

MONITORING HIV DRUG RESISTANCE WITH CADRE

Overview

Use of antiretroviral therapy (ART) has increased significantly over the past decade. Nearly 80% of all people living with HIV worldwide received ART in 2022. In countries supported by the U.S. President's Emergency Plan for AIDS Relief (PEPFAR), over 90% of people living with HIV achieve viral suppression. Achieving viral suppression preserves the health of the person living with HIV and prevents transmission to sexual partners. The emergence of HIV drug resistance, however, can compromise the effectiveness of antiretroviral drugs and efforts to reduce the spread of HIV, prevent severe HIV disease, and prevent HIV-related deaths.

It is a priority to monitor the emergence of and understand the risk factors for HIV drug resistance, especially resistance to dolutegravir (DTG)-based regimens, which account for 92% of ART dispensed with PEPFAR support. Surveillance of HIV drug resistance is critical for minimizing the emergence and spread of HIV drug resistance.

CDC Leads Surveillance of HIV Drug Resistance with CADRE

CDC leads an international surveillance effort to estimate the occurrence of HIV drug resistance among people with HIV who are taking dolutegravir (DTG)-based treatments. This surveillance effort utilizes Cyclical Acquired HIV Drug Resistance Surveillance (CADRE), a laboratory-based HIV drug resistance monitoring process.

CDC strengthens surveillance of HIV drug resistance in PEPFAR-supported countries by supporting laboratories with procurement of equipment and supplies; and by providing training, technical support, and quality assurance. CADRE uses existing laboratory networks to conduct genetic testing on leftover viral load specimens that are routinely collected for patient care. Data from CADRE can be used to monitor for emergence of HIV drug resistance, understand the risk factors for HIV drug resistance, and inform HIV treatment guidelines.

Data from CADRE can be used to:



Understand how often resistance to DTG occurs



Understand the factors that make it more likely for someone to develop drug resistance



Identify which treatment options would still be effective if resistance were to occur

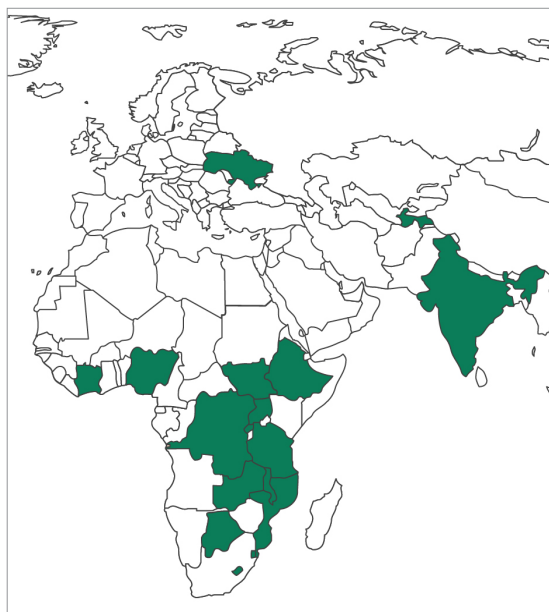
Generating Data to Inform Treatment Guidelines

CADRE fills an important gap in monitoring HIV drug resistance in settings where it is not feasible to conduct patient-level drug resistance testing. The routine collection and analysis of specimens through CADRE will also allow for cost-effective and continuous monitoring of DTG resistance in PEPFAR programs. With CADRE, CDC seeks to create a stronger surveillance database for in-depth analysis of factors contributing to HIV drug resistance. This will offer crucial data to guide treatment choices for the large number of patients struggling with HIV on DTG-based regimens, preventing severe disease and virus transmission.

CADRE Implementation

CDC is helping build capacity for surveillance, strengthening laboratories, and leading the implementation of CADRE in 15 countries, with support from PEPFAR (Figure 1, right).

Table 1 (below) presents findings from drug resistance surveillance studies conducted between 2020 and 2022. Clinic-based surveys were conducted in Malawi and Mozambique. Lab-based surveys utilizing CADRE were conducted in Uganda and Ukraine. The surveys provide data to understand levels of drug resistance to DTG-based regimens. Findings indicate that the percentage of patients experiencing clinically significant resistance to DTG-based regimens is low, indicating that DTG-based regimens remain effective for the majority of patients with a high viral load.



- Botswana
- Cote d'Ivoire
- DRC
- Eswatini
- Ethiopia
- India
- Lesotho
- Malawi
- Mozambique
- Nigeria
- Rwanda
- South Sudan
- Tajikistan
- Tanzania
- Uganda
- Ukraine
- Zambia

Figure 1: Map of Countries Where CDC is Implementing CADRE with support from PEPFAR

	Malawi Weighted Rate (95% CI)	Mozambique Unweighted Rate** (95% CI)	Uganda Weighted Rate (95% CI)	Ukraine Weighted Rate (95% CI)
% of Cases with Low, Intermediate, or High (Clinically Significant) DTG Resistance	8.6 (5.3, 11.9)	19.7 (14.5, 26.1)	3.9 (0.7, 7.1)	6.6 (2.3, 10.9)

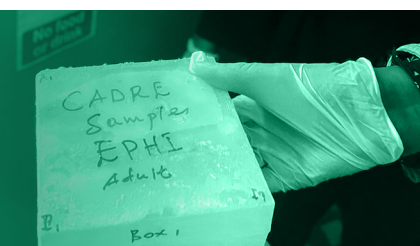
Table 1: Levels of Drug Resistance to DTG-based Treatment Regimens

Early Results

[Recent studies supported by PEPFAR](#) in low- and middle-income countries show that 3.9% to 19.6% of people on DTG-based regimens may have developed resistance to DTG. These data show that DTG-based regimens remain effective and that current levels of DTG resistance do not require a change in regimen for most people living with HIV.

When treatment failure occurs, it is likely due to challenges that patients face adhering to the treatment. Helping patients adhere to their treatment by providing support, education, and addressing any challenges they may face in following their treatment plans should be the main management strategy for patients for whom DTG-based regimen is failing.

DTG-based regimens remain effective. Current levels of DTG resistance do not require a change in regimen for most people living with HIV. Data from CADRE can help monitor and assess trends in HIV-resistance and inform treatment guidelines.



What's Next for CADRE?

Once fully implemented, the CADRE database will provide a unique opportunity to analyze DTG resistance across a substantial number of cases. This will allow for statistical analyses to understand the factors that increase patients' chances of developing resistance to HIV drugs. Understanding how often HIV drug resistance occurs in people for whom the DTG-based regimen is not effective and how that resistance develops will inform treatment guidelines and HIV prevention strategies.