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DATA NOTE

Younger ages at risk of Covid-19 mortality in communities of color [version 1; peer review: 2 approved]

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Abstract
More than 85% of Covid-19 mortality in high income countries is among people 65 years of age or older. Recent disaggregated data from the UK and US show that minority communities have increased mortality among younger age groups and in South Africa initial data suggest that the majority of deaths from Covid-19 are under 65 years of age. These observations suggest significant potential for increased Covid-19 mortality among younger populations in Africa and South Asia and may impact age-based selection of high-risk groups eligible for a future vaccine.

Keywords
COVID-19, Africa, Youth, Mortality, Communities of Color
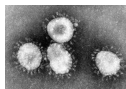
This article is included in the Coronavirus (COVID-19) collection.

Open Peer Review

Reviewer Status ✔ ✔

	Invited Reviewers	
	1	**2**
version 1 26 Jun 2020	✔ report	✔ report

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Any reports and responses or comments on the article can be found at the end of the article.

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Author roles: Klugman KP: Formal Analysis, Writing – Review & Editing; **Zewdu S**: Writing – Review & Editing; **Mahon BE**: Data Curation, Formal Analysis, Writing – Review & Editing; **Dowell SF**: Writing – Review & Editing; **Srikantiah P**: Writing – Review & Editing; **Laserson KF**: Validation, Visualization, Writing – Review & Editing; **Tappero JW**: Writing – Review & Editing; **Zaidi AK**: Writing – Original Draft Preparation, Writing – Review & Editing; **Mundel T**: Writing – Review & Editing

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Developed countries, even those overwhelmed for a time by Covid-19 like Italy and the UK, have had most of their deaths among the elderly. In Italy, with one of the oldest populations in the world, only 4% of deaths were in people under age 60[1]. This has led to speculation that Africa and South Asia, with younger populations, may be spared most of the mortality of this pandemic. Recent national data from the UK, US and South Africa suggest that this may not be the case.

In the UK, the racial disparity in Covid-19 mortality is clear, with non-white minorities dying at higher rates than whites[2]. The reasons for this disparity are not yet clear but may include higher rates of exposure due to socio-economic factors reducing ability to social distance, poorer access to or quality of care, and / or higher rates of severe disease among infected persons. In England and Wales, black males are 4.2 times more likely to die of Covid-19 than are white males, and black women are 4.3-fold more likely to die of Covid-19 than white women, in analyses adjusted for differences in age between these communities[2].

In addition, England and Wales have reported concerning racial differences in age at death from Covid-19. Although age-specific death rates have not yet been reported for different racial groups, just 9.8% of white patients in England and Wales who died of Covid-19 were under age 65, whereas among those with black ancestry, 24.2% were under age 65, as were 20.9% of those with ancestry from India, Bangladesh or Pakistan[2]. In sum, the data from the UK[2] show both excess mortality, particularly in black communities, and increased proportions of death in younger age groups. This pattern cannot be explained just by younger age structure in these communities. Age is the most important risk factor for Covid-19 mortality in all these communities[2]. Therefore, in communities with younger age structures it is expected that there would be less total mortality, not more mortality, than in older age structured communities. The excess mortality at younger ages relative to Caucasian people in the UK therefore reflects excess risk—of exposure, of severe disease in infected persons, or both—despite younger age.

Similar concerning data have now been released by the CDC[3], showing that, while just 9.7% of white Americans who die from Covid-19 are under 65 years of age, that percentage among black Americans is 24.2%. Among Hispanic Americans 35.6% are less than age 65 at the time of their Covid-19-related death, as are 40.4% of American Indians or Alaska Natives, and 42.9% of Hawaiians or Other Pacific Islanders.

Major comorbidities for Covid-19 mortality, including diabetes, hypertension and chronic lung disease are concentrated in poorer communities, as illustrated in data from across multiple counties in the US[4].

These data thus may pose major problems for both South Asia and Africa, where poverty and lack of access to care may further increase risk of these risk factors for Covid-19 mortality. Major comorbidities that increase the risk for severe Covid-19 disease may explain some of this disparity in mortality. Untreated hypertension and diabetes are increasing rapidly in Africa and South Asia, particularly in urban centers. A 2017 paper surveying a representative sample of 16,287 adults over age 2, in three cities in South Asia--Chennai, Delhi and Karachi--documented that 30.1% of men and 26.89% of women living in those cities had hypertension, with only 1/7 on treatment[5]. The Covid-19 pandemic portends greater mortality at younger ages in these settings than in rich countries with generally better access to care of comorbid conditions.

As of the first week of June 2020, the epidemic continues to expand in Latin America, and is gaining significant momentum in both South Asia and Africa. In the data on the first 752 Covid-19 deaths with known age in South Africa, 66.4% were aged less than 65[6]. While only 5% of the South African population at their last census were aged 65 or older, fully 26.5% of the population is 40-65 years of age, the age group associated with 58% of deaths[6]. The majority of deaths in South Africa at this early stage of their epidemic are in the Western Cape, reflecting increased risk of importation from travelers, and the increase in deaths at younger ages is becoming more pronounced each week, as local transmission in poor communities increases[6]. In the past week the first preliminary data on poor quality of care as a risk for Covid-19 mortality have been presented for the Western Cape in South Africa[7], showing increased mortality for people with untreated and poorly treated diabetes, compared to well controlled diabetes. Also, the first data suggesting HIV infection may increase risk for Covid-19 mortality have just been released. These data are not yet published or peer-reviewed, but if they hold up under review, they will suggest significantly increased risks for mortality in younger South Africans consistent with the large fraction of deaths in younger age groups[6].

These data raise important questions on implications for access to what are likely to be limited initial quantities of a vaccine. While many factors will determine access to vaccine and specific groups such as first responders may get first access to vaccine, age-based indications for early doses of Covid-19 vaccines will be confounded by these data. Will age-based risk be taken into account to protect the majority of those at risk for age related Covid-19 mortality? This is not only a global question, it also will need to be addressed in the US, as shown in Table 1, where vaccine given at ages 65 years of age and above addresses 90% of the mortality burden in non-Hispanic white people, but only 64% of Hispanic or Latino people and 57% of Hawaiian and other Pacific Islanders.

Table 1. **US Covid-19 mortality data from the National Center for Health Statistics[3].** Bold numbers indicate the age group above which 89% or more of covid-19 deaths have occurred.

Age	All	Non-Hispanic White	Non-Hispanic Black	Non-Hispanic Indian or Alaska Native	Non-Hispanic Asian	Non-Hispanic Hawaiian and other Pacific Islander	Hispanic or Latino
All	88243	46965	20288	463	4648	63	14455
≥65	71186 (81%)	**42196 (90%)**	14723 (73%)	276 (60%)	3621 (78%)	36 (57%)	9316 (64%)
≥55	**81772 (93%)**		**18195 (90%)**	363 (78%)	**4282 (92%)**	49 (78%)	11976 (83%)
≥45				**413 (89%)**		**56 (89%)**	**13516 (94%)**

Equitable age-based vaccination strategies will need to consider adjustment for age specific patterns of mortality in some communities.

Data availability
All data underlying the results are available as part of the article and no additional source data are required.

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   Reference Source

2. Office for National Statistics: **Coronavirus (COVID-19) related deaths by ethnic group, England and wales: 2 March 2020 to 10 April 2020.** 2020.
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   Reference Source

Open Peer Review

Current Peer Review Status: ✓ ✓

Version 1

Reviewer Report 14 July 2020

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This article, published on Gates Open Research, discusses the emerging evidence that people of younger age in minority communities are at increased risk of death from COVID-19 when compared with people living in high income countries, where most deaths occur in the elderly.

This issue is raised by the authors in consideration of the implications this may have on access to what are likely to be limited initial quantities of a vaccine for this infection. The authors further indicate that risk factors for COVID-19 severity and mortality, such as diabetes mellitus, hypertension, and chronic lung disease, are more common in poorer communities; many studies suggest that these are occurring at younger ages. Coupled with poverty, reduced ability to practice social distancing, possible lack of access to care, and resultant poor treatment, this may place younger people in these communities at greater risk of COVID-19 mortality.

While it is acknowledged by the authors that there will be many factors that will determine access to the vaccine, they suggest that simple age-based recommendations may be confounded by these facts, and if age based recommendations are introduced to protect those at risk of age related COVID-19 mortality, they will need to be adjusted for age-specific patterns of risk factors in certain communities.

While we would agree with these recommendations regarding age, there also needs to be consideration of the importance of much further research into what the exact factors are that are related to these community-based differences. This includes the additional consideration of the potential role of nutritional deficiencies, as well as obesity, genetic differences such as polymorphisms in the ACE2 receptor that may put some populations at greater risk, as well as our understanding of what treatments are being offered in different communities in cases with active COVID-19 infection. One important understanding that is still urgently needed is what the COVID-19 risk is for people living with HIV (PLWH). Although the

authors indicated that the initial data from Cape Town, South Africa, as yet not peer reviewed or published, suggested a greater risk for PLWH, data from a study from Johannesburg, South Africa, of their first 100 COVID-19 cases, suggested that PLWH were not at greater of COVID-19 infection than the general population, and none of the HIV-positive patients in their study had died (Zamparini *et al.*, 2020[1]). There have been other studies published that suggest that HIV is not a major risk factor, and knowledge of the real risk associated with HIV infection, as well as the other issues mentioned above, may assist in better stratifying risks in different populations and prioritising them for vaccine use. Perhaps these additional points should be included in the paper.

References
1. Zamparini J, Venturas J, Shaddock E, Edgar J, et al.: Clinical characteristics of the first 100 COVID-19 patients admitted to a tertiary hospital in Johannesburg, South Africa. *Wits Journal of Clinical Medicine*. 2020; **2** (2): 105-114 Reference Source

Is the rationale for creating the dataset(s) clearly described?
Yes

Are the protocols appropriate and is the work technically sound?
Yes

Are sufficient details of methods and materials provided to allow replication by others?
Yes

Are the datasets clearly presented in a useable and accessible format?
Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Respiratory infections, particularly community-acquired pneumonia, including COVID-19

We confirm that we have read this submission and believe that we have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Reviewer Report 10 July 2020

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There are a number of difficulties in following the age specific impact of Covid-19 in the middle of the pandemic when much of the information is tentative. However, that does not mean that analysis of epidemiologic findings should not be done. In fact, it is essential for planning purposes to use the data

that are available, with appropriate caveats. Issues in dealing with data on the differential impact of the pandemic in different racial and ethnic groups in the US include the lack of necessary information in many of the data sources available and also the very spotty nature of viral outbreaks. An example of the latter is the heavy contribution of nursing or care homes in terms of mortality data. Residents are typically older than the population from which they are drawn, and deaths in these outbreaks will skew the age distribution upward. While it is clear in the US that minority groups in major cities were more heavily infected and had worse outcomes, it is not clear why that is the case. As the pandemic evolves, it is becoming more definite that close contact over time is likely to increase likelihood of transmission, which is more common in disadvantaged communities. They also have more underlying conditions at a younger age, so the combination will lead to higher mortality at a younger age in these populations. The situation in the UK is similar in many respects. Of concern there is the fact that it is not clear how care home data are being handled. Also, there is significant suggestion that socioeconomic status is driving some of the racial/ethnic differences. There is even one report of little difference in that factor in a more affluent suburb of London, a report which is at odds with other reports of racial differences in health care workers and other populations.

The current data note examines distribution of deaths by age initially in the UK and in the US. It takes the position that, since deaths are occurring at lower ages in minority communities in these countries, it will probably also be the case in Africa and parts of Asia. The evolving situation in the Western Cape of South Africa is given in support. I agree with this conclusion but am concerned that there will also be another factor at play in following the severity of the outbreak in places which do not have the level of intensive care present in the US and UK, necessary to ensure survival. There also seems to be a systematic underreporting of Covid mortality going on in some of these countries, driven by deaths at home not being properly attributed and others in hospital being counted as being caused by the comorbidities and not by the SARS-CoV-2 virus. Those issues are not easily solved but should be factored into estimates of impact.

The note mainly uses proportions rather than estimated incidence or age specific mortality rates. That is based on the data available, but it might be more reflective of impact on, for example, the health care system to estimate what that would translate to in actual mortality rates.

Is the rationale for creating the dataset(s) clearly described?
Yes

Are the protocols appropriate and is the work technically sound?
Yes

Are sufficient details of methods and materials provided to allow replication by others?
Yes

Are the datasets clearly presented in a useable and accessible format?
Yes

Competing Interests: No competing interests were disclosed.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.