Resolving the CD4-testing crisis to help end AIDS-related deaths

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WHO defines advanced HIV disease in adults and adolescents as having a CD4 cell count less than 200 cells per µL or WHO clinical stage 3 and 4 disease.[1] Despite programmatic advances, 30% of people with HIV who present or re-present for care worldwide have advanced HIV disease.[2] People with advanced HIV disease are at high risk of death from tuberculosis, cryptococcal meningitis, *Pneumocystis* pneumonia, and severe bacterial infections.[2]

CD4 testing is essential for the diagnosis of advanced HIV disease. In 2017, WHO issued management guidance for advanced HIV disease that requires CD4 testing to implement evidence-based packages of prophylaxis, screening, and pre-emptive treatment to avert morbidity and mortality.[1] However, evidence from Uganda has shown substantial declines in CD4 testing since the introduction of WHO's test-and-treat policy and due to budget constraints, with HIV programmes often forced to prioritise viral load monitoring instead of CD4 testing.[3]

As the 2025 and 2030 Sustainable Development Goals approach, a new crisis in access to near-bedside and point-of-care CD4 testing in low-income and middle-income countries (LMICs) has occurred. In May, 2022, Abbott Laboratories (Chicago, IL, USA) announced that it would no longer produce its near-bedside Pima CD4 platforms; only CD4 cartridges and maintenance for existing machines are now available. Similarly, Becton Dickinson Biosciences (Franklin Lakes, NJ, USA) confirmed the discontinuation of their near-bedside FACSPresto CD4 platform from the end of 2024, with no access to cartridges or maintenance services from 2026 onwards. With the crisis worsening, many HIV programmes in LMICs either have no access to CD4 testing or have access to only one novel, lateral-flow-based CD4 semi-quantitative assay that increasingly shows its limitations in terms of diagnostic performance and feasibility, particularly when used at the point of care as opposed to in controlled laboratory settings.[4–10]

The only commercially available lateral-flow assay worldwide currently is the VISITECT CD4 Advanced Disease (AccuBio, Alva, UK) semi-quantitative test, which indicates whether CD4 count is less than, more than, or equal to 200 cells per µL. Five peer-reviewed assessments of diagnostic accuracy published since 2020 have shown a sensitivity of the VISITECT CD4 Advanced Disease assay of 93–100% for diagnosis of advanced HIV disease.[4–6,8,9] Reported specificity, however, is lower, ranging from 86% in optimal laboratory conditions to 61% with finger-prick blood conducted by various staff.[5,6] Furthermore, positive predictive values are 46–88% in settings with high prevalence of advanced HIV disease.[5] The assay also imposes a substantial time and workload burden on health-care workers;[10] the test takes 45 min to process and only 57% of users interviewed found the timing of the multiple steps manageable.[4,6,10] Moreover, slight alteration to the incubation steps of the test could change the final test result, suggesting that the test should be done by a dedicated clinic or laboratory health-care worker.[4]

In June, 2023, the Fight AIDS Coalition and the Diagnostics Equity Consortium wrote an open letter to express their concern and seek clarification on how Abbott Laboratories and Becton Dickinson Biosciences would mitigate the repercussions of their announcements. Abbott Laboratories indicated that their decision had been precipitated by market forces, specifically reductions in CD4 testing with their Pima instruments. However, they committed to continue working with global health agencies, including WHO, donor organisations, civil society, and people living with HIV, to predict CD4 test demand, devise a re-deployment strategy, increase use of existing instruments (including Pima cartridges), and facilitate technology transfer. Becton Dickinson Biosciences responded that their decision was due to suppliers discontinuing several crucial components of their FACSPresto CD4 platform, and noted a substantial decrease in CD4-testing demand due to multiple market factors, including a shift to viral-load testing as the preferred method to monitor HIV treatment. In January, 2024, the Fight AIDS Coalition wrote to WHO demanding their leadership in addressing the CD4 crisis.

2 years after the announcements by Abbott Laboratories and Becton Dickinson Biosciences, the urgency to resolve the CD4 crisis has only increased. The

For the **Diagnostics Equity Consortium** see https://oneill.law.georgetown.edu/projects/diagnostics-equity-consortium/

***Panel:* Recommendations to address and end the CD4-testing crisis**

Funding requirements
- Guaranteed, coordinated funding for CD4 testing from donors and governments
- An advanced HIV-disease industry forum for:
  - Urgent and immediate investment in new CD4 technologies and optimisation of existing platforms by global funders, expert organisations, and governments
  - Facilitation of expedited technology transfer from Abbott Laboratories and Becton Dickinson Biosciences and reinforcement of maintenance and service agreements
- Independent funding for community representatives and people living with HIV to continue essential advocacy efforts, including for CD4-platform price reductions due to increases in cartridge prices

Policy recommendations
- Clear policy messaging on the crucial importance of CD4 testing at initiation and re-initiation of antiretroviral therapy, and incorporation into national guidelines
- Specific guidance on which CD4 test should be used in which context (eg, type of operators, training, and advanced HIV-disease prevalence) to ensure cost-effectiveness
- Increased CD4-testing coverage to allow effective implementation of WHO-recommended packages of care for advanced HIV disease to reduce AIDS-related deaths

Data requirements
- New epidemiological, advanced HIV-disease data to inform predictions, including collation of CD4-testing coverage data
- Tracking of CD4-testing policy and practice at national and global levels
- Implementation of new, advanced HIV-disease indicators, including mortality, within existing national monitoring and evaluation frameworks
- Prioritisation of feasibility and efficacy studies of new and existing CD4 platforms

Investments to strengthen health-care systems
- Situational analyses of laboratory and supply-chain barriers and facilitators for CD4 testing, including diagnostic-network optimisation
- Investment in strengthening laboratory and supply-chain systems for accurate laboratory, near-bedside, and point-of-care CD4 testing by donors and governments

For the **End Aids Action Group** see https://endaidsaction.group/

2025 and 2030 goals to end both the HIV epidemic and preventable, unacceptable AIDS-related deaths cannot be achieved without adequate and sustainable access to CD4 testing. Emerging data on point-of-care CD4 testing suggest these assays are unlikely to provide this adequate and sustainable access, and an array of assays (ie, laboratory, bedside, and point of care) are required in LMICs.[4–10] We therefore propose a set of recommendations to provide a comprehensive action plan (panel), as market forces cannot be allowed to undo decades of progress in HIV response. The feasibility of research into improved care for and treatment of people with advanced HIV disease is currently compromised as advanced HIV disease cannot be accurately identified without CD4 testing in many LMICs, where disease burden is greatest. The HIV epidemic can and should be ended; the crisis in access to validated CD4 tests in LMICs needs an urgent, comprehensive, and collaborative effort involving all global health stakeholders and industry. Four decades into the HIV epidemic, ending AIDS deaths has become a test case for all global health efforts, and our collective failure to end it is a source of lessons for all global health programmes.

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