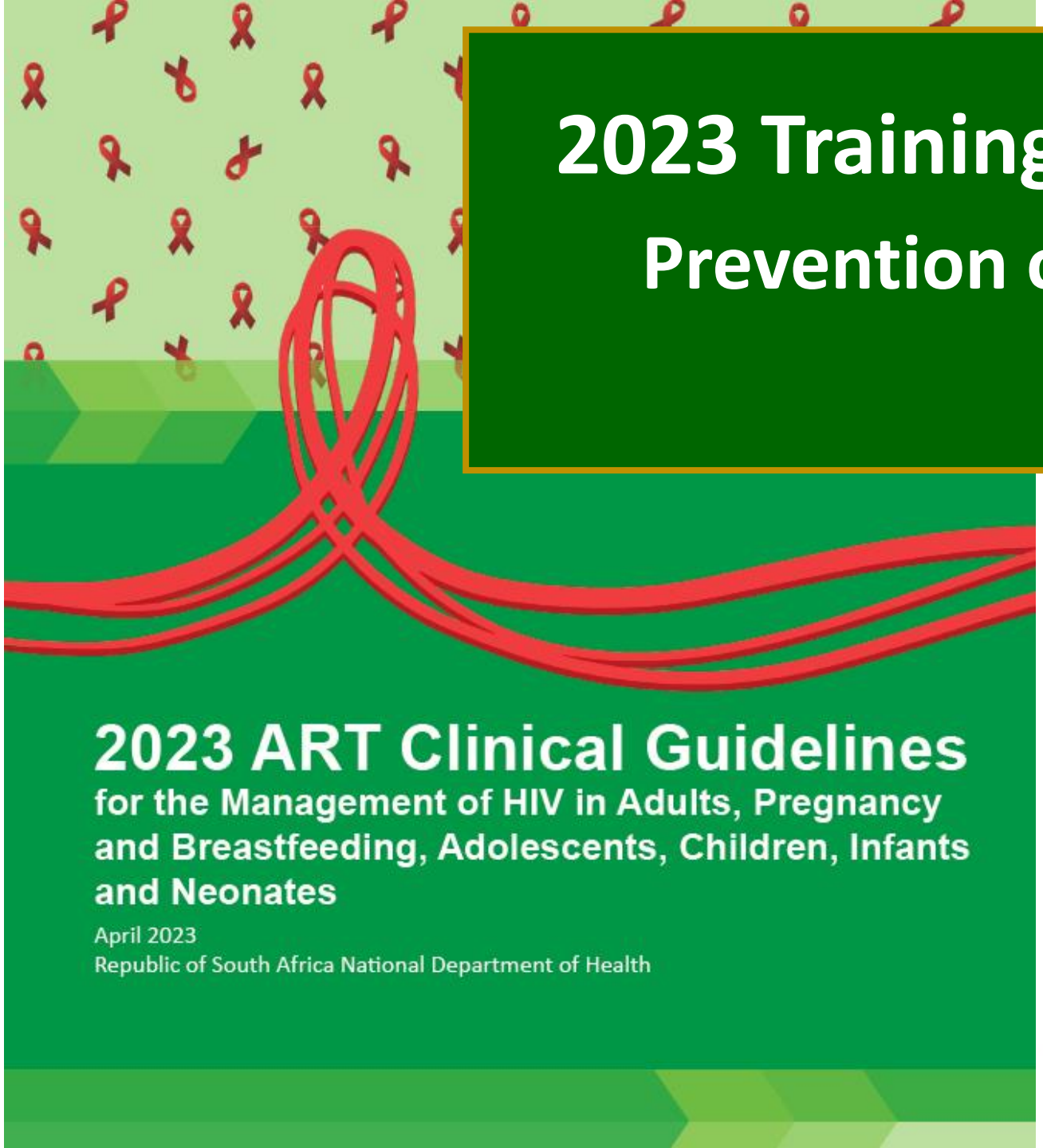
2023 Training on updates to ART and Prevention of Vertical Transmission Guidelines



health
Department:
Health
REPUBLIC OF SOUTH AFRICA

CLINTON HEALTH ACCESS INITIATIVE

World Health Organization

unicef

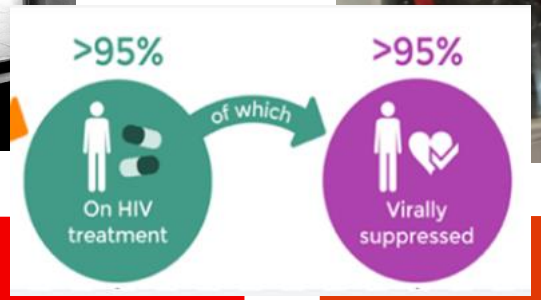
Objectives Session 2

Detailed changes to ART Clinical Guidelines for Adults and Adolescents

- **Background and Rationale for changes**
- **Changes for the Stable client**
- **Changes to TB screening guidelines**
- **Changes relating to the unstable client**
- **Changes to the management of Cryptococcal Meningitis**

Background and rationale

South African HIV program big challenges….



Sub-optimal retention

especially in the first 12 year on ART

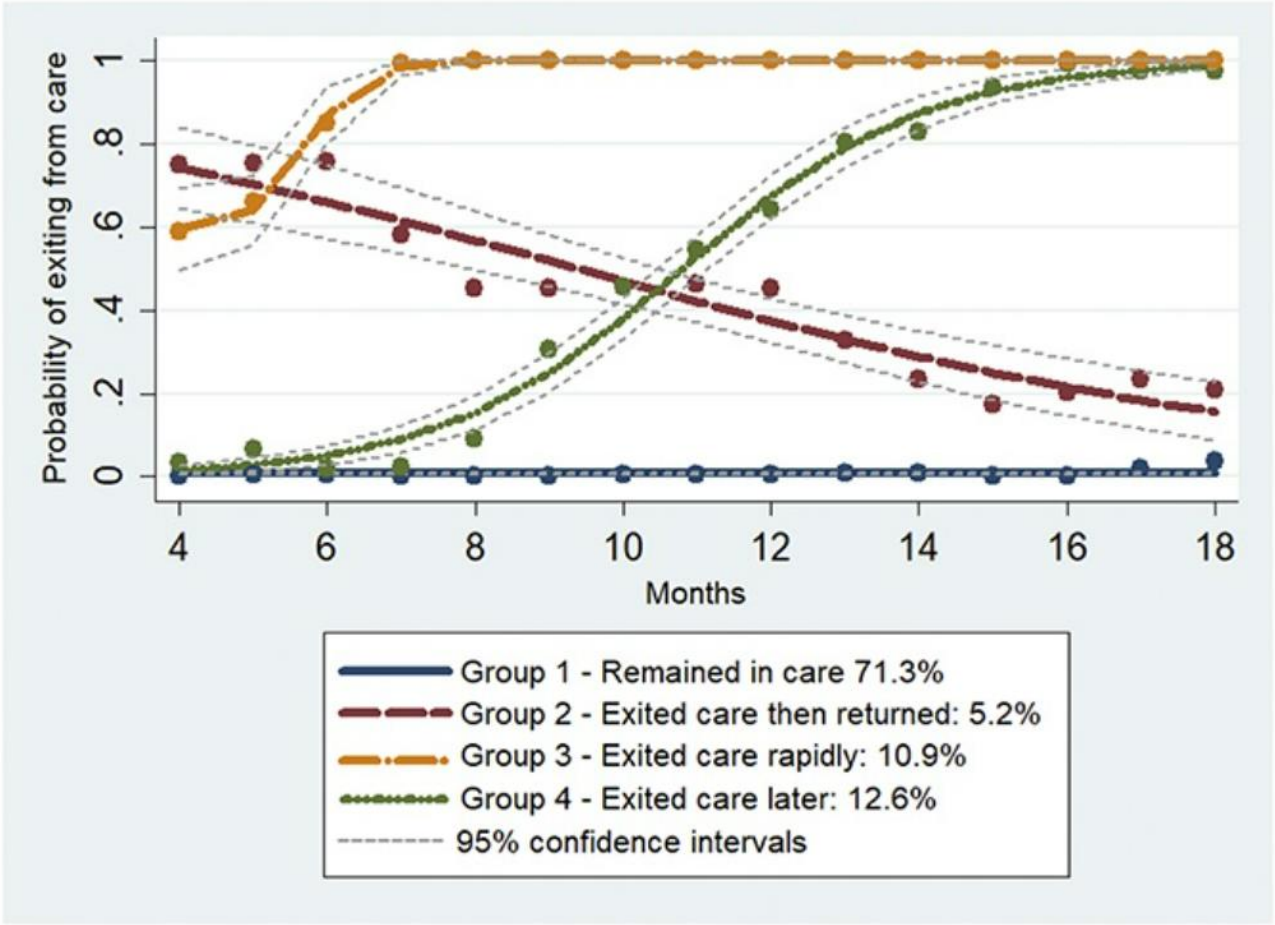
(including for returning clients)

Sub-optimal VL suppression (<50 copies/ml)

Massive health system burden high number of people living with HIV and people at risk of acquiring HIV requiring ongoing **HIV treatment and prevention services**

Disengagement approx. 15% by 6 months on ART

+ further 9% by 12 months on ART



Care trajectories in trial clinics over 18 months of clinical follow-up among patients eligible for ART initiation at the first visit (ANRS 12249 TasP trial, n = 777).

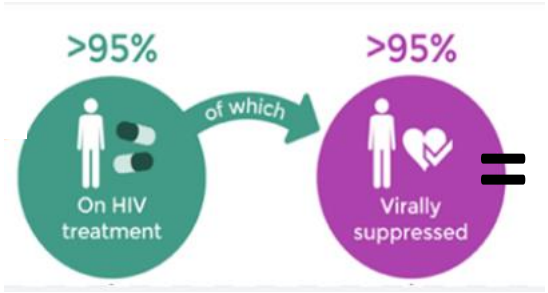
Gosset, Andréa MSc[a,b]; Protopopescu, Camelia PhD[a]; Larmarange, Joseph PhD[c,d]; Orne-Gliemann, Joanna PhD[e,f]; McGrath, Nuala PhD[g,c,h]; Pillay, Deenan PhD[c,i]; Dabis, François PhD[e,f]; Iwuji, Collins MRCP[j,c,h]; Boyer, Sylvie PhD[a]. Retention in Care Trajectories of HIV-Positive Individuals Participating in a Universal Test-and-Treat Program in Rural South Africa (ANRS 12249 TasP Trial). JAIDS Journal of Acquired Immune Deficiency Syndromes 80(4):p 375-385, April 1, 2019.

Critical consideration for this update:

1. Reducing disengagement in the first 6-12 months on treatment (including after re-engagement)

Continue? Disengage?

A critical consideration for this update:
2. Improving long-term viral load suppression (VLS)

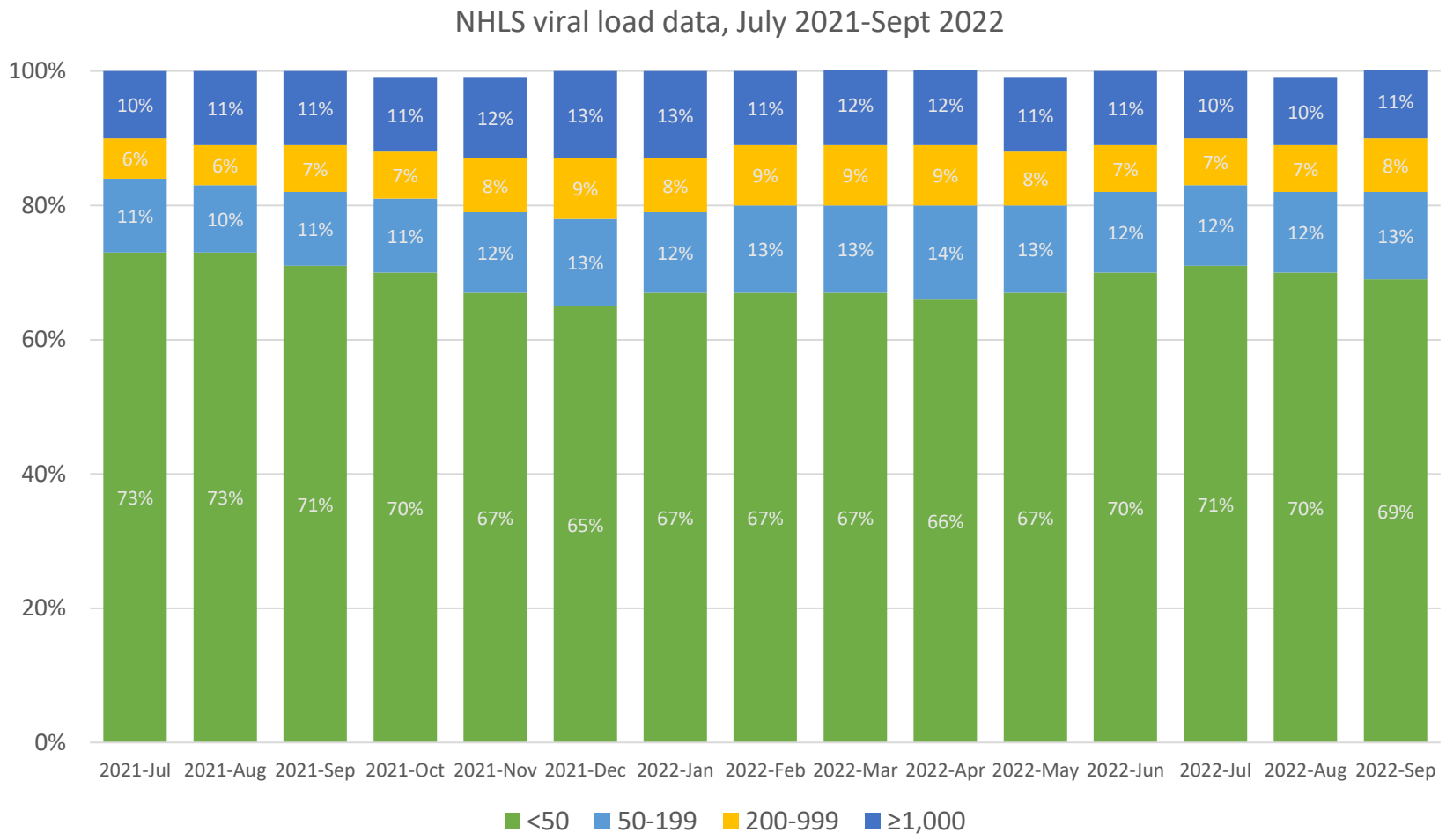


= 86%

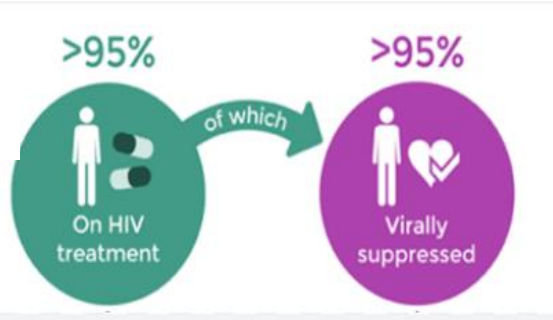
10-13% > 1000 c/ml

low level viraemia:
16-23% 50-1000 c/ml
yellow & light blue

Only 68-70% of VLs are < 50 c/ml



Aims of ART Clinical Guideline predominantly on 2nd & 3rd 95 Targets



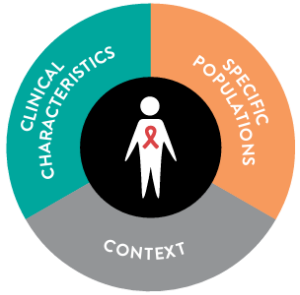
- **Aim 1: Implement optimized regimens**
- **Treat as many people with DTG containing regimens as possible**
- **Aim 2: Create an enabling environment to support engagement in care and adherence**
- **Prioritize patient-centred service delivery**
  - ➢Empower clients with the knowledge and skills they need
  - ➢Identify adherence challenges earlier
  - ➢Reduce unnecessary visits and increase convenience (clinical or ART refill)
  - ➢Integrate service delivery including alignment of visits

Guideline Approach

Aim 1: Implement optimized ART regimens

Clinical updates

Aim 2: Create an enabling environment to support engagement in care and adherence



Patient-centred service delivery updates

Note: Differentiated models of care (DMOC) fully integrated into the ART clinical guidelines. DMOC SOPs form part of ART guidelines.

Previously called "adherence guideline SOPs"

Integration of clinical and service delivery components

Toolkit

Tools for Clinical Management

TLD

Monitoring on ART

Preventing and managing STIs, NCDs and OIs with TPT and CPT

Tools for Differentiated Care (DMOC SOPs)

New patient	Stable patient	Non-stable patient
SOP 1 FTIC	SOP 5 RPCs SOP 6 Switch in RPCs	SOP 2 EAC SOP 7 Trace SOP 8 Re-engagement

SOP 3 Disclosure

SOP 4 MMD

Tools for the Provision of Integrated Care

Visit schedules to align EPI visits with paeds ART, maternal ART, maternal contraception, maternal PrEP, TB treatment and ART

Who decides which tool is used where??

Part 1: Implementing optimized regimens

Part 1: Implementing optimized regimens

Definition

An Optimised ART Regimen means we provide PLHIV with the best-available ART in the most efficient and cost-effective manner possible

An optimized regimen using DTG:

- simplifies regimens with reduced pill burden and dosing frequency
- enhances tolerability
- reduces toxicity
- reduces potential drug-drug interactions
- maintains viral suppression without jeopardizing future treatment options through the development of drug resistance

Background evidence that informed decisions in the GL revision

Benefits of Dolutegravir

EClinicalMedicine 28 (2020) 100573

Contents lists available at ScienceDirect

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journal homepage: https://www.journals.elsevier.com/eclinicalmedicine

Research Paper

Comparative efficacy, tolerability and safety of dolutegravir and efavirenz 400mg among antiretroviral therapies for first-line HIV treatment: A systematic literature review and network meta-analysis

Steve Kanters[a,*], Marco Vitoria[b], Michael Zoratti[c], Meg Doherty[b], Martina Penazzato[b], Ajay Rangaraj[b], Nathan Ford[b], Kristian Thorlund[c], Prof. Aslam H. Anis[a,d], Mohammad Ehsanul Karim[a,d], Lynne Mofenson[e], Rebecca Zash[f,g], Alexandra Calmy[h], Tamara Kredo[i], Nick Bansback[a,d]

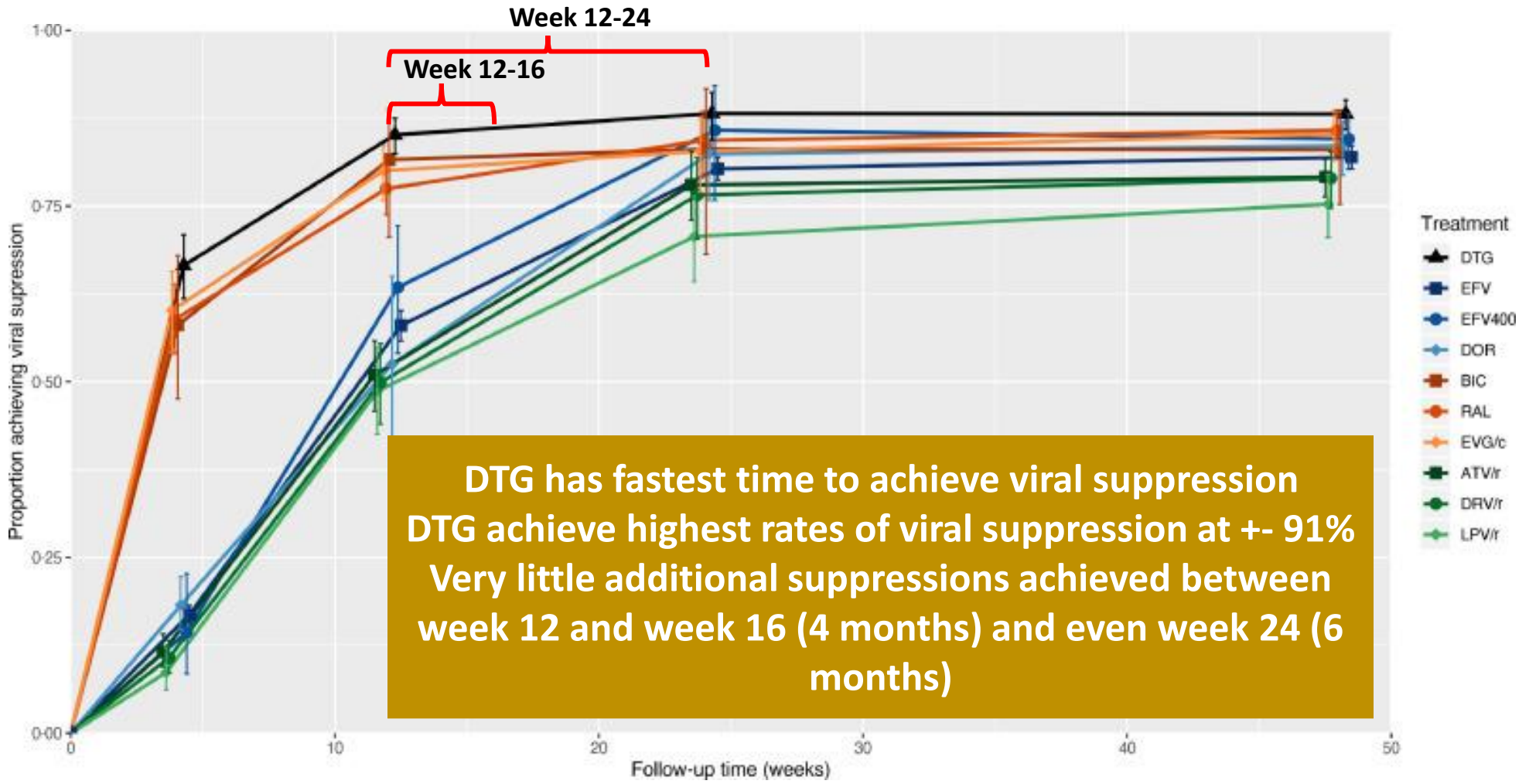
[a] School of Population and Public Health, University of British Columbia, Vancouver, British Columbia, Canada
[b] Department of HIV/AIDS, WHO, Geneva, Switzerland
[c] Departments of Health Research Methods, Evidence and Impact, McMaster University, Hamilton, Canada
[d] Centre for Health Evaluation and Outcome Science, University of British Columbia, Vancouver, Canada
[e] Elizabeth Glaser Pediatric AIDS Foundation, Washington, DC, USA
[f] Division of Infectious Diseases, Beth Israel Deaconess Medical Center, Boston, USA
[g] Botswana – Harvard AIDS Institute Partnership, Gaborone, Botswana
[h] HIV/AIDS Unit, Division of Infectious Diseases, Geneva University Hospital, Geneva, Switzerland
[i] South African Medical Research Council, Cape Town, South Africa

Systematic review of 156 publications
To inform and update WHO guidelines

- DTG had **improved odds of viral suppression**
- DTG was **protective of drug-resistance**
- DTG led to **fewer discontinuations** due to better tolerance and low side effect profile
- Evidence supported dolutegravir use among TB-HIV co-infected persons and **pregnant women.**

No additional risk of NTDs!!

Treatment comparison with respect to viral suppression over time relative to treatment initiation



DTG has fastest time to achieve viral suppression
DTG achieve highest rates of viral suppression at +- 91%
Very little additional suppressions achieved between week 12 and week 16 (4 months) and even week 24 (6 months)

Recycling of TDF in second-line regimens

- **Nucleosides And Darunavir/Dolutegravir In Africa (NADIA)**
- **This trial evaluated options for second-line antiretroviral therapy in patients failing on a non-nucleoside reverse transcriptase inhibitor (NNRTI) and tenofovir (TDF)-based first-line regimen. The trial aimed to answer the following:**
  1. Is a **DTG**-containing regimen as effective as a darunavir-containing **(DRV/r)** regimen in 2nd-line?
  2. Is continuing **TDF and 3TC** in your second-line regimen as effective as using **AZT and 3TC.**

NADIA trial conclusions:

DTG in combination with NRTIs was as effective as DRV/r

including in those with extensive NRTI resistance in whom no NRTIs were predicted to have activity.

TDF was superior to AZT as second-line therapy.

Implications of NADIA

- **TDF may safely be reused in 2nd-line therapy following 1st-line failure with TDF-containing regimens.**
- **TDF to replace AZT for patients on second-line ART. Benefits of TDF:**
  - Better viral suppression than AZT
  - Better tolerated than AZT
  - Less intense initial monitoring
  - Fewer tablets per day
  - Once daily (vs twice-daily)
  - Available as a fixed-dose combination (TLD)
  - It is cheaper
  - Greater harmonisation with first line TDF-based regimens would likely improve 2nd-line drug stock challenges.

Implications of NADIA: “Simple switches from TEE to TLD

- **Simple switch i.e. non-VL dependent**
- **Why were switches VL –dependent in the 2019 ART GL?**
  - It differentiated between a switch to TLD (first-line)
  - and a switch to AZT, 3TC and DTG (i.e., “second-line”)
- **In the 2023 ART GL, whether**
  - they switch from TEE to TLD as “first-line” (with a suppressed VL)
  - Or if they switch from TEE to TLD as “second-line” (if they were “failing” TEE)
  - → the regimen is still the same, i.e. TLD!!

- **We do not need a VL to distinguish between which regimen they will get!**
- **Therefore, the VL need not delay the switch**
- **BUT, an elevated VL must still be managed !!**

A paradigm shift

In the new ART era of dolutegravir, TLD used as a

First-line regimen

Second-line regimen

Part of
Third-line regimens

→need to rethink our terminology related to "1st and 2nd-line"

TLD 1

Clients on a DTG-containing regimen, who **have never failed** a previous regimen
(old "1st line" terminology)

TLD 2

Clients on a DTG-containing regimen, who **have failed** a previous regimen
(old "2nd line" terminology)

Who is eligible for a "simple"/non-VL dependent switch to TLD?

Switching Existing Clients to DTG-containing Regimens
(Adults, adolescents or children)

Non VL-dependent regimen switches Regimens where the VL result will not influence nor delay the decision to switch to a DTG-containing regimen			
VL considerations	**Current Regimen**	**Criteria for switch**	**Regimen if change indicated**
Switching regardless of VL result	**TEE** ABC/3TC/EFV (or NVP*) AZT/3TC/EFV (or NVP*) AZT/3TC/DTG Any LPV/r or ATV/r regimen for **less than 2 years**	**Switch all to a DTG-containing regimen, regardless of VL result** Review VL in last 12 months. If VL in last 12 months was not suppressed, continue to switch same day, but do ABCDE assessment and provide enhanced adherence counseling (EAC) if needed. If VL was not done in last 12 months, do it at this visit, but do not wait for the result to switch	**TLD** provided no renal dysfunction and age ≥ 10 yrs and weight ≥ 30 kg If client does not qualify for TDF **ABC[1]/3TC/DTG** If client does not qualify for TDF and has ABC hypersensitivity **AZT/3TC/DTG**

VL dependent switches

- Relevant to all clients who have been on PI-based regimens for more than two years
- Their VL result in the last 12 months will influence the decision of how and when to switch to a DTG-containing regimen
- If they are failing a PI regimen, this WILL influence regimen selection, because if they have already failed a PI, they have no “backup” regimen if they fail DTG
- They may require a resistance test to determine if they indeed have PI resistance
- If resistance is confirmed, they will require an individualised regimen (to be determined in consultation with an expert)

Switching Existing Clients to DTG-containing Regimens

(Adults, adolescents or children who have never used a DTG-containing regimen in the past)

VL-dependent regimen switches Relevant to all clients who have been on PI-based regimens for more than two years: their VL result in the last 12 months will influence the decision of how and when to switch to a DTG-containing regimen			
VL considerations	**Current Regimen**	**Criteria for switch**	**Regimen if change indicated**
VL < 1000 c/mL	**Any LPV/r or ATV/r regimen** for **more than 2 years**	**Switch all to a DTG-containing regimen** If VL in last 12 months was ≥ 50 c/mL, continue to switch same day, but do ABCDE assessment, provide EAC if needed, and repeat the VL after 3 months as per ***"The VL non-suppression algorithm" on page 19***	**TLD** provided no renal dysfunction and age ≥ 10 yrs and weight ≥ 30 kg If clients does not qualify for TDF **ABC[1]/3TC/DTG**
[2] Two or more VLs ≥ 1000 c/mL taken **two or more years** after starting PI regimen	Adult or adolescent on any **LPV/r or ATV/r** regimen and adherence **less than 80%[3]**	**Switch all to a DTG-containing regimen** **Do not do a resistance test** These clients are unlikely to have PI resistance mutations. Rather switch to a more tolerable once daily FDC regimen which is likely to support adherence. Manage as per ***"The VL non-suppression algorithm" on page 19***	**TLD** provided no renal dysfunction and age ≥ 10 yrs and weight ≥ 30 kg If clients does not qualify for TDF **ABC[1]/3TC/DTG**
	Adult or adolescent on any **LPV/r or ATV/r** regimen and adherence **more than 80%[3]**	Clients who meet the definition of confirmed virological failure and have confirmed adherence more than 80% may need a resistance test. **These clients do not qualify for a same-day switch.** Discuss with an HIV expert[4] to authorise and interpret a resistance test. Provide individualised regimen as recommended by HIV expert. Repeat VL 3 months after the regimen change to confirm re-suppression, as per the ***"Management of Confirmed Virological Failure on TLD" on page 21***	
	Child < 10 years, or weight < 30 kg on any **LPV/r or ATV/r regimen**	These clients do not yet qualify for TLD and may require a resistance test. Refer to algorithm ***"Switching children on PI-containing regimens to DTG-containing regimens" on page 16***	

Before switching to TLD

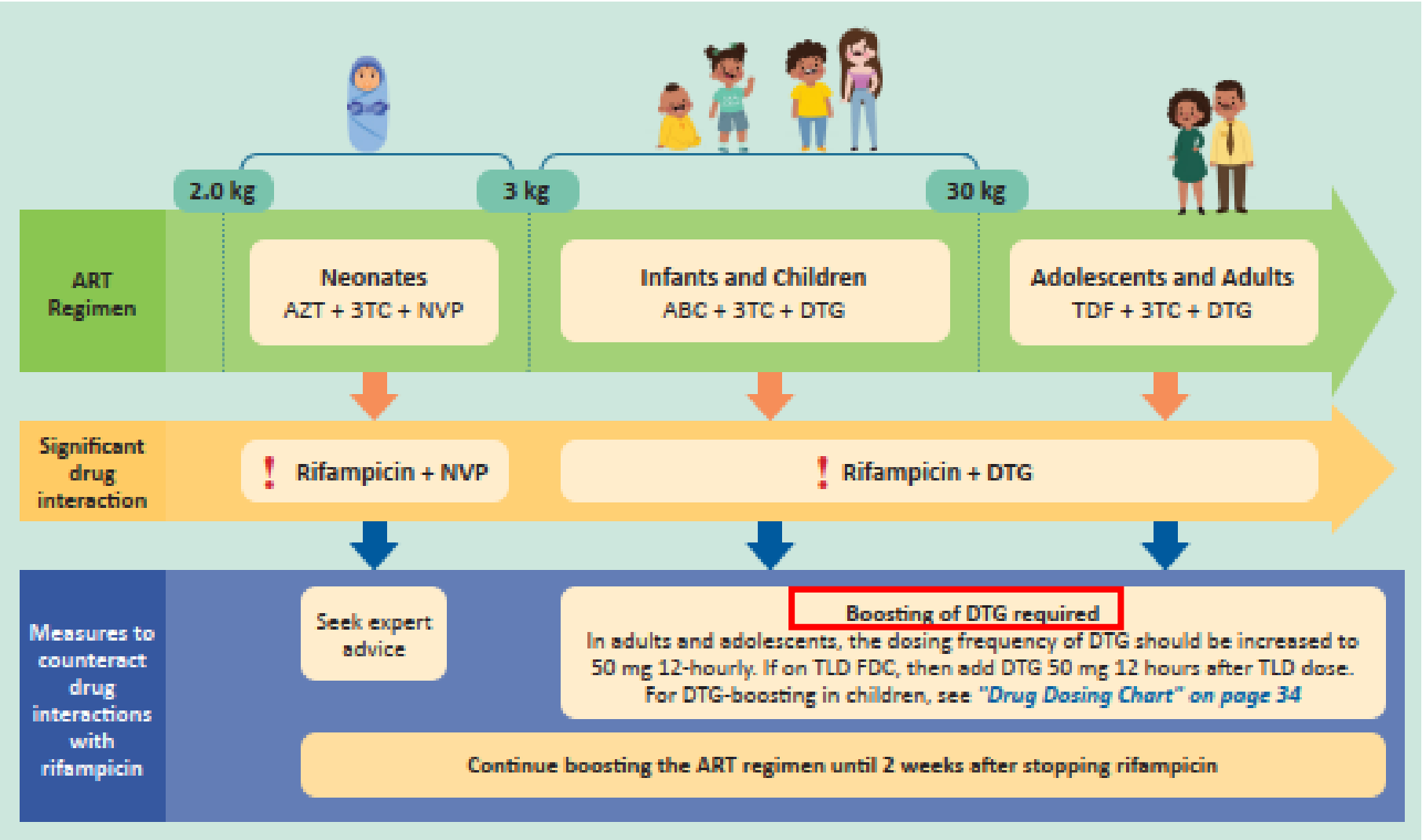
Counsel the client about:

- **The change to their medication that you are recommending**
- **Why it is being changed**
- **Potential new side effects (insomnia, although rare)**
- **Important drug interactions with common over-the-counter medications e.g. multivitamins and antacids**
- **There will be no extra blood tests**
- **They are welcome to return if she has any problems**

Drug interactions with DTG

Interacting Drug[1]	Effect of Co-Administration	Recommendation
Rifampicin	↓ Dolutegravir	Increase DTG dose to 50 mg 12-hourly. If on TLD FDC, add DTG 50 mg 12 hours after TLD dose. For interactions with paediatric regimens see *"Drug Interactions with DTG and Rifampicin-containing TB Treatment" on page 13*
Polyvalent cations (Mg^{2+}, Fe^{2+}, Ca^{2+}, Al^{3+}, Zn^{2+}) e.g. antacids, sucralfate, multivitamin and nutritional supplements*	↓ Dolutegravir	Calcium supplements decrease DTG concentrations if taken together on an empty stomach. To prevent this, DTG and calcium supplements can be taken at the same time if taken with food. It is safe to dissolve the DTG dispersible tablets in breast milk. Iron supplements decrease DTG concentrations if taken together on an empty stomach. To prevent this, DTG and iron supplements can be taken at the same time if taken with food. However, calcium and iron supplements must be taken at least 4 hours apart. Magnesium/aluminium containing antacids decrease DTG concentrations regardless of food intake and should be taken a minimum of 2 hours after or 6 hours before DTG
		* Many over the counter (OTC) medications contain polyvalent cations. Clinicians should regularly ask clients about OTC medication use and advise about possible interactions
Anticonvulsants: • Carbamazepine • Phenobarbital • Phenytoin	↓ Dolutegravir	Avoid coadministration if possible. Alternative agents that do not interact with DTG include valproate, lamotrigine, levetiracetam, and topiramate. Remember that valproate is contra-indicated during pregnancy. Double DTG dose to 50 mg 12-hourly for carbamazepine, phenytoin, or phenobarbital if an alternative anticonvulsant cannot be used
Metformin/DTG	↑ Metformin	DTG increases metformin concentrations. Maximum metformin dose 500 mg 12-hourly

Drug interactions between DTG and Rifampicin



First-Line ART Regimens in Adults, Adolescents, Pregnant Women, Children, Infants, and Neonates

All Adult and Adolescent Females and Males ≥ 30 kg and ≥ 10 years of Age

TDF + 3TC + DTG (TLD)

Neonates, Infants and Children 0 to < 10 years of Age

For further detail on transitioning between regimens, see "Switching existing clients to DTG-containing regimens" on page 13-14

2.0 kg — Birth to < 4 weeks of age[1]

Neonates
AZT + 3TC + NVP

For further details on initiating ART in term and pre-term neonates see pages 20-21

3 kg — and ≥ 4 wks of age, to < 10 years of age

Infants and Children
ABC + 3TC + DTG

Transition does not require a VL before switching

30 kg — and ≥ 10 years of age

Adults and Adolescents
TDF + 3TC + DTG (TLD)

Transition does not require a VL before switching
Ensure adequate renal function[2]

[1] For neonates with severe anaemia, obtain advice from an expert or through one of the helplines provided on page 18

[2] Before switching to TDF, ensure adequate renal function by checking eGFR/creatinine as outlined in table on page 7

TLD will be used as:

A First-line regimen

A Second-line regimen

Part of Third-line regimens

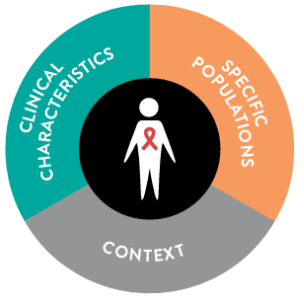
If TLD is the most optimised regimen we have, and it can be used in 1st, 2nd, and third-line regimens, that means that:

All new clients should be initiated on TLD, or…

Clients already on ART should have been switched to TLD, or…

…be IN THE PROCESS of switching to TLD

Clinical updates



Patient-centred service delivery updates

The Stable Client in the 1st year of ART and onwards

First year on ART for the stable client

DC =

dispensing cycle whether 28 or 30 days

MMD =

multi-month dispensing

RPCS =

repeat prescription collection strategies (external pick-up points, facility pick-up points and adherence clubs)

Visit Schedule for Adults, Adolescents and Children 5 Years and Older on ART

DC/ Months* on ART	Routine monitoring tests	Overview of Management
0	**Baseline clinical and lab assessment as outlined on pages 4 to 6 ART initiation and session 1 of fast track initiation counselling**	
1	**Review test results**	• Session 2 of fast track initiation counselling including planning for travel and VL education • Clinical assessment and routine monitoring as outlined on page 17 • Integrated services for family planning and NCDs • **2 months ART dispensed (2MMD) - DMOC SOP 4**
3	**3-month* VL sCR and eGFR**	• Clinical assessment including VL and any other routine monitoring bloods as outlined on page 17 • Integrated services for family planning and NCDs

4	**Review test results**	• Clinical assessment and review of VL and any other monitoring results
		• Integrated services for family planning and NCDs
		• Assess eligibility for Repeat Prescription Collection strategies (RPCs) (South Africa's differentiated models of care for stable patients)
		  • VL < 50 c/mL
		  • Clinically well
		  • No OIs, including TB
		  • Not pregnant
		Repeat Prescription Collection strategies (DMOC for stable patients)
		Facility Pick-up Point (FAC-PUP) (DMOC SOP 5.1) / Adherence Clubs (AC) Facility or community-based support groups (DMOC SOP 5.2) / External Pick-up point (EX-PUP) (DMOC SOP 5.3)
		• Renew prescription for next 6 months, with first 3 month's supply issued today from the facility
		• If not eligible for RPCs or refused RPCs:
		Assess eligibility for facility provided multi-month dispensing (MMD) – DMOC SOP 4

7		• Collect medication from preferred RPCs
10	**10-month* VL sCR and eGFR CD4 count**	• Clinical assessment including VL and any other monitoring bloods as per "Monitoring on ART" on page 17 • Integrated services for family planning and NCDs • Check TPT eligibility • Renew prescription for next 6 months • Do not require clients to return to the facility in 1 month to review the VL results, unless other clinical indications exist that require review. Rather, recall to the facility only those clients with elevated VLs
11+		• 12-monthly clinical assessment and family planning review as per "Monitoring on ART' on page 17 • 12-monthly routine monitoring of VL, sCR and eGFR • Check that chosen RPCs option is still suitable • Collect medication from preferred RPCs

Non-stable clients

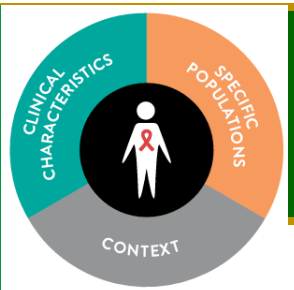
If at any stage the client becomes clinically non-stable and /or non-adherent i.e. a client who has:

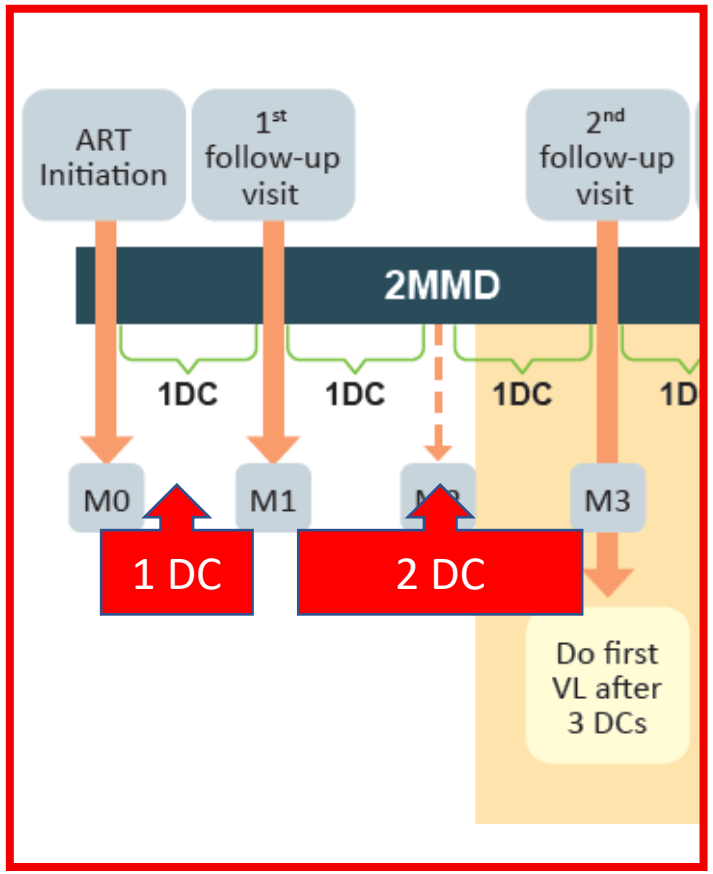
- missed a scheduled appointment by more than 28 days (including in an RPCs) (see also re-engagement algorithm on page 12)
- a VL ≥ 50 c/ml
- possible signs or symptoms of clinical failure, e.g. if the client is acutely unwell, or develops a new OI such as TB

A clinician should:

- If in an RPCs, return the client to regular care to ensure more frequent clinical follow-up until they are stable again.
- Provide appropriate clinical management
- If clinically well and struggling with visit frequency: provide multi-month dispensing (DMOC SOP 4)
- If experiencing side effects or the child cannot tolerate their medication: switch drugs/formulation
- If struggling to take ART as prescribed: enhanced adherence counselling (See Annexure 3)

ART initiation to 1st Viral load





DC/ Months* on ART	Routine monitoring tests	Overview of Management
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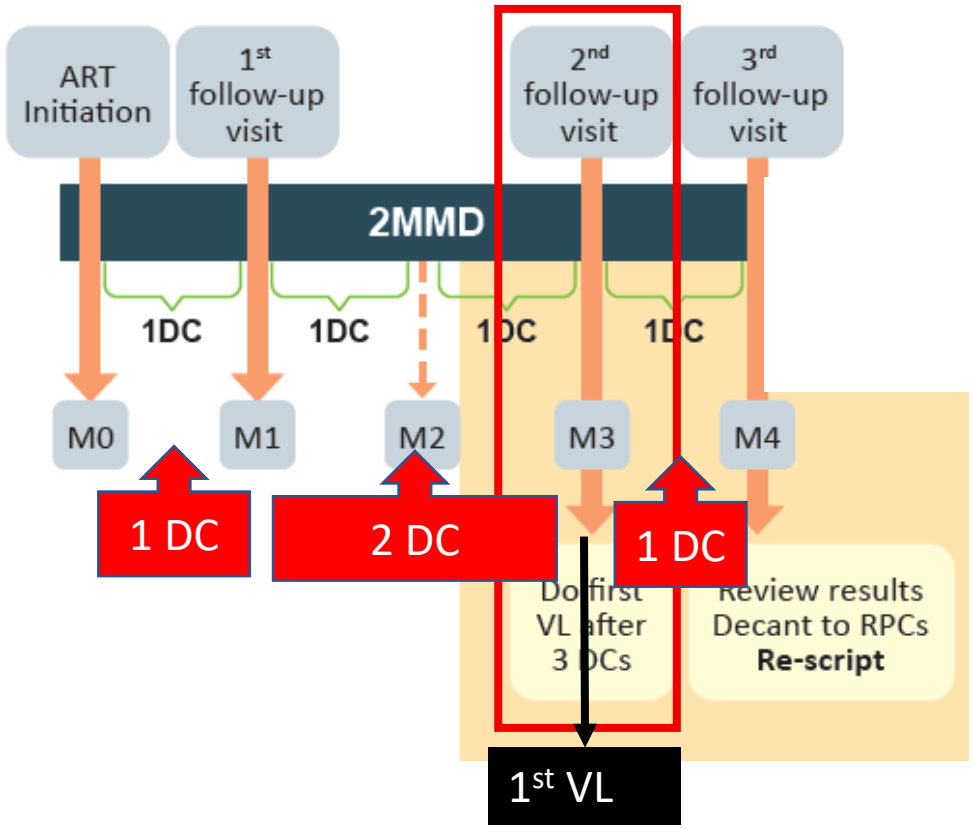
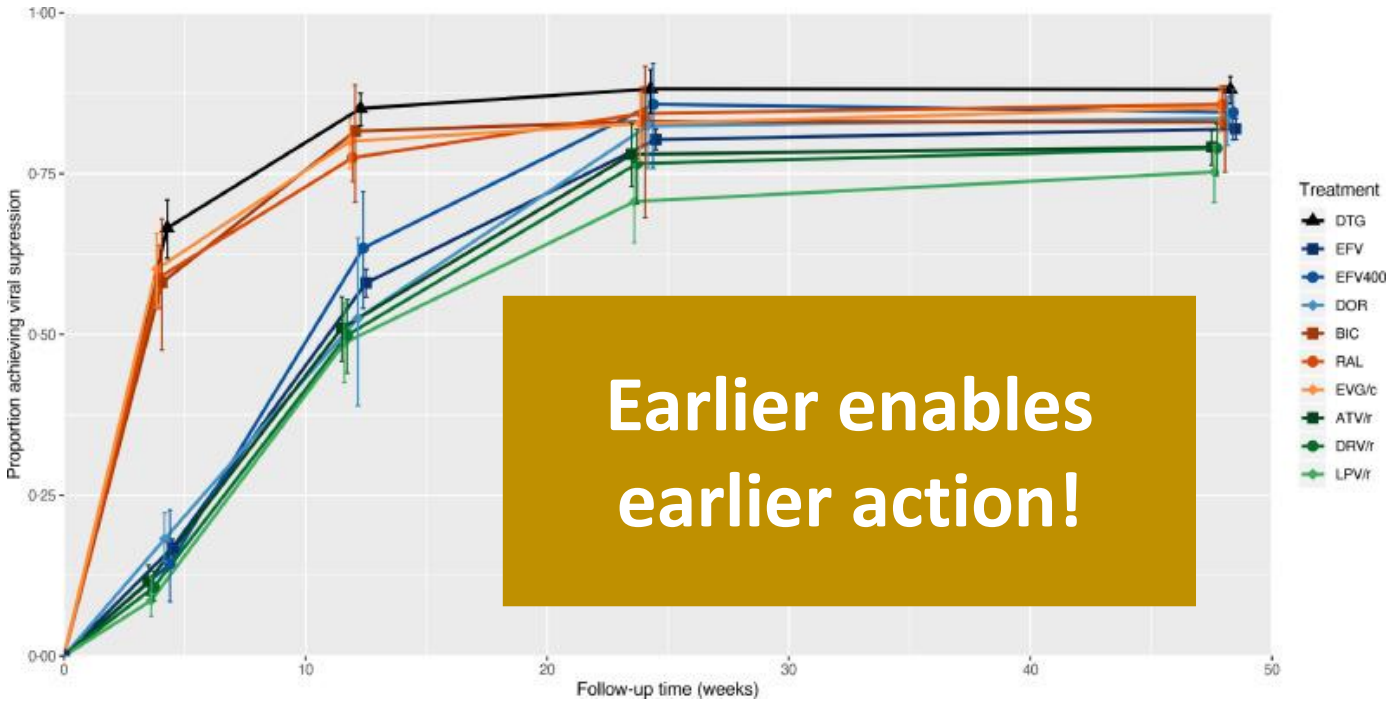
1	**Review test results**	• Session 2 of fast track initiation counselling including planning for travel and VL education • Clinical assessment and routine monitoring as outlined on page 17 • Integrated services for family planning and NCDs • **2 months ART dispensed (2MMD) - DMOC SOP 4**
3	**3-month* VL sCR and eGFR**	• Clinical assessment including VL and any other routine monitoring bloods as outlined on page 17 • Integrated services for family planning and NCDs

1st viral load

DC/ Months* on ART	Routine monitoring tests	Overview of Management
3	3-month* VL sCR and eGFR	• Clinical assessment including VL and any other routine monitoring bloods as outlined on page 17 • Integrated services for family planning and NCDs

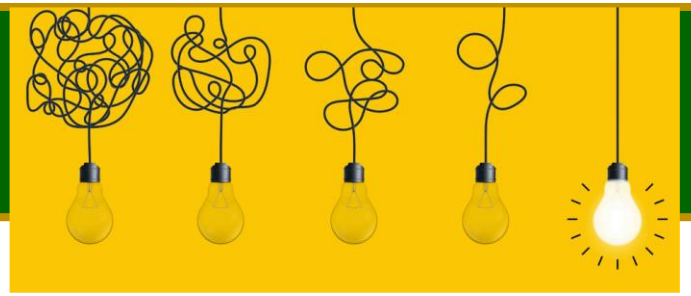


- **After 3 consecutive DCs (M3 visit) – takes 1st viral load**



Earlier enables earlier action!

Aligning viral load timing



- Elevated VL: Repeat VL after 3 DCs
- Pregnant and start ART: First VL after 3 DCs in ANC
- Re-engagement after LTFU: VL at 3 DCs after re-engagement
- Start ART: First VL after 3 continuous dispensing cycles (3 DCs)

Simpler = easier to train, implement and monitor

VL review to next clinical review

<table>
<tr><td rowspan="5">4</td><td rowspan="5">Review test results</td><td colspan="3">• Clinical assessment and review of VL and any other monitoring results
• Integrated services for family planning and NCDs
• Assess eligibility for Repeat Prescription Collection strategies (RPCs) (South Africa's differentiated models of care for stable patients)
  • VL < 50 c/mL
  • Clinically well
  • No OIs, including TB
  • Not pregnant</td></tr>
<tr><td colspan="3">Repeat Prescription Collection strategies
(DMOC for stable patients)</td></tr>
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<tr><td colspan="3">• Renew prescription for next 6 months, with first 3 month's supply issued today from the facility
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Assess eligibility for facility provided multi-month dispensing (MMD) – DMOC SOP 4</td></tr>
<tr><td colspan="3"></td></tr>
<tr><td>7</td><td></td><td colspan="3">• Collect medication from preferred RPCs</td></tr>
</table>

1st viral load REVIEW

VIRAL LOAD SUPPRESSED + CLINICALLY WELL = STABLE

4	Review test results	• Clinical assessment and review of VL and any other monitoring results
		• Integrated services for family planning and NCDs
		• Assess eligibility for Repeat Prescription Collection strategies (RPCs) (South Africa's differentiated models of care for stable patients)
		  • VL < 50 c/mL
		  • Clinically well
		  • No OIs, including TB
		  • Not pregnant

		Repeat Prescription Collection strategies (DMOC for stable patients)
		Facility Pick-up Point (FAC-PUP) (DMOC SOP 5.1) / Adherence Clubs (AC) Facility or community-based support groups (DMOC SOP 5.2) / External Pick-up point (EX-PUP) (DMOC SOP 5.3)

- **Client is adherent to ART**
- **Important to start making longer-term adherence easier and more convenient**
- **No benefit for the client to require frequent clinical reviews, ART collections or rescripts**
  - Time to differentiate care…..

Why focus on VLS and clinical stability only?

- **Previous time on ART eligibility criteria matched VL timeline:**
  - 2016: 1st and 2nd VL timeline (12 months)
  - 2019: 1st VL timeline (6 months)

As time on ART had no separate purpose, this has been removed.

1st viral load REVIEW:
Assess RPCs eligibility → *DMOC for stable patients*

DC/ Months* on ART	Routine monitoring tests	Overview of Management

4	Review test results	• Clinical assessment and review of VL and any other monitoring results
		• Integrated services for family planning and NCDs
		• Assess eligibility for Repeat Prescription Collection strategies (RPCs) (South Africa's differentiated models of care for stable patients)
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If eligible, explain and offer all repeat prescription collection strategies (RPCs) available at your facility:

- External pick-up points
- Fast track facility pick-up point
  - One stop ART pick-up point – do not retrieve folder or see clinician
- Facility or community adherence club

1st viral load REVIEW:
Scripting and ART supply for RPCs

DC/ Months* on ART	Routine monitoring tests	Overview of Management		

4	Review test results	• Clinical assessment and review of VL and any other monitoring results
		• Integrated services for family planning and NCDs
		• Assess eligibility for Repeat Prescription Collection strategies (RPCs) (South Africa's differentiated models of care for stable patients)
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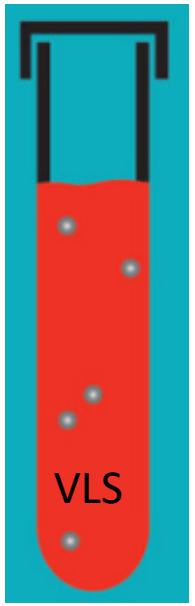
		  • No OIs, including TB
		  • Not pregnant		

		Repeat Prescription Collection strategies (DMOC for stable patients)		
		Facility Pick-up Point (FAC-PUP) (DMOC SOP 5.1)	Adherence Clubs (AC) Facility or community-based support groups (DMOC SOP 5.2)	External Pick-up point (EX-PUP) (DMOC SOP 5.3)
		• Renew prescription for next 6 months, with first 3 month's supply issued today from the facility		

- If client chooses an RPCs option, script for 6 months with max 2 ART refills
- 1st supply provided by facility pharmacy
- 2nd supply to be collected at RPCs location

2nd VL and quality clinical review and thereafter…



DC/ Months* on ART	Routine monitoring tests	Overview of Management
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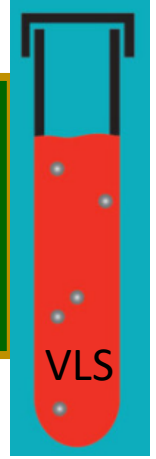
11+		• 12-monthly clinical assessment and family planning review as per "Monitoring on ART' on page 17 • 12-monthly routine monitoring of VL, sCR and eGFR • Check that chosen RPCs option is still suitable • Collect medication from preferred RPCs

- **2nd VL after 10 DCs (after completion of 6-month script)**
- **Further VLs will be done every 12 DCs thereafter**
- **Quality clinical review – not just a rescript**
  - Cost benefit for the client and the health system

Rescripting and recall high VLs



- Remember these clients are stable – last VL suppressed
- If in RPCs, immediately rescript based on previous VL.
- **Do not require return for VL result review**
- Explain to client if they are not recalled its means their VL is suppressed. They will be recalled if elevated.

DC/ Months* on ART	Routine monitoring tests	Overview of Management
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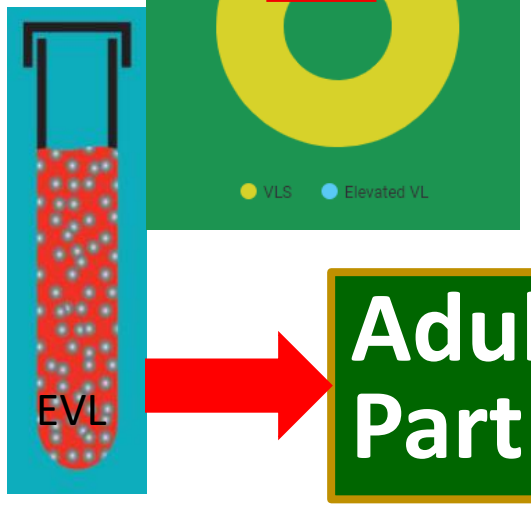


Recall clients with elevated VLs (<5% of clients with previously suppressed VL will now have an elevated VL)

Adult HIV: Non-stable: See Part 3

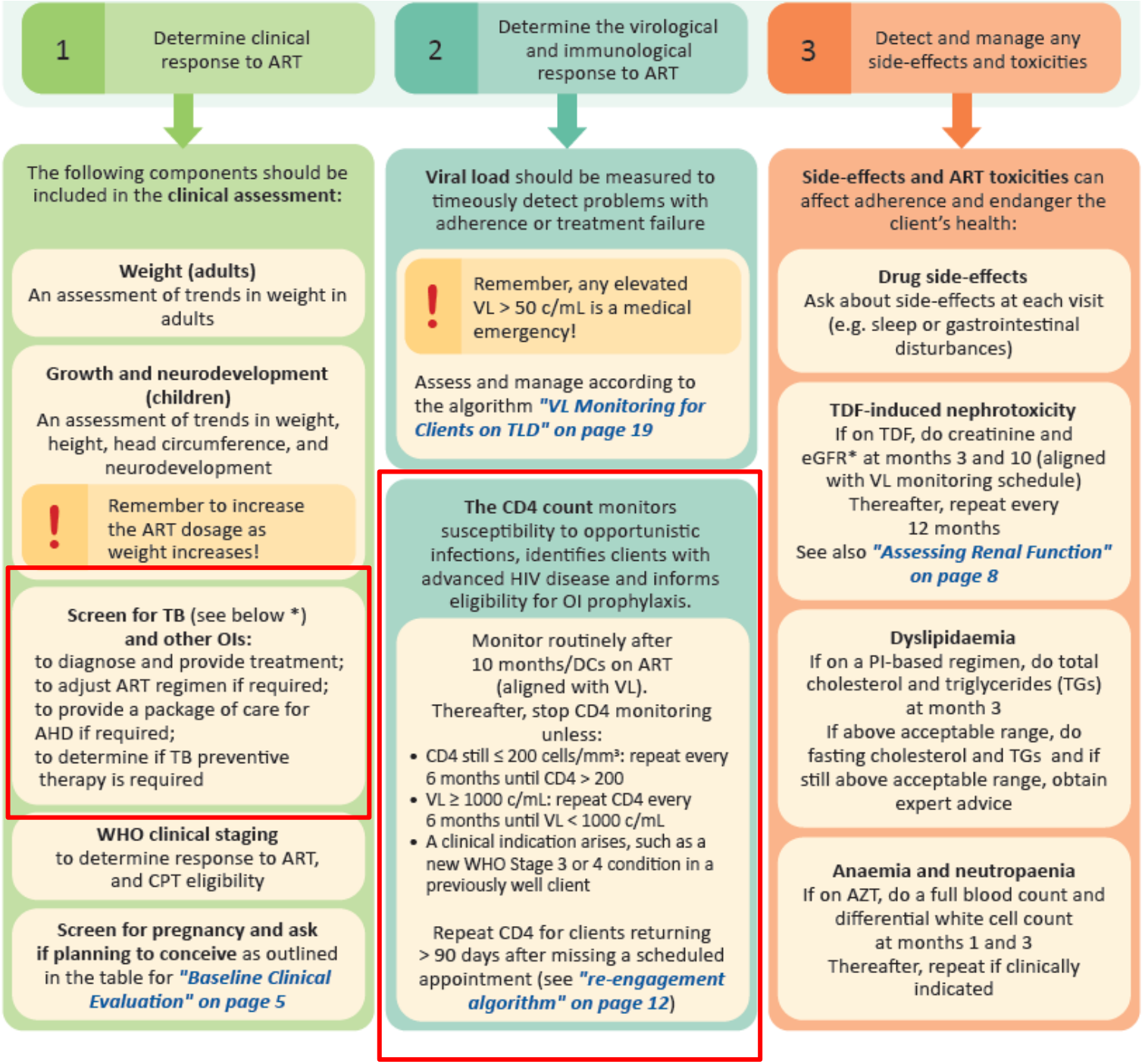
Monitoring on ART

Creatinine and eGFR aligned to new VL monitoring schedule

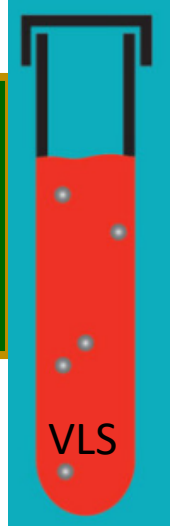
New TB screening recommendations to be covered in separate sections

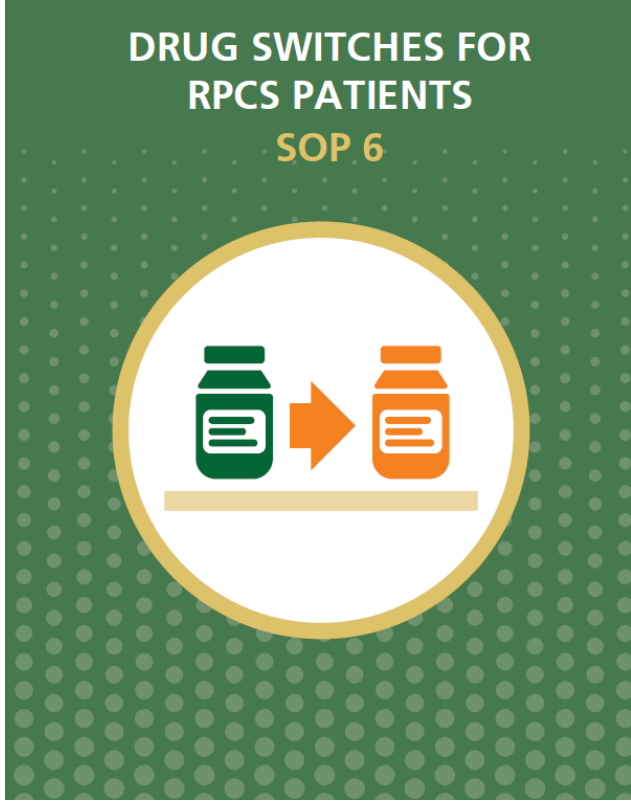
Note repeat CD4 every 6 months for children <5 yrs if less 25%

When monitoring on ART integrate monitoring for other chronic conditions
(HPT, DM, and mental health)



Switching stable clients on ART to TLD in RPCs





- All clients in RPCs must also be considered for switch to TLD at next clinical review (and rescript)
- Must remain in RPCs – not a reason to return to facility care *(unless their VL comes back elevated)*.
- Provide TLD 6-month RPCs script immediately
- No additional clinical reviews required

Sub-section

The Clients Journey in the 1st year of ART:

Change to TB screening guidelines

Response: National SOP on the **FAST** Approach

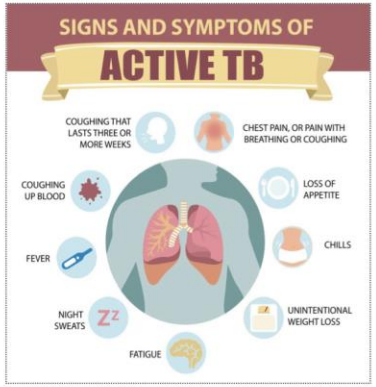
Finding people with TB **A**ctively, **S**eparate safely, and **T**reating effectively, is a quality improvement intervention aimed at preventing the spread of TB in congregate settings.

Targeted Universal Testing for TB (TUTT)

STUDY DESIGN

Standard of care of clinics

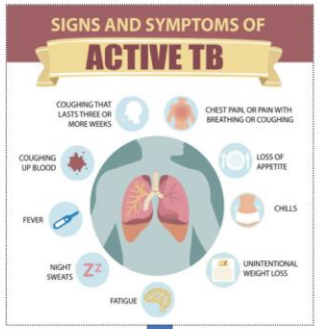
30 PHC Clinics



Xpert Ultra MTB/RIF

Study Intervention clinics

30 PHC Clinics



Xpert Ultra MTB/RIF

+

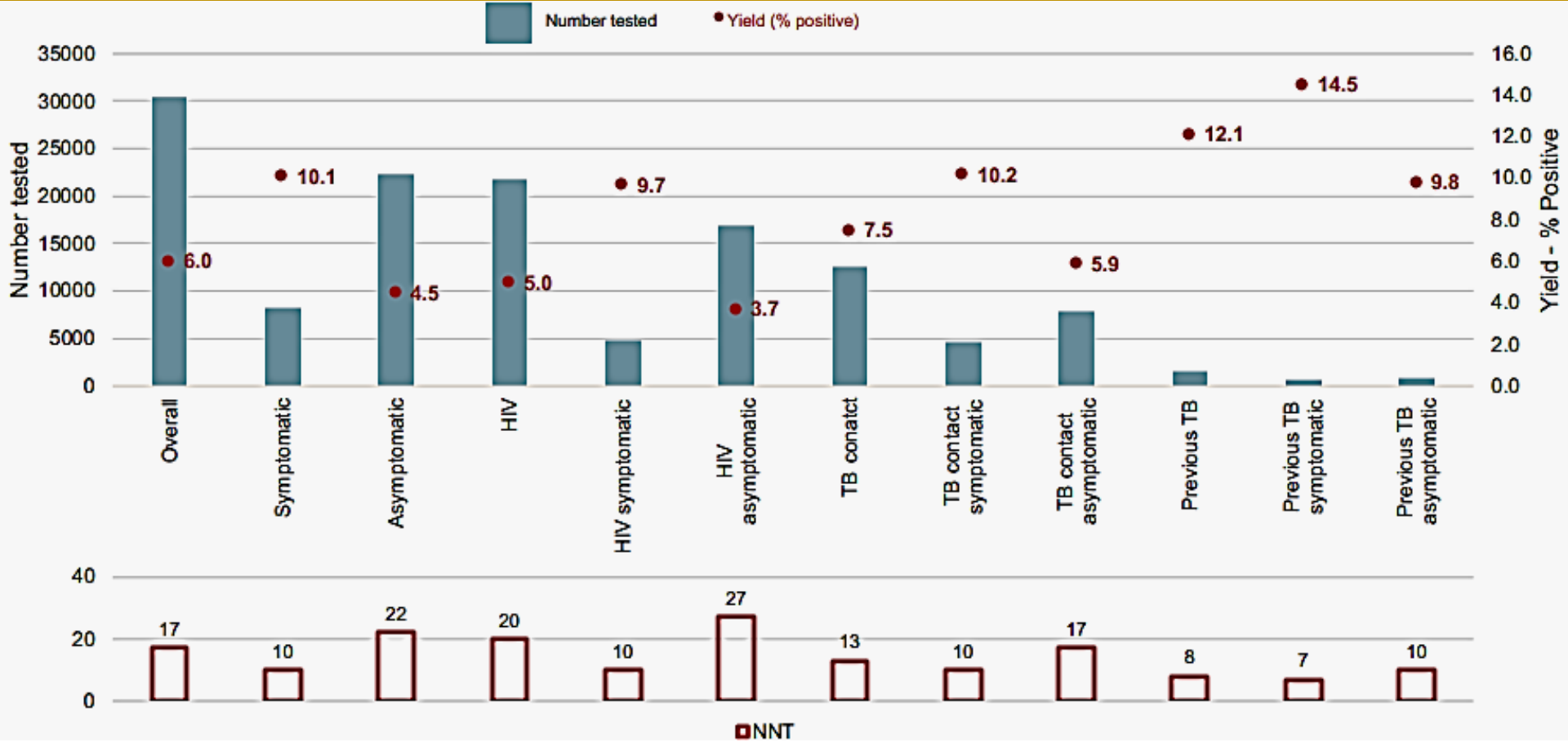
ALL
HIV infected
Previous TB
TB contacts

Xpert Ultra MTB/RIF & MGIT culture

Martinson et al. A Cluster Randomized Trial of Systematic Targeted Universal Testing for Tuberculosis in Primary Care Clinics of South Africa (The TUTT Study). Available at SSRN: https://ssrn.com/abstract=4092970

Targeted Universal TB Testing (TUTT) study

RESULTS: YIELD BY RISK FACTOR AND SYMPTOMS



Universal TB testing for patients at high risk for TB using Xpert and culture irrespective of the presence of TB symptoms resulted in a 6% overall yield in laboratory confirmed TB.

TUTT Study Conclusions

- Systematic screening with Xpert & or culture diagnosed more TB cases in clinics
  - Overall: 6%
  - HIV-infected: 5%
- Clinics are diagnosing 8% fewer patients with TB year on-year under the standard of care
- The TUTT intervention resulted in a 17% net increase in TB cases diagnosed per clinic per month as compared to the standard of care clinics.
- Systematic screening with Xpert is recommended in sub-populations at high risk of TB

Who must be tested for TB?

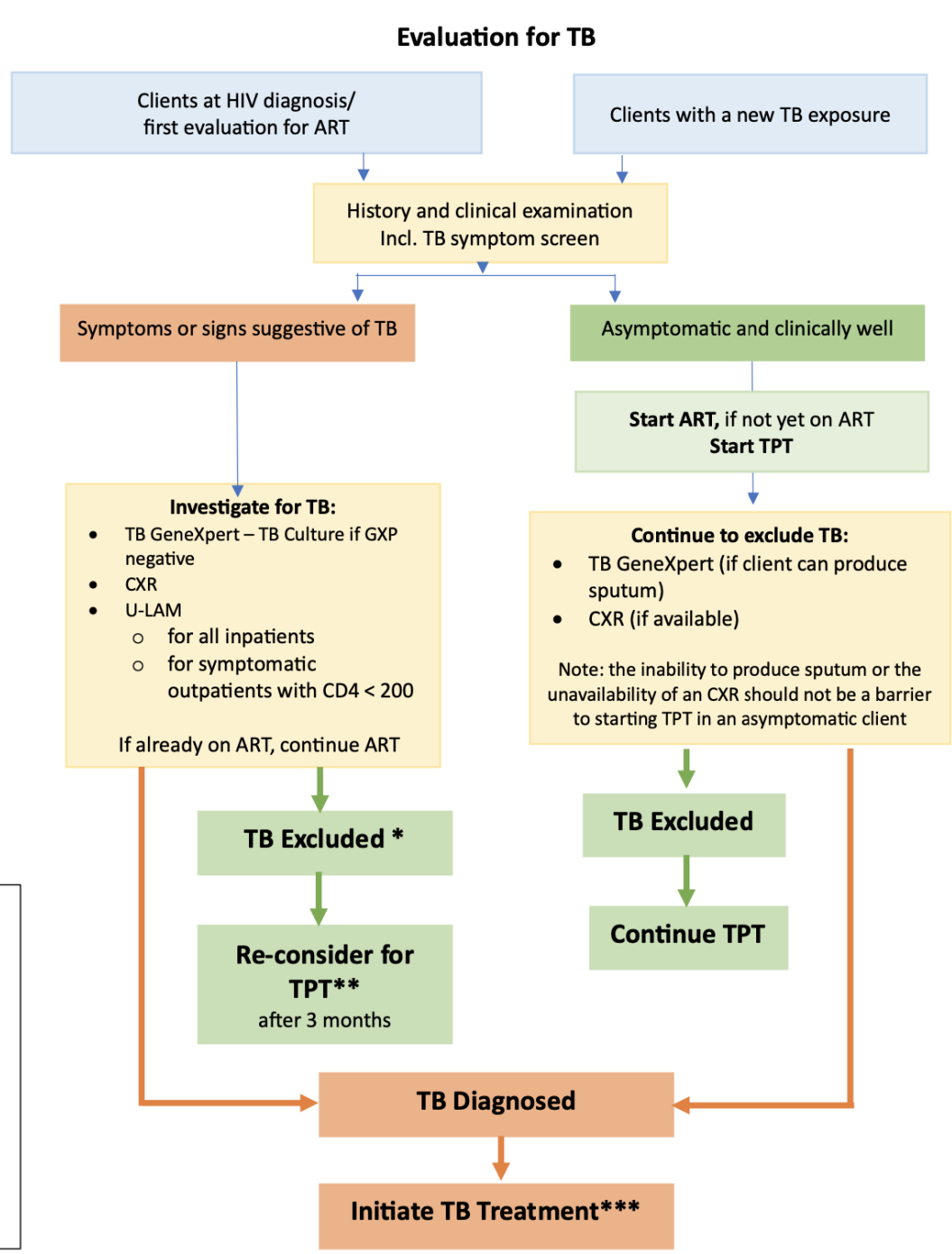
A specimen must be collected for TB testing in the following groups:

- People (children, adolescents, and adults) with any one of the TB symptoms
- People who have been in close contact with a person diagnosed with TB or TB treatment in the past year irrespective of TB symptoms
- People who have been treated and completed TB treatment in the past two years irrespective of TB symptoms.
- Newly diagnosed PLHIV irrespective of symptoms

Frequency of testing

1. General population
    - Only when they present with any TB symptom or chest x-ray changes suggestive of TB
2. People living with HIV
    - At the time of HIV diagnosis
    - On enrolment in Antenatal care for pregnant women
    - Annually for PLHIV on treatment linked to VL monitoring follow up visits
3. Household contacts of people diagnosed with TB
    - After each exposure to a person with a confirmed TB diagnosis
4. People previously treated for TB
    - Annually for a period of two years

Evaluation for TB



*Based on a clinician's assessment of the symptomatic client's clinical condition and all special investigations, and subsequently deciding that the client does not have TB

**Symptomatic clients who were who subsequently considered NOT to have TB, should not immediately be initiated on TPT. They can be reconsidered for TPT 3 months later. However, at this later time, they should be screened and tested for TB again, before being considered for TPT

***Clients who are asymptomatic and were initiated on TPT, and who were then subsequently diagnosed with TB, can stop TPT and initiate TB treatment. There is no risk of developing INH resistance in the short period of time that the client would have taken INH alone

Algorithm to support TB evaluation approach

PATIENT CATEGORY		WHAT TO DO	REGIMEN
ncluding children ≥25kg	HIV-positive	**PLHIV**: Test for TB regardless of ART status and give TPT once TB disease is excluded. If newly diagnosed with HIV, start ART immediately and TPT within the next two weeks.	3HP* or 12H
		Post TB treatment: Offer TPT to all PLHIV ≥25 kg after successfully completing treatment for TB disease, after active TB disease has again been excluded.	
		Previously treated with TPT: If re-exposed to any close contact with TB, retest for TB and give TPT once TB disease has been excluded.	
		Evaluate all **HIV-positive pregnant women** regardless of CD4 count and give TPT once TB disease has been excluded.	12H

TPT Regimen Options for infants and children weight < 25 kg

Infants and children <25kg	HIV -positive	Children living with HIV (CLHIV): Evaluate all children older than 14 weeks of age living with HIV for TB and start TPT once active TB has been excluded. ART should be started immediately if newly diagnosed with HIV. TPT should be started within two weeks of ART initiation.	6H**
		Contacts: Evaluate all TB-exposed CLHIV and start TPT after TB disease has been excluded, regardless of previous treatment or TPT.	
	HIV-negative	**Contacts:** Evaluate HIV-negative children in close contact with a TB patient and start TPT after active TB disease has been excluded.	3RH
		Test other **HIV-negative at-risk children** (weakened immune system e.g., cancer, diabetes, autoimmune diseases, transplant patients on immunosuppressive drugs, receiving dialysis, or inherited immunodeficiencies) for TB and start TPT once TB disease has been excluded	

Important to Note

- PLHIV present with pauci-bacillary PTB or EPTB therefore a negative Xpert MTB RIF result must be followed by clinical assessment, chest x-ray and culture and DST to confirm the diagnosis of TB.
- People who are asymptomatic but test positive on Xpert MTB RIF must be clinically assessed for TB (including proper history taking), chest x-rays, culture and DST or other tests must be conducted to confirm TB.
- In people who completed TB treatment in the past two years, a “Positive” or “Trace” Xpert MTB RIF test result may indicate presence of live (active TB disease) or dead (left over from previous TB episode) bacilli or DNA. Therefore, the test result must be considered along with the clinical findings before treatment initiation and a TB culture conducted to confirm active TB disease.

Summary (1/2)

- All clients entering the health facility must be screened for symptoms of TB and Covid-19
- Where available, a chest x-ray may be conducted for people without TB symptoms to screen for TB
- People who present with any of the TB symptoms or who have an abnormal chest x-ray suggestive of TB must have a sputum sample collected for Xpert MTB RIF testing
- People living with HIV must have a sputum sample collected for Xpert MTB RIF Ultra testing, irrespective of TB symptoms

Summary (2/2)

- People who are close contacts of TB patients must have a sputum sample collected for Xpert MTB RIF Ultra testing, irrespective of TB symptoms
- People who have been previously treated for TB must have a sputum sample collected for Xpert MTB RIF Ultra testing irrespective of TB symptoms
- Always offer an HIV test to people who do not know their HIV status and those who tested negative more than 3 months ago

Part 3: The non-stable Client

Training Approach:
Part 2 Patients Journey

Including separate sub-sections on

1. management of TB diagnosed once a person is already on ART
2. management of cryptococcal meningitis

Visit Schedule for Adults, Adolescents and Children 5 Years and Older on ART

DC/ Months* on ART	Routine monitoring tests	Overview of Management
0	**Baseline clinical and lab assessment as outlined on pages 4 to 6 ART initiation and session 1 of fast track initiation counselling**	
1	**Review test results**	• Session 2 of fast track initiation counselling including planning for travel and VL education • Clinical assessment and routine monitoring as outlined on page 17 • Integrated services for family planning and NCDs • **2 months ART dispensed (2MMD) - DMOC SOP 4**
3	**3-month* VL sCR and eGFR**	• Clinical assessment including VL and any other routine monitoring bloods as outlined on page 17 • Integrated services for family planning and NCDs

4	**Review test results**	• Clinical assessment and review of VL and any other monitoring results
		• Integrated services for family planning and NCDs
		• Assess eligibility for Repeat Prescription Collection strategies (RPCs) (South Africa's differentiated models of care for stable patients)
		  • VL < 50 c/mL
		  • Clinically well
		  • No OIs, including TB
		  • Not pregnant
		Repeat Prescription Collection strategies (DMOC for stable patients)
		Facility Pick-up Point (FAC-PUP) (DMOC SOP 5.1) / Adherence Clubs (AC) Facility or community-based support groups (DMOC SOP 5.2) / External Pick-up point (EX-PUP) (DMOC SOP 5.3)
		• Renew prescription for next 6 months, with first 3 month's supply issued today from the facility
		• If not eligible for RPCs or refused RPCs: Assess eligibility for facility provided multi-month dispensing (MMD) – DMOC SOP 4

7		• Collect medication from preferred RPCs
10	**10-month* VL sCR and eGFR CD4 count**	• Clinical assessment including VL and any other monitoring bloods as per "Monitoring on ART" on page 17 • Integrated services for family planning and NCDs • Check TPT eligibility • Renew prescription for next 6 months • Do not require clients to return to the facility in 1 month to review the VL results, unless other clinical indications exist that require review. Rather, recall to the facility only those clients with elevated VLs
11+		• 12-monthly clinical assessment and family planning review as per "Monitoring on ART' on page 17 • 12-monthly routine monitoring of VL, sCR and eGFR • Check that chosen RPCs option is still suitable • Collect medication from preferred RPCs

Non-stable clients

If at any stage the client becomes clinically non-stable and /or non-adherent i.e. a client who has:

- missed a scheduled appointment by more than 28 days (including in an RPCs) (see also re-engagement algorithm on page 12)
- a VL ≥ 50 c/ml
- possible signs or symptoms of clinical failure, e.g. if the client is acutely unwell, or develops a new OI such as TB

A clinician should:

- If in an RPCs, return the client to regular care to ensure more frequent clinical follow-up until they are stable again.
- Provide appropriate clinical management
- If clinically well and struggling with visit frequency: provide multi-month dispensing (DMOC SOP 4)
- If experiencing side effects or the child cannot tolerate their medication: switch drugs/formulation
- If struggling to take ART as prescribed: enhanced adherence counselling (See Annexure 3)

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What about people “failing” TLD with an elevated VL?

- **There have been very few 1st line DTG Failures due to resistance (only 1 described in literature!!)**
  - 99,99% of elevated VLs on DTG are due to adherence issues!!
- **The best chance they have of good adherence and a suppressed VL is on a TLD because:**
  - TLD is one tablet once a day
  - TLD is very well tolerated with few side-effects
  - Low toxicity
  - DTG has the fastest time to achieve viral suppression (see next slide)
  - DTG achieves the highest rates of viral suppression at +- 91%
- **Resistance on TLD 2 has been described, but only when they have been on DTG for > 2 years**

A paradigm shift

Historically we've been taught:
"never leave a client on a failing regimen"

- **In the era of "first-line" EFV → it meant a change in regimen to LPV/r**
  - low genetic barrier to resistance
  - Accumulation of other mutations that results in cross resistance to drugs other than EFV
- **In the era of "first-line" DTG (TLD1) → it means fix adherence and stay on DTG**
  - High genetic barrier to resistance
  - Very low possibility of resistance
  - More efficacious than any other regimen
  - Best chance good adherence better tolerated than any alternatives

Under which circumstance should someone change from “second-line” DTG (TLD2) to an alternative PI-based regimen?

- Only if DTG is proven to be in-active in a “second-line” DTG (TLD2) regimen
- This requires a resistance test

Does that mean everyone failing TLD2 should get a resistance test?

- **No!!**
- **Only clients failing "second-line" TLD2 and meeting the following criteria for "confirmed virological failure"**
  - On a DTG-based regimen for more than 2 years
  - Two or more consecutive VLs ≥ 1000 c/mL, taken two or more years after starting DTG regimen
  - Adherent on their regimen
- **All Resistance tests will need to be authorised**

VL Monitoring for Clients on TLD

(also applicable to ALD and other DTG-containing regimens)

Routine VL monitoring for virally suppressed clients as outlined in the algorithm
"Routine HIV VL Monitoring on ART" on page 18

VL < 50 c/mL

VL unsuppressed (VL ≥ 50 c/ml)
(This includes previous VL level of 50-999 and VL > 1000 c/ml)

Do a thorough assessment of the cause of an elevated VL. Consider the possibility of:

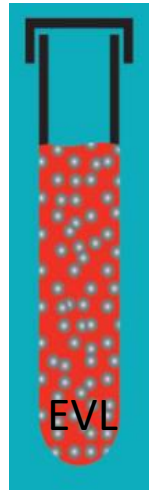
A. **A**dherence problems *(see **"Enhanced Adherence Support" on page 20**)*
B. **B**ugs (Intercurrent infections)
C. In-**C**orrect ART dosage *(see Annexure 5 **"Drug Dosing Chart" on page 34**)*
D. **D**rug Interactions *(see **"Drug Interactions with DTG and Rifampicin-containing TB Treatment" on page 13**)*
E. R**E**sistance (if > 2 years on treatment)

Implement interventions to re-suppress the VL, including **Enhanced Adherence Support** if indicated
(See Annexure 3 Enhanced Adherence Counselling)
Recommend **condom use and contraception** as appropriate

Repeat VL after 3 months

Repeat VL after 3 months

Repeat VL **unsuppressed** [1] **(VL > 50 c/ml)**



Re-assess and resolve adherence issues! [2]
*(See **"ABCDE assessment of an Elevated Viral Load" on page 20** and Annexure 3 **"Enhanced Adherence Support" on page 20**)*

On TLD for **at least 2 years**

On TLD **less than** 2 years [3]

If **Adherence > 80%** [4], and
Two or more **VLs ≥ 1000 c/mL**
taken two or more years after starting TLD regimen
or at least one VL ≥ 1000 c/mL and either
CD4 < 200 cells/mm3 or an opportunistic infection

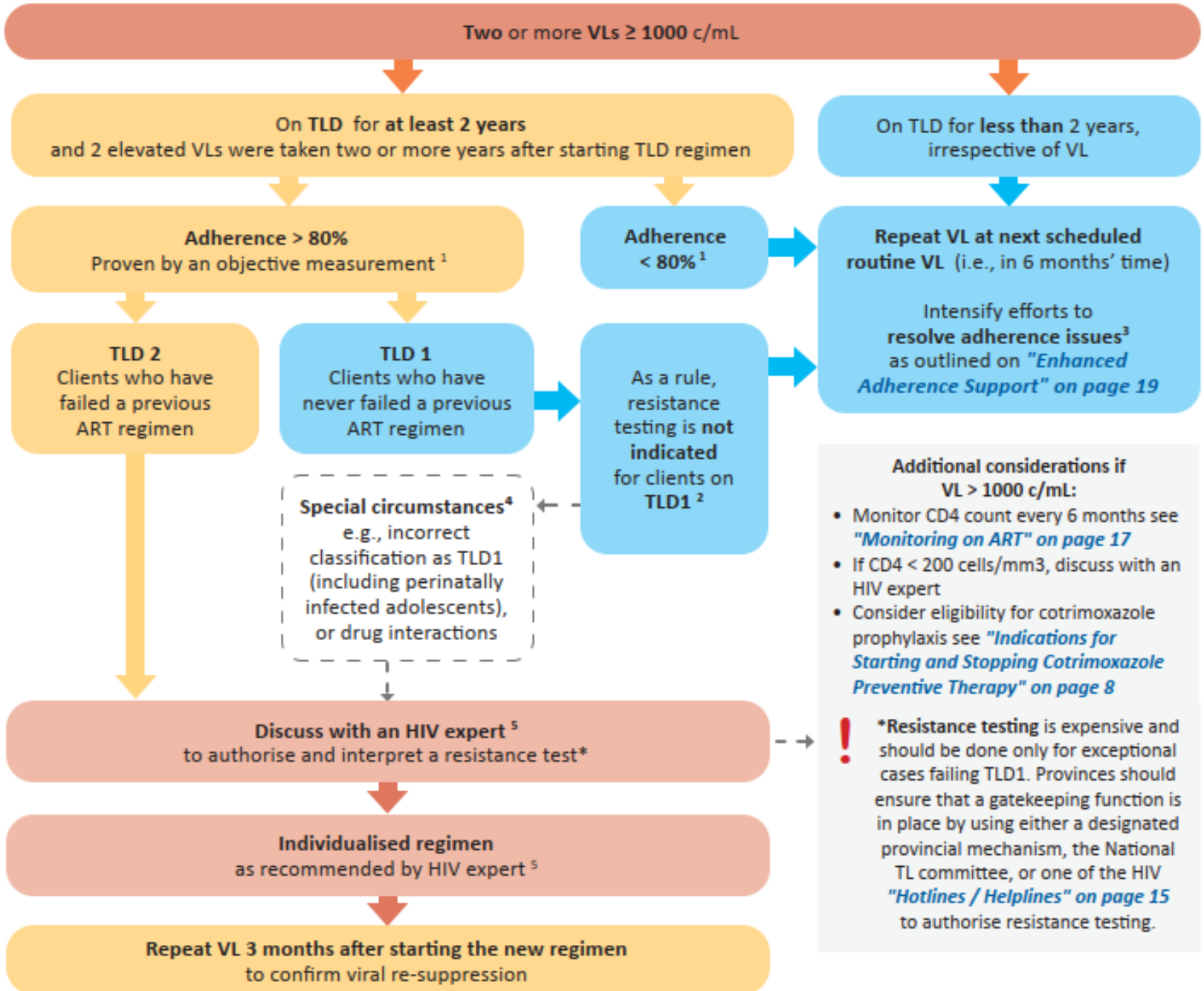
If adherence still
suboptimal [4],
or persistent low-level viraemia
(2 or more consecutive VLs between
50 and 999 c/mL)

Go to the algorithm for
"Management of Confirmed Virological Failure on TLD" on page 21

Repeat VL at next scheduled routine VL
(i.e., in 6 months' time)
Intensify efforts to **resolve adherence issues** [2]

Management of Confirmed Virological Failure on TLD

(also applicable to other DTG-containing regimens)



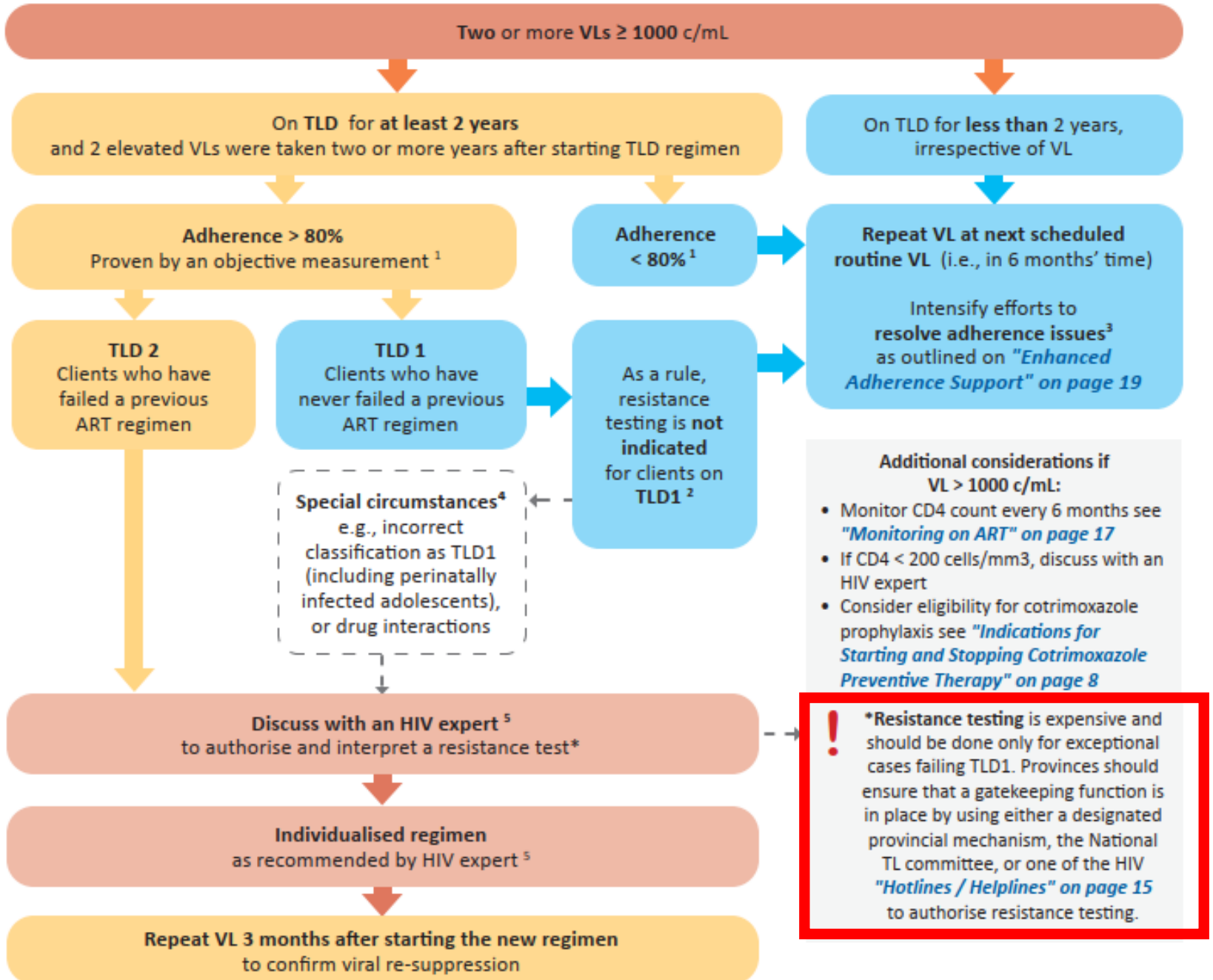
Footnote 4: Special circumstances that may warrant a resistance test for clients on TLD1 include

- Incorrect classification as TLD1 (clients who declare themselves as never having had ART before, but who have actually been exposed to ART and may have failed a regimen in the past)
- Perinatally infected adolescents: Unless a clearly documented drug history is available, perinatally infected adolescents should be classified as TLD2 due to the high likelihood of ART exposure and virological failure in the past
- Current or previous drug interactions with rifampicin, carbamazepine, phenytoin, phenobarbital, or the polyvalent cations may have resulted in the development of resistance. Drug interactions may also warrant an expert discussion and authorisation of a resistance test earlier than 2 years on the regimen.

In these types of exceptional circumstances, TLD1 clients with persistent virological failure despite confirmed good adherence may be discussed with an expert to authorise a resistance test on a case-by-case basis.

Management of Confirmed Virological Failure on TLD

(also applicable to other DTG-containing regimens)



Mechanisms for authorisation of RTs

1. **National Third-line ART committee**
2. **One of the 3 HIV Helplines**
3. **Infectious disease specialists**
4. **Provincial gatekeepers**
   - Consisting of 5-10 additional nominated experts
     - The lab will have a list of all nominated experts from provinces
     - All nominated experts will be provided with a code by NHLS that will authenticate authorisations

Return from RPCs to clinician-managed care

1. **Clients are returned to clinician-managed care at the facility when:**
   - VL > 50 copies ml
   - Clinically unwell including diagnosed with TB or other OI or an other condition that requires clinical review more frequentl than 6 monthly
   - More than 28 days late for their appointment

➢ **Explain to client:**
   - Benefits of more intensive clinical management
   - Timeline back to return to RPCs

CRITERIA FOR RETURN TO REGULAR CARE

- RPCs patient did not return to the facility or RPCs within 28 calendar days of their scheduled RPCs appointment date.
- RPCs patient is assessed as clinically unstable requiring more frequent clinical management, including diagnosed with TB or any other opportunistic infection or any other opportunistic infection.
- Other safety lab test results are abnormal.
  - For HIV: VL ≥50 copies/ml (unless clinician confirms persistent viraemia)
  - For Diabetes: HbA1c >8%
  - For Hypertension: BP >140/90
- RPCs patient becomes pregnant and is referred to integrated MNCWH services.

All patients must be advised that they are being returned to regular care to ensure more frequent clinical care until they are stable again. Patients can return to their RPCs (or alternative preferred RPCs) after a single normal result and meeting other RPCs criteria (also see Re-engagement SOP 10).

Enhance Adherence Counselling

Enhance Adherence Counselling focuses on:

- Providing education on the outcome of their latest clinical assessment and VL results
- Understanding what the client already knows or doesn't know regarding their treatment and the importance of VL suppression
- Doing a mental health screen
- Correcting any misconceptions and allowing flexibility around the most common barriers to adherence (such as alcohol/ drug consumption, forgetting doses due to a rigid schedule, etc.).
- Understanding the client's experiences, assessing and understanding the barriers that affect the client's adherence
- Developing adherence strategies to overcome these

Return from RPCs to clinician-managed care
How to manage: Drug switch-MMD-EAC

2. Assess if enhanced adherence counselling would be helpful

i. Drug side effects impacting adherence?
- ➢ If yes and drug/s switched no need for EAC

ii. Difficulty getting to facility to collect treatment probably no need for EAC
- ➢ If difficulty getting to facility for treatment, provide 2 or 3-month supply until next NECESSARY clinical visit to support improved adherence
- ➢ **New DMOC SOP 4** explains facility provided MMD aligned to clinical review dates including for TB and elevated VL

iii. Challenges with taking/remembering to take treatment
- ➢ Provide EAC session 1 (annexure 3 of ART guidelines/DMOC SOP 2)

A clinician should:

- If in an RPCs, return the client to regular care to ensure more frequent clinical follow-up until they are stable again.
- Provide appropriate clinical management

ii. Enable adherence
- If clinically well and struggling with visit frequency: provide multi-month dispensing (DMOC SOP 4)

i. Enable adherence
- If experiencing side effects or the child cannot tolerate their medication: switch drugs/formulation

iii. Enable adherence
- If struggling to take ART as prescribed: enhanced adherence counselling (See Annexure 3)

Multi-month dispensing (MMD)

NEW

- **Previously MMD was only included in Repeat Prescription Collection Strategies (RPCs) SOPs.**
- **New SOP that specifically enables longer refills by facilities between clinical reviews for people:**
  - People who are NOT eligible for RPCs
    - **Elevated VL after EAC**
    - **Re-engaging (if clinically well)**
    - **TB continuation phase**
    - **6 months old to 5 yrs old**
    - **Travelling**
    - **6-months post-natally**
  - Eligible but do not want RPCs/no RPCs suitable option at their facility

Facility-based MMD Not RPCS therefore not supplied by CCMDD

Sub-section to Part 3

The not-stable client

The Integrated visit schedule for clients on TB and ART

TB: Eligibility/exit from RPCs

2019 ART guidelines

- Only eligible for RPCs if no OI
- If unwell or **screen positive for TB** – return to regular care for clinical management

2023 ART clinical guidelines

- No changes for RPCs eligibility
- **Change to exit criteria – only exit if unwell OR diagnosed with TB**
  - **TB screening now includes annual GeneXpert – do not return all clients to regular care while waiting for GeneXpert result**
- **Added facility-based MMD to support TB continuation phase**

Months on ART	Routine monitoring tests	Overview of Management
0	**Baseline clinical and lab assessment as outlined on pages 4 to 6 ART initiation and session 1 of fast track initiation counselling**	
1	**Review test results**	• Session 2 of fast track initiation counselling including planning for travel and VL education • Clinical assessment and routine monitoring as outlined on page 15 • Integrated services for family planning and NCDs • **2 months ART dispensed (2MMD) - AGL SOP 4**
3	**3-month VL sCR and eGFR**	• Clinical assessment including VL and any other routine monitoring bloods as outlined on page 15 • Integrated services for family planning and NCDs

4	**Review test results**	• Clinical assessment and review of VL and any other monitoring results
		• Integrated services for family planning and NCDs
		• Assess eligibility for repeat prescription collection strategies (RPCs)
		  • VL < 50 c/mL
		  • Clinically well
		  • No OIs, including TB
		  • Not pregnant
		Facility Pick-up Point (FAC-PUP) (AGL SOP 5) | Adherence Clubs (AC) Facility or community-based support groups (AGL SOP 6) | External Pick-up point (EX-PUP) (AGL SOP7)
		• Renew prescription for next 6 months, with first month's supply issued today from the facility
		• If not eligible for RPCs or refused RPCs: Assess eligibility for facility provided multi-month dispensing (MMD) – AGL SOP 4

5 - 9		• Collect medication from preferred RPCs
10	**10-month VL sCR and eGFR CD4 count**	• Clinical assessment including VL and any other monitoring bloods • Integrated services for family planning and NCDs • Renew prescription for next 6 months. • Do not require the clients to return to the facility in 1 month to review the VL results. Rather, recall to the facility only those clients with elevated VLs
11+		• Collect medication from preferred RPCs • Annual clinical assessment as outlined on page 15 • 12-monthly routine monitoring of VL, sCR and eGFR

Non-stable clients

If at any stage the client becomes clinically non-stable and /or non-adherent i.e. a client who has:

- missed a scheduled appointment by more than 28 days (including in an RPCs) (see also re-engagement algorithm on page 10)
- a VL ≥ 50 c/ml
- possible signs or symptoms of treatment failure

A clinician should:

- If in an RPCs, return the client to regular care to ensure more frequent clinical follow-up until they are stable again.
- Provide appropriate clinical management
- If clinically well and struggling with visit frequency: provide multi-month dispensing (Adherence Guideline SOP 4)
- If experiencing side effects or the child cannot tolerate their medication: switch drugs/formulation
- If struggling to take ART as prescribed: enhanced adherence counselling (See Annexure 3)

ART patient diagnosed with TB not in RPCs yet:

Clinicians should provide integrated TB management at clinical consultation visits and reduce visit schedules to limit disengagement

Integrated visit schedule for a client on ART who develops DS-TB (not in RPCs)		Months (M) on TB Treatment (Rx)						
		Intensive Phase (IP) (months 1-2)				Continuation Phase (CP) (months 3-6)		
		TB M0	TB M1 (4 completed weeks)	7 wks	TB M2 (8 completed weeks)	TB M4 (16 completed weeks)	23 wks	TB M6 (24 completed weeks)
Integrated TB/ ART clinical consult	TB screening as part of routine care	TB diagnosis and TB Rx initiation	Clinician-managed care at facility		Assess smear conversion and transition to CP of TB Rx, if smear result is negative	Clinician-managed care at facility		Confirm TB Rx completion Assess for RPCs enrolment
Investigations	TB GeneXpert and any other investigations as clinically indicated	Review result		Smear	Review result		Smear	Review end-of-Rx result
ART/TB script	Script ART for 1 month	Combined script for 1 month of IP TB Rx and ART	Combined script for 1 month of IP TB Rx and ART		Combined script for 2 months** of CP TB Rx and ART	Combined script for 2 months** CP of TB Rx and ART"		If eligible for RPCs: RPCs ART script for 6 months
ART-TB drug supply dispensed by facility	Dispense ART for 1 month	Dispense 1 month of IP TB Rx and DTG boosted ART	Dispense 1 month of IP TB Rx and DTG boosted ART		Dispense 2 months of CP TB Rx and 2 months DTG boosted ART	Dispense 2 months of CP TB Rx and 2 months DTG boosted ART		Dispense 3 months of ART
Ask client to return:	If client has TB symptoms or is unwell, ask client to return in 5-7 days for review *	After 4 weeks for clinical review	After 3 weeks for sputum smear	After 1 week for smear results	After 8 weeks for clinical review	After 7 weeks for end of Rx smear	After 1 week for smear results	If eligible and enrolled in RPCs: return for next ART supply at RPCs pick-up point after 3 months

Sub-section to Part 3

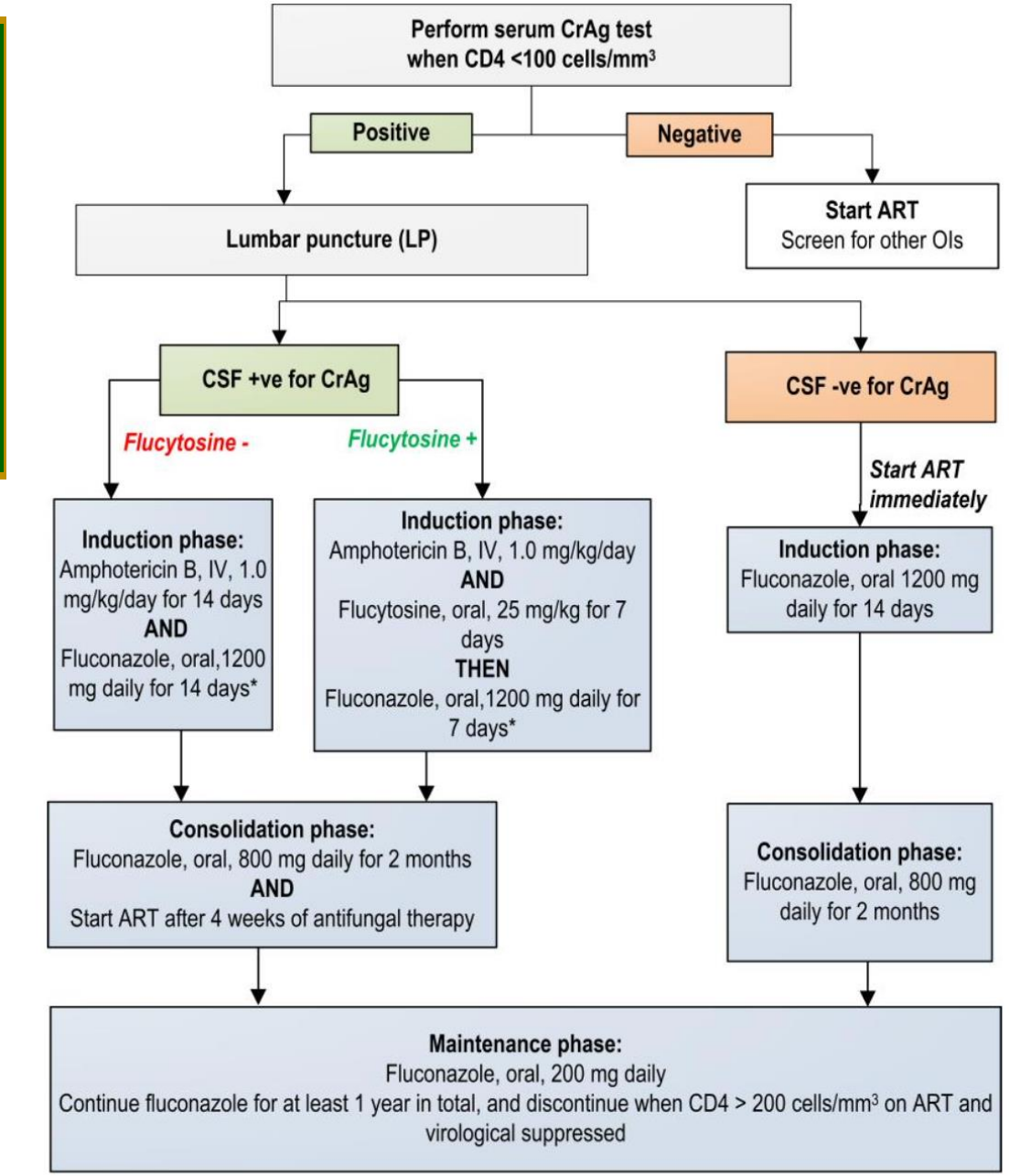
The not-stable client

Changes to Management of Cryptococcal Meningitis

Cryptococcal Antigen (CrAg) screening guidelines

- **Currently a reflex CrAg test is performed on all CD4 samples <100.**
- **If CrAg test positive, all patients should have a lumbar puncture, regardless of whether symptoms of meningitis are present, since asymptomatic cryptococcal meningitis may be present.**
    - Give first fluconazole dose 1200mg oral
- **Fluconazole prophylaxis should be continued for at least 1 year, can be stopped once the CD4 count increases to > 200cells/mm3 on ART and Viral load is suppressed.**
    - If the CD4 count does not increase continue treatment indefinitely.

Screening for and Management of Cryptococcal Disease



Note: If there is a delay in performing LP, obtaining LP results or in starting amphotericin B therapy, start fluconazole 1200 mg immediately.

SA Recommended Treatment Regimen using Flucytosine

INDUCTION	CONSOLIDATION	MAINTENANCE
1 week regimen: Flucytosine, oral 25 mg/kg 6 hourly for 7 days + Amphotericin B (1mg/kg/day).[same dose children & adolescents] followed by 1 week of fluconazole (1200 mg daily for adults; 12 mg/kg/day for children and adolescents to a maximum of 800 mg daily	8 weeks Fluconazole (800mg daily) 6-12 mg/kg/day for children & adolescents -max 800 mg daily	Fluconazole (200 mg/day). For at least 12 months and until a single CD4 count is >200 cells/µl and the HIV viral load is suppressed 6 mg/kg/day children and adolescents - max 200 mg daily

Hospital Level (Adults) Standard Treatment Guidelines and Essential Medicines List 2nd Edition, SA - 2019

Indications for CM treatment

- Serum CrAg+ with symptoms of meningitis (1st instance detected)
  - LP should always be done unless declined by the patient
- Detection in CSF, regardless of symptoms (1st instance detected)
  - CSF India ink positive or CSF CrAg positive (better diagnostic performance than india ink) or CSF culture positive
- Recurrent symptomatic episode with CSF culture+
- Culture + ve from any specimen (disseminated cryptococcosis)
  - For Mx of pulmonary crypto, cryptococcomas, and other disseminated disease seek expert advice / consult 2010 IDSA guidelines

Post discharge – CrAg positive patients and those completing hospital induction therapy

- Adherence support is recommended for all patients who screen CrAg-positive and are followed up as outpatients
- Particularly among those who decline an LP as may have subclinical meningitis
- Provide supply on discharge and ensure knows how to get resupply
- Provide patient information on discharge – if any symptoms to urgently return to hospital
- Try to ensure there is a treatment buddy who can support adherence and identify symptoms of meningitis if they develop
- If patient stops fluconazole maintenance prematurely then restart

Summary: ART Regimens

ART Regimens	**All adult and adolescent clients > 30 kg and > 10 years of age, including pregnant and breastfeeding women**	• The preferred first-line ART regimen is **tenofovir disoproxil fumarate-lamivudine-dolutegravir (TLD)** for those adult and adolescent clients initiating ART. • TDF weight-related eligibility criteria decreased from **35 kg to 30 kg** • All clients already on ART and not on dolutegravir (DTG), whether on first-line or second-line regimens, should be evaluated for a switch to a dolutegravir-containing regimen.
		• TDF may safely be reused in 2nd-line therapy following 1st-line failure with TDF-containing regimens. TLD will therefore be used as both first (TLD 1) and second (TLD 2) line regimens and in certain cases, 3rd line regimens as well • Simplified **switching from TEE to TLD not dependant on VL**
	New formulations	• **DTG 10 mg dispersible tablets** for children from ≥ 3kg and ≥ 4 weeks of age • DTG-containing fixed-dose combination: Abacavir (ABC) 600 mg + lamivudine (3TC) 300 mg + DTG 50 mg (ALD FDC). ALD FDC can be prescribed for clients ≥ 25 kg
	Children ≥ 3 kg and ≥ 4 weeks of age until 29,9 kg or 9 years of age	• The preferred first-line ART regimen is **abacavir-lamivudine-dolutegravir (ALD)**. • All paediatric clients already on ART and not on dolutegravir (DTG), whether on first-line or second-line regimens, should be evaluated for a switch to a dolutegravir-containing regimen.
	Other antiretrovirals	• **Abacavir** is the preferred alternative agent if TDF cannot be used • Zidovudine (AZT) no longer part of any standard ART regimen. AZT will be reserved only for cases with **both** renal failure **and** ABC hypersensitivity • **Atazanavir/r** replaces lopinavir/r as the preferred protease inhibitor except when on TB treatment

Summary: Monitoring on ART

Monitoring on ART	**VL monitoring**	**First VL** after ART initiation to be done after 3 dispensing cycles
	Creatinine and eGFR	eGFR previously done at 'month' 6 moves to 'month' 3 (i.e. after 3 dispensing cycles) to align with the new VL monitoring schedule

Summary of changes Virological Failure

Virological Failure	• **Definition:** two or more VLs ≥ 1000 c/mL taken two or more years after starting a DTG/PI-containing regimen and adherence > 80% • **Focus on improved adherence:** Resistance to DTG is very uncommon. If other reasons for an unsuppressed VL (including drug interactions) have been addressed or excluded, the highest probability of improving adherence would be to remain on a once-daily, well-tolerated, fixed-dose combination regimen (TLD) while identifying and addressing the underlying root causes of non-adherence. • **No regimen changes without a resistance test:** Switching off a DTG-containing regimen should only happen if InSTI resistance has been confirmed by a resistance test • Resistance testing can only be authorised by a member of the National Third-line committee, one of the helpline consultants, or a nominated provincial expert

Summary

Other updates	• 2 high quality counselling sessions at ART start and at follow-up a month later
	• Reduces health facility visits in the first year on ART to support continued engagement in care, including visit schedule for first year on treatment.
	• Removes time on ART from repeat prescription collection strategies (RPCs) eligibility criteria, enabling access as soon as first VL is suppressed.
	• Reduces visits once enrolled in RPCs with a maximum of 2 visits per 6-month scripting cycle.
	• Returns clients in RPCs with VL 50-1000 c/mL to clinician care for TLD switch and VL management
	• Enables multi-month dispensing (MMD) by the facility between clinical visits including for people not eligible for RPCs - children from 6 months of age, post-natal women, people co-infected with TB, with elevated viral loads or re-engaging in care.
	• Introduces a differentiated approach to management on re-engagement.
	• Integrates contraception and TB preventative therapy into all service delivery models
	• Aligns ART visit schedules to TB management and infant EPI schedules to enable integration
	• Incorporates tools for:
	  • enhanced adherence counselling
	  • mental health assessment

Help Line

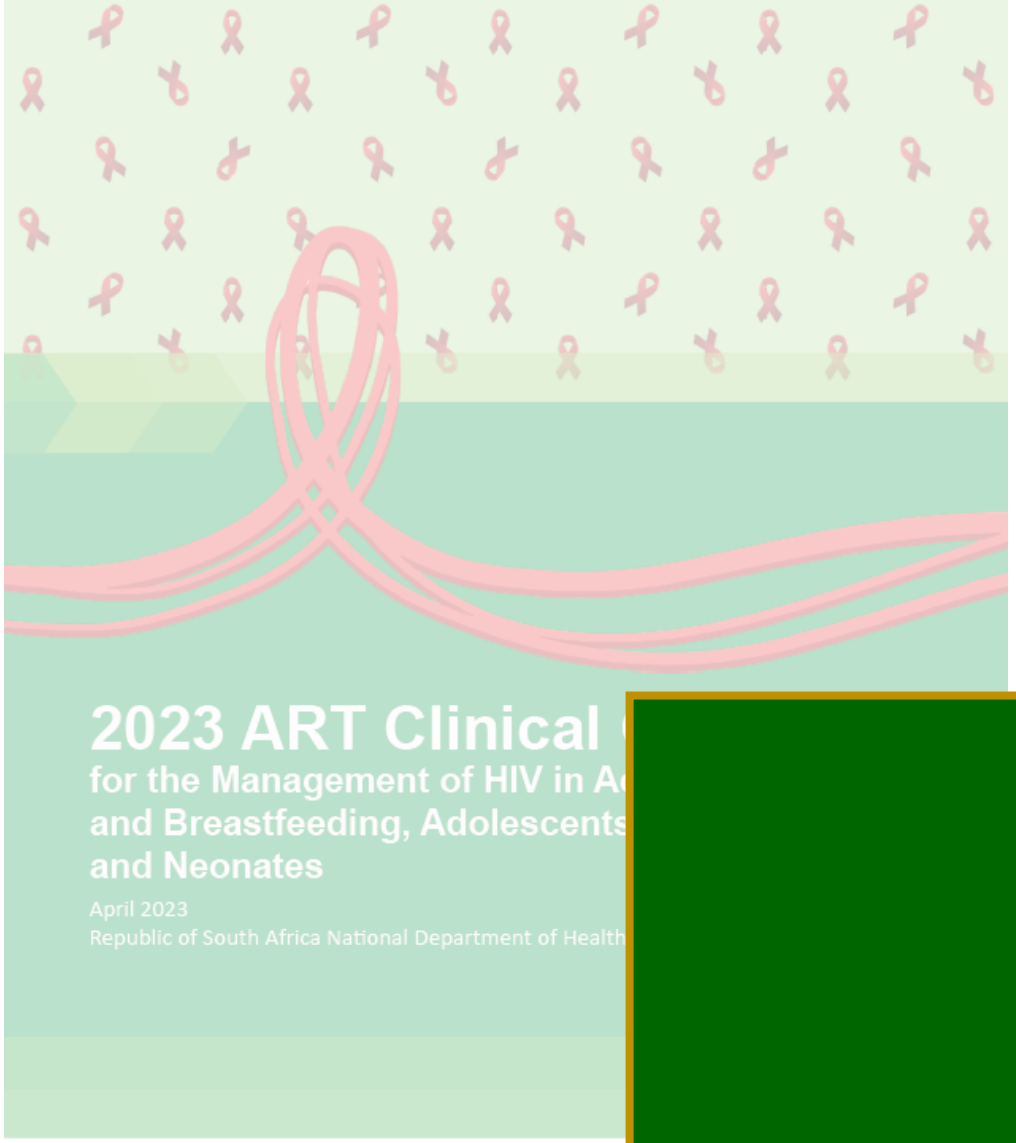
HELPLINES

If in doubt about any aspect of viral load management or switching to second-line, contact one of the following resources:

National HIV & TB Health Care Worker Hotline: **0800 212 506**

Right to Care Paediatric, Adolescent and Adult HIV Helpline: **082 352 6642**

KZN Paediatric Hotline: **0800 006 603**



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Thank you!

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