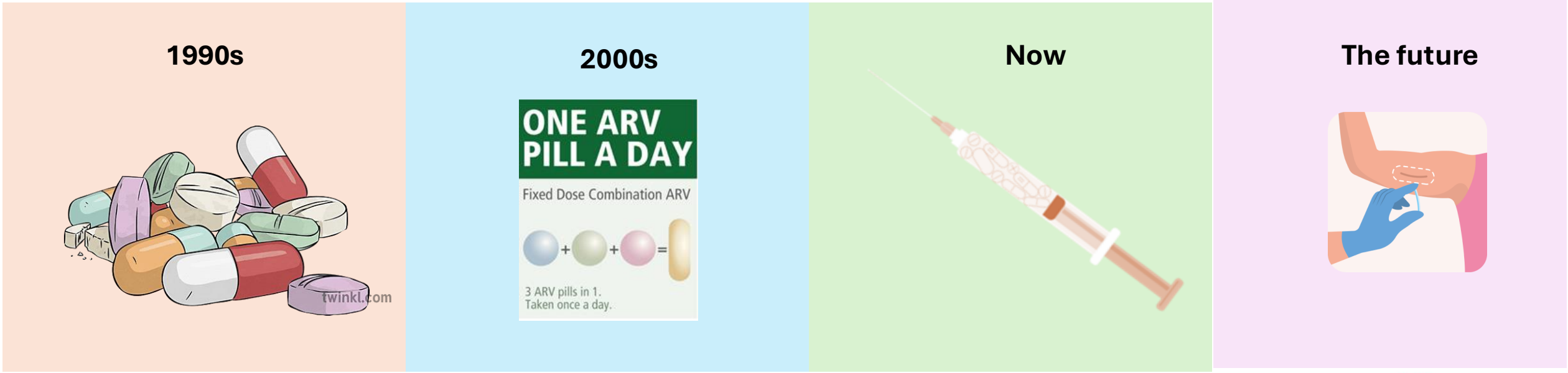


Durability by Design:
Individualising ART for success

Linda-Gail Bekker

Desmond Tutu Health Foundation & HIV Centre

Science of Scale Session

Continuum Conference 2026

San Juan, Puerto Rico 23 June 2026

Relevant disclosures

- DTHF has received grants and research product from Johnson and Johnson, ViiV Healthcare and Gilead Sciences.
- LGB has served on advisories for
  - ViiV Healthcare
  - Merck Pty LTD
  - Gilead sciences

UNAIDS HIV/AIDS Targets for 2030

95

percent of people living with HIV knowing their HIV status

95

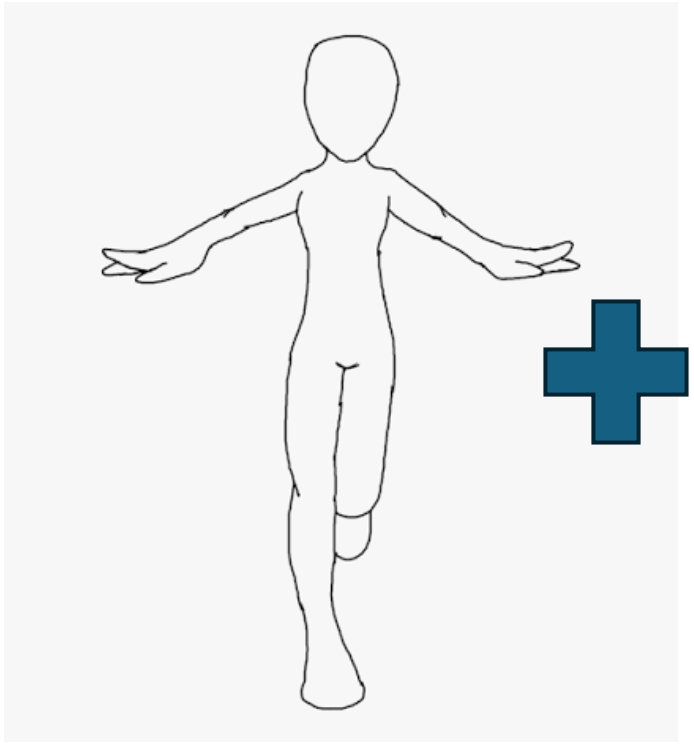
percent of people who know their status receiving treatment

95

percent of people on HIV treatment being virally suppressed

EPIDEMIC CONTROL

For the Individual Person……



+

+

=

WELLBEING
HEALTH

HEALTH
VIRAL
SUPPRESSION

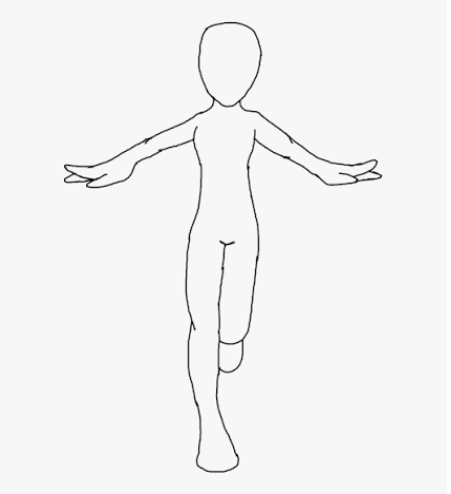
Person:
personality
life stage
Reproductive choices

Current realities:
houseless
two jobs
violent relationship

Health system:
Complexity
regimen
cost

Outcome:
Person
Provider

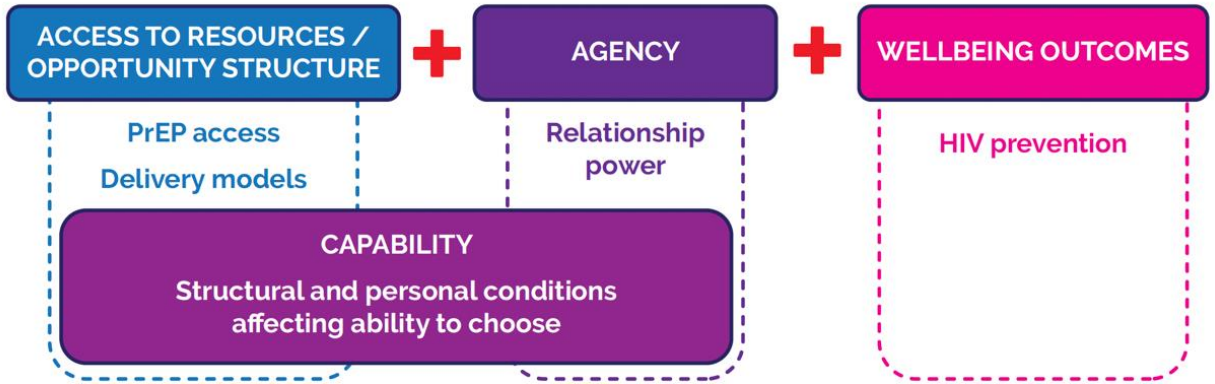
The person in front of us…..

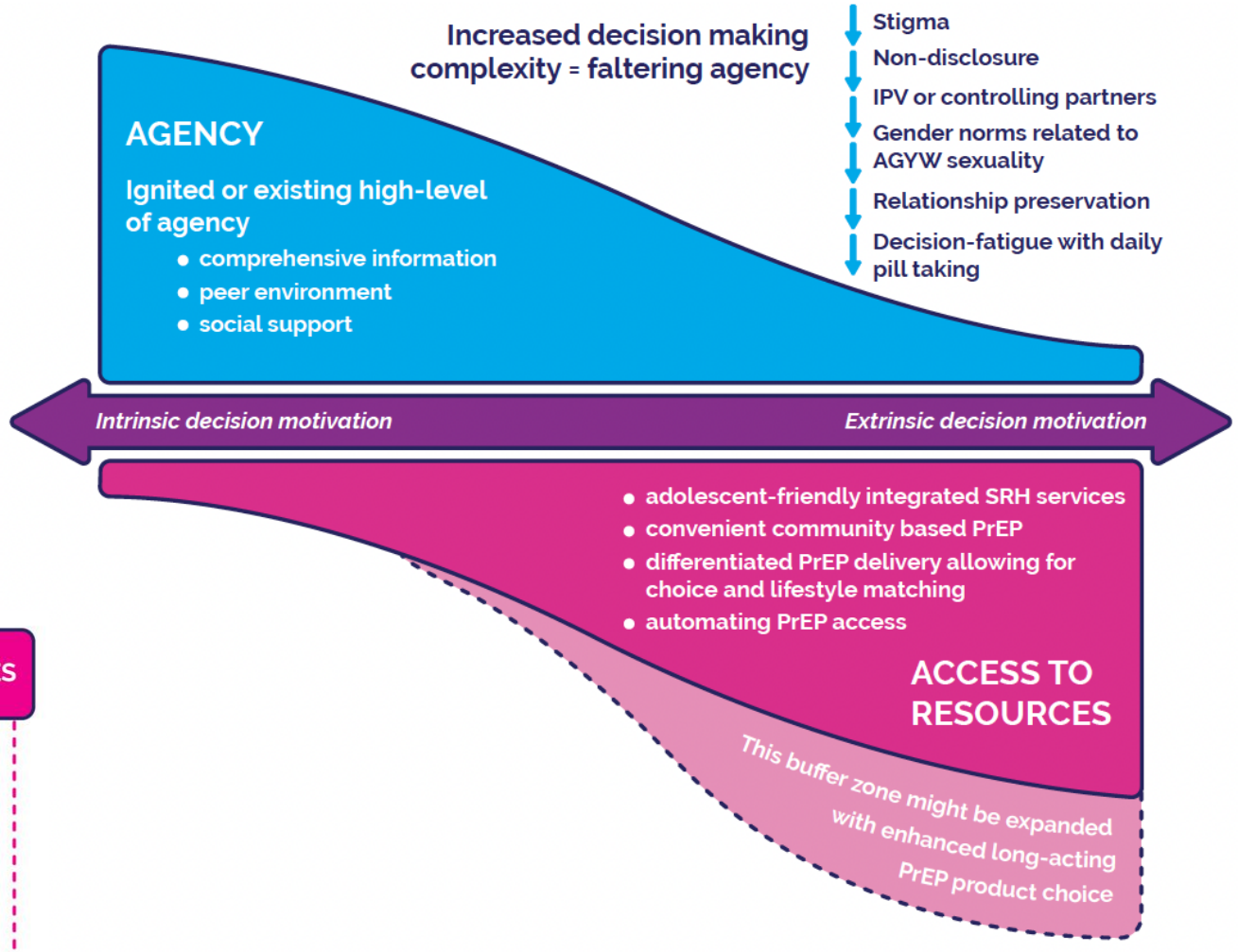


- Naïve to ART…..an “unknown” but clues
- On ART and suppressed and happy
- On ART and suppressed but navigating ”risky” waters…
- On ART and suppressed but not happy….tired, restless,
- On ART and suppressed but heard about simpler newer option….
- On ART but various toxicities/side effects eroding well being
- On ART (but not really…..) not suppressed and struggling
- On ART – but navigating life and neither ART nor VS is top priority

Filling the gap between PrEP interest and use

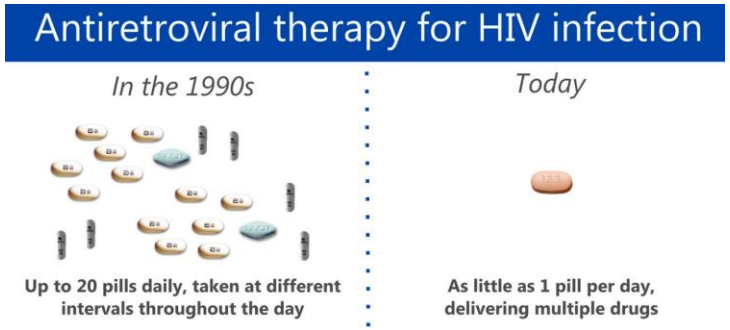
- Gap between PrEP interest, PrEP uptake, and PrEP persistence
- PrEP is ”pitched” as user-controlled but with high levels of agency needed (especially in AGYW – HIV burden in ESA) – can they independently access and use PrEP
- Optimal HIV prevention means **products AND services** that suit the user.





Rousseau et al (2024)

HIV therapy of old.... For 20yo LWHIV



- 1996, life expectancy: 39 years.
- 2011, life expectancy: 70 years.
- 2020, life expectancy: 77 years (and up to 87 years if ART initiated at a CD count >500) (Marcus et al., CROI 2020)

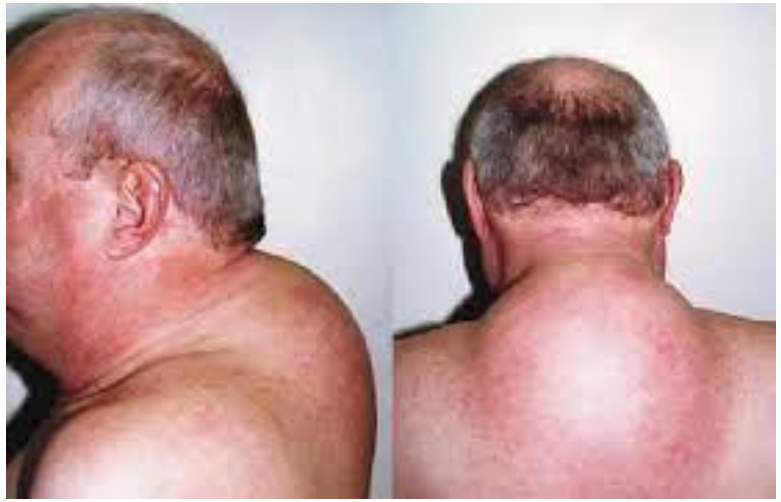
LISBON patient dies aged 100 years old in 2019

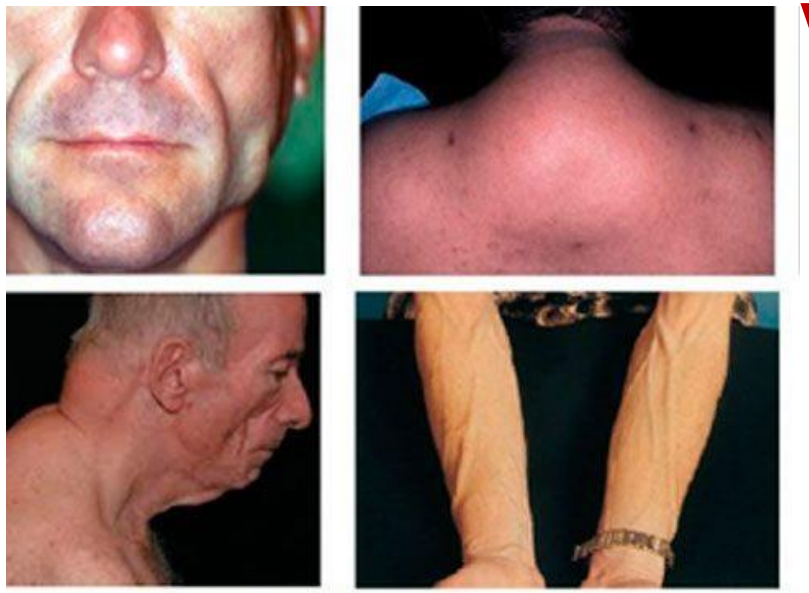
Swiss Cohort:

- 78% of deaths between 1988 and 1995 were due to AIDS-related causes.
- Between 2005 and 2009: 15 % due to AIDS related causes.

But, 16 year study amongst >380 000 PLHIV showed that although life expectancy was similar, PLHIV still live with substantially more comorbidities – specifically PLHIV were found to present with health problems 16 years earlier than their HIV- counterparts.
E.g. presented 24 years earlier with liver disease, 17 years earlier with kidney disease, and 8-9 years earlier with diabetes, cancer, and CVS disease.
(Marcus et al., CROI 2020)

ART of the 90s vs ART today!





Vs

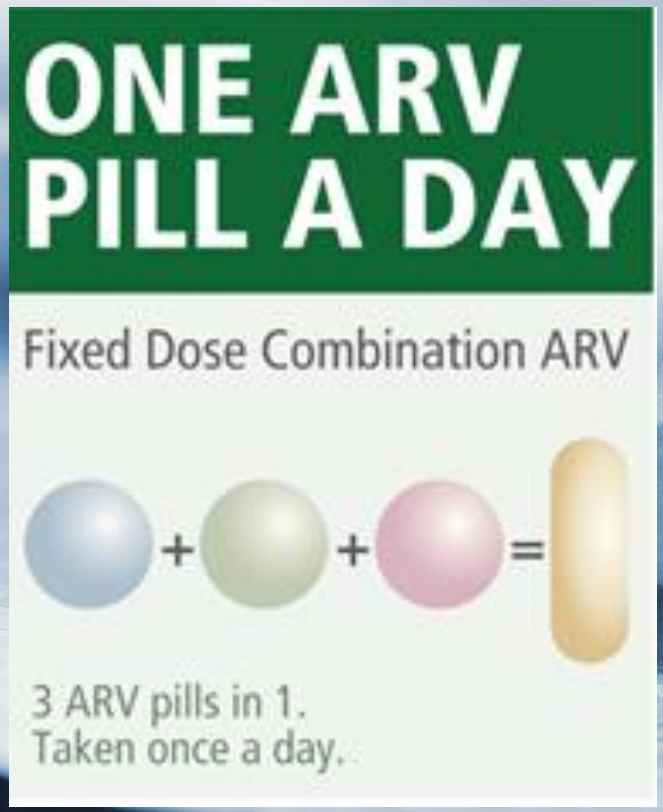
The fabulous, activist-advocate Yvette Raphael and daughter

“ My health is my wealth- living with HIV and on ART since this one was a baby. Take nothing for granted – I live every day positively!
We now run a business together!”

Triple therapy today....

- Potent Integrase inhibitor (DTG, BTG, ETV) or
- NNRTI (RPV, DOR, EFV) or
- (b)PI (DRV, LPV) and
- 2 NRTIs (TDF, 3TC, FTC)

- Magic sauce: Excellent Viral suppression, easy tolerance, high barrier to resistance
- Once per day dosing (QD)
- Single Tablet Regimen (STR)



Reasons to Consider Regimen Optimization in Setting of Viral Suppression: "STIFF Cost"

- **S**implification: reduce pill burden and/or dosing frequency; **S**witch to long-acting injectable regimen to relieve pill fatigue, decrease potential stigma or disclosure concerns associated with daily oral medications
- **T**olerability: enhance tolerability and/or decrease short- or long-term toxicity
- **I**nteractions: prevent or mitigate drug–drug interactions
- **F**ood/fluid requirements: eliminate food or fluid requirements
- **F**ertility: allow for optimal use of ART during pregnancy or in cases where pregnancy may occur
- **Cost**: reduce costs

Considerations When Switching Regimens in Virologically Suppressed Patients

Drug Resistance:

- Review ART history for possible Viral Failure
- Review all available resistance test results
- If earlier resistance uncertain, only consider switch if new regimen likely to maintain suppression of resistant virus
- Caution when switching from boosted PI to another class if full treatment/resistance history not known
- Consult an expert when switching if resistance to ≥ 1 class
- Within-class switches usually maintain virologic suppression if no resistance to drugs in that class are present

Safety:

- Review ART history for intolerance
- Must be HLA-B*5701 negative if considering ABC
- Consider drug–drug interactions with comedications

Comorbidity:

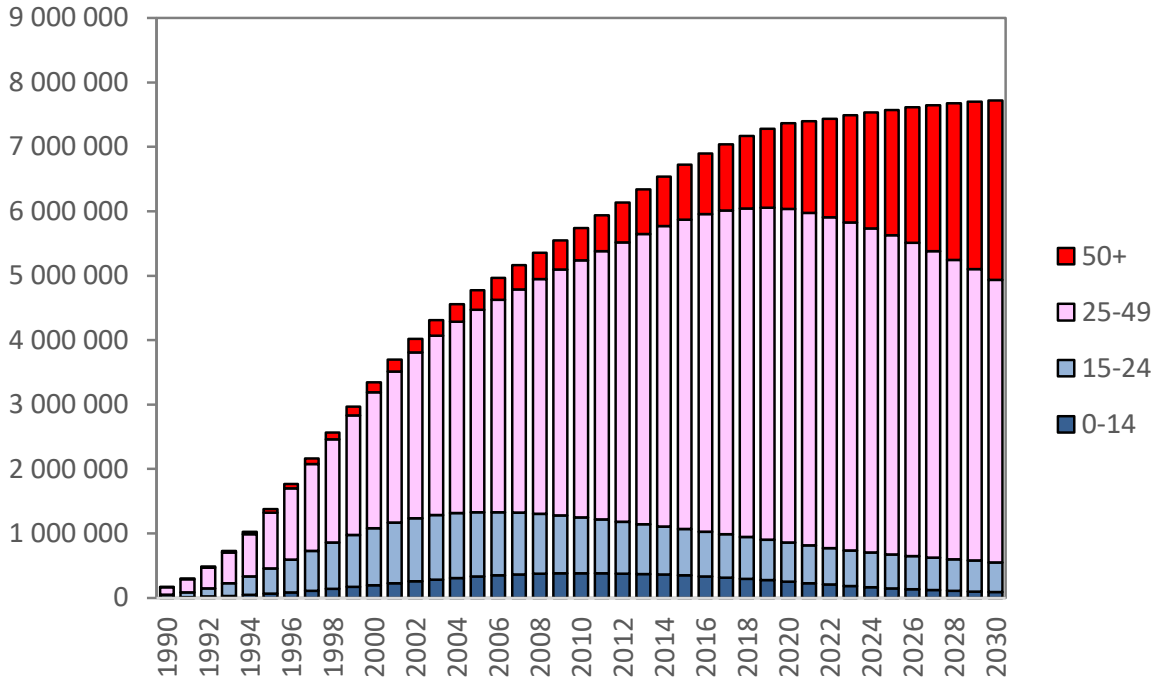
- HBV coinfection
- Cardiovascular disease or risk
- Renal function
- Bone mineral density
- Pregnancy
- Other coinfections

DHHS ART Guidelines. December 2019.

Principle to Optimizing ART in the Setting of Virologic Suppression

- *"People with HIV who have no history of drug-resistance mutations or virologic failure can likely switch to* ***any regimen that has been shown to be highly effective in ARV-naive patients"***

HIV with a touch of gray!

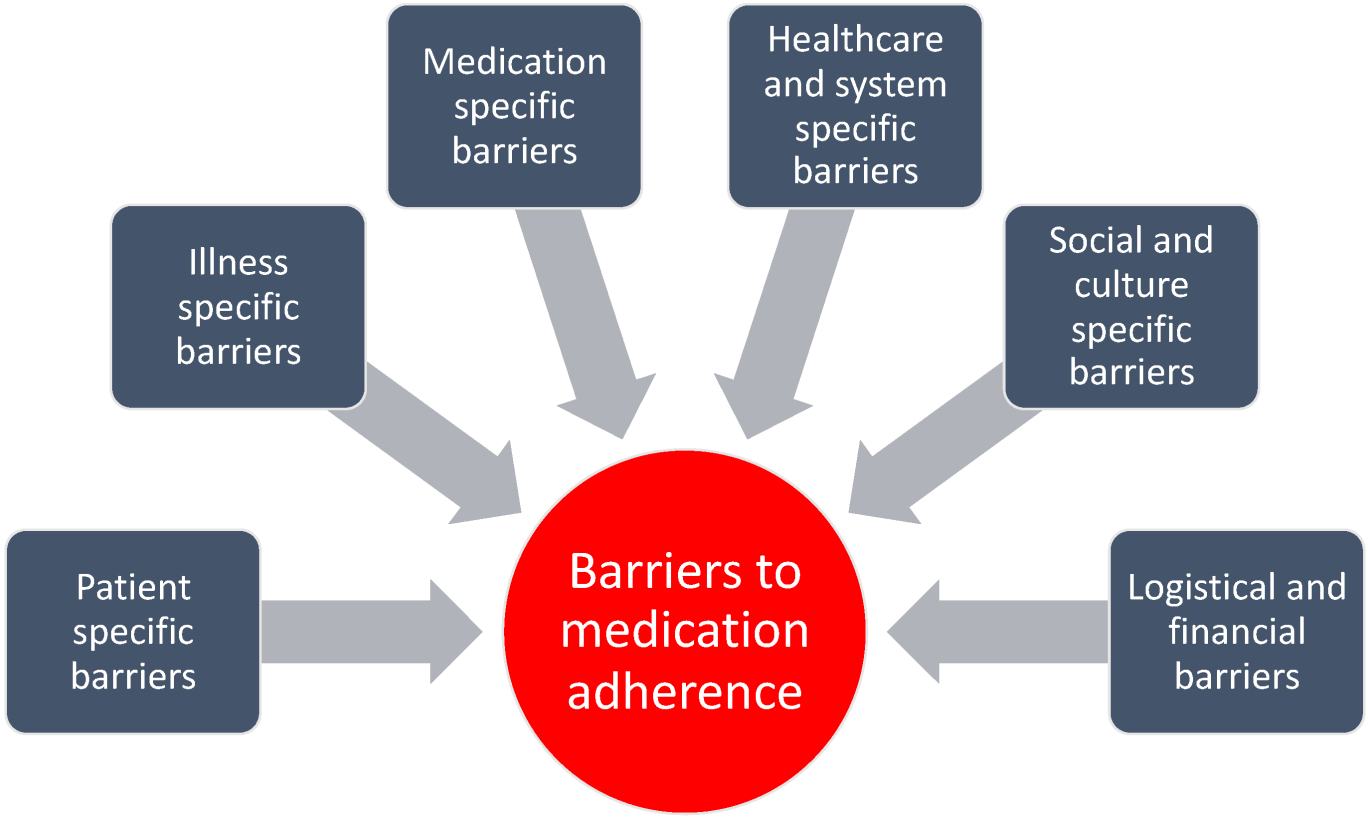


Leigh Johnson: Thembisa 4.7 model 2024

DHHS Adult and Adolescent ART Guidelines. March 2023.

But for the “Not suppressed” …..or just struggling

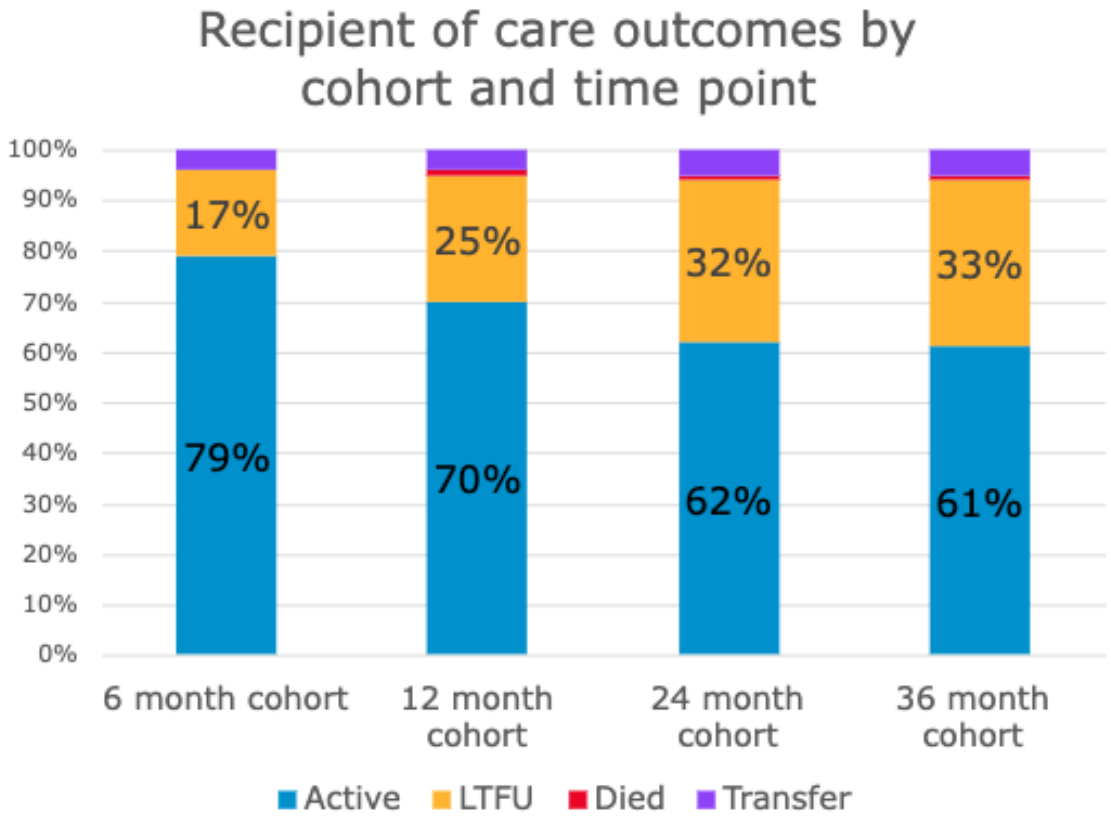
- Many people living with HIV struggle to adhere to daily oral antiretroviral treatment
- This results in inadequate viral suppression, poor outcomes and ongoing HIV transmission
- **Less frequent visits may offer a solution to adherence challenges**



Kvarnström et al. *Pharmaceutics* **2021**

AIDS 2024

Two largest challenges: Sub-optimal 12-month retention and viral suppression



- 80% of cohort has a viral load done. Of those:
  - 907,658 have a VL 50-1000 copies/mL
  - 321,462 have a VL >1000 copies/mL
- 2023 Guideline update focused on 2nd and 3rd 90s – keeping people on treatment (especially in the first 12 months) and virally suppressed

https://www.differentiatedservicedelivery.org/wp-content/uploads/5_Reengagement-satellite_Musa-Manganye_FINAL.pdf

Anna Grimsrud 2024

Revised ART & differentiated models of care (DMOC) guidelines central approach

AIDS 2024

Aim 1: Implement optimized ART regimens

- Clinical updates

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

- Person-centred service delivery updates

- Updated clinical **and** service delivery guidance at the same time
- Coordinated national technical working group
- Reviewed previous re-engagement algorithm

DMOC and ART Clinical Guidelines assume full integrated approach in South Africa

- The first time **clinical** and **service delivery** guidelines were revised together to ensure coordinated approach to of both components of HIV care

Anna Grimsrud 2024

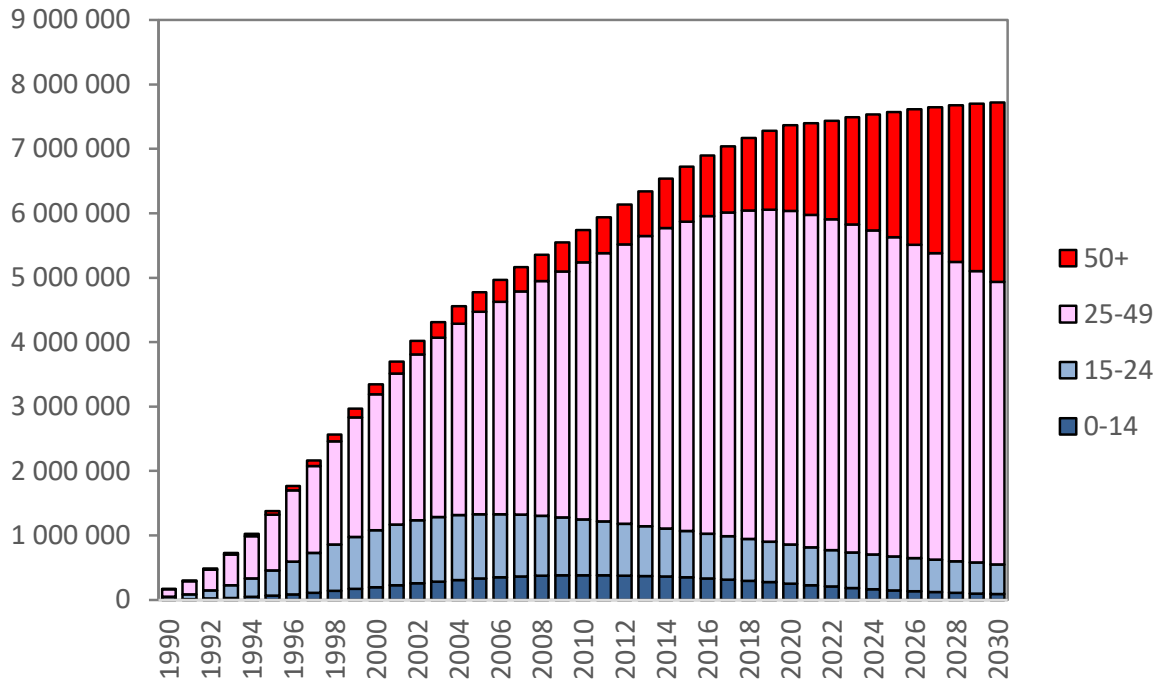
Where South African policy is “ahead” on treatment.

- **Integration**
  Adherence guidelines that address HIV alongside TB and NCDs (RPCs for chronic stable people living with HIV)

- **Earlier first viral load**
  - Taken at month 3 for action at month 4

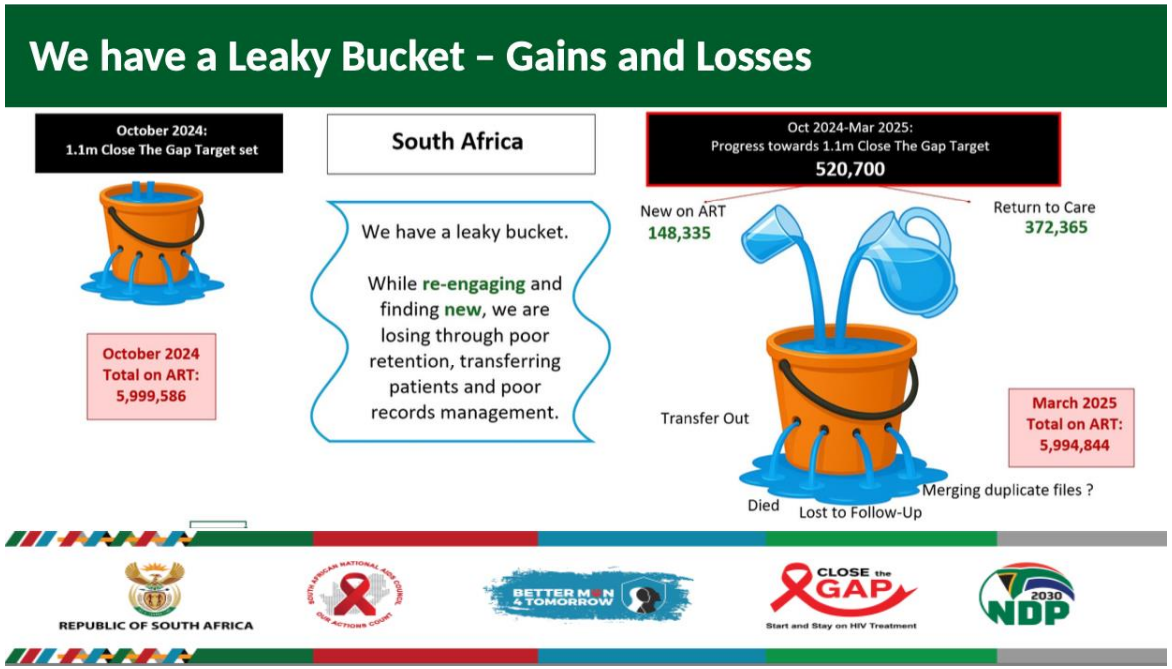
- **Differentiation at re-engagement**
  - Re-engagement algorithm

HIV with a touch of gray



Leigh Johnson: Thembisa 4.7 model 2024

Close the Gap Campaign: Find 1.1 Million



On World AIDS Day 2024, the Minister committed to 30% of eligible people receiving 6MMD by mid-2025.

Only province implementing based on emergency circular is the Western Cape (24,500 people on 6MMD)

Implementation plan for 90 facilities (10/province) to reach a target of 200,000 by 1 April 2026.

Anna Grimsrud 2024

Shift from daily to longer-acting regimens

Introducing the less frequently dosed injectables, infusibles, implantables

Oral Weekly ISL + LEN in People Virologically

i-base

On 8 June 2026, Gilead Sciences and Merck/MSD released top-line results of the phase 3 ISLEND-1 and ISLEND-2 studies using an experimental once-weekly oral formulation of islatravir 2 mg/lenacapavir 300 mg (ISL/LEN).

The press statement only noted that the primary endpoints of non-inferiority at week 48 had been met for both studies, compared to either daily Biktarvy or standard of care ART, respectively.

More detailed results will be presented at future meetings.

No unexpected side effects were reported.

Although the press release notes that results will be filed with global regulatory authorities, these are not specified.

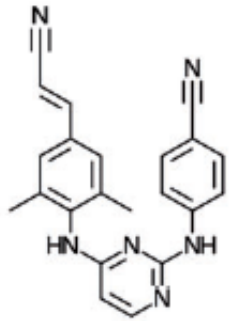
Some agencies might require longer follow-up out to 96 weeks.

HIV-1 RNA ≥50 c/mL	HIV-1 RNA <50 c/mL	No Data in Window

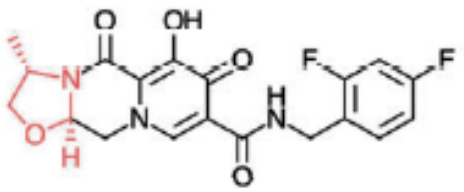
▪ 95% CI; P value	-0.04 to -0.01; .6301

Colson. CROI 2024. Abstr 208.

Rilpivirine



Cabotegravir



LA CAB/RPV completed trials

	n	Arms	Population	Eligibility
LATTE-2	286	LAI CAB/RPV 4 weekly LAI CAB/RPV 8 weekly Oral CAB +ABC-3TC OD	5 high income countries (USA/Europe)	ART naïve
FLAIR	566	LAI CAB/RPV 4 weekly Oral DTG/ABC/3TC OD	11 countries (USA/Europe/South Africa)	ART naïve
ATLAS	616	LAI CAB/RPV 4 weekly 2NRTIs+INSTI/NNRTI/PI	13 Countries (USA/Europe/ South Africa/Australia, Asia)	On ART >6 months, suppressed
ATLAS-2M	1045	LAI CAB/RPV 4 weekly LAI CAB/RPV 8 weekly	Same as ATLAS	On ART >6 months, suppressed
SOLAR*	670	LAI CAB/RPV 8 weekly Oral BIC/FTC/TAF OD	USA/Europe/ Japan	On ART >6 months, suppressed

*preliminary month 12 results presented at CROI 2023

LATTE-2 experience

- There are side-effects…but it's worth it!
- Greater confidentiality and privacy
- Psychosocial and emotional benefits
  - ART is a daily unwanted reminder of HIV

PROVIDERS:

- Does not eliminate all adherence barriers
- Concern about resistance and the tail
- Concern about clinic flow

PLOS ONE

RESEARCH ARTICLE

Experiences with long acting injectable ART: A qualitative study among PLHIV participating in a Phase II study of cabotegravir + rilpivirine (LATTE-2) in the United States and Spain

Deanna Kerrigan[1☯*], Andrea Mantsios[1☯], Miguel Gorgolas[2], Maria-Luisa Montes[3], Federico Pulido[4], Cynthia Brinson[5], Jerome deVente[6], Gary J. Richmond[7], S. Wilson Beckham[1‡], Paige Hammond[1‡], David Margolis[8], Miranda Murray[9]

"In reality, taking the pill everyday keeps it [HIV] present . . .and the shot is just once a month. . .you remember it when you come in and the rest of the time you can basically forget it"

DHHS Guideline Recommendations: Optimizing ART in the Setting of Virologic Suppression

- **LA injectable CAB + RPV is an optimization option** for patients who:
  - Are **engaged** in care
  - Have experienced **3-6 mo of viral suppression on oral therapy**
  - Agree to **every 1- to 2-mo clinic visits**
- No history of resistance to regimen components

DHHS Adult and Adolescent ART Guidelines. March 2023.

FDA-Approved Use of LA Cabotegravir + Rilpivirine

Optimal Candidates

- Virologically suppressed on oral regimen for at least 3-6 mo
- Any renal function
- Engaged with their healthcare
- Agree to make frequent clinic visits

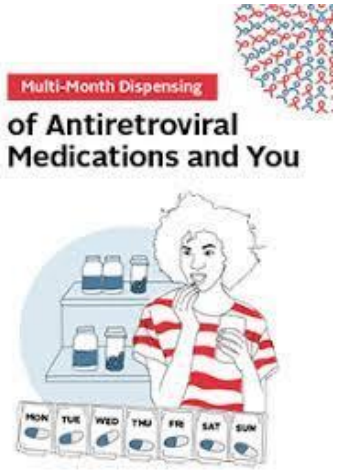
Contraindications

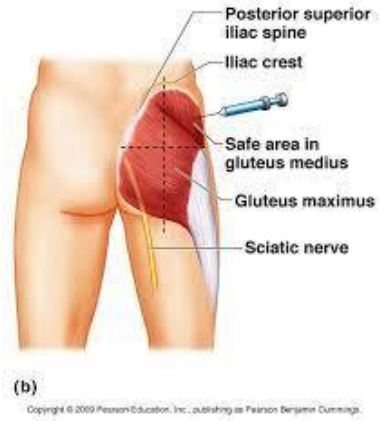
- Prior INSTI or NNRTI resistance (except K103N)
- Prior virologic failure
- Chronic HBV infection (active or occult)

Cabotegravir extended-release injectable suspension; rilpivirine extended-release injectable suspension PI. Updated December 2023.
DHHS Guidelines. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV. May 2023.

Challenges for injectable c

- Health system challenges
  - rewind on multi month dispensing
- Identification of eligible patients
  - stable? suppressed?
- Logistical requirements
  - cold chain
- Patients' management challenges
  - re-medicalization; stopping; travelling
- Provider and staff training
  - IMI administration
- Consumer challenges
  - stopping; travelling





HHS Public Access
Author manuscript
Curr Opin HIV AIDS. Author manuscript; available in PMC 2018 March 12.

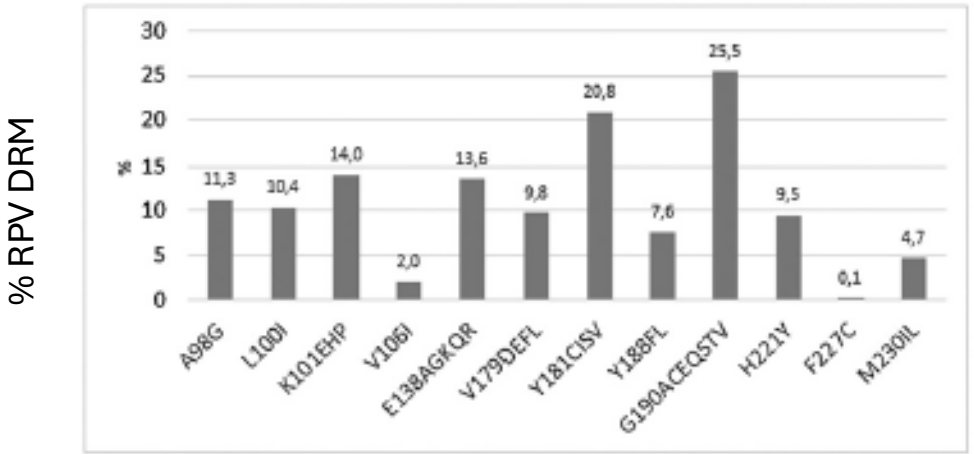
Published in final edited form as:
Curr Opin HIV AIDS. 2015 July ; 10(4): 282–289. doi:10.1097/COH.0000000000000158.

Implementation challenges for long-acting antivirals as treatment

Diane Havlir and Monica Gandhi
Department of Medicine, HIV/AIDS Division, University of California, San Francisco, San Francisco, California, USA

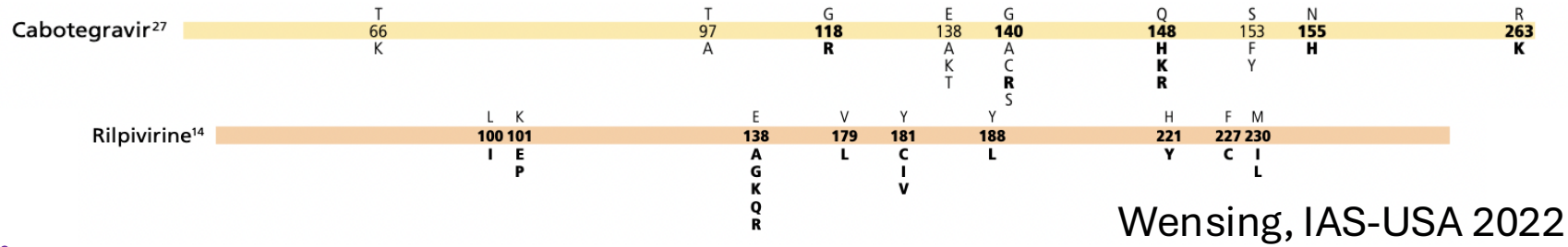
Impact of rilpivirine cross-resistance on long-acting cabotegravir-rilpivirine in low and middle income countries

12% Naïve and 74% Failures



Steegen K et al AIDS2023

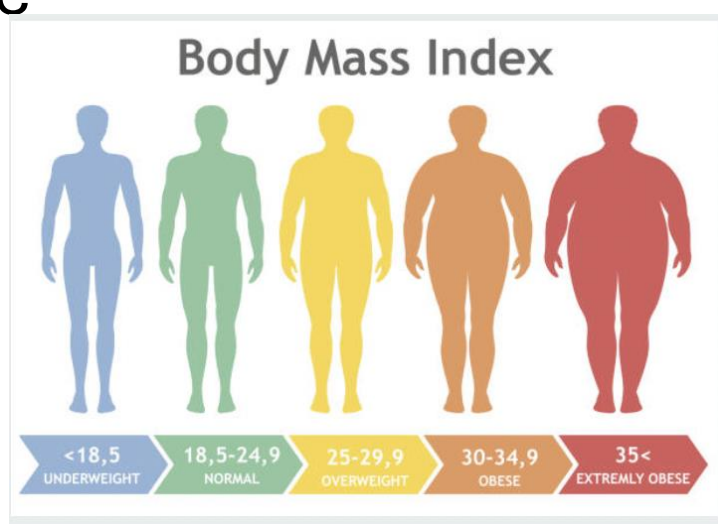
Challenges



Wensing, IAS-USA 2022

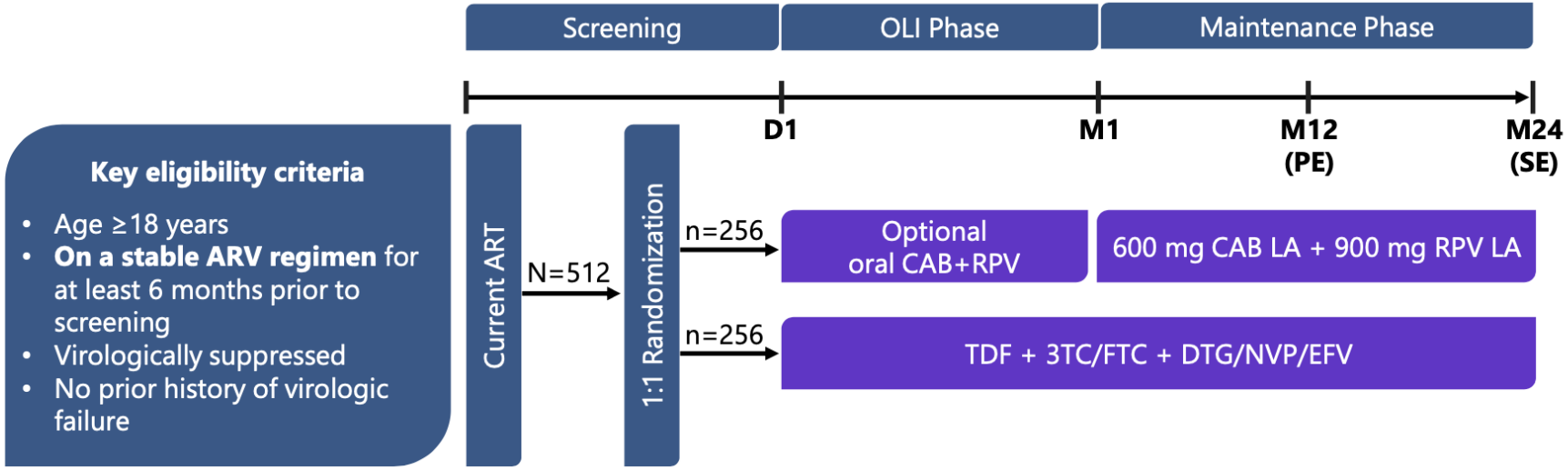
Risks of resistance:

- Transmitted NNRTI mutations (countries with high NNRTI exposure): RPV RAMs a known risk for failure; no baseline resistance testing.
- High BMI: 35.2% of SA women of childbearing age were obese in 2017. (Nglazi, BMC Health 2022)
- Covering the very long tail with adherence to oral therapy (CAB/RPV = 48 weeks; LEN = 72 weeks)



CARES: Study Design
(Kenya, South Africa, Uganda)

Objective: Efficacy and safety in adults on stable cART in SSA



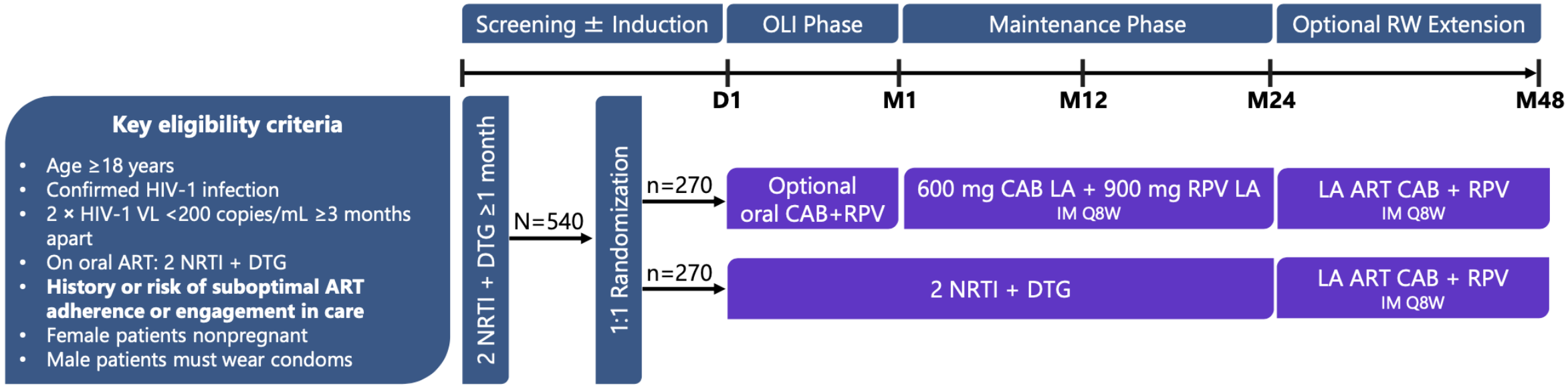
Primary outcome

- Noninferiority of CAB + RPV LA every 2 months vs daily cART over 12 months in a resource-limited setting

- **97% viral suppression at week 96.**
- **1.6% with CVF (n=4) – three resuppressed on TLD**
- **Increased treatment satisfaction; Well tolerated**

IMPALA: Study Design
(Kenya, South Africa, Uganda)

Objective: Efficacy and retention in care for adults with a history or risk of suboptimal adherence or engagement in SSA



Primary outcome

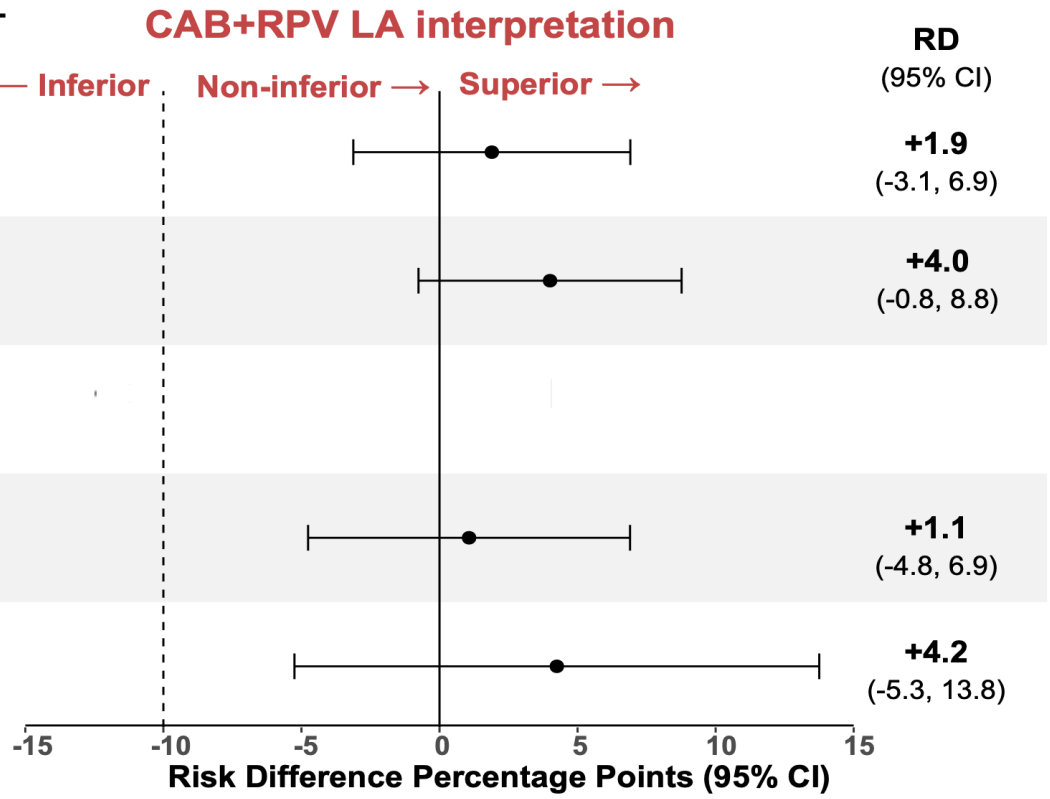
- Noninferiority of CAB + RPV LA every 2 months vs daily cART over 12 months in people with a history or risk of suboptimal adherence

IMPALA outcomes

Primary outcome at Week 48

- 99.0% retention. 98% of 2159 injections given within window

HIV-1 VL <50 c/mL	CAB+RPV % (n/N)	Oral ART % (n/N)	RD (95% CI)
Primary analysis (ITT-e)	**91.0%** (244/268)	**89.2%** (240/269)	**+1.9** (-3.1, 6.9)
Per protocol analysis	**93.9%** (229/244)	**89.9%** (223/248)	**+4.0** (-0.8, 8.8)
ITT-e subgroup analysis:			
Body mass index <30	**90.0%** (180/200)	**89.0%** (194/218)	**+1.1** (-4.8, 6.9)
Body mass index ≥30	**94.1%** (64/68)	**90.2%** (46/51)	**+4.2** (-5.3, 13.8)



High efficacy: CAB/RPV non-inferior to DTG-based therapy in an African population with prior sub-optimal HIV control

No baseline resistance testing.

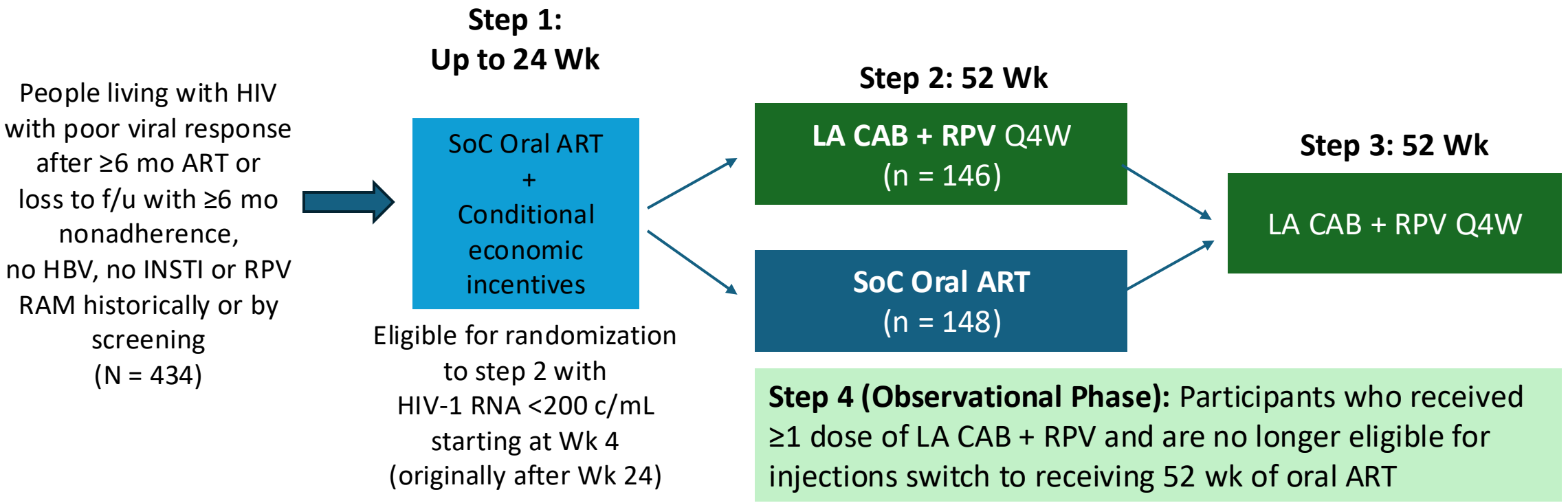
5 VF: <2% - with DTG resistance; all resuppressed (4 on TLD, 1 on PI/r).

Studies of LA CAB + RPV Treatment in People With Adherence Challenges or Viremia

- LATITUDE Study (ACTG A5359)
- OPERA
- WARD 86
- Other real world experiences ….

ACTG A5359 LATITUDE: LA ART as a Potential Tool for People With Challenges to Oral ART

- Prospective, randomized, open-label phase III trial



Rana. CROI 2024. Abstr 212.

ACTG A5359 LATITUDE: Efficacy Outcomes

Primary Outcome

Secondary Outcomes

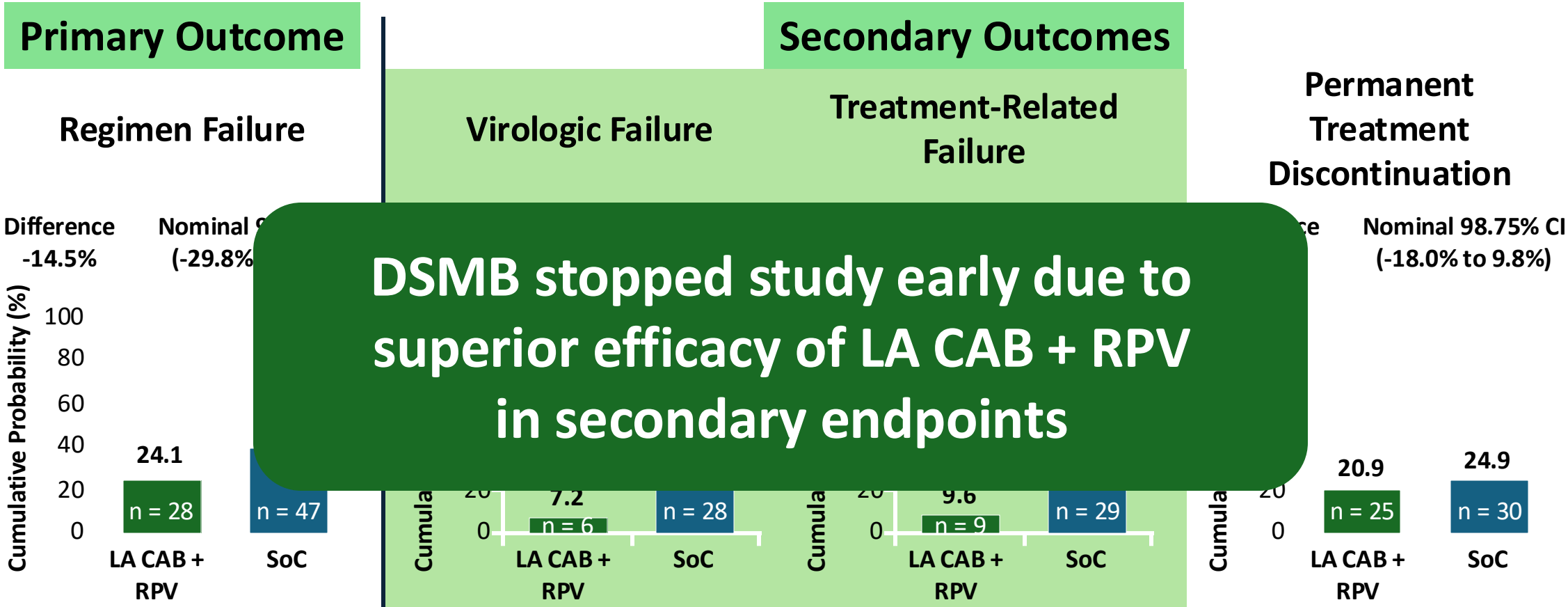
Regimen Failure

Virologic Failure

Treatment-Related Failure

Permanent Treatment Discontinuation

DSMB stopped study early due to superior efficacy of LA CAB + RPV in secondary endpoints



1 additional virologic failure after Wk 24 included in secondary endpoints, but not primary

Rana. CROI 2024. Abstr 212.

Table. Characteristics of Individuals With and Without Viremia (≥30 Copies/mL) Initiating Cabotegravir/Rilpivirine

Characteristic	No. (%)		
	Viremia (n = 129)	No viremia (n = 241)	Overall (n = 370)
Age at referral, median (range), y	48.0 (25.0-67.0)	44.0 (21.0-70.0)	45.0 (21.0-70.0)
Race and ethnicity[a]			
American Indian	3 (2.3)	9 (3.7)	12 (3.2)
Asian	6 (4.7)	23 (9.5)	29 (7.8)
Black	32 (24.8)	53 (22.0)	85 (23.0)
Mixed	3 (2.3)	4 (1.7)	7 (1.9)
White	56 (43.4)	95 (39.4)	151 (40.8)
Not specified	29 (22.5)	57 (23.7)	86 (23.2)
Gender[a]			
Cisgender men	111 (86.0)	191 (79.3)	302 (81.6)
Nonbinary	1 (0.8)	6 (2.5)	7 (1.9)
Transgender women	14 (10.9)	42 (17.4)	56 (15.1)
Other	1 (0.8)	1 (0.4)	2 (0.5)
Missing	2 (1.6)	1 (0.4)	3 (0.8)
Housing			
Housing unstable (SRO, shelter, outdoors, vehicle)	67 (51.9)	97 (40.2)	164 (44.3)
Stable (rent or own)	62 (48.1)	144 (59.8)	206 (55.7)
$CD4^+$ count at cabotegravir/rilpivirine initiation, cells/mm^3			
≥200	30 (23.3)	88 (36.5)	118 (31.9.)
<200	88 (68.2)	106 (44.0)	194 (52.4)
Missing	11 (8.5)	47 (19.5)	58 (15.7)
Substance use			
No current or past substance use	51 (39.5)	148 (61.4)	199 (53.8)
Current or past substance use	78 (60.5)	93 (38.6)	171 (46.2)

Abbreviation: SRO, single-room occupancy.

[a] Participants selected their race and ethnicity and their gender as part of the medical record, with options defined by the health system, and classified by the investigators. Race and ethnicity were assessed to track disparities in achieving virologic suppression in each group.

Research Letter

FREE

HIV Viral Suppression With Use of Long-Acting Antiretroviral Therapy in People With and Without Initial Viremia

Matthew A. Spinelli, MD, MAS[1]; Megan J. Heise, PhD[1]; Nathanial Gistand, BS[1]; et al

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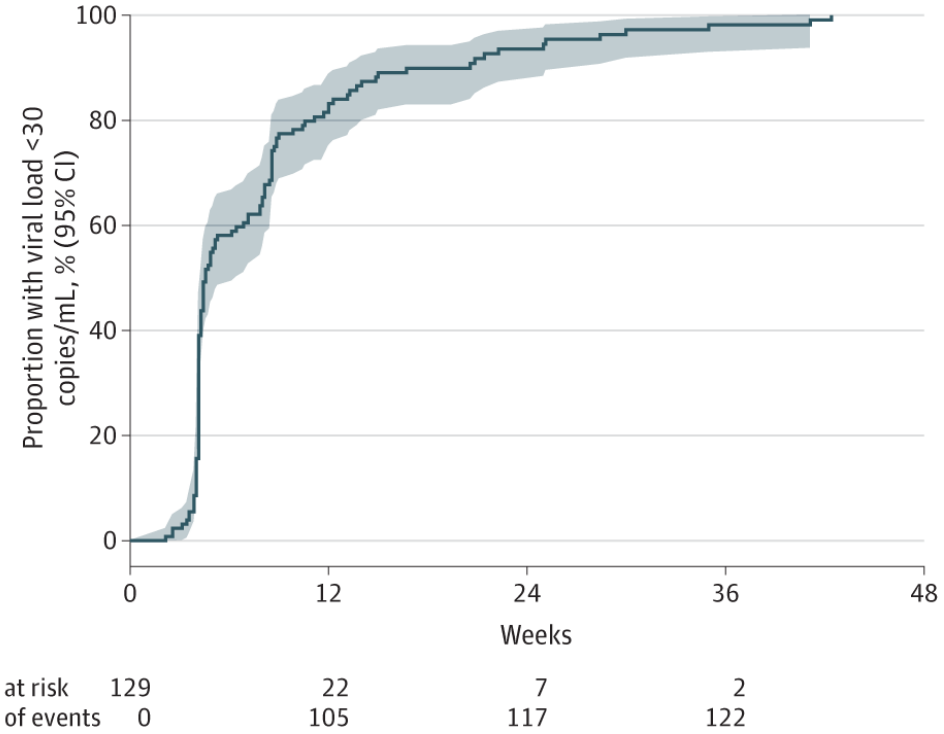
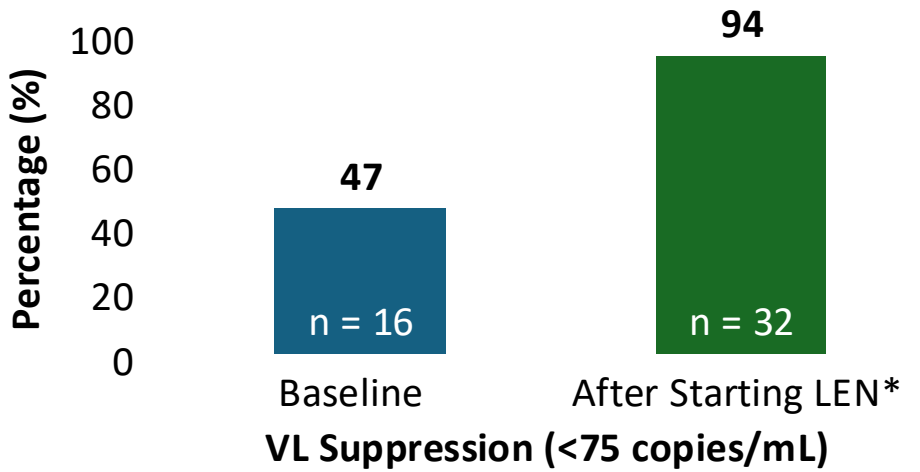


Time to Achieve a Viral Load Less Than 30 Copies/mL for People With HIV Starting Cabotegravir/Rilpivirine With Viremia. Time to achieve a viral load less than 30 copies/mL is plotted on a Kaplan-Meier curve for people with HIV starting cabotegravir/rilpivirine with viremia (viral load ≥30 copies/mL). Shaded region indicates 95% CIs. Events indicate the number of individuals who achieved virologic suppression at each point. No individuals achieved virologic suppression past 43 weeks.

Off-Label Use of LA CAB (± RPV) + LEN: Case Series

- LA CAB + RPV only recommended as a complete LA ART regimen, but not approved by WHO in LMICs
  - Many LMICs have >10% resistance to NNRTIs
  - Disparities in availability of LA ART
- Case series of 4 US clinics where use of LA CAB (± RPV) + LEN off-label is occurring for selected people due to adherence challenges with oral ART (N = 34)
  - Most common reason for off-label combination use was NNRTI mutations
- Call for trial to study LA CAB + LEN in those with NNRTI resistance worldwide

Patient Characteristics/Results	All Patients (N = 34)
Male/cis or trans female, %	76/24
Black/Latino/a, %	41/38
CAB Q4W/CAB Q8W, %	29/71
Reason(s) for using LA CAB (± RPV) + LEN, n (%) ▪ Documented/suspected NNRTI mutations ▪ Integrase mutations ▪ High VL ▪ Cont. viremia on LA CAB + RPV alone	 21 (59) 5 (15) 6 (18) 4 (12)



*Suppression occurred a median of 8 (4-16) wk after starting LEN.

Gandhi. CROI 2024. Abstr 629. who.int/publications/i/item/9789240086319

Updated IAS-USA Recommendations for LA CAB + RPV March 1, 2024

- *When supported by **intensive follow-up** and **case management services**, injectable LA CAB + RPV may be **considered for people with viremia** who meet the criteria below when **no other treatment options are effective** due to a patient's persistent inability to take oral ART:*
  - ***Unable to take oral ART** consistently despite extensive efforts and clinical support*
  - ***High risk of HIV disease progression** (CD4 cell count <200/µL or history of AIDS-defining complications)*
  - ***Virus susceptible to both CAB and RPV***
- *If applicable, patients should also be referred for treatment of substance use disorder and/or mental illness.*

Sax. JAMA. 2024;[Epub].

WHO recent guidance

Dual ARV oral regimens:

Dolutegravir (DTG) + 3TC can be used for treatment simplification for adults and adolescents with undetectable HIV viral load on three-drug antiretroviral regimens and without active hepatitis B infection. (Conditional recommendation, moderate-certainty evidence)

Long-acting injectable regimens:

Long-acting injectable cabotegravir + rilpivirine can be used as an alternative switching option for adults and adolescents with undetectable HIV viral load on oral ART and without active hepatitis B infection.(Conditional recommendation, moderate-certainty evidence)

High Acceptability and Perceived Feasibility of Long-Acting Injectable Antiretroviral Treatment Among People Living with HIV Who Are Viremic and Health Workers in Uganda

Caitlin E. Kennedy, PhD, MPH,[1] Tongying Zhao, MSPH,[1] Anh Van Vo, MSPH,[1] Rosette Nak
Proscovia Nabakka, BA,[2] Jade Jackson, MSW,[3] Joseph G. Rosen, PhD, MSPH,[1] Larry W. Cha
Steven J. Reynolds, MD, MPH,[4,5] Thomas C. Quinn, MD, MS,[5] Gertrude Nakigozi, MBchB
Godfrey Kigozi, MBchB, MPH, PhD,[2] Joseph Kagaayi, MBchB, MPH, PhD,[2] Fred Nalugod
William G. Ddaaki, MSc,[2] M. Kate Grabowski, PhD, ScM,[3] and Neema Nakyanjo,

Acceptability and feasibility of long-acting injectable antiretroviral therapy for HIV-infected persons who inject drugs in Vietnam: a qualitative study

Sarah E. Rutstein,[a]* Adams L. Sibley,[b] Hanna E. Huffstetler,[b] Trang Thu Do Nguyen,[c] Ha Viet Tran,[c] Giang Le Minh,[c] Teerada Sripaipan,[b] Minh Nguyen,[b] William C. Miller,[d] Joseph J. Eron,[a] Cynthia L. Gay,[a] and Vivian F. Go[b]

RESEARCH

Key informant views on potential acceptability and feasibility of long-acting antiretroviral treatment for HIV in Kenya

Anne Kaggiah[1*], Catherine N. Maina[1], John Kinuthia[1,2], Douglas Barthold[3], Brett Hau
Jane M. Simoni[5] and Susan M. Graham[2,6,7]

RESEARCH ARTICLE

Acceptability of long-acting antiretroviral therapy among people living with HIV who use drugs in Vancouver, Canada: A qualitative study

Koharu Loulou Chayama[1,2], Cara Ng[1], Isabella Brohman[1], Manal Mansoor[1], Will Small[1,2], Morgan Philbin[4,5], Alexandra B. Collins[6], Ryan McNeil[1,7,8]*

ORIGINAL PAPER

Factors Associated with Preferences for Long-Acting Injectable Antiretroviral Therapy Among Adolescents and Young People Living with HIV in South Africa

Elona Toska[1,2,3,8] · Siyanai Zhou[1,4] · Jenny Chen-Charles[3] · Lesley Gittings[1,5] · Don Operario[6] · Lucie Cluver[3,7]

MOCHA/IMPAACT2017 *(Lowenthal et al, 2024)*

- 12 ers did in-depth interviews
- **CA**
  - ly pill-taking
  - st in the provider the big factor

> *"Take the shot once a month, be over with it and you can actually live a normal life instead of taking pills in front of people every day or looking at yourself like you're not a real human or something."*

- **ADOLESCENTS:**
  - Not having to worry about hiding pills
  - Concern about ability to maintain injec
  - Many would prefer the injection to be g

> *"Especially for that teenager who's already not liking to be reminded that they're HIV positive. Then actually having to go to the clinic every month would not be necessarily a positive experience for them."*

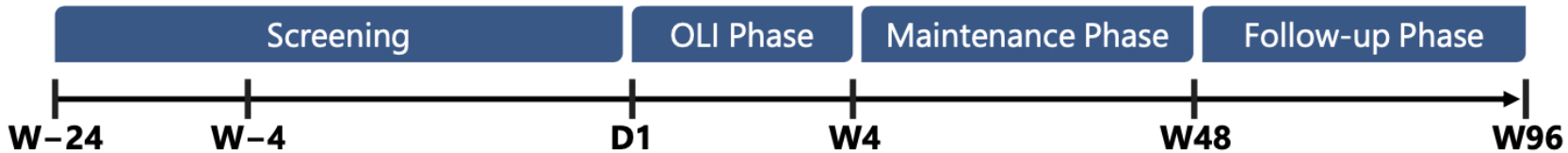
Adolescents and ART

- In RSA : The number of adolescents on ART has rapidly increased.
- Adolescents have the lowest adherence rates of all age groups.
- Only 23.2% of adolescents were fully virally suppressed in the preceding year
- Adolescents continue to perform poorly on the UNAIDS 95-95-95 targets (compared to adults)
- For adolescents, significant barriers to HIV treatment, retention and adherence include stigma, fear of being judged, fear of disclosure, treatment fatigue, adolescent lifestyle

(Maskew et al., Lancet HIV. 2019) *(Lowenthal E et al., Lancet Infect Dis 2014)* *(Haghighat R et al., BMC Infect Dis. 2021)* *(Enane LA et al., JVE, 2018)* *(Hlope LD et al., PONE, 2023)*

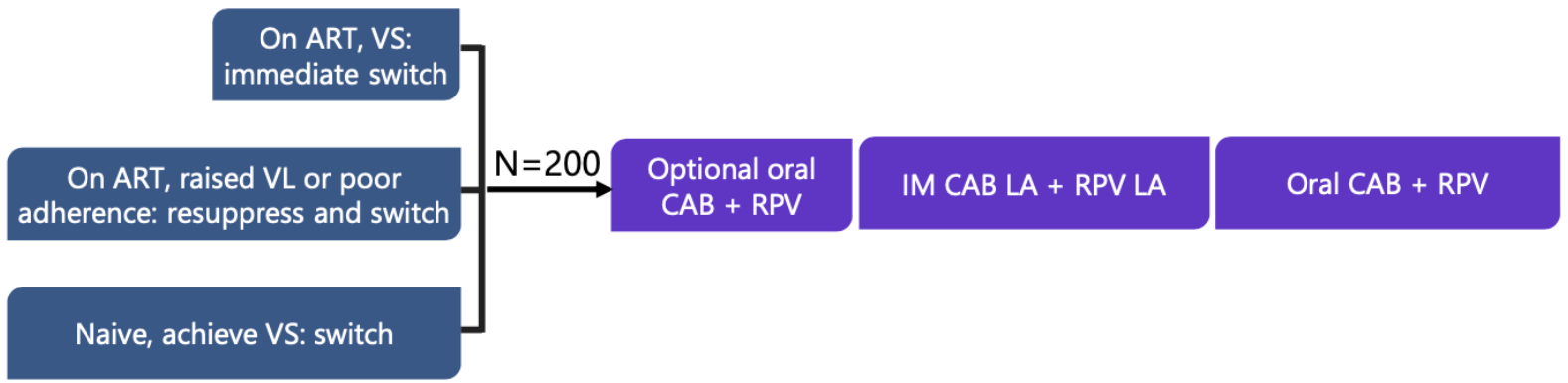
AFINAty: Study Design
(South Africa)

Objective: Effectiveness, acceptability, and feasibility of community AYA implementation in SSA



Key eligibility criteria

- HIV-1 positive
- **Age 12–24 years**
- Clinically well (no current HIV-related illnesses)
- Virologically suppressed

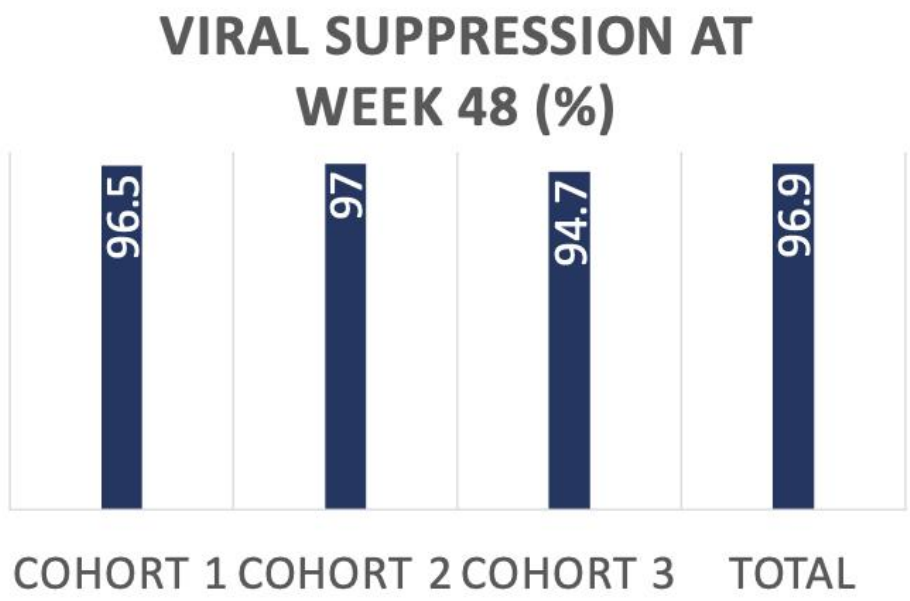


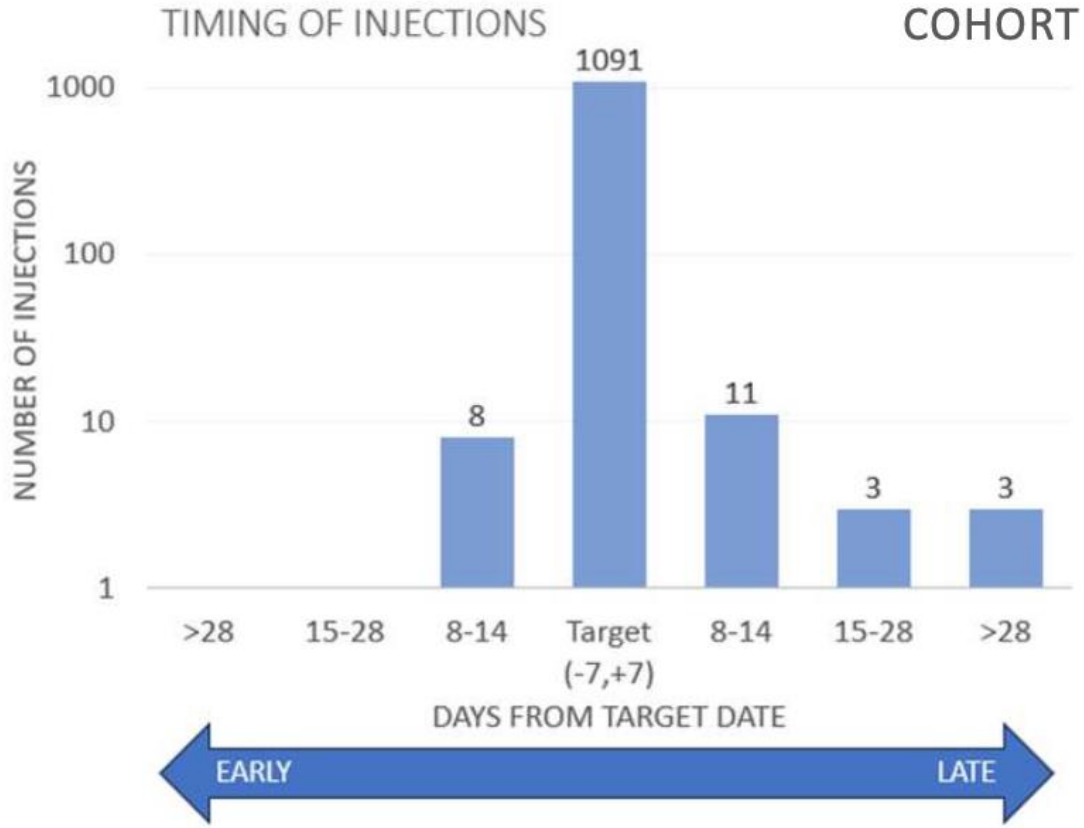
Primary outcomes

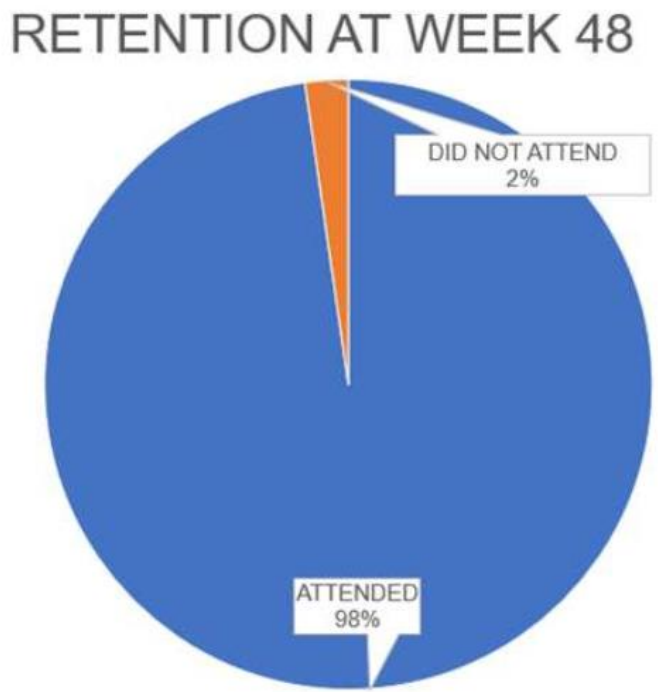
- Acceptability and tolerability of IM delivery
- Feasibility of IM delivery in a community setting
- Adherence

AFINAty outcomes

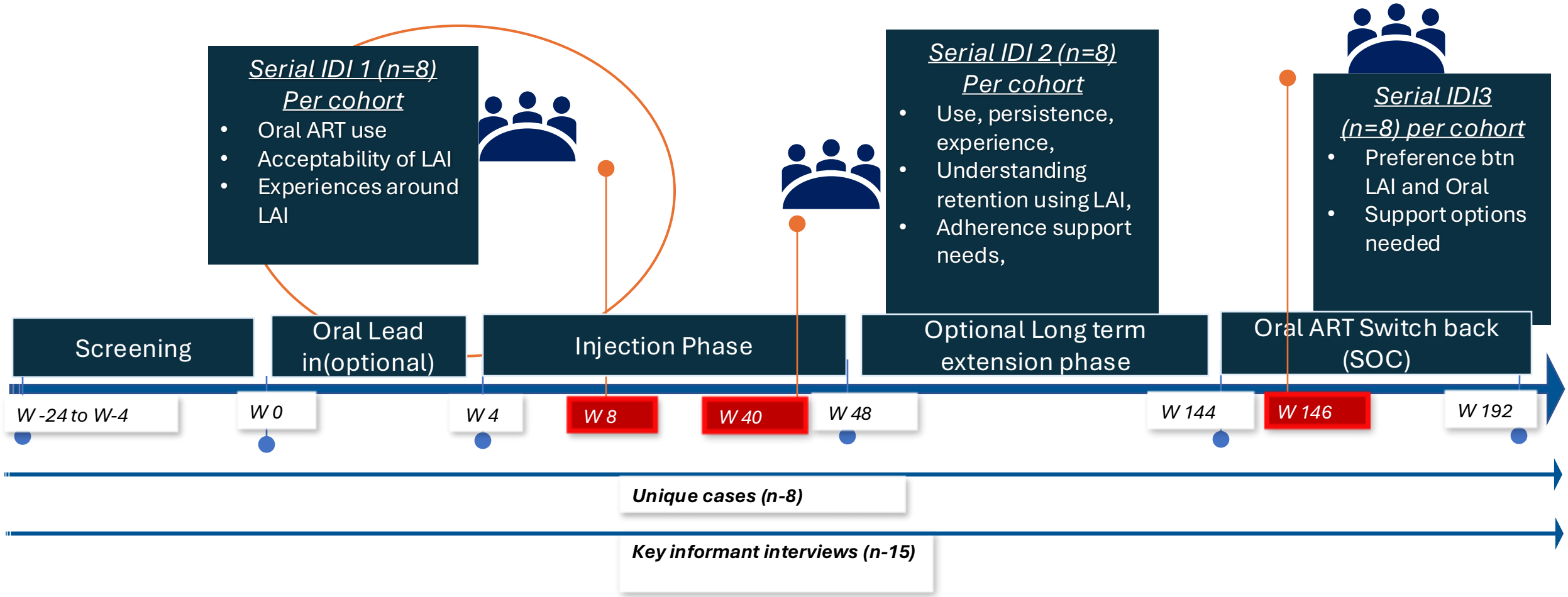
Age & gender	Cohort 1	Cohort 2	Cohort 3
Total	59	35	40
Female sex at birth: n(%)	37 (63.8)	15 (42.86)	31 (81.6)
Age (years): mean (SD)	19.1 (15.7-22.5)	19.3 (16.5-22.2)	20.3 (18.3-22.4)
Under 18 years: n(%)	18(31)	9(25.1)	4 (10.3)







AFINAty: Qualitative Study Design



Cohort summary narratives

Cohort 1: VL suppressed adolescents

- Ages 13-24 years
- Majority living with perinatally acquired HIV.
- Long history of treatment (average 8 years).
- *Consistently taking their medication for better health.*

Cohort 2: Adolescents with adherence challenges

- Ages 15-24 years
- Majority living with perinatally acquired HIV
- Long history of treatment (average 13 years)
- *Struggling with medication due to fear of judgement, stigma and disclosure.*

Cohort 3: ART naïve adolescents

- Ages 17-23 years
- Mostly sexually acquired HIV
- Treatment naïve
- *Struggling to balance their new diagnosis, its complications, and establishing a schedule for oral ART.*

AFINAty: Qualitative findings

- Overwhelmingly acceptable across all cohorts
- Side-effects described as minor compared to the burden of daily treatment

"I chose injectables because I was tired of taking medication."
(22 years, Female, Cohort 1, on ART for 13 Years)

"What I like about the injection is that you don't have to keep being reminded about the pills, it's just in your body always." (Male, 20 years, Cohort 3)

Cohort 1 (VS switch): Living freely as if you were HIV negative

- Injectables simplified their lives
  - Removes constant reminder of illness
  - Enables easier planning of routine
  - Alleviates burden on self and family

"I like the fact that I can be stress free…I don't have to worry about pills. So ja, it's just one injection, actually two, then I'm done."
(16 years, Male, Cohort 1)

So, the injection would just minus everything [takes away these burdens completely]. So I am just living fully now."
(23 years, Male, Cohort 1)

Cohort 2 (Struggling to suppress): The injection is discreet

- Daily pill-taking is visible – persistent concerns about disclosure
- Significant emotional and logistical stress
- Routine activities require planning

The fact that I no longer have to hide myself in a certain place or go to the bathroom to take my medication, among other things.
(25 years, Male, Cohort 2)

"If there is noise then obviously people will think that you are carrying pills, especially my friends. So, the injection is better because you don't have to carry anything and there won't be any sound "
(20 years, Female, Cohort 2)

Cohort 3 (Naïve, suppress, start): Navigating life with HIV

- Injections remove the additional worry of remembering to take a pill, while adjusting to life with HIV.
- Emotional and practical challenges of establishing a new routine
- Injections offer a sense of control and stability

"When I was still taking the pills it was hard because no one at home knew…I had to look and make sure that when I went to go fetch them, no one saw me." (23 years, Male, Cohort 3, on ART for ≤6 months)

"The injection allows you to chill. With the pills, I have to wake up every day at eight. I have to be worried about the pills. So I like that the injection doesn't have that. I get my injection and I'm good." (17 years, Female, Cohort 3, on ART for ≤6 months)

In summary

- An additional tool to achieve durable viral suppression as well as healthy wellbeing is to add long-acting treatment regimens to our HIV-treatment toolkit LAI treatment does not only have medical and logistical benefits
- It improves psychological well-being and fosters a sense of normalcy
- LAI does not address all adherence issues and may not be feasible or suitable for all populations
- But is possible for patients who prefer non daily, non-pill options
- And an option for patients who struggle with logistics of daily pills…..
- Additional new 2 drug regimens with novel mechanisms of action are in the pipeline.
- As always – affordability and access will be key to success!

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The AFINAty site team
The AFINAty participants

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