

THE ROLE OF HIV VIRAL SUPPRESSION IN IMPROVING INDIVIDUAL HEALTH AND REDUCING TRANSMISSION

POLICY BRIEF



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ISBN 978-92-4-005517-9 (electronic version)

ISBN 978-92-4-005518-6 (print version)

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Suggested citation. The role of HIV viral suppression in improving individual health and reducing transmission: policy brief. Geneva: World Health Organization; 2023. Licence: CC BY-NC-SA 3.0 IGO.

Cataloguing-in-Publication (CIP) data. CIP data are available at <http://apps.who.int/iris>.

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KEY MESSAGES

- HIV viral suppression is critical to improve individual health, prevent sexual transmission, and reduce perinatal transmission.
- There are three key categories for HIV viral load measurements: unsuppressed (>1000 copies/mL), suppressed (detected but ≤ 1000 copies/mL) and undetectable (viral load not detected by test used).
- People living with HIV who have an undetectable viral load using any WHO-prequalified combination of sample and testing platform, including dried blood spot samples, and continue taking medication as prescribed have zero risk of transmitting HIV to their sexual partner(s).
- People living with HIV who have a suppressed but detectable viral load and are taking medication as prescribed have almost zero or negligible risk of transmitting HIV to their sexual partner(s).
- HIV viral load test results can be a motivation for adhering to treatment and achieving the ultimate goal of being undetectable. Emphasizing and strengthening adherence counselling during antiretroviral therapy initiation and throughout treatment are essential, including communicating about the prevention benefits of viral load suppression to all people living with HIV.
- Current WHO-prequalified tests, including point-of-care and alternative sample types such as dried blood spot samples, can support the goals of treatment programmes to accurately measure and report viral load results as unsuppressed, suppressed and undetectable.

Understanding HIV viral load measurements and testing approaches is needed. This policy brief is for a wide audience, including people living with HIV, providers, laboratory staff, program managers, global and national policymakers, and clinical and diagnostic partners.



1. INTRODUCTION

Antiretroviral therapy has transformed the lives of people living with HIV. All over the world, people living with HIV who have been diagnosed and treated early and take their medication as prescribed can now live longer and pursue as healthy a life as people who are HIV-negative. Further, people living with HIV who maintain an undetectable viral load by taking their antiretroviral therapy as prescribed have zero risk of transmitting HIV to their sexual partner(s) and minimal risk of transmitting HIV vertically to their children. Accurate, reliable testing for viral load is critical for realizing the benefits of antiretroviral therapy at both the individual and population levels.

This policy brief describes key HIV viral load thresholds and the available viral load testing approaches for monitoring how well antiretroviral therapy is working for people living with HIV. It provides clarification for and elaborates upon the current treatment monitoring algorithm from the *Consolidated guidelines on HIV prevention, testing, treatment, service delivery and monitoring: recommendations for a public health approach (1)*. This information can help people living with HIV to live healthy lives, ensure that HIV is not transmitted to other people and support policy-makers in determining the optimal allocation of resources for scaling up viral load testing and communicating the results.

2. WHAT IS VIRAL SUPPRESSION AND HOW CAN IT BE ACHIEVED?

When taken as prescribed, HIV medicine suppresses the replication of HIV inside a person's body. Most people who have reliable access to HIV medicines and take their medication as prescribed will eventually reach a point where this suppression is so complete that HIV is not detectable in their blood or genital secretions by even the most sensitive viral load testing methods currently available. However, this state of viral suppression can be reversed if a person loses access or stops taking the medication as prescribed. Thus, supporting people living with HIV to start and stay on antiretroviral therapy as prescribed has enormous personal and public health benefits.

In addition to taking medication as prescribed, people living with HIV need regular health checks to make sure that antiretroviral therapy is working well. These checks include a blood test to measure any virus. Known as a viral load test, this is done by taking a blood sample and performing a test called polymerase chain reaction (PCR) to measure the amount of virus in the blood, which is reported in copies of virus per millilitre of blood. When a viral load is equal to or below 1000 copies/mL, we say that person is virally suppressed. When a viral load is so low the test cannot measure it, we say that the person's HIV is undetectable.

Taking antiretroviral therapy for life can feel daunting, especially when a person does not know about and understand the tremendous benefits of viral suppression. People living with HIV find different ways to ensure they do not miss any doses, including by supporting one another and, when possible, through the support of their close family and friends. Further, being able to take their medication as prescribed relies heavily on the health system: drug stockouts, treatment interruptions, incorrect drug regimens prescribed, and stigma and discrimination in healthcare settings can all have a severe impact on one's treatment goals. Communicating the benefits of antiretroviral therapy, especially its ability to prevent transmitting HIV to someone who is HIV-negative, can provide motivation and inspiration to adhere to a treatment programme. Further, people living with HIV should be provided information about what viral load results mean, receive encouraging adherence counselling messages and feel empowered to control and manage their own health.

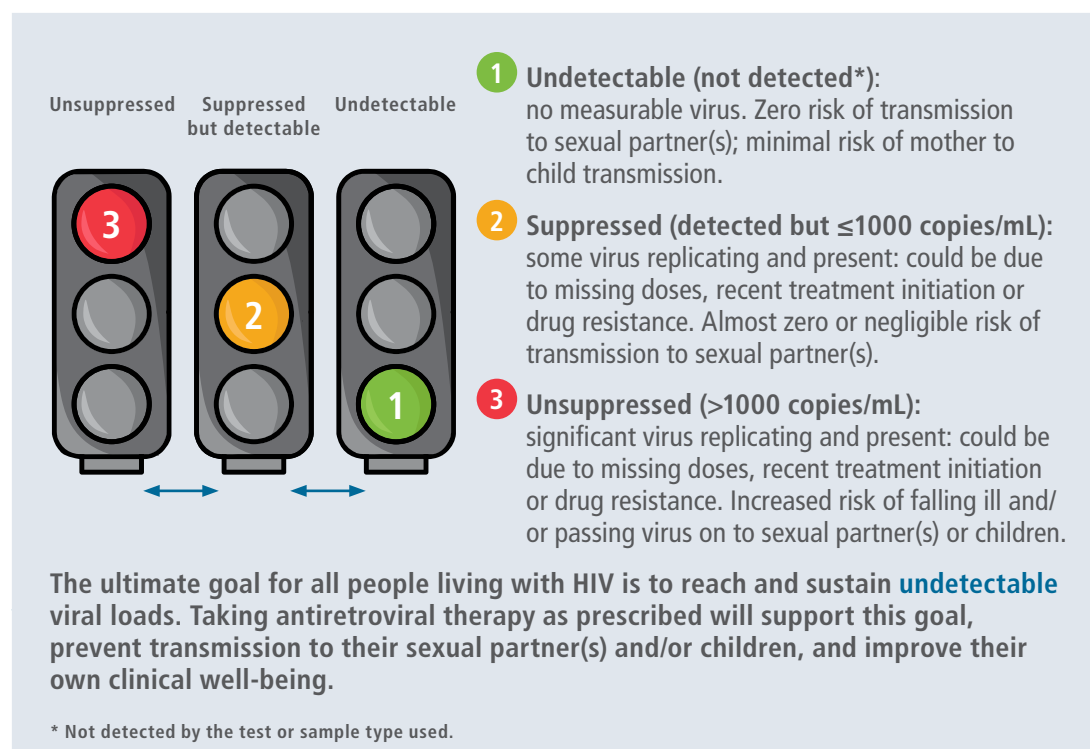
3. THE UPDATED TREATMENT MONITORING ALGORITHM AND ITS THREE CATEGORIES OF VIRAL LOAD LEVELS

3.1 Updated treatment monitoring algorithm

WHO's HIV treatment monitoring algorithm was updated in 2021 to support people living with HIV to achieve viral suppression, with the ultimate goal of maintaining an undetectable viral load (2). The updated algorithm introduced two distinct thresholds: >1000 copies/mL to identify people living with HIV who are unsuppressed and for whom treatment might be failing; and undetectable to identify people living with HIV whose viral load cannot be detected. This policy brief aims to explain the rationale behind these thresholds and to provide additional information regarding implementation considerations.

3.2 Three categories of viral load levels

There are three key categories of viral load suppression: unsuppressed, suppressed, and undetectable. The viral loads of people living with HIV can fluctuate between these categories depending on their access and adherence to antiretroviral therapy. These are illustrated and detailed in the figure below.



The 2025 Global AIDS Targets calls for all people receiving antiretroviral therapy to achieve viral suppression by 2025. (3). People living with HIV with an undetectable viral load as well as those with a suppressed viral load (detected but ≤ 1000 copies/mL) should be included in the numerator when calculating the last 95 (viral suppression) target.

Anyone with a detectable HIV viral load, even if suppressed (≤ 1000 copies/mL), should be supported with adherence counselling and follow-up viral load testing (see Annexes 1 and 2 for the updated treatment monitoring algorithm and implementation considerations for treatment monitoring of pregnant women and breastfeeding women, respectively); however, only those with persistent unsuppressed viral loads¹ should be considered for a treatment regimen switch.

¹ Two consecutive viral load tests performed three months apart that are >1000 copies/mL, with adherence counselling between tests.

4. VIRAL LOAD THRESHOLDS IN THE CONTEXT OF INDIVIDUAL HEALTH AND HIV TRANSMISSION

4.1 Individual health and well-being

The benefits of antiretroviral therapy for the health and well-being of people living with HIV have been well documented. Within weeks after treatment initiation, clinical and immune improvement and viral suppression can be expected. Good adherence to treatment improves survival and long-term life expectancy.

A systematic review was conducted to understand the clinical impact of being suppressed but detectable (≤ 1000 copies/mL) (4). The available evidence showed that viral loads between 200 and 1000 copies/mL have been associated with future suspected treatment failure (persistent viral load >1000 copies/mL). Further, the evidence showed that viral loads that are detectable but ≤ 1000 copies/mL have been associated with the development of drug resistance mutations. However, these studies included people living with HIV taking older drug regimens. The relevance, frequency and likelihood of these events among people living with HIV taking preferred antiretroviral drugs, such as dolutegravir, are unknown because little evidence currently indicates any risk of drug resistance and/or treatment failure with dolutegravir-based first-line therapy. In addition, the prevalence of low-level viraemia remains relatively low: one study found that among people with a suppressed viral load (≤ 1000 copies/mL), 95% had an undetectable viral load (5).

4.2 HIV transmission during pregnancy, delivery and breastfeeding

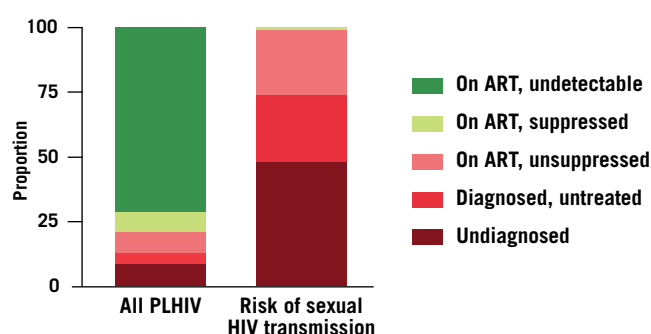
Available evidence suggests that if a mother living with HIV is taking antiretroviral therapy and maintains a suppressed viral load during pregnancy, delivery and breastfeeding, the risk of vertical HIV transmission can be as low as $<1\%$ (6–8). If a mother is taking antiretroviral therapy and is undetectable prior to and throughout pregnancy and delivery, there is no risk of transmitting to the infant during pregnancy. Vertical HIV transmission during pregnancy, delivery and breastfeeding is considerably more frequent when the mother's viral load is unsuppressed. WHO guidance indicates that a pregnant mother living with HIV whose viral load is suppressed within four weeks of delivery is at low risk of transmitting HIV to their infant and recommends breastfeeding for women taking antiretroviral therapy (1,9).

4.3 HIV transmission during sex

All available evidence suggests that people living with HIV who have an undetectable viral load have zero risk of transmitting HIV sexually and those with a suppressed viral load (detectable but ≤ 1000 copies/mL) have almost zero risk of transmitting HIV to a sexual partner. A recent summary of the available evidence (4) found that three studies showed no evidence of HIV transmission between adult couples when the HIV-positive partner had viral loads of less than 200 copies/mL, while three studies showed no transmission events when the viral loads were less than 1000 or 1500 copies/mL, respectively. Finally, one study observed one transmission event when the index partner had two viral load results of ~ 850 copies/mL (10); however, the viral load at transmission was unknown. **Therefore, viral loads under 1000 copies/mL are not clearly associated with sexual transmission of HIV.**

Without antiretroviral therapy, median viral load values tend to be considerable: anywhere from 30 000 to $>500\,000$ copies/mL, depending on the stage of infection (11). High viral loads are known to be associated with high rates of HIV transmission (12). Furthermore, recent modelling from sub-Saharan Africa has shown that 75% of all sexual HIV transmissions occur when the index partner is undiagnosed or diagnosed yet untreated (Fig 1) (13). The remaining sexual HIV transmissions occur when the index partner is diagnosed, on ART, but unsuppressed. From the most recent global HIV report, an estimated 68% of people living with HIV are virally suppressed (14). Prevention strategies should, therefore, prioritize identifying all people living with HIV and linking them to optimal and successful antiretroviral therapy.

Fig. 1 Proportion of viral load categorization of all people living with HIV and by risk of sexual transmission



People living with HIV who have an undetectable viral load have zero risk of transmitting HIV to their sexual partner(s).

People living with HIV who have a suppressed but detectable viral load have almost zero or negligible risk of transmitting HIV to their sexual partner(s).

Research suggests that the prevention benefits of HIV treatment are highly motivating to people living with HIV and that, when people living with HIV are informed of these benefits, they are more likely to adhere to their medication (15). Community-led initiatives that communicate these benefits to people living with HIV, such as Undetectable = Untransmittable (U=U) campaigns, provide helpful messages and tools to encourage people living with HIV to achieve and maintain viral suppression and to reduce anxiety about transmitting HIV to sexual partners, support safer conception in serodiscordant couples and reduce community stigma. WHO guidance encourages the use of these messages as part of counselling, educational information and demand creation activities (16).

4.4 HIV transmission through needle-sharing

The transmissibility of HIV by sharing injecting drug use equipment when a person's viral load is undetectable or suppressed has not been studied (4).

5. IMPLEMENTATION CONSIDERATIONS FOR VIRAL LOAD TESTING OF PEOPLE LIVING WITH HIV

5.1 Tests and sample types to measure the viral load of people living with HIV

Countries and health-care workers have many choices to consider among viral load testing methods available for people living with HIV (17-19). The options range from complex, high-throughput laboratory-based technologies to simpler, decentralizable point-of-care tests. Although plasma samples provide the most sensitive results for HIV viral load testing (lowest limits of detection), alternative tests and sample types that provide high-quality results and enable broader scale-up and sustainable access to viral load testing can be beneficial and are often preferable (17). To use plasma samples for viral load testing, blood samples must generally arrive to and be processed at the laboratory within 24 hours of sample collection. This can be a considerable limitation in many settings with a high burden of HIV prevalence. Using alternative sample types, such as dried blood spot samples, considerably expands access to viral load testing where distances may be far, roads poor or sample transport challenging.

There are advantages and disadvantages to each test and sample type available for consideration. These should be carefully reviewed and selected within an integrated, optimized diagnostic network based on the country needs and context. Some of these test and sample type options have a higher limit of detection (LOD), generally because of smaller sample volumes. Nevertheless, all HIV viral load tests and sample types available and with WHO prequalification are capable of accurately identifying people living with HIV using the three viral load categories presented above, enabling them to play an important role in a tiered, optimized diagnostic network.

For example, some point-of-care tests or dried blood spot samples with smaller sample volumes and higher limits of detection (300–900 copies/mL) can accurately distinguish between samples that are undetectable, suppressed (detected but ≤ 1000 copies/mL) and unsuppressed (> 1000 copies/mL) (20, 21). Note that a result “below the limit of detection” typically means that there is indeed a detectable viral load but its quantification is simply below the threshold used by the viral load technology (see the next section). A suppressed viral load would yield a result of “ $< \text{LOD}$ ” (below the limit of detection), “ $< \text{LLOQ}$ ” (below the lower limit of quantification), or a viral load value that is ≤ 1000 copies/mL. Further, an undetectable viral load would yield a result of “target or viral load not detected”.

5.2 Understanding limits of detection, viral load results, and inherent assay variability

Reinforced clinical and laboratory training are important for understanding and interpreting viral load results correctly. A limit of detection is defined as the lowest amount of virus that can be detected 95% of the time. This does not preclude technologies from being able to detect a viral load below their stated limit of detection. In fact, all technologies that are WHO prequalified report viral load results that are below the limit of detection without providing a precise value (report output: $< \text{LOD}$ or $< \text{LLOQ}$). In nearly all cases, these would be considered viral load results that are suppressed (detected but ≤ 1000 copies/mL). The box summarizes the typical range of outputs provided by viral load technologies.

Typical viral load technology reporting outputs

- Not detected = undetectable: the test could not detect any virus in the sample
- <LOD or <LLOQ = the test detected some virus but less than the limit of detection (<LOD) or lower limit of quantification (<LLOQ) (in nearly all cases these would be suppressed, detected but ≤ 1000 copies/mL)
- Viral load copies/mL value = the quantified value of viral load detected
- >ULOQ = detectable viral load that is more than the upper limit of quantification (>ULOQ) (generally >1 million copies/mL or higher)

Therefore, regardless of HIV viral load test and sample type, treatment monitoring programmes can use all WHO-prequalified options to accurately identify people living with HIV using the three key viral load categories: **unsuppressed, suppressed and undetectable.**

Viral load testing uses PCR technology that is known to be inherently variable (22–24), even using the most sophisticated and accurate reference standards. For example, a viral load of 1000 copies/mL (even if using a plasma specimen and a laboratory-based assay) has a known and accepted variability in the range of 500–2000 copies/mL, meaning that if you repeated the test the result would likely be anywhere within that range (22–24).

Although the lower limits of detection of some tests and sample types tend to be higher than plasma because of the smaller sample volume, this does not preclude the technologies from correctly classifying people living with HIV as unsuppressed, suppressed or undetectable. Therefore, limits of detection should not be the primary metric for consideration when reviewing test or sample type performance or selecting one for routine use. Further, **alternative tests and sample types often enable significantly greater access to viral load testing and should be considered by national programmes to ensure that viral load testing is available for all people living with HIV.**



6. CONCLUSIONS AND IMPLICATIONS

6.1 Understanding HIV viral load for people living with HIV

- An undetectable viral load is the ultimate goal of antiretroviral therapy for all people living with HIV, for their own health and to prevent onward transmission to their sexual partner(s) and children. People living with HIV who have an undetectable viral load have zero risk of transmitting HIV through sex as long as they continue to take their antiretroviral therapy as prescribed.
- People living with HIV who have a suppressed but detectable viral load have almost zero or negligible risk of transmitting HIV through sex as long as they continue to take their antiretroviral therapy as prescribed. Taking antiretroviral therapy as prescribed will also improve their individual health and enable them to live a healthy life.
- People living with HIV should have confidence in the technologies used to measure and confirm their viral load as unsuppressed, suppressed or undetectable.

6.2 Understanding HIV viral load for clinicians and other health facility staff delivering HIV care

- An undetectable viral load is the ultimate goal of antiretroviral therapy for all people living with HIV, for their own health and to prevent onward transmission to their sexual partner(s) and children. This message should be reinforced at every visit, while reaching viral suppression should be a cause for celebration.
- People living with HIV who have an undetectable viral load should be told that, along with achieving better health, there is zero risk of transmitting HIV through sex as long as they continue to take their antiretroviral therapy as prescribed.
- People living with HIV who have a suppressed but detectable viral load should be told that, along with achieving better health, there is almost zero or negligible risk of transmitting HIV through sex as long as they continue to take their antiretroviral therapy as prescribed. Further, they should receive encouragement for reaching this threshold while addressing adherence and exploring other barriers that may exist to reaching an undetectable viral load.
- It is important to share viral load test results as soon as they are available with people living with HIV who fall into any of the three viral load categories: unsuppressed, suppressed and undetectable. Although those whose unsuppressed viral load results may need to be rapidly called back to the clinic for further counselling, all people living with HIV should be told their test results.

6.3 Understanding HIV viral load for national programmes and policy-makers

- An undetectable viral load is the ultimate goal of every HIV programme, at both the individual and community levels, to accelerate progress towards epidemic control. Improving and ensuring widespread access to viral load testing, motivating people living with HIV to reach and sustain viral suppression and improving reporting systems will help achieve this goal.
- When selecting viral load testing technologies, HIV programmes should consider all available options and sample types giving priority to widespread access. PCR is inherently variable, yet all WHO prequalified viral load technologies can identify people living with HIV as unsuppressed, suppressed and undetectable. Dried blood spots, in particular, will support national programmes to ensure access to viral load for all people living with HIV, complementing plasma sampling.
- National programmes, with support from civil society organizations and networks of people living with HIV, should create and disseminate tools to educate people living with HIV and communities about the benefits of antiretroviral therapy and viral suppression, and these messages may also help reduce stigma associated with HIV.
- Quickly reporting unsuppressed viral load results to health-care facilities and people living with HIV will support follow-up clinical actions. Point-of-care testing technologies can support this expedited reporting, especially for high priority, vulnerable or high-risk populations (1). Likewise, it is important to develop materials and mechanisms to ensure consistent and reliable reporting of viral load results that are suppressed and undetectable to allow for clear, positive celebratory messages and consider eligibility for differentiated clinical services.

When reviewing current treatment monitoring policies, a public health approach should be considered that takes into account HIV viral load access, current treatment regimens, tests and sample types available, sample transport options, result utilization and individual and national goals. The priority for national HIV programmes is to increase access to viral load testing – current testing approaches, sample types and assay precision should not be considered a barrier to doing so.

ACKNOWLEDGEMENTS

This policy brief was drafted and led by Lara Vojnov, Andy Seale, and Meg Doherty (Department of Global HIV, Hepatitis, and Sexually Transmitted Infections Programmes, WHO).

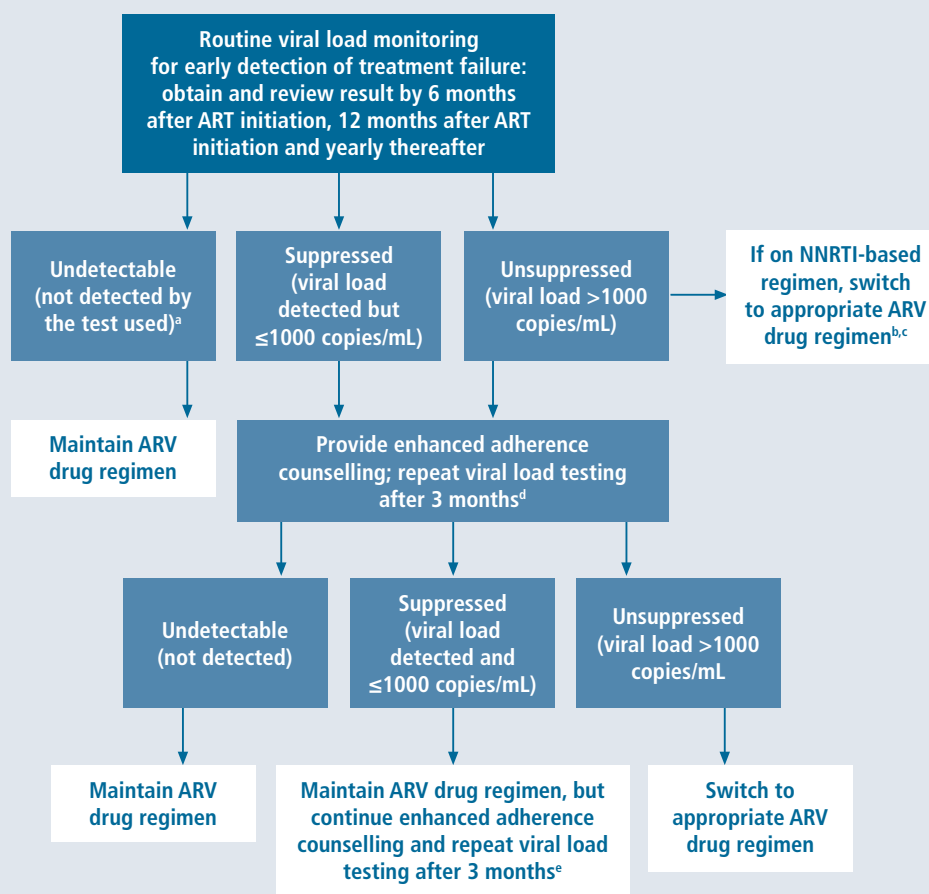
WHO gratefully acknowledges the contributions of many individuals to develop this policy brief.

These include George Alemnji (PEPFAR, USA), Heather Alexander (US Centers for Disease Control, USA), David Allen (Bill & Melinda Gates Foundation, USA), Florence Riako Anam (Global Network of People Living with HIV, Kenya), Moherndran Archary (King Edward VIII Hospital affiliated to the Nelson Mandela School of Medicine, South Africa), Helen Ayles (London School of Hygiene and Tropical Medicine (Zambart), Zambia), Iskandar Azwa (Universiti of Malaya, Malaysia), Solange Baptiste (International Treatment Preparedness Coalition, South Africa), Rachel Baggeley (WHO), Linda-Gail Bekker (The Desmond Tutu HIV Centre, South Africa), Debi Boeras (Global Health Impact Group, USA), Laura Broyles (Global Health Impact Group, USA), Pedro Cahn (Fundacion Huesped, Argentina), Alexandra Calmy (Hôpitaux Universitaires de Genève, Switzerland), Mohamed Chakroun (Infectious Diseases at Fattouma Bourguiba Teaching Hospital, Tunisia), Myron Cohen (University of North Carolina School of Medicine, USA), Ben Collins (ReShape/IHP, United Kingdom of Great Britain and Northern Ireland), Paul Drain (University of Washington, USA), Mandisa Dukashe (HIV Survivors and Partners Network, South Africa), Nathan Ford (WHO), Catherine Godfrey (Office of the Global AIDS Coordinator, USA), Eric Goemaere (Médecins Sans Frontières, South Africa), Maureen Goodenow (National Institutes of Health Office of AIDS Research, USA), Raffy Gorospe (Office of AIDS Research of the National Institutes for Health, USA), Beatriz Grinsztejn (Instituto Nacional de Infectologia Evandra Chagas-Fiocruz, Brazil), Andrew Grulich (Kirby Institute, Australia), Nina Hasen (Population Services International, USA), Diana Havlir (University of California San Francisco, USA), Micheal Ighodaro (U=U Win-Win Advocacy Coalition, USA), Cadi Irvine (WHO), Andreas Jahn (Training and Education Centre for Health, Malawi), John Kinuthia (Kenyatta National Hospital, Kenya), Eline Korenromp (UNAIDS), Nagalingeswaran Kumarasamy (VHS-Infectious Diseases Medical Centre, Voluntary Health Services, India), Imelda Mahaka (Pangaea Zimbabwe AIDS Trust, Zimbabwe), Mary Mahy (UNAIDS), Lynne Mofenson (Elizabeth Glaser Pediatric AIDS Foundation, USA), Joseph Murungu (Pangaea Zimbabwe AIDS Trust, Zimbabwe), Angela Mushavi (Ministry of Health and Child Care, Zimbabwe), Landon Myer (University of Cape Town, South Africa), Kogieleum Naidoo (Centre for the AIDS Programme of Research in South Africa, South Africa), Tom Ngaragari (Population Services International, Kenya), Emi Okamoto (Clinton Health Access Initiative, USA), Roger Paredes (Hospital Universitari Germans Trias i Pujol, Spain), Andrew Philips (University College London, United Kingdom of Great Britain and Northern Ireland), Elliot Raizes (US Centers for Disease Control, USA), Bruce Richman (Prevention Access Campaign, USA), Alison Rodger (University College London, United Kingdom of Great Britain and Northern Ireland), Kenly Sikwese (AfroCAB, Zambia), Kat Sleeman (US Centers for Disease Control, USA), Anna Turkova (University College London, United Kingdom of Great Britain and Northern Ireland), Jeffrey Walimbwa (Global Black Gay Men Connect, Kenya), Jacque Wambui (AfroCAB Treatment Access Partnership, Kenya), Jason Williams (USAID, USA), Clement Zeh (US Centers for Disease Control, USA).

REFERENCES

1. Consolidated guidelines on HIV prevention, testing, treatment, service delivery and monitoring: recommendations for a public health approach, 2021 update. Geneva: World Health Organization; 2021 (<https://apps.who.int/iris/handle/10665/342899>, accessed 30 June 2022).
2. Updated recommendations on HIV prevention, infant diagnosis, antiretroviral initiation and monitoring: March 2021. Geneva: World Health Organization; 2021 (<https://apps.who.int/iris/handle/10665/340190>, accessed 30 June 2022).
3. Global AIDS Strategy 2021-2026 - End Inequalities. End AIDS. Geneva: UNAIDS; 2021 (https://www.unaids.org/sites/default/files/media_asset/global-AIDS-strategy-2021-2026_en.pdf, accessed 12 June 2023).
4. Broyles LN, Luo R, Boeras D, Vojnov L. The risk of sexual transmission of HIV in individuals with low-level HIV viraemia: a systematic review. *Lancet* 2023; published online July 21. [https://doi.org/10.1016/S0140-6736\(23\)00877-2](https://doi.org/10.1016/S0140-6736(23)00877-2).
5. Chang G, Bingham T, Sleeman K, Benech I, Duong Y, Justman J et al. Population-based HIV impact assessments and viral load results: implications for U=U. 2020 Conference on Retroviruses and Opportunistic Infections, 8–11 March 2020, Boston, MA, USA. Abstract 1082.
6. Gill MM, Hoffman HJ, Ndatimana D, Mugwaneza P, Guay L, Ndayisaba GF, et al. 24-month HIV-free survival among infants born to HIV-positive women enrolled in Option B+ program in Kigali, Rwanda: The Kabeho Study. *Medicine*. 2017 Dec;96(51):e9445.
7. Myer L, Phillips TK, McIntyre JA, Hsiao N-Y, Petro G, Zerbe A, et al. HIV viraemia and mother-to-child transmission risk after antiretroviral therapy initiation in pregnancy in Cape Town, South Africa. *HIV Med*. 2017 Feb;18(2):80-88.
8. Townsend CL, Byrne L, Cortina-Borja M, Thorne C, de Ruiter A, Lyall H, et al. Earlier initiation of ART and further decline in mother-to-child HIV transmission rates, 2000-2011. *AIDS*. 2014 Apr;28(7):1049-57.
9. Global guidance on criteria and processes for validation: elimination of mother-to-child transmission of HIV, syphilis, and hepatitis B virus. Geneva: World Health Organization; 2021 (<https://apps.who.int/iris/handle/10665/349550>, accessed 30 June 2022).
10. Mujugira A, Coombs R, Heffron R, Celum C, Ronald A, Mugo N, et al. Seminal HIV-1 RNA detection in heterosexual African men initiating antiretroviral therapy. *J Infect Dis*. 2016 Jul;215(2):212.
11. Selik R, Linley L. Viral loads within 6 weeks after diagnosis of HIV infection in early and late stages: observational study using national surveillance data. *JMIR Public Health Surveill*. 2018 Oct-Dec;4:e10770.
12. Anderson RM, May RM. Epidemiological parameters of HIV transmission. *Nature* 1988; 333:514–9.
13. Edun O, Okell L, Chun H, Milligan K, Dirlikov E, Shiraishi RW et al. Sexual risk and role of low-level viremia to HIV transmission in sub-Saharan Africa. 30th Conference on Retroviruses and Opportunistic Infections. 2023, Abstract 868.
14. In Danger: UNAIDS Global AIDS Update 2022. Geneva: UNAIDS; 2022 (https://www.unaids.org/sites/default/files/media_asset/2022-global-aids-update_en.pdf, accessed 12 June 2023).
15. Okoli C, Van de Velde N, Richman B, Allan B, Castellanos E, Young B et al. Undetectable equals untransmittable (U= U): awareness and associations with health outcomes among people living with HIV in 25 countries. *Sex Transm Infect*. 2021;97:18-26.
16. What works for generating demand for HIV testing services. Geneva: World Health Organization; 2019 (<https://www.who.int/publications-detail-redirect/WHO-CDS-HIV-19.33>, accessed 27 June 2022).
17. HIV molecular diagnostics toolkit to improve access to viral load testing and infant diagnosis. Geneva: World Health Organization; 2019 (<https://apps.who.int/iris/handle/10665/325961>, accessed 30 June 2022).
18. HIV/AIDS diagnostics technology landscape. 5th ed. Geneva: Unitaid; 2015 (http://www.unitaid.org/assets/UNITAID_HIV_Nov_2015_Dx_Landscape-1.pdf, accessed 30 June 2022).
19. WHO list of prequalified in vitro diagnostic products. Geneva: World Health Organization; 2022 (https://extranet.who.int/pqweb/sites/default/files/documents/220420_List_PQ_IVD_Products.pdf, accessed 30 June 2022).
20. Sacks JA, Fong Y, Gonzalez MP, Andreotti M, Baliga S, Garrett N et al. Performance of Cepheid Xpert HIV-1 viral load plasma assay to accurately detect treatment failure. *AIDS*. 2019;33:1881-9.
21. Vojnov L, Carmona S, Zeh C, Markby J, Boeras D, Prescott MR et al. The performance of using dried blood spot specimens for HIV-1 viral load testing: a systematic review and meta-analysis. *PLoS Med*. 2022 Aug;19(8):e1004076.
22. Cobb BR, Vaks JE, Do T, Vilchez RA. Evolution in the sensitivity of quantitative HIV-1 viral load tests. *J Clin Virol*. 2011;52 (Suppl. 1): S77-82.
23. Jennings C, Harty B, Granger S, Wager C, Crump J, Fiscus SA et al. Cross-platform analysis of HIV-1 RNA data generated by a multicenter assay validation study with wide geographic representation. *J Clin Microbiol*. 2012;50:2737-2747.
24. Lelie N, van Drimmelen H. Accuracy of quantitative HIV-1 RNA test methods at 1000 copies/ml and the potential impact of differences in assay calibration on therapy monitoring of patients. *J Med Virol*. 2020;92:3246-53.
25. HIV diagnosis and ARV use in HIV-exposed infants: a programmatic update. Geneva: World Health Organization; 2018 (<https://apps.who.int/iris/handle/10665/273155>, accessed 30 June 2022).

ANNEX 1. TREATMENT MONITORING ALGORITHM FOR PEOPLE LIVING WITH HIV



Adherence counselling should be provided at all visits to ensure that viral suppression is maintained or given priority throughout care

- a. Not detected by the test or sample type used. This is updated from ≤ 50 copies/ml from (1).
- b. Switch after a single elevated viral load should be considered if treatment experience is likely.
- c. A second viral load may be considered before regimen switch if DTG-based regimens are unavailable and the results of a viral load test can be returned and acted on rapidly.
- d. Conduct same-day testing using point-of-care viral load testing for a repeat viral load test, where available, to expedite the return of results. If not available, viral load specimens and results for a repeat viral load should be given priority across the laboratory referral process (including specimen collection, testing and return of results). See subsection 3.2 of (2).
- e. Consider therapy switch for those receiving NNRTI-based regimens and based on clinical considerations and no adherence concerns.

ANNEX 2. IMPLEMENTATION CONSIDERATIONS FOR TREATMENT MONITORING OF PREGNANT AND BREASTFEEDING WOMEN

- **Whenever possible, use same-day point-of-care testing for viral load testing of pregnant and breastfeeding women** to expedite the return of results and clinical decision-making. If this is not available, viral load specimens and results for pregnant and breastfeeding women should be given priority across the laboratory referral process (including specimen collection, testing and return of results).
- **Adherence counselling** should be provided at all antenatal care and postnatal visits to ensure that viral suppression is maintained throughout pregnancy and breastfeeding.
- **For all pregnant women, regardless of ART initiation timing:** conduct viral load testing at 34–36 weeks of gestation (or at the latest at delivery) to identify women who may be at risk of treatment failure and/or may deliver infants at higher risk of perinatal transmission.

Action: if viral load >1000 copies/mL, follow the treatment monitoring algorithm^a and provide enhanced postnatal prophylaxis^b for the infant. Where available, consider infant nucleic acid testing at birth.^b

In addition:

- (a) **For pregnant women receiving ART before conception:** conduct a viral load test at the first antenatal care visit (or when first presenting) to identify women at increased risk of in utero transmission.

Action: If viral load >1000 copies/mL, follow treatment monitoring algorithm^a and consider infant nucleic acid testing at birth,^b where available.

- (b) **For pregnant women starting ART during pregnancy:** conduct a viral load by three months after ART initiation to ensure that there has been rapid viral suppression.^c

Action: If viral load >1000 copies/mL,^a follow the treatment monitoring algorithm.^a Regardless of the maternal viral load, the infants of mothers starting ART at any time during pregnancy could be considered for birth testing,^b where available.

- **For all breastfeeding women, regardless of when ART was initiated:** conduct a viral load test three months after delivery and every six months thereafter to detect viraemic episodes during the postnatal period.

Action: if viral load >1000 copies/mL,^a follow the treatment monitoring algorithm,^a conduct infant HIV testing immediately^d and consider reinitiating enhanced postnatal prophylaxis for the infant.^{b,e}

a. See Annex 1.

b. See the programmatic update on HIV diagnosis and ARV use in HIV-exposed infants (25).

c. If viral load testing is expected to be undertaken in close proximity to the planned viral load at 34–36 weeks of gestation (see above), the first viral load test can be delayed until weeks 34–36 of gestation.

d. Conduct same-day testing using point-of-care infant diagnosis, where available, to expedite the return of results. See subsection 3.1 of (2).

e. Consider reinitiating and continuing enhanced postnatal prophylaxis until the results are returned or same-day testing is negative. Begin ART if the infant is diagnosed with HIV (see the programmatic update on HIV diagnosis and ARV use in HIV-exposed infants (25)).

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