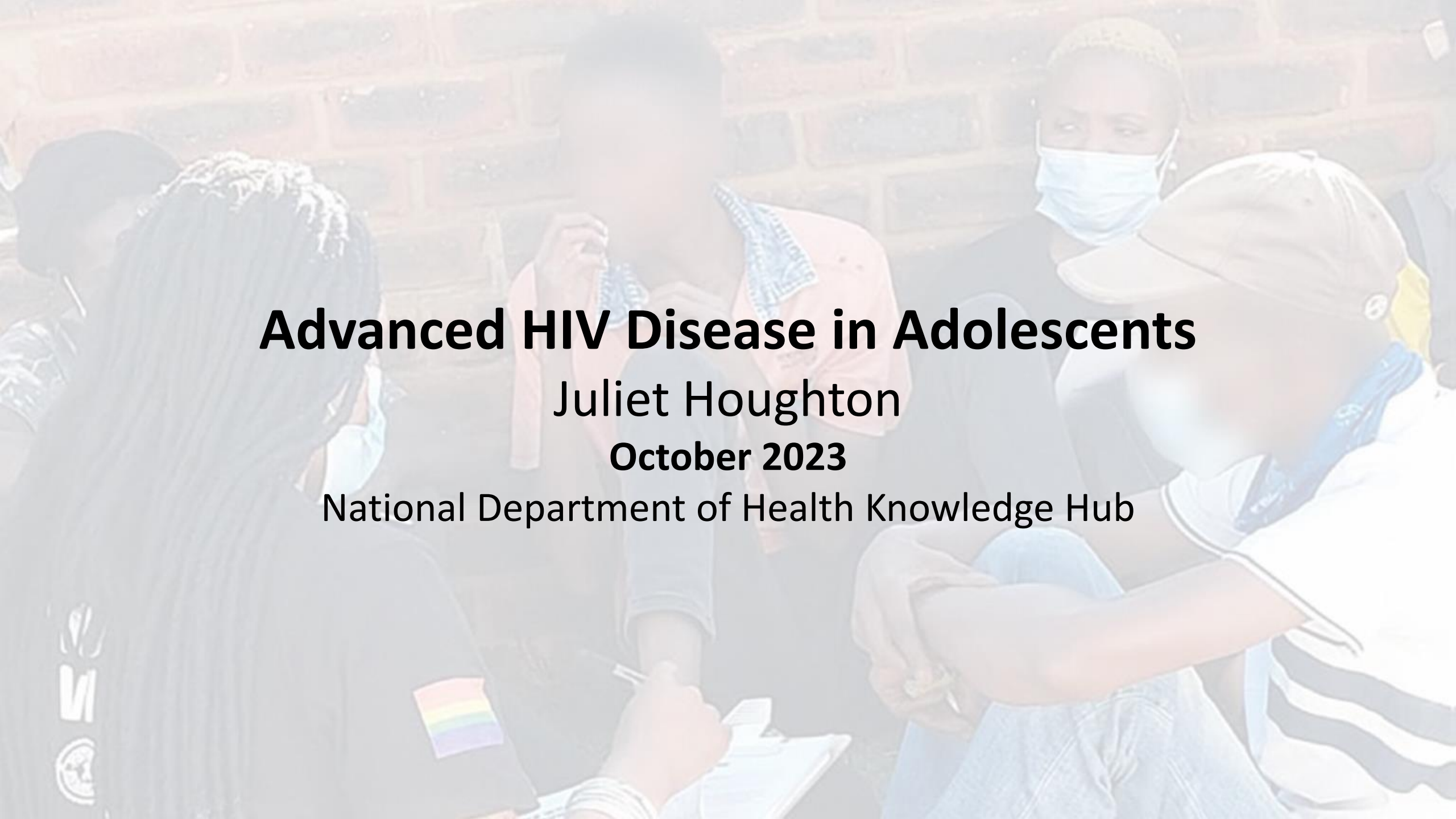


Advanced HIV Disease in Adolescents

Juliet Houghton

October 2023

National Department of Health Knowledge Hub

Aims

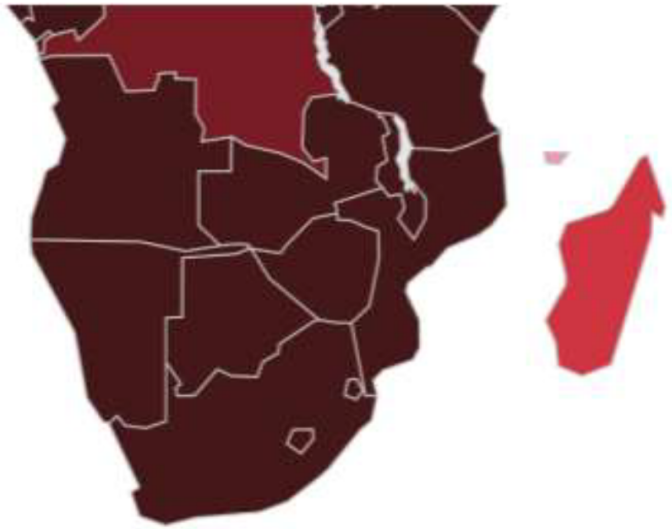
- Explore epidemiology of adolescents living with HIV
- Understand clinical staging of adolescents
- Identify virological failure in an adolescent
- Explore management plan options for an adolescent with virological failure
- Describe models of care tailored to meet needs of adolescent clients

Learning Outcomes

- Identify virological failure in adolescents living with HIV
- Understand clinical staging of adolescents
- Describe challenges and mechanisms leading to treatment failure
  - clinical aspects
  - adolescent aspects
  - social aspects
- Outline management plan options for an adolescents within different models of adolescent care

Epidemiology

Epidemiology of Child and Adolescent HIV in South Africa



New HIV infections in 2020

- Children (<15 years): 12 000 (6900 – 31 000)
- Adolescents (10-19 years): 38 000 (5 400 - 77 000)
- All Ages: 230 000 (150 000 – 310 000)

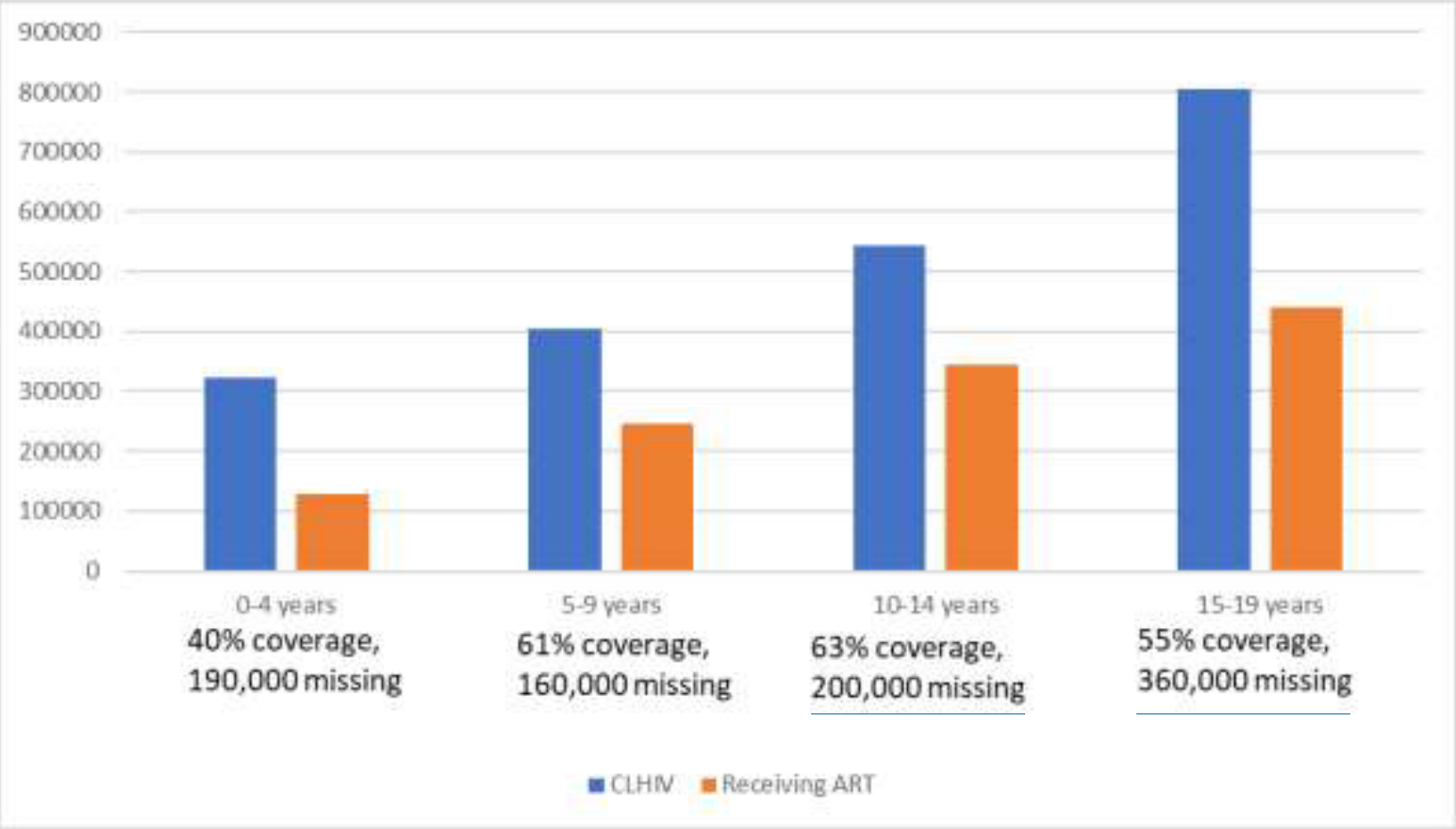
People living with HIV

- Children (<15 years): 310 000 (200 000 – 540 000)
- Adolescents (10-19 years): 370 000 (190 000 - 550 000)
- All Ages: 7 800 000 (5 200 000 – 10 000 000) – Prevalence 17.7 (11.7 – 22.5)

ART Coverage in Adolescents in Sub-Saharan Africa

There are an estimated **200,000** younger adolescents (10-14) years who are not on ART in SSA

Worse still, the coverage for older adolescents is only **55%** of ALHIV receiving ART; representing around **360,000** older adolescents not on ART

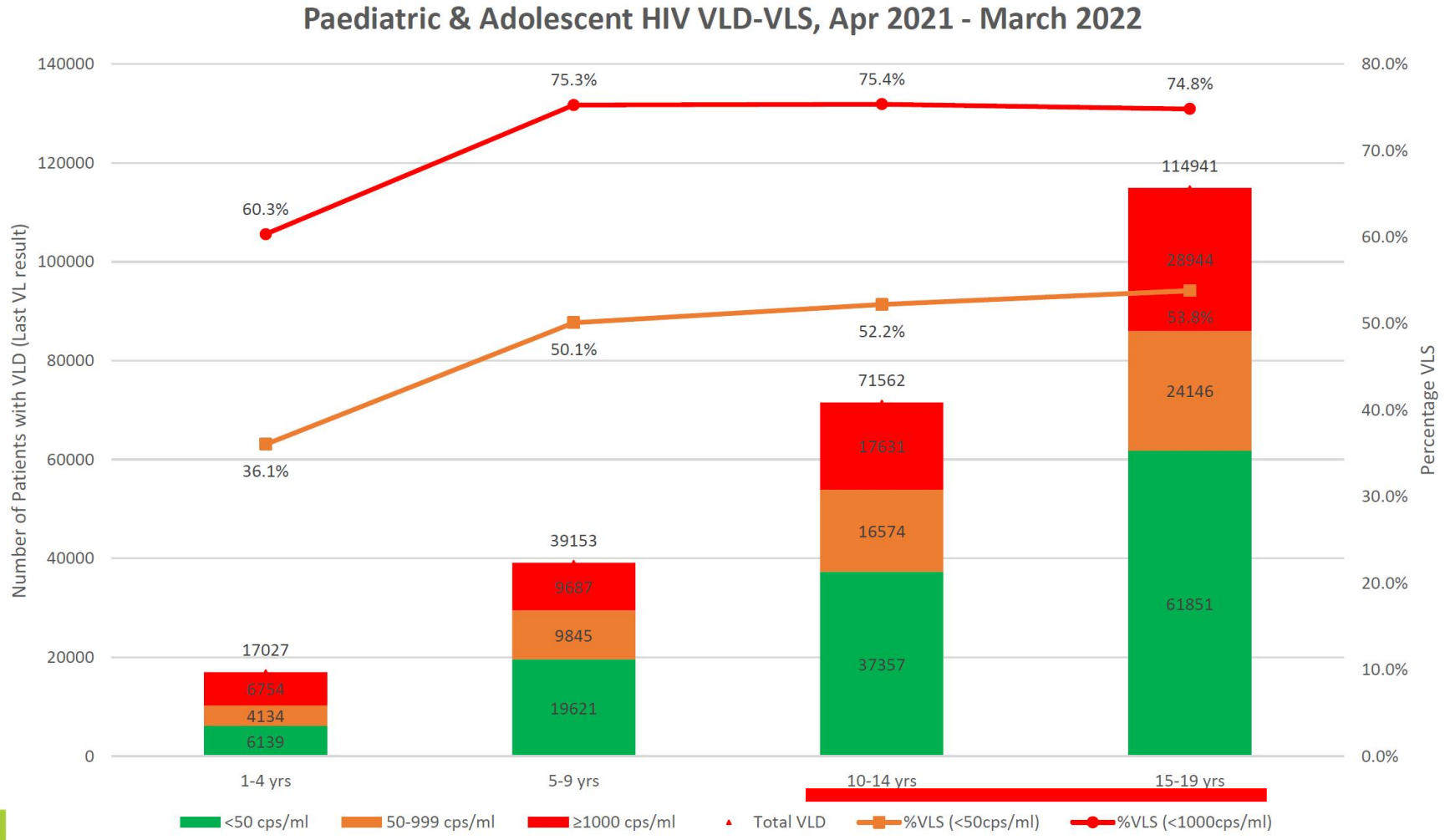


HIV VL Suppression in C+ALHIV in South Africa

The total % of VLD in adolescents on ART in SA dropped slightly over the year

The total % of VLS <50cps/ml is only **52.2%** in younger adolescents and **53.8%** in older adolescents

A further **21%** of adolescents who had VLD had VLS between 50 – 1000 cps/ml



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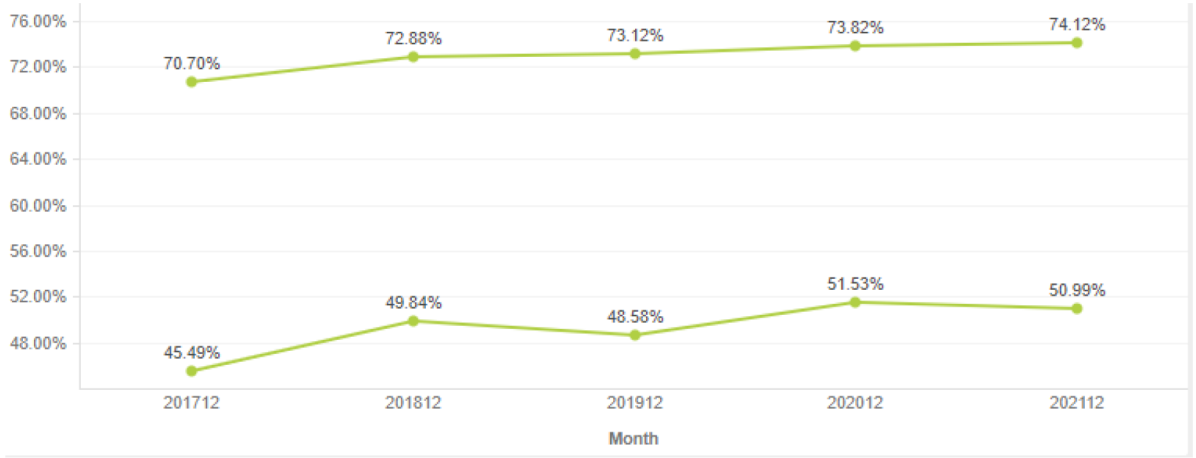
Trends in HIV VL Suppression in Children and Adolescents in South Africa

South Africa: NHLS VLS <15 Years: 2017 – 2021



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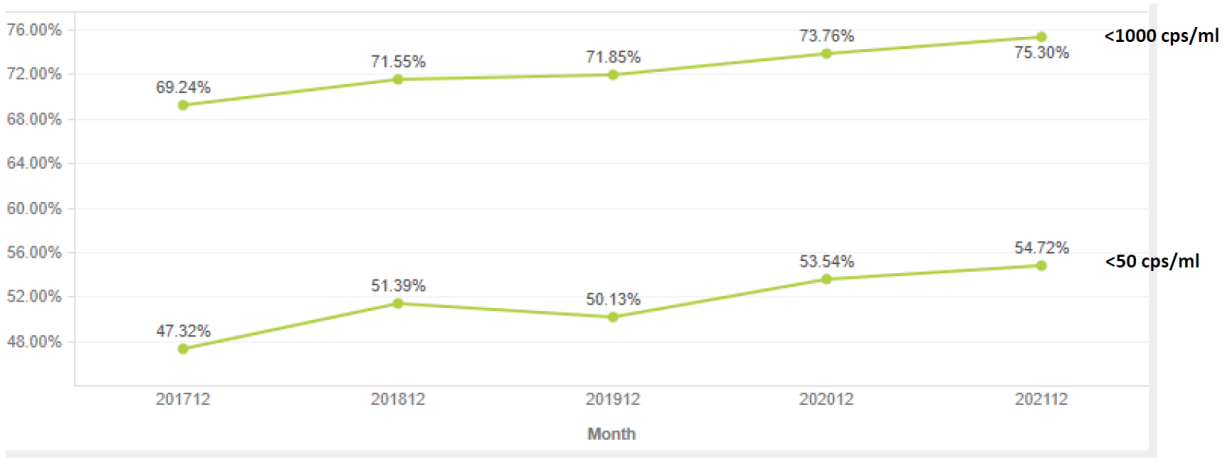
VL suppression has been static over last 5 years

? Improvement to come with switch from LPV/r syrup to DTG dispersible tablets and FDCs for children?

South Africa: NHLS VLS 15 - 19 Years: 2017 – 2021

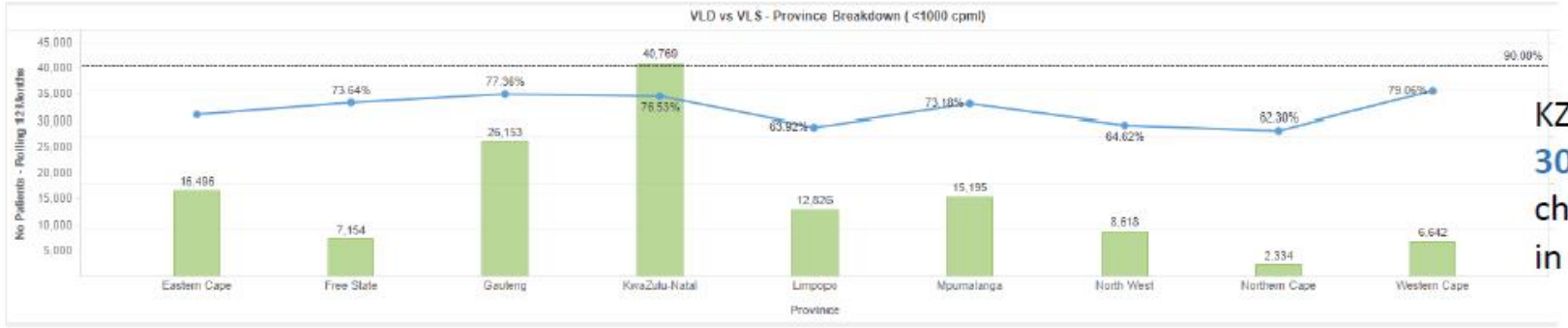


HIV VL Suppression: Breakdown of Older Adolescents in KZN

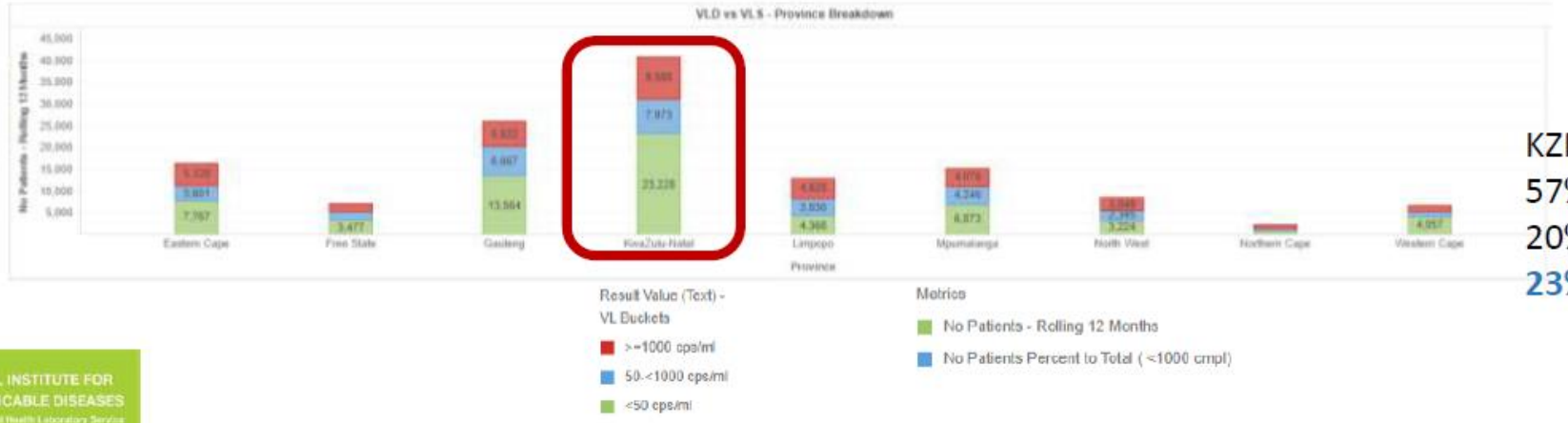
Provincial NHLS VLD & VLS 0<15 Years: Apr 2021 – Mar 2022

Viral Suppression: Provincial Breakdown

Provincial NHLS VLD & VLS <15yrs, Apr 2021 – March 2022



KZN accounts for **30% of 136 187** children <15 years in chronic care



KZN
57% - < 50 c/ml
20% - 50-1000 c/ml
23% - > 1000 c/ml

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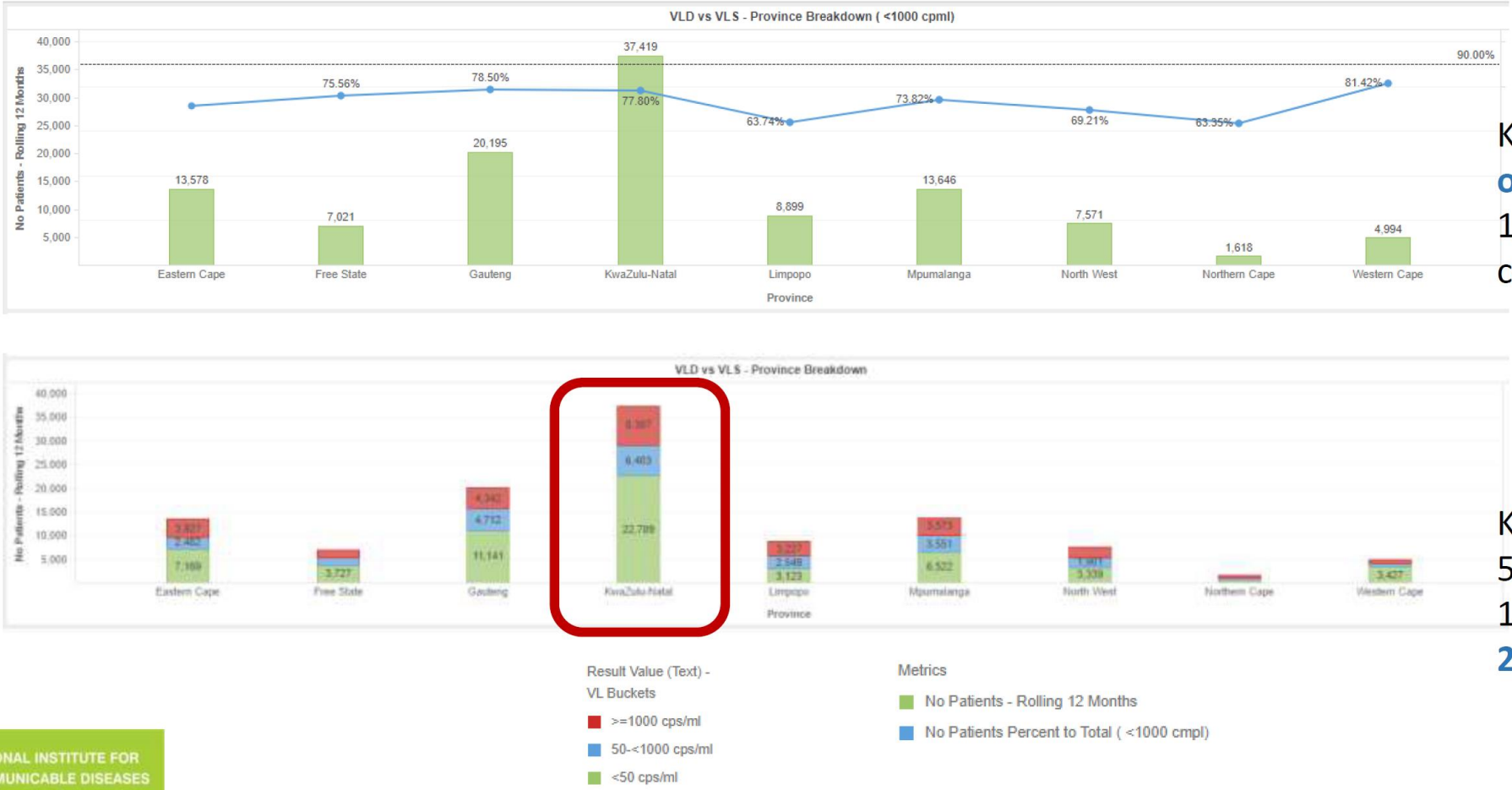
HIV VL Suppression: Breakdown of Older Adolescents in KZN

Provincial NHLS VLD & VLS 15-19 Years: Apr 2021 – Mar 2022



KZN accounts for **33% of 114 941 adolescents** 15-19 years in chronic care

KZN
55% - < 50 c/ml
17% - 50-1000 c/ml
22% - > 1000 c/ml

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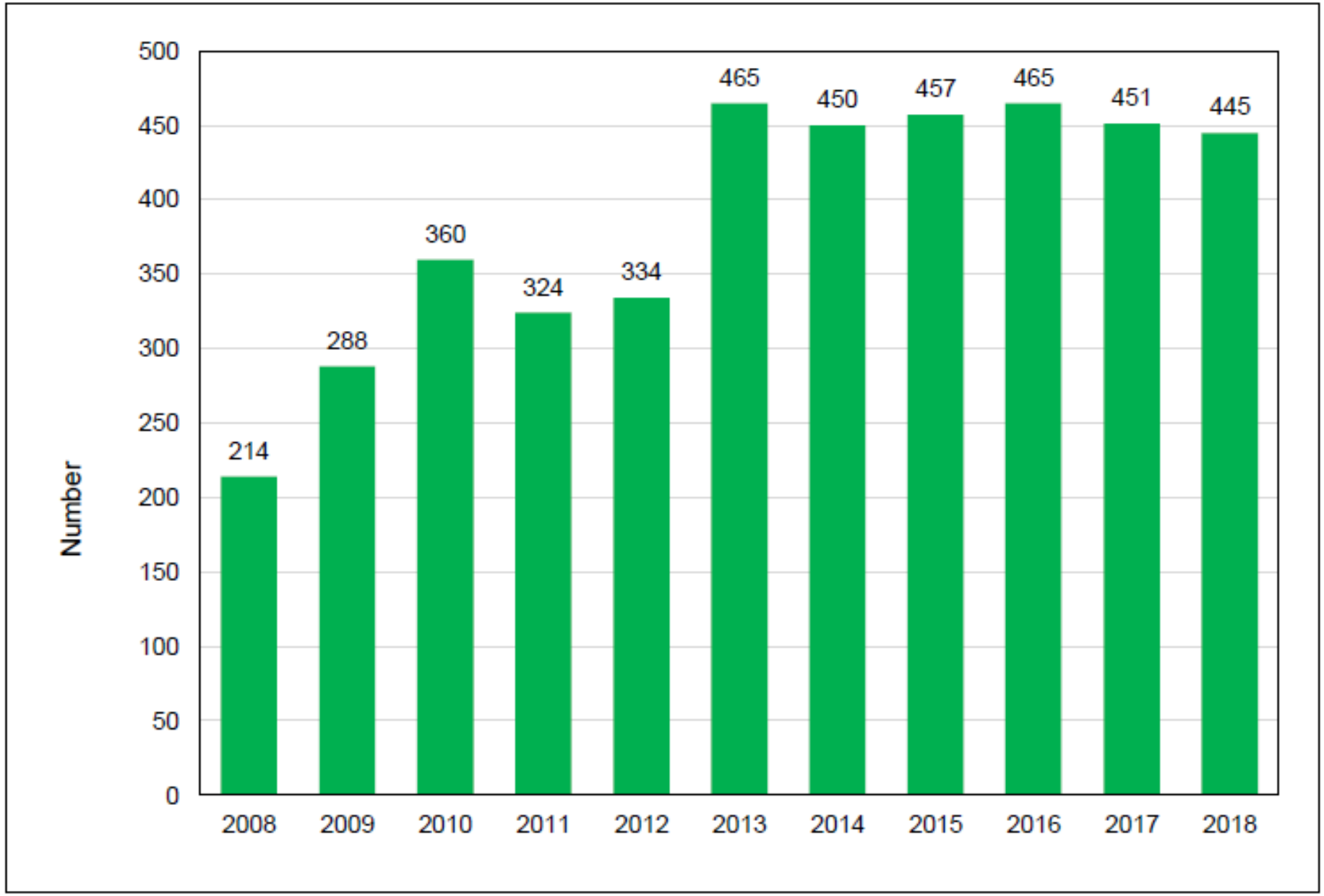
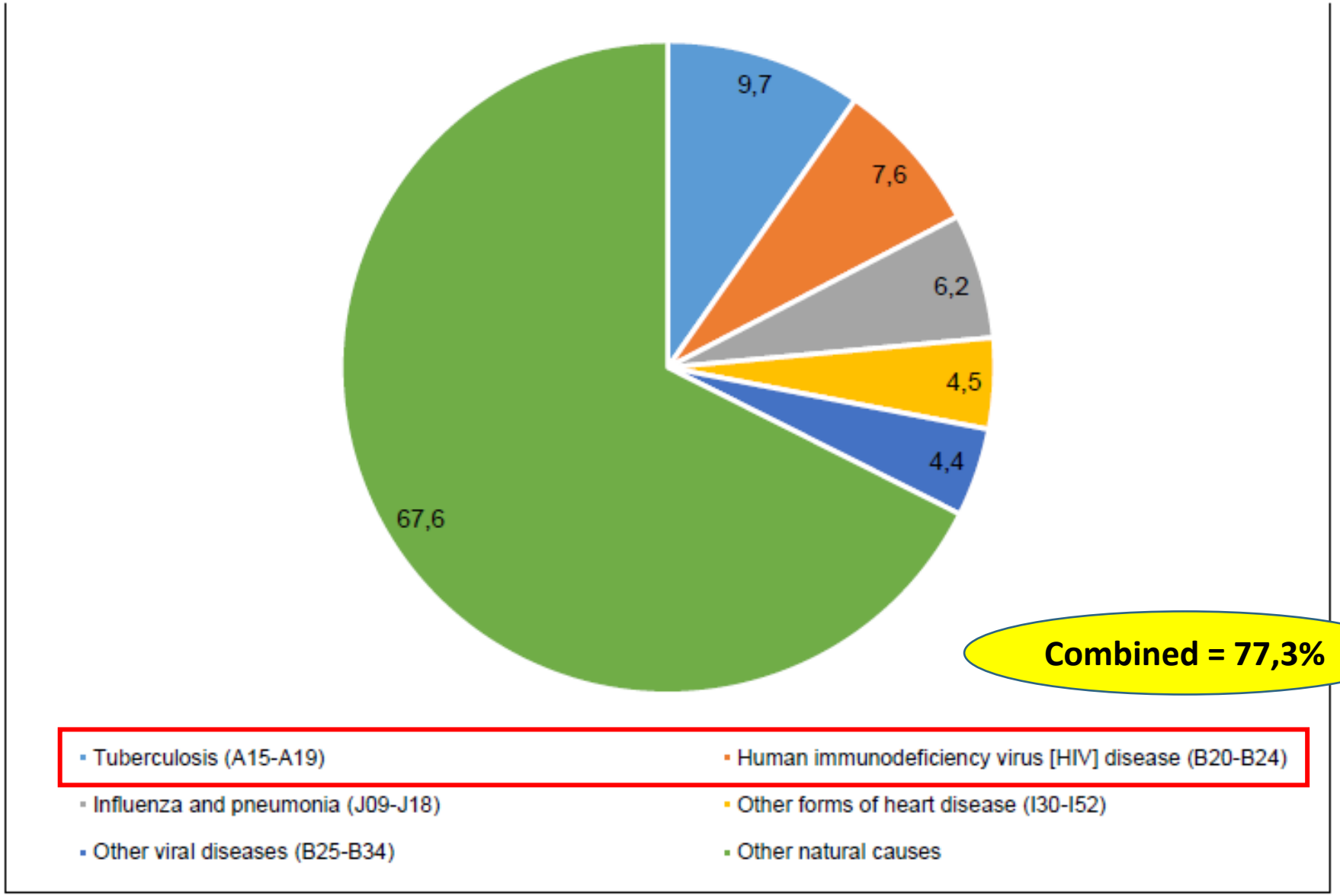
Figure 14.8: Number of deaths from HIV among adolescents by year



Source: Mortality and causes of death, 2008-2018

Source : Stats SA Adolescent report – 2022 p. 65

Figure 13.4: The five leading natural causes of death among adolescents (n = 5 820)



Source: Mortality and causes of death, 2018

Source : Stats SA Adolescent report – 2022 p. 56

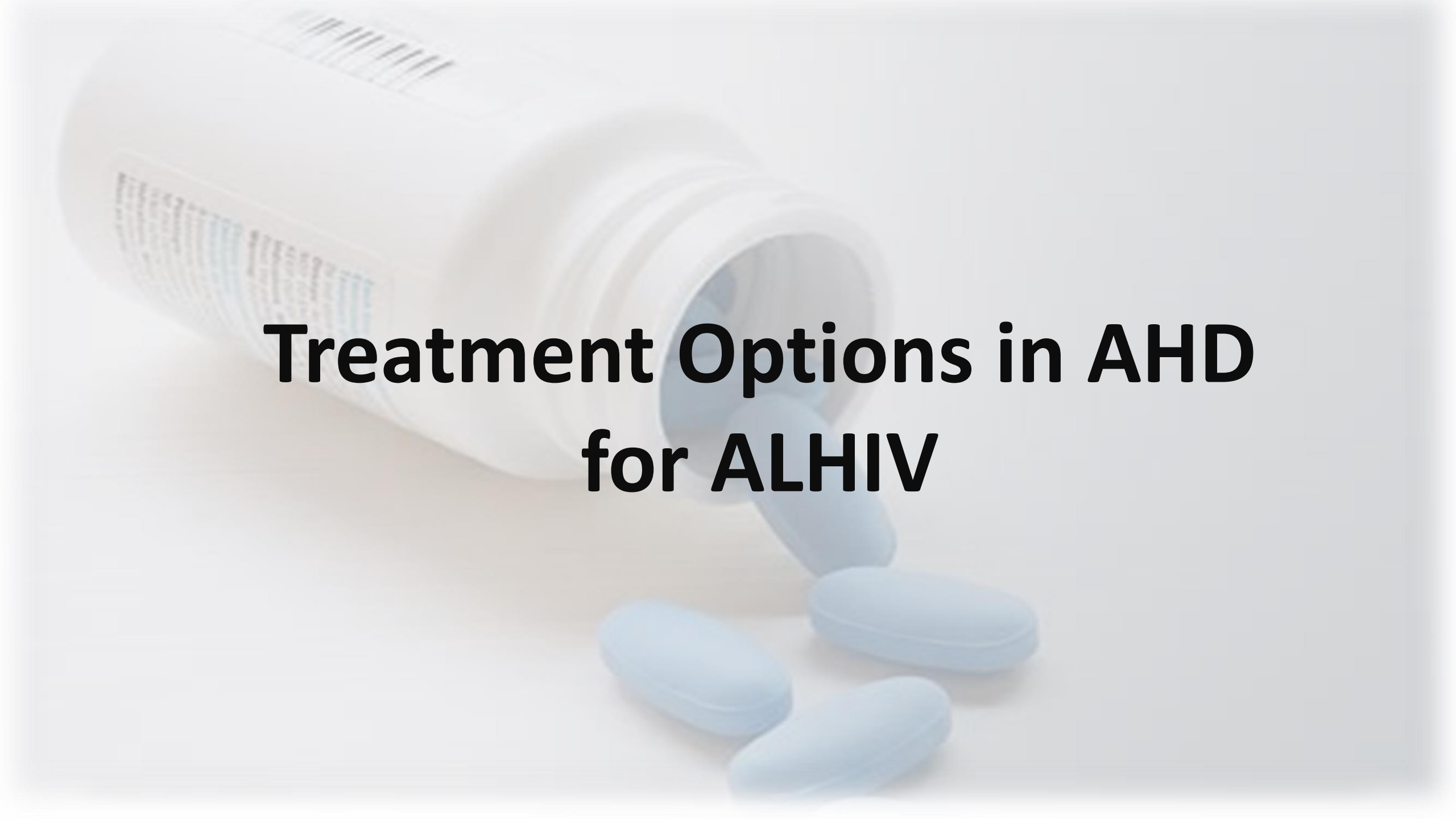
QUESTION 1

The largest number of ALHIV in South Africa live in which province?

a) **Gauteng**

b) **KwaZulu-Natal**

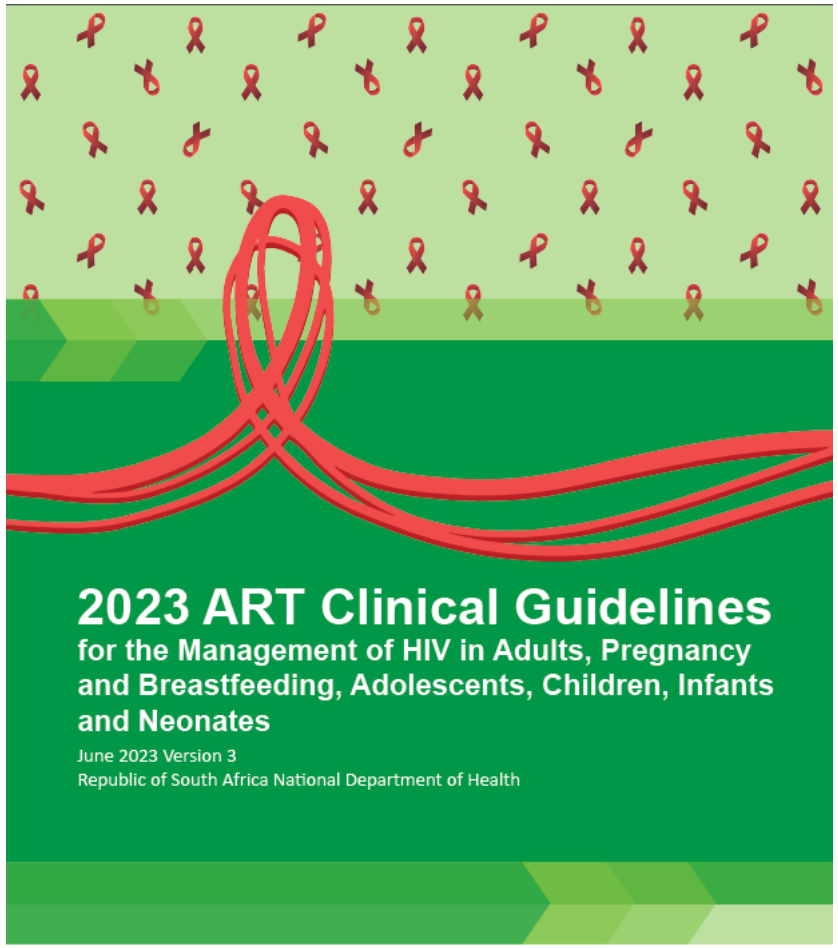
c) **Eastern Cape**



Treatment Options in AHD for ALHIV

Treatment Options in AHD for ALHIV

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**



health
Department:
Health
REPUBLIC OF SOUTH AFRICA

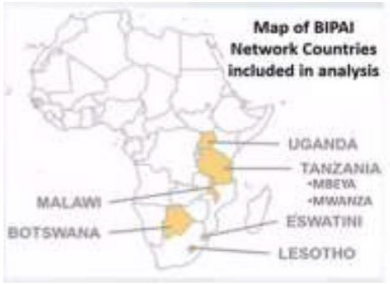
World Health Organization

2030 NDP

Shifting from PI-Based ART to DTG-ART Achieves and Maintains Viral Suppression

Bacha J et al. International Pediatric HIV Workshop, Montreal July 2022, Abs. 21; AIDS 2022 Ab)AB0203

- Retrospective review from 7 BIPAI sites in 6 countries on 1,475 children enrolled in care and optimized from **PI- to DTG**-based ART
  - Median age 14.0 year (range 3.6-19.9 years)
  - Time on PI (72% LPV/r, 28% ATV/r) ART prior to switch to DTG 9.8 years
  - Suppression (VL <1,000) on **PI ART 88.9%**



- FU on DTG 212 days (7-1017 days); **post-DTG VL suppression 89.8%,** with no difference by PI
- 118 youth were **unsuppressed on PI**; **68% suppressed after switch to DTG**
- VL suppression was lower for <u>both</u> PI and DTG ART in **females and adolescents 15-19 years**

→Switch from PI to DTG ART effective at maintaining and achieving viral suppression.

→Continued attention to support females and older adolescents needed.

Cohort	Added VLS among previously unsuppressed (n=118 with pre and post-DTG VL)		
	VLS on DTG	Total on DTG	VLS rate post DTG
All	80	118	67.8%

	Females	Males	p-value
VLS on PI-based ART	**86.4%** (451/522)	92.7% (548/591)	<0.001
VLS on DTG-based ART	**87.2%** (574/658)	90.4% (722/799)	0.05

	15-19yo	10-14yo	p-value
VLS on PI-based ART	**86.9%** (432/497)	91.4% (361/395)	0.03
VLS on DTG-based ART	**85.5%** (538/629)	90.1% (465/516)	0.02

	15-19yo	5-9yo	p-value
VLS on PI-based ART	**86.9%** (432/497)	94.0% (203/216)	<0.01
VLS on DTG-based ART	**85.5%** (538/629)	93.5% (257/275)	<0.01

Principles of ART in ALHIV: Aim for…

- Once daily dosing
- Fixed Dose combinations
- Reduction in no of tablets to a minimum (avoid suspensions!)
- No food restrictions
- Medication that can all be taken together
- Fitting their Rx into their lifestyle – ask about it!
- Twice daily does not = 12 hourly
- Continued supervision/support (watch them swallow it)
- Identifying a Treatment Buddy wherever possible

ART Amenable to Once Daily Dosing for ALHIV

Drugs amenable to once daily dosing:

- 3TC
- FTC
- ABC
- EFV
- RPV
- LPV/r (PI naïve patients (< 3 PI mutations))
- ATV/r
- DRV/r dosed 800mg + 100mg RTV (if no DRV mutations)
- TDF
- DTG

Don’t Forget Mental Health of ALHIV

Review of 8 studies in mental health disorders in C+ALHIV aged 8-21 years found:

- Attention Deficit Disorder - **28%**
- **6-fold** increased risk ratio

- Anxiety Disorder - **29%**

  3.8-fold increased risk ratio

- Depression **25%**

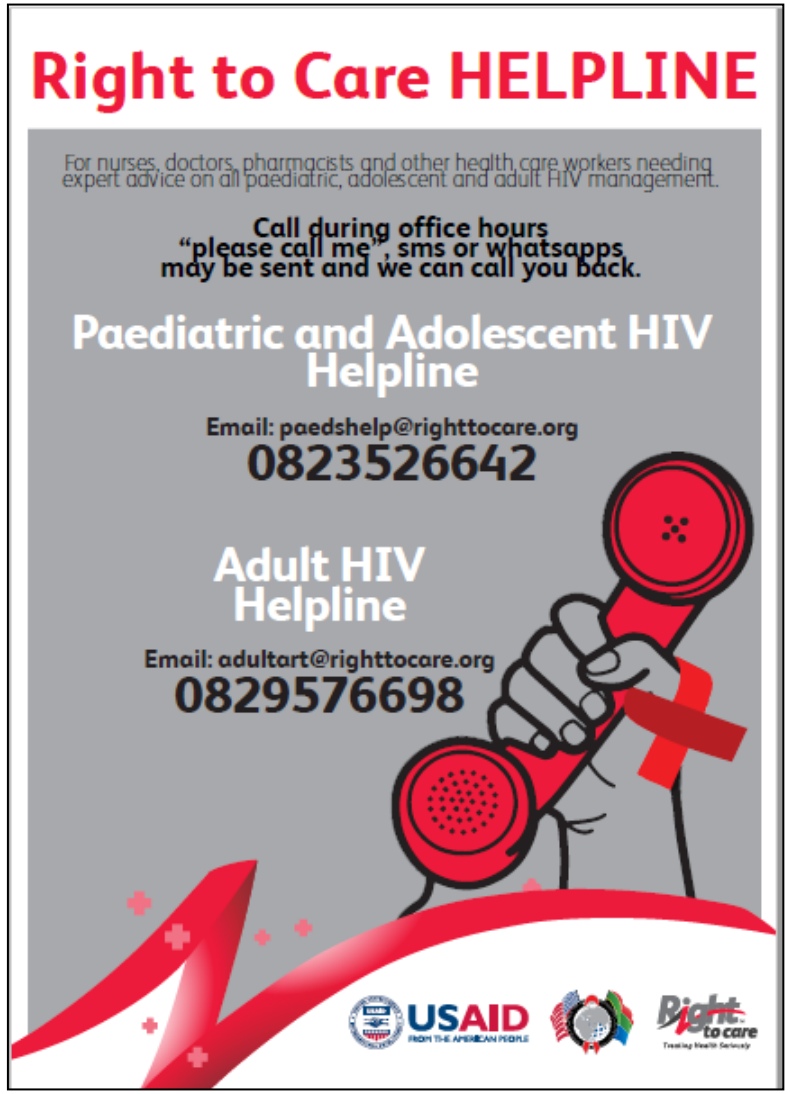
  7.1-fold increased risk ratio

AIDS Care 2006:18:441-5

Simplify ART Regimens Further

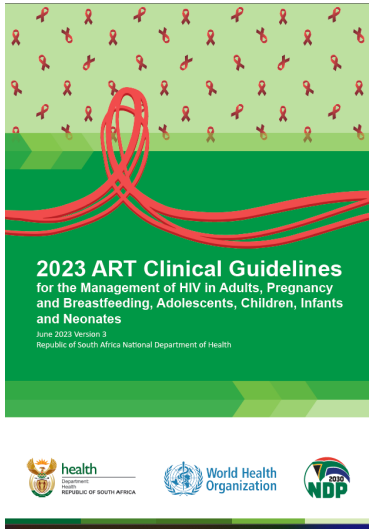
Drugs available in Fixed Dose Combinations in South Africa:

- ABC + 3TC
- AZT + 3TC
- TDF + FTC
- TDF + 3TC + DTG
- TDF + FTC + EFV
- Lopinavir/r
- Atazanavir/r
- TDF + FTC + RPV



Assessment of an Elevated Viral Load

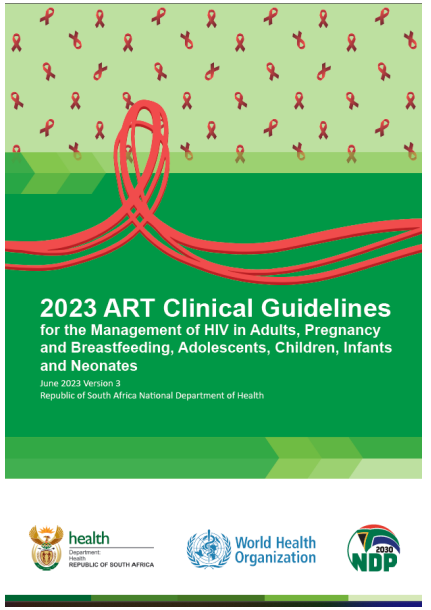
A thorough assessment is essential for any client with a viral load measuring ≥ 50 c/ml			
Adherence	A	Is adherence to medication poor? Ask about factors that may influence adherence e.g. Direct cost of clinic visits to patient, e.g. transport, loss of income, cost of paying another person to take on social responsibilities • Taking time away from existing work, finding work and/or social care responsibilities • Needing to travel for extended periods of time • Medication side-effects • Unpalatable medications • Depression or other mental health conditions • Alcohol or substance abuse • Poor social support and/or GBV • Non-disclosure Pregnant women may experience nausea/vomitting, heartburn, and constipation. Assess the need for symptomatic treatment with an anti-emetic, anti-diarrhea agent, or fiber supplement. Adherence difficulties in young children are often linked to poor tolerability of unpalatable formulations, particularly LPV/r solution. It is important to ask the caregiver about how the child tolerates the medication e.g., does the child refuse to swallow the medicine or spit, or vomit the medicine out?	**Tips** Ask open ended questions e.g. "What makes it difficult for you to collect or take your treatment?", and "How many doses have you missed this week?" Statements like "we all miss a dose now and then" can encourage a client to be more open. Create a safe and non-judgemental space for your client to discuss challenges.
Bugs	B	Check for symptoms and signs of infection. Do a TB and STI screen.	Remember that immune compromised, malnourished, and pregnant clients may not exhibit overt symptoms of TB. If in doubt, do a TB GXP.
Correct Dose	C	Is the client on the correct dose for their weight? This is especially applicable to growing children, or clients with deteriorating renal function or previous renal impairment	
Drug	D	Are there any potential drug interactions? Consider: • Other prescribed treatment e.g. rifampicin, anti-epilepsy drugs and pregnancy supplements (iron, calcium) • Over the counter treatment e.g., antacids, multivitamins • Other supplements and herbal/traditional medications e.g. St John's wort	See also *"Drug Interactions with DTG and Rifampicin-containing TB Treatment" on page 13* If in any doubt, call the **HIV Hotline 0800 212 506** or one of the *"Helplines" on page 23*
REsistance	E	Consider HIV drug resistance if other causes of virological failure have been excluded and the client is adherent to their medication by an objective measure.	Refer to the algorithm *"Management of Confirmed Virological Failure on TLD" on page 23*



NDoH Guidelines

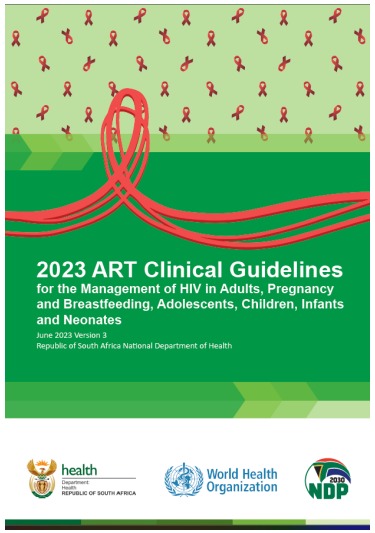
Non VL-Dependent Regimen Switches for ALHIV

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 Regimen Switches for ALHIV

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 21***	**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 consecutive 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 21***	**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 23***	



NDoH Guidelines

Management of Confirmed Virological Failure on TLD

Two or more consecutive VLs ≥ 1000 c/mL

On **TLD** for **at least 2 years**
and 2 elevated VLs were taken two or more years after starting TLD regimen

On TLD for **less than** 2 years, irrespective of VL

Adherence > 80%
Proven by an objective measurement [1]

Adherence < 80% [1]

Repeat VL at next scheduled routine VL (i.e., in 6 months' time)

Intensify efforts to **resolve adherence issues**[3] as outlined on *"Enhanced Adherence Support" on page 22*

TLD 2
Clients who have failed a previous ART regimen

TLD 1
Clients who have never failed a previous ART regimen

As a rule, resistance testing is **not indicated** for clients on **TLD1** [2]

Special circumstances[4]
e.g., incorrect classification as TLD1 (including perinatally infected adolescents), or drug interactions

Discuss with an HIV expert [5]
to authorise and interpret a resistance test*

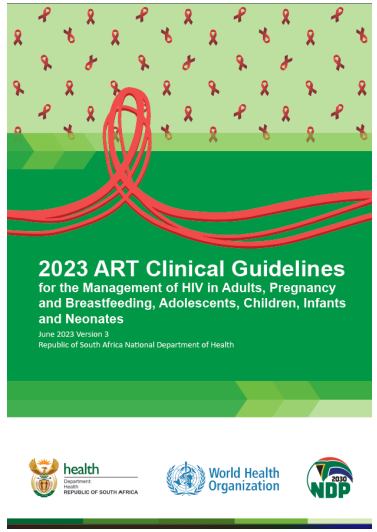
Individualised regimen
as recommended by HIV expert [5]

Repeat VL 3 months after starting the new regimen
to confirm viral re-suppression

Additional considerations if VL > 1000 c/mL:

- Monitor CD4 count every 6 months see *"Monitoring on ART" on page 19*
- If CD4 < 200 cells/mm3, discuss with an HIV expert
- Consider eligibility for cotrimoxazole prophylaxis see *"Indications for Starting and Stopping Cotrimoxazole Preventive Therapy" on page 8*

! ***Resistance testing** is expensive and should be done only for exceptional cases failing TLD1. Provinces should ensure that a gatekeeping function is in place by using either a designated provincial mechanism, the National TL committee, or one of the HIV *"Helplines" on page 23* to authorise resistance testing.



QUESTION 2

Which statement below is TRUE:

a) **Management of ART in adolescents is the same as in adults**

b) **Management of ART in adolescents is the same as adults for all >30kgs and >10 years**

c) **Management of ART in adolescents is dependent on their age only**

Advanced HIV Disease in Adolescents

What's Different for ALHIV?

- ALHIV are a complex population comprising of those with peri/postnatally acquired HIV (PaALHIV) aging up into adolescence as well as those who have recently acquired HIV during adolescence
- PaALHIV often have more advanced HIV disease with related co-morbidities and developmental challenges associated with delayed HIV treatment and lifelong HIV
- Many PaALHIV are highly ART experienced with increased experience and risk of treatment failure and resistance
- Regardless of the cause of HIV acquisition, all ALHIV are navigating their developmental transition from childhood to adulthood whilst dealing with a chronic and sexualy transmissible health condition
- ALHIV are at increased risk of lost to follow up and death

Lamb, M.R., Fayorsey, R., Nuwagaba-Biribonwoha, H., Viola, V., Mutabazi, V., Alwar, T., Casalini, C. and Elul, B., 2014. High attrition before and after ART initiation among youth (15–24 years of age) enrolled in HIV care. *AIDS (London, England)*, *28*(4), p.559.

Judd, A., Chappell, E., Doerholt, K., Galli, L., Giaquinto, C., Gibb, D., Goetghebuer, T., Le Coeur, S., Julian, A.N., Turkova, A. and Goodall, R., 2016. Long-term trends in mortality and AIDS-defining events among perinatally HIV-infected children across Europe and Thailand.

WHO Definition of AHD

- For **adults and adolescents, and children older than five years**, advanced HIV disease is defined **as CD4 cell count <200cells/mm^3 or a WHO stage 3 or 4 event at presentation for care**
  - *Includes both ART naïve individuals and those who interrupt treatment and return to care*
- **All children younger than five years old with HIV are considered as having advanced HIV disease**

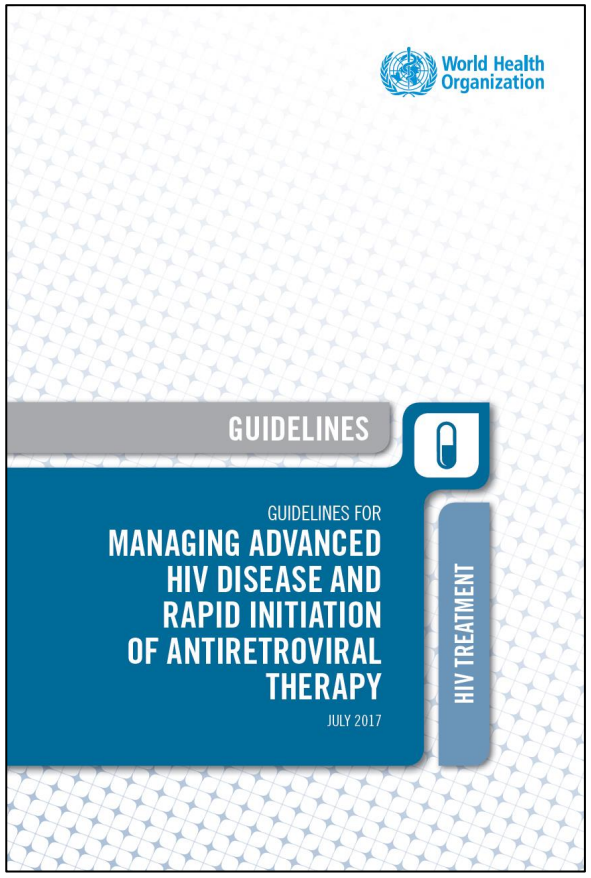
In spite of increasing access to treatment, the **number of people with advanced HIV at the time of diagnosis remains high** and is not declining very fast, especially among males

The **mortality rate** among people with advanced HIV disease is **very high even with access to ART. The risk of death is higher with low CD4 cell count, especially with CD4 cell count <100 cells/mm^3**

WHO AHD in Adolescents: Definitions Cont…

- A **seriously ill** adolescent is defined as having **any** of the following danger signs, including:

  - Respiratory rate **≥30** breaths per minute
  - Heart rate **≥120** beats per minute
  - Unable to walk unaided
  - Systolic BP **<90mmHg**
  - SaO2 **>90%**
  - Altered/reduced mental state/GCS
  - Moderate/severe dehydration

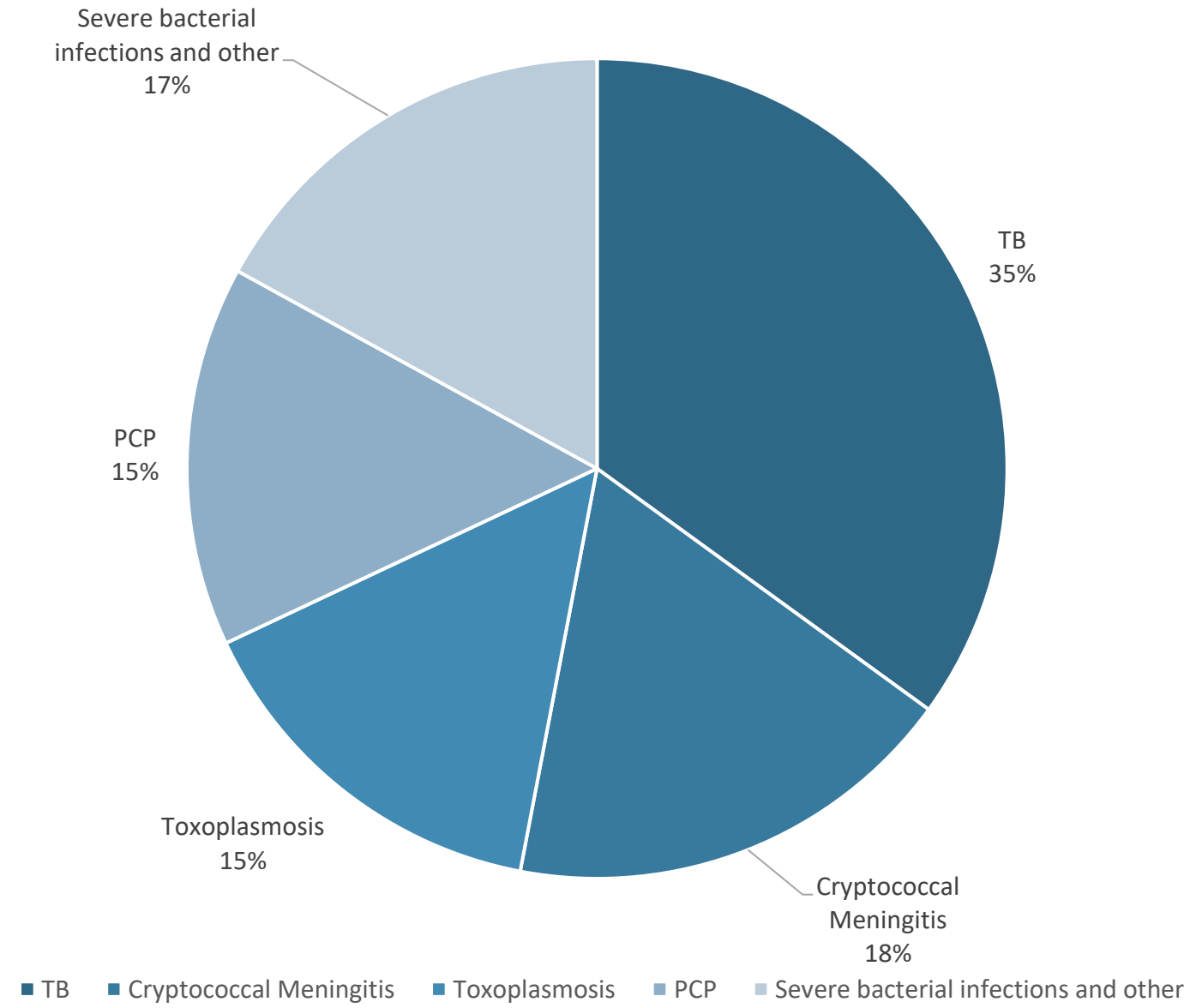


- A severely immune-compromised adolescent is defined as having a CD4 cell count **<50 cells/mm³**

Causes of Mortality in AHD

AHD-related mortality is driven by a small number of Opportunistic Infections, including TB and fungal infections like Cryptococcus

The majority of AHD-related deaths of hospitalised adults are caused by opportunistic infections, including TB, PCP (PJP), Cryptococcal Meningitis and Toxoplasmosis



Source: WHO AHD Guidelines, 2017.

WHO Clinical Staging for Adolescents and Adults

	Description
	Clinical Stage 1
1	Asymptomatic
2	Persistent generalized lymphadenopathy
	Clinical Stage 2
1	Moderate unexplained weight loss (<10% of presumed or measured body weight)
2	Minor mucocutaneous manifestations (seborrheic dermatitis, papular pruritic eruptions, fungal nail infections, recurrent oral ulcerations, angular cheilitis)
3	Herpes zoster
4	Recurrent upper respiratory tract infections (sinusitis, tonsillitis, bronchitis, otitis media, pharyngitis
	Clinical Stage 3
1	Unexplained severe weight loss (over 10% of presumed or measured body weight)
2	Unexplained chronic diarrhea for longer than one month
3	Unexplained persistent fever (intermittent or constant for longer than one month)
4	Persistent oral candidiasis
5	Oral hairy leukoplakia
6	Pulmonary tuberculosis
7	Severe bacterial infections (e.g., pneumonia, empyema, pyomyositis, bone or joint infection, meningitis, bacteraemia)
8	Acute necrotizing ulcerative stomatitis, gingivitis or periodontitis
9	Unexplained anemia (below 8g/dl), neutropenia (below 0.5 x 109/l) and /or chronic thrombocytopenia (below 50 x 109/l)

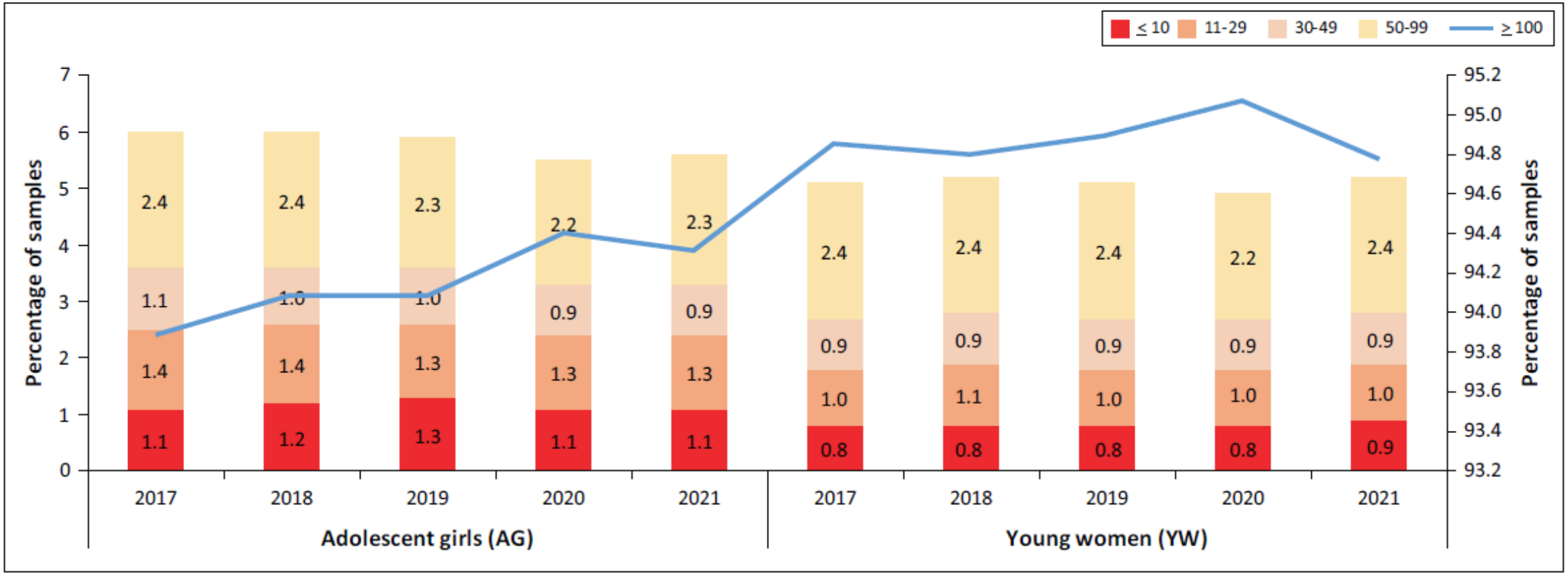
https://apps.who.int/iris/handle/10665/43699

WHO Clinical Staging for Adolescents and Adults Cont..

	Clinical Stage 4
	Conditions where a presumptive diagnosis can be made using clinical signs or simple investigations
1	HIV wasting syndrome
2	*Pneumocystis jiroveci* pneumonia (PCP)
3	Recurrent severe bacterial pneumonia (>2 episodes within 1 year)
4	Cryptococcal meningitis
5	Toxoplasmosis of the brain
6	Chronic oro-labial, genital or ano-rectal herpes simplex infection for > 1 month
7	Kaposi Sarcoma
8	HIV encephalopathy
9	Extra-pulmonary tuberculosis
	Conditions where confirmatory diagnosis testing is necessary:
1	Cryptosporidiosis, with diarrhea > 1 month
2	Isosporiasis
3	Cryptococcosis (extra-pulmonary)
4	Disseminated non-tuberculosis mycobacterial infection
5	Cytomegalovirus (CMV) retinitis or infection of the organs (other than liver, spleen, or lymph nodes)
6	Progressive multifocal leucoencephalopathy (PML)
7	Any disseminated mycosis (e.g., histoplasmosis, coccidioidomycosis)
8	Candidiasis of the oesophagus or airways
9	Non-typhoid salmonella (NTS) septicaemia
10	Lymphoma cerebral or B cell non-Hogdkins's Lymphoma
11	Invasive cervical cancer
12	Visceral leishmaniasis
13	Symptomatic HIV-associated nephropathy or HIV-associated cardiomyopathy

https://apps.who.int/iris/handle/10665/43699

Assessing very advanced HIV disease in adolescent girls and young women



AG, adolescent girls; YW, young women; NHLS, National Health Laboratory Service.

FIGURE 2: National analysis of the percentage of CD4 specimens with a count ≤ 10 cells/μL, 11 cells/μL – 29 cells/μL, 30 cells/μL – 49 cells/μL, 50 cells/μL – 99 cells/μL and ≥ 100 cells/μL by calendar year for AG and YW between 2017 and 2021. AG was defined as ages 15–19 years compared to 20–24 for YW. The ≥ 100 cells/μL category is reported on the secondary *y*-axis. Data are reported for public-sector testing by the NHLS, South Africa.

Southern African Journal of HIV Medicine
ISSN: (Online) 2078-6751, (Print) 1608-9693

Factors Associated with AHD in AGYW

A myriad of factors are associated with HIV vulnerability among AGYW

Recent systematic reviews cite:

Southern African Journal of HIV Medicine
ISSN: (Online) 2078-6751, (Print) 1608-9693

- A history of sexually transmitted infections
- Alcohol use
- Multiple partners
- Early marriage
- Being out of school
- Inconsistent condom use
- Engaging in transactional sex

- It has been reported by *Karim et al.* that AGYW have the least power in society and bear an enormous burden of both intimate partner violence (IPV) and HIV. A key intervention to reduce gender-based violence (GBV) is primary and secondary education of AGYW

Karim QA, Baxter C. The dual burden of gender-based violence and HIV in adolescent girls and young women in South Africa: Guest editorial. S Afr Med J. 2016;106(12):1151–1153. https://doi.org/10.7196/SAMJ.2016.v106i12.12126

Basic Package of Care for ALHIV with AHD

1. Cryptococcus antigen (CrAg screening) and Fluconazole pre-emptive therapy:
   CD4 ≤ 100

2. Gene Xpert and Urine Lam for TB diagnosis

3. TB preventive therapy: for ALL after Active TB is ruled out

4. CTX: CD4 ≤ 350 or WHO stage 3 or 4

5. Rapid ART initiation if no TB or /crypto meningitis (same day if possible)
   - ART should be deferred for 6 weeks if client is diagnosed with cryptococcal meningitis
   - ART should be started within 2 weeks of starting TB treatment

6. Enhanced counselling and adherence support

Monitoring of ALHIV with AHD

1. Monitor for the following after ART initiation:

- Clinical Response
- Development of IRIS
- Treatment interruption of ART, prophylaxis or other treatments prescribed (and OTC/traditional)
- Mental health
- Objective measures of adherence

Note:

- As the availability of HIV PrEP continues to expand across South Africa, it is important to remember to enquire as to any prior ART exposure (not just VTP)

Objective Measures of Adherence

1. Objective measures of good adherence include at least one of:
   - Pharmacy refills > 80% in the last 6-12 months (if this is known)
   - Attendance of > 80% of scheduled clinic visits in the last 6-12 months (if this is known)
   - Detection of current antiretroviral drug/s in the client's blood or urine, if available

   Note: Self-reported adherence is not considered a measure of good adherence!

Objective vs self-reported measures of adherence:

- It *may* be helpful to do pill counts with adolescents when they visit the facility – but they are not stupid! They may simply dispose of any missed medication prior to the pill count

- Establishing rapport and asking open-ended questions (without blame or judgement) may lead to more accurate reporting but this can also be hampered by their desire to please us!

Addressing Adherence Challenges with ALHIV

Address the **individual** client factors, including:

- Age (and developmental level) of the adolescent
- Check prescriptions – correct drugs and dosage (simplify wherever possible)
- Check understanding of dosage, timings etc.
- Check understanding of HIV and need for lifelong treatment
- Look at clinic file for clues to adherence problems
- Review if short/long treatment interruptions have been seen before
- Any documentation of adherence problems including toxicity/tolerability problems
- Check understanding and beliefs (including religious and traditional) around HIV and ART

Addressing Adherence Challenges with ALHIV Cont..

Assess for any **clinical** factors, including:

- Previous use of ARVs (pMTCT, PrEP, PEP)
- Risk of primary drug resistance (understanding current and previous partners' ART use)
- Concomitant medication – prescribed, over-the-counter, traditional, alternative and complementary
- Adverse effects especially those likely to affect adherence and absorption (e.g. diarrhoea, vomiting)
- Mental state/cognitive impairment
- Substance misuse (alcohol, recreational drugs etc.)

Addressing Adherence Challenges with ALHIV Cont..

Assess for any **social** factors, including:

- Household living arrangements
- Disclosure – any disclosure to household members, partner, friends
- Anyone else taking ART at home
- Stigma/discrimination (internal or external)
- Care responsibilities (including siblings, elderly/sick relatives)
- Education/employment – pattern of attendance, location to home, disclosure to teacher/employer?
- Food security
- Financial – source of individual or family income? grants?
- Transport/distance to clinic
- Clinic experience/staff attitudes
- SGBV/IPV

Assessing for Danger Signs in AHD

Patient identified as new stage 3 or 4 disease or with CD4 < 200 (ART naïve or experienced)

- **Screen for danger signs** (Respiratory rate >30, Heart rate >120, Systolic BP <90, Temperature >39°C, moderate/severe dehydration, Unable to walk unaided, Saturation <90%, altered mental state/GCS, other neurological problems)

ABSENT

- Complete clinical history and assessment for TB and other OIs
- Conduct appropriate labs: CD4, TB LAM, Serum CrAg

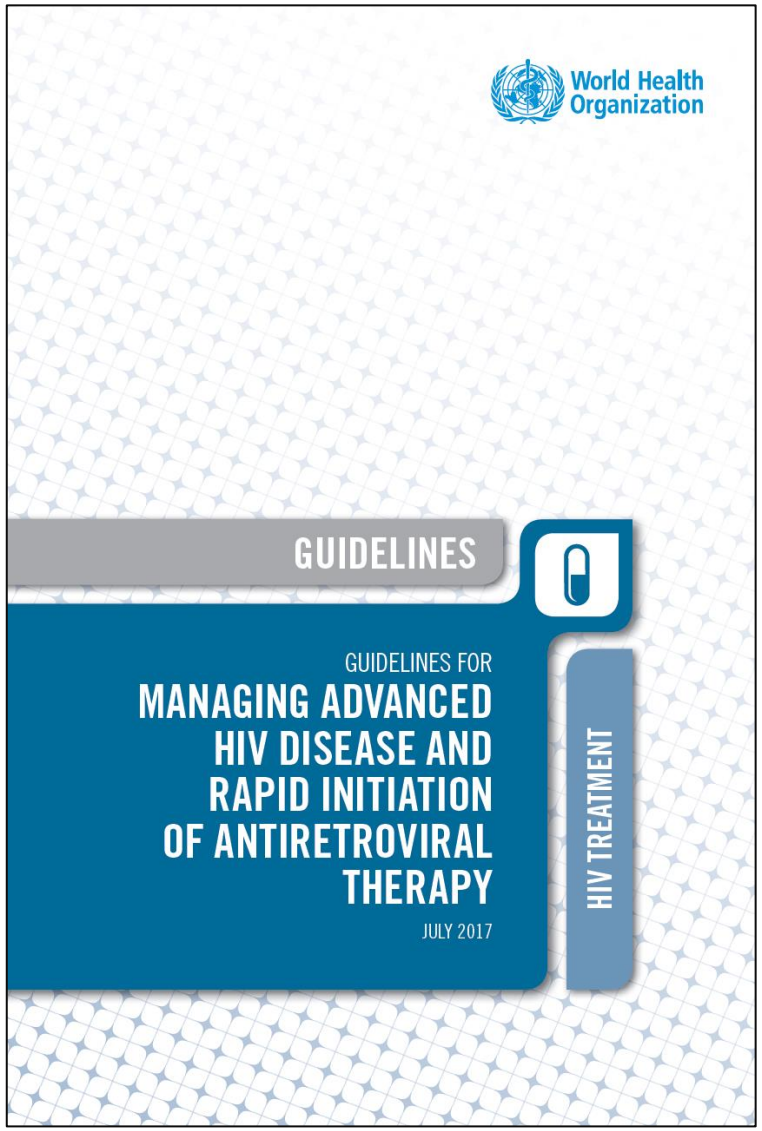
Further management is based on two key criteria:
Is the patient ART-naïve or Treatment experienced client returning to care

PRESENT

- **CRITICALLY UNWELL patient**
- Provide **urgent labs**, supportive management (e.g. oxygen, IV fluids)
- Start **urgent treatment**: (e.g. antibiotics, TB treatment, etc.).
- **Refer to Hospital**

https://differentiatedservicedelivery.org/Resources/Resource-Library/Global-Advanced-HIV-DiseaseToolkit

AHD in Adolescents: Rapid Initiation of ART



Rapid initiation of antiretroviral therapy

Rapid ART initiation[a] should be offered to all people living with HIV following a confirmed HIV diagnosis and clinical assessment.

(Strong recommendation: high-quality evidence for adults and adolescents; low-quality evidence for children)

[a]Rapid initiation is defined as within seven days from the day of HIV diagnosis; people with advanced HIV disease should be given priority for assessment and initiation.

ART initiation should be offered on the same day to people who are ready to start.

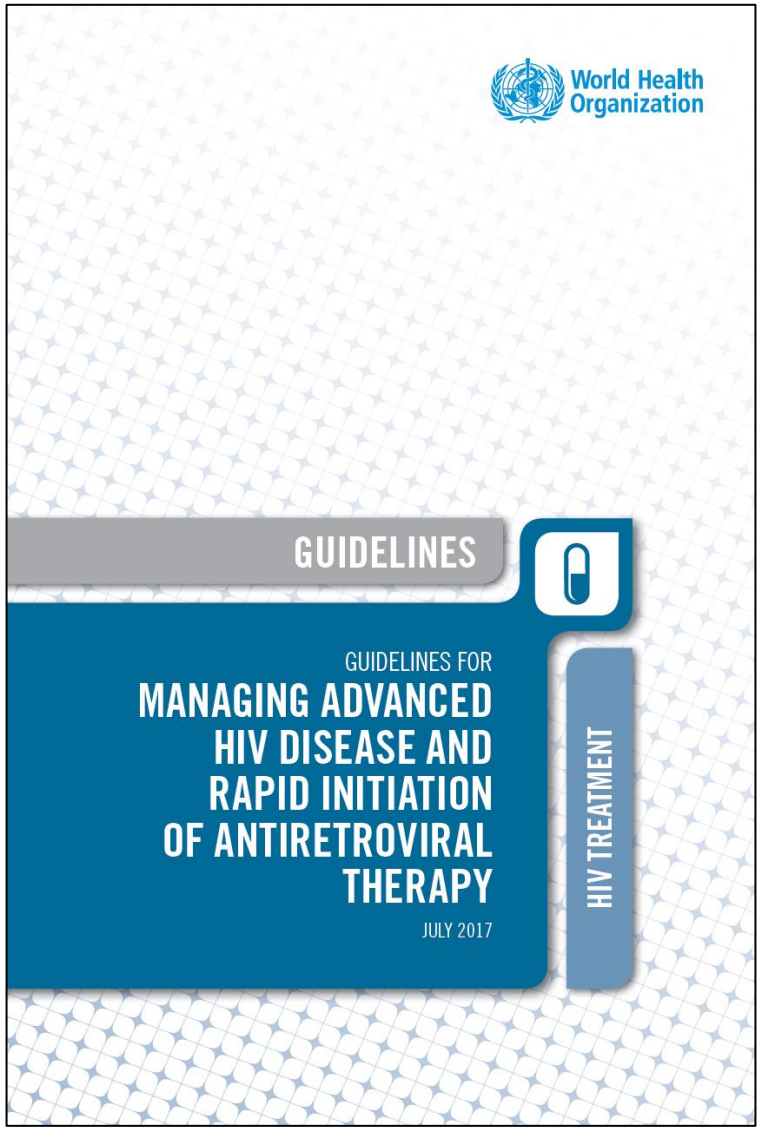
(Strong recommendation: high-quality evidence for adults and adolescents; low-quality evidence for children)

Good practice statement

ART initiation should follow the overarching principles of providing people-centred care. People-centred care should be focused and organized around the health needs, preferences and expectations of people and communities, upholding individual dignity and respect, especially for vulnerable populations, and should promote engaging and supporting people and families to play an active role in their own care by informed decision-making.

The introduction of the "treat all" recommendation (ART for all people living with HIV regardless of CD4 cell count) supports the rapid initiation of ART, including the offer of same-day initiation where there is no clinical contraindication. People with no contraindication to rapid ART initiation should be fully informed of the benefits of ART and offered rapid ART initiation, including the option of same-day initiation. Rapid ART start is especially important for people with very low CD4 cell count, for whom the risk of death is high. People should not be coerced to start immediately and should be supported in making an informed choice regarding when to start ART.

AHD in Adolescents: Common Conditions



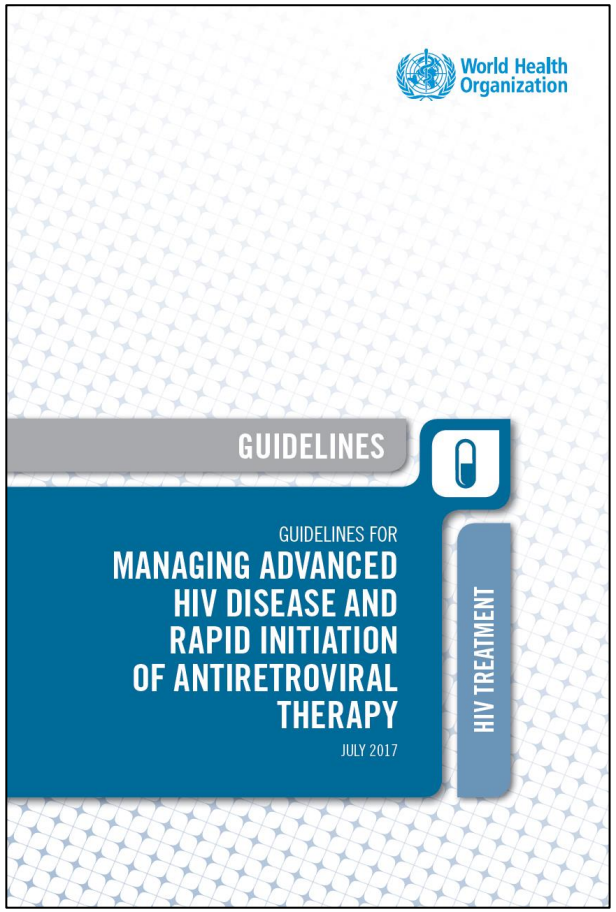
Tuberculosis (TB)

TB is the leading cause of morbidity and mortality among people living with HIV, accounting for **one third** of the estimated 1.1 million people dying from AHD globally in 2015, with most of these TB-associated deaths (200 000 cases) occurring among men

TB also remains a leading cause of HIV-associated hospitalisation among adults and children living with HIV worldwide

The 2016 WHO consolidated ARV guidelines summarise the WHO recommendations for the prevention, diagnosis and treatment of TB among people living with HIV

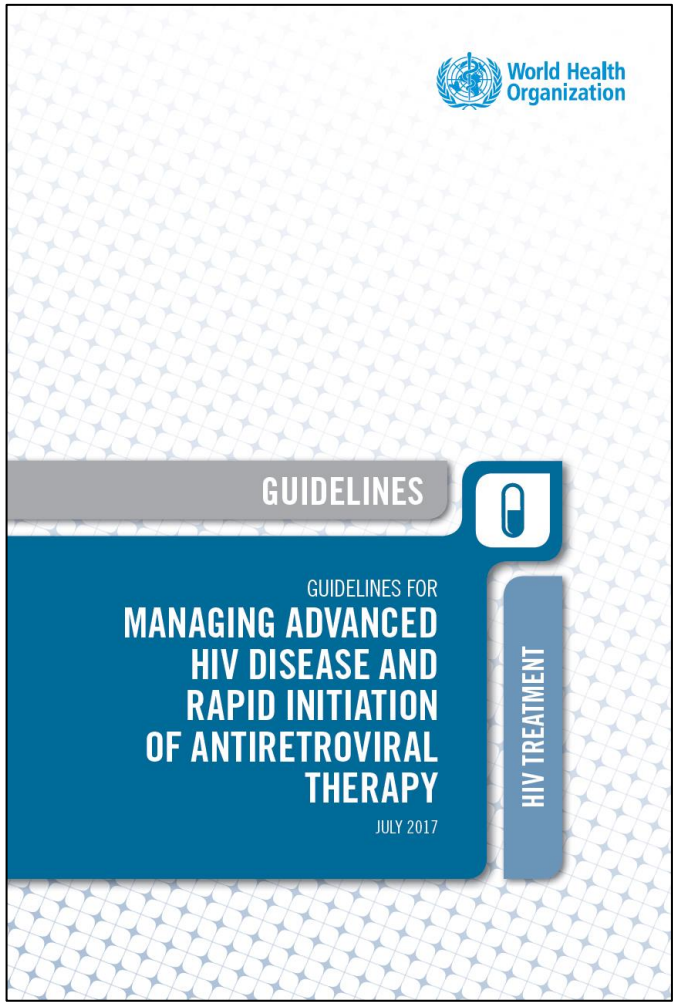
AHD in Adolescents: Common Conditions Cont..



Cryptococcal meningitis

- The incidence of cryptococcal meningitis remains substantial despite scale-up of ART
- A recent review estimated that there were 223,100 incident cryptococcal meningitis cases globally in 2014, with **73%** of the cases occurring in sub-Saharan Africa
- Cryptococcal meningitis is a leading cause of mortality among hospitalised adults living with HIV
- Pre-emptive therapy for cryptococcal antigen–positive asymptomatic adolescents is a key strategy to prevent cryptococcal meningitis

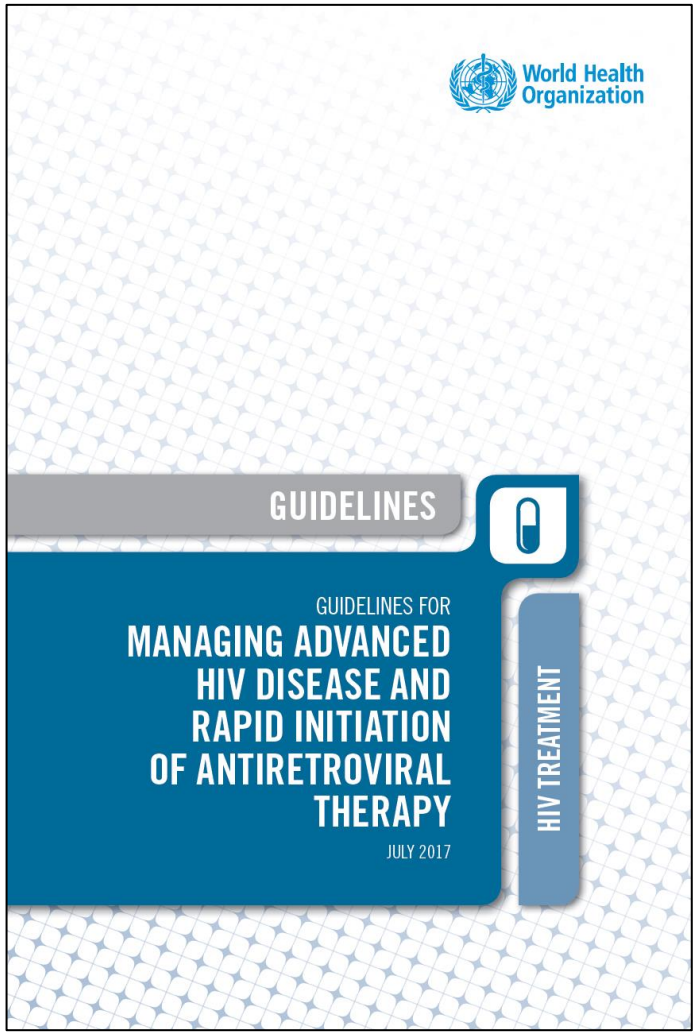
AHD in Adolescents: Common Conditions Cont..



Toxoplasmosis

- Cerebral toxoplasmosis is the most frequent cause of expansive brain lesions among adults living with HIV **not receiving co-trimoxazole**
- Toxoplasmosis is a common protozoan infection among PLWHIV, with the prevalence of concomitant HIV and Toxoplasmosis especially high in sub-Saharan Africa (**45%**)
- People with latent toxoplasmosis are at risk of developing cerebral toxoplasmosis when their CD4 count falls below 200 cells/mm^3
- About **15%** of the those dying from AHD do so from cerebral toxoplasmosis

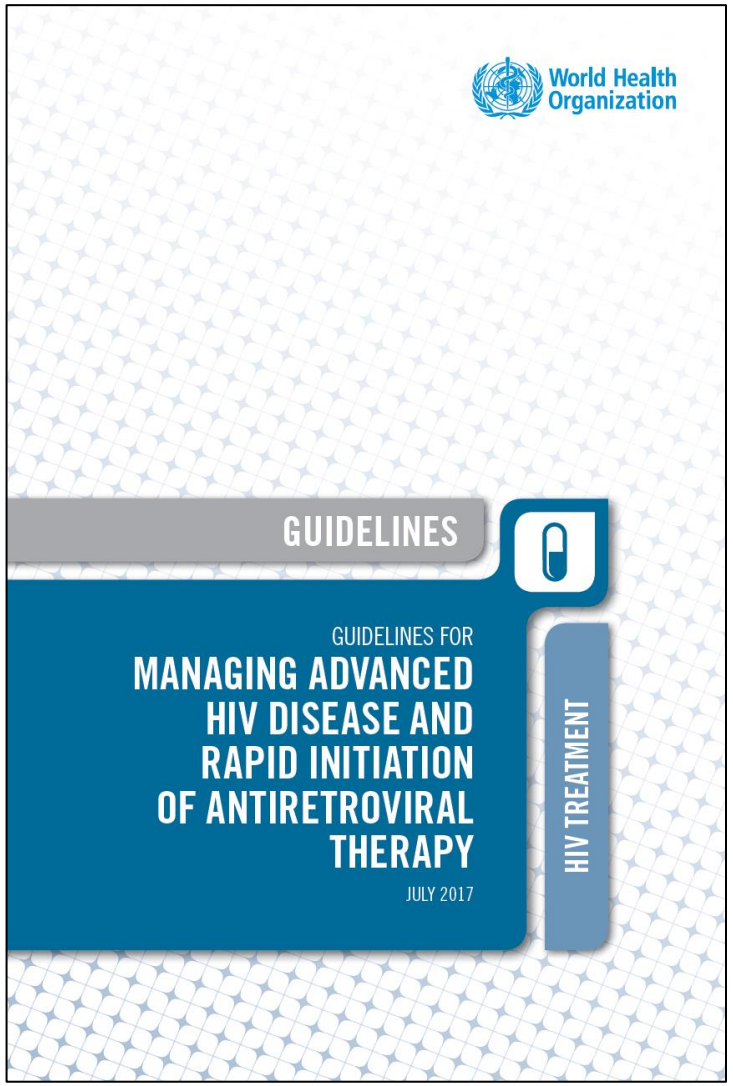
AHD in Adolescents: Common Conditions Cont..



Pneumocystis jirovecii pneumonia (PJP)

- PJP is a leading cause of mortality among hospitalised adults (**13%**) and children (**29%**) living with HIV
- However, the global burden of morbidity and mortality attributable to Pneumocystis jirovecii pneumonia is poorly characterised because appropriate diagnostic facilities are lacking in most settings
- This highlights the need for more accurate and feasible diagnostic approaches and improved access to co-trimoxazole and ART

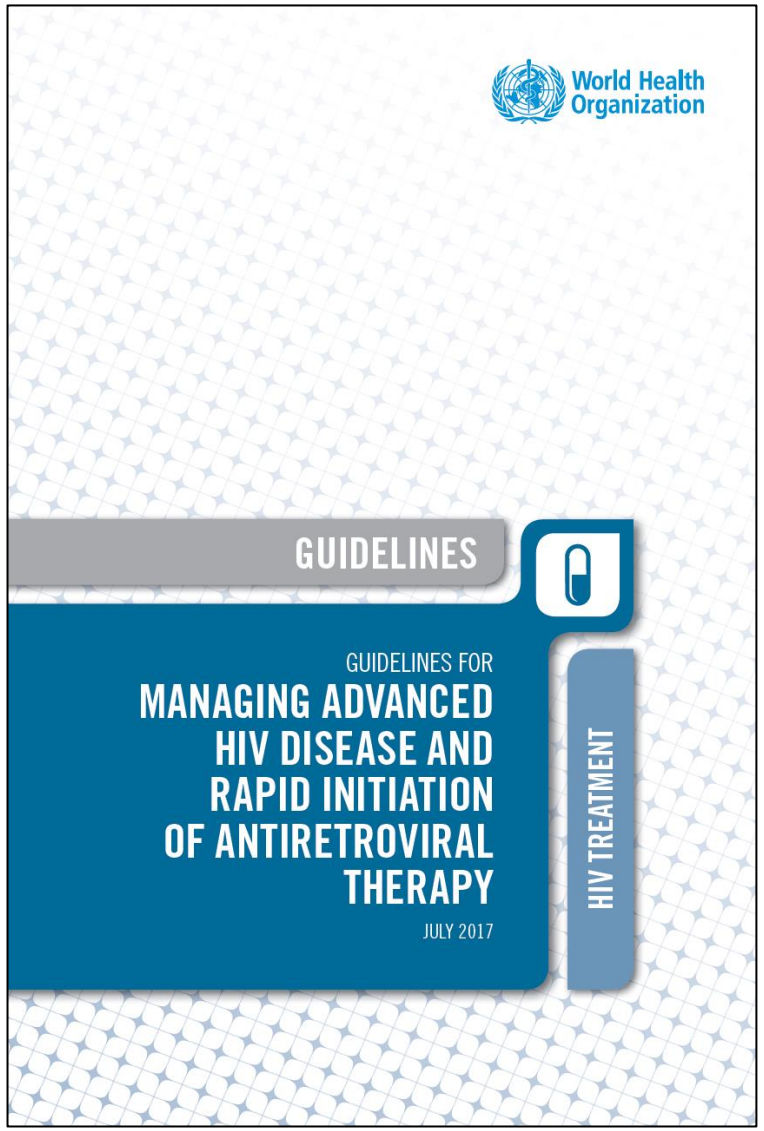
AHD in Adolescents: Common Conditions Cont..



Cytomegalovirus (CMV)

- Cytomegalovirus infection is a systemic viral infection that usually manifests as cytomegalovirus retinitis among severely immunocompromised people
- The reported prevalence of CMV retinitis is highest in Asia and appears to be low in Africa (but is more commonly seen in children with AHD in our context)
- Since cytomegalovirus is a systemic infection, improving access to early diagnosis and affordable, oral systemic treatment with valganciclovir is a priority

AHD in Adolescents: Common Conditions Cont..



Severe bacterial infections

- Adolescents with AHD frequently have severe bacterial infections, including bloodstream, respiratory, central nervous system and gastrointestinal infections
- Severe bacterial infections are estimated to cause more than **one third** of the hospitalisations among PLHIV worldwide
- Co-trimoxazole prophylaxis provides protection against some but not all severe bacterial infections
- Increasing resistance to antimicrobial drugs can complicate the treatment of adolescents with severe bacterial infections

QUESTION 3

Advanced HIV disease in adolescents is defined as:

a) **WHO stage 2 or 3 and a CD4 cell count <200cp/mm^3**

b) **WHO stage 3 or 4 and a CD4 cell count <350cp/mm^3**

c) **WHO stage 3 or 4 and a CD4 cell count <200cp/mm^3**

Models of Adolescent Care in AHD Management

What do ALHIV Need?

Business Unusual! Consider modifying (differentiating) services to include:

- Adolescent friendly staff
- Flexible after school hours clinics (or weekends!)
- Early (but timely) HIV disclosure
- Mental health, drug and alcohol support
- Peer support (one-to-one, group and mHealth options)
- Support for ALHIV in transitioning to adult services

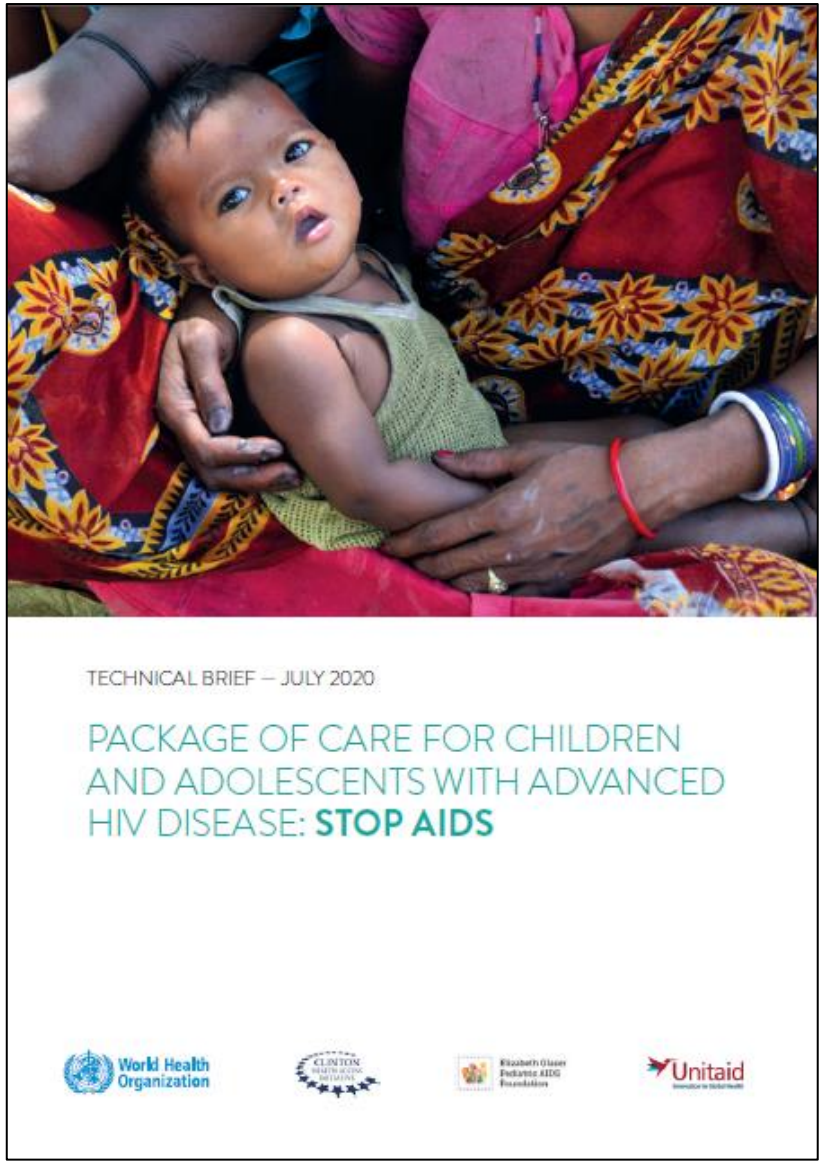
- Support for HCPs for adolescents growing up and remaining at PHC (it is the HCP who has to transition their way of working with ALHIV)

What do ALHIV Need Cont…?

Also consider:

- Decentralising health services (mobile clinics/community-based delivery)
- Integrated service delivery (e.g ART, contraceptives, STI screening, nutritional assessment)
- Simplified, low SE ART regimens and prophylaxis
- CCMDD once stable and adherence is good
- Community navigators
- Economic or nutritional support

Models of AHD Management in ALHIV



This publication builds on the 2017 guidelines cited earlier and highlights existing WHO recommendations and implementation considerations that are relevant to the care of children and adolescents with advanced HIV disease

The '*STOP*' approach is a straightforward guide to approaching AHD management in adolescents

AHD in Adolescents: STOP Approach

The 2017 WHO guidelines focus on providing an enhanced package of prophylactic, diagnostic and therapeutic interventions for adolescents with AHD

The main interventions to reduce morbidity and mortality are summarised as **S**creen, **T**reat, **O**ptimise and **P**revent

In addition, routine interventions – including immunisation, deworming, growth monitoring, iron and vitamin A supplementation should all be provided

AHD in Adolescents: STOP Approach Cont…

Box 1. Screen, Treat, Optimize and Prevent AIDS

Screen[a]

TB

- Screen for TB using a clinical algorithm[b] followed by X-ray when indicated and if available
- Use the following diagnostic tests to confirm TB as applicable:[c]
  - Rapid molecular diagnostic (Xpert® MTB/RIF or Ultra) on (induced) sputum, stool, gastric aspirate or nasopharyngeal aspirate or other extrapulmonary samples if relevant
  - Lateral flow urine lipoarabinomannan (LF-LAM) assay[d]

Cryptococcal infection among adolescents

- Serum or plasma or blood cryptococcal antigen screening followed by lumbar puncture if positive or symptomatic

Malnutrition

- Weight-for-height
- Height-for-age
- Mid-upper arm circumference among children 2–5 years old

AHD in Adolescents: STOP Approach Cont…

Treat

TB, severe pneumonia, severe bacterial infections, cryptococcal meningitis and **severe acute malnutrition** according to WHO guidelines

Optimize

Rapid antiretroviral therapy start – within seven days with optimal regimens[e]

Antiretroviral therapy counselling

[a] Screening refers to screening and diagnostics throughout this publication.
[b] See Fig. 3 in *Guidance for national tuberculosis programmes on the management of tuberculosis in children (9).*
[c] A negative test result does not exclude TB in children living with HIV in whom there is a strong clinical suspicion of TB.
[d] See Table 2 and the text for recommendations.
[e] Unless TB or cryptococcal disease is diagnosed *(10).*

AHD in Adolescents: STOP Approach Cont…

Prevent

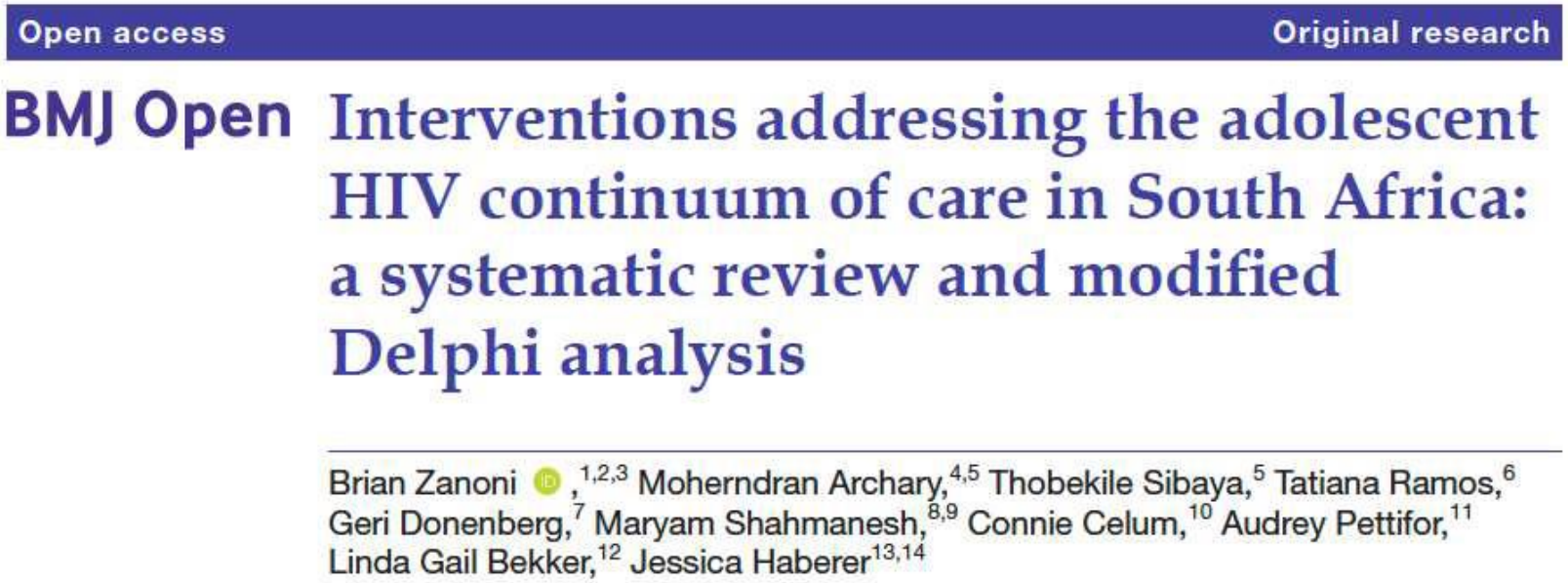
Bacterial infections and *Pneumocystis* pneumonia
- Co-trimoxazole prophylaxis

TB
- TB preventive treatment

Cryptococcal meningitis among adolescents
- Fluconazole pre-emptive therapy

Vaccinations
- Pneumococcal vaccine
- Human papillomavirus
- Measles
- BCG

What Works for ALHIV in South Africa?



Open access Original research

BMJ Open

Interventions addressing the adolescent HIV continuum of care in South Africa: a systematic review and modified Delphi analysis

Brian Zanoni ,[1,2,3] Moherndran Archary,[4,5] Thobekile Sibaya,[5] Tatiana Ramos,[6] Geri Donenberg,[7] Maryam Shahmanesh,[8,9] Connie Celum,[10] Audrey Pettifor,[11] Linda Gail Bekker,[12] Jessica Haberer[13,14]

- **Adherence** to ART among adolescents improved with the provision of food support, attendance in HIV support groups and parental supervision

- Two interventions improved **retention in care**: one focused on adolescent friendly services by providing an after-school hours clinic with peer support, counselling and meals and the other by providing in-home support for HIV education, psychosocial support and assistance with applications to government grants

Zanoni, B., Archary, M., Sibaya, T., Ramos, T., Donenberg, G., Shahmanesh, M., Celum, C., Pettifor, A., Bekker, L.G. and Haberer, J., 2022. Interventions addressing the adolescent HIV continuum of care in South Africa: a systematic review and modified Delphi analysis. *BMJ open*, *12*(4), p.e057797.

Retention in Care for ALHIV

Authors Title	Publication and Date	Number of Subjects	Study Type	Intervention Description	Overall Results	Median Overall Score Round 1
Retention in Care						
Zanoni, et al. **Higher Retention and Viral Suppression with Adolescent-Focused HIV Clinic in South Africa**	PLoS One 2017	254 HIV+ Adolescents	Retrospective Cohort Analysis	**Weekend adolescent-focused clinic** with peer support, group activities, counseling, and meals compared to standard of care.	Retention: 95% in adolescent-friendly clinic vs. 85% in standard clinic (OR 3.5; 95% CI 1.2 – 11.1; p=0.018). Viral Suppression: 91% adolescent-friendly clinic vs. 80% in standard clinic. (OR 2.5; 95% CI 1.1 – 5.8; p=0.028	88
Fatti, et al. **The Effectiveness and Cost-Effectiveness of Community-Based Support for Adolescents Receiving Antiretroviral Treatment: An Operational Research Study in South Africa**	Journal of the International AIDS Society 2018	6706 Adolescents	Retrospective Cohort Study	**Community based support (CBS)** included home-based ART-related education, psychosocial support, symptom screening for opportunistic infections and support to access government grants. CBS was compared to standard of care.	Cumulative LTFU was 40% lower amongst participants receiving CBS (29.9%) compared to participants without CBS (38.9%), aHR = 0.60 (95% CI: 0.51 to 0.71); p < 0.0001). Viral failure: at 3 years – no difference; at five years 18.8% CBS participants versus 37.2% non-CBS participants had viral failure, adjusted odds ratio = 0.24 (95% CI: 0.06 to 1.03).	80

Service Models: Adolescent Clubs

- These clubs are a specific adaptation of the chronic club model designed to support adolescents

- The eligibility criteria should be flexible to support adolescents, including those with detectable viral loads (ideally in separate clubs)

- Clubs providing ART refills should have a clinician to support this service

- Clubs should be divided by age and development level, and the size of the club should be adjusted based on the capacity of the facility

Goal

- To achieve and maintain virally suppressed ALHIV

Service Models: Adolescent Clubs Cont..

Objectives include:

- To enable adolescents to access support, learning and clinical care with their peers
- To empower adolescents to take responsibility for their lives – including their health
- To support ALHIV to understand the importance of treatment adherence
- To enable adolescents to live with HIV as an important but not dominant or limiting element
- To foster self-confidence and awareness to facilitate onward disclosure and reduce stigma

Service Models: Adolescent Transitioning Clubs

Adolescents currently receiving care in a paediatric facility will also require support that is tailored to address the challenges of transitioning to adult services

Key components of support for ALHIV include:

- Providing adolescent-friendly services (ideally supported by adult clinicians)
- Recognising that transition isn't necessarily easy and identifying any risks
- Identifying any developmental or cognitive challenges
- Fostering peer support and providing psychosocial support to enable the adolescent to cope with the normal feelings and concerns about transition
- Supporting self-management of medication, appointments and referrals
- Supporting disclosure to enable sharing of their HIV status to other healthcare workers, peers and family, thereby increasing their support systems
- Addressing the reality that transition is inevitable

Adolescent Transitioning Clubs: Assessing Transition Readiness

Checklist for successful transitioning of adolescents into adult care services

- Acceptance of a chronic medical condition and orientation towards future goals and hopes, including long-term survival and health
- Establishment of a good working relationship with healthcare providers at the paediatric/adolescent site
- Has learned the skills needed to negotiate appointments and multiple providers in an adult practice setting
- Has achieved personal and medical independence and is able to assume responsibility for his/her treatment and participate in decision-making

Adolescent Transitioning Clubs: Checklist Cont..

- Can identify symptoms and describe them
- Arrives to appointments on time
- Requests prescription refills correctly and allow enough time for refills to be processed before medications run out (not missing visits)
- Is receiving psychosocial support (peer, family, facility) and entitlements are in place (home care/ housing, transportation)
- Knowledgeable about SRHR and family planning including condom use skills

QUESTION 4

Which model(s) of care for adolescents work for ALHIV

a) **Adolescent Club Model**

b) **Adolescent Transition Model**

c) **Adolescent & Youth Friendly Services (AYFS) Model**

d) **mHealth Model**

e) **All of the above**

Conclusions

- Across the continuum of care, ALHIV are faring worse than either their adult or paediatric counterparts
- Morbidity and mortality in ALHIV remains unacceptably high
- The clinical management of AHD in ALHIV is the same as for adults so nothing new or uncommon
- However AHD management for ALHIV needs to take into account their specific needs and challenges
- We need to strengthen our collaborations with other stakeholders (including CHWs, schools, DSD, SASSA etc) to meet their diverse and often complex needs

Acknowledgments

Prof Mo Archary (UKZN)

Dr Mary Mahy (UNAIDS)

NDoH Knowledge Hub

Dr Leon Levin (RtC)

Prof Lynne Mofenson (EGPAF)

Prof Brian Zanoni (Emory)

Dr Dean Solomon (Kheth'Impilo)

Prof Linda-Gail Bekker (DTHF)

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