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presage rising HIV incidence during the precarious time ahead when HIV services need strengthening.

How might viral load metrics add to HIV prevention and treatment strategies? Individual viral load monitoring is crucial for patient management and is the global standard.<sup>7</sup> Clinic-aggregated viral load metrics are also now used to optimise HIV care delivery. However, viral load monitoring must be expanded and harnessed for maximum impact beyond individual and clinic-level care. We must shift population viral load metrics from the realm of observational epidemiology into triggers for rapid action to improve HIV prevention and care.<sup>128</sup>

The potential value of population viral load metrics for this purpose is two-fold. First, estimates of population viral load, which include people who are undiagnosed and people who are out of care, can help rapidly target resources to optimise the HIV care cascade spanning from diagnosis to linkage to retention (appendix). Second, PDV—by acting as a so-called community level biomarker of HIV incidence<sup>5,8</sup>—can allow for rapid and adaptive targeting of HIV prevention resources to areas of greatest need. Taken together, tracking community and population viral load and PDV can offer a roadmap to identify which HIV services need strengthening, where, and when.

These uses of viral load metrics might be particularly high-impact for PWID and MSM who are often harder to reach and durably engage, receive fewer direct services, have higher morbidity related to HIV and co-infections including hepatitis C, and are often subject to persistent criminalisation, stigma, and chronic underfunding of care.<sup>9</sup> In the authors' original trial, they successfully integrated HIV prevention and treatment services with other co-located services for these vulnerable populations.<sup>10</sup> Recently, this concept has burgeoned, and more tools for delivering streamlined multi-disease care have emerged. In the coming years, these tools will include novel longacting pre-exposure prophylaxis and ART, expanded service locations and times, and other innovations. The current study suggests that the impact of these efforts could be further improved by better use of viral load metrics to match resources to needs.

Viral load monitoring and aggregated population viral load metrics hold great promise for improving HIV care delivery and HIV prevention. Viral load is easily measured, and novel point-of-care viral load technologies are expanding. Investments in populationlevel data collection and analyses could enable viral load to serve as a warning indicator and spur to action, helping us expand the impact of viral load from individual to community health.

We declare no competing interests.

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- Montaner JS, Lima VD, Barrios R, et al. Association of highly active antiretroviral therapy coverage, population viral load, and yearly new HIV diagnoses in British Columbia, Canada: a population-based study. *Lancet* 2010; **376**: 532–39.
- 2 Havlir D, Lockman S, Ayles H, et al. What do the Universal Test and Treat trials tell us about the path to HIV epidemic control? J Int AIDS Soc 2020; 23: e25455.
- Jain V, Petersen ML, Liegler T, et al. Population levels and geographical distribution of HIV RNA in rural Ugandan and Kenyan communities, including serodiscordant couples: a cross-sectional analysis. Lancet HIV 2017; 4: e122–33.
- 4 Tanser F, Vandormael A, Cuadros D, et al. Effect of population viral load on prospective HIV incidence in a hyperendemic rural African community. *Sci Transl Med* 2017; **9:** eaam8012.
- 5 Patel EU, Solomon SS, Lucas GM, et al. Temporal change in population-level prevalence of detectable HIV viraemia and its association with HIV incidence in key populations in India: a serial cross-sectional study. *Lancet HIV* 2021; published online July 28. https://doi.org/10.1016/ S2352-3018(21)00098-9.
- 6 Balzer LB, Ayieko J, Kwarisiima D, et al. Far from MCAR: obtaining population-level estimates of HIV viral suppression. *Epidemiology* 2020; 31: 620–27.
- 7 WHO. Updated recommendations on HIV prevention, infant diagnosis, antiretroviral initiation and monitoring. 2021. https://www.who.int/ publications-detail-redirect/9789240022232 (accessed June 11, 2021).
- Tanser F, Bärnighausen T, Grapsa E, Zaidi J, Newell ML. High coverage of ART associated with decline in risk of HIV acquisition in rural KwaZulu-Natal, South Africa. Science 2013; 339: 966–71.
- 9 Parashar S, Collins AB, Montaner JS, Hogg RS, Milloy MJ. Reducing rates of preventable HIV/AIDS-associated mortality among people living with HIV who inject drugs. Curr Opin HIV AIDS 2016; 11: 507–13.
- 10 Solomon SS, Solomon S, McFall AM, et al. Integrated HIV testing, prevention, and treatment intervention for key populations in India: a cluster-randomised trial. *Lancet HIV* 2019; **6**: e283–96.



## Epidemiology of severe COVID-19 from South Africa

Published Online August 4, 2021 https://doi.org/10.1016/ \$2352-3018(21)00183-1 Despite the global importance of the COVID-19 pandemic, its impact remains poorly characterised in low-income and middle-income countries, including

most of those in Africa. As of Aug 1, 2021, only 3.4% of recorded COVID-19 cases and 4.0% of COVID-19-related deaths were from Africa, where 17% of the global

population live. South Africa, where 4.4% of Africa's population live, accounted for 36.7% of COVID-19 cases and 42.3% of COVID-19 deaths recorded on the continent. Factors contributing to inadequate characterisation of the burden of COVID-19 in Africa include insufficient diagnostic capabilities for testing of SARS-CoV-2, with South Africa reporting the highest testing rate (248 per 1000 population), which nevertheless is one-fourteenth of testing done in the UK.1 Furthermore, inadequacy in surveillance infrastructure is major challenge in most African countries, limiting the availability of robust readily accessible data. Consequently, many uncertainties about SARS-CoV-2 epidemiology remain in Africa.

The analysis of people admitted to hospital with COVID-19 by Waasila Jassat and colleagues in The Lancet HIV addresses key knowledge gaps in the epidemiology of COVID-19 in an African setting.<sup>2</sup> In South Africa, 9.1% of the 59.6 million population are older than 60 years, and there is a high prevalence of underlying medical conditions among adults, including HIV (19%), diabetes (8–13%), hypertension (44–46%), and obesity (11-41%).<sup>3</sup> Impressively, the analyses by Jassat and colleagues were based on expeditiously establishing a national electronic surveillance database (DATCOV), soon after the COVID-19 pandemic was declared in March, 2020. DATCOV eventually encompassed data on COVID-19 hospital admissions and outcomes from all hospitals in South Africa. A question probed was the role of underlying HIV and past or present tuberculosis in COVID-19 deaths during the first two waves of COVID-19 in South Africa.

The findings indicated that underlying HIV and past and present tuberculosis were independently associated with 1.34-fold and 1.48-fold higher odds of death, respectively, following hospital admission with COVID-19. Among people living with HIV, those not receiving antiretroviral therapy (ART), or with a history of a HIV viral load of 1000 copies or more per mL or CD4 counts of less than 200 cells per  $\mu$ L in the past year had a higher odds of in-hospital COVID-19-associated death. Nevertheless, the prevalence of HIV among patients admitted to hospital with COVID-19 even when restricting analysis to only public hospitals (20.4%), was similar to the population prevalence of HIV (19%). This finding suggests that, similar to population-based observational studies from the UK and a few other places, underlying HIV is not necessarily a risk factor for See Articles page e554 COVID-19 hospitalisation or severe disease.<sup>4</sup>

Missing data on key covariates were a recognised limitation of the DATCOV dataset. Nevertheless, a high prevalence of mainly non-communicable underlying medical conditions was evident in people with HIV (57.5%) and HIV-uninfected individuals (65.2%), the presence of which was independently associated with increased odds of death. Notably, for individuals admitted to hospital with available data, the absolute numbers of COVID-19 deaths associated with underlying diabetes (n=14707) and hypertension (n=19668), which were independently associated with higher risk of COVID-19 death, far exceeded deaths in people with HIV (n=3407) or past and present tuberculosis (n=307). Furthermore, older age group was independently associated with greater likelihood of COVID-19 death, including 5.32 higher odds among people aged 40-59 years (16285 deaths) and 20.67 higher odds among people aged 80 years or older (6015 deaths) compared with people aged younger than 20 years. These data are consistent with the global experience, indicating that even in an African setting with high HIV and tuberculosis prevalence, advanced age and non-communicable disease are the major risk factors for COVID-19 deaths. The data provide guidance on which individuals need to be prioritised for COVID-19 vaccination in settings such as South Africa, where access to COVID-19 vaccines remains constrained despite more than half of adult populations in high-income countries already having been vaccinated.<sup>1</sup>

Despite the laudable efforts by Jassat and colleagues, another major issue relates to extrapolating the findings of this analysis to the general population. Modelling for excess mortality from May 3, 2020, to March 27, 2021, by the South African Medical Research Council reported 150271 excess deaths in individuals older than 1 year (including compared with 52648 [35.0%] COVID-19 deaths officially recorded in South Africa), which was strikingly similar to the 51037 deaths reported by Jassat and colleagues at the same timepoint.5 Notably, the trajectory of excess deaths reported in South Africa during the first and second COVID-19 waves is almost completely synchronous with the reported COVID-19 deaths, indicating the majority of excess deaths are probably due to COVID-19. Reasons for the discrepancy between COVID-19 deaths imputed with the excess mortality

estimate and recorded deaths could include deficiencies in investigation of possible cases and reporting of COVID-19 deaths. Furthermore, individuals might choose not to access or be unable to gain timely access to health care, particularly when health-care facilities are overwhelmed at the time when the COVID-19 waves peak. All indications are that the discrepancy between reported and imputed COVID-19 deaths using excess mortality estimates are widening in the current wave being experienced in South Africa largely because of infections by the delta variant, compared with the earlier two waves. This poses further challenges in fully characterising the epidemiology of COVID-19 even in South Africa, despite the admirable efforts by its scientists.

SAM has been the lead investigator on COVID-19 epidemiology and vaccine trials that are funded by BMGF and Novavax. JN is a lead South African investigator on COVID-19 treatment trials undertaken by WHO Solidarity accelerated COVID-19 treatment trials. All funding goes to their institutions.

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- Ritchie H, Ortiz-Ospina E, Beltekian D, et al. Coronavirus pandemic (COVID-19). 2020. https://ourworldindata.org/covid-cases (accessed Aug 1, 2021).
- 2 Jassat W, Cohen C, Tempia S, et al. Risk factors for COVID-19-related in-hospital mortality in a high HIV and tuberculosis prevalence setting in South Africa: a cohort study. *Lancet HIV* 2021; published online Aug 4. https://doi.org/10.1016/S2352-3018(21)00151-X.
- 3 National Department of Health, Statistics South Africa, South African Medical Research Council, and ICF. South Africa Demographic and Health Survey 2016. January, 2019. https://www.samrc.ac.za/sites/default/files/ attachments/2019-01-29/SADHS2016.pdf (accessed July 7, 2021).
- Bhaskaran K, Rentsch CT, MacKenna B, et al. HIV infection and COVID-19 death: a population-based cohort analysis of UK primary care data and linked national death registrations within the OpenSAFELY platform. Lancet HIV 2021; 8: e24–32.
- 5 South African Medical Research Council Burden of Disease Unit. Report on weekly deaths in South Africa. April 14, 2021. www.samrc.ac.za/sites/ default/files/files/2021-04-14/weekly10Apr2021.pdf (accessed July 7, 2021).



### Call for abstracts: HIV and Healthy Longevity

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To submit an abstract for consideration see https://app. oxfordabstracts.com/ stages/3129/submitter

For more on The Lancet Summit: HIV and Healthy Longevity see http://www. thelancetsummit.com/HIV-Healthy-Longevity We invite submission of abstracts for oral presentation at The Lancet Summit: HIV and Healthy Longevity, a virtual meeting to be held Feb 24–25, 2022.

Earlier this year, *The Lancet* journals marked the 40th anniversary of the first cases of HIV/AIDS being described in medical literature and the incredible advances in the understanding, management, treatment, and prevention of HIV in the past four decades. While helping to curtail HIV transmission and substantially increasing healthy life expectancy, the phenomenal success of antiretroviral therapy around the world has led to more people living and ageing with HIV than ever before. These individuals face major challenges including multimorbidity, complications from polypharmacy, and stigma associated with both age and HIV. Their pathophysiology may offer important insights regarding the role of immune dysfunction and chronic inflammation in ageing more generally.

Additionally, HIV has been viewed as a highly morbid condition affecting young people, but as management has improved, many people ageing with HIV remain healthy and sexually active and may continue to use substances. This combined with substantial delays in diagnosis among older individuals, leads to risk of HIV transmission often unappreciated by the individual or their health-care provider. As global populations age more older people will be at risk of acquiring HIV and outreach may need to be better tailored to this group.

In recognition of this demographic shift in people affected by HIV, *The Lancet Healthy Longevity* and *The Lancet HIV* will host The Lancet Summit: HIV and Health Longevity. This virtual meeting aims to bring together key opinion leaders in HIV and geroscience to present new research, analysis, and discussion, and to nurture cross-boundary collaboration.

At The Lancet Summit, we hope to inspire new work that will help address specific challenges in HIV prevention, diagnosis, and treatment among older individuals. To facilitate this, we invite submission of research abstracts for presentation at the meeting on any topic related to HIV and longevity. We are particularly interested in clinical and implementation research that will help to guide practice and policy in the coming decades in a variety of health-care settings. Abstracts accepted for presentation will be published in one of the two journals. Deadline for submission is October 15.

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