What we know vs what is happening

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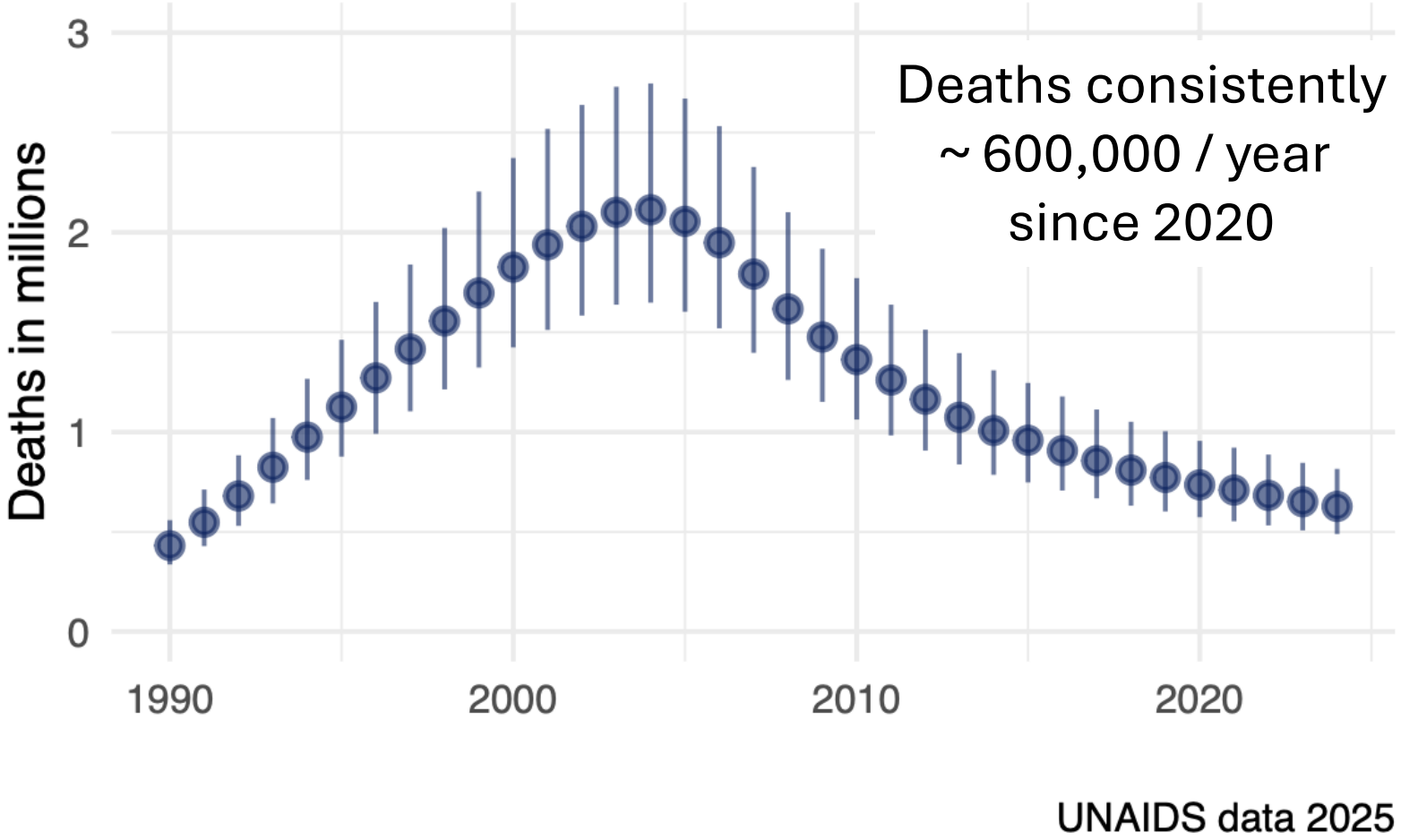
Unfinished business: Ending preventable deaths from advanced HIV disease in a changing HIV response

AIDS 2026

26–31 July • Rio de Janeiro, Brazil

aids2026.org

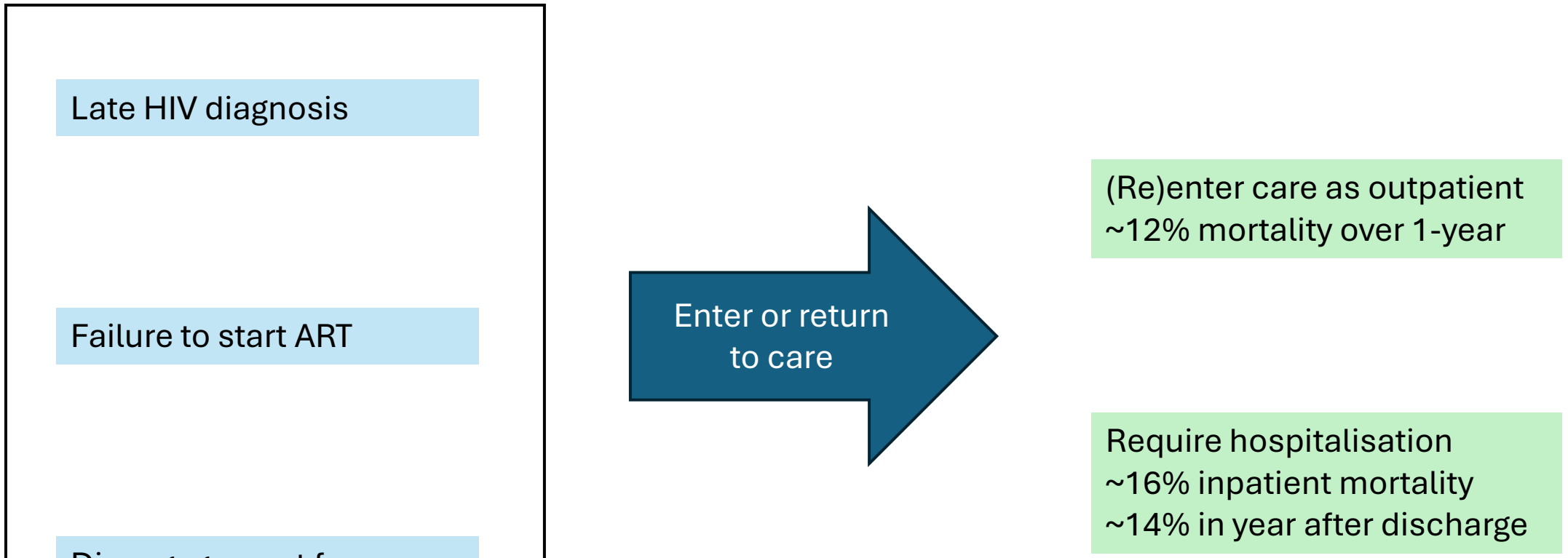
Rate of decline in HIV-related deaths has slowed



Estimated 1.9 million people living with AHD in sub-Saharan Africa

Stelzle
Lancet Glob Health 2025;13:e437

Drivers of AHD and settings it is encountered



Scheier, AIDS 2026;40:967
Burke, JIAS 2026;29:e70134
Ford, Lancet HIV 2022;9:e150

Drivers of AHD and settings it is encountered

Late HIV diagnosis

Testing strategies

Failure to start ART

Linkage strategies

Disengagement from care

Retention & early return strategies

Not in care

Enter or return to care

(Re)enter care as outpatient
~12% mortality over 1-year

AHD package of care

Require hospitalisation
~16% inpatient mortality
~14% in year after discharge

Improved hospital management & linkage to outpatient care

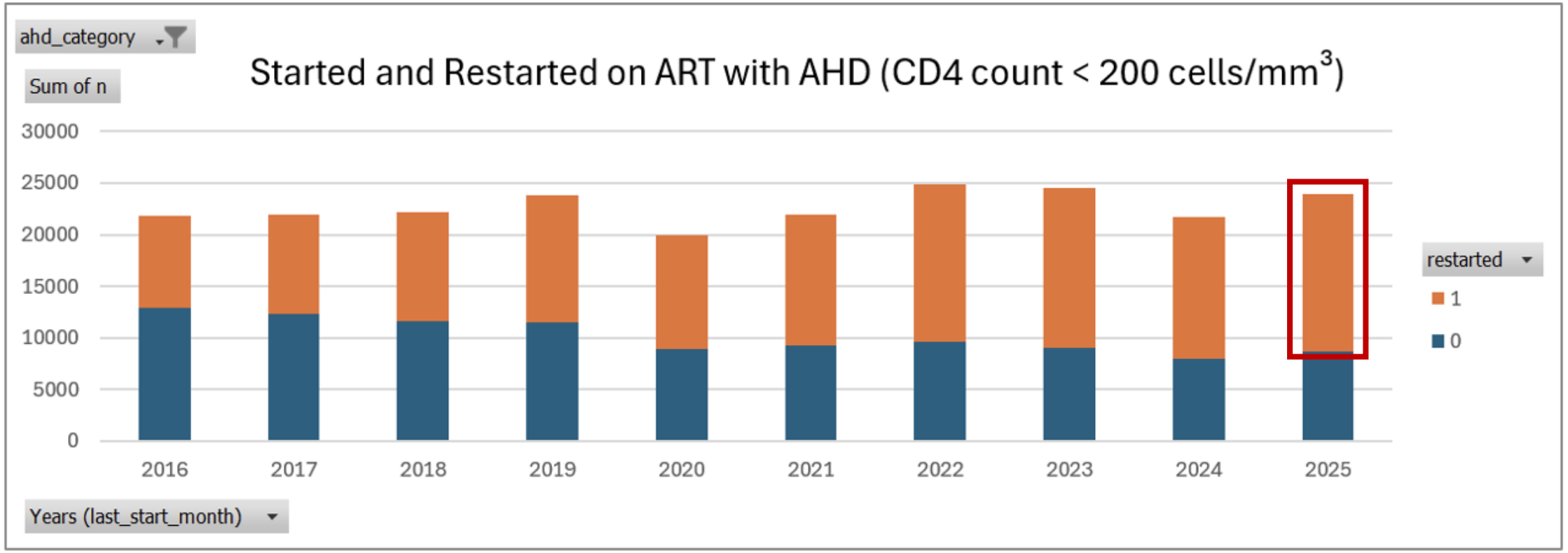
Issues to be covered

1. **Disengagement** as a driver of AHD

2. Implementation of **AHD package of care** and role of **CD4 testing**

3. Management of those **hospitalized** with AHD

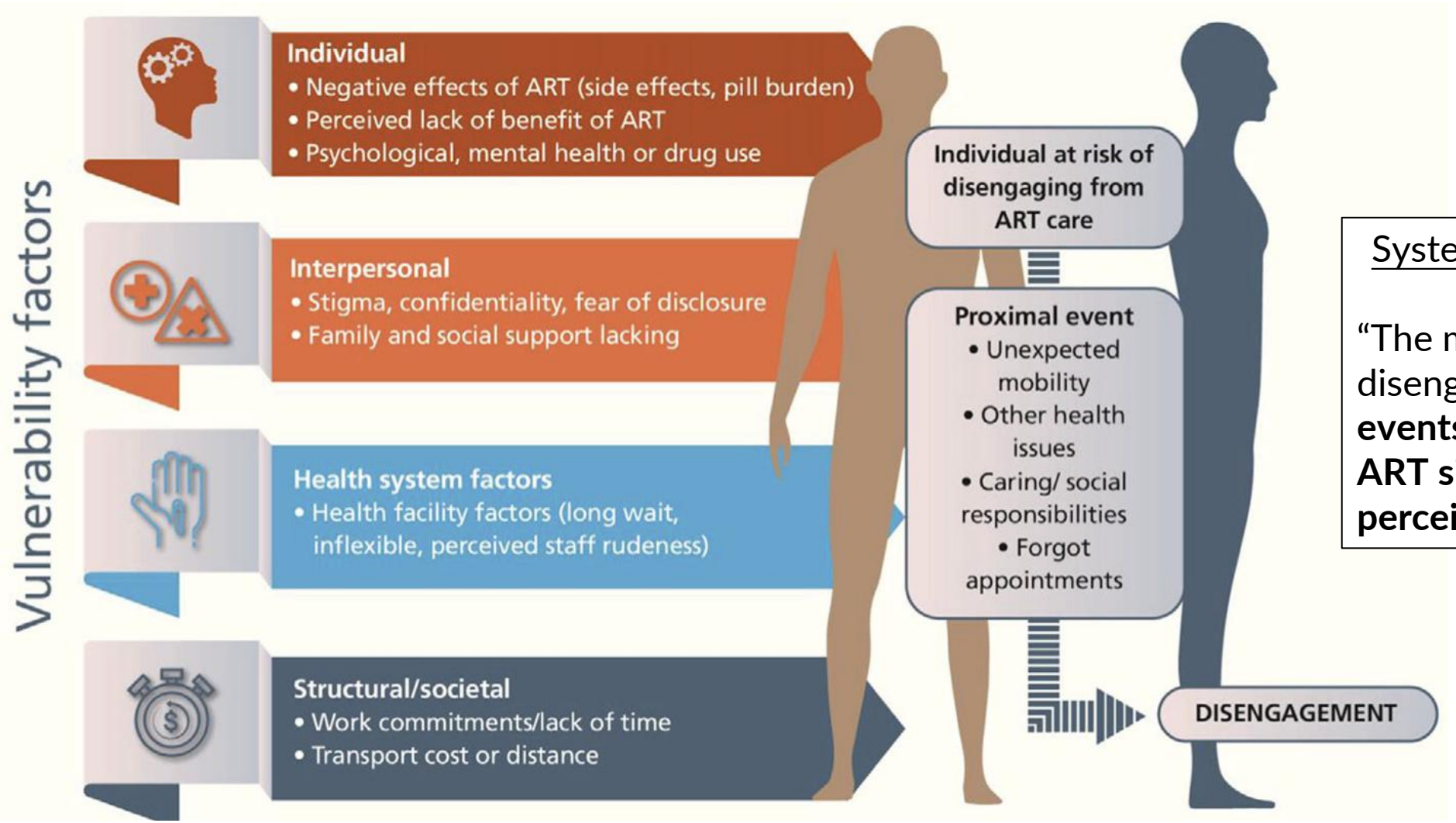
Western Cape, South Africa: Return to care with AHD



2025: 65% of those with CD4 < 200 are re-entering care (rather than entering for first time)

Euvrard et al, Western Cape Data Centre

What are the reasons for disengagement?



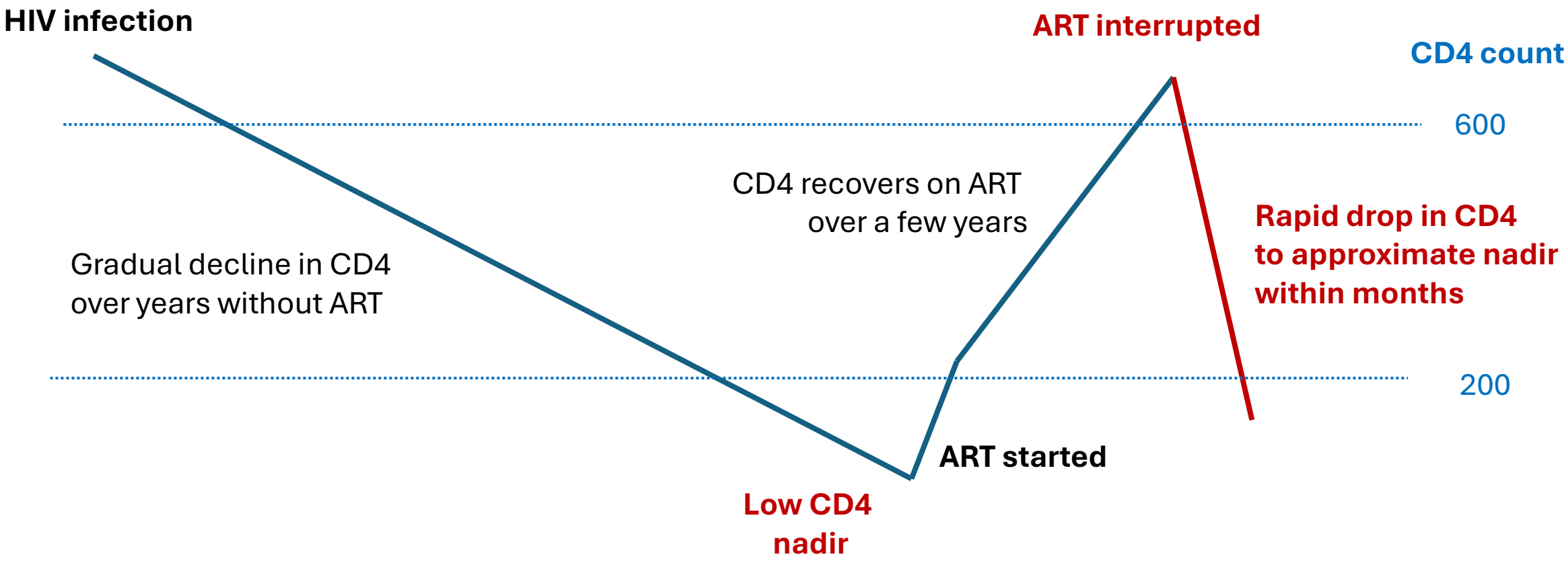
Systematic review of 21 studies (LMICs, 2015 -2022):

"The most common reasons for disengagement were **unexpected events, socio-economic reasons, ART side effects or lack of perceived benefit of ART"**

Burke, J Int AIDS Soc 2024,27:e26230

Disengagement from ART care = key AHD driver

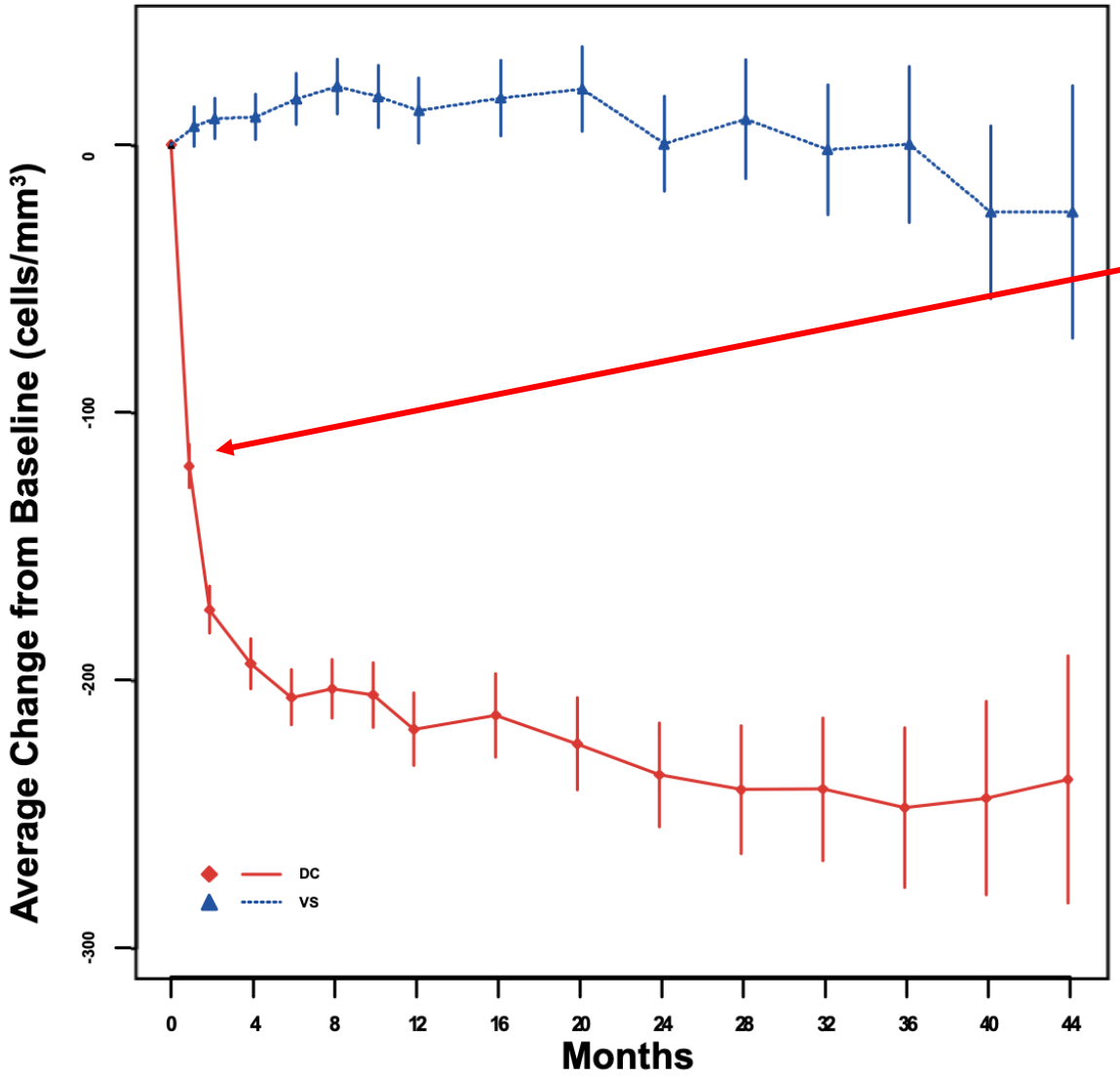
Especially patients who have low CD4 nadir



East Africa IeDEA Collaboration: CD4 increases after ART reinitiation much slower than those before disengagement

Thomadakis
Am J Epidemiol 2023;192(7):1181

In majority of people with low CD4 count nadir, when stop ART CD4 count drops in 3-6 months to approximate that CD4 nadir



SMART trial evaluated planned ART interruption strategy:
CD4 dropped by ~ 200 in 4 months following ART interruption

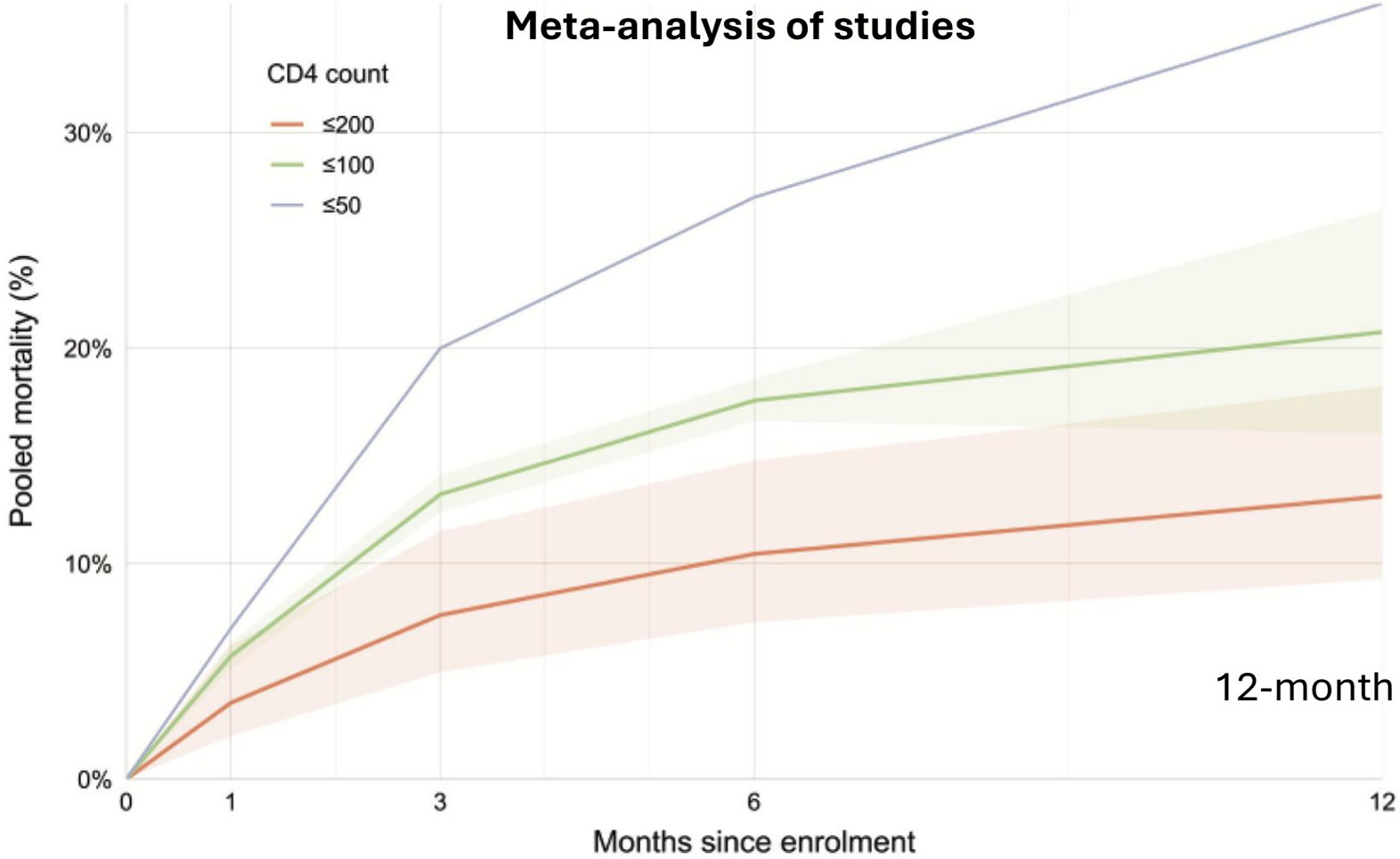
SMART Study Group
N Engl J Med 2006;355:2283

Interventions to address disengagement

- Funding cuts will negatively impact PEPFAR-funded retention and outreach activities to find patients who have disengaged

- Need to intensify strategies for retention/early re-engagement
  - Design services to work around life demands of PLHIV and their mobility
  - Welcoming, person-centered services
  - Including multi-month dispensing and dispensing outside facilities
  - Adherence support and education about consequences of disengagement
  - Outreach to find those disengaged; including mHealth solutions

Substantial mortality after entering/re-entering care with CD4 < 200



CD4 < 50

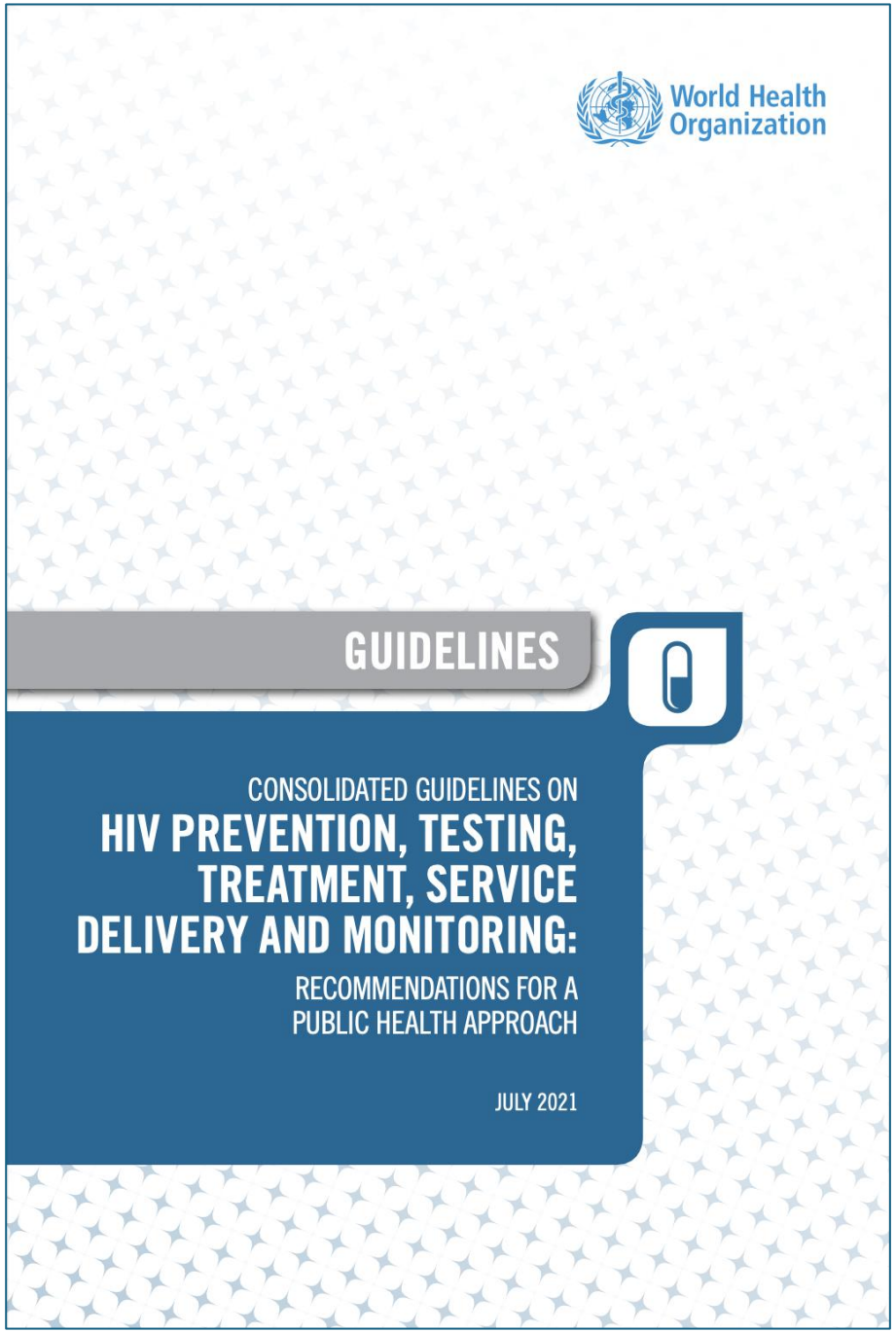
CD4 < 100

CD4 < 200

12-month mortality

Fig. 5. Pooled mortality by time since enrolment, stratified by CD4⁺ cell count. Only studies reporting mortality at all specified timepoints were included. Number of studies: CD4⁺ cell count ≤200 cells/mm³: 5; CD4⁺ cell count ≤100 cells/mm³: 2; CD4⁺ cell count ≤50 cells/mm³: 1. Shaded areas represent 95% confidence intervals (not included for the CD4⁺ cell count <50 stratum as this was based on a single study).

Scheier, AIDS 2026;40:967–981



WHO package of care for people with AHD

Screening and diagnostics

TB symptoms screen
Sputum NAAT
Urine LAM
CrAg screening recommended if CD4 <= 100 (consider if CD4 <= 200)

Prophylaxis

Co-trimoxazole if CD4 <=350 or stage 3 or 4
TB preventive therapy
Fluconazole pre-emptive treatment if CrAg+

ART initiation

Rapid, but defer if symptoms of TBM or CM

Adapted adherence support

Include home visits if feasible

Integrated into WHO 2021 Consolidated HIV guidelines

Evidence behind AHD package of care

- Urine LAM reduces deaths among hospitalised PWH
  - **TB NEAT LAM trial:** 25 to 21%
  - **STAMP trial:** 21 to 18%
- CrAg screening / pre-emptive fluconazole + adherence support
  - **REMSTART trial:** reduced deaths by 28% in those with CD4 < 200
- Co-trimoxazole prophylaxis with ART
  - **Meta-analysis:** reduced death by 60% when started at CD4 < 350
- Isoniazid preventive therapy for TB with ART
  - **IPT-ART trial:** reduced incidence of TB by 37%
  - **TEMPRANO trial:** reduced TB by 56% and death by 37%
  - **PREVENT TB:** 3HP non-inferior to isoniazid preventive therapy

Peter, Lancet 2016;387:1187
Gupta-Wright, Lancet 2018;392:292
Mfinanga, Lancet 2015;385:2173
Suthar, Lancet HIV 2015; 2: e137
Rangaka, Lancet 2014;384:682
TEMPRANO, N Engl J Med 2015;373:808
Badje, Lancet Glob Health 2017;5:e1080
Sterling, N Engl J Med 2011;365:2155

CD4 testing: recommendations and coverage

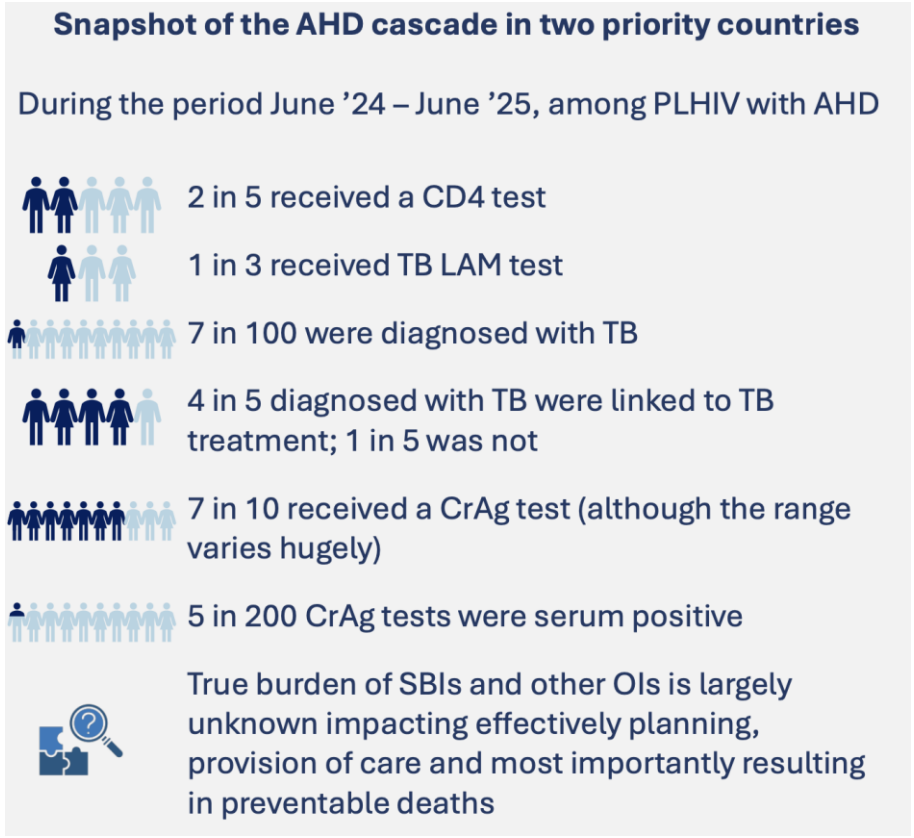
- **CD4 testing critical for identifying patients for AHD package of care**
  - WHO recommendation 2026: *CD4 testing is recommended as the preferred method to identify AHD among PLHIV*

    (Strong recommendation, moderate-certainty evidence)
- Funding constraints, national policy, market forces affects provision
- Manufacture of new machines stopped
  - Abbott stopped production of Pima, but now committed to limited production
  - BD no longer produce FACSPresto
- Main option now = semi-quantitative VISITECT (AccuBio)
- CD4 testing declined 35% from 2024 to 2025 (6 countries in SSA)

WHO Guideline update 2026
Syarif, Lancet Glob Health 2025;13:e26
CHAI HIV Market Impact Memo, June 2026

AHD Rapid Landscape Assessment

- **Survey of 6 countries in southern Africa (2025)**
- Critical challenges with supply chain and funding
- **CD4 testing coverage** remains inconsistent, ranging from as low as **16%** of new ART initiates in one country to **80%+** in another
- **CrAg and TB LAM screening** gaps are severe, with one of the five countries reporting **3%** of eligible AHD clients receiving either test, and highest reporting coverage rates only **~50%**



Acknowledgment: Ana Moore (CHAI)

REVIVE
Reducing Mortality in Adults with Advanced HIV Disease

REVIVE trial

RCT evaluating **Azithromycin** prophylaxis (250mg for 4 weeks) in patients with CD4 < 100 entering or returning to care to reduce mortality (related to **severe bacterial infections**)

Enrolling in 57 sites across 11 countries

6000 of target 8000 participants enrolled

Results anticipated Q4 of 2027

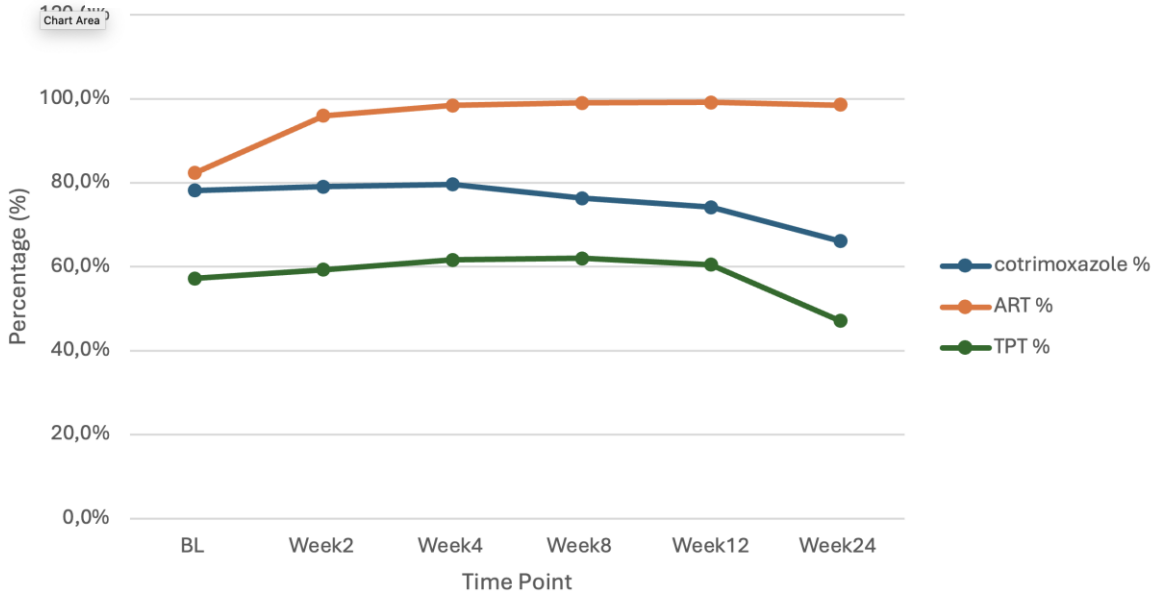
Population Health Research Institute
HEALTH THROUGH KNOWLEDGE

University of Cape Town · Universiteit van Kaapstad · iYunivesithi yaseKapa

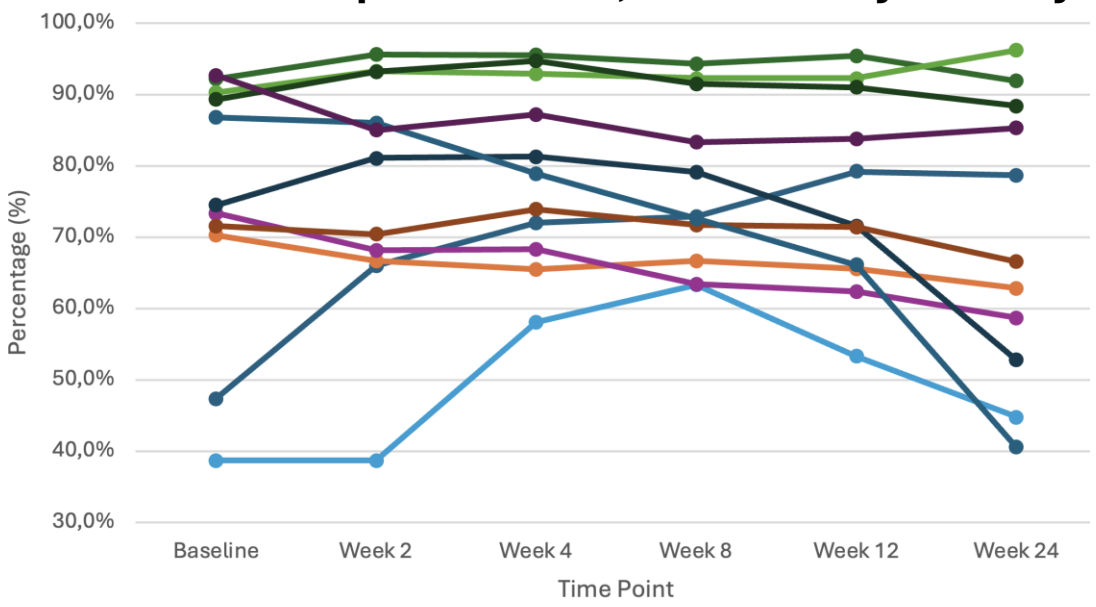
Gates Foundation

REVIVE: Co-trimoxazole preventive therapy (CPT)

Prescription over time for ART, CPT, and TPT



Prescription of CPT, stratified by country



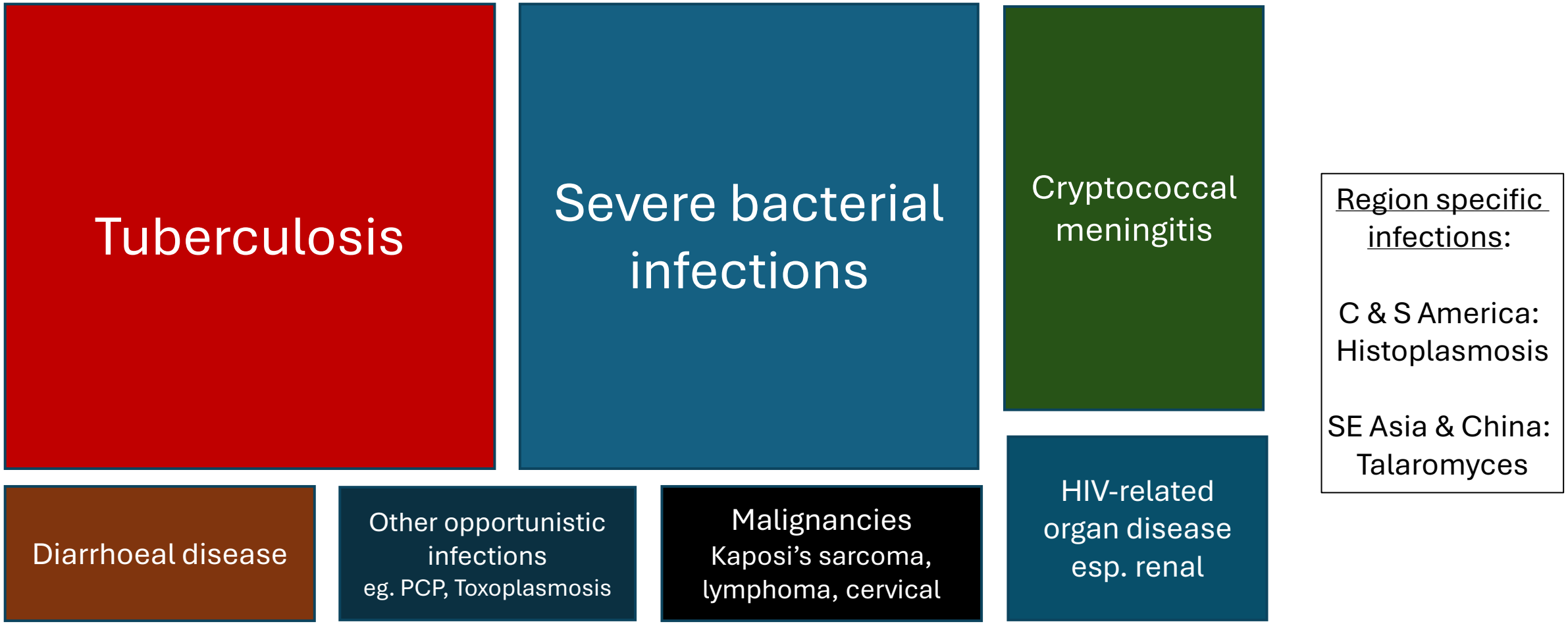
<u>Reasons for non-prescription of CPT</u>:
Supply issues, funding cuts, out of pocket, misunderstanding of guidelines

This is clinical trial – worse in routine care?

Data for n=4041

Wasserman, Scheier, REVIVE investigators
Unpublished

Causes of hospitalization and death in AHD



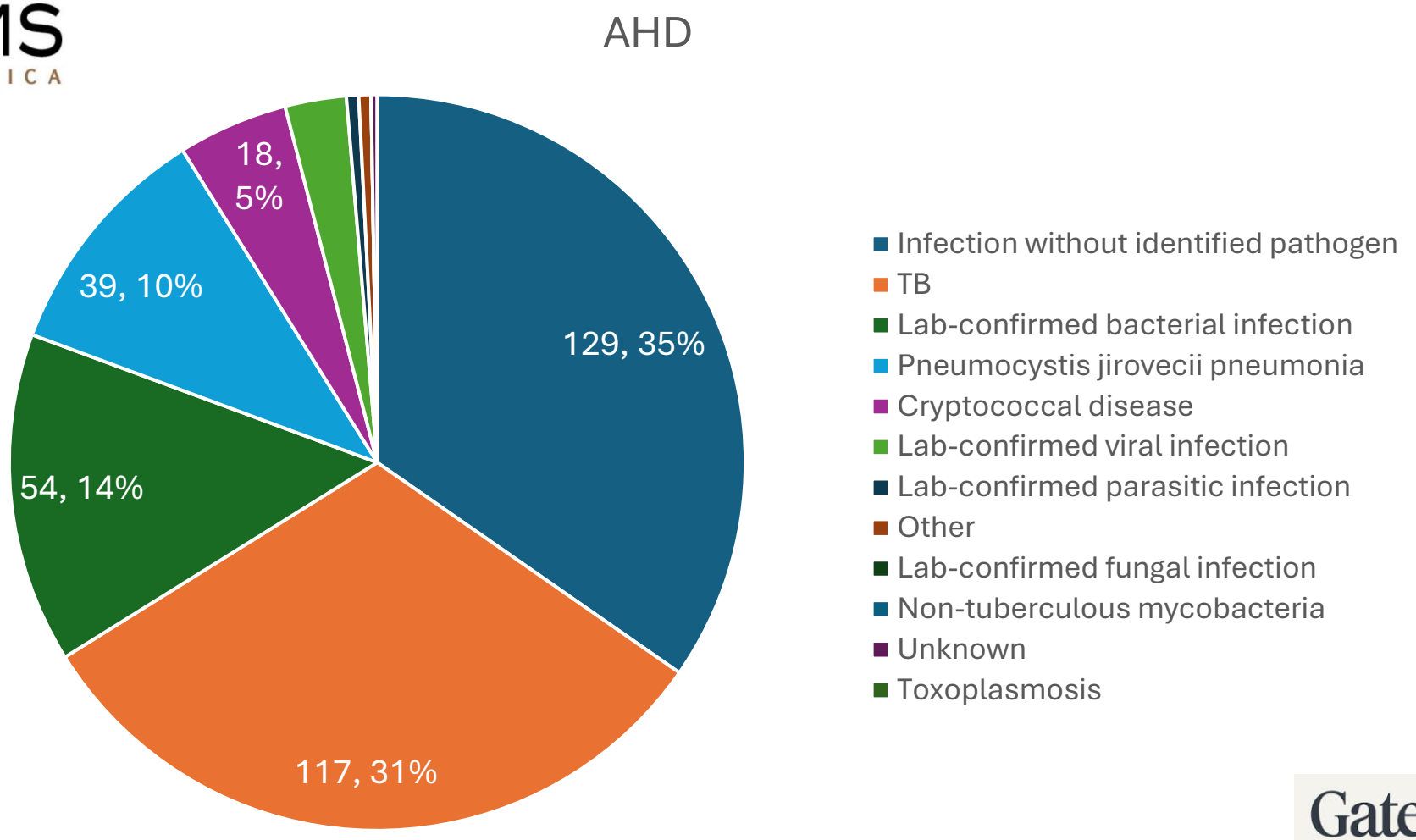
Burke, Lancet HIV 2025;12:e355; Burke, JIAS 2026;29:e70134; Gupta, AIDS 2015, 29:1987–2002; Meintjes, Medicine 2015;94:e2269; Rajasingham, Lancet Infect Dis 2022;22:1748

TIER 2 - Sentinel Facility-level Surveillance

Infection-related admissions are most commonly of unknown cause, followed by TB, bacteria, PCP and crypto

ADVANCE GERMS SOUTH AFRICA

Aim: to determine the causes and contribution of severe and AMR infections to severe illness and death for hospitalized patients with AHD



Prophylaxis in last year

- CPT 2%
- TPT 3%

Gates Foundation

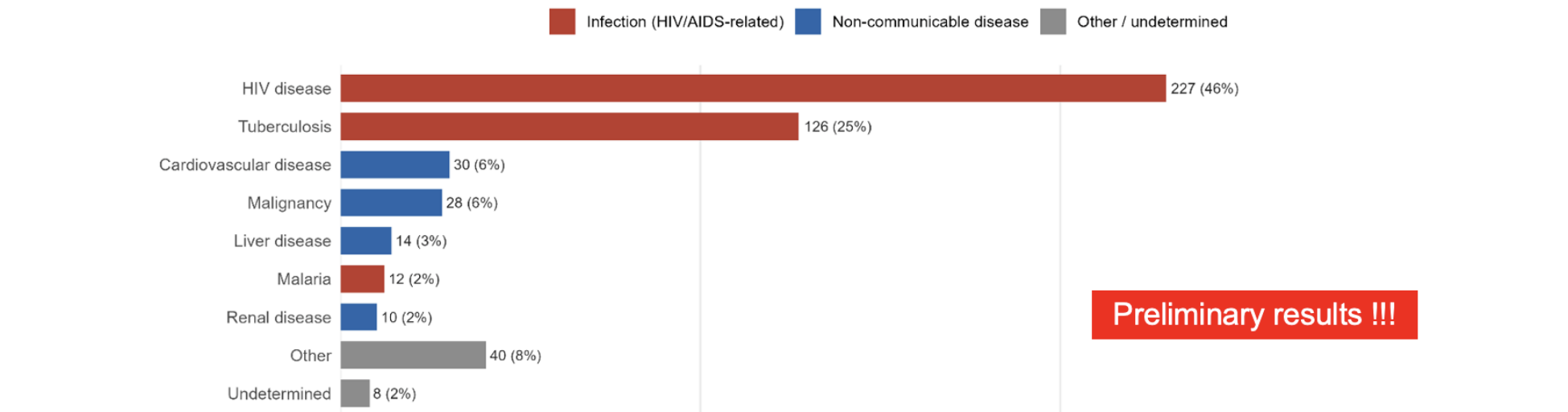
CHAMPS

South Africa
Kenya
Mozambique
Sierra Leone

Using Minimally Invasive Tissue Sampling to Determine Causes of Death among Adults with HIV across Four Sub-Saharan African Countries in the Era of Widespread ART Access to ART.

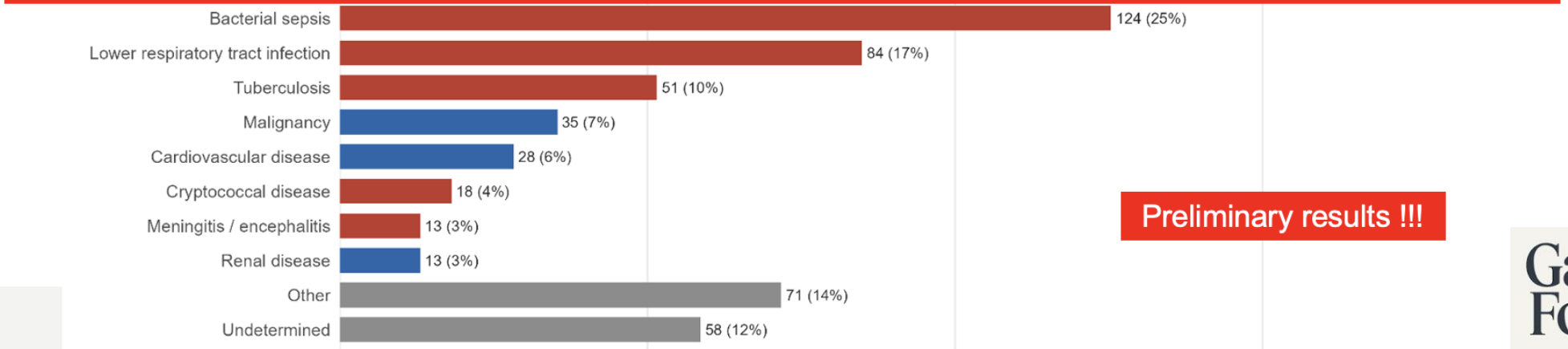
(MITADH study)

Underlying Causes of Death among HIV-Positive Decedents (N = 495)



Preliminary results !!!

Immediate Causes of Death among HIV-Positive Decedents (N = 495)



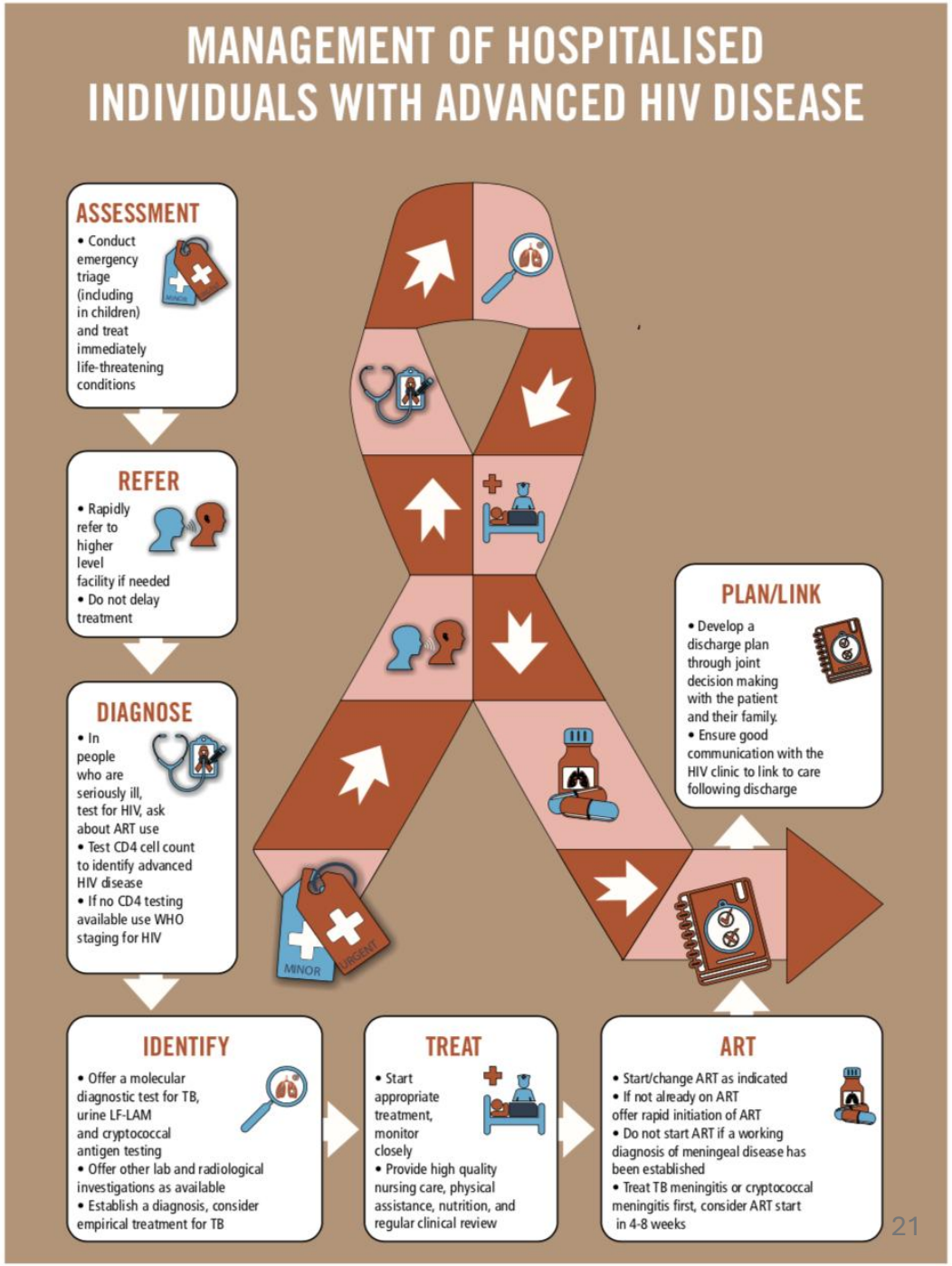
Preliminary results !!!

Gates Foundation

PROVIDING CARE TO PEOPLE WITH ADVANCED HIV DISEASE WHO ARE SERIOUSLY ILL

POLICY BRIEF

World Health Organization



Minimum package for managing AHD in hospitals

DIAGNOSTICS

FBC
Chemistry
CSF analysis
Chest X-ray
Ultrasound
CT scan (at central facility)
NAAT test for TB
Urine LAM
Cryptococcal antigen test
Stool microscopy

SUPPORTIVE MANAGEMENT

Oxygen
IVI fluids
Electrolyte supplementation
Nutritional supplementation
Adherence support (especially for linkage)

MEDICATION

TB treatment (Rifampicin, INH, PZA, Ethambutol)
Broad-spectrum IVI and oral antibiotics
ART
Co-trimoxazole
Ampho B (preferably liposomal), flucytosine, fluconazole

CHAI HIV Market Impact Memo (2026) highlights **critical threats to supply chain for CM medication** (short supply and stock outs of ampho B and flucytosine)

Linkage of PLHIV at hospital discharge

- 60–65% link to care within 1 month of discharge; 42% in a meta-analysis
- Meta-analysis: Interventions (eg. pre-discharge care planning, post-discharge follow-up) may improve linkage to care and reduce readmission, but **no mortality benefit**
- WHO recommendation (2025):

Katuramu, BMC Public Health 2025;25:3571
Ford OFID 2025;12(4):ofaf175

Interventions to provide at hospital discharge	
New, 2025	Hospitalized people with HIV may be provided interventions to support transitions to outpatient care and reduce avoidable readmissions. *(Conditional recommendation, low-certainty evidence)* Interventions may include: • pre-discharge goal setting • medication review • transitional care planning • telephone follow-up • home visits by health-care providers and/or peer supporters • individualized support.

Priorities

- Initiatives upstream to prevent AHD
  - Improve retention in care and ensure early re-engagement
  - Person-centered program innovations, adherence support, patient education, community outreach, mHealth solutions

- Ensure optimal coverage of CD4 testing and AHD package of care commodities for patients entering/returning to care in clinics
  - Especially first 6 months of ART start/restart

- Care of people hospitalised with AHD
  - Management often outside HIV program
  - Educating hospital health care professionals in AHD management
  - Commodity supply for OI diagnosis and management
  - Interventions at discharge
  - Linkage to outpatient care after discharge and follow-up

Acknowledgements

- Nathan Ford
- Tendai Nyagura
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- Jonathan Euvrard