The Role of HIV Viral Suppression in Improving Individual Health and Reducing Transmission

Department of Global HIV, viral hepatitis and sexually transmitted infections Programmes

12 October 2023
## The history of diagnostics within treatment monitoring

<table>
<thead>
<tr>
<th>Year</th>
<th>Description</th>
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</thead>
<tbody>
<tr>
<td>2006</td>
<td>ART initiation of PLHIV with a CD4 ≤200 cells/ul</td>
</tr>
<tr>
<td>2010</td>
<td>ART initiation of PLHIV with a CD4 ≤350 cells/ul; viral load suggested</td>
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<tr>
<td>2013</td>
<td>Viral load as the preferred method to identify treatment failure</td>
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<tr>
<td>2016</td>
<td>ART should be initiated in ALL PLHIV, regardless as to CD4 cell count</td>
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<tr>
<td>2017</td>
<td>CD4 is critical to identifying people living with advanced HIV disease</td>
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</table>
The evolution of optimized ART: towards smarter and better treatment options

- **Cabotegravir**
- **Lencaprevir**
- **Rilpivirine**

Long Acting ARVs

- CAB/RPV (2021)
  - 1 injection every 2 months

Adherence

Costs

Long Acting ARVs

- CAB/RPV (2021)
  - 1 injection every 2 months

Adherence

Costs

Department of Global HIV, viral hepatitis and sexually transmitted infections Programmes
Low-level viremia associated with poorer individual health

Low-level viremia associated with:
- Virological failure
- Switch to 2nd line
History of treatment monitoring algorithm: 2016 to 2020

Targeted viral load monitoring (suspected clinical or immunological failure)

- Test viral load
- Viral load >1000 copies/ml
- Evaluate for adherence concerns
- Repeat viral load testing after 3–6 months
  - Viral load ≤1000 copies/ml
    - Maintain first-line therapy
  - Viral load >1000 copies/ml
    - Switch to second-line therapy

Routine viral load (early detection of virological failure)
Key goals for the 2021 treatment monitoring algorithm

- Appreciating the role and benefits of notifying PLHIV of an undetectable viral load
- Available evidence for optimal treatment monitoring algorithm considering DTG and TLD roll-out
- Impact of low-level viremia on HIV transmission
- Role of low-level viremia on individual health, and if possible within the context of DTG and TLD roll-out
- Timing of the first viral load
- Increasing rates of NNRTI-based drug resistance and quick switching to ‘2nd line’
- Clarifying timing of repeat viral load after an initial unsuppressed viral load
History of treatment monitoring algorithm: 2016 to 2020

Targeted viral load monitoring (suspected clinical or immunological failure)

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Routine viral load monitoring for early detection of treatment failure: obtain and review result by 6 months after ART initiation, 12 months after ART initiation and yearly thereafter

- Undetectable (≤50 copies/ml)
  - Maintain ARV drug regimen
- Viral load >50 to ≤1000 copies/ml
  - Provide enhanced adherence counselling; repeat viral load testing after 3 months
- Viral load >1000 copies/ml
  - If on NNRTI-based regimen, switch to appropriate regimen

Adherence counselling should be provided at all visits to ensure that viral suppression is maintained or given priority throughout care
Three studies showed no HIV transmission when the person living with HIV had a viral load less than 200 copies/mL. Most transmission events occurred when the person living with HIV had a viral load between 30,000 and 750,000 copies/mL.

Across the remaining four prospective studies, there were 323 transmission events; none were in patients considered stably suppressed on ART.

Among all studies, there were two cases of transmission when person living with HIV’s most recent viral load was less than 1000 copies/mL (~700 and ~850 copies/mL). However, in both cases the viral load test was taken 50+ days prior to the transmission event.

No studies were identified evaluating the transmissibility of HIV through the sharing of injection drug use equipment when a person’s viral load is less than 1000 copies/mL.
Ongoing challenges for people living with HIV

- Continued and regular stigma and discrimination
  - Family
  - Friends
  - Health care providers
  - General public
- Punitive laws resulting in criminalization of PLHIV
Evidence improving public health messaging

Evidence consolidation and review of the risks of sexual HIV transmission based on viral load levels

Reflecting on the benefits and harms of the evidence, impact of positive messaging, and challenges with stigma, discrimination, and criminalization
Clear, celebratory messaging for people living with HIV

Three categories of viral load levels

1. Undetectable (not detected*): no measurable virus. Zero risk of transmission to sexual partner(s); minimal risk of mother to child transmission.

2. Suppressed (detected but ≤ 1000 copies/mL): some virus replicating and present: could be due to missing doses, recent treatment initiation or drug resistance. Almost zero or negligible risk of transmission to sexual partner(s).

3. Unsuppressed (>1000 copies/mL): significant virus replicating and present: could be due to missing doses, recent treatment initiation or drug resistance. Increased risk of falling ill and/or passing virus on to sexual partner(s) or children.

The ultimate goal for all people living with HIV is to reach and sustain **undetectable** viral loads. Taking antiretroviral therapy as prescribed will support this goal, prevent transmission to their sexual partner(s) and/or children, and improve their own clinical well-being.

* Not detected by the test or sample type used.
The evolution of optimized ART: towards smarter and better treatment options

- DTG/TLD have clinical and programmatic advantages over old regimens, including higher barrier to drug resistance
- Transition to TLD almost completed globally. The next action is to define what and how to monitor
- Some barriers to complete TLD transition: NTD concerns, local production of old drugs, BWG
- Concerns related to potential long-term toxicity (cardiometabolic issues) and resistance risk - WHO developed tools to monitor it

Adoption of TDF+3TC (or FTC)+DTG as the preferred first-line antiretroviral combination for treatment inflation in national guidelines for adults and adolescents, July 2022

By July 2022, 108 countries (88%) adopting DTG as part of the preferred first-line antiretroviral therapy for adults and adolescents, an 80% increase from 68 countries in 2020 when data for this indicator was first collected.

Rapid global uptake of TLD: adopted in +100 LMICs and used by >80% of PLHIV on ART

Source: Global AIDS Monitoring (UNAIDS/WHO/UNICEF) and Global HIV, Hepatitis and STIs Programmes (HHS), WHO, 2023
The majority of people living with HIV are not at risk of sexually transmitting the virus

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).
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.
How can dried blood spot samples be used?

**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, ≤ 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)

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.
## Performance of dried blood spot samples for viral load testing

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<tr>
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<th>Hologic Aoptima</th>
<th>Roche COBAS TaqMan HIV-1 FVE</th>
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<th>Siemens VERSANT HIV-1 RNA</th>
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<tbody>
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<td>DBS:plasma threshold comparisons</td>
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<td>800:800</td>
<td>95.04 (91.45–97.17)</td>
<td>92.59 (82.86–96.99)</td>
<td>91.55 (4.60–99.96)</td>
<td>98.64 (43.94–99.99)</td>
<td>85.36 (80.27–89.32)</td>
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<td>92.95 (0.04–100.00)</td>
<td>98.55 (60.16–99.97)</td>
<td>88.87 (83.99–92.40)</td>
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<td>98.40 (66.61–99.95)</td>
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<td>95.99 (91.31–98.20)</td>
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Performance of near point-of-care viral load testing

Jillian A. Sacks, Yuoi Fong, Mercedes Perez Gonzalez, Mauro Andretti, Shekala Balla, Nigel Garrett, Jeanne Jordan, Etienne Kartou, Sima Kalari, Omen Mut, Fanta Mboh, Zibusiso Ndlou, Jean-Claude Planteur, Sunnukar Saravanan, Lesley Scott, Trevor Peter, Nigel Doherty and Lara Volpov

Table

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<tr>
<td><strong>Cepheid Xpert</strong></td>
<td>Median viral load (copies/ml)</td>
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<td><strong>Comparator</strong></td>
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<td>Difference in medians (copies/ml)</td>
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Threshold comparisons

**Sensitivity (UCL-LCL)**

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Viral suppression remains a key global, public health and individual goal

- 95% of HIV-positive people know their HIV status
- 95% of people diagnosed with HIV receive sustained ART
- 95% of people on ART have viral suppression
Acknowledgements

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- Francoise Renaud (WHO)
- Omar Sued (WHO)
- Maëva Villard (IAS)
- Elena Vovc (WHO)
- Saltanat Yegeubayeva (WHO)

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