TOOLKIT

HIV MOLECULAR DIAGNOSTICS TOOLKIT TO IMPROVE ACCESS TO VIRAL LOAD TESTING AND INFANT DIAGNOSIS

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HIV TREATMENT AND CARE

World Health Organization

HIV molecular diagnostics toolkit to improve access to viral load testing and infant diagnosis

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1. INTRODUCTION: MOLECULAR DIAGNOSTICS FOR HIV VIRAL LOAD TESTING AND INFANT DIAGNOSIS

Treatment failure monitoring

Monitoring people receiving antiretroviral therapy is important to ensure successful treatment, identify adherence problems and determine whether antiretroviral therapy regimens should be switched in case of treatment failure. In 2013, WHO recommended viral load testing as the preferred monitoring approach to diagnose and confirm antiretroviral therapy failure *(1)*. Compared with clinical or immunological monitoring, viral load provides an early and more accurate indication of treatment failure. Measuring viral load can help to distinguish between drug resistance and non-adherence when coupled with robust enhanced adherence counselling. Further, viral load can serve as a proxy measure for the risk of transmission and effectiveness of prevention interventions at both the individual and population levels.

Updated 2016 WHO guidelines recommend routine viral load monitoring be carried out at 6 months, 12 months after initiation of antiretroviral therapy and then every 12 months thereafter if the person is stable on antiretroviral therapy *(2)*. If viral load is not routinely available, CD4 count and clinical monitoring should be used to assess treatment failure. Further, dried blood spot specimens using venous or capillary whole blood can be used to determine the HIV viral load. A threshold of 1000 copies/mL should be used to determine treatment failure when using dried blood spot specimens, as similarly defined for testing using plasma.

Treatment failure is defined by a persistently detectable viral load exceeding 1000 copies/mL *(2)*: that is, two consecutive viral load measurements within a three-month interval with adherence support between measurements after at least six months of starting a new antiretroviral therapy regimen (Box 1).

In addition, viral load may support differentiated service delivery strategies for people living with HIV, including those who are stable on antiretroviral therapy *(2)*. Stable individuals are defined as those who have received antiretroviral therapy for at least one year and have no adverse drug reactions that require regular monitoring, no current illnesses or pregnancy, are not currently breastfeeding and have good understanding of lifelong adherence and evidence of treatment success (two consecutive viral load measurements below 1000 copies/mL). The package of care for stable individuals can include less frequent clinic visits and medication pickup, community-based care and cessation of CD4 count monitoring if viral load testing is available.

Box 1. Assessing advanced HIV disease

Since CD4 count is the best predictor of disease status and immediate risk of death, it should be used to identify people with advanced HIV disease. Everyone entering or re-entering care should receive a CD4 test at treatment baseline and as clinically indicated for people who are clinically unstable or have symptoms of advanced HIV disease *(2,3)*. Further, it is strongly recommended that people with advanced HIV disease (CD4 count below 200 cells/mm^3 or WHO stage 3 or 4) receive a package of care *(4)*.

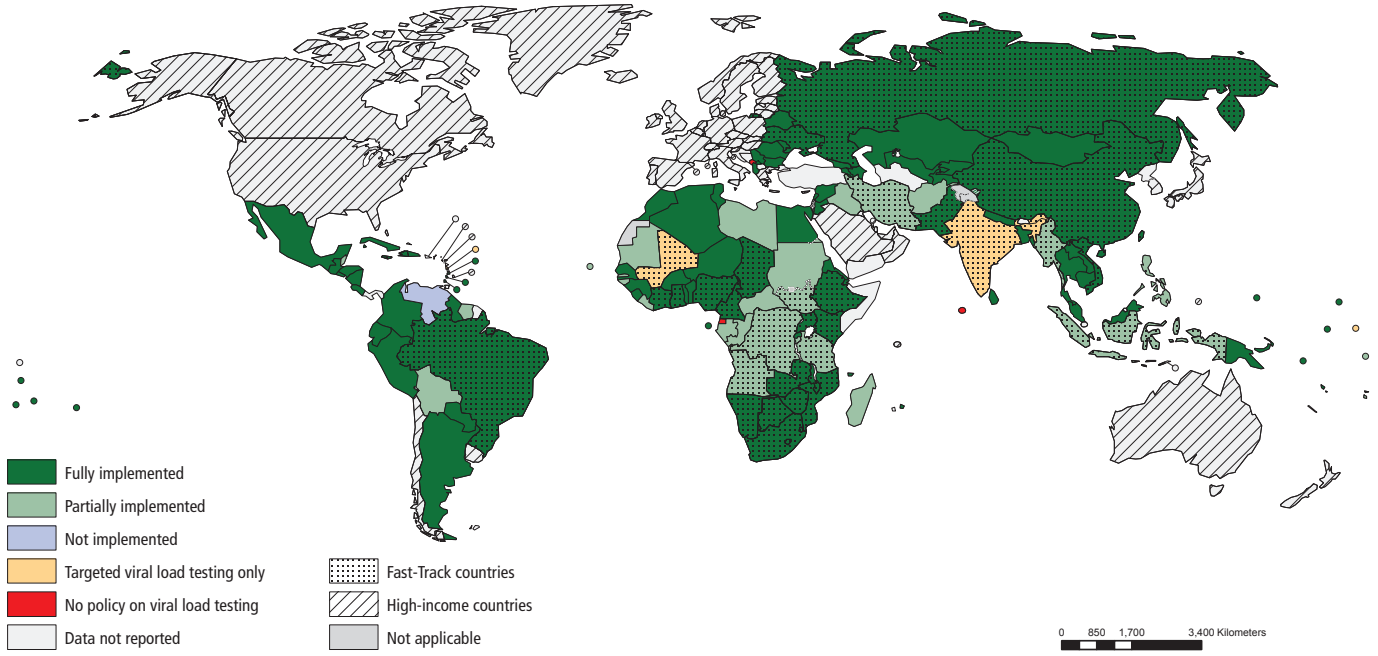
Many national guidelines now recommend and are scaling up access to viral load testing for treatment monitoring (Fig. 1).

The proportion of yearly viral load tests performed has increased significantly since 2013 (Fig. 2) *(5)*. About 15 million viral load tests were conducted in 2017, and projections suggest that nearly 29 million tests may be performed in 2022. Despite increasing volumes, the total coverage of the demand of viral load testing remained below 60% in 2017.

As national viral load test volumes are large and continue to grow, this will add significantly more costs to national testing budgets. Fortunately, several recent pricing commitments have been negotiated to support viral load testing expansion and access *(6–8)*.

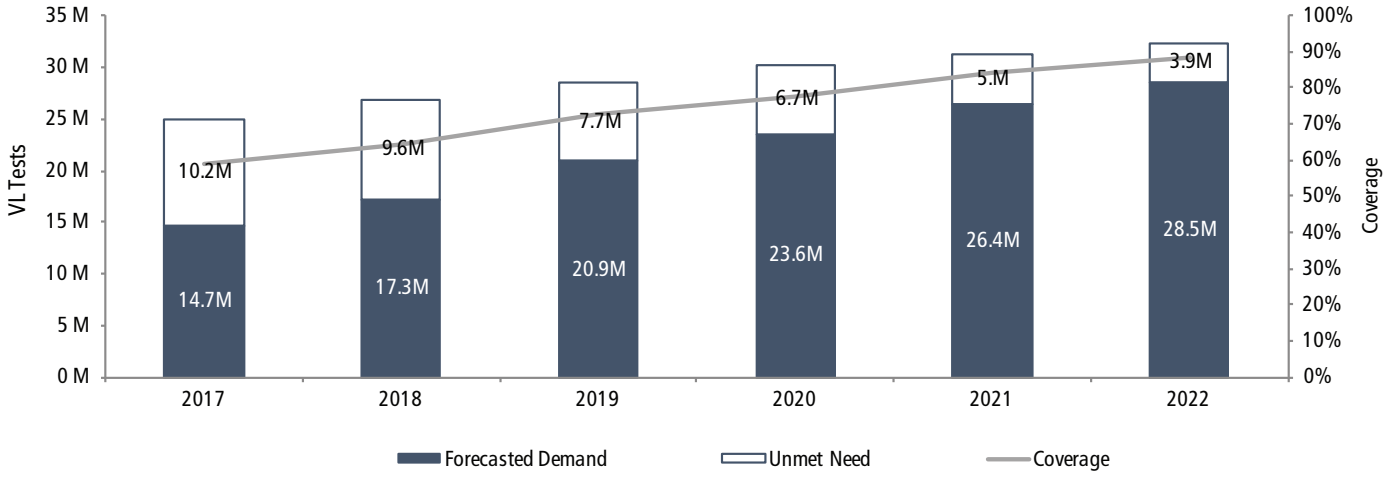
Numerous technologies, both laboratory-based and near-point-of-care assays, currently exist to support the scaling up of viral load testing and infant diagnosis. Several additional technologies are being developed *(9,10)*.

Fig. 1. National policy on routine viral load testing for monitoring ART and level of implementation for adults and adolescents in low- and middle-income countries (situation as of July 2019)



Source: Global AIDS Monitoring (UNAIDS/WHO/UNICEF) and WHO HIV Country Intelligence Tool, 2019

Fig. 2. Estimated viral load forecast in low- and middle-income countries globally



Source: 2018 CHAI HIV Market Report.

Infant diagnosis

Infant diagnosis consists of testing throughout the exposure period of HIV-exposed infants. Depending on the age, this can comprise either nucleic acid–based testing or serological testing. More specifically, early infant diagnosis refers specifically to nucleic acid-based testing of infants within two months of birth. See Annex 1 for the infant diagnosis algorithm.

Coverage of early infant diagnosis (testing within two months of birth) has remained stagnant in recent years, with about 51% of HIV-exposed infants receiving a nucleic acid test within the first two months of life in 2018 *(11)*. The proportions of HIV-exposed infants tested at nine months or at the end of the exposure period have been difficult to gather.

Current forecasts for nucleic acid testing suggest moderate growth and sustained volumes through 2022 (Fig. 3) *(5)*. About 1.4 million infant nucleic acid tests were performed in 2017, with more than 2 million projected to be needed for 2022.

Since 2010, several key recommendations have been made to support access to and expanded scale-up of infant diagnosis *(2,12)*.

- An indeterminate range should be used to improve the accuracy of all nucleic acid–based infant diagnosis assays (strong recommendation, moderate-quality evidence).
- Among infants with an initial positive nucleic acid test result, it is strongly recommended that antiretroviral therapy be started without delay and, at the same time, a second specimen be collected to confirm the initial positive test (strong recommendation, low-quality evidence).
- It is strongly recommended that children (18 months or older) with suspected HIV infection or HIV exposure have HIV serological testing performed according to the standard diagnostic HIV algorithm used for adults to determine final diagnosis (strong recommendation, high-quality evidence).
- In generalized epidemic settings, infants and children with unknown HIV status who are admitted for inpatient care or attending malnutrition or TB clinics should be routinely tested for HIV (strong recommendation, low-quality evidence).
- In generalized epidemic settings, infants and children with unknown HIV status should be offered HIV testing in outpatient or immunization clinics (conditional recommendation, low-quality evidence).
- Nucleic acid–testing technologies that are developed and validated for use at or near to the point of care can be used for infant HIV testing (conditional recommendation, low-quality evidence).
- Addition of nucleic acid testing at birth to existing infant diagnosis approaches can be considered to identify HIV infection among HIV-exposed infants (conditional recommendation, low-quality evidence).
- Consideration should be given to replace serological testing at nine months of age with nucleic acid–based testing.

Fig. 3. Estimated infant diagnosis forecast in low- and middle-income countries globally