COVID-19: First data from Africa

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Africa is no stranger to infectious disease pandemics prior to SARS-CoV-2, with recent major outbreaks spanning ebola to listeria and measles, and ongoing high background incidence of malaria, HIV and TB. Most countries on the continent have severe health resource constraints, and the focus of many far richer countries hit by the SARS-CoV-2 epidemic – PCR-guided contact tracing to prevent spread, reliance on intensive-care and ventilation to deal with those who became severely ill - struck fear into African public health practitioners, health workers and the public, where sophisticated laboratory infrastructure and high-tech intensive care is often severely rationed (1).

There was speculation that the continent may be relatively protected from the worst of COVID by its younger population age structure (and fewer associated chronic comorbidities linked to COVID-19 mortality), limited public transport, possibly greater circulating seasonal coronaviruses, and even antiretroviral therapy programs with anti-coronavirus activity. However, the possibility of HIV and TB being risk factors for COVID severe events, both relatively unusual in the richer countries, could mean worse consequences in these populations (2).

Dr Mary-Anne Davies presents important data from the Western Cape Province, the epicenter for South Africa's initial wave of infections, in this edition of CID (3). South Africa as a major business and tourism hub was always likely to be one of the earliest African countries struck. Initial severe lockdown measures were announced in March as the first internal cases in international travelers were reported. Community seeding, especially in poorer and more densely populated communities, was delayed, but infections rapidly accelerated, and at the time of writing (late August 2020), the country has the fifth largest epidemic in the world (4).

This data is from an ongoing surveillance cohort that has previously generated rich data on disease patterns in the Western Cape, and currently continues to provide near real-time updates on the impact of PCR-confirmed SARS-CoV-2 on factors ranging from death to oxygen consumption within hospitals. Data from electronic clinical information systems is synthesized with laboratory, pharmacy and administrative data, providing a powerful population level dataset. Reported data from other national surveillance systems from across the country confirms much of Davies' findings, although her dataset is remarkable in its detail. Key strengths of the paper include a dataset covering over 3 million healthcare users in the Western Cape Province, and the use of both hospitalized and non-hospitalized cases and deaths

Davies' data shows similar mortality risk factors, including age, sex, diabetes (especially uncontrolled diabetes), hypertension and renal disease to other cohorts from richer countries.

The data do provide vital information on South Africa's other two continuing pandemics, with HIV and past or current TB all giving a roughly two-fold increased risk of death. Earlier reports from Europe and North America had not found a clear association with mortality, but they were limited by small sample sizes and selection biases. Davies' cohort had about 4000 HIV positive patients with COVID in it – about 40 times more than all the other published case series combined to date (5). The dataset shows an association between HIV infection and increased mortality, with a hazard ratio after adjusting for age, sex and other comorbidities of 2.14 (95% CI 1.7-2.7). The possibility of residual confounding exists, but Davies makes a plausible case for HIV being an independent risk factor for COVID-19-related death. Interestingly, Davies' dataset does suggest a higher mortality in HIV patients with virological failure and/or pre-COVID CD4 counts under 200 cells/μL compared with those who were virally suppressed, though there is substantial overlap in the confidence intervals,

and may be confounded by social factors associated with non-adherence, as well as COVID-19 mortality.

Whether antiretroviral therapy somehow mitigates COVID outcomes has been widely speculated in the HIV scientific literature, with in-vitro data suggesting tenofovir has activity against coronaviruses (6). Intriguingly, in the multivariate analysis Davies found that patients receiving tenofovir disoproxil fumarate as part of their antiretroviral therapy saw a statistically significant reduction in mortality (aHR 0.41, p=0.007). This supports observational data from a Spanish cohort that similarly suggested better outcomes for those on tenofovir-based antiretroviral therapy (5). However, extreme care should be taken interpreting the tenofovir data, as the association is at high risk of confounding and channeling bias. Patients not on tenofovir in South Africa are very likely to have underlying renal dysfunction, or be on second-line therapy, which is often again associated with coexisting social issues that may make them more vulnerable to COVID-19 consequences.

Davies' data again makes a substantial addition to the COVID-19 literature with respect to tuberculosis, a previously unreported topic. Both active tuberculosis and past tuberculosis were associated with an elevated risk of mortality in the study, the latter presumably on the basis of residual lung damage and consequent poor respiratory reserve.

What does this data mean for the rest of Africa? We should be wary of extrapolating too far –Africa has enormous diversity, and Western Cape demographics differ markedly even from the rest of South Africa. However, the data is broadly similar to other regions in the world, and so the immediate priority for African health systems remains to rapidly and practically design systems to protect the elderly and those with chronic diseases or TB.

For South Africa, a sigh of relief at a relatively small increase in mortality in HIV and TB should be quickly tempered; diabetes was the second commonest cause of death in the country pre-COVID-19, and most patients in the country have poor glucose control, a major risk factor from Davies' data (7). In addition, obesity is an independent risk factor for COVID-19 mortality in other cohorts, and while this was not collected in this dataset (weight and height was not available for this cohort), the country's obesity epidemic, especially among women, is well documented. Among HIV patients, again more among women, the large-scale introduction of dolutegravir in late 2019 may markedly aggravate obesity and COVID mortality in the near-6 million South African patients on antiretrovirals (8).

Sadly, South Africa has not learnt from other African countries and their epidemics (2). When ebola struck in West Africa, the consequence of locking down the society and suspending vaccine programs extracted a mortality from measles alone estimated to be similar to that from ebola (9). Initially lauded by the WHO for the speed and severity of COVID-19 lockdown measures, the South African response became increasingly militarised (over 200 000 people charged or incarcerated since the start), characterized by bizarre decisions on commerce, an incoherent PCR-based testing and tracing program, poor food support programs, corruption around procurement of personal protective equipment, and chaotic re-opening of schools, with a temporary decimation of vaccination and HIV and TB programs (10). The country will face years of continuing infectious and other diseases well beyond this SARS-CoV-2 era, that may well lead to a far greater mortality than COVID-19. Low-and-middle income countries will need to ponder future pandemic responses that pit any current epidemic against hard-won public health interventions.

Finally, the value of having integrated surveillance systems such as the Western Cape's that can rapidly inform urgent public health responses in real time are demonstrated in this paper. African governments and donors should invest more in these systems, as a major adjunct to public health programs.

Potential Conflicts of Interest

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