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Session 2A
2.3 Re-engagement and AHD

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Key global statistics for Advanced HIV disease and opportunistic infections

630,000

AIDS-RELATED DEATHS IN 2022

>20-30%

AHD AT BASELINE, SOMETIMES HIGHER (UPTO 50%)

187,000

DEATHS FROM TB AMONG PLHIV IN 2021

112,000

DEATHS FROM CRYPTOCOCCAL INFECTION IN 2021

380,000

AIDS-RELATED DEATHS IN THE WHO AFRICAN REGION

1.5M
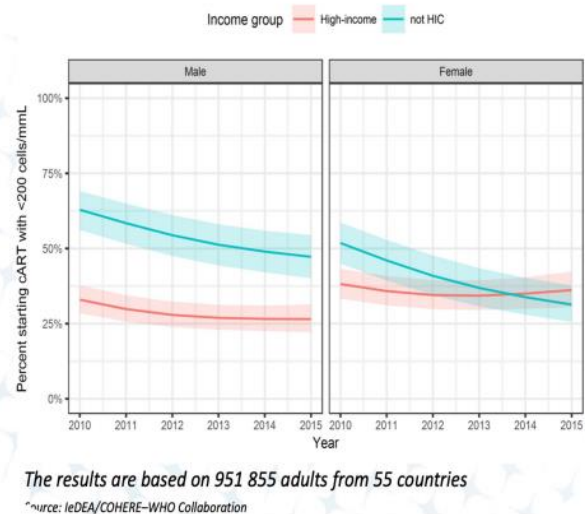
CHILDREN LIVING WITH HIV
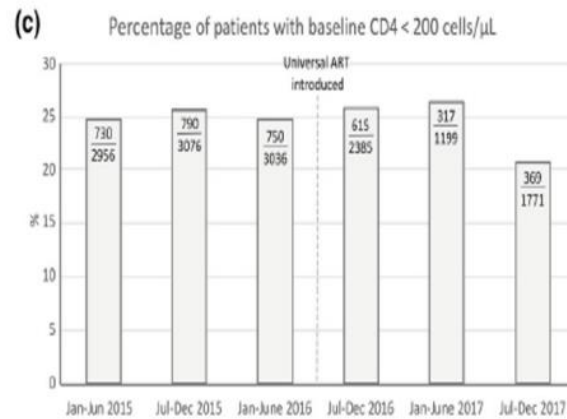
84,000

AIDS-RELATED DEATHS IN CHILDREN WITH HIV

2.1M

ADULTS LIVING WITH AHD in SSA

Despite scaleup of HIV treatment, large cohort of AHD

The results are based on 951 855 adults from 55 countries
Source: IeDEA/COHERE–WHO Collaboration

38% AHD

(from 55 countries)

25% AHD

(Botswana 2015-18)

36-37% AHD

(RSA and Kenya)

IedeA/COHERE collaboration, 2016
Lemme HIV Med 2020
Brennan, JIAS 2019
Huerga, OFID 2021

Estimates of AHD (PHIA surveys)

- Rates higher in men, ages 30-49, and urban residence

Stezle et al 2023
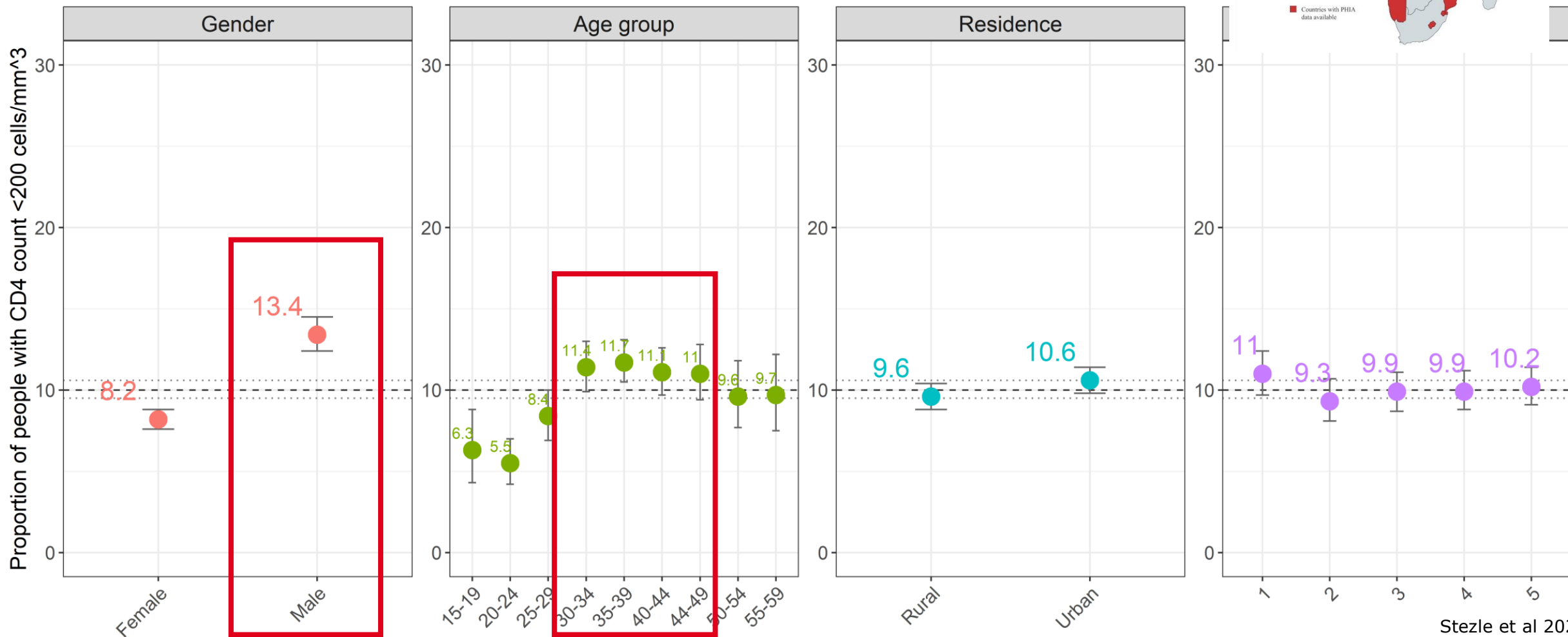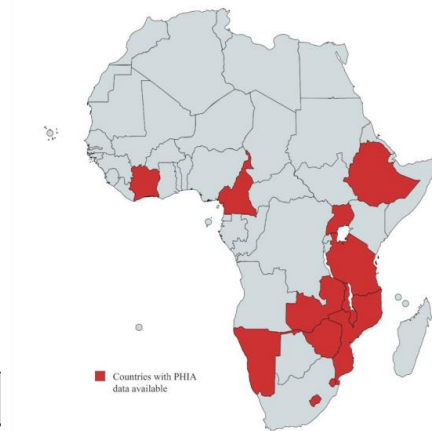
AHD by the HIV testing and treatment cascade, by gender

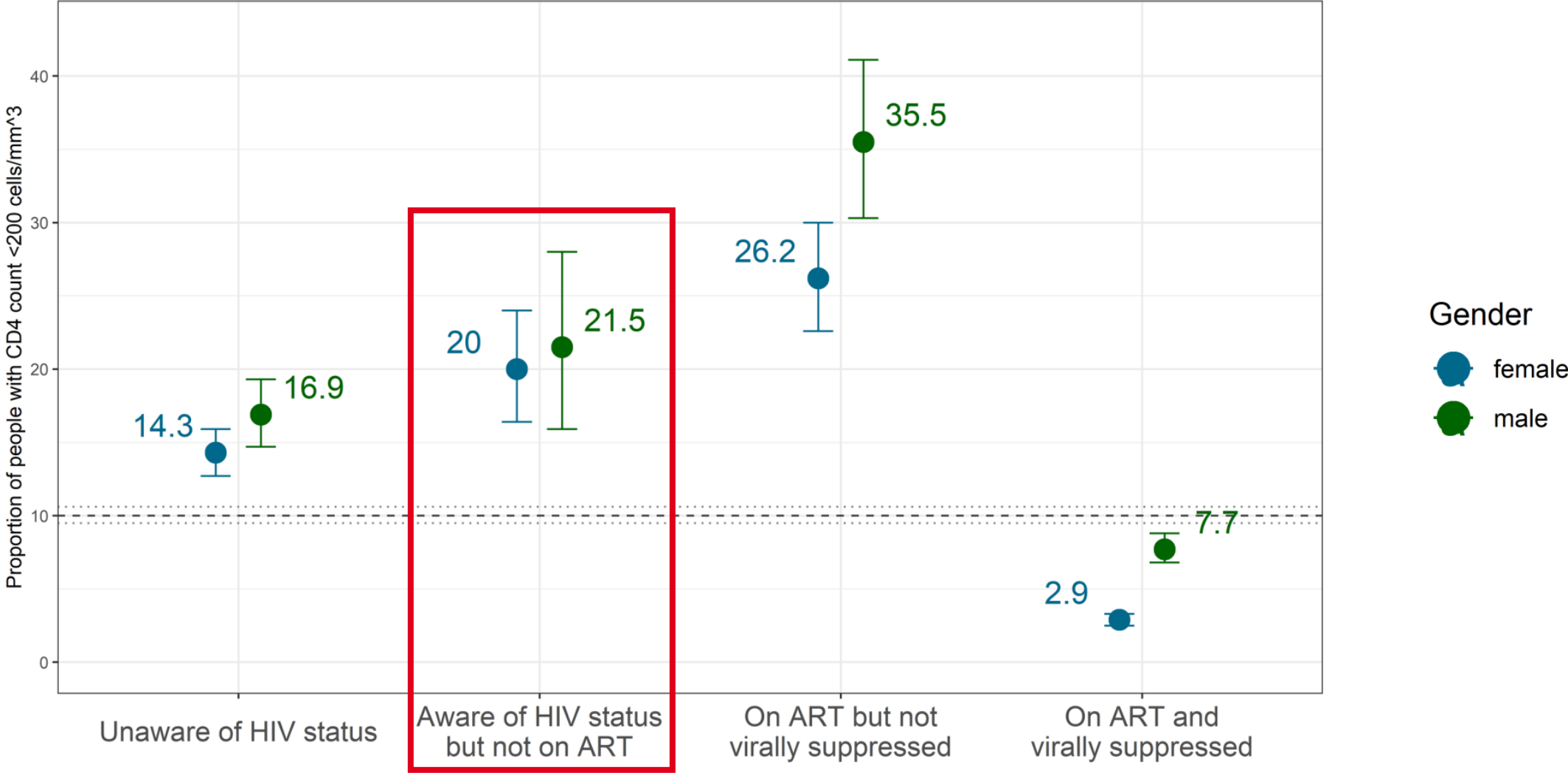# Distribution of AHD by treatment cascade, by country
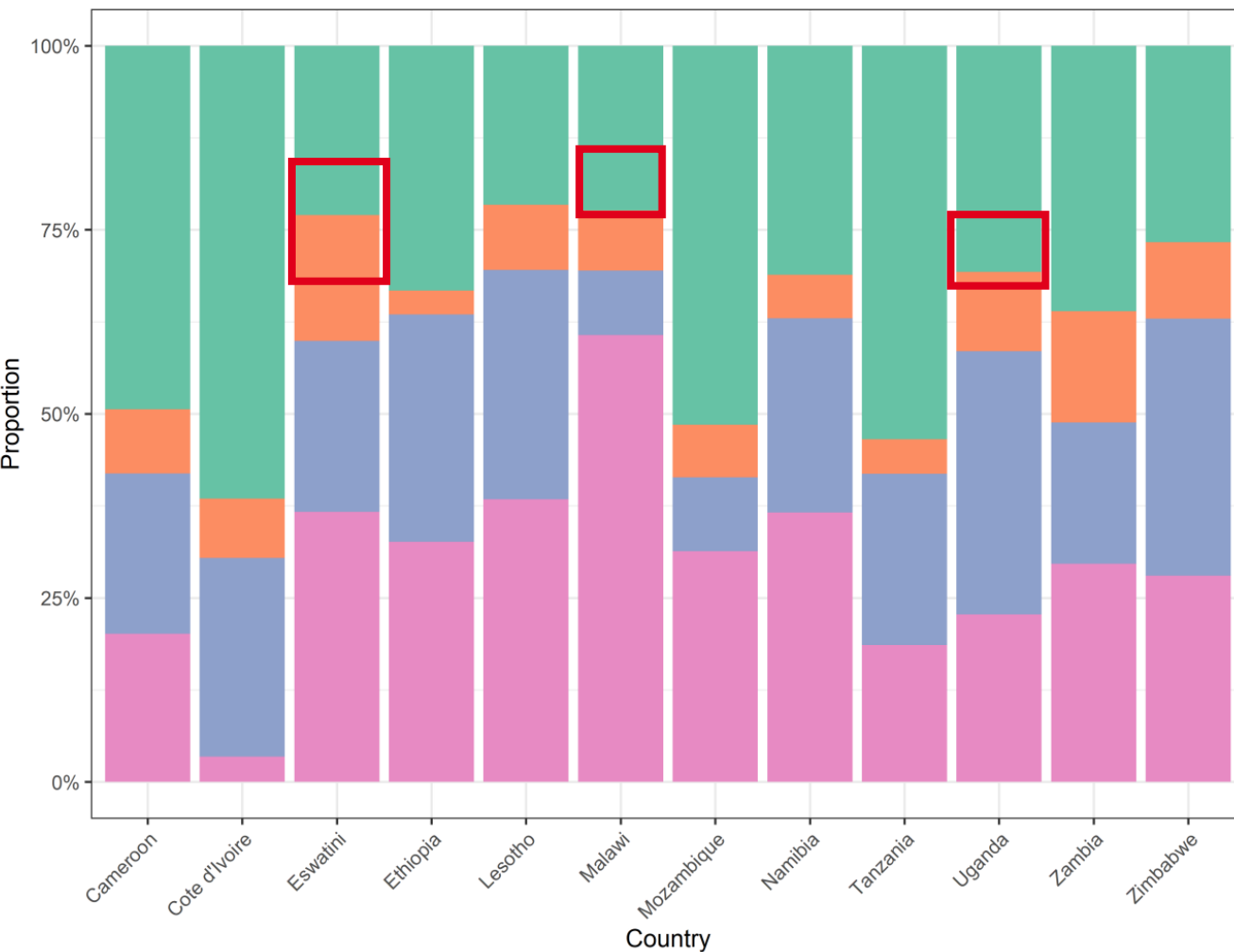
Disaggregation of all people with AHD	n = 2151	%
Not aware of HIV status	706	32.5
Aware of status but not on ART	216	9.9
On ART but not virally suppressed	543	25.0
Virally suppressed	686	31.6

Legend:
- CD4 count <200 cells/mm³ and not aware of HIV status
- CD4 count <200 cells/mm³ aware of HIV status but not on ART
- CD4 count <200 cells/mm³ on ART but not virally suppressed
- CD4 count <200 cells/mm³ on ART and virally suppressed

https://www.croiconference.org/abstract/high-prevalence-of-advanced-hiv-disease-in-sub-saharan-africa-an-analysis-of-11-household-surveys/

What about access to CD4?

	% of initiations with CD4 performed	% of initiations with CD4 < 200 cells/mm3
Eswatini		
Kenya		
Malawi		
Uganda	85%	25%

What data is available in your setting?

Effect of ARVs on CD4 count and viral load
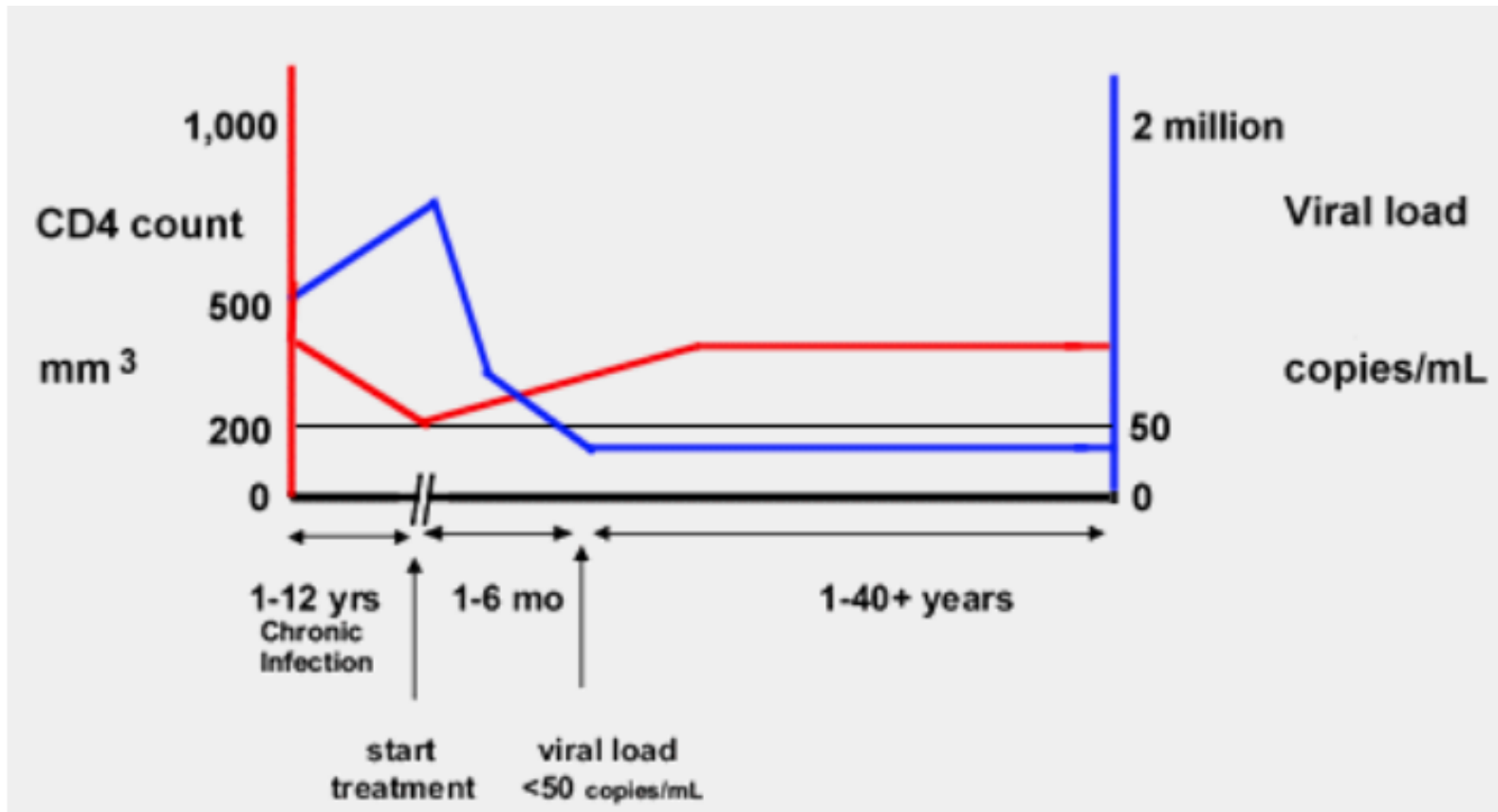
Impact of treatment interruptions on CD4

The average CD4+ count decreased **by 87 cells per cubic millimeter per month during the first 2 months after randomization**

After reinitiation of antiretroviral therapy in the drug conservation group, the median time to an HIV RNA level of 400 copies per milliliter or less was **3.1 months**

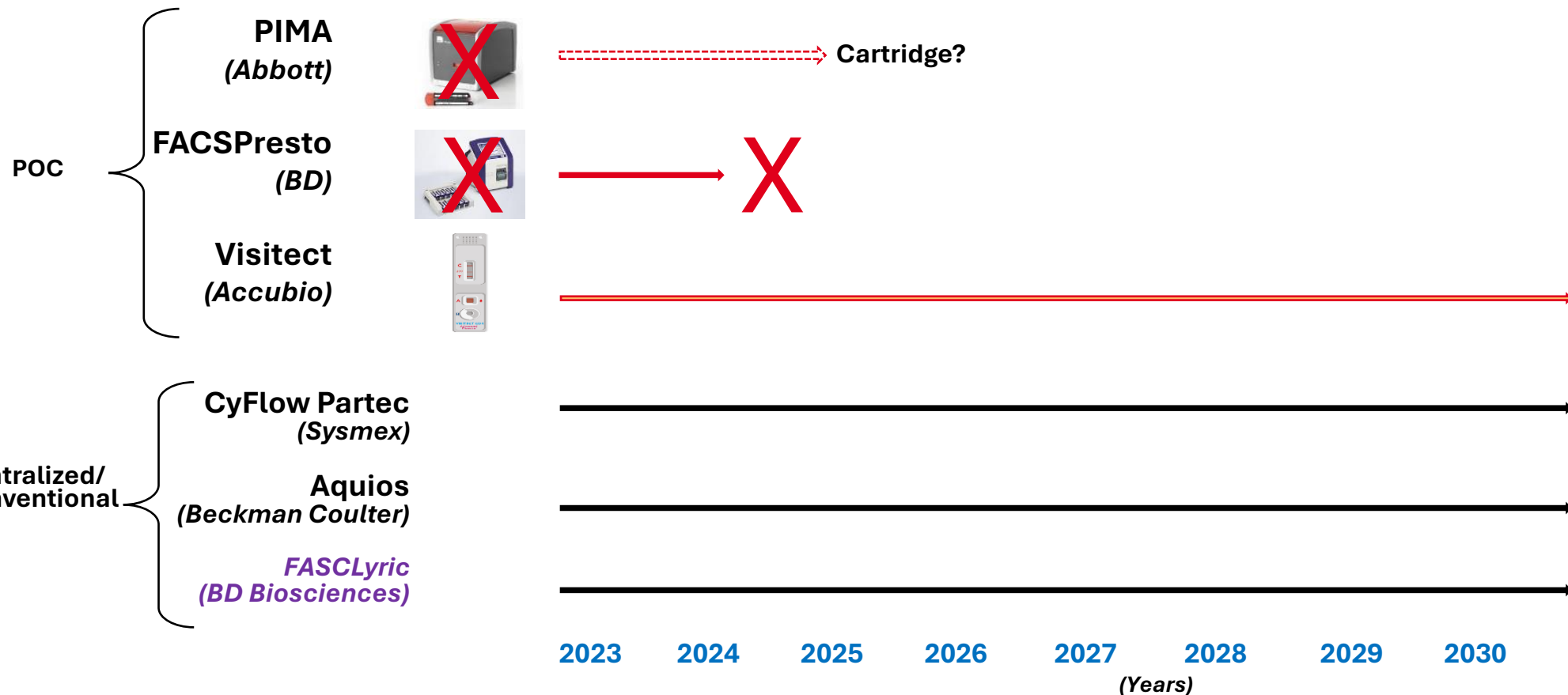| Thomadakis C et al.The Effect of HIV Treatment Interruption on Subsequent Immunological Response. Am J Epidemiol. 2023 Jul 7;192(7):1181-1191. **_East Africa data_** | Availability of CD4 Cell-Count Data After Reengagement in ART | | | | | | | | | P Value |
	CD4 Data Available(n = 8,501)			CD4 Data Not Available (n = 2,460)			Total (n = 10,961)			
	No.	%	Median (IQR)	No.	%	Median (IQR)	No.	%	Median (IQR)	
Sex										0.883
Female	5,636	66.3		1,627	66.1		7,263	66.3		
Male	2,865	33.7		833	33.9		3,698	33.7		
Age at disengagement from care, years			37.8 (32.0–44.7)			37.6 (31.2–44.7)			37.8 (31.9–44.7)	0.017
CD4 cell count at ART initiation, cells/µL			139.0 (67.0–208.1)			138.0 (58.0–217.8)			139.0 (64.0–210.0)	0.244
CD4 cell count available at disengagement	1,826	21.5		772	31.4		2,598	23.7		
CD4 cell count at disengagement (<2 months prior to last visit before disengagement), cells/µL			293.5 (175.0–432.8)			314.0 (136.0–495.2)			297.0 (166.0–452.8)	0.040
CD4 cell-count measurements from reengagement to ART restart available[a]	3,985	36.4		0	0.0		3,985	36.4		
CD4 cell count from reengagement to ART restart[a], cells/µL			248.0 (126.0–412.0)			N/A			248.0 (126.0–412.0)	
Time from ART initiation to disengagement, months			12.9 (4.9–25.5)			10.8 (3.4–23.0)			12.5 (4.5–25.1)	<0.001
Time from disengagement to reengagement, months			2.7 (2.1–5.0)			3.2 (2.2–7.1)			2.7 (2.1–5.4)	<0.0
Restart of ART	8,156	95.9		2,131	86.6		10,287	93.9		
ART restart at reengagement in care	7,003	82.4		2,021	82.2		9,024	82.3		
Time from disengagement to ART restart, months[b]			2.9 (2.2–6.0)			3.5 (2.2–9.6)			3.0 (2.2–6.6)	<0.001

CD4 cell count testing dilemma

POC
- PIMA *(Abbott)* — Cartridge?
- FACSPresto *(BD)*
- Visitect *(Accubio)*

Centralized/Conventional
- CyFlow Partec *(Sysmex)*
- Aquios *(Beckman Coulter)*
- FASCLyric *(BD Biosciences)*

2023 2024 2025 2026 2027 2028 2029 2030
(Years)

Pipeline CD4 technologies
1. Accesso Biotech (POC instrument based)

- **Little or no consultative-stakeholder opinion** for these huge manufacturing changes
- Is use of POC LFA CD4 feasible in all clinics or is sample transport still needed
- **How will we prevent AIDS deaths without this tool?**

»How can DSD principles be used to deliver the AHD package?

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Two scenarios:

Re-engagement with AHD from in-patient department	Re-engagement with AHD from out-patient department/ primary health centre

Components to consider when designing the building blocks for DSD models for clients with AHD at re-engagement

- Identifying AHD
- Clinical package to screen, prevent and treat opportunistic infections (OIs) in patients with advanced HIV disease
- Rapid ART initiation and/or regimen switch
- **Linkage in-patient department (IPD) out-patient department (OPD)/ Primary health care (PHC) for ongoing care**
- Intensive follow up first 3 months
- Management of HVL

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What are the opportunities for **decentralization** and **task sharing** for delivery of the advanced HIV disease package?

What policy changes are needed to enable this?

	Component 1: Identifying advanced HIV disease	
	Identifying clinical signs and symptoms	**Performing CD4**
WHEN Service frequency	At initiation Each clinical visit **At re-engagement** Any time in the community	
WHERE Service location	Facility Out of facility	
WHO Service provider	Doctor Nurse Community cadre (including CATS, key population peer supporter, CARG member) Client	
WHAT Service package	Identification of red flags and danger signs and symptoms	

	Component 1: Identifying advanced HIV disease	
	Identifying clinical signs and symptoms	Performing CD4
WHEN Service frequency	At initiation Each clinical visit At re-engagement Any time in the community	At time of HIV diagnosis **Re-engaging in care after more than 3 months off ART** If VL >1000 copies/ml Presenting clinically unwell on ART
WHERE Service location	Facility Out of facility	Facility Out of facility
WHO Service provider	Doctor Nurse Community cadre (including CATS, key population peer supporter, CARG member) Client	Laboratory technician/scientists Microscopist Nurse Primary counsellor
WHAT Service package	Identification of red flags and danger signs and symptoms	CD4, where possible at POC

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	Component 2: Clinical package to screen and prevent AHD (WHEN)					
	TB LAM	XPERT MTB/RIF	Blood CrAG	Fluconazole pre-emptive treatment	CTX	TPT
WHEN Service frequency	Outpatient and inpatient settings: in adults, adolescents and children with HIV • With signs and symptoms of TB • With advanced HIV disease • Who are seriously ill • Irrespective of signs and symptoms of TB and with a CD4 cell count <200 cells/mm^3	Whenever presenting with TB symptoms	If CD4 <200 cells/mm^3	If blood CrAG is positive and LP CrAG (if feasible) is negative	WHO clinical Stages 2, 3 and 4 CD4 cell count <350 cells/mm^3	TB screening negative Assessment for TPT repeated every three years

"When" – derived from national clinical guidance
Ideally same time as HIV testing/initiation

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	Component 2: Clinical package to screen and prevent AHD (WHERE)					
	TB LAM	XPERT MTB/RIF	Blood CrAG	Fluconazole pre-emptive treatment	CTX	TPT
WHERE Service location	POC at same site as CD4 testing (inpatient, outpatient, primary care, **out-of-facility site** where trained cadre present) where possible Or Sent to nearest testing site			Inpatient Outpatient Primary care site	Inpatient Outpatient Primary care site Out-of-facility site where trained cadre present	Inpatient Outpatient Primary care site Out-of-facility site where trained cadre present

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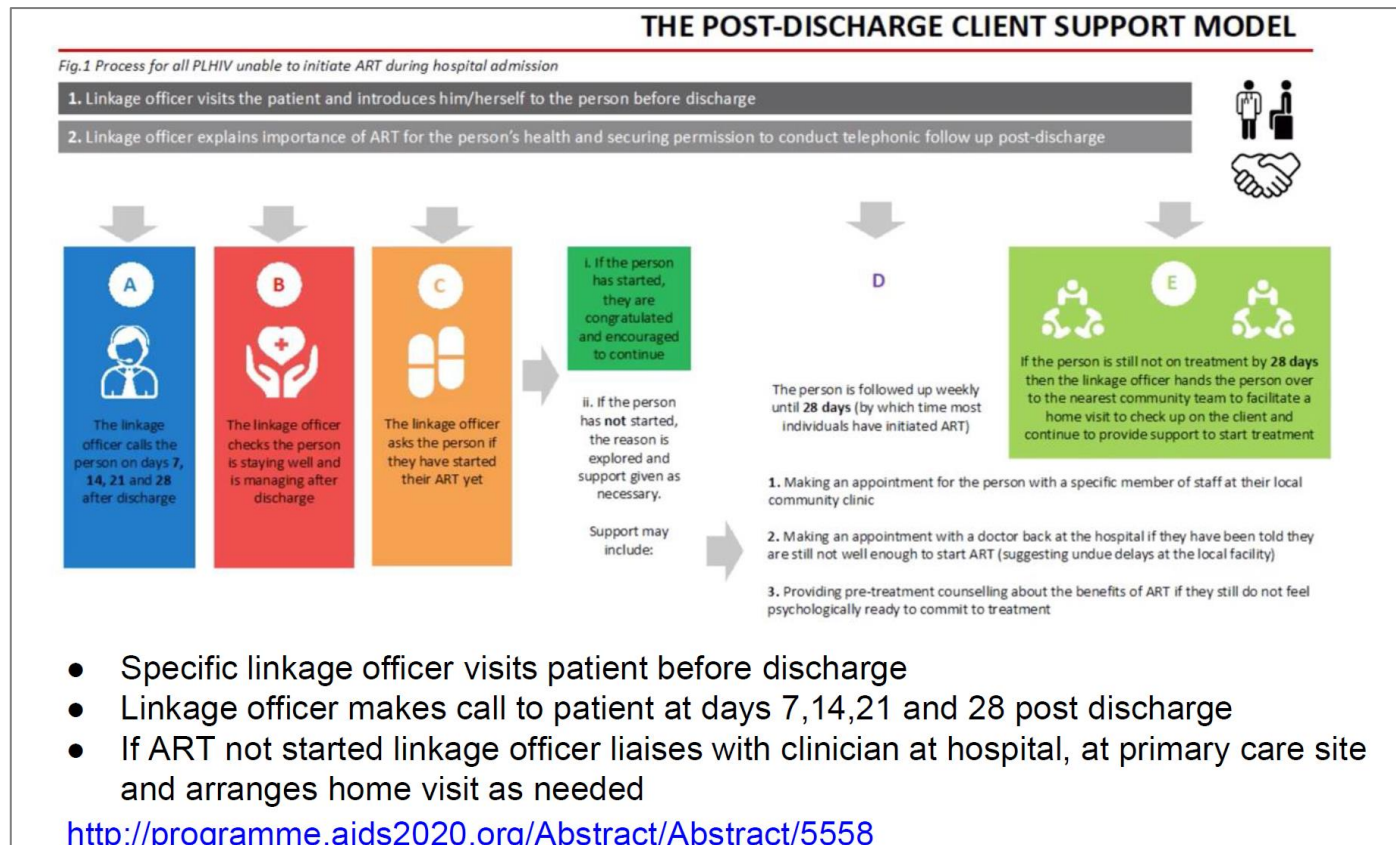| Component 2: Clinical package to screen and prevent AHD (WHO)						
	TB LAM	XPERT MTB/RIF	Blood CrAG	Fluconazole pre-emptive treatment	CTX	TPT
WHO Service provider	Laboratory technician/scientists Microscopist Nurse Primary counsellor			Doctor Nurse	Doctor Nurse	Doctor Nurse Primary counsellor for telehealth follow-up

Viewpoint

CrossMark **Framework for the implementation of advanced HIV disease diagnostics in sub-Saharan Africa: programmatic perspectives**

Ndlovu Z et al Lancet HIV. 2020 Jul;7(7):e514-e520. doi: 10.1016/S2352-3018(20)30101-6.

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What about re-engagement at IPD?
Linkage between district hospital and outpatient/PHC/community follow up

THE POST-DISCHARGE CLIENT SUPPORT MODEL

Fig.1 Process for all PLHIV unable to initiate ART during hospital admission

1. Linkage officer visits the patient and introduces him/herself to the person before discharge

2. Linkage officer explains importance of ART for the person's health and securing permission to conduct telephonic follow up post-discharge

A The linkage officer calls the person on days 7, 14, 21 and 28 after discharge

B The linkage officer checks the person is staying well and is managing after discharge

C The linkage officer asks the person if they have started their ART yet

i. If the person has started, they are congratulated and encouraged to continue

ii. If the person has not started, the reason is explored and support given as necessary.

Support may include:

D The person is followed up weekly until 28 days (by which time most individuals have initiated ART)

1. Making an appointment for the person with a specific member of staff at their local community clinic

2. Making an appointment with a doctor back at the hospital if they have been told they are still not well enough to start ART (suggesting undue delays at the local facility)

3. Providing pre-treatment counselling about the benefits of ART if they still do not feel psychologically ready to commit to treatment

E If the person is still not on treatment by 28 days then the linkage officer hands the person over to the nearest community team to facilitate a home visit to check up on the client and continue to provide support to start treatment

- Specific linkage officer visits patient before discharge
- Linkage officer makes call to patient at days 7,14,21 and 28 post discharge
- If ART not started linkage officer liaises with clinician at hospital, at primary care site and arranges home visit as needed

http://programme.aids2020.org/Abstract/Abstract/5558

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- Before implementing the model, an average of **55%** of clients needing ART were confirmed to have initiated treatment following hospital admission.

- After implementation, **over 90%** of clients had initiated ART within 28-days post-discharge

- This model can be described using the building blocks approach

WHEN	At discharge ; Days 7,14,21 and 28 post discharge
WHERE	Remotely Initiation at Primary care
WHO	Designated Linkage Officer
WHAT	Asked if staying well Asked if ART initiated – if not reason explored and referral made if needed

http://programme.aids2020.org/Abstract/Abstract/5558

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Differentiated follow-up schedule (first 3 months after initiation/switch)

Follow-up in the first three months is differentiated into:

- Standard

- Intensive

Activity	Criteria for intensive follow-up
Clinical monitoring	Active OIs or AHD identified
Counselling	Mental health condition identified, drug or substance misuse, adolescents, pregnant or breastfeeding women, key populations
Viral load monitoring	Earlier VL at month three for pregnant and breastfeeding women Where available, use of POC VL for children, adolescents, pregnant and breastfeeding women Where POC not available, flag specimen as urgent on request form for children, adolescents, pregnant and breastfeeding women

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Key messages

- Still significant (at least one in four initiations) number of clients with AHD at initiation

- Duration of dis-engagement increases the risk of presenting with AHD. Are our tracking procedures having an impact?

- DSD principles can be applied to the design of service delivery models for clients with AHD at re-engagement