Several studies have reported a higher rate of COVID-19 mortality in men.[1–6] A higher rate of COVID-19 mortality has also been reported in black and minority ethnic (BAME) groups,[6–8] especially among the healthcare providers.[9,10]

The exact reasons for these disparities are not known but may be due to differential susceptibility based on biological sex,[11] as well as gender differences in health behaviors (e.g. smoking, physical activity) giving rise to differences in comorbidities (e.g., cardiovascular disease) that increase the risk of COVID-19 mortality in men.[12] However, there are social influences that could make women more susceptible to exposure and infection compared to men, e.g., women are more likely to be involved in service sector work/healthcare.[6,12] In regards to ethnic differences, people from BAME background may be more likely to be in frontline, exposed, jobs; they may be more likely to live in overcrowded multi-generation households making it challenging to maintain physical distancing from elderly family members.[13]

In the context of gender and ethnic differences in COVID-19 mortality, additional important policy-related issues include our understanding of (i) whether there are ethnic variations in COVID-19 mortality in men and women, (ii) whether there is heterogeneity in gender differences within individual ethnic groups, and (iii) whether we could identify some factors that may help explain these disparities, if any.

Most studies of COVID-19 mortality have statistically "adjusted" for factors (e.g., socioeconomic deprivation) that may potentially help to explain gender and ethnic disparities.[14] While often necessary, these adjustments are seldom sufficient.[15]*"sufficient" for what? Meaning of this sentence is unclear. You can probably drop it. Frequently, we do not have complete information on the causal pathways. Many known or hypothesised factors that could account for gender/ethnic disparities in health are not readily available in routine health records[15] and methodological and analytic approaches may also affect these conclusions.

For example, in the context of COVID-19 mortality, if sex is "adjusted" in a statistical model, it assumes that the ethnicity-specific risk estimates are fixed in men and women i.e., it renders invisible any heterogeneity in gender differences within individual ethnic groups. Similarly, if ethnicity is adjusted, the model assumes that the gender-specific risk estimates are fixed in different ethnic groups i.e., it masks any ethnic variation in men and women. Therefore, just because an association is reported as 'adjusted', it is no panacea.

We elaborate these issues further drawing on results from three recent reports published using the UK data. The OpenSAFELY study reported that the COVID-19 mortality risk in men was twice as high compared to women.[3] Since this study adjusted for both gender and ethnicity, it assumes that the

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increased risk of COVID-19 mortality in men is fixed regardless of ethnicity, and that the ethnicity-specific risks are also fixed in men and women. However, the results from the UK Office for National Statistics (ONS) showed that there was substantial heterogeneity in the risks of COVID-19 mortality in different ethnic groups, both in men and women.[7]

However, the ONS results do not allow the comparison of risks in men and women within individual ethnic groups because the study estimated the risk in men against White men, and that in women against White women. Therefore, to be able to directly compare the gender-specific risks in COVID-19 mortality in individual ethnic groups, we need to precisely know the gender difference in COVID-19 mortality in the reference (White) population. The unadjusted risk in White men (compared to White women) was approximately 1.5 in the ONS study,[7] while the age-adjusted risk was approximately 2.0 in the recent study by Public Health England (PHE).[6] Applying these estimates (1.5 and 2.0) to the ONS regression results, we find that the increased risk in men varies considerably across the ethnic groups (depending on the ONS statistical models, the risk in men varies between 1.3 and 3.5 times that in women).

After adjusting for a range of socioeconomic and structural factors, the ONS study showed that a considerable portion of ethnic variability could be explained by socioeconomic and structural factors (e.g., deprivation, household composition, regional variabilities). However, we do not know if this is true for gender differences within individual ethnic groups. In the context of gender differences in COVID-19 mortality, it will be invaluable to understand whether the differences in men and women could potentially be explained by determinants related to biological sex or to social factors (gender). These findings will help shape individualised policies on the prevention and treatment of COVID-19.

A growing body of research is attempting to examine the relationship between sex hormones and COVID-19 susceptibility, which could potentially help explain the sex (biological) differences.[11] Future studies should explore the effects of additional factors, including (but not limited to) pattern, sequence, and duration of multimorbidity, on COVID-19 susceptibility/mortality within the context of individual ethnic groups to disentangle these issues.

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