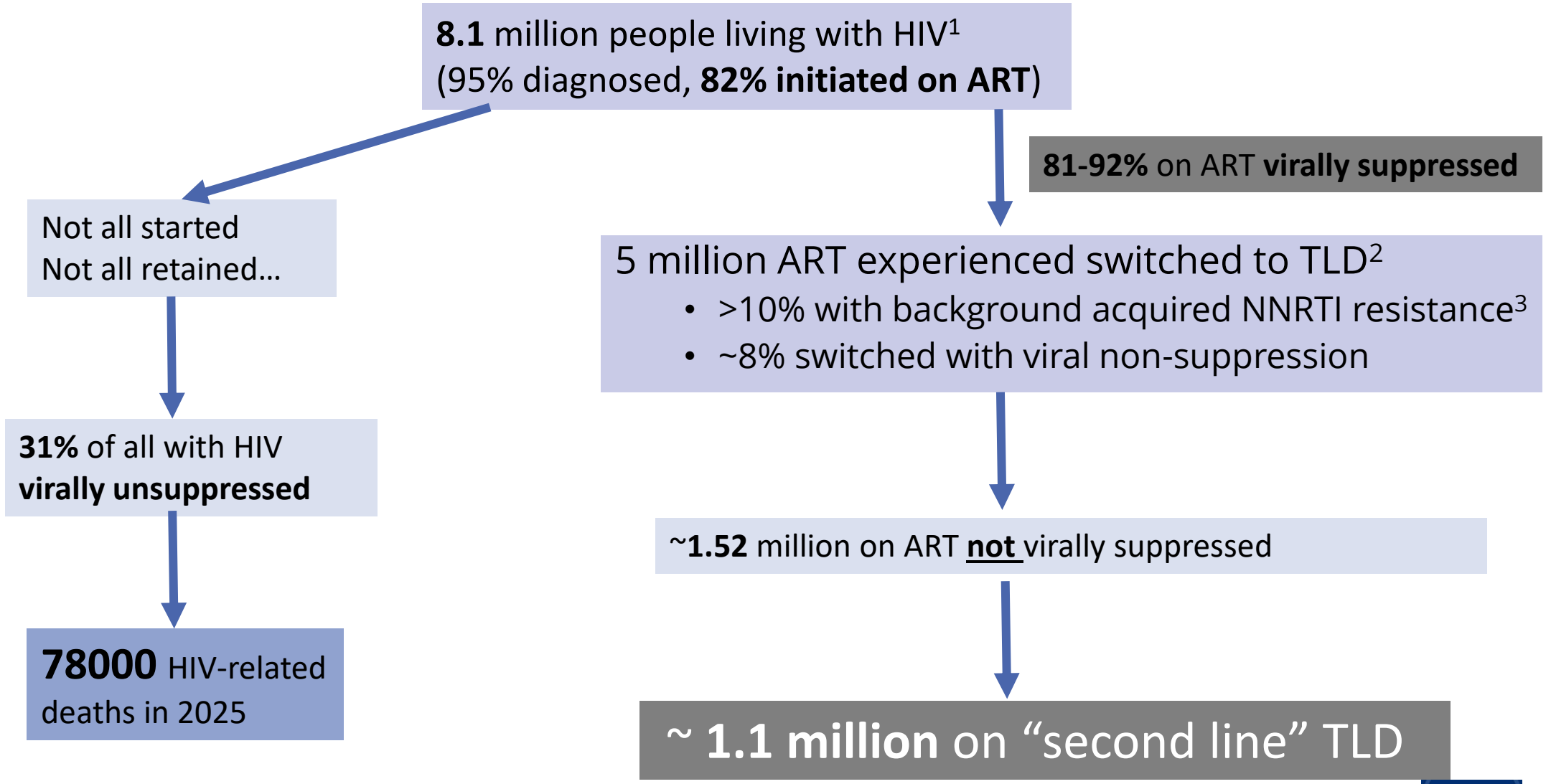
A Person-Centred Approach to Persistent HIV Viraemia & Drug Resistance

Bridging the gap between biological failure and the human experience

Dr Natasha Davies
Infectious Diseases Unit, CMJAH
24 April 2026

South Africa: HIV Programme Overview



[1]Thembisa model 4.8, March 2025

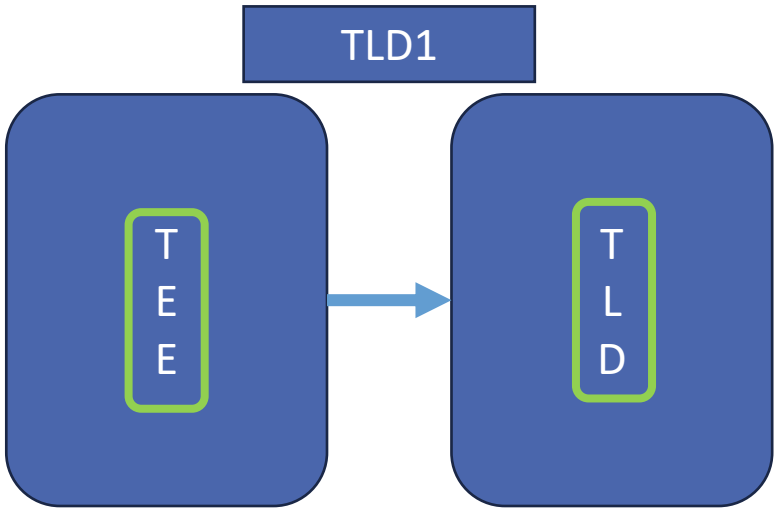
[2]NICD, 2023

[3]Chimukangara et al, 2019

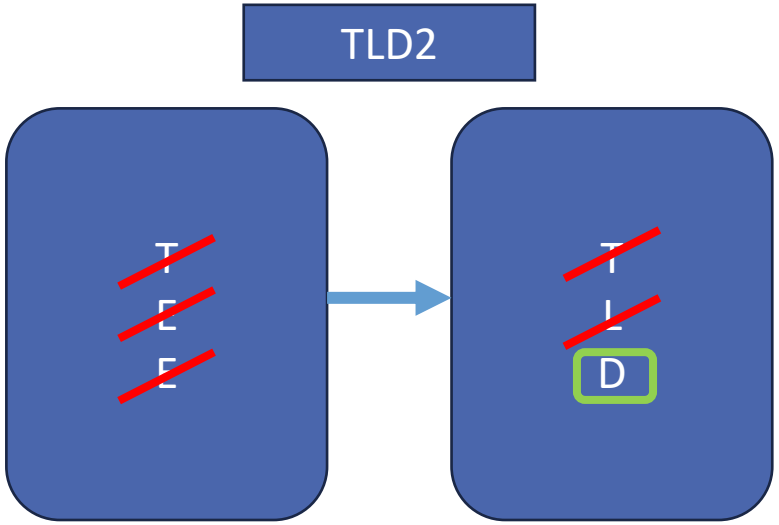
TLD2 and why it matters

TLD 1 (or ALD 1 in children)	Clients on a DTG-containing regimen, who have **never failed** any other regimen (previous "first-line" terminology)
TLD 2 (or ALD 2 in children)	Clients on a DTG-containing regimen, who **have failed** an earlier regimen (previous "second-line" terminology)

Remember: >50% of 'new' (TLD1) clients are silently returning to care – they may be missed TLD2



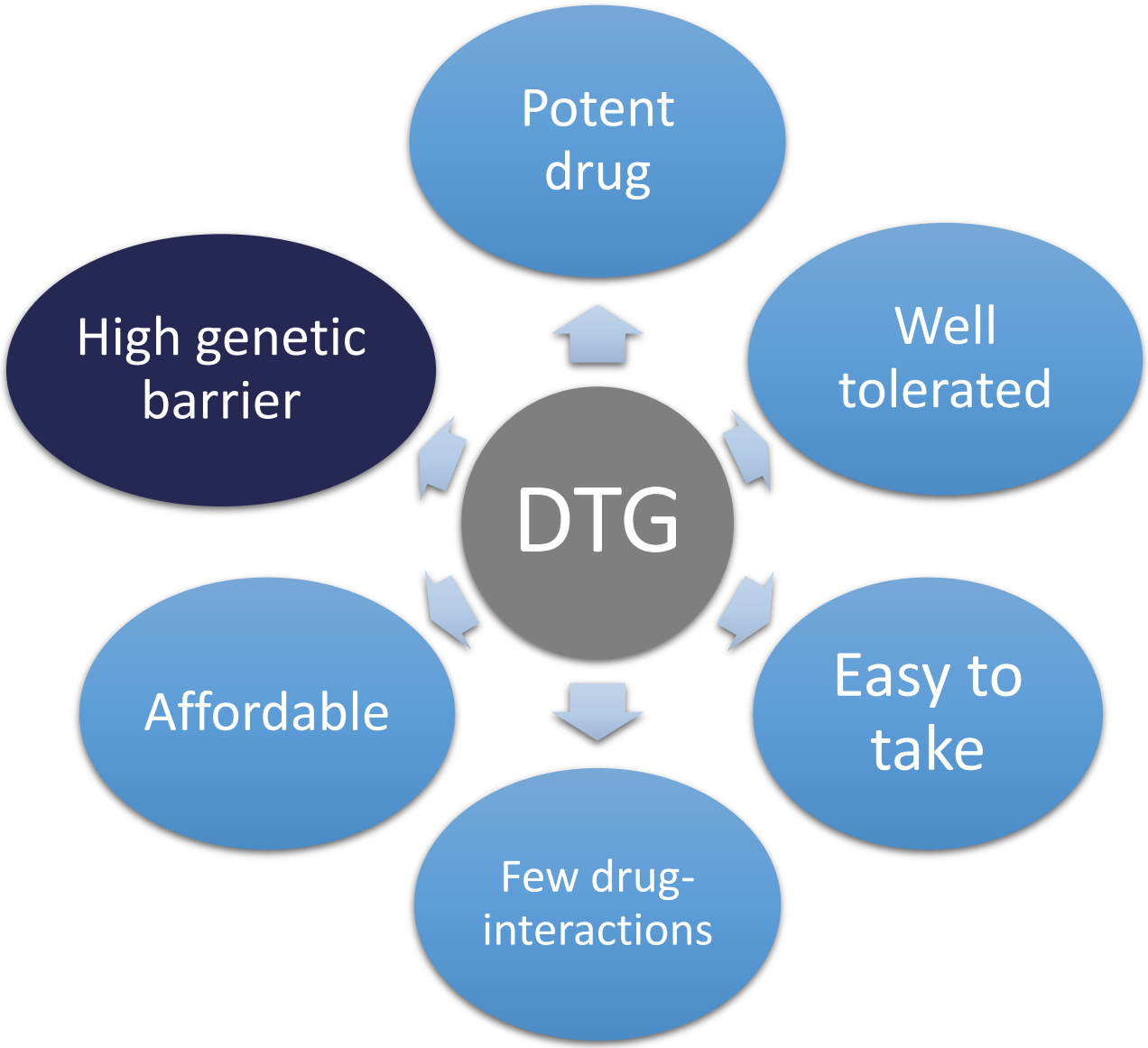
No prior failure = likely all 3 TLD drugs working



Prior failure = likely only DTG working

Mavhandu et al SA J of HIV Med 2021 Sithole AIDS Behav. 2021

Dolutegravir (DTG) – Anticipated as HIV's silver bullet



DTG - expectations vs reality

Clinical Trials

- 0-5% viral non-suppression (VNS)
- <1% DTG resistance if naïve/suppressed at TLD switch (TLD1)
- **20% DTG resistance if VNS** at TLD switch (TLD2)

Programmatic Outcomes

- Globally **3.9 – 27%** DTG resistance if VNS

South Africa

- 24%-41.6% DTG resistance if VNS
- **National programme**: DTG resistance in **26%** of resistance tests

SA modelling: **42%** DTG resistance with VNS by 2035

DTG is highly effective
BUT support within real world programmes is failing

WHO, 2024 HIV Drug resistance Report; Kanise et al, Viruses, 2024; Hans et al, 2023; Loosli et al, 2025

Resistance: A broken copy machine and a perfect storm

No ART

HIV factory

No resistance

Optimal adherence

ARV padlock closes factory

No resistance

Clinical trials: keep most people here

Intermittent adherence

Perfect storm: intermittent drug pressure

Resistance

Real world : more people exist here

Resistance does not result from stopping treatment completely

Resistance emerges with intermittent adherence;

Driven by the reality of being human with a life long condition

Preventing resistance relies on preventing viraemia

Optimal adherence

No resistance

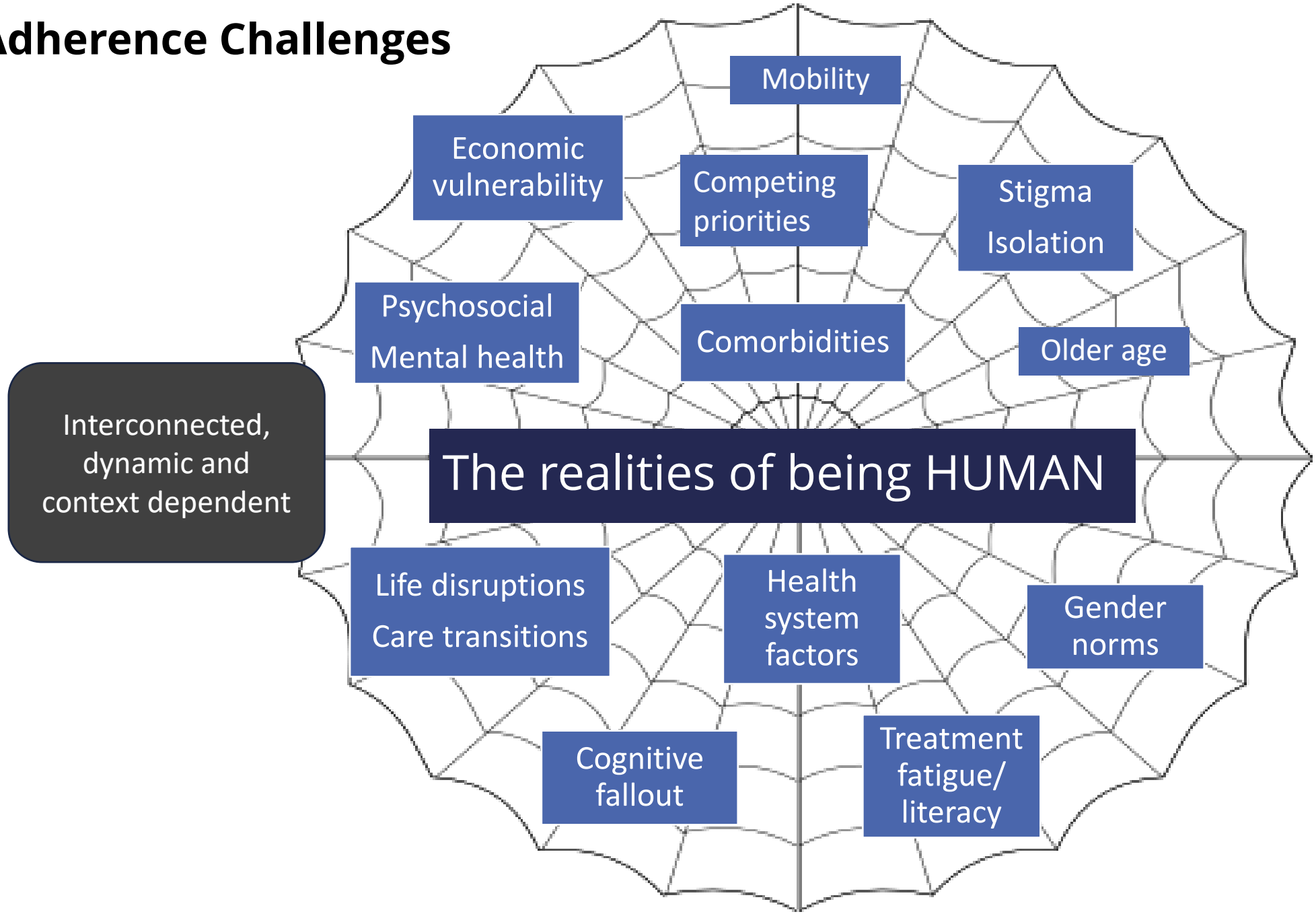
- Ultimate goal - keep the padlock on
- Optimise adherence
- **Not by switching ART drugs**

but

- By helping people take their drugs well

Except if you don't,
Because, sometimes you won't

Adherence Challenges



Heestermans et al., 2016; Moosa et al., 2019; Enslin & Mallya, 2022; Almeida et al., 2024; Seunanden et al, 2025; Tindikali & Mpambije, 2025

Persistent viraemia - the ultimate clinical question

Is this adherence?

No Resistance

Goal – adherence support[1] to achieve resuppression on SAME regimen[2,3]

+/-

Is this resistance?

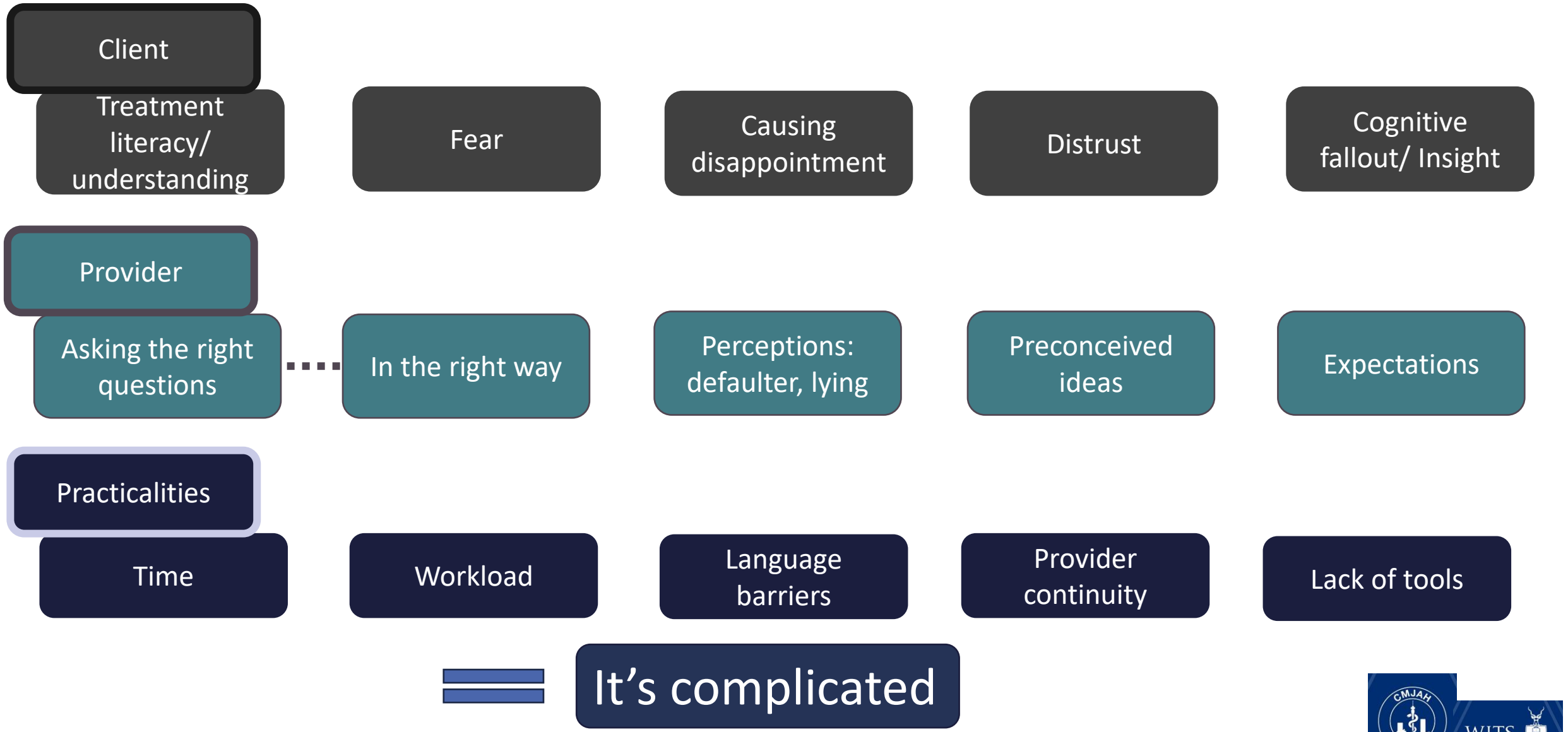
Chronic adherence challenges - "perfect storm" leads to resistance

Goal - support resuppression on NEW regimen and MAINTAIN suppression[4]

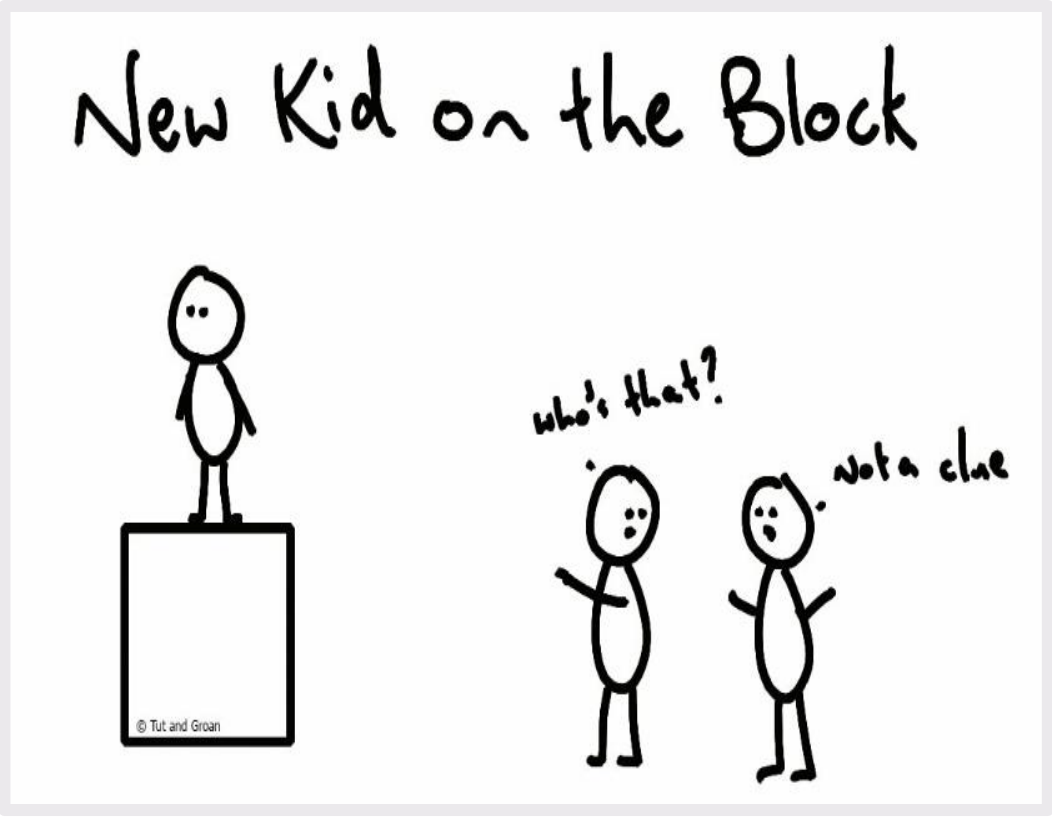
Both groups: **adherence issues must be addressed**
Crucial: understand **WHY** the person **struggles** not just **WHY** they are **viraemic or if they have resistance**

[1] Damulak et al, 2021 [2] Akpan et al, 2022 [3] Mitiju Kidie et al, 2025 [4] Bakari et al, 2024

Assessing adherence is difficult



DTG exposure testing



- **New triage tool** helps identify:
  - Those who **need resistance testing**
  - Those who **need adherence support**

  And saves money (fewer resistance tests)

- **55-80%** of viraemic individuals
  - **no detectable DTG** in blood
  - <2% have DTG resistance (NPP 98%)

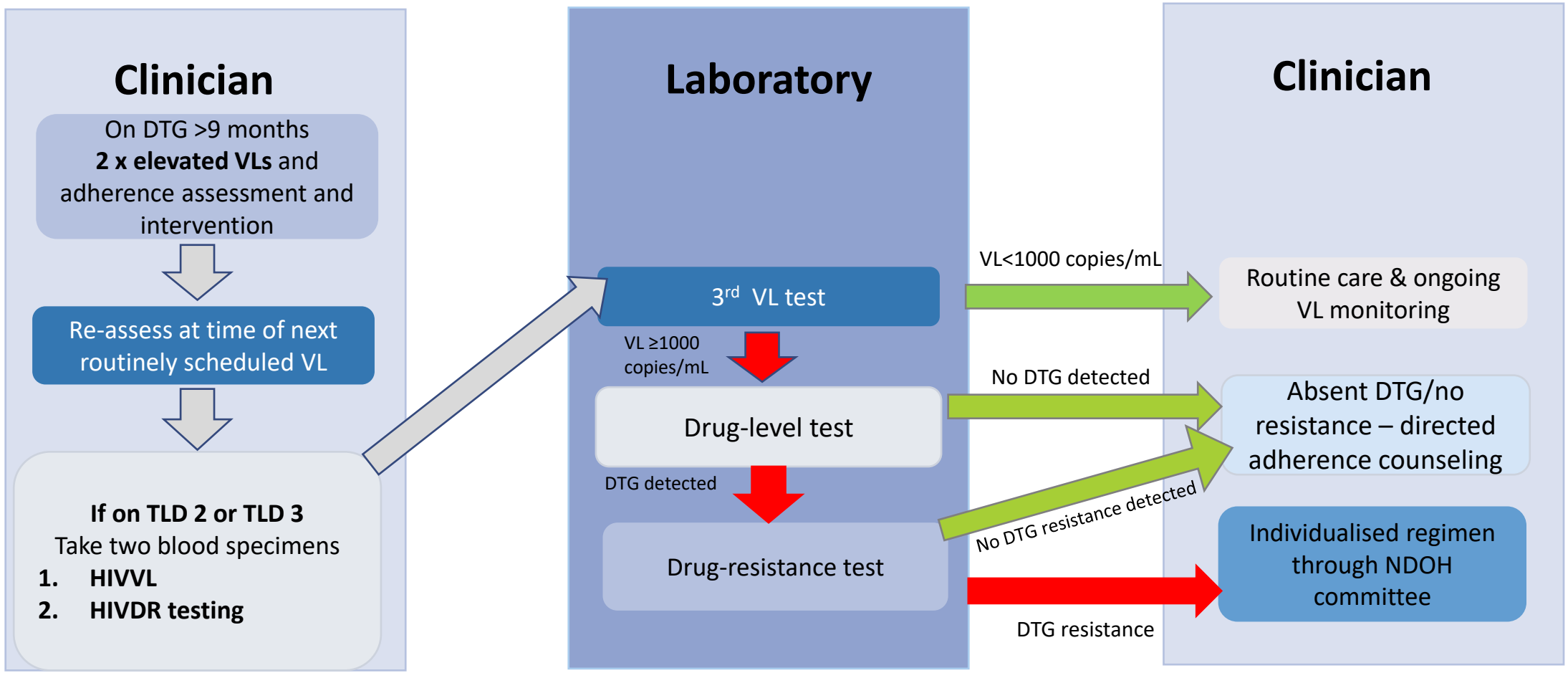
BUT

- **If DTG present – 50% have resistance**

Steegen et al., 2023 , Coetser et al., 2025, Steegen et al, 2025, Steegen et al, 2026,

Updated 2026 National ART Guidelines

p100 of guideline
Curtesy of Dr J Wessels



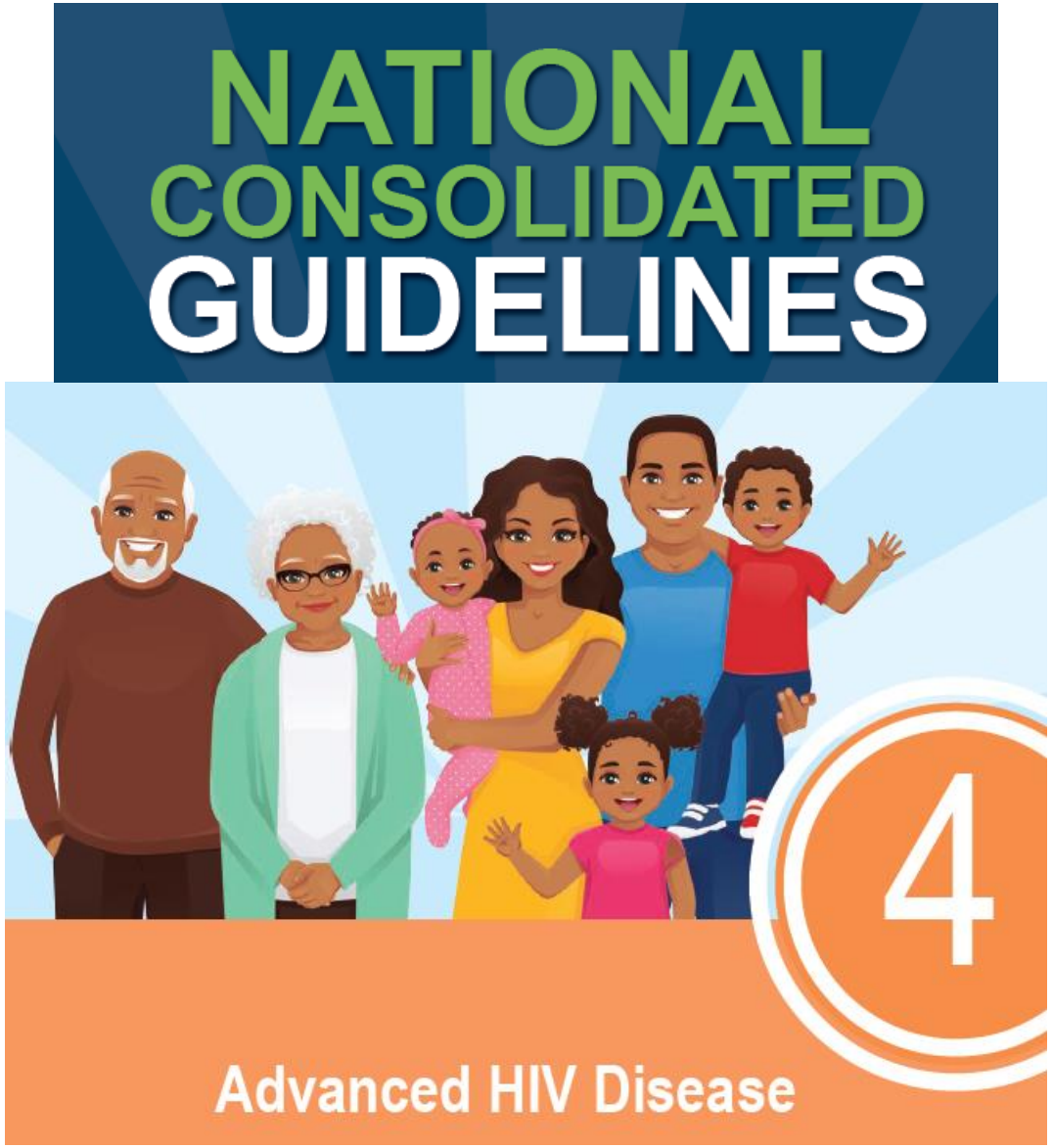
IMPORTANT
This helps with:
1. **WHAT** is happening (adherence vs resistance)
2. Optimising treatment/ regimen switch

It does ***not*** help with
1. **WHY** individual has persistent viraemia if no resistance
2. Addressing underlying issues if low adherence
3. Guiding appropriate adherence support

Viral non-suppression, AHD and mortality are closely linked

AHD mortality study *(Fieggen et al, 2026)*

- Majority (60%) with AHD in South Africa are now treatment experienced:
  - 40% currently disengaged from care – with inevitable viral non-suppression
  - **20% taking ART but not virally suppressed**
- AHD hinders viral suppression *(Kachingwe et al, 2025)*
  - 57% of AHD clients did not achieve viral suppression within 6 months of (re)initiating ART
- The **highest mortality** was seen in those **on ART, with viraemia**
  - 17% overall mortality
  - **50% mortality** within the **first year** (median 7 months)
  - AHD and mortality highest in **men, >45 years, CD4 <100**
  - **VL >1000 = independent** mortality **risk factor**



Viraemia Drives CD4 decline

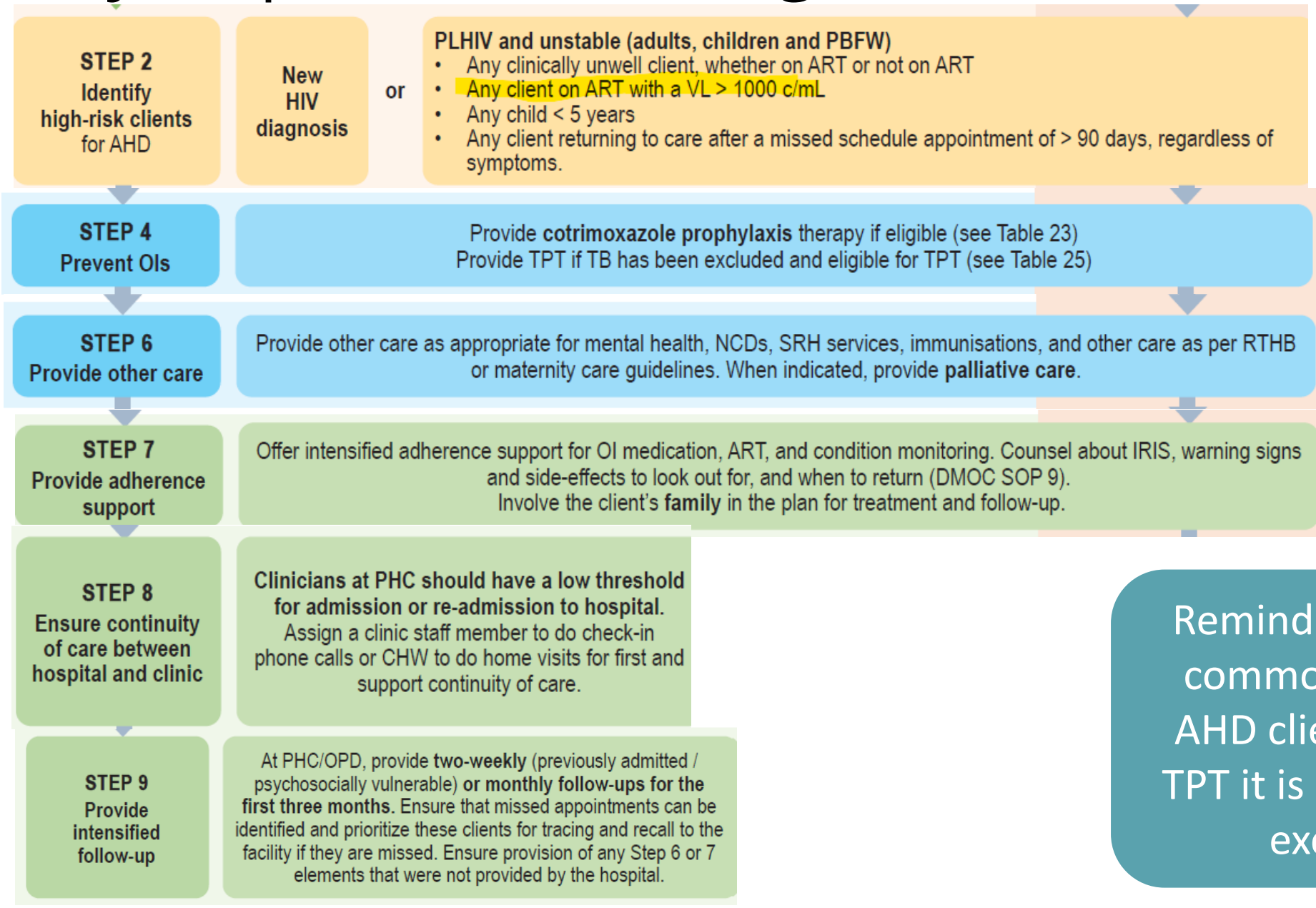
CD4 counts generally lower in those with DTG NOT detected

- AHD develops **more rapidly with adherence issues** than with resistance
  - Low adherence = **wild type** virus = **more virulent,** faster replication = **faster CD4 decline**
  - Resistance = mutated virus = crippled replication = slower CD4 decline
- Be vigilant in both groups but **DTG NOT detected = red flag**
    - Monitor **CD4 6 monthly** if VL >1000
    - Need to **quickly get to underlying adherence barriers** to avert mortality

Take home messages

- Any viraemia requires rapid, effective management to avoid AHD and reduce mortality
- Persistent viraemia: must maintain dual focus on monitoring viral load and CD4
- Patients with viraemia and AHD are particularly vulnerable and need parallel, comprehensive management of both complications
- If we, as clinicians, can catch viraemia early, and achieve resuppression, we will prevent a new wave of AHD clients

Key Steps of AHD Management for Viraemic Clients



Reminder: TB remains most common cause of death in AHD clients. Before starting TPT it is essential to carefully exclude active TB

Reframing “failure” through person centred care (PCC)

Resistance is not only a virological phenomenon

It reflects missed opportunities for person-centred care

PCC reorientates care towards

- Responsivity to lived realities
- Empowering agency and co-management
- Health systems alignment rather than individual blame

PCC is not optional

It is a **foundational mechanism** through which optimal chronic care becomes

Achievable **Sustainable** **Equitable**

PCC Framework

Duncombe et al, 2015; Grimsrud et al, 2016; Murray et al, 2017;WHO; 2023; Mead & Bower, 2000

PCC as a clinical intervention to manage persistent viraemia

Current System

Fragmented, high-volume care
- Many, short visits
- Many clinicians, no continuity

Patient experience
- Not known / not heard
- Generic counselling/ poor understanding
- Low trust/ emotional burden ignored

Behaviour
- Intermittent adherence
- Missed visits
- Treatment interruptions

Outcome
- Persistent viraemia
- Drug resistance

PCC Approach

Relational, person-centred care
- Micro-continuity
- Listening-led
- Shared understanding and decisions

Patient experience
- Known and respected
- Trust
- Barriers known, goals aligned

Behaviour
- Consistent adherence and retention
- Improved motivation and engagement

Outcome
- Viral resuppression
- Reduced resistance
- Improved staff satisfaction

Case Discussions
Persistent Viraemia
Understanding the WHY

*Stories shared with permission

Case 1 – 51 year old male

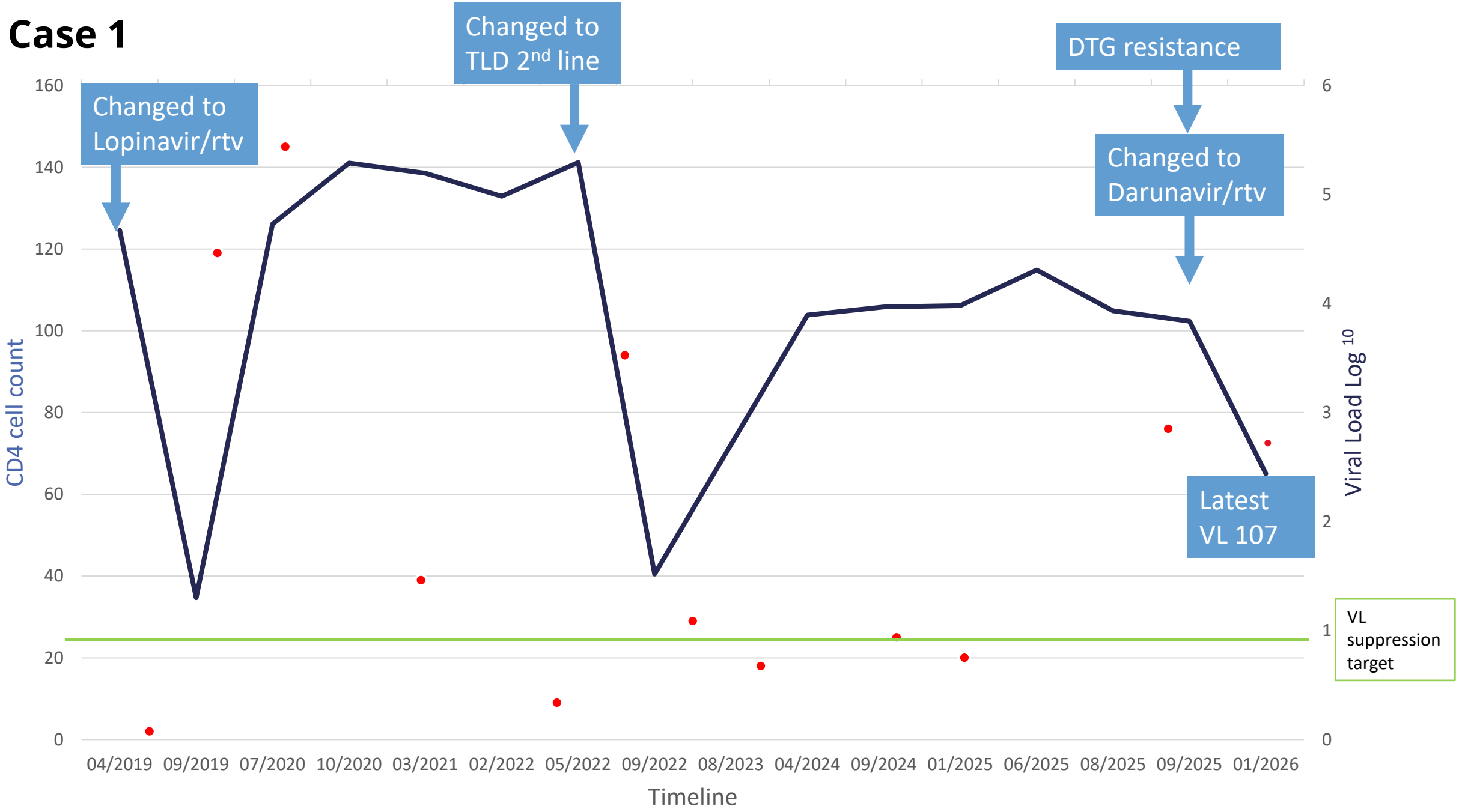
13 years on ART

- Multiple ART regimens
  - 1st line **virological failure**
  - Ongoing VNS on PI regimen (no resistance)
  - 2nd line TLD from May 2022
- Advanced HIV Disease (AHD) for over 10 years
- **33 visits, 22 different doctors** past 8 years

Adherence History

- Intermittent adherence for many years
- Recurrent treatment interruptions
  - Work commitments → weeks/months off ART, missed clinic visits
  - Night driving c/o drowsiness → missed doses
- Heavy weekend alcohol use → missed doses

Case 1


Changed to Lopinavir/rtv
Changed to TLD 2nd line
DTG resistance
Changed to Darunavir/rtv
Latest VL 107
CD4 cell count
Viral Load Log 10
VL suppression target
Timeline
160
140
120
100
80
60
40
20
0
6
5
4
3
2
1
0
04/2019
09/2019
07/2020
10/2020
03/2021
02/2022
05/2022
09/2022
08/2023
04/2024
09/2024
01/2025
06/2025
08/2025
09/2025
01/2026

Case 1 – the biology

HIV Viral Load:

HIV Viral Load	7939	copies/mL
Log Conversion	3.90	Log(copies/mL)
Input Volume	0.600	mL
Methodology	Abbott Alinity M HIV-1 Test	

Drug levels:

Dolutegravir — Detected

Limit of detection set at 0.01 ug/mL for plasma dolutegravir.

Please note: multiple factors can affect plasma drug levels including dosing, dosing frequency, sample timing, sample handling, drug-drug interactions and drug metabolism. Please consult with an appropriate expert before making treatment adjustments.

Drug Resistance Interpretation: INI

INI major resistance mutations	R263K
INI minor resistance mutations	None

Integrase Inhibitors:

Bictegravir (BIC)	Intermediate resistance
Cabotegravir (CAB)	High-level resistance
Dolutegravir (DTG)	Intermediate resistance
Elvitegravir (EVG)	Intermediate resistance
Raltegravir (RAL)	Low-level resistance

Case 1 – the humanity

Missed Opportunities

- Addressing lifestyle and competing priorities (night driving, mobility)
- Treatment literacy assumed – impact of missed doses not known
- Simplified TLD regimen but actual issues remained unaddressed
- No provider continuity for 8 years

Learning Points

- Simplified regimens don’t always solve the real problem
- Low treatment literacy can persist for years if not tackled
  - Explain health condition and treatment – don’t underestimate individual’s ability to understand

Case 2 - 53yr old male

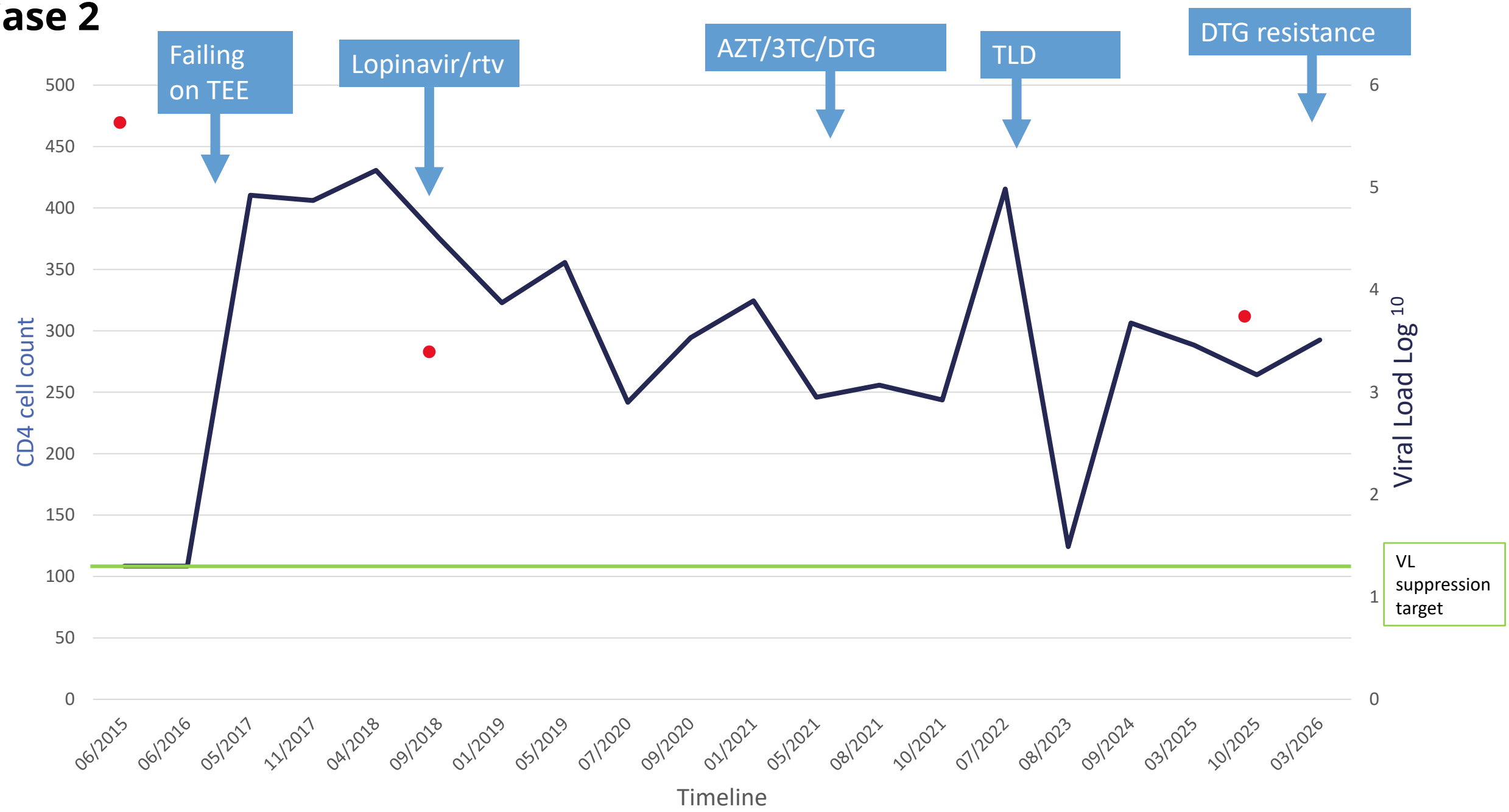
13 years on ART

- Multiple ART regimens
  - 1st line **virological failure**
  - Ongoing VNS on PI regimen (no resistance test done)
  - 2nd line TLD from Dec 2023
- CD4 >200 maintained
- **33 visits, 27 different doctors** past 9 years

Adherence History

- Repeated prolonged treatment interruptions
  - Cross border worker – sometimes couldn't return
  - Missed visits, ran out of meds – multi-month dispensing avoided because non-suppression
- Incarcerated in 2018 - no treatment provided

Case 2


Failing on TEE
Lopinavir/rtv
AZT/3TC/DTG
TLD
DTG resistance
CD4 cell count
Viral Load Log 10
VL suppression target
Timeline
500
450
400
350
300
250
200
150
100
50
0
6
5
4
3
2
1
0
06/2015
06/2016
05/2017
11/2017
04/2018
09/2018
01/2019
05/2019
07/2020
09/2020
01/2021
05/2021
08/2021
10/2021
07/2022
08/2023
09/2024
03/2025
10/2025
03/2026

Case 2 - the biology

HIV Viral Load:

HIV Viral Load	3233	copies/mL
Log Conversion	3.51	Log(copies/mL)
Input Volume	0.600	mL
Methodology	Abbott Alinity M HIV-1 Test	

Drug levels:

Dolutegravir Detected

Limit of detection set at 0.01 ug/mL for plasma dolutegravir.

Integrase Inhibitors:

Bictegravir (BIC)	Intermediate resistance
Cabotegravir (CAB)	High-level resistance
Dolutegravir (DTG)	Intermediate resistance
Elvitegravir (EVG)	High-level resistance
Raltegravir (RAL)	High-level resistance

Case 2 – the humanity

Missed Opportunities

- Structural barriers driving interruptions
  - Cross border mobility – he tried accessing treatment near border, turned away
  - Incarceration without health access – human rights abuses
  - Considered 'ineligible' for multi-month dispensing
- Not educated on rights or treatment literacy

Learning Points

- Highly mobile clients need
  - Treatment literacy – planning ahead where possible
  - Health rights education – care at any clinic, no transfer needed
  - Buffer medication supply to avoid interruptions
  - Appointment date flexibility

Case 3 - 53 year old female

20 years on ART

- Suppressed for 15 years (2006 – 2021)
- Interrupted x 1 year
- Restarted Dec 2022 DTG-based regimen
- **17 visits, 12 doctors** over 4 years

Adherence History

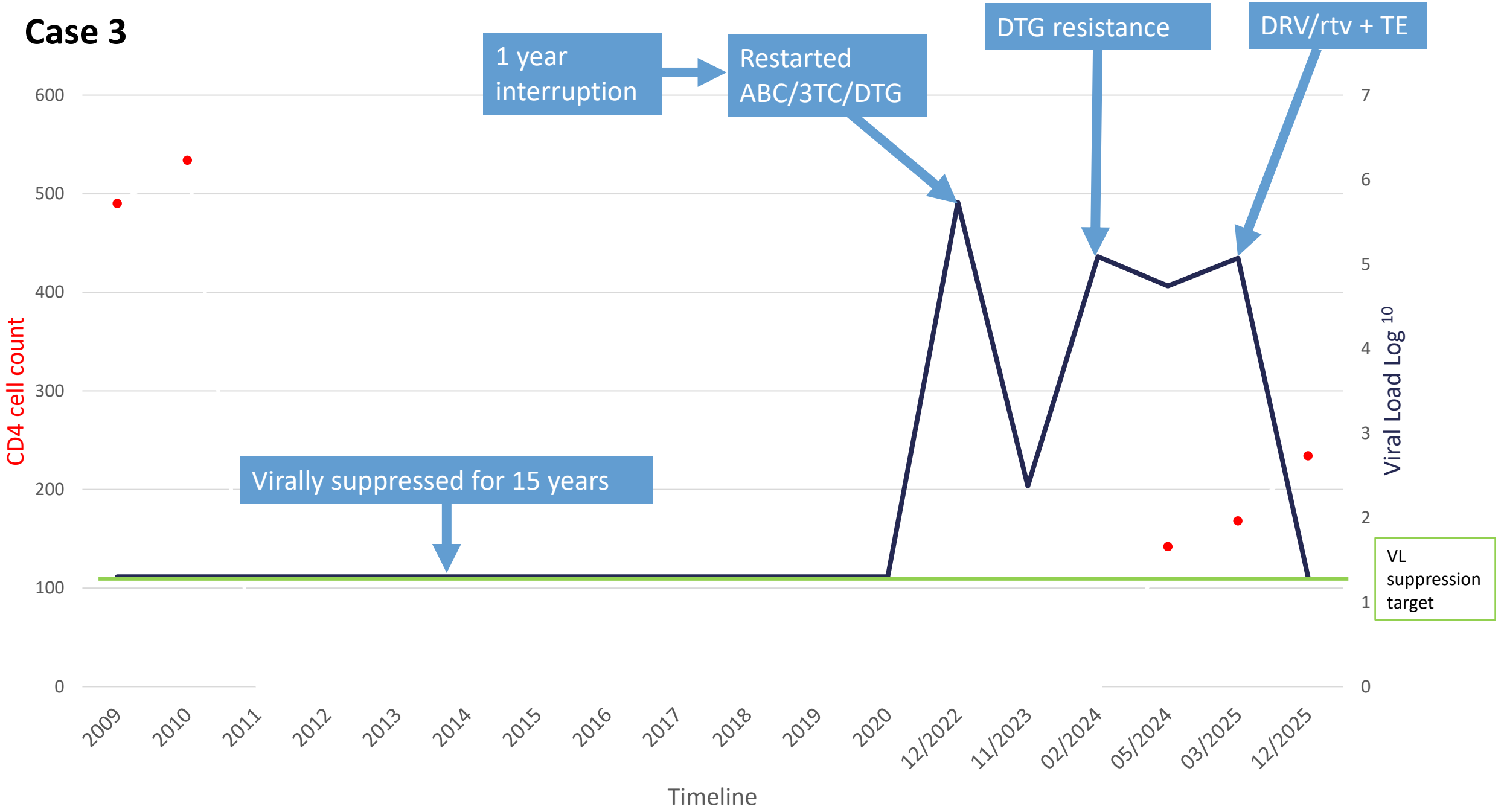
- Treatment interruption during 8m admission for CVA – ? Why no ART
- 2023 - 7 family members die in MVA → undiagnosed depression → low adherence
- 2026 - grandmother and nephew die of poisoning – 2 week interruption

Comorbidities & Polypharmacy

- HIV with AHD
- HPT
- Dyslipidaemia
- Diabetes
- CVA
- Depression

14 tablets daily + s/c injections

Case 3


1 year interruption
Restarted ABC/3TC/DTG
DTG resistance
DRV/rtv + TE
Virally suppressed for 15 years
CD4 cell count
Viral Load Log 10
VL suppression target
Timeline
600
500
400
300
200
100
0
7
6
5
4
3
2
1
0
2009
2010
2011
2012
2013
2014
2015
2016
2017
2018
2019
2020
12/2022
11/2023
02/2024
05/2024
03/2025
12/2025

Case 3 - the biology

HIV Viral Load:

HIV Viral Load	123000	copies/mL
Log Conversion	5.09	Log(copies/mL)
Input Volume	0.500	mL
Methodology	Cobas 6800/8800	HIV-1 Test

Drug levels:

Dolutegravir — Not detected

Limit of detection set at 0.01 ug/mL for plasma dolutegravir.

Retrospective genotype in DTG pilot

Integrase Strand Transfer Inhibitors

bictegravir (BIC)	Intermediate Resistance
cabotegravir (CAB)	High-Level Resistance
dolutegravir (DTG)	Intermediate Resistance
elvitegravir (EVG)	Intermediate Resistance
raltegravir (RAL)	Low-Level Resistance

Case 3 - the humanity

Missed Opportunities

- Trauma, life disruptions common → mental health impacts
  - Nobody recognised the sudden change in how she was doing
  - Depression/anxiety undiagnosed for 3 years
- Polypharmacy complicates adherence

Learning Points

- DTG has high genetic barrier but 1 mutation is enough
  - Slow response to viraemia can blow it
- Comorbidity → polypharmacy → pill burden → low adherence for all conditions requiring comprehensive approach
- Mental health screening essential component of care
- Avoid “defaulted/defaulter” – fails to acknowledge complexities

Case 4 - 28yr old male

20 years on ART

- Diagnosed at 9yrs, disclosed to at 11yrs, adult care from 20yrs
- 1st line failure
- Unsuppressed on PI with no resistance
- **2nd line TLD since 2023**
- **AHD, CD4** <50 for years, latest **8**
- **68 visits, 26 doctors** over 9 years

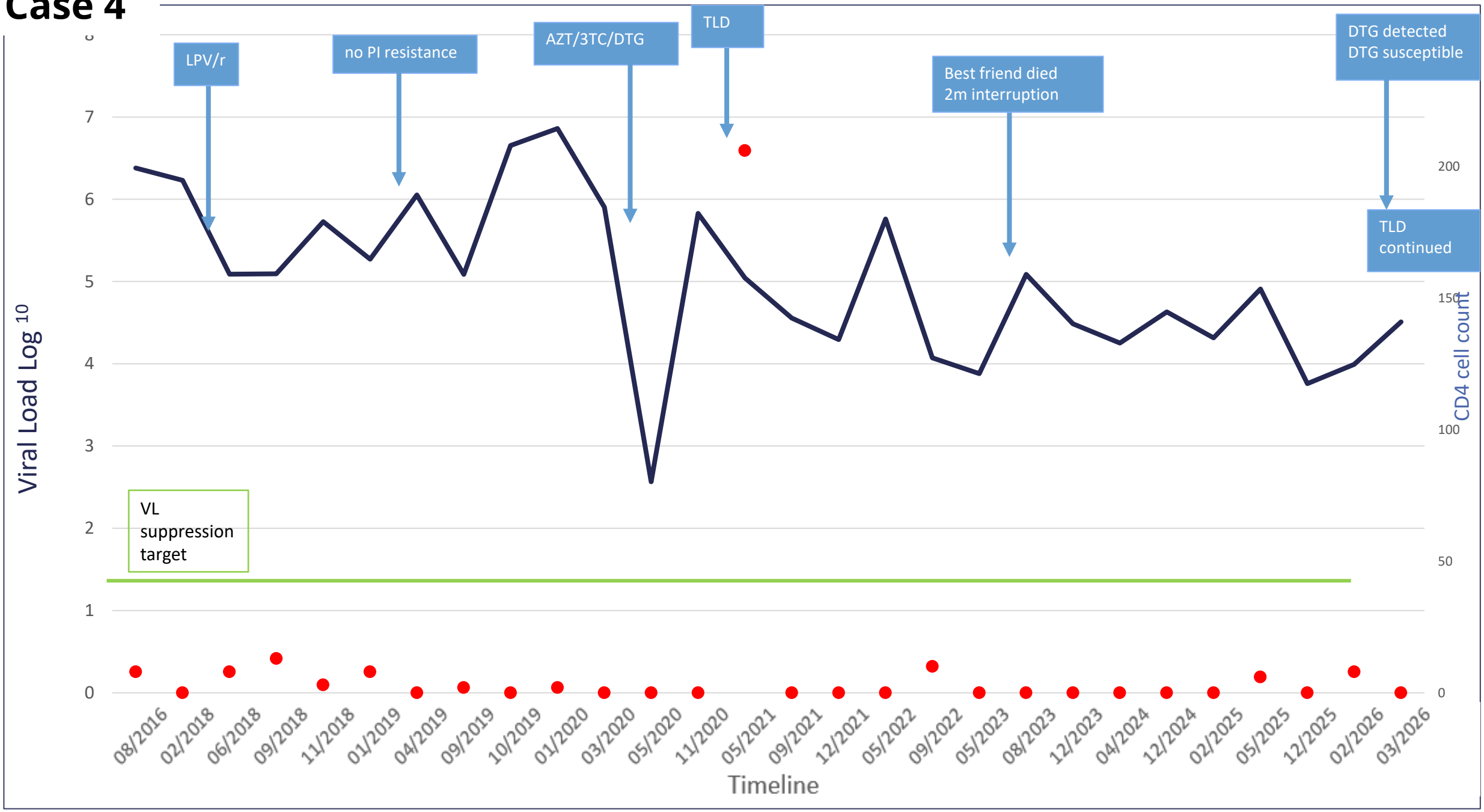
Adherence History

- None to very low adherence with brief periods of improvement

Undiagnosed mental health issues

- Worse after death of best friend, socially isolated
- Suicide attempt (2024) – no psych care
- Describes not caring if he lives or dies, low motivation to adhere
- Work prioritised over visits and adherence
- Longstanding AHD → cognitive fallout → forgetfulness

Case 4


LPV/r
no PI resistance
AZT/3TC/DTG
TLD
Best friend died
2m interruption
DTG detected
DTG susceptible
TLD
continued
VL
suppression
target
Viral Load Log 10
CD4 cell count
Timeline
0
1
2
3
4
5
6
7
50
100
150
200
08/2016
02/2018
06/2018
09/2018
11/2018
01/2019
04/2019
09/2019
10/2019
01/2020
03/2020
05/2020
11/2020
05/2021
09/2021
12/2021
05/2022
09/2022
05/2023
08/2023
12/2023
04/2024
12/2024
02/2025
05/2025
12/2025
02/2026
03/2026

Case 4 - the biology

HIV Drug Resistance Input Data:

HIV viral load	32315	copies/mL
HIV viral load log	4.51	Log(copies/mL)
HIV viral load date	05/03/2026	

Drug levels:

Dolutegravir	Detected

Limit of detection set at 0.01 ug/mL for plasma dolutegravir.

Integrase Inhibitors:

Bictegravir (BIC)	Susceptible
Cabotegravir (CAB)	Susceptible
Dolutegravir (DTG)	Susceptible
Elvitegravir (EVG)	Potential low-level resistance
Raltegravir (RAL)	Potential low-level resistance

"white coat adherence"

Case 4 - the humanity

Missed Opportunities

- Poorly supported transition from adolescent to adult care, no continuity
- Missed significant mental health issues (PHQ down from 19-6)
- Non-judgemental conversations to address ‘white coat’ adherence
- Low treatment literacy, treatment fatigue, competing priorities not addressed

Learning Points

- Importance of kindness, patience and being approachable – he never disclosed his suicide attempt
- Normalise the struggle
- Mask your frustration – patients don’t want to feel they let us down
- Long term survivors often isolated, battling with wanting ‘normality’

Sidebar: Persistent viraemia requires AHD Safety Net Approach

- CD4 monitoring 6 monthly when viral load >1000
- Advanced HIV disease = CD4<200 or WHO 3/4
- AHD requires comprehensive package of care – **NEW: Chapter 4 of National Guideline (p51+)**
  - Cotrimoxazole prophylaxis
  - TB preventive therapy: 3HP or 12H
    - Exclude TB thoroughly first: TB NAAT, urine TB LAM, TB blood culture (if available)
  - CrAG +/- LP + appropriate treatment: if CrAG +, fluconazole for minimum 1 year

This creates a **Clinical Tension: A Pill Burden Paradox**

- Clinician must balance need for prophylaxis with possible negative adherence impact
  - Shared decision-making: discuss trade-off between mortality and pill burden and allow patient to decide

  - Watch for OIs, including IRIS if they start adhering/change regimen and rapidly suppress
  - Nutrition assessment: monitor weight at every visit, low BMI – refer dietician, social worker, apply for SASSA disability grant
  - Cognitive assessment: cognitive decline impacts memory - impacts adherence – family support
  - Check Hb and ALT, Hep B, STI screen
  - Ensure females have had pap smear

Other things to discuss:
- Contraception if females
- Partner? - ?need for PrEP

Case 5 - 24 year old female

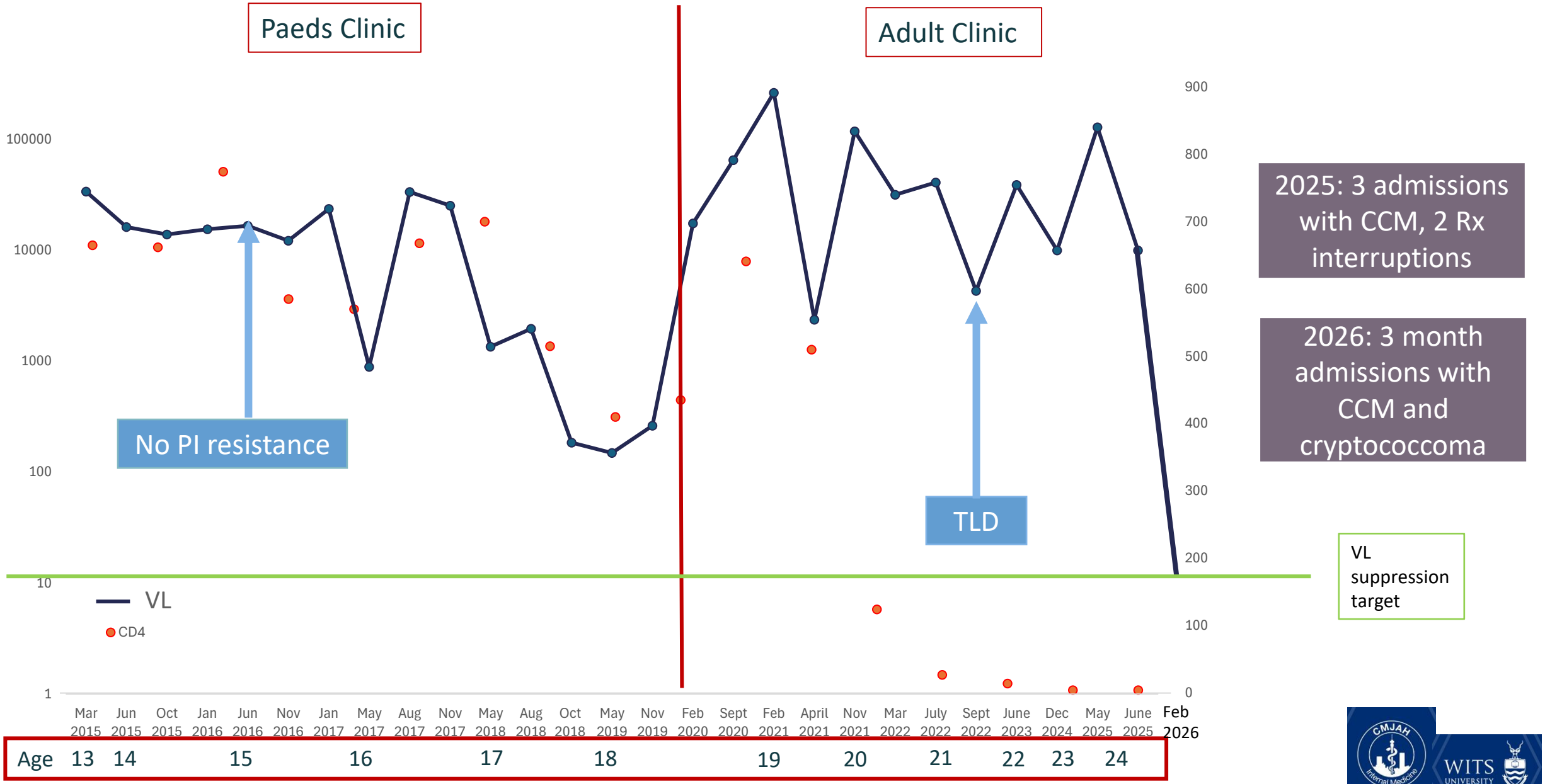
18 years on ART

- Diagnosed at 6yrs, disclosed to at 13yrs, adult care from 18yrs
- 1st line failure after disclosure
- Unsuppressed from 13yrs, no PI resistance
- **2nd line TLD since 2022**
- **AHD, CD4** <50 for years, latest **4**
- **19 visits, 17 doctors** over 5 years at adult clinic

Adherence History

- Late disclosure → stigma, low self-esteem, anger and frustration, loss of trust
- Hearing impairment, blind right eye, cognitive fall out impacted understanding → low adherence
- Mom & Dad both very supportive, 5 siblings all HIV uninfected – “unfair”

Case 5


Paeds Clinic
Adult Clinic
No PI resistance
TLD
2025: 3 admissions with CCM, 2 Rx interruptions
2026: 3 month admissions with CCM and cryptococcoma
VL suppression target
VL
CD4
100000
10000
1000
100
10
1
900
800
700
600
500
400
300
200
100
0
Mar 2015
Jun 2015
Oct 2015
Jan 2016
Jun 2016
Nov 2016
Jan 2017
May 2017
Aug 2017
Nov 2017
May 2018
Aug 2018
Oct 2018
May 2019
Nov 2019
Feb 2020
Sept 2020
Feb 2021
April 2021
Nov 2021
Mar 2022
July 2022
Sept 2022
June 2023
Dec 2024
May 2025
June 2025
Feb 2026
Age 13 14 15 16 17 18 19 20 21 22 23 24

Case 5 - the biology

HIV Molecular Investigations:

HIV Viral Load:

HIV Viral Load	67191	copies/mL
Log Conversion	4.83	Log(copies/mL)
Input Volume	0.200	mL
Methodology	Abbott Alinity M HIV-1 Test	

Drug levels:

Dolutegravir	Not detected

Limit of detection set at 0.01 ug/mL for plasma dolutegravir.

HIV drug resistance test not done

Approaching an Absent DTG Level Result: Drug Level Informed Counselling

Discussing **absent** DTG takes skill and a person-centred approach

Kindness first

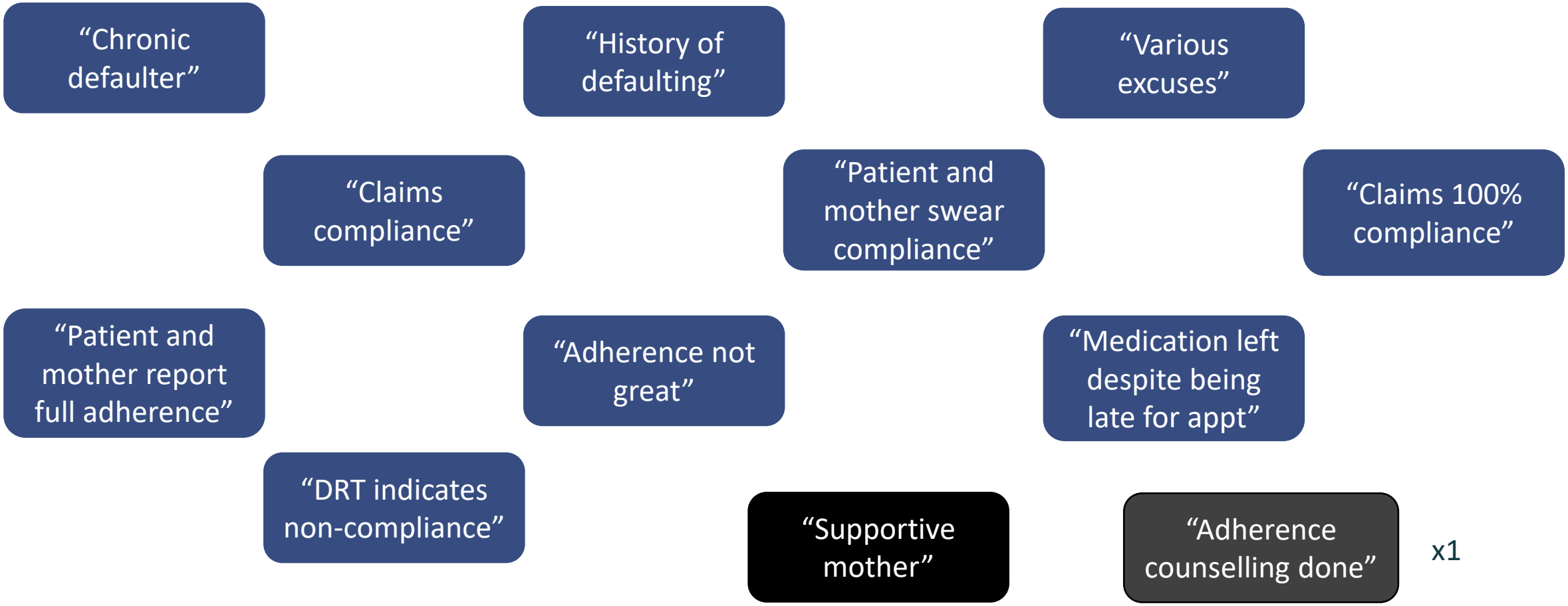
- **Shared understanding**
- **Safe space and rapport**
- **Open, neutral discussion**
- **Empathy and validation**
- **Normalise challenges**
- **Be supportive and flexible**
- **Remember mental health**

- **Avoid judgement**
- **No punitive response**
- **Don’t make assumptions**
- **Watch your language**
- **Don’t compare with others**

The most powerful clinical tool

A gentle, listening ear

Providers' Written Notes for Case 5



Language reflects mindset - Mindset shapes care - Care shapes outcomes

Case 5's feelings about taking ART

Case 5 - the humanity

Missed Opportunities

- Transition to adult clinic → loss of continuity
- Lack of recognition of KB's personhood – overlapping grief, disability, depression, social isolation, treatment fatigue, cognitive fall out
- 'defaulter' label coloured future clinical engagements

Learning Points

- Human first, illness second
- Active listening crucial
- Language used in notes matters
- Acknowledging tough realities individual → feels seen/heard
- Never give up! – she is now doing well – CD4 299, viral load <20

Reframing “Treatment Failure”

Commonalities

- Lack of
  - Continuity
  - Shared understanding
  - Therapeutic relationships
  - Individualised problem-solving
  - Shared decision making

Ask the question sooner:
What is the underlying WHY preventing the person from taking treatment optimally?

With improved person-centred care:

- Relational, responsive care
- Trust and shared understanding
- Earlier identification of barriers
- Sustained engagement, improved adherence
- Optimal, faster viral (re)suppression
- Avoid emergent drug resistance

Mead & Bower, 2000; Grimsrud et al, 2016

Micro-continuity for small wins

- Many patients, many providers, little time – this isn't going to change in our constrained setting
- **Create** a *sense* of continuity
  - Optimally use each interaction to create continuity of **thinking**

- **Short patient summaries**
  - Person's **main barriers**
  - Agreed **plan**
  - **What matters** to the patient
  - Brief **personal details**

30 seconds of well written context
can improve the next interaction **(if it's read…)**

- Repetitive, standardised counselling becomes **relational engagements**
  - Ask why it's hard for **them** right now - normalise struggles
  - Identify real barriers: structural vs psychosocial vs treatment vs cognitive
- Actively listen
- Choose one small, achievable, shared goal
  - Record this so next doctor can do focused check-in

Simple things can make a difference

Without making consultations longer or harder…

Relate

- Introduce yourself
- Greet person by name
- Make eye contact (and smile??)
- Don't show frustration

Communicate

- Small notes about family member's including names – ask how they are
- Avoid blame/judgement
- Congratulate progress
- Create microcontinuity

Educate

- Explain one thing each visit - while you write your script
- Explain blood/ investigation results
- Explain any changes made

The two easiest…

#hello my name is…

"See me as a person first, before my disease. Individuals are more than just their illness, they are human beings with lives beyond this interaction"

Conclusion

- There will always be individuals who face adherence struggles
- DTG exposure testing is a useful new tool
  - Differentiates adherence from resistance
- But, for **all** viraemic individuals, addressing underlying challenges remains crucial
  - PCC has become an imperative
  - We cannot afford **NOT** to be person-centred
  - This is true for all chronic conditions, not just HIV

- Even in this challenging context, we can choose how we

Relate Communicate Educate

to positively influence our patients' experiences and outcomes