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Data-driven HIV programming to maximise health benefits

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From the perspective of the ongoing COVID-19 pandemic, where evidence on effective prevention and treatment interventions for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections is limited, the near perfect efficacy of antiretroviral therapy (ART) for HIV treatment is enviable. ART prevents individual level HIV-associated morbidity and mortality, restoring life expectancy to near normal,[1] and prevents transmissions by decreasing viral load to undetectable levels.[2] To translate ART efficacy to population level health benefits, the Joint United Nations Programme on HIV/AIDS (UNAIDS) set goals to diagnose 90% of people living with HIV, link 90% of those diagnosed to ART, and achieve 90% viral suppression among people on ART by 2020.[3] In the 6 years since UNAIDS set the 90-90-90 goal, four large community randomised trials tested ART as a strategy to decrease HIV incidence with mixed results.[4] Clinical trials are the gold standard—a way to measure the underlying true efficacy while keeping everything else the same. Health programmes based on well executed trials are generally expected to have lower real-world effectiveness due to differences in intervention delivery and measurement of outcomes. In *The Lancet HIV*, Claire Steiner and colleagues[5] present the outcomes of the Bukoba Combination Prevention Evaluation (BCPE) in Tanzania in which they describe a data-driven approach to maximise the health benefits of HIV programming. By addressing gaps in the HIV care continuum, the authors more than halved the fraction of people living with HIV who were undiagnosed and more than doubled those with HIV on ART, improving on the observed efficacy in some clinical trials.

Because the results from ART community randomised trials were mixed, with only the SEARCH trial achieving high population viral suppression,[6] the BCPE investigators incorporated strategies to extend the reach of testing and more closely follow individuals through the continuum of HIV care.[7] First, they used a combination of community-based and facility-based HIV testing to reach men and young people who otherwise do not seek care at clinics. Second, same-day ART start was supported in the community and at clinics. Last, peer counsellors provided linkage and retention services, seeking out those individuals who had not been seen in the last 90 days or those lost-to-care. The welcome back to the clinic service included treatment navigation and expedited services—a stark contrast to standard measures for clients perceived as not engaged in care. The cost of the intervention was low, at US$18 per client. Overall, intervening throughout the continuum achieved higher viral suppression but fell just short of the 90-90-90 goal (64% [76% × 93% × 91%] *vs* 73% UNAIDS goal). Critically, their data driven approach identified gaps for future interventions to reach men, people who use alcohol, and those living in poverty, thus closing the gaps in HIV care.

Whereas clinical trials test hypotheses, quantitative and qualitative effectiveness evaluations identify gaps in coverage and can guide programmes as new interventions are integrated into existing health systems. This iterative process allows programmes to keep strategies that work, discard those that do not work, and maximise health benefits.[8] Pragmatic evaluations of HIV services will now occur in a world drastically altered by the COVID-19 pandemic. The last 6 months of this pandemic have focused attention on how to deliver HIV testing, linkage, and ART to people living with HIV with as little disruption as possible. This delivery must be better in low-income and middle-income countries (LMICs) where overstretched health systems to manage COVID-19 have resulted in fewer services for diagnosis, treatment, and prevention of HIV, tuberculosis, and other health conditions. For HIV, client-focused, streamlined, differentiated service delivery for HIV care as well as promising strategies such as telemedicine (allowing visits by phone or videoconference), community-based or home-based ART delivery, and multi-month scripting[9,10] could take us closer to the new 95-95-95 UNAIDS goals. Taking what we have learnt from clinical trials and programme evaluations, incorporating innovations and data-driven adaptations with ongoing monitoring and evaluation, we can maximise health benefits from HIV prevention and treatment programmes and achieve the UNAIDS goals. In many LMICs, inequities produced by the social determinants of health drive HIV infection and COVID-19. As we prepare to live

with the coronavirus, we might have to adjust from an HIV-focused approach to one that accommodates this new pandemic.

We declare no competing interests.

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INSTIs and weight gain in pregnancy

In 2019, WHO updated HIV treatment guidelines to recommend dolutegravir as first-line antiretroviral therapy (ART) for all individuals, including women living with HIV who are pregnant and breastfeeding.[1] Dolutegravir, an integrase-strand-transfer inhibitor (INSTI), is well tolerated and has better virological outcomes compared with existing first-line efavirenz-based regimens.[2,3] Unsuppressed viral load is the strongest risk factor for mother-to-child HIV transmission and adverse maternal and child clinical outcomes. Thus, the rapid scale-up of dolutegravir to women living with HIV who are pregnant has the potential to reduce mother-to-child HIV transmission and improve outcomes in low-income and middle-income countries (LMICs) where the burden of HIV is greatest.

However, scaling up dolutegravir during pregnancy can come at a cost. In two randomised controlled trials from Cameroon (NAMSAL)[2] and South Africa (ADVANCE),[3] which are reported in *The Lancet HIV*, adults initiating dolutegravir with either tenofovir disoproxil fumarate or tenofovir alafenamide had greater weight gain and treatment-emergent obesity compared with those initiating efavirenz up to 96 weeks. In the ADVANCE trial,[3] larger increases in fat mass were observed for participants initiating dolutegravir compared with efavirenz. The largest increases in weight gain and fat mass were among women (who were not pregnant).

Obesity during pregnancy is increasing in many LMICs, where INSTI-associated gestational weight gain is likely to adversely affect maternal and child metabolic health. Prepregnancy obesity and excessive gestational weight gain increase the risk of pregnancy complications, including gestational diabetes, hypertensive disorders of pregnancy, delivery complications, and large-for-gestational-age infants.[4] Moreover, obesity in pregnancy is associated with maternal type 2 diabetes and hypertension long term, and childhood obesity.[5] For women living with HIV, overlapping risk factors (eg, alcohol use) could increase the risk of obesity during pregnancy.

INSTIs might increase cardiometabolic risk for pregnant women living with HIV and their children. Data for the cardiometabolic effects of INSTIs in pregnancy are scarce. However, in a study of 265 women living with HIV,[6] INSTIs were associated with a nearly threefold increased risk of hypertensive disorders of pregnancy, compared with women taking protease inhibitors (25% with INSTIs *vs* 10% with protease inhibitors; adjusted risk ratio 2·8, 95% CI 1·5–5·1). Hypertensive disorders of pregnancy have long-term health implications. For example, women with pre-eclampsia