing some kind of wider study of all cause mortality. We agree that this is a limitation, and as above, have added it to the discussion.

9. The conclusion that 'Primary, secondary, and tertiary prevention should target BAME communities

in Wales' is quite vague and doesn't really stem from the findings of this particular study or point to specific recommendations for public health planning or policy.

Thanks. We agree. The discussion has been expanded to give some example of more recent preventative work being carried out.

Minor points:
The Williamson et al. Publication can now be updated from a MedRxiv preprint to published.

Thanks. Updated.

VERSION 2 – REVIEW

REVIEWER	Lassale, Camille Institut Hospital del Mar d'Investigacions Mediques
REVIEW RETURNED	14-May-2021

GENERAL COMMENTS	Nice revision, the paper is improved. However I was surprised not to see a point by point response to the referee's comments

REVIEWER	Mathur, Rohini London School of Hygiene and Tropical Medicine, Department of Non-Communicable Disease Epidemiology
REVIEW RETURNED	04-May-2021

GENERAL COMMENTS	I thank the authors for their considered responses to my comments. I think the paper has been strengthened greatly by the additional analyses, the clarification of wording in the abstract and methods, and by the more detailed and nuanced discussion section. I agree with the reviewers decision/argument for keeping minority ethnic groups together for some of the reported results as these are disaggregated later on. The new results on testing are interesting and in-line with what has been reported in other parts of the UK- this paper now reads like a more comprehensive appraisal of ethnic inequalities in Wales and the value of the ONOMAP tool in assessing this.