

Multiple HIV testing strategies are necessary to end AIDS

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In 2021, 40 years after the emergence of the global HIV pandemic and despite impressive scale-up of antiretroviral therapy (ART) worldwide, there were still an estimated 690 000 AIDS-related deaths and 1.7 million new HIV infections, far above the 2020 global goals of less than 500 000 deaths and 500 000 new infections [1]. The cornerstone of the global AIDS control effort is currently universal test-and-treat (UTT) strategy to identify all people with HIV (PWH), promptly initiate ART and achieve sustained viral load suppression to improve health outcomes and prevent onward HIV transmission [2], yet an estimated one in five PWH globally are unaware of their HIV status [1].

On the basis of a General Assembly meeting in June 2021, the UNAIDS *'End inequalities. End AIDS. Global AIDS strategy 2021–2026 report'* identifies ambitious targets: 95% of people at risk for HIV will use combination prevention, 95% of PWH will know their status, 95% of newly diagnosed individuals initiate ART, and 95% of those starting ART will be virally suppressed [3]. But new infections are not evenly distributed in populations or in settings. For example, key populations and their sexual partners constituted ~62% of all new HIV infections in 2019, despite representing only a small fraction of the world's population [3]. Testing people unlikely to have HIV might be considered a poor investment in the fight to end AIDS [4].

In Botswana, a country with ~2.3 million people, of whom ~20% are PWH, care cascade indicators are among the highest reported for sub-Saharan Africa: an

estimated 92% of PWH know their status and 79% of PWH are virally suppressed. Although Botswana is getting close to the UNAIDS 95–95–95 targets, there is a push by its PEPFAR programme to target people with the highest likelihood of undiagnosed HIV for HIV testing. In response, Rowlinson *et al.* [5] identified predictors for an algorithm to improve the efficiency of facility-based HIV testing. The investigators used retrospective data collected as part of HIV testing procedures in over 130 Ministry of Health facilities during two distinct periods in 2018–2020 to develop and validate a predictive score for HIV testing. They excluded from model development all data from testing for which targeting was deemed unacceptable [i.e. patients with tuberculosis or sexually transmitted infections, pregnant women, voluntary counseling and testing (VCT) or partner testing, pediatric testing], making these a priori testing criteria. This work resulted in a set of characteristics that could be used as a screening tool to identify patients for HIV testing.

In period 1 (when few characteristics were collected), three factors were significantly associated with HIV positivity, including citizenship of a nation other than Botswana, age at least 30 years, and testing in emergency departments. In period 2 (when additional data were collected), 12 factors were identified, including 3 from period 1 as well as female sex, cohabitation, being divorced, self-employment, no prior HIV test, HIV testing more than 12 months ago, inpatient medical ward testing, and having TB or HIV symptoms. In period 1, application of a risk score cut-off at least 1.0 would result

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in 50% fewer tests performed and capture 61% of positives. In period 2, a cut-off at least 1.0 would result in 13% fewer tests and capture 96% of positives. The authors estimated that testing costs averted ranged from 12.1 to 52.3% depending on the risk score cut-off applied. Importantly, the costs of missed diagnoses and onward transmission were not considered.

Why should we aim to target testing in Botswana? Outpatient provider-initiated testing and counselling (PITC) constituted the vast majority (75% in period 1, 70% in period 2) of tests conducted. If three in four HIV tests in Botswana are taking place in busy outpatient departments and HIV positivity is 4–5% as in the Rowlinson study, clearly all patients should be tested and healthcare staff not be bothered with complicated test algorithms that need additional validation and would require periodic updating. In their article, authors arrive at a similar conclusion and caution policy makers: ‘adopting a more focused approach to testing – even one guided by substantial risk data – comes at a cost; curtailing testing would result in delayed HIV diagnoses in 4–17% of HIV-positive patients and would disproportionately impact younger persons’. In Kenya, the country with the fifth largest HIV epidemic, analysis of data from PEPFAR-funded HIV testing and counselling programmes between July 2017 and June 2018 found a new diagnosis yield of only 1.4% in over 13 million tests performed, of which 77% were categorized as PITC [6]. As stated by de Cock *et al.* [6] there is an ethical imperative not to let HIV go undiagnosed and untreated in healthcare settings, especially in sub-Saharan Africa, where PITC often has an HIV test positivity rate above 1%.

But the reality is that funding to end AIDS by 2030 is in competition with other pandemics, and funding agencies, such as PEPFAR, want testing to be as cost-effective as possible. Although studies, such as that by Rowlinson and our own work in Kenya highlight the importance of testing persons who have never tested, or tested more than 12 months ago [7], it also provides a cautionary note to funders looking for short-term savings: all score cut-offs evaluated in period 2 led to disproportionate numbers of young and single people not being diagnosed. HIV-testing approaches that miss infections, especially those among young, sexually active individuals, may be penny-wise and pound-foolish if they miss individuals who are likely to transmit to one or more partners. Currently, PITC is only offered to about one in five patients in sub-Saharan Africa [8], and is most often targeted at those with obvious signs of immunosuppression, reducing preventive impact [9]. The costs of delayed diagnosis and onward transmission are important considerations that can only be addressed through careful modelling and cost-effectiveness studies, and analyses evaluating only testing cost are misleading.

Many different HIV testing strategies will be needed to target testing to individuals at high risk for transmission and ensure access to care of key and priority populations (e.g.

people who inject drugs, adolescent girls and young women [10], sexual minority individuals, young and mobile men [11,12], and people with sexually transmitted infection symptoms [13]). In fact, as knowledge of HIV status increases, the use of antigen-based or HIV-1 RNA testing may become more important to contain transmission, as modelling shows that 10–50% of transmission takes place during acute and early infection, before rapid antibody tests are positive [14,15]. Early diagnosis through multiple testing strategies and targeting of key and priority populations to ensure access, remain the cornerstone of strategies to reach 95–95–95 goals and end the epidemic. We should be looking harder for undiagnosed HIV infection, not stepping on the brakes.

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Conflicts of interest

There are no conflicts of interest.

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