# The missing link in ethnicity and covid-19 research – time to separate the risk of infection from the risk of severe disease

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Ethnic minority groups, such as those of Black and Asian backgrounds, continue to be disproportionately affected by covid-19.[1] A large number of studies have emerged investigating the relationship between covid-19 and clinical outcomes, often with conflicting results, especially as to whether those of ethnic minority groups are at increased risk of infection, intensive therapy unit (ITU) admission, and death.[2] These studies usually follow one of three approaches. The first kind of study investigates patients with confirmed or clinically suspected covid-19 in a hospital setting and assesses whether ethnicity is a predictor of severe disease, by looking at rates of ITU admission or mortality. The second are transmission studies which use a community dataset to investigate the role of ethnicity and infection from covid-19. The third involve large datasets representative of a population linked to national databases of death from covid-19. All three studies can be extremely large (ranging from 5 million to over 13 million) and therefore thought to be robust, especially when multiple key confounders, such as age, comorbidity, socioeconomic status and deprivation are adjusted for.[3–5]

Although all of these studies ask relevant research questions, none so far make the distinction between the risk of infection and the risk of severe disease once infected. Variables relating to both outcomes are often grouped together and consequently, the ability to delineate differences in risk by ethnic background continues to be severely inhibited. For example, whilst studies of hospitalized cohorts can adjust for differences between ethnic groups at admission, they miss the crucial information of those who were infected but did not present or get admitted to hospital – which can only be adjusted for in studies which encompass both community and hospitalized patients. However, no transmission studies present the proportion of patients hospitalized, or had died from covid-19, and no population studies investigating the role of

ethnicity have yet adjusted for the simple risk of testing positive for covid-19 when examining mortality.

Compared to non-communicable diseases, where predictors for the development and progression of cardiovascular, chronic lung disease, or chronic kidney disease are similar (eg, smoking, lifestyle habits and the presence of other comorbidities), the risk of getting covid-19 is more related to settings where high intensity, long-duration interactions occur, such as within households or workplaces with poor ventilation, with no definitive evidence yet of an association between environmental virus exposure and subsequent disease severity.[6,7] The risk of severe covid-19 on the other hand is related to obesity, older age, and cardiometabolic comorbidities.[8] In other words, factors relating to increased risk of infection are more likely to be in the public health domain, compared to factors relating to increased risk of disease severity, which are more biological. Ethnicity, being a social construct is intrinsically related to all these variables—but it remains uncertain whether the risk is mainly weighted towards risk of infection or severity of disease.

The simplest method of addressing this problem is for large population studies to acquire data on the number of participants that have been infected with SARS-CoV-2, and adjust for this in subsequent analysis on hospitalization or death. In the UK, this can be done by linking with Pillar 1 and Pillar 2 data from Public Health England, which include community and hospital test results.[9] Transmission studies investigating factors relating to the risk of SARS-CoV-2 infection in the community should also expand to explore how the risk of infection contributes to ITU admission and mortality as secondary outcomes. Finally, prospective biomarker, therapeutic, and vaccine trials must also investigate markers of disease severity or therapeutic efficacy in relation to ethnic group. Recently, the Pfizer BioNTech vaccine appears to be equally

effective across multiple ethnic groups, suggesting that the disproportionate risk of covid-19 on clinical outcomes in these groups may be more likely to be related to increased exposure to the virus rather than severe disease.[10]

If ethnicity is more strongly associated with an increased risk of infection, it would be important to communicate to the general population that for most, simply belonging to an ethnic minority group does not mean they are more likely to die if they get covid-19. A targeted public health approach, focused on risk factors relating to increased risk of infection in ethnic minority groups would also prevent disproportionate death. This will be of particular importance given the emergence of two new variants of SARS-CoV-2 in the UK, both of which appear to have increased infectivity.[11,12] However, should ethnic minorities be found to mainly have a higher risk of disease severity once infected, this provides a powerful argument for the early initiation of effective therapeutics, including prioritising vaccination to these cohorts. To move forward with covid-19 public health policies involving ethnic groups, it is time we acknowledge that the risks of infection are very different to those for severe disease.

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**Declaration of interests**

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