HIV VIRAL LOAD

Presented by: Dr Nomfundo Nhlapo

Dr Jeremy Nel is acknowledged for the development of the slides

PRETORIA, SATURDAY 17TH FEBRUARY 2018
A quick recap... HIV life cycle
Current cost ART in RSA: R 6 billion / annum

Smits RL et al. Frontiers Genetics 2013
WHAT IS THE VIRAL LOAD? And how it is measured?
WHAT IS THE VIRAL LOAD?

The viral load is a measure of the number of HIV copies present in the sample.

In practice, it’s almost always the serum (from the blood) that’s of interest, hence “serum viral load”.

- In certain situations, the viral load of other compartments can be useful – e.g. cerebrospinal fluid viral load.

It’s often expressed as copies per millilitre (copies/mL)

- For instance, a serum viral load of 50,000 copies/mL means that there are 50,000 HIV particles in each millilitre of the patient’s serum.
COPIES VS LOGARITHM OF COPIES

But since it can be difficult to deal with such large numbers when writing viral loads (e.g. 2,105,277), the viral load can also be expressed as a logarithm with base 10.

For example, a viral load of 10,000 copies per mL is equal to 4 log copies/mL.

<table>
<thead>
<tr>
<th>Viral load (copies/mL)</th>
<th>Logarithm(_{10}) (copies/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>10,000</td>
<td>4</td>
</tr>
<tr>
<td>50,000</td>
<td>4.69</td>
</tr>
<tr>
<td>100,000</td>
<td>5</td>
</tr>
<tr>
<td>500,000</td>
<td>5.69</td>
</tr>
</tbody>
</table>

In this scale, an increase of 1 log is equal to an increase of ten times the copies/mL (the viral load increases from 10,000 to 100,000 (10 times increase) between log 4 and log 5).
WHAT IS THE RANGE OF VIRAL LOADS SEEN IN TREATMENT-NAIVE HIV-INFECTED PATIENTS?

Without treatment, the range of viral loads seen is anything from undetectable to >10 million copies/mL.

However, most patients fall within the range of approximately 10,000 to 200,000 copies/mL, if you do random viral loads on them.


But each individual goes through several distinct phases:
NATURAL COURSE OF HIV VIRAL LOAD

If untreated
Phases of HIV Infection

- Primary infection
- Acute HIV syndrome
  - Wide dissemination of virus
  - Seeding of lymphoid organs
- Clinical latency
- Symptoms of AIDS
  - Opportunistic diseases
  - Constitutional symptoms
  - Death
- CD4+ Lymphocyte Count (cells/mm³)
- HIV RNA Copies per mL plasma

Weeks

Years
EXPLAINING THE “NATURAL COURSE” OF HIV VIRAL LOAD (WITHOUT TREATMENT)

**Red curve = viral load**

1. Starts from almost zero (new infection)

2. Within a few weeks, it rapidly climbs to a very high level, often > 1,000,000 copies/mL (1,000,000 corresponds to $10^6$ copies/mL on graph)

Why? At this point, there is little effective immunity that the body has developed against HIV.
3. Once the body develops an adaptive immune response to the HIV, the viral load declines again.

This partial immune control is driven by cytotoxic T cells (CD8 cells) and antibodies against HIV.
4. But this immune response is only partially effective:

- The viral load never goes back to zero

- Over time, the viral load rises as the virus slowly causes CD4 cell depletion (blue curve). The rise in viral load is slow for many years (while there are still moderate numbers of CD4 cells) and more rapid at the end (when the CD4 cells are almost depleted).

- As the CD4 cells get more and more depleted, symptoms of AIDS, opportunistic disease, and death can occur. This happens because there are not enough CD4 cells to fight the HIV as well as other infections in the body.
WHAT HAPPENS WHEN YOU START SOMEONE ON ANTIRETROVIRAL THERAPY?

All antiretroviral drugs work by inhibiting the replication cycle of HIV at some point, so all antiretroviral drugs will cause a decrease in the viral load.

If there is no resistance to the drugs, they will work to reduce the viral load to zero.
There are many reasons why drug resistance can occur, the main one being treatment related:

- Inadequate drug potency
- Inadequate drug levels, sub-optimal dosing, and drug interactions
- Inadequate adherence

Viral replication continues when patients are not virally suppressed on treatment, allowing more mutations to occur, and resistance to develop.

Other reasons for drug resistance are pre-existing resistance (which can occur in those who have been on antiretroviral drugs in the past), or infection with a drug resistant strain of HIV.
Differente antiretroviral drugs reduce the viral load at different speeds:

The quickest reductions in viral loads are generally seen with the integrase inhibitors.

HOW QUICKLY SHOULD VIRAL LOAD FALL ON APPROPRIATE THERAPY?

Most patients are fully suppressed by 3 months.

A subset of patients who start with a very high VL may not be fully suppressed at three months despite excellent adherence, but such patients would have had a $>2 \log_{10}$ drop in VL from baseline (i.e. the viral load is $1/100^{th}$ of what it was at baseline).

E.g. if baseline viral load was 3,000,000 copies/mL ($6.3 \log_{10}$) at 3 months it should be 3,000 copies ($4.3 \log_{10}$) at the highest.

This would considered to be a good response to treatment as there is more than a 2 log$_{10}$ drop in the VL.
Viral blips are transient and low-level increases in the viral load in a patient who had previously demonstrated viral suppression.

- Typically between 50-200 copies/mL. Never more than 1000.
- Can represent laboratory error, laboratory processing artefacts, intermittent poor adherence, or transient bursts of HIV replication.
- Not usually associated with subsequent virological failure.
WHY ARE THESE NOT BLIPS?

**Too high**
(generally 20-200 copies/mL, never more than 1000)

**Too sustained**
(Viral load should return to undetectable shortly thereafter)
WHAT TO DO ABOUT BLIPS?

**HIV Clinicians society guidelines:** if any detectable viral load found:

- **Give (repeat) adherence counselling, and**

- **Repeat next viral load in 2-3 months** (rather than every 6-12 months) – to check the elevated viral load is not sustained (in which case it would be a sustained viraemia, and not a blip).
If a virus becomes resistant to the patient’s therapy, or
If a patient stops taking their antiretroviral therapy, then

... the viral load will undergo a (sustained) increase. A sustained increase in the viral load is considered to be virological failure.
EXCEPTIONS: HIV CONTROLLERS AND LONG-TERM NONPROGRESSORS
HIV CONTROLLERS

“HIV controllers” are HIV-infected patients who are able to control their viral load without antiretroviral therapy. Their viral loads (without treatment) usually sit at <500 copies/mL.

- HIV controllers make up <1% of HIV patients.  

AIDS 2009, 23:1163–1169

A subset of these HIV controllers are “elite controllers” – with viral loads that are undetectable despite not being on therapy.

N.B. If you suspect a patient may be an “elite controller”, it is vital to exclude other possibilities, such as lab error or false-positive HIV results. Consider repeating the HIV test, the viral load, and an alternative confirmatory test such as an HIV PCR or Western Blot.
HOW DO HIV CONTROLLERS CONTROL THEIR HIV?

No single answer.

Likely several different mechanisms, with different ones (or combinations) operating in different patients
HOW DO ELITE CONTROLLERS DO?

Interestingly, compared to patients with a suppressed viral load from ART, elite controllers:

- Have increased immune activation and inflammation
- May be more likely to be hospitalised (especially with cardiovascular problems)
SHOULD ELITE CONTROLLERS BE TREATED?

The group isn’t well studied (small numbers), but on balance, the answer is probably “yes”.

HIV Clinician Society Guidelines specifically address this issue: “We advise starting ART in elite controllers too, with the same caveats regarding the patient being prepared.”

VIRAL LOAD AS (AN EXCELLENT) SURROGATE MARKER FOR OUTCOMES
TREATED OR UNTREATED, A HIGHER VIRAL LOAD PREDICTS A FASTER PROGRESSION TO AIDS-DEFINING ILLNESSES AND DEATH.
In one representative study, a low CD4 count was only 58% sensitive and 75% specific for detecting virological failure. (In other words, in only 58% of cases did the CD4 count effectively detect virological failure).

Viral load identified failure significantly earlier than CD4 count (median 10.4 vs 15.6 months, (p<0.0001).
VIRAL LOAD AS AN EXCELLENT SURROGATE MARKER FOR OUTCOMES IN HIV

The corollary is important: people monitored without viral load are more likely to develop treatment failure (since the initial warning signs aren’t picked up on early enough in as many cases).
VIRAL LOAD MONITORING

HIV Clinicians Society 2017 Adult ART guidelines recommendations:

VL monitoring at baseline, at 3 months, at 6 months, and then 6 monthly.
If the VL is undetectable for >12 months, then monitoring can be reduced to 12 monthly.
A viral load of >50 ml/copies should prompt adherence counselling and repeat viral load testing in 2-3 months.
VIRAL LOAD MONITORING

NDoH 2019 ART guidelines recommendations:

- VL monitoring at 6 months, and then 12 monthly (count from day of initiation).
- If the VL is undetectable (<50c/mL) for >12 months, then monitoring every 12 months.
- A viral load is more than 1000, do thorough assessment of the cause of an elevated VL. Consider the possibility of:
  - A. Adherence problems
  - B. Bugs (Intercurrent infection)
  - C. Incorrect ART dosage
  - D. Drug interaction
  - E. Resistance should prompt adherence counselling and

- Repeat viral load testing in 3 months. If viral load is under 1000, but is increasing more than a blip, must advocate for viral load.
VL AND PREGNANCY

- ART naïve pregnant women - 1<sup>st</sup> VL at 3 months then repeat at delivery if suppressed
- Known HIV positive on ART - VL at the first/booking visit in ANC if suppressed repeat VL at delivery
- Known HIV positive currently not on ART but previously exposed (previous PMTCT, or ART discontinued - VL before re-starting ART (but don’t wait for the results before starting ART
  - Repeat in one month
  - If more than one log drop in VL- continue and repeat VL in 2 months
  - If suppressed repeat VL at delivery
- VL at 6 months after delivery regardless of breastfeeding status
- VL 6 monthly during breastfeeding, aligned to 6 months, 12 months and 18 months well child visits
WHAT ABOUT VIRAL LOADS <1000?
VIROLOGICAL FAILURE: WHAT LEVEL?

The goal of ART is to suppress viral replication. ANY detectable viral load therefore could potentially represent viral failure.

But remember to exclude viral blips!
Virological Failure: What Level?

<table>
<thead>
<tr>
<th>Organisation</th>
<th>Virological failure threshold</th>
</tr>
</thead>
<tbody>
<tr>
<td>US Department of Health and Human Services</td>
<td>200 copies/mL</td>
</tr>
<tr>
<td>European AIDS Clinical Society</td>
<td>Any detectable viral load</td>
</tr>
<tr>
<td>World Health Organization</td>
<td>1000 copies/mL</td>
</tr>
<tr>
<td>Southern African HIV Clinicians Society</td>
<td>1000 copies/mL</td>
</tr>
<tr>
<td>South African Department of Health</td>
<td>1000 copies/mL</td>
</tr>
</tbody>
</table>

Note: all guidelines emphasize that a viral load should be repeated after 2-3 months, before virological failure is definitively diagnosed.
BUT THERE IS GOOD EVIDENCE THAT SUSTAINED VIRAL LOADS BELOW <1000 PREDICT SUBSEQUENT VIROLOGICAL FAILURE

Effect of HIV-1 low-level viraemia during antiretroviral therapy on treatment outcomes in WHO-guided South African treatment programmes: a multicentre cohort study

Lucas E Hermans, Michelle Moorhouse, Sergio Carmona, Diederick E Grobbee, L Marije Hofstra, Douglas D Richman, Hugo A Tempelman, Willem D F Venter, Annemarie M J Wensing

Lancet Infect Dis 2018; 18: 188–97
VIRAL LOAD AND TRANSMISSIBILITY
MULTIPLE TRIALS HAVE SHOWN THAT A SUSTAINABLY UNDETECTABLE VIRAL LOAD ESSENTIALLY PREVENTS HIV TRANSMISSION TO OTHERS

Antiretroviral Therapy for the Prevention of HIV-1 Transmission (HPTN 052 trial)

There were zero transmissions of HIV from HIV-positive patient to HIV-negative partner in over 8500 partner-years when the viral load was stably suppressed.

Sexual Activity Without Condoms and Risk of HIV Transmission in Serodifferent Couples When the HIV-Positive Partner Is Using Suppressive Antiretroviral Therapy (PARTNER trial)

Specifically enrolled people engaging in condomless sex. There were zero transmissions of HIV from HIV-positive patient to HIV-negative partner after a median of 1.2 years when the viral load was <200 copies/mL.
THANK YOU!
MONITORING ON ART AND SWITCHING REGIMENS
ROUTINE MONITORING ON ART: OVERVIEW

No additional testing needed for DTG-based regimens. Monitoring on TLD remains the same as for TEE

<table>
<thead>
<tr>
<th>Time on ART</th>
<th>Creatinine (only if on TDF)</th>
<th>CD4</th>
<th>VL</th>
<th>Total Cholesterol and TG (LPV/r)</th>
</tr>
</thead>
<tbody>
<tr>
<td>At ART initiation</td>
<td>√</td>
<td>√</td>
<td></td>
<td>No baseline cholesterol tests</td>
</tr>
<tr>
<td>Month 3</td>
<td>√</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Month 6</td>
<td>√</td>
<td></td>
<td>√</td>
<td></td>
</tr>
<tr>
<td>At 1 year</td>
<td>√</td>
<td>√</td>
<td>√</td>
<td></td>
</tr>
<tr>
<td>12-monthly</td>
<td>√</td>
<td>If clinically indicated</td>
<td>√</td>
<td>No routine annual cholesterol monitoring</td>
</tr>
</tbody>
</table>

Do HB and HBsAg if switching from 1st to 2nd line ART
**IMPORTANT PRINCIPLES IN VL MONITORING**

Virological suppression is defined as VL of < 50 c/mL

Any VL > 50 c/mL requires action

**VL 50 -999 c/ml**
- Transient viral blip
- Might be the start of virological failure

**VL ≥ 1000 c/ml**
- Work-up for possible virological failure

A **thorough assessment** is essential for any patient with a viral load measuring ≥ 50 c/ml
A thorough assessment is essential for any patient with a viral load measuring \( \geq 50 \text{ c/ml} \)

| **A** Adherence | **Is adherence to medication poor?**  
| Ask about factors that may influence adherence e.g.  
| • Medication side-effects,  
| • Depression,  
| • Alcohol or substance abuse,  
| • Poor social support or  
| • Non-disclosure.  
| Pregnant women may experience nausea, heartburn, and constipation. Assess the need for symptomatic treatment with an anti-emetic, anti-diarrhea agent, or fiber supplement. | **Tips**  
| Ask open ended questions e.g. "What makes it difficult for you to take your treatment?", and "How many doses have you missed this week?"  
| Be non-judgmental. Statements like "we all miss a dose now and then" can encourage a client to be more open. |

| **B** Bugs (Infections) | **Check for symptoms and signs of infection. Do a TB and STI screen.**  
| **Remember that immune compromised and pregnant clients may not exhibit overt symptoms of TB. If in doubt, do a TB GXP.** |

| **C** Correct Dose | **Is the client on the correct dose for her weight?**  
| This is especially applicable to young or malnourished girls who may have recently gained weight, or clients with previous renal impairment. |

| **D** Drug Interactions | **Are there any potential drug interactions? Consider:**  
| • Other prescribed treatment e.g. rifampicin, anti-epilepsy drugs  
| • Over the counter treatment e.g. antacids  
| • Supplements and herbal/traditional medications e.g. St John's wort  
| **If in any doubt, call the HIV Hotline 0800 212 506** |

| **E** RE-sistance | **Consider HIV drug resistance if other causes of virological failure have been excluded and the client is adherent to their medication. The need for 2nd-line ART is determined by her current regimen and how long she has been on ART.**  
| **Refer to the 2019 Consolidated ART Guideline for further management** |
Important principle when considering single drug substitutions:

NEVER CHANGE ONLY ONE DRUG IN A FAILING REGIMEN!

Remember......the threshold for failure is 1000 c/ml

<table>
<thead>
<tr>
<th>VL &lt; 50 c/mL</th>
<th>VL 50 -999 c/ml</th>
<th>VL ≥ 1000 c/mL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Virological suppression</td>
<td>Transient viral blip, might be the start of virological failure</td>
<td>Work-up for possible virological failure</td>
</tr>
<tr>
<td>Safe to switch one drug in the regimen? Yes!!</td>
<td>Safe to switch one drug? We don’t know?? They might be on their way to failure, therefore assess first and repeat VL</td>
<td>Safe to switch one drug? No!! Work-up for possible failure Switch to 2nd line</td>
</tr>
</tbody>
</table>
SWITCHING BETWEEN EFV AND DTG IN STABLE PATIENTS

If you have determined that the client is not progressing to outright failure (VL < 1000), and is eligible for a single drug substitution from EFV to DTG

Also remember to:
• Counsel patients on risks and benefits of DTG vs EFV, and the low risk for NTDs in subsequent pregnancies in WOCP
• Provide counselling on contraception for WOCP
• Check for potential drug interactions
• Warn the client about new side effects that may be experienced when switching to a new drug
• Offer patient a choice of remaining on EFV or switching to DTG
Once virological failure is confirmed with 2 VL > 1000, an entire regimen switch is required to DTG-based 2nd line with new NRTI backbone.

Never change only one drug in a failing regimen!
IMPORTANT PRINCIPLES WHEN CONSIDERING VIROLOGICAL FAILURE

Virological failure is now defined by:

**The regimen** the client is currently failing NNRTI vs. InSTI/PI

**Time** on the regimen

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**NNRTI**

2 VLs > 1000 c/mL on at least 2 occasions.

**DTG / PI-based regimen**

VL > 1000 c/mL on at least three occasions over the course of two years, or VL > 1000 c/mL with signs of immunological or clinical failure (i.e. declining CD4 and/or opportunistic infections).
**2ND LINE REGIMENS IN ADULTS AND ADOLESCENTS**

Progression will be:

1. **NNRTI-based regimen**
   - EFV

2. **InSTI-based regimen**
   - DTG

3. **PI-based regimen**
   - LPV/r
   - ATZ/r

PI as alternative if DTG not suitable i.e. women wanting to conceive
**2ND LINE REGIMENS IN CHILDREN**

Progression will be:

- **< 20kg**
  - NNRTI-based regimen
  - **EFV**
  - **ATZ/r**
  - Resistance test required
  - Must ensure that at least 1 NRTI is active

- **≥ 20kg**
  - PI-based regimen
  - **LPV/r**
  - **DTG**
  - Resistance test needed

- **< 20kg**
  - PI-based regimen
  - **LPV/r**
  - **ATZ/r**
  - Resistance test needed
  - Must ensure that at least 1 NRTI is active

## NNRTI-based regimen

- **EFV**

## PI-based regimen

- **LPV/r**
- **ATZ/r**

## INSTI-based regimen

- **DTG**
Management of Viral Load Results in Infants, Children, Adolescents and Adults

Part 1

Routine VL monitoring at 6 months on ART, 12 months on ART, and 12-monthly thereafter

- **VL < 50 c/mL**
  - Continue routine VL monitoring

- **VL 50 - 999 c/mL**
  - Do a thorough assessment of the cause of an elevated VL.
    - Consider the possibility of:
      A. Adherence problems
      B. Bugs (Intercurrent infections)
      C. In-Correct ART dosage
      D. Drug Interactions
      E. Resistance

- **VL ≥ 1000 c/mL**
  - Implement interventions to re-suppress the VL, including enhanced adherence support as outlined in the Adherence Guideline for HIV, TB and NCDs

Repeat VL after 3 months
Part 2

VL MONITORING – INTERPRETING THE RESULTS OF THE VL REPEATED AFTER 3 MONTHS

Switching for virological failure will now depend on

- **Current regimen** (NNRTI vs InSTI/PI)
- **Duration on ART**
### Second-line ART Regimens for Adults with Confirmed Virological Failure

<table>
<thead>
<tr>
<th>Regimen</th>
<th>First-Line Regimens</th>
<th>Second-Line Regimens</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>NNRTI-based Regimen</td>
<td>InSTI-based Regimen for &gt; 2 years</td>
</tr>
<tr>
<td>TDF + 3TC/FTC + EFV/NVP</td>
<td>TDF + 3TC/FTC + DTG</td>
<td>AZT/TDF + 3TC/FTC + LPV/r or ATV/r</td>
</tr>
<tr>
<td>Resistance Testing</td>
<td>Resistance test not required</td>
<td>Resistance testing may be required under expert consultation</td>
</tr>
<tr>
<td>Resistance Test results</td>
<td>Not applicable</td>
<td>Not applicable</td>
</tr>
<tr>
<td>HBV Co-infection Status</td>
<td>HBV-negative</td>
<td>HBV-negative</td>
</tr>
<tr>
<td>¹</td>
<td></td>
<td></td>
</tr>
<tr>
<td>New Regimen</td>
<td></td>
<td></td>
</tr>
<tr>
<td>AZT + 3TC/FTC + DTG²</td>
<td>TDF¹ + AZT + 3TC/FTC + DTG²</td>
<td>AZT + 3TC/FTC + LPV/r</td>
</tr>
<tr>
<td>If DTG not suitable²,</td>
<td>If DTG not suitable²,</td>
<td></td>
</tr>
<tr>
<td>AZT + 3TC/FTC + LPV/r</td>
<td>TDF + 3TC/FTC + LPV/r</td>
<td></td>
</tr>
</tbody>
</table>

1. For HBV co-infection, ART should be adjusted to avoid the risk of resistance development.
2. Alternative regimens may include tenofovir alafenamide (TAF) or tenofovir disoproxil fumarate (TDF) as per national guidelines.
3. Resistance testing may be required under expert consultation.
4. If intolerance to LPV/r is affecting adherence, discuss possible substitutions with an expert.
5. Refer to Third-Line Committee. Regimen will be determined by results of resistance test.
### Second and Third-line ART Regimens for Children and Adolescents with Confirmed Virological Failure

All children and adolescents with confirmed virological failure should be discussed with an expert.

<table>
<thead>
<tr>
<th>Regimen</th>
<th>NNRTI-based Regimen</th>
<th>PI-based Regimen for &gt; 2 years</th>
<th>InSTI-based Regimen for &gt; 2 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABC/AZT/TDF + 3TC/FTC + EFV/NVP</td>
<td>ABC/AZT/TDF + 3TC/FTC + LPV/r or ATV/r</td>
<td>ABC/AZT/TDF + 3TC/FTC + DTG</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Resistance Testing</th>
<th>Resistance test not required</th>
<th>Resistance test required</th>
<th>Resistance test required</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resistance Test Results</td>
<td>Not applicable</td>
<td>No PI resistance</td>
<td>PI resistance (or genotype unsuccessful)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Weight</th>
<th>&lt; 20 kg</th>
<th>≥ 20 kg</th>
<th>&lt; 20 kg</th>
<th>≥ 20 kg</th>
<th>All</th>
<th>All children/adolescents on DTG will be ≥ 20 kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>New Regimen or Other Action Required</td>
<td>ABC/AZT + 3TC + LPV/r</td>
<td>2 NRTIs + DTG&lt;sup&gt;2&lt;/sup&gt; In consultation with an expert, ensure that at least 1 NRTI is active&lt;sup&gt;3&lt;/sup&gt;</td>
<td>Continue current regimen and address adherence</td>
<td>2 NRTIs + DTG&lt;sup&gt;2&lt;/sup&gt; In consultation with an expert, ensure that at least 1 NRTI is active&lt;sup&gt;3&lt;/sup&gt;</td>
<td>Refer to Third-line committee</td>
<td>Refer to Third-line committee</td>
</tr>
<tr>
<td></td>
<td>If NRTI activity cannot be confirmed, expert will recommend 2 NRTIs + PI/r</td>
<td></td>
<td>If NRTI activity cannot be confirmed, expert will recommend 2 NRTIs + PI/r. Adherence must be addressed</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<sup>1</sup> DNA resistance testing required. Refer to Third-line committee if DNA resistance testing is not available.

<sup>2</sup> May also consider more intensive scheduling of laboratory monitoring if resistance test shows resistance to at least one of the NRTIs or PI.

<sup>3</sup> When initiating ART in a child or adolescent infected vertically with HIV, there may be situations where no history of NRTI or PI resistance is available. In these situations, the child or adolescent should be monitored closely for virological failure and adherence issues should be addressed promptly.
THANK YOU!