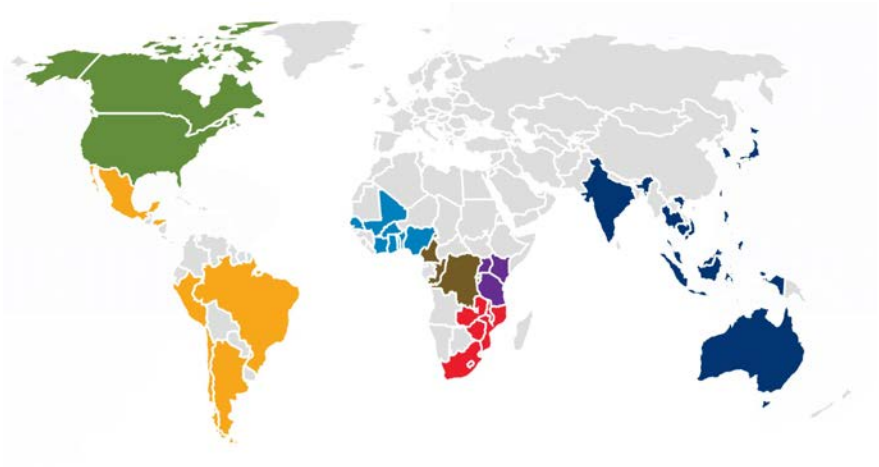
IeDEA Global Cohort Consortium

2024 Research Highlights



Website: iedea.org

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- Regional acknowledgements of site investigators, cohorts, study teams and administrators, data managers, and coordinating and data centers are available at: https://www.iedea.org/resources/

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2024 IeDEA Asia-Pacific Research Highlights

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HIV Treatment Outcomes After 10 years on ART in the TREAT Asia Observational Database and Australian HIV Observational Database

- Assess long-term immunological and survival outcomes among PWH from Asia (TAHOD) and Australia (AHOD)
- PWH receiving ART for ≥10 years included; factors associated with CD4 count in years 11–15 of ART analyzed using repeated measures linear regression; survival after 10 years analyzed using competing risk regression
- 7139 PWH included: 68% from TAHOD; 76% men; 51% heterosexual HIV exposure; median age 10 years after ART 46 years; 56% on NRTI + NNRTI at 10 years

Jiamsakul, A; Rupasinghe, D; Woolley, I; Choi, JY; et al. HIV Treatment Outcomes After 10 years on ART in the TREAT Asia Observational Database and Australian HIV Observational Database. JAIDS, 2024 Dec 15;97(5):460-47.

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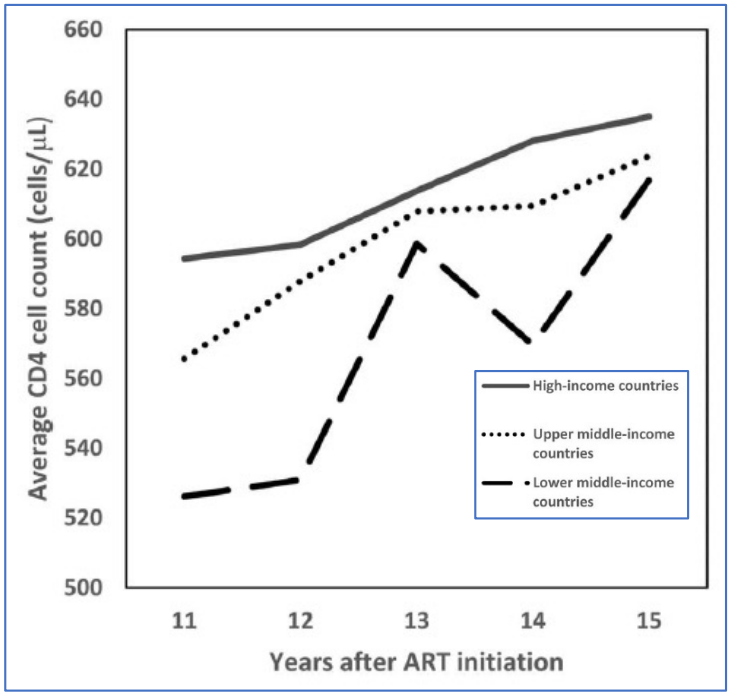
- Higher CD4 levels after 10 years observed if nadir CD4 in 1st decade higher
- Previous PI-based ART and treatment interruptions (TI) of 14 days to 3 months and >6 months associated with lower CD4 counts after 10 years
- Mortality rate 1.04 per 100py
  - Virological failure associated with subsequent mortality (sHR 1.34, 95% CI 1.04-1.71)
- <u>Sustaining high CD4 and minimizing TI has benefits beyond 1st decade of ART</u>

Figure: Average CD4 cell counts after 10 years on ART, by World Bank country income grouping



Jiamsakul, A; Rupasinghe, D; Woolley, I; Choi, JY; et al. HIV Treatment Outcomes After 10 years on ART in the TREAT Asia Observational Database and Australian HIV Observational Database. JAIDS, 2024 Dec 15;97(5):460-47.

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Risk factors for toxoplasmosis in people living with HIV in the Asia-Pacific region

- Assess prevalence of toxoplasmosis and risk factors among PWH
- Retrospective and prospective cases of toxoplasmosis reported in TAHOD between 1997-2020 included; sites without cases excluded
- Toxoplasmosis cases matched to 2 controls from the same site
- 269/9576 (2.8%) PWH diagnosed with toxoplasmosis across 19 sites
  - 227 (84%) reported retrospectively; 42 (16%) prospective diagnoses after TAHOD enrollment

Lee KH, Jiamsakul A, Kiertiburanakul S, Borse R, Khol V, Yunihastuti E, et al. Risk factors for toxoplasmosis in people living with HIV in the Asia-Pacific region. PLoS One, 2024 Jul 1;19(7):e0306245.

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- Median age 33 years, 80% male, 75% not on ART, at toxoplasmosis diagnosis
- Abstaining from ART, IDU HIV exposure and positive HBsAg associated with toxoplasmosis; toxoplasmosis less likely with increasing CD4 count
- Symptomatic toxoplasmosis rare but still occurs in the context of delayed diagnosis
- <u>Early HIV diagnosis and ART remain a priority in Asian PWH</u>

Table 2. Risk factors associated with toxoplasmosis.

	Number of subjects		Univariate analysis			Multivariate analysis		
	Control group	Case group	OR	95% CI	*p*	OR	95% CI	*p*
Total	538	269						
Age (years)					0.839			
≤30	205	95	1					
31–40	213	117	1.18	(0.85, 1.65)	0.320			
41–50	84	40	1.03	(0.65, 1.63)	0.899			
>50	36	17	1.02	(0.54, 1.92)	0.950			
Sex								
Male	359	214	1					
Female	179	55	0.49	(0.34, 0.71)	<0.001			
Mode of HIV exposure					<0.001			0.045
Heterosexual	378	168	1			1		
MSM	47	19	0.87	(0.48, 1.56)	0.636	1.88	(0.79, 4.47)	0.152
Injecting drug use	82	71	2.69	(1.69, 4.28)	<0.001	2.27	(1.15, 4.47)	0.018
Other/Unknown	31	11	0.80	(0.39, 1.64)	0.535	0.72	(0.23, 2.29)	0.580
ART					0.007			0.003
NRTI+NNRTI	153	51	1			1		
NRTI+PI	18	9	1.76	(0.72, 4.31)	0.213	1.96	(0.49, 7.79)	0.337
Other	16	8	1.97	(0.77, 5.05)	0.156	1.83	(0.45, 7.49)	0.401
None	351	201	2.24	(1.43, 3.53)	<0.001	3.62	(1.81, 7.24)	<0.001
CD4 (cells/μL)					<0.001			<0.001
≤50	16	125	1			1		
51–100	19	37	0.35	(0.16, 0.77)	0.010	0.41	(0.18, 0.96)	0.039
101–200	44	30	0.15	(0.07, 0.32)	<0.001	0.14	(0.06, 0.34)	<0.001
>200	123	14	0.02	(0.01, 0.05)	<0.001	0.02	(0.01, 0.06)	<0.001
Not tested	336	63						
VL (copies/mL)								
<1000	60	16	1					
≥1000	27	64	9.83	(4.4, 21.96)	0.000			
Not tested	451	189						
HBV co-infection								
Negative	390	187	1			1		
Positive	35	29	1.71	(1.02, 2.86)	0.042	3.19	(1.41, 7.21)	0.005
Not tested	113	53						
HCV co-infection								
Negative	300	140	1					
Positive	91	69	1.90	(1.22, 2.94)	0.004			
Not tested	147	60						
Prior AIDS								
No	434	0	N/A					
Yes	104	269						
Prophylactic cotrimoxazole use								
No	450	214	1					
Yes	88	55	1.35	(0.91, 1.99)	0.136			

Lee KH, Jiamsakul A, Kiertiburanakul S, Borse R, Khol V, Yunihastuti E, et al. Risk factors for toxoplasmosis in people living with HIV in the Asia-Pacific region. PLoS One, 2024 Jul 1;19(7):e0306245.

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Prevalence and incidence of anal HSIL in a cohort of cisgender men and transgender women who have sex with men diagnosed and treated during acute HIV acquisition

- Describe prevalence, incidence and factors associated with anal HSIL progression among cisgender men and TGW who began ART during acute HIV acquisition
- Consenting participants in an acute HIV acquisition cohort in Bangkok, Thailand, were enrolled
- HPV genotyping, high-resolution anoscopy (HRA) and anal biopsy as indicated, conducted at baseline and 6-monthly visits
- 89 MSM and 4 TGW included: median age 26 years; baseline anal HSIL prevalence 11.8%

Thitipatarakorn S, Teeratakulpisarn N, Nonenoy S, Klinsukontakul A, Suriwong S, et al. Prevalence and incidence of anal high-grade squamous intraepithelial lesions in a cohort of cisgender men and transgender women who have sex with men diagnosed and treated during acute HIV acquisition in Bangkok, Thailand. JIAS, 2024 May;27(5):e26242.

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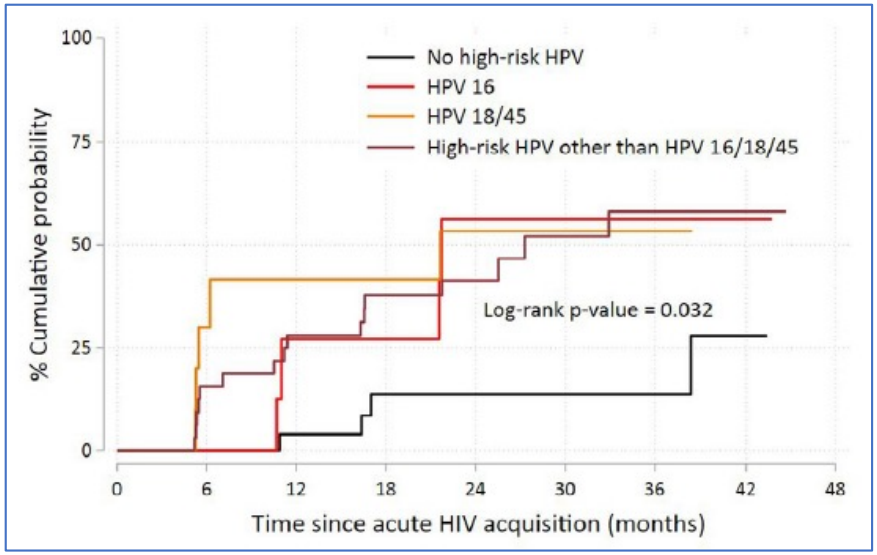
- Incidence of anal HSIL: 19.7 per 100 py (over 147 PY follow-up)
- Associated with incident anal HSIL:
  - Anal HPV 16, anal HPV 18/45, and other anal high-risk HPV
  - Syphilis infection and CD4 count <350 cells/mm^3
- <u>Screening and management of anal HSIL a crucial part of long-term HIV care for all MSM</u>

Figure: Kaplan–Meier curve of the cumulative probability of initial anal HSIL among participants free of prevalent anal HSIL, stratified by anal high-risk HPV infection status



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Long-term risk of mortality and loss to follow-up in children and adolescents on antiretroviral therapy in Asia

- Assess mortality and loss to follow-up (LTFU) in children and adolescents under care for >5 years following initiation of ART
- Patients followed from 5 years after ART until earlier of 25th birthday, last visit, death, or LTFU; Cox regression assessed predictors of mortality; competing risk regression assessed factors associated with LTFU
- 4488 children and adolescents initiating ART between 1997-2016
  - Median age 5.2 years; 51% male; median CD4 820 cells/mm^3 and 66% viral load <50 copies/mL at 5 years on ART

Nimkar S, Kinikar A, Mave V, Khol V, Du QT, et al. Long-term risk of mortality and loss to follow-up in children and adolescents on antiretroviral therapy in Asia. HIV Medicine, 2025 Jan;26(1):140-152

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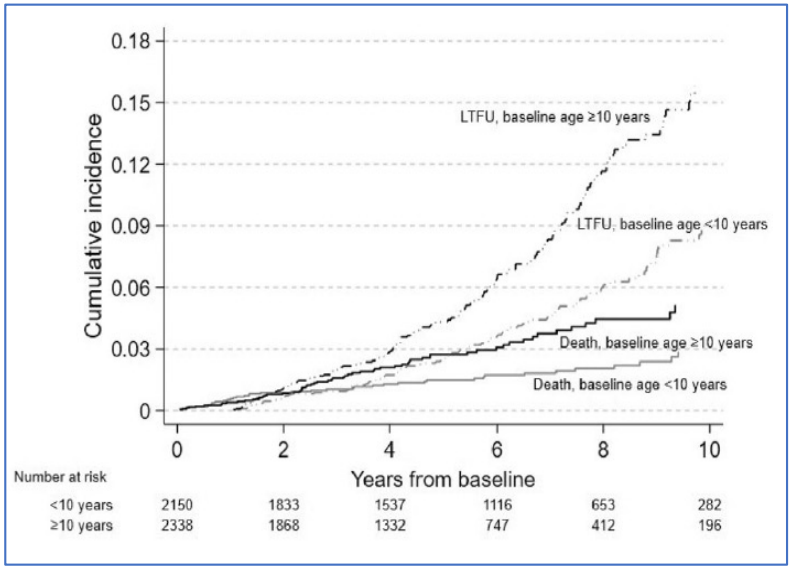
- 107 (2%) died; 271 (6%) LTFU
- Mortality rate 4.35; LTFU rate 11.01 per 1000 PY
- Mortality associated with AIDS diagnosis, lower CD4 count, higher VL and exposure to >1 ART regimen
- LTFU associated were male sex, higher VL and later ART start
- <u>For children/adolescents surviving 5 years on ART, current CD4 and VL remain strong indicators for monitoring but additional efforts needed for patients switching ART</u>

Figure: Cumulative incidence of mortality and LTFU after 5 years on ART



Nimkar S, Kinikar A, Mave V, Khol V, Du QT, et al. Long-term risk of mortality and loss to follow-up in children and adolescents on antiretroviral therapy in Asia. HIV Medicine, 2025 Jan;26(1):140-152

High mortality in adolescents and young adults with perinatally-acquired HIV in Thailand during the transition to adulthood

- Assess treatment outcomes and mortality among Thai AYA-PHIV aged 18–24 years who started ART during childhood at 5 pediatric HIV clinics in Thailand
- Data from cohort database, medical records, and the Thai National AIDS Program database: November 2020–July 2021
- 811 eligible AYA-PHIV: 754 (93%) alive; 57 (7%) had died
- Of those alive: median age 22 years; 71% current HIV care in adult clinic; median duration on ART 16 years; 56% NNRTI ART; 78% HIV RNA <200 copies/ml

Ounchanum P, Aurpibul L, Teeraananchai S, Lumbiganon P, Songtaweesin WN, et al., on behalf of the Thai PAPAYA study team. High mortality in adolescents and young adults with perinatally-acquired HIV in Thailand during the transition to adulthood. AIDS Care, 2024 Jul;36(7):964-973. .

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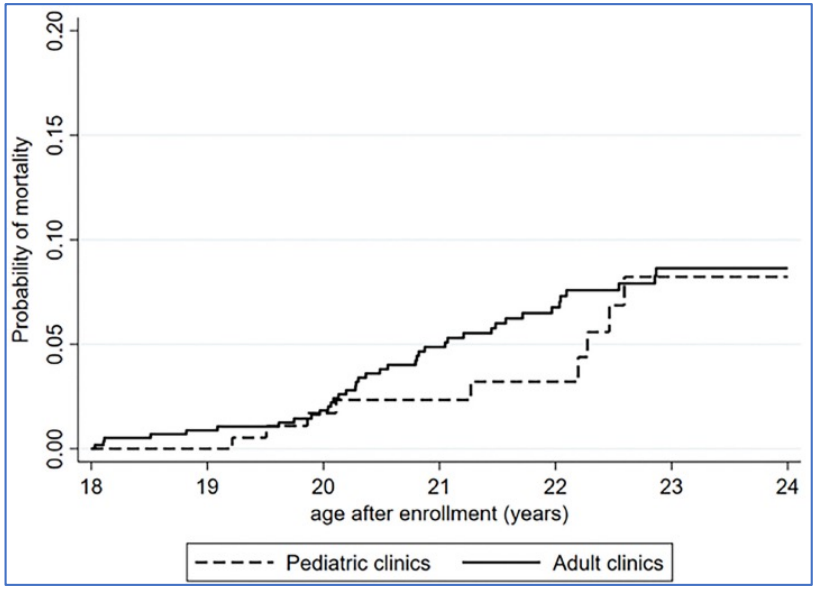
- Of those who died: median age at death 20.8 years; 88% AIDS-related deaths; mortality after age 18 was 1.76 per 100 PY
  - CD4 <200 cell/mm^3 at age 15 associated with higher risk of mortality (aHR 6.16, 95% CI 2.37–16.02)
  - No statistical difference in probability of mortality by clinic type (p=0.54)
- <u>High mortality among Thai AYA-PHIV indicates need for better AYA-PHIV support systems during transition</u>

Figure: Probability of mortality of adolescents and young adults with perinatally acquired HIV 18–25 years, by type of HIV clinic



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CCASAnet Publication Highlights 2024

IeDEA
International epidemiology Databases to Evaluate AIDS

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RESEARCH ARTICLE

Clinical outcomes and risk factors for immune recovery and all-cause mortality in Latin Americans living with HIV with virological success: a retrospective cohort study

Gabriel Castillo-Rozas[1,2,*], Shengxin Tu[3,*], Paula Mendes Luz[4], Fernando Mejia[5], Juan Sierra-Madero[6], Vanessa Rouzier[7], Bryan E. Shepherd[3] and Claudia P. Cortes[2,8,9,10,§]

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Introduction: The study examines immune recovery after ART initiation in Latin American PLWH, linking poor recovery to higher long-term morbidity and mortality despite viral suppression. It aims to identify factors affecting outcomes and survival.

Methods: Retrospective cohort study included PLWH ≥18 years who initiated ART with three-drug therapy, maintained follow-up for ≥24 months, and achieved viral suppression. Patients were categorized into four groups based on CD4 T-cell increase after 2 years (<150, [150, 250), [250, 350], >350 cells/mm³).

Primary outcomes were all-cause mortality, AIDS-defining events, and non-communicable diseases occurring >2 years post-ART. Factors influencing CD4 T-cell recovery were analyzed using a cumulative probability model.

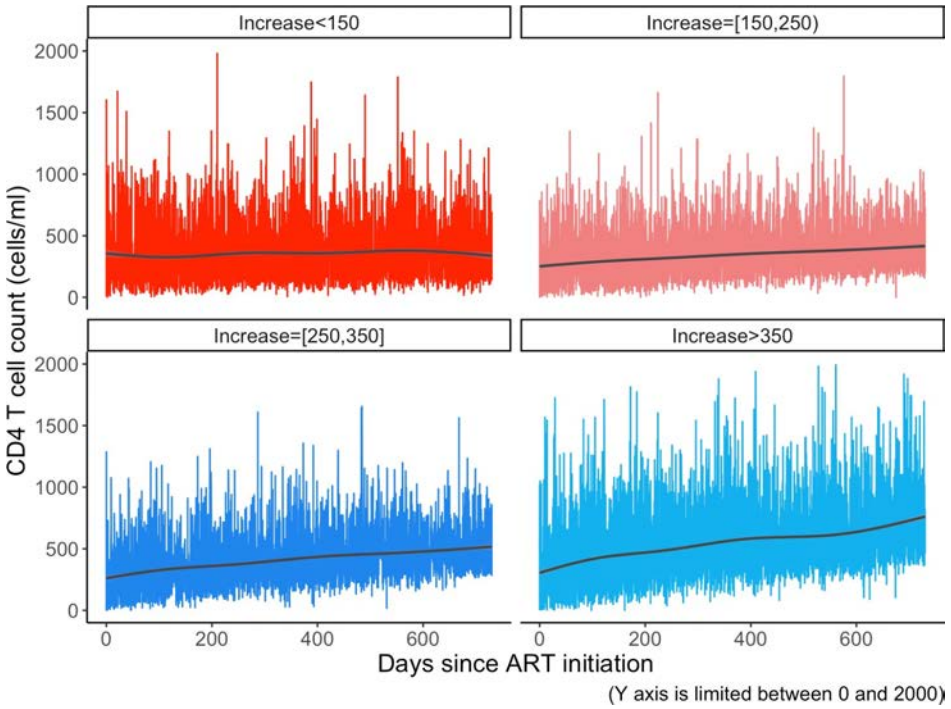

Figure S2. CD4 T cell count trends for each group (defined according to CD4 T cell count at 2 years of ART initiation).

Study Population:

✓ 4,496 PLWH from Brazil (30%), Chile (15%), Honduras (5%), Mexico (19%), and Peru (32%).

✓ 80% male; median age of 35 years at ART initiation (IQR: 29–43).

✓ CD4 T-cell Recovery Groups:

- <150 cells/mm³: 23% (1,048 participants)
- 150–249 cells/mm³: 25% (1,102 participants)
- 250–350 cells/mm³: 21% (962 participants).
- >350 cells/mm³: 31% (1,384 participants).

✓ Men and older individuals tended to have lower CD4 T-cell increases.

Factors associated with worse immunological performance: after 2 years of treatment.

- ✓ Older age (>40) at ART initiation
- ✓ Higher baseline CD4 T-cell count,
- ✓ Shorter time from diagnosis to ART initiation
- ✓ Lower baseline viral load
- ✓ Male sex,
- ✓ Starting regimens with AZT
- ✓ Starting a NNRTI-based regimen (compared to a PI-based regimen)

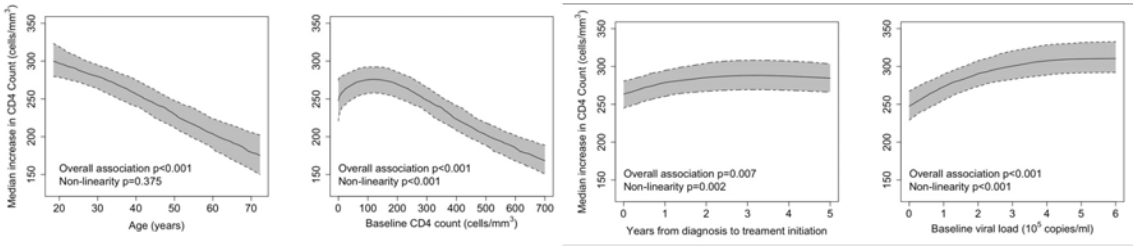

Figure 1. Baseline CD4 T-cell count, time from diagnosis to ART initiation, and baseline viral load had significant non-linear relationships with increase in CD4 T-cell count, adjusting for other covariates

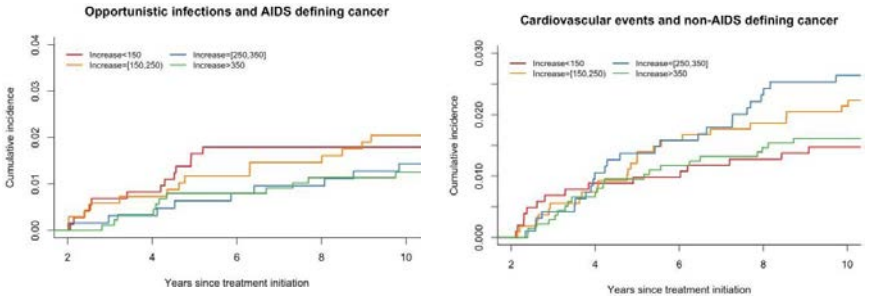

Figure 4. No statistical difference in the AIDS and non-AIDS related comorbidities among the groups.

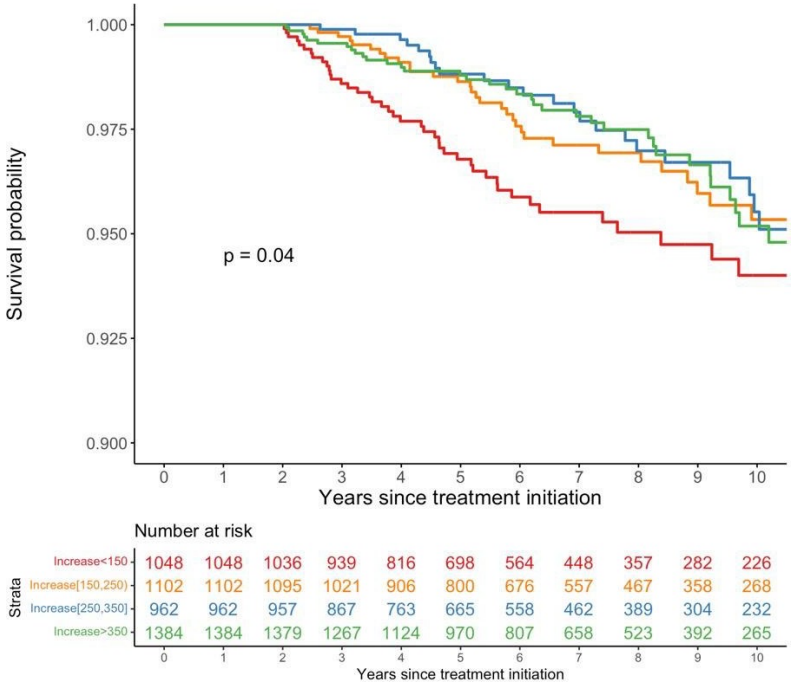

Figure 2. Survival probability based on CD4-cell count increases at the first two years of ART initiation over 10 years after ART initiation.

Assessment of all-cause mortality:

✓ Patients with an increase <150 cells/mm3 at 2 years had the lowest survival probability.

✓ Lower increase in CD4 T-cell count over 2 years was associated with a higher risk of all-cause mortality, adjusting for baseline CD4 T-cell count, age, time from diagnosis to ART initiation, sex, starting regimens, and HIV center.

Contents lists available at ScienceDirect

Public Health in Practice

journal homepage: www.sciencedirect.com/journal/public-health-in-practice

The impact of earthquakes in Latin America on the continuity of HIV care: A retrospective observational cohort study

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Study Population:

- Adults receiving HIV care at CCASAnet clinical sites experiencing at least a "moderate intensity" (Modified Mercalli scale) earthquake {Figure S1}
- Enrolled/receiving care from 2003 to 2017
- Interrupted Time Series models were fit with discontinuities at site-specific earthquake dates (Sept. 16, 2015 in Chile; Apr. 18, 2014 and Sept. 19, 2017 in Mexico; and Aug. 15, 2007 in Peru) to assess weekly outcomes (Y) such as clinical visit, CD4 measure, viral load measure, and ART initiation rates, both 3 and 6 months after versus before earthquakes:

$$\log(Y) = \beta_0 + \beta_1 Week + \beta_2 AfterQuake + \beta_3 Week \times AfterQuake + \log(P)$$

{log(P) is an offset accounting for the total number of patients in care}

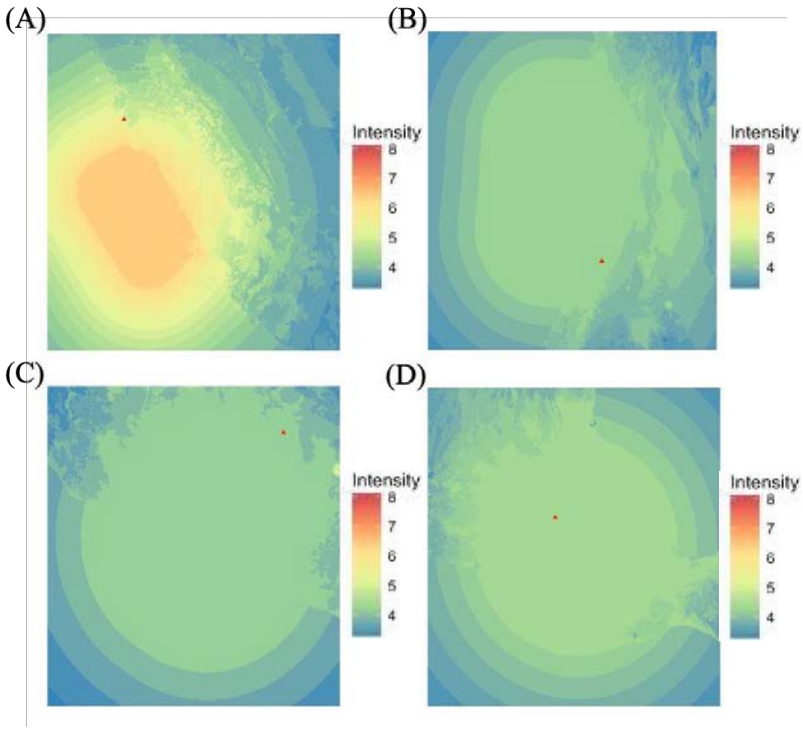

Figure S1. Shakemaps depicting the Modified Mercalli Intensity (MMI) of the earthquake in (A) Peru on August 15, 2007; (B) Chile on September 16, 2015; (C) Mexico on April 18, 2014; (D) Mexico on September 19, 2017. The red triangles indicate the location of the relevant CCASAnet clinic sites.

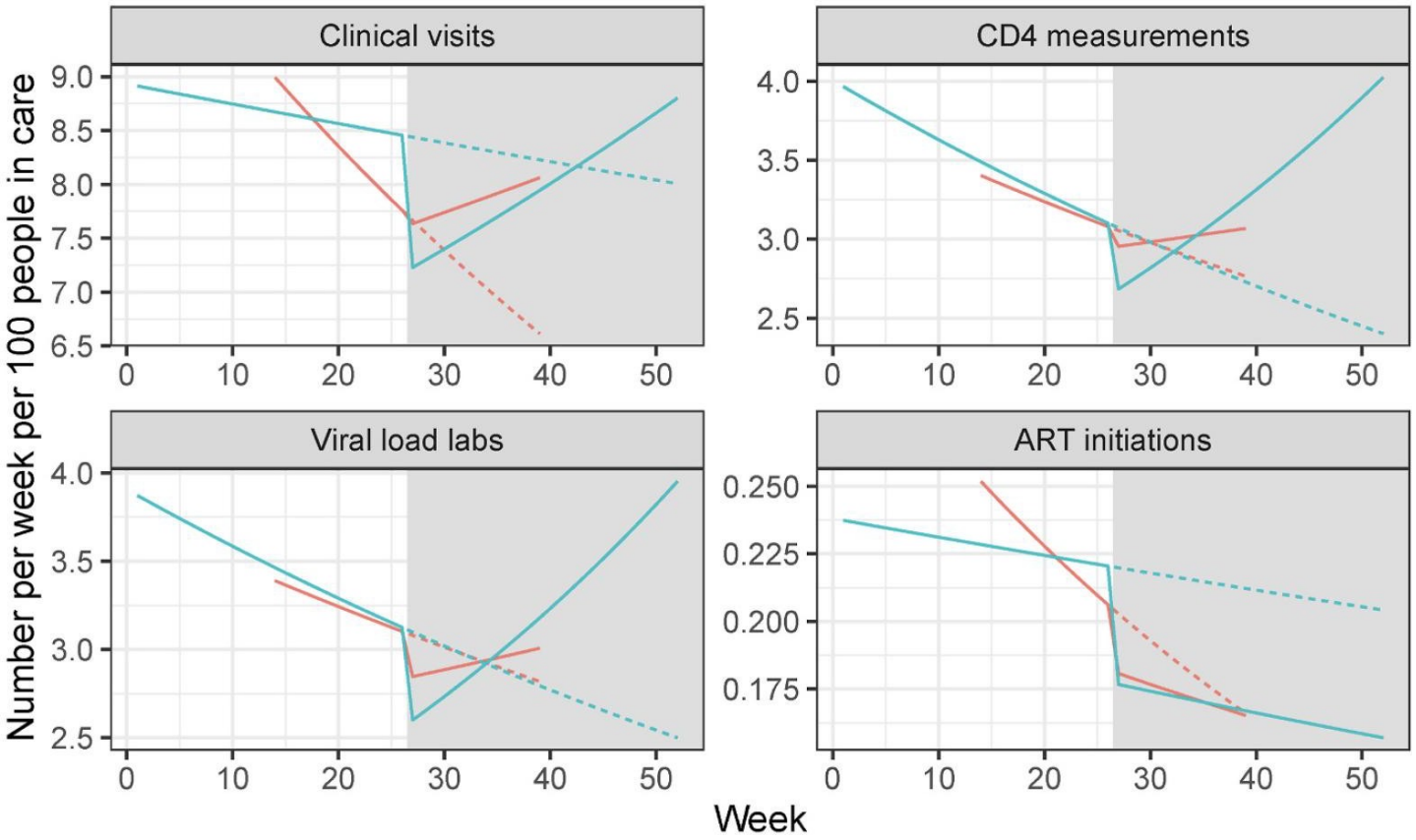

Figure 1. Interrupted Time Series models with discontinuities at the time of an earthquake to illustrate post-earthquake fitted trajectories (**solid lines**) for comparison against the pre-quake counterfactual trajectories (**dotted lines**) based on the 3-month and 6-month windows before and after the events.

- Comparing post-earthquake to pre-earthquake periods, there was a sharp drop in median HIV care visit rates (IRR = 0.79, 95% CI: 0.68–0.91)
- Viral load lab collection rates per week also decreased (IRR = 0.78, 95% CI: 0.62–0.99) across a 3-month window
- CD4 measurement rates also decreased (IRR = 0.43; 95% CI: 0.37–0.51), though only across a 6-month window

- Earthquakes occur frequently in Latin America & the Caribbean and have potential to disrupt care for chronic conditions like HIV
- Here we show short-term impacts on the numbers of clinic visits and CD4 and viral load measures over 3 months post-earthquake, but that these were largely overcome by 6 months post-earthquake
- Our data speak to the need for HIV clinical centers to develop disaster preparedness plans to help mitigate such disruptions in care following natural disasters

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Addressing Multiple Detection Limits with Semiparametric Cumulative Probability Models

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CCASAnet

Detection Limits (DLs) are common in biomedical research, including HIV/AIDS research

- For example, HIV-1 RNA (viral load; VL) is measured with DLs: People living with HIV who have suppressed VL have a VL below the DL (e.g., 40 copies/mL) but this is a non-zero value.

Data with DLs are often challenging to analyze; most of the common approaches have limitations:

- Dichotomize as detectable vs. undetectable (most common approach used for the analysis of VL in HIV research): This approach loses information because it treats all values above the DL as equivalent (e.g., 41 copies/mL = 4.1×10^6 copies/mL).
- Imputation of values below the DL (e.g., singly impute all values below DL as the DL itself, DL/2, or 0; or multiply impute values below DL based on some assumed distribution): Results may be sensitive to the arbitrary choice of the imputation value or the assumed distribution.

These analysis challenges are compounded when DLs differ across sites and time as is the case in practice (see Figure).

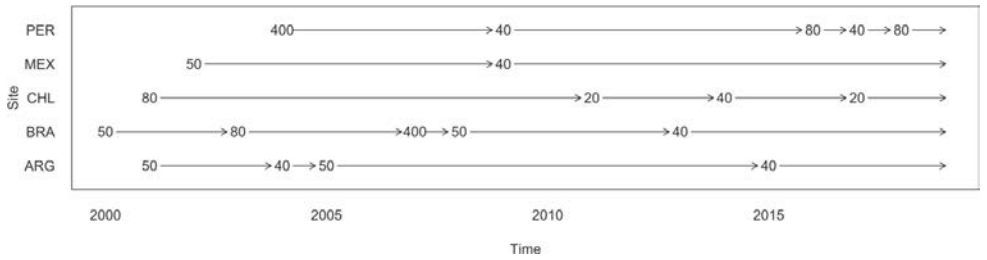


Figure. Most frequent DL values for VL by year at CCASAnet sites.

Method

We developed a statistical method that handles multiple DLs without dichotomizing variables or imputing value below the DLs.

Our approach is based on a widely used ordinal regression model, the cumulative probability model (CPM).

The CPM is a rank-based, semiparametric linear transformation model that can handle mixtures of continuous and ordinal variables.

These features are key for analyzing data with DLs because while observations above the DL are continuous, those below the DL can be thought of as belonging to some lower ordinal category.

With a single lower DL, CPMs assign values below the DL as having the lowest rank.

With multiple DLs, the CPM likelihood can be modified to appropriately distribute probability mass.

Adjusted odds ratios, conditional quantiles, and conditional exceedance probabilities can be easily extracted from these models.

Our paper derives properties of the method, shows good performance with simulations, and applies it to CCASAnet data.

We believe this approach is the new gold standard for analyzing data with DLs.

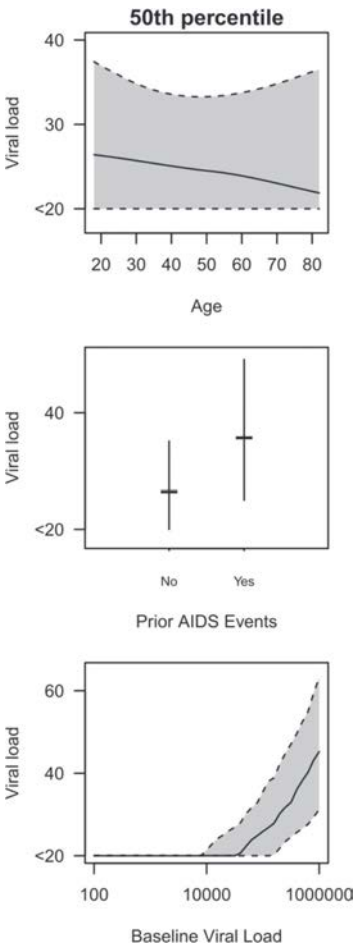
Factors associated with viral load (VL) 6 months after ART initiation

Data from 5301 PWH at 6 CCASAnet sites, 56% with VL < DLs.
Table shows adjusted odds ratios

- e.g., those with prior AIDS event at ART initiation have 24% increased odds of having a higher 6-month VL than those without AIDS after controlling for other variables in table.

Figure shows estimated median 6-month VL as a function of age, prior AIDS events, and VL at ART initiation (baseline), holding all other variables constant at their medians/modes.

Predictor	Odds ratio (95% CI)	*p*-value
Age (per 10 years)	0.98 (0.93, 1.03)	0.418
Sex		0.201
Male (reference)	1	
Female	0.90 (0.76, 1.06)	
Study center		<0.001
Peru (reference)	1	
Argentina	1.26 (0.98, 1.61)	
Brazil	1.07 (0.91, 1.26)	
Chile	1.07 (0.90, 1.26)	
Mexico	0.59 (0.49, 0.70)	
Route of infection		0.408
Homosexual/Bisexual (reference)	1	
Heterosexual	0.96 (0.83, 1.10)	
Other/unknown	0.79 (0.62, 1.01)	
Prior AIDS event		0.001
No (reference)	1	
Yes	1.24 (1.09, 1.41)	
Baseline CD4 (per 1 square root cells/μL)	1.09 (1.08, 1.10)	<0.001
Baseline VL (per 1 $\log_{10}$ copies/mL)	1.44 (1.34, 1.54)	<0.001
ART regimen		0.007
NNRTI-based (reference)	1	
INSTI-based	0.55 (0.40, 0.75)	
PI-based	1.10 (0.95, 1.29)	
Other	2.57 (1.28, 5.16)	
Months to VL measure	0.95 (0.92, 0.98)	0.002
Calendar year	0.89 (0.88, 0.91)	<0.001



Prediction Models for Adverse Drug Reactions During Tuberculosis Treatment in Brazil

Felipe Ridolfi,[1,2] Gustavo Amorim,[3] Lauren S. Peetluk,[4,5] David W. Haas,[1] Cody Staats,[1] Mariana Araújo-Pereira,[6,7] Marcelo Cordeiro-Santos,[8,9] Afrânio L. Kritski,[10] Marina C. Figueiredo,[1] Bruno B. Andrade,[1,6,7,11,12,13] Valeria C. Rolla,[2,a] and Timothy R. Sterling[1,a]; for the Regional Prospective Observational Research in Tuberculosis (RePORT)–Brazil Consortium

The Journal of Infectious Diseases

MAJOR ARTICLE

The Journal of Infectious Diseases, Volume 229, Issue 3, 15 March 2024, Pages 813–823, https://doi.org/10.1093/infdis/jiae025

RePORTBrazil
Regional Prospective Observational Research for Tuberculosis

Objectives 1. Development of prediction models for ADR during standard TB treatment
2. Evaluation of ADR-related factors

Eligibility drug-susceptible, culture-confirmed, pulmonary TB, standard TB treatment

Methods

- Prediction models ➔ bootstrapped backward selection approach and performance evaluation
- ADR-associated factors ➔ Cox regression
- ADR definition: TB-treatment related ADR (TB-ADR)

Results

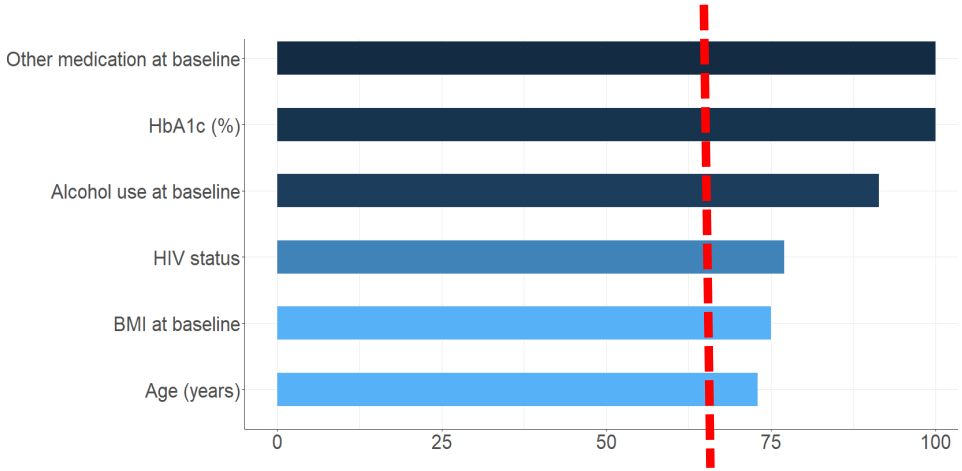
945 participants, 11% (N=102) of TB-ADR

- Grade 2 (78%), during the intensive phase (77%), hepatic (53%), "likely" related to TB treatment (46%)

Six variables were most predictive of ADR

- Main prediction model: baseline variables only (Figure 1)
- Alternative prediction model: included NAT2 variable (not shown)

Figure 1. Bootstrapped backward selection. Variables for the main prediction model (>70%)



Results

Increased risk of ADR ➔ Concomitant medication use and HIV-positivity (Figure 2)

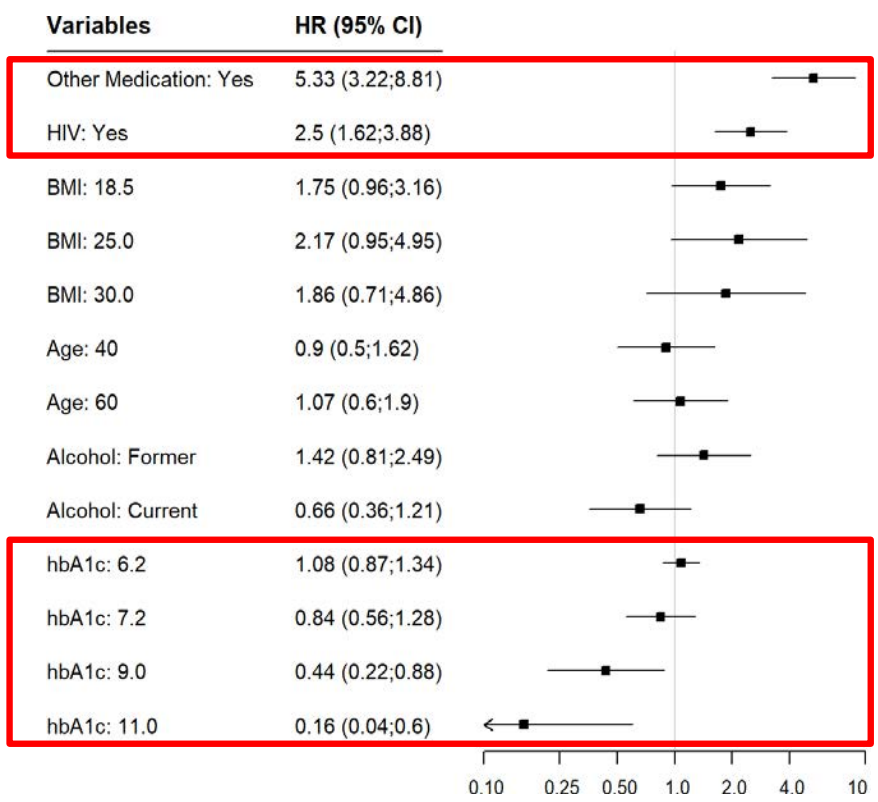
- 27 classes of concomitant medication
- unable to explore the risk of specific class of medication
- paracetamol vs non-paracetamol ➔ no difference in association with TB-ADR risk

Decreased risk of ADR ➔ Elevated levels of HbA1c

Conclusions

- The models were highly predictive of developing TB-ADR
- Concomitant medication and HIV-positivity were independent risk factors for TB-ADR
- Elevated levels of HbA1c were protective for TB-ADR

Figure 2 Coefficient plot. Baseline factors and association with ADR during TB treatment.



Footnote: HR; hazard ratio. Reference categories for other medication: no; for HIV: no/HIV-negative; Body Mass Index (BMI):15, for age: 20; for alcohol: never; for HbA1c:5.5.

Prenatal syphilis and adverse pregnancy outcomes in women with HIV receiving ART in Brazil: a population-based study

Jessica L. Castilho,[a,*] Fernanda F. Fonseca,[b,e] Ahra Kim,[d] Emilia Jalil,[e] Shengxin Tu,[d] Andréa M. B. Beber,[c] Adele S. Benzaken,[b] Valdiléa G. Veloso,[e] Beatriz Grinsztejn,[e] Bryan E. Shepherd,[d] and Angélica E.B. Miranda,[c] on behalf of the National Cohort Study of Dolutegravir and Pregnancy Outcomes in Brazil

The Lancet Regional Health - Americas 2024;39: 100894
Published Online 10 October 2024

Background: Rates of prenatal syphilis are rising globally and are associated with adverse pregnancy outcomes (stillbirth, miscarriage, preterm delivery, low birth weight) and congenital syphilis. In women with HIV, prenatal syphilis may also increase risk of vertical HIV transmission but there is limited data of prenatal syphilis in women with HIV in the current epidemic.

Methods: In this **nationally-representative, observational, retrospective study of pregnant women with HIV receiving ART in Brazil in 2015-2018,** we analyzed factors associated with prenatal syphilis, syphilis screening, prenatal care quality (based upon observed vs. recommended timing of entry into care and number of prenatal visits), and adverse pregnancy outcomes using multivariable logistic regression models. Prenatal syphilis included clinical diagnoses with receipt of treatment or any positive syphilis test within 30 day before conception and delivery.

PMID: 39839683 PMCID: PMC11747186

CCASAnet

Results:

7.8% [95%CI: 6.5-8.8%] overall prevalence of prenatal syphilis (166 / 2169 women)

91% of women with prenatal syphilis had documentation of receipt of treatment

Table 1. Characteristics of pregnant women with and without syphilis

	Women without prenatal syphilis (n=2003)	Women with prenatal syphilis (n=166)
Age at conception, median (IQR)	27.7 (22.7-32.9)	25.9 (21.2-32.3)
Race, n (%)		
White	701 (35.1)	43 (26.1)
Black	227 (11.4)	36 (21.8)
Pardo/Mixed	899 (45.0)	75 (45.5)
All others & unknown	168 (8.4)	11 (6.6)
Years of education, n (%)		
0-3 years	120 (6.4)	8 (5.2)
4-7 years	619 (33.0)	66 (42.6)
8-11 years	902 (48.2)	75 (48.4)
≥12 years	232 (12.4)	6 (3.9)
History of tobacco use, n (%)	372 (18.6)	56 (33.7)
History of alcohol use, n (%)	323 (16.1)	51 (30.7)
History of substance use, n (%)	216 (10.8)	48 (28.9)
History of crack/cocaine use, n (%)	140 (7.0)	35 (21.1)

Results:

46% of women received inadaquate prenatal care and only 29% received recommended syphilis screening based upon timing of prenatal care entry

- Median number of prenatal visits = 7 (IQR: 5-9) for both women with and without prenatal syphilis
- Median gestational age at prenatal care entry = 12.0 and 12.8 weeks for women with and without prenatal syphilis, respectively
- Prenatal syphilis was more frequent among women with inadequate prenatal care (12%) vs. women with intermediate or adequate prenatal care (8%)

In unadjusted and multivariable analses, prenatal syphilis was not associated risk of composite of any adverse pregnancy outcomes:
aOR 0.91 [95%CI: 0.64-1.30]

Pregnancy outcomes among women with and without prenatal syphilis

	Women without prenatal syphilis (n=2039)	Women with prenatal syphilis (n=168)
Pregnancy outcome, n (%) Live births Stillbirths Spontaneous abortions	 1970 (96.6) 20 (1.0) 49 (2.4)	 161 (95.8) 2 (1.2) 5 (3.0)
Multiple fetus[c], n (%)	69 (3.6)	4 (2.5)
Estimated gestational age at birth (weeks), median (IQR)	38.9 (3.0-39.4)	39.0 (38.0-40.0)
Birthweight (grams), median (IQR)	3040 (2755-3355)	3085 (2782-3370)
Preterm delivery[d], n (%)	405 (21.3)	34 (21.4)
Small for gestational age[e], n (%)	179 (9.7)	17 (11.0)
Any congenital abnormality, n (%)	96 (5.0)	11 (6.9)

[a]Stillbirth defined as fetal demise at or after EGA 22 weeks. [b]Abortion defined as fetal demise before EGA 22 weeks. All presumed spontaneous as elective abortions are illegal in Brazil. [c]Multiple fetus includes fetus of twin or more pregnancy. [d]Preterm delivery defined as live birth occurring before 37 weeks EGA and only assessed for singleton pregnancies [e]Small for gestational age defined as birthweight of live birth only below the 10th percentile for the Brazilian population as predicted by EGA at birth and sex (male or female). Only assess in live birth outcomes from singleton pregnancies.

Conclusions: Prenatal syphilis was prevalent among pregnant women with HIV in Brazil. Prenatal syphilis was not associated with adverse pregnancy outcomes. Inadequate prenatal care and lack of receipt of recommended syphilis was common. Greater attention to syphilis screening, prevention, and treatment is especially needed among marginalized women.

PMID: 39839683 PMCID: PMC11747186

Central Africa IeDEA

2024 Research Highlights

IeDEA

Availability of substance use screening and treatment within HIV clinical sites across seven geographic regions within the IeDEA Consortium

Lancaster KE, Stockton M, Remch M, Wester CW, Nash D, Brazier E, Adedimeji A, Finlayson R, Freeman A, Hogan B, Kasozi C, Kwobah EK, Kulzer JL, Merati T, Tine J, Poda A, Succi R, Twizere C, Tlali M, Groote PV, Edelman EJ, Parcesepe AM; IeDEA Consortium. Availability of substance use screening and treatment within HIV clinical sites across seven geographic regions within the IeDEA consortium. Int J Drug Policy. 2024 Feb;124:104309. doi: 10.1016/j.drugpo.2023.104309.

AIM:

- To assess the availability and implementation of alcohol and substance use disorder screening and treatment across HIV clinical sites globally, with a focus on regional differences, facility characteristics, and national policies related to alcohol and substance use.

METHODS:

- **Design:** The 2020 site assessment survey collected data from HIV care sites across 41 countries to evaluate alcohol and substance use disorder (AUD/SUD) screening and treatment practices.
- **Population:** The survey included 223 sites, with 68% urban, 77% in low- and middle-income countries, and representation from regions such as East Africa (33%) and Asia-Pacific (23%).
- **Measurements:** Data were collected on the use of validated AUD/SUD screening instruments and the availability of treatments such as counseling, detoxification, medication, and syringe exchange programs.
- **Analysis:** Descriptive analyses assessed variations in AUD/SUD screening and treatment by site characteristics, including income, rurality, and national alcohol and harm reduction policies.

IeDEA

Availability of substance use screening and treatment within HIV clinical sites across seven geographic regions within the IeDEA Consortium

RESULTS:

- A total of 32% (n=71) of sites reported the use of validated screening tools for Alcohol Use Disorder (AUD), with significantly higher prevalence in high-income countries (49%) compared to low-income countries (8%).
- 31% (n=69) of sites provided both AUD screening and at least one treatment modality (i.e., counseling, brief intervention, medication, or detoxification).
- Substance Use Disorder (SUD) screening was less prevalent, with only 12% (n=27) of sites utilizing validated instruments, predominantly in North America (38%).
- Sites located in countries with national alcohol or harm reduction policies exhibited higher rates of both AUD and SUD screening, as well as greater availability of associated treatment interventions.
- Regional differences were pronounced, with no sites in West or Central Africa reporting AUD or SUD screening, highlighting geographic disparities in service provision.

Lancaster KE, Stockton M, Remch M, Wester CW, Nash D, Brazier E, Adedimeji A, Finlayson R, Freeman A, Hogan B, Kasozi C, Kwobah EK, Kulzer JL, Merati T, Tine J, Poda A, Succi R, Twizere C, Tlali M, Groote PV, Edelman EJ, Parcesepe AM; IeDEA Consortium. Availability of substance use screening and treatment within HIV clinical sites across seven geographic regions within the IeDEA consortium. Int J Drug Policy. 2024 Feb;124:104309. doi: 10.1016/j.drugpo.2023.104309.

IeDEA

Long-term HIV care outcomes under universal HIV treatment guidelines: A retrospective cohort study in 25 countries

Brazier E, Tymejczyk O, Wools-Kaloustian K, Jiamsakul A, Torres MTL, Lee JS, Abuogi L, Khol V, Mejía Cordero F, Althoff KN, Law MG, Nash D; International epidemiology Databases to Evaluate AIDS (IeDEA). Long-term HIV care outcomes under universal HIV treatment guidelines: A retrospective cohort study in 25 countries. *PLoS Med*. 2024 Mar 18;21(3):e1004367. doi: 10.1371/journal.pmed.1004367.

AIMS:

- To estimate loss-to-clinic (LTC) at 12, 24, and 36 months after enrollment in HIV care, comparing adults ≥15 years enrolling before and after country-level adoption of universal HIV treatment guidelines.
- To estimate clinic retention, viral load (VL) testing, and VS at 12, 24, and 36 months after ART initiation.

METHODS:

- **Design**: Retrospective cohort analysis of patients enrolling in HIV care between 24 months before and 12 months after national adoption of universal HIV treatment guidelines, occurring 2012-2018.
- **Population**: ART-naïve patients aged ≥15 years at care enrollment in 25 countries in IeDEA's Asia-Pacific, Central Africa, East Africa, Central/South America, and North America regions.
- **Analysis**: Competing risks and cause-specific Cox proportional hazards regression models used to estimate the crude cumulative incidence of LTC and hazards of LTC at 12, 24, and 36 months after enrollment, before and after national adoption of universal treatment guidelines. Modified Poisson regression models used to estimate relative risks of care retention, viral load (VL) monitoring, and viral suppression (VS) at 12, 24 and 36 months after ART initiation, before and after universal treatment guideline adoption.

IeDEA

Long-term HIV care outcomes under universal HIV treatment guidelines: A retrospective cohort study in 25 countries

RESULTS:

- Among 66,963 patients enrolling in HIV care at 109 clinics (69.4% enrolling before guideline adoption and 30.6% enrolling afterwards), the crude cumulative incidence of LTC was 23.8% at 12 months, 31.0% at 24 months, and 37.2% at 36 months.
- Adjusting for patient characteristics and clinic setting, enrolling in care and initiating ART after guideline adoption was associated with increased hazard of LTC at 12 months (aHR: 1.25, 95% CI: 1.08, 1.44); 24 months (aHR: 1.38, 95% CI: 1.19, 1.59); and 36 months (aHR 1.34, 95% CI 1.18, 1.53) compared with enrollment before guideline adoption, with no before-after differences among patients with no record of ART start.
- Among patients retained on ART, VL monitoring was low, with little improvement after guideline adoption.
- Among those with VL monitoring, VS was high at each time point among patients enrolling before guideline adoption, with no substantive difference associated with guideline adoption.

Brazier E, Tymejczyk O, Wools-Kaloustian K, Jiamsakul A, Torres MTL, Lee JS, Abuogi L, Khol V, Mejía Cordero F, Althoff KN, Law MG, Nash D; International epidemiology Databases to Evaluate AIDS (IeDEA). Long-term HIV care outcomes under universal HIV treatment guidelines: A retrospective cohort study in 25 countries. *PLoS Med*. 2024 Mar 18;21(3):e1004367. doi: 10.1371/journal.pmed.1004367.

IeDEA

Association of cardiovascular disease risk with liver steatosis and fibrosis in people with HIV in low- and middle-income countries

Kuniholm MH, Murenzi G, Shumbusho F, Brazier E, Plaisy MK, Mensah E, Wandeler G, Riebensahm C, Chihota BV, Samala N, Diero L, Semeere AS, Chanyachukul T, Borse R, Nguyen DTH, Perazzo H, Lopez-Iniguez A, Castilho JL, Maruri F, Jaquet A. AIDS. Epub 2024 Sep 11. doi: 10.1097/QAD.0000000000004012.

AIMS:

- To understand the relationship between cardiovascular disease (CVD) risk and liver steatosis and fibrosis among people with HIV (PLWH) on antiretroviral therapy (ART) in low and middle income countries (LMIC).

METHODS:

- **Design:** Cross-sectional analysis of data collected between December 2020 and September 2022 across nine sites in Brazil, Cote d'Ivoire, India, Kenya, Mexico, Rwanda, Togo, Zambia and Zimbabwe.
- **Population:** Participants were ≥40 years and receiving HIV care at Sentinel Research Network (SRN) sites. Participants with viral hepatitis, hazardous alcohol consumption, and unsuppressed HIV viral load were excluded from the analysis
- **Measurements:** Ten-year CVD risk was calculated using 2019 World Health Organization (WHO) non-laboratory and laboratory models. Transient elastography was used to assess liver disease.
- **Analysis:** Logistic regression was used to estimate odds ratios, adjusting for study site, CD4 T cell count, stavudine and didanosine exposure, and in models stratified by sex and geographic region.

IeDEA

Association of cardiovascular disease risk with liver steatosis and fibrosis in people with HIV in low- and middle-income countries

RESULTS:

- There were 1750 participants from nine LMIC. The median age of participants was 51 years of age [interquartile range (IQR): 46–57], and a majority (61%) were women.
- Median CVD risk was 3% for both non-laboratory and laboratory-based models.
- Adjusted odds ratios (ORs) for steatosis and significant fibrosis associated with laboratory CVD risk (10 vs. <5%) were OR=1.83; 95% CI=1.21–2.76; P=0.004 and OR=1.62; 95% CI=0.85–3.07; P=0.14, respectively.
- Associations of CVD risk with steatosis were stronger in men and among participants at study sites outside Africa (Figure)

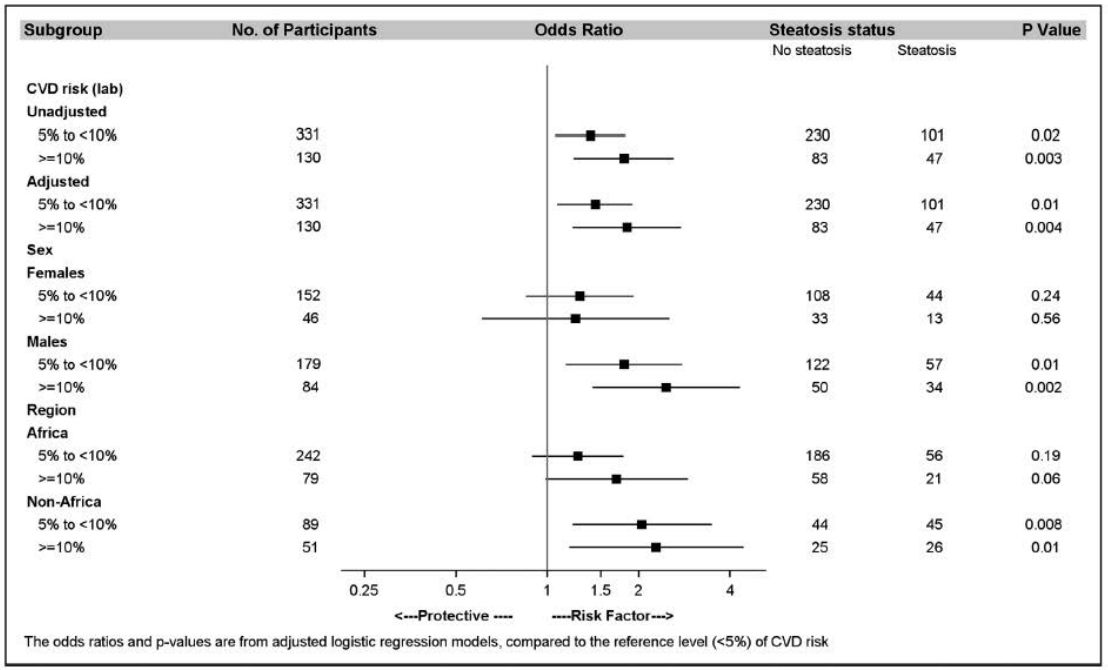


Fig. 2. Associations of cardiovascular disease risk (laboratory) with liver steatosis in people with HIV, ≥40 years of age, and on antiretroviral therapy >6 months.

Kuniholm MH, Murenzi G, Shumbusho F, Brazier E, Plaisy MK, Mensah E, Wandeler G, Riebensahm C, Chihota BV, Samala N, Diero L, Semeere AS, Chanyachukul T, Borse R, Nguyen DTH, Perazzo H, Lopez-Iniguez A, Castilho JL, Maruri F, Jaquet A. AIDS. Epub 2024 Sep 11. doi: 10.1097/QAD.0000000000004012.

IeDEA

Accuracy of nine-item Patient Health Questionnaire against psychiatric diagnosis for depression among people with HIV

Yotebieng M, Zotova N, Bernard C, Goodrich S, Awoh AR, Watnick D, Nsonde DM, Moungang EFT, Noumedem JLN, Mbongo'o GCN, Minga A, Seydi M, Gandou P, Kwobah EK, Atwoli L, Jaquet A, Wools-Kaloustian K, Anastos K; IeDEA Consortium. AIDS. 2024 Oct 1;38(12):1765-1773. doi: 10.1097/QAD.0000000000003963.

AIM:

To assess the performance of the nine-item Patient Health Questionnaire (PHQ-9) against psychiatrist diagnosis in people with HIV (PWH)

METHODS:

- **Design:** Cross-sectional analysis of data collected between January 2018 and July 2022 across five sites in Cameroon, Cote d'Ivoire, Kenya, Senegal, and the Republic of Congo.
- **Population:** Participants were ≥18 years and receiving HIV care at the participating site
- **Measurements**: PHQ-9 was administered by study staff followed by a psychiatrist's evaluation within 3 days.

IeDEA

Accuracy of nine-item Patient Health Questionnaire against psychiatric diagnosis for depression among people with HIV

RESULTS:

- Overall, 778 participants with complete data were included: 297 (38.2%) in Cameroon, 132 (17.0%) in Congo, 148 (19.0%) in Cote d'Ivoire, 98 (12.6%) in Kenya, and 103 (13.2%) in Senegal.
- For the common cut-off score ≥10, sensitivity was low: 50% or lower in Cameroon, Congo and Senegal, 66.7% in Kenya and 70.6% in Cote d'Ivoire.
- However, PHQ-9 score was highly predictive of psychiatric diagnosis with area under the curve ranging from 0.935 [95% confidence interval (CI): 0.893, 0.977] in Cote d'Ivoire to 0.768 (95% CI: 0.589, 0.947) in Congo and
- Negative predictive values (NPV) were high: 98.9% (95% CI: 96.9%, 99.8%) in Cameroon, 96.1 (95% CI: 91.1, 98.7) in Cote d'Ivoire, 96.3% (95% CI: 89.7%, 99.2%) in Kenya, 95.7% (95% CI: 90.2%, 98.6%) in Congo, and 89.0% (95% CI: 81.2%, 94.4%) in Senegal.

Yotebieng M, Zotova N, Bernard C, Goodrich S, Awoh AR, Watnick D, Nsonde DM, Moungang EFT, Noumedem JLN, Mbongo'o GCN, Minga A, Seydi M, Gandou P, Kwobah EK, Atwoli L, Jaquet A, Wools-Kaloustian K, Anastos K; IeDEA Consortium. Accuracy of nine-item Patient Health Questionnaire against psychiatric diagnosis for depression among people with HIV. AIDS. 2024 Oct 1;38(12):1765-1773. doi: 10.1097/QAD.0000000000003963.

IeDEA

Cancer risk among people living with Human Immunodeficiency Virus (HIV) in Rwanda from 2007 to 2018

Dusingize JC, Murenzi G, Muhoza B, Businge L, Remera E, Uwinkindi F, Hagenimana M, Rwibasira G, Nsanzimana S, Castle PE, Anastos K, Clifford GM. Int J Cancer. 2024 Dec 15;155(12):2149-2158. doi: 10.1002/ijc.35091.

AIM:

To assess the risk of cancer among people living with Human Immunodeficiency Virus (HIV) in Rwanda from 2007 to 2018.

METHODS:

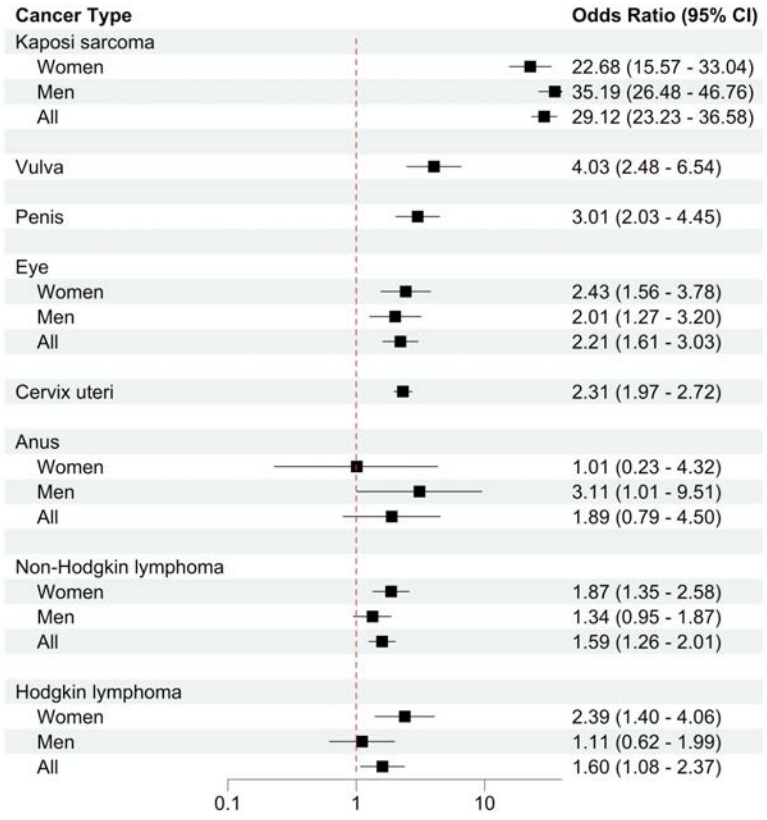
- **Data:** Population-based cancer registry data from 2007 to 2018 were used to identify cancer cases among both people living with HIV (PLHIV) and HIV-negative individuals. A probabilistic record linkage approach between the HIV and cancer registries was employed to supplement HIV status ascertainment in the cancer registry.
- **Analysis**: Unconditional logistic regression models were employed to evaluate the association between HIV infection and different cancer types, controlling for potential confounding factors.

IeDEA

Cancer risk among people living with Human Immunodeficiency Virus (HIV) in Rwanda from 2007 to 2018

RESULTS:

- From 2007 to 2018, the cancer registry recorded 17,679 cancer cases, of which 7% were diagnosed among PLHIV.
- Cancers were diagnosed at a younger age among PLHIV (median age 43 years) compared to HIV-negative individuals (median age 50 years), with a higher proportion of cases found in women than men (60% vs. 40%).
- We found significant associations between HIV infection and Kaposi's sarcoma (OR: 29.1, 95% CI: 23.2-36.6), non-Hodgkin lymphoma (1.6, 1.3-2.0), Hodgkin lymphoma (1.6, 1.1-2.4), cervical (2.3, 2.0-2.7), vulvar (4.0, 2.5-6.5), penile (3.0, 2.0-4.5) and eye cancers (2.2, 1.6-3.0).
- Men living with HIV had a higher risk of anal cancer (3.1, 1.0-9.5) than men without HIV, but women living with HIV did not have higher risk than women without HIV (1.0, 0.2-4.3).



Dusingize JC, Murenzi G, Muhoza B, Businge L, Remera E, Uwinkindi F, Hagenimana M, Rwibasira G, Nsanzimana S, Castle PE, Anastos K, Clifford GM. Int J Cancer. 2024 Dec 15;155(12):2149-2158. doi: 10.1002/ijc.35091.

IeDEA

East Africa

IeDE

INTERNATIONAL EPIDEMIOLOGY
DATABASES TO EVALUATE AIDS

2024 Research Highlights

IeDEA

Adaptation of the Client Diagnostic Questionnaire (CDQ)

Objective:

-To culturally adapt the Client Diagnostic Questionnaire (CDQ), a mental health and substance use questionnaire designed in the United States for use by non-medical specialists with PLWHIV to conduct screening for depression, anxiety disorders, post-traumatic stress disorder, psychosis and substance use (including drugs and alcohol).

Validation:

-90 participants (30 from each site) were selected for a diagnostic interview with a mental health professional for criterion validation

-Kappa statistics assessed the strength of agreement between the non-specialists and the mental health professionals' diagnoses

Location	Eldoret, Kenya	Kisumu, Kenya	Mbarara, Uganda
Language of local CDQ adaptation	Swahili[1]	Dholuo[2]	Runyankole -Rukiga[3]
Group members conducting translations to local language and face validation[4]	Psychiatrist (2) General Medicine clinician Psychologist Nurse Community representative	Psychiatrist Interpersonal psychotherapist General Medicine clinician (2) Mental Health study coordinator Translator	Psychiatrist Study PI Study coordinator
Use of unique expert translator for local language back translation from to English.	Yes	Yes	No[5]
Psychiatrist evaluation of local language and back translated CDQ	Yes (2)	Yes (1)	Yes (1)

-Translational ambiguity was observed (more than one meaning for a word)

Example: "alcoholic drink" was translated into both "pombe" and " vileo" in Swahili

-Semantic equivalence was often difficult

May require direct translation or a more pragmatic approach to achieve the intended meaning (use of multiple words or phrase)

IeDEA

Adaptation of the Client Diagnostic Questionnaire (CDQ)

Criterion Validation
-There was agreement between the Psychiatrist and the RA using the CDQ 75.5% of the time (original English agreement was 85% and 79% in South Africa)
-RAs were more likely to over diagnoses a problem (17.8%) with the CDQ compared with the mental health professional, but this can be mitigated with mental health referrals
-Under diagnosis by the RA with the CDQ was less common (6.7%)

	Non-Specialist Locally Translated CDQ Administration Results	
Psychiatrist	**Positive N (%)**	**Negative N (%)**
Positive	39 (43.3%)	6 (6.7%)
Negative	16 (17.8%)	29 (32.2%)

Summary
-The CDQ was successfully translated into several languages and adapted for use in East Africa
-Trained non-specialists can use the CDQ with a sensitivity of 86.7% (91% in original study) and a specificity of 65% (same as the original study)
-Over diagnosis will lead to further evaluation that may be negative, but will be less likely to miss an existing diagnosis

Kwobah et al. PLOS Global Health, 2024

IeDEA

Modeling the HIV Cascade of Care Using Routinely Collected Clinical Data to Guide Programmatic Interventions and Policy Decisions

Study design: retrospective cohort

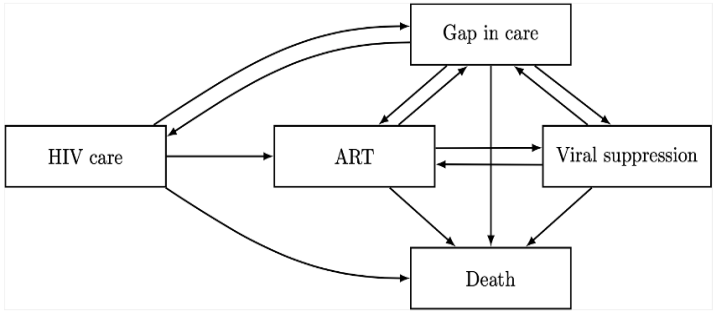
Sample: 35,649 people living with HIV and receiving care at 78 clinics in East Africa between 2014 and 2020

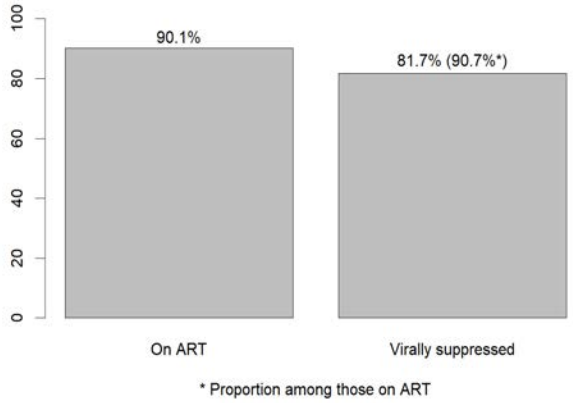
Eligibility criteria:
- Age ≥ 15 years
- Enrollment in one of the EA-IeDEA clinics between 2014-2020
- At least 1 viral load measurement

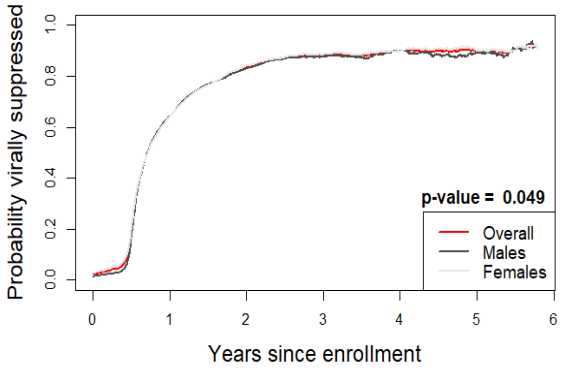
Outcomes:
- Gap in care: missing any scheduled visit by > 30 days
- Viral suppression (VS) <1000 copies/mL
- Death

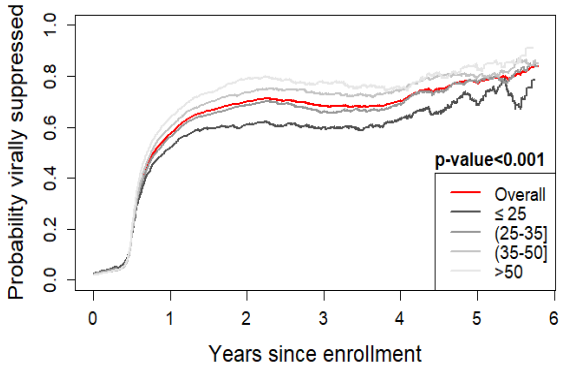
IeDEA

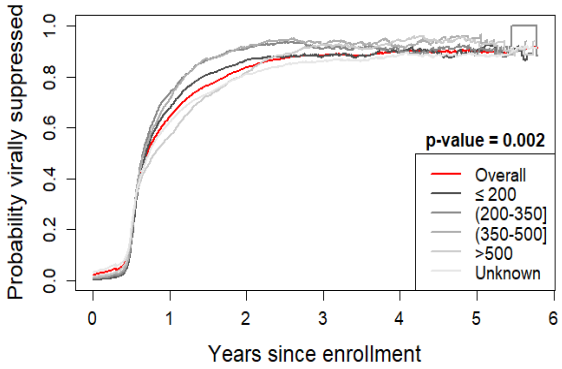
Modeling the HIV Cascade of Care Using Routinely Collected Clinical Data to Guide Programmatic Interventions and Policy Decisions

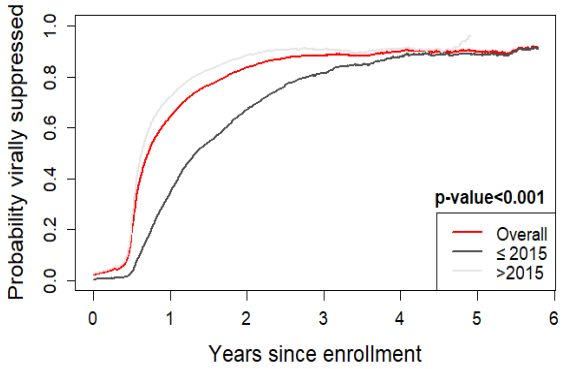












IeDEA

High Prevalence of Unconfirmed Positive HIV PCR Test Results among African Infants with HIV Exposure in the International epidemiology Databases to Evaluate AIDS (IeDEA) Consortium

Study design: retrospective cohort

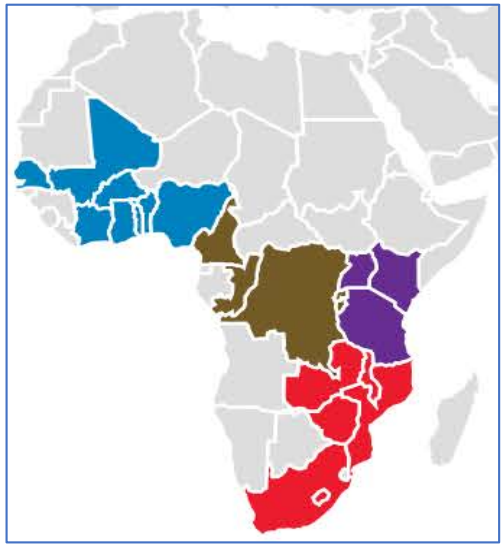
Setting: Four IeDEA regions; Central Africa, East Africa, Southern Africa, and West Africa

Eligibility criteria: All Infants with HIV exposure (IHE), born from 2004–2021, and enrolled in care at an IeDEA-affiliated site at age <18 months of age.

Definitions & Outcomes:

- "Unconfirmed positives" = IHE with only one positive virologic test (qualitative or quantitative DNA and/or RNA PCRs) at <18 months of age and no additional positive virologic or antibody test at ≥18 months of age
- Primary outcomes:
  (i) prevalence of unconfirmed positives among all IHE
  (ii) among those with any positive virologic test

Objective: To determine the prevalence of unconfirmed positive HIV PCR test results among African IHE in the IeDEA consortium



https://www.iedea.org/regions/

Carlucci et al, *Clin Infect Dis*, 2024

IeDEA

44% of infants with ≥1 positive virologic test lacked a confirmatory positive test

Results:

	CA 2004-20	EA 2004-21	SA 2014-17	WA 2004-18	All Regions
1. Infants with perinatal HIV exposure [n]	10,520	47,015	8,600	6,483	72,618
2. Any positive virologic test at <18 months, *among #1* [n (%)]	415 (4%)	2,980 (6%)	154 (2%)	103 (2%)	3,652 (5%)
3. Only one positive test ("**unconfirmed positives**"), *among #2* [n(%)]	240 (58%)	1,256 (42%)	20 (13%)	94 (91%)	1,610 (44%)
4. No additional virologic test performed after the initial positive test, *among #3* [n(%)]	192 (80%)	1,095 (87%)	19 (95%)	87 (93%)	1,393 (87%)
5. Additional (≥1) virologic test performed and not positive, *among #3* [n(%)]	48 (20%)	161 (13%)	1 (5%)	7 (7%)	217 (13%)

Conclusions:

- Unconfirmed positive HIV test results were highly prevalent among IHE in this cohort
- Efforts are needed to ensure confirmatory testing to reduce the risk of potentially false-positive results
- Future research will investigate (i) the contexts in which unconfirmed positive results occur, and (ii) whether unconfirmed false-positive results might have led to misdiagnoses that need to be addressed

Carlucci et al, *Clin Infect Dis*, 2024

IeDEA

Effects of alcohol use on patient retention in HIV care in East Africa

- Little is known about the long-term association between hazardous alcohol use and gaps in care for people living with HIV in East Africa.
- Adults who participated in our previously published Phase I* study of hazardous alcohol use at HIV programs in Kenya and Uganda were eligible at their 42 to 48 month follow-up visit.
- Participants who re-enrolled were followed for an additional ~12 months. Hazardous alcohol use behavior was measured using the Alcohol Use Disorders Identification Test (AUDIT) tool.
- The proportion of patients experiencing a gap in care at a specific time point was based on a nonparametric moment-based estimator. A semiparametric Cox proportional hazard model was used to determine the association between hazardous alcohol use at enrollment in Phase I (AUDIT score ≥8) and gaps in care.

Monroy et al, 2024

*Patsis et al, 2020

IeDEA

Effects of alcohol use on patient retention in HIV care in East Africa

- Of the 731 study-eligible participants from Phase I, 5.5% had died, 10.1% were lost to follow-up, 39.5% transferred, 7.5% declined/not approached, and 37.3% were enrolled.
- Phase II participants were older, had less hazardous drinking and had a lower WHO clinical stage than those not re-enrolled.
- Hazardous drinking in the re-enrolled was associated with a Hazard Ratio (HR) of 1.88 [p-value = 0.016] for a gap in care.
- Thus, hazardous alcohol use at baseline was associated with an increased risk of experiencing a gap in care and presents an early target for intervention.

Monroy et al, 2024

IeDEA

The Tuberculosis Sentinel Research Network (TB-SRN) of the International epidemiology Databases to Evaluate AIDS (IeDEA): protocol for a prospective cohort study in Africa, Southeast Asia, and Latin America

- Tuberculosis (TB) is a leading infectious cause of death globally, and the most common cause of morbidity and mortality in people with HIV.
- Individuals who complete TB treatment may be at risk for post-TB lung disease (PTLD), a focus of emerging research with very limited data in populations affected by HIV.
- The TB-SRN is a prospective, observational cohort study that will assess drivers and correlates of treatment and post-treatment outcomes of individuals aged ≥15 years with pulmonary TB (microbiologically confirmed or clinically diagnosed), with and without HIV. Target enrollment is 2,600 participants across 16 sites in 11 countries across 6 IeDEA regions.

Enane et al, *BMJ Open*, In press

IeDEA

The Tuberculosis Sentinel Research Network (TB-SRN) of the International epidemiology Databases to Evaluate AIDS (IeDEA): protocol for a prospective cohort study in Africa, Southeast Asia, and Latin America

- Data regarding clinical and sociodemographic factors, mental health, health-related quality of life, pulmonary function, and laboratory and radiographic findings will be collected through harmonized procedures and using standardized questionnaires and data collection tools, beginning from TB treatment initiation, through 12 months after the end of treatment.
- The **TB-SRN provides a unique platform for global observational research in TB-HIV epidemiology**; generating key data for drivers and correlates of TB treatment and post-treatment outcomes, across a diverse global cohort. Findings from this project will inform policy and practice regarding TB treatment, and further research efforts.

Enane et al, *BMJ Open,* In press

IeDEA

IeDEA Southern Africa

Research highlights 2024

IeDEA

MR190: Transition to dolutegravir-based ART in 35 low- and middle-income countries: a global survey of HIV care clinics

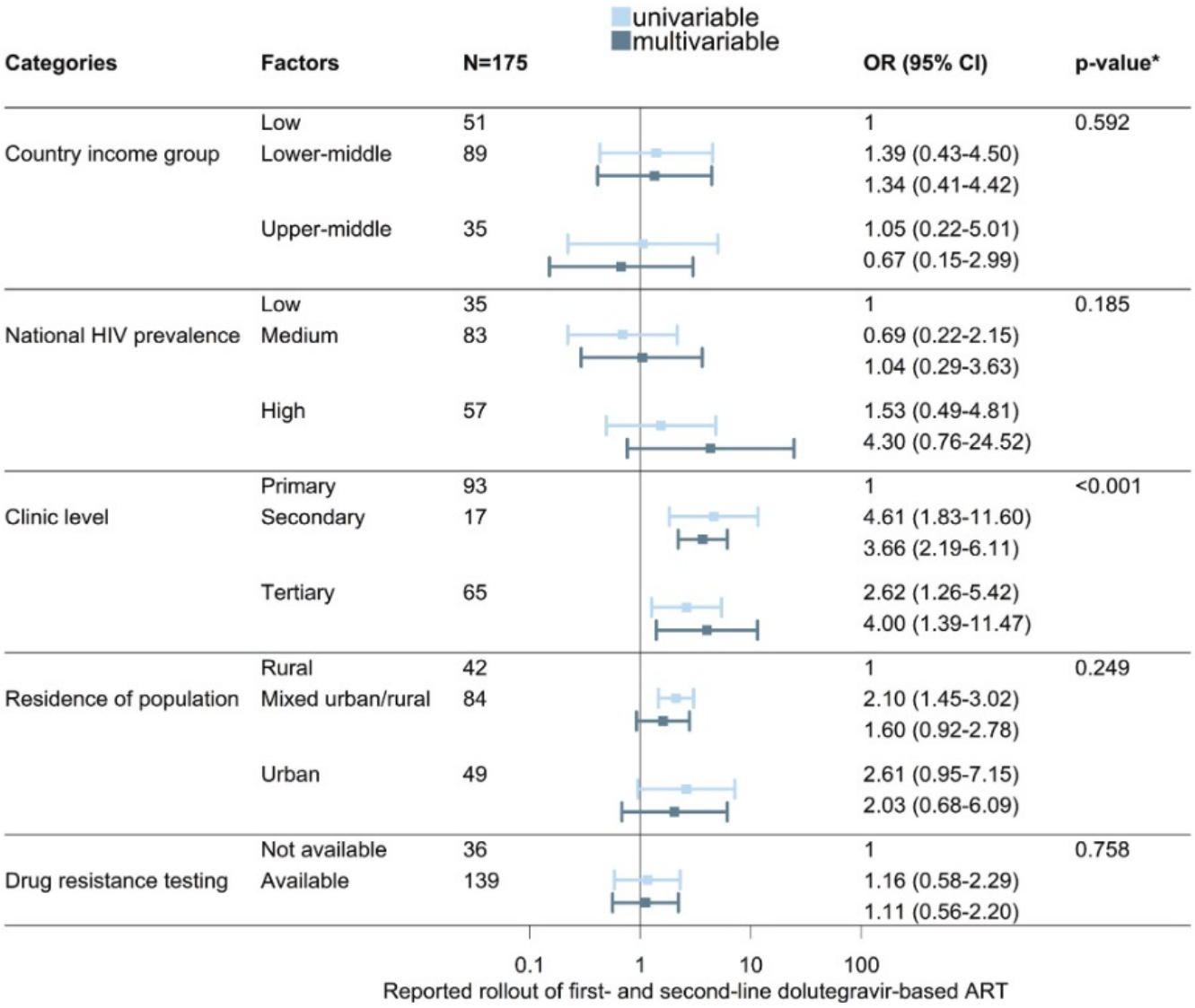
- We assessed the status of dolutegravir (DTG) rollout and viral load (VL) and drug resistance (DR) testing practices in IeDEA
- Site Assessment 4.0 data collected in 2020-2021
- 175 clinics: 137 (78%) in Africa, 30 (17%) in the Asia-Pacific, 8 (5%) in Latin America
  - 90% of clinics rolled out DTG, most for first- or second-line ART, 55% for both lines
  - 59% of clinics that introduced first- or second-line DTG required recent viral load testing before switching, 15% performed genotypic resistance testing at switch

Many sites switched persons to DTG without recent VL testing and DR testing was rarely performed.

Drug resistance among persons switching to DTG may go undetected.

Zaniewski et al., AIDS, 2024; DOI:10.1097/QAD.0000000000004007

IeDEA



Univariable and multivariable logistic regression of DTG rollout both first- and second-line regimens among 175 IeDEA clinics

Zaniewski et al., AIDS, 2024

IeDEA

Long-term Hepatitis B and Liver Outcomes Among Adults Taking Tenofovir-Containing Antiretroviral Therapy for HBV/HIV Coinfection in Zambia

Background

- Chronic hepatitis B virus (HBV) infection affects around 250 million individuals and causes up to 1 million deaths per year from cirrhosis and/or hepatocellular carcinoma.
- To mitigate the increased risk of liver-related mortality with HBV/HIV coinfection versus HBV alone, universal tenofovir-containing antiretroviral therapies (ART) are recommended for people with coinfection.
- However, in sub-Saharan Africa, long-term data on HBV outcomes, including in people with HIV, are extremely limited.

Methods

- Prospective cohort of adults with HIV and hepatitis B surface antigen (HBsAg)-positivity enrolled at ART initiation.
- On tenofovir-containing ART, we ascertained HBV viral load (VL) non-suppression, alanine aminotransferase (ALT) elevation, serologic end-points, progression of liver fibrosis based on elastography, and hepatocellular carcinoma (HCC) incidence.

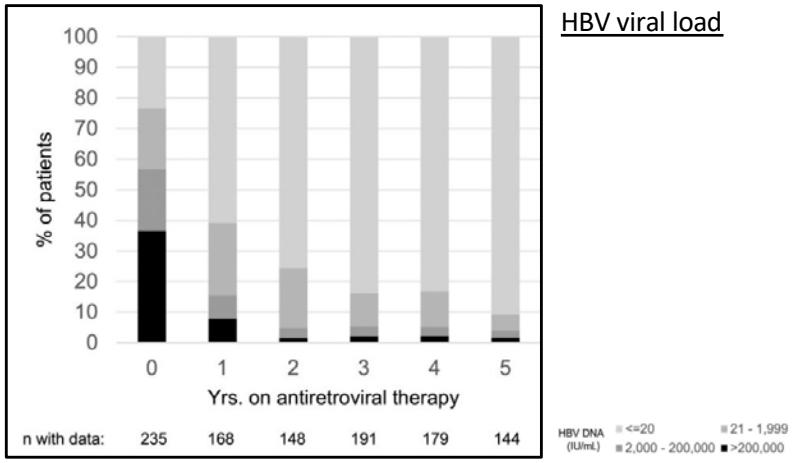
Vinikoor et al. Clin Infect Dis. 2024 Jun 14;78(6):1583-1590. PMID: 37997691

IeDEA

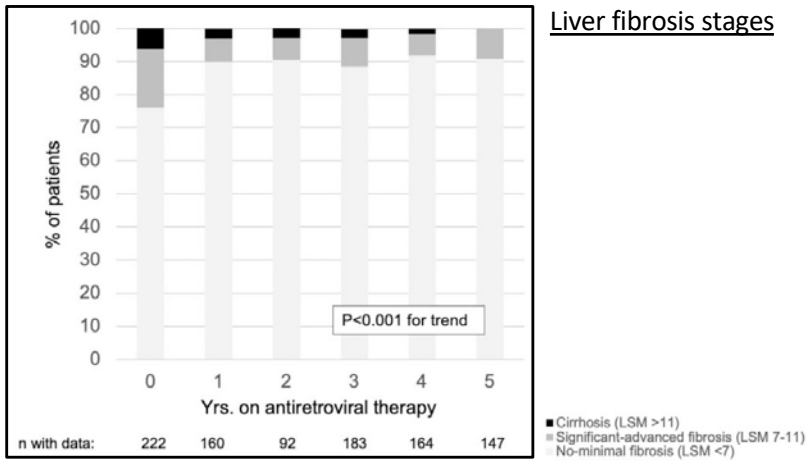
Results

- Among 289 participants, median age was 34 years, 40.1% were women, median CD4 count was 191 cells/mm3, 44.2% were hepatitis B e antigen-positive, and 28.4% had liver fibrosis/cirrhosis.
- Over median 5.91 years of ART, 13.6% developed HBV viral non-suppression. Regression of fibrosis was common, progression to cirrhosis was absent, and no cases of HCC were ascertained. HBsAg seroclearance was 9.4% at 2 and 15.4% at 5 years.

HBV viral load



Liver fibrosis stages



Conclusion

- Reassuring long-term liver outcomes were ascertained during tenofovir-based ART for HBV/HIV coinfection in Zambia.
- Higher than expected HBsAg seroclearance during ART underscores the need to include people with HIV in HBV cure research.

IeDEA

The Effect of Care Interruptions on Mortality in Adults Resuming Antiretroviral Therapy

- Estimate the relative rate of mortality of those on ART with a history of interruptions compared to those with no previous interruptions in care.
- Retrospective cohort study of 63 692 adults with HIV from 4 South African IeDEA sites, contributing 162 916 person-years of observation between 2004 and 2019.
- Interruption defined as a gap in contact longer than 180 days. Observation time prior to interruption allocated to “no interruption group”. Time after interrupting allocated to “early” or “late” interruption groups, based on whether the first interruption started before or after 6 months on ART.
- Cox regression to estimate adjusted hazard ratios.

Moolla H, et al. AIDS. 2024 July 1, 38(8):1198-1205. doi: 10.1097/QAD.0000000000003859

IeDEA

Figure 1: Survival curves by interruption status

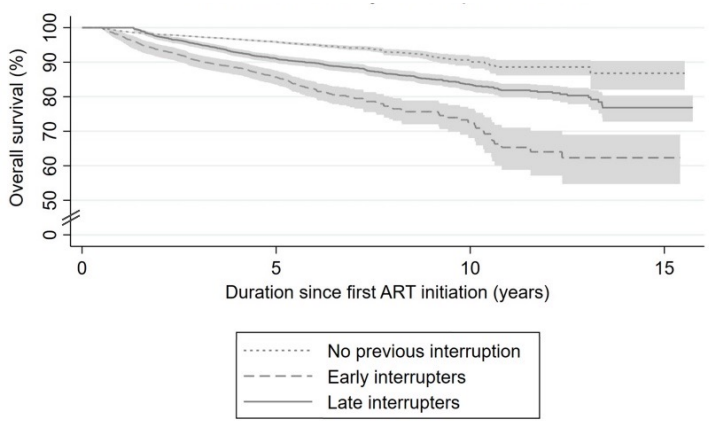


Table 1: Selected adjusted hazard ratios for all-cause mortality

Variable		Adjusted hazard ratio (95% CI)
Interruption status	No interruption	1 (reference)
	Early interrupters	4.37 (3.87-4.95)
	Late interrupters	2.74 (2.39-3.15)
Sex	Female	1 (reference)
	Male	1.38 (1.25-1.51)
Baseline age (years) at first ART initiation	15-24	1 (reference)
	25-34	1.08 (0.89-1.31)
	35-44	1.44 (1.19-1.75)
	45-54	2.15 (1.76-2.64)
	55-64	3.35 (2.63-4.27)
	65+	5.91 (4.03-8.66)
Baseline CD4 count (cells/mm^3) at first ART initiation	500+	1 (reference)
	350-499	1.14 (0.84-1.54)
	200-349	1.36 (1.04-1.78)
	100-199	2.01 (1.54-2.61)
	50-99	2.34 (1.78-3.08)
	<50	2.99 (2.29-3.92)

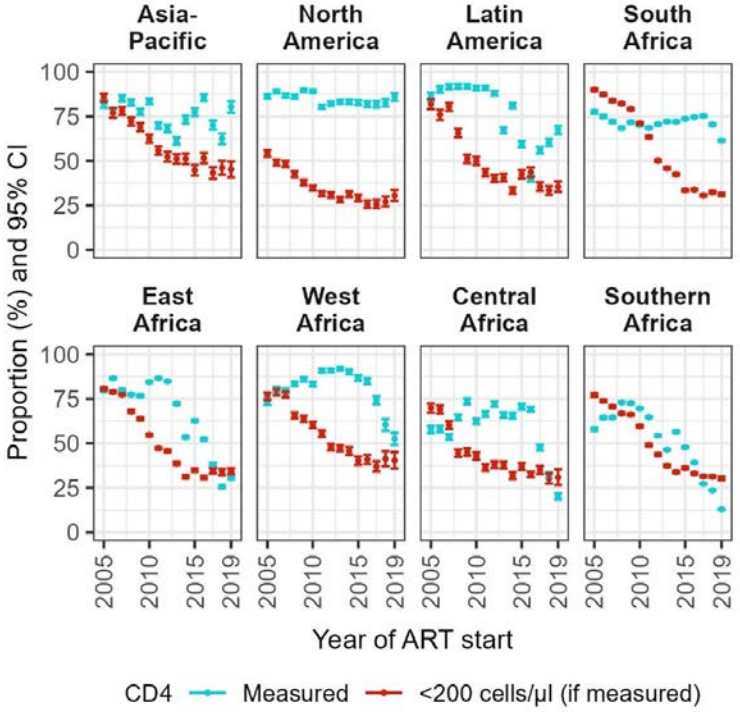
- Those resuming care following an interruption experienced increased mortality compared to those with no interruptions: hazard ratios were 4.37 [3.87-4.95] and 2.74 [2.39-3.15] for early interrupters and late interrupters, respectively.
- Hazard ratios varied by clinic site, suggesting that care should be taken when applying the results in other settings.
- There is a clear need to improve retention in care, regardless of treatment duration. Programmes to encourage return to care also need to be strengthened.

The effect of care interruptions on mortality in adults resuming antiretroviral therapy. Moolla H, et al. AIDS. 2024 July 1, 38(8):1198-1205. doi: 10.1097/QAD.0000000000003859

IeDEA

Global trends in CD4 count measurement and immunosuppression at first ART initiation (adults and children)

Background: Despite its importance for individual care and programmatic monitoring, measurement of CD4 count has decreased since the implementation of Treat-All recommendations, particularly in low- and middle-income countries. Prevalence of advanced HIV disease, and severe immunosuppression remains relatively high. ART coverage and mortality in children remains higher than in adults.



We described global trends in:

- CD4 count measurement at ART initiation (within 6 months before to 2 weeks after) and;
- Prevalence of CD4 <200 cells/µL at ART initiation

Among 1,355,104 PWH aged 15-80 years who started ART in 2005-2019:

- CD4 measurement at ART initiation declined from 68% in 2012 to 17% in 2019 in sub-Saharan Africa (except RSA) and LA.
- Amongst those with a CD4, prevalence of CD4<200 declined over time in all regions, then plateaued after 2015 at around 26% (NA); 32-34% (CA, EC, SA, RSA, LA); 40% (WA) and 47% (AP).

de Waal R et al. Global trends in CD4 count measurement and distribution at first antiretroviral treatment initiation. *Clin Infect Dis*. 2024 Nov 6.

Global trends in CD4 count measurement and immunosuppression at first ART initiation (adults and children)

We described the proportion of children with:

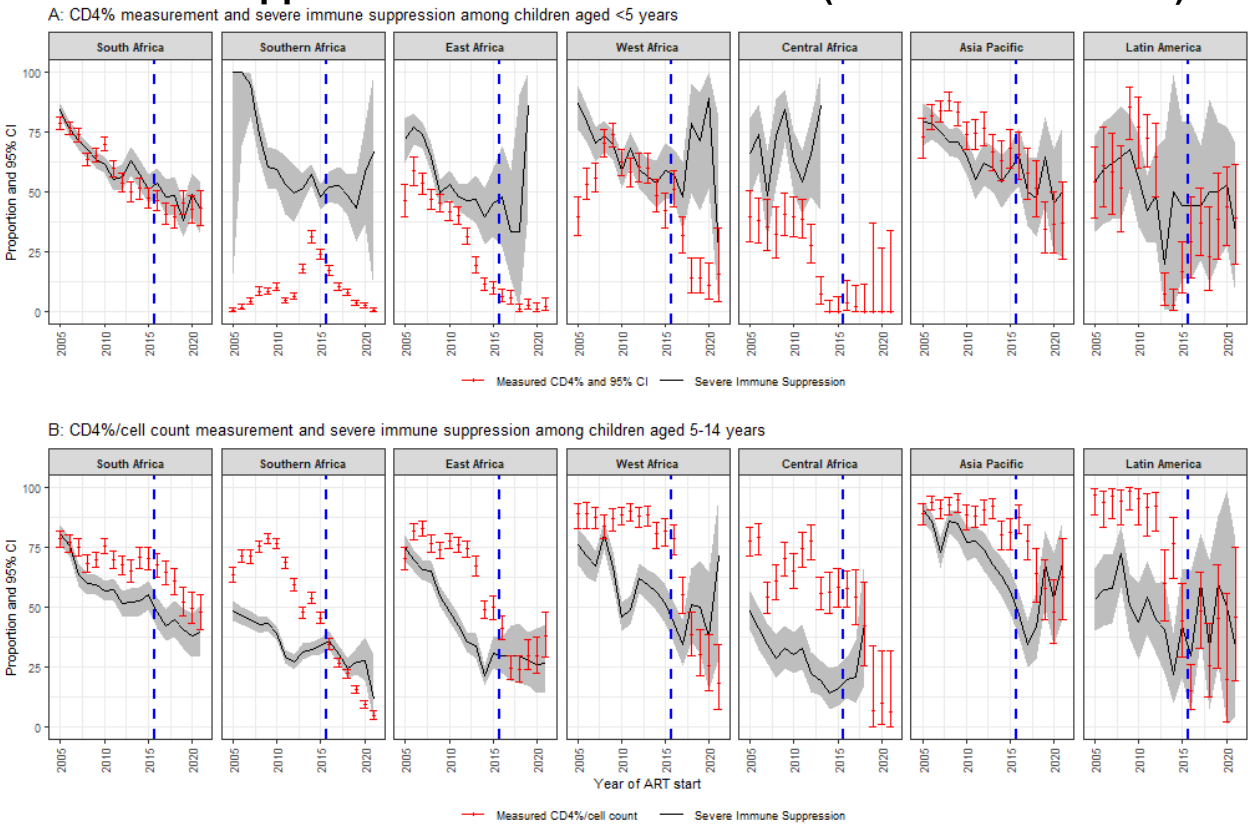
- a CD4 measure at ART initiation (for children <5 years: CD4%, for those 5-14 years: CD4% or cell counts) and;
- Prevalence of Severe Immune Suppression (SIS) defined according to WHO 2007 criteria

Among 47,937 children aged <5 years:

- CD4% testing declined from 51% in 2005 to 12% in 2021
  - In African regions (excl RSA), by 2021 CD4% testing ranged from 0% to 15%
- SIS prevalence decreased from 82% in 2005 to 42% in 2021

Among 49,516 children aged 5-14 years:

- CD4 count testing declined from 74% in 2005 to 20% in 2021
  - In African regions (excl RSA) by 2021, CD4 count testing ranged from 5% to 38%
- SIS prevalence decreased from 66% in 2005 to 37% in 2021



Conclusions:

Measurement of CD4 has declined to very low levels, especially in sub-Saharan Africa (excluding South Africa). The ongoing high proportion of adults with CD4<200 cells/μL and children with SIS at ART initiation is of concern. Meaningful conclusions about AHD/SIS prevalence in recent years are difficult due to extremely low CD4 measurement.

To better monitor and evaluate ART programmes, and to guide individual care, CD4 measurement should be more widely adopted and adequately funded as recommended by WHO guidelines.

Patten G et al, under review PIDJ

IeDEA

The contribution of non-communicable and infectious diseases to the effect of depression on mortality: a longitudinal causal mediation analysis

Didden C, Egger M, Folb N, Maartens G, Rohner E, Kassanjee R, Mesa-Vieira C, Kriel A, Seedat S, Haas AD

- **Background**: Physical diseases contribute to higher mortality in individuals with mental illness.
- **Study Aim**: Quantify the effect of major depressive disorder (MDD) on mortality and decompose it into indirect effects mediated through six leading causes of death in South Africa.
- **Participants:** 981,540 beneficiaries aged 18+ from a private South African medical insurance scheme.
- **Case Definitions:** ICD-10 codes, lab test results, and medication claims. Diseases were treated as chronic.
- **Key Variables:**

  Exposure: MDD (ICD-10 codes: F32-33).

  Mediators: HIV, TB, cardiovascular diseases (CVDs), respiratory diseases, diabetes & kidney disease, cancers.

  Outcome: All-cause mortality.

  Time-Dependent Covariates: Hypertension, anxiety disorders.

  Baseline Covariates: Sex, age, population group.
- **Method:** Longitudinal mediation analysis with interventional effects using data from 2011-2020.
- **Subgroup Analyses:** by sex and age group (<40, ≥40 years).

Epidemiology. 2025 Jan 1;36(1):88-98. PMID: 39589015, PMCID: PMC11594557

IeDEA

Results

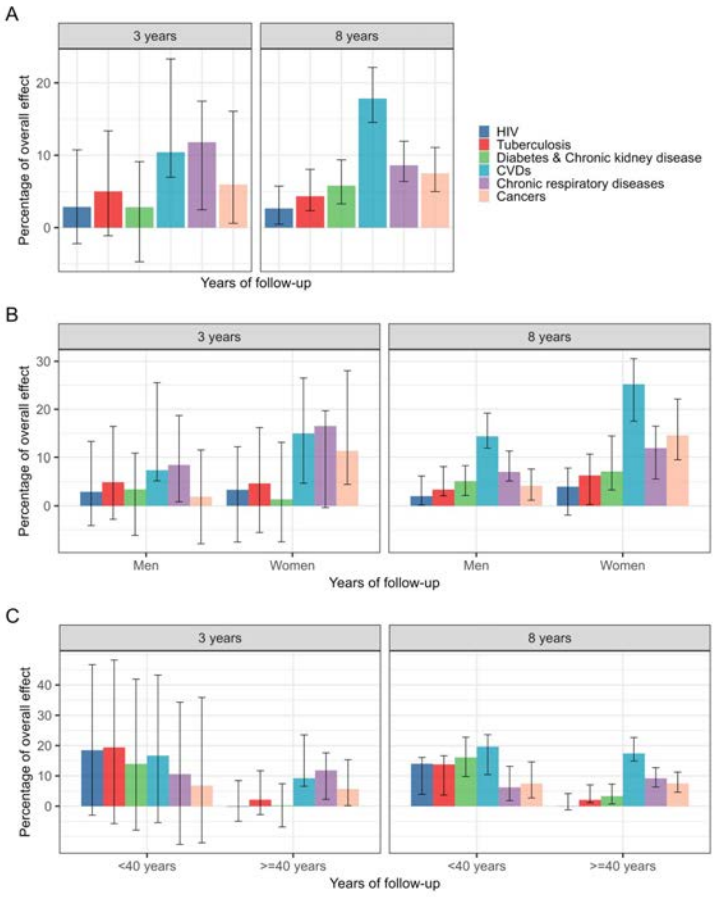


Figure: Indirect effects through phyical diseases, presented as percentages of the overall effect of MDD on mortality. Panel A: total sample population, Panels B & C: stratified by sex (B) and age group (C).

Based on our modelling assumptions, we find that

- **MDD increases mortality** (Risk ratio (RR): 1.23, 95% CI: 1.20-1.27).
- **Highest RR in men** (1.28, 95% CI: 1.24-1.32).
- **Most important mediators of the effect of MDD on mortality:** Non-communicable diseases, especially CVDs.
- **HIV and TB**: Minor role overall, except for those <40 years.

Key message:

MDD increases the risk of physical diseases, and this increased risk of physical diseases contributes to higher mortality. CVDs, in particular, are key contributors to the effect of MDD on mortality.

West Africa -IeDEA

Research highlights 2024

IeDEA

Sex-Based Disparities in the Transition to Dolutegravir-Based Antiretroviral Therapy in West African HIV Cohorts

Tiendrebeogo et al., Open Forum Infect Dis. 2024

Background

- WHO recommended DTG as preferred first-line ART globally (2018) with initial safety concerns in pregnancy, resolved by 2019 updated
- Many West African countries initiated DTG transition with varied implementation timelines and patterns
- Need to understand real-world DTG implementation and outcomes in West African context to monitor transition patterns

Objective

- To assess DTG transition and examine predictors of the switch to DTG among ART-experienced persons living with HIV (PLHIV) in West Africa during the 2019–2021 period

Methods

Retrospective cohort analysis using IeDEA West Africa cohort data (2017-2021)

- Cumulative incidence functions for DTG switch
- Cox proportional hazards models with Competing risks and random effect on clinic site

Sex-Based Disparities in the Transition to Dolutegravir-Based Antiretroviral Therapy in West African HIV Cohorts

Population Characteristics

- 21,167 ART-experienced PLHIV from 5 HIV clinics across 3 countries
- 69% female, median age 45 years, median follow-up 8 years
- Baseline ART regimen: EFV-based (63%), NVP-based (15%), PI-based (21%)

DTG Transition Patterns

- Transition started in 2019 across all sites
- Initial faster uptake among men
- Women showed catchup phase in later period
- Sex disparity mainly observed in patients <50 years

Factors Associated with DTG Switch

- Male sex (early period)
- Age <50 years
- Non-protease inhibitor-based regimens
- Viral suppression

Conclusion

- Heterogeneous implementation across clinics
- Gap between men and women gradually closing
- Ongoing monitoring needed to ensure equitable access

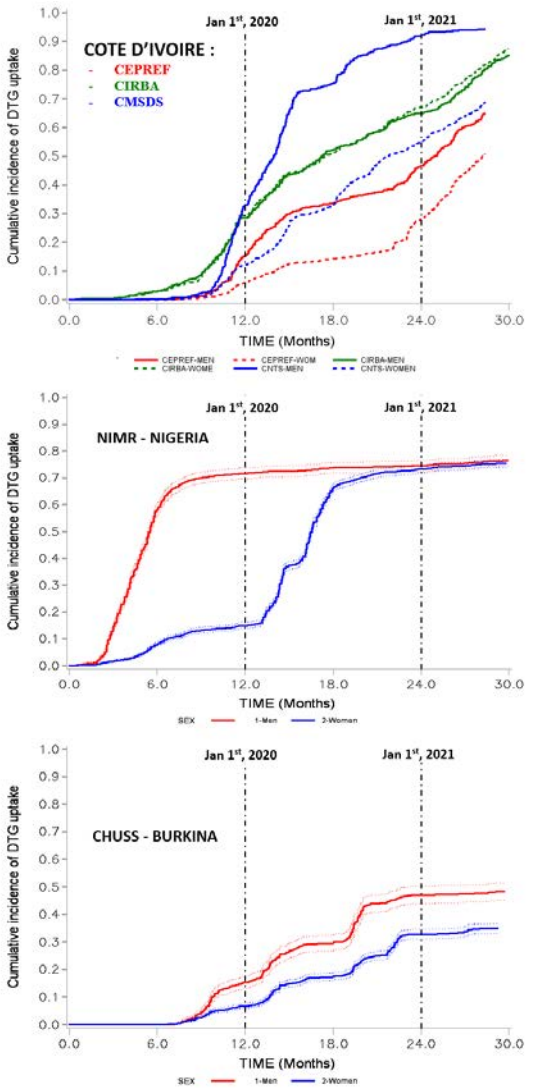


Figure 1. Cumulative incidence function of Dolutegravir uptake by sex according to participating cohorts & countries. The IeDEA West Africa Collaboration 2019-2021

Impact of switching to a dolutegravir-based regimen on body weight changes: insights from West African adult HIV cohorts

Tiendrebeogo et al., JIAS 2024

Background

- Dolutegravir (DTG) shows superior efficacy but weight gain concerns emerge in developed countries
- Limited data available from sub-Saharan Africa despite widespread DTG adoption
- Rising cardiometabolic diseases in PLHIV necessitate careful monitoring

Objective

- To explore changes in body weight pre- and post-switch to DTG-based regimen and assess the association between DTG switch and significant weight gain (≥10% increase over a 12-month period) in PLHIV on ART in West Africa

Methods

Two-part analysis using IeDEA West Africa cohort data (2017-2021)

- Piecewise linear mixed modeling for weight changes (Two years pre-switch / One year post-switch to DTG)
- Emulated target trials with inverse probability weighting

Impact of switching to a dolutegravir-based regimen on body weight changes: insights from West African adult HIV cohorts

Population Characteristics

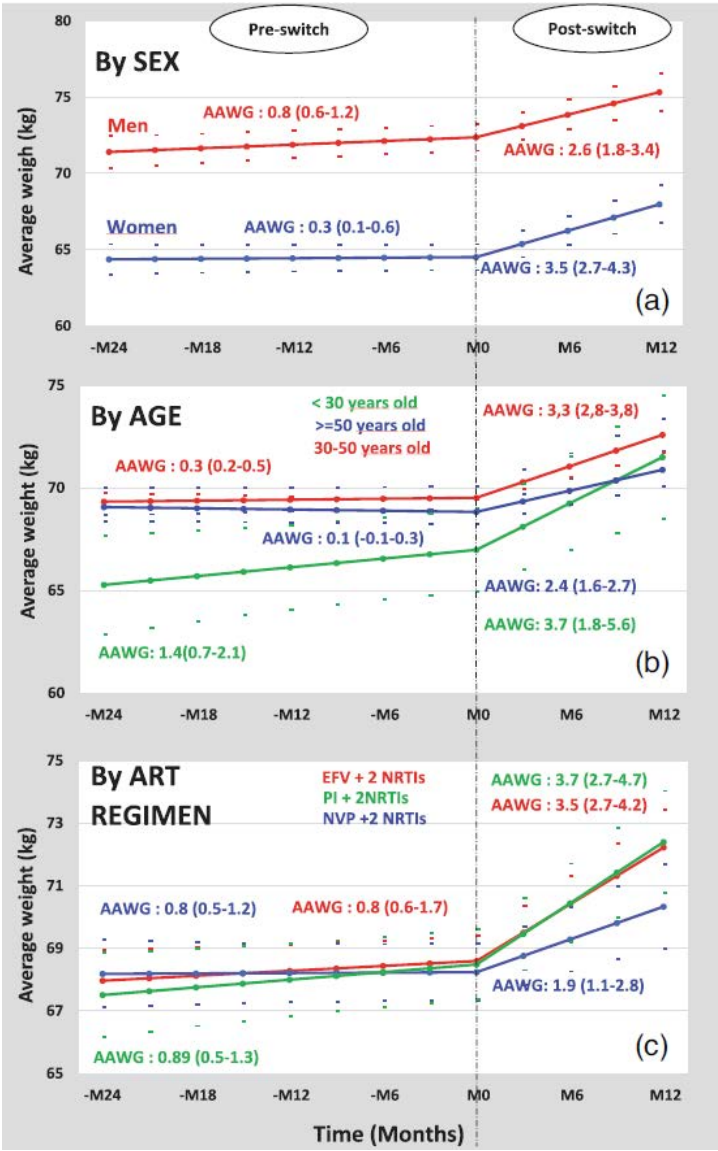
- 6,705 PLHIV from Burkina Faso, Côte d'Ivoire, Nigeria
- 63% female, median age 48 years, median follow-up 9 years
- Pre-switch ART: EFV-based (56.6%), NVP-based (30.9%)

Key Findings

- Pre-switch annual weight gain: 0.62 kg/year [95% CI: 0.36-0.88]
- Post-switch annual weight gain: 3.07 kg/year [95% CI: 2.33-3.80]
- Greater weight gain in patients previously on EFV and PI-based ART vs. NVP-based ART
- Switching to DTG was significantly associated with substantial weight gain (aOR = 2.54; 95% CI = 2.18-2.97)

Clinical Implications

Continuous weight monitoring and metabolic profiling is imperative in HIV cohorts to delineate the long-term cardiometabolic impact of DTG



Accuracy of alternative PHQ-9 scoring algorithms to screen for depression in people living with HIV in Sub-Saharan Africa

Bernard C, Font H, Zotova N, Wools-Kaloustian K, Goodrich S, Kwobah EK, Awoh AR, Mbongo'o GCN, Nsonde DM, Gandou P, Minga A, Tine JM, Ndiaye I, Dabis F, Seydi M, de Rekeneire N, Yotebieng M, Jaquet A, IeDEA Cohort Collaboration. J Acquir Immune Defic Syndr 2025 Feb 1;98(2):143-149.

Objective: To assess the performance of alternative PHQ-9 scoring for screening depression in Sub-Saharan African PLWH

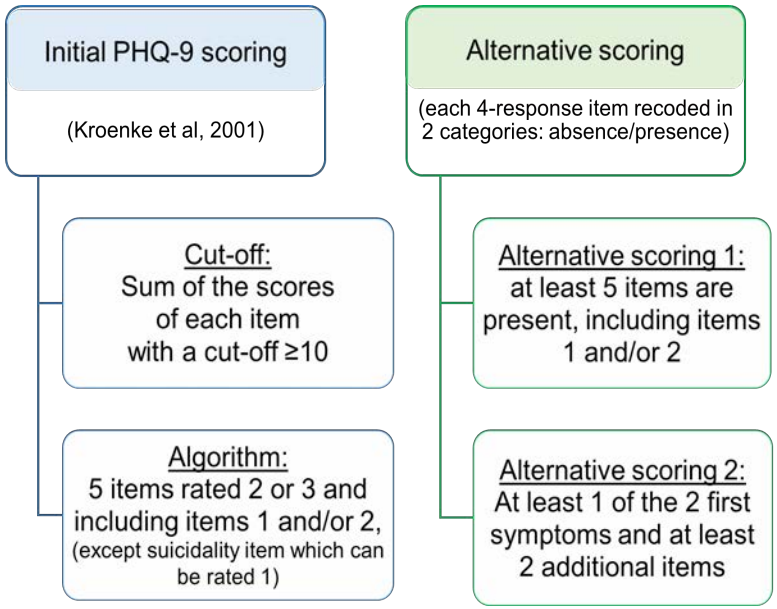
Countries: Cameroun, Côte d'Ivoire, Kenya, Senegal, Republic of Congo

Initial PHQ-9 scoring: Two previously used PHQ-9 scorings compared to alternative scoring

Alternative scoring:

1- Simplified recoding of each item responses in two categories : absence or presence instead of rating

2- Presence of at least one mood symptom
+ other symptoms listed in the PHQ-9



Gold standard: Psychiatrist diagnosis

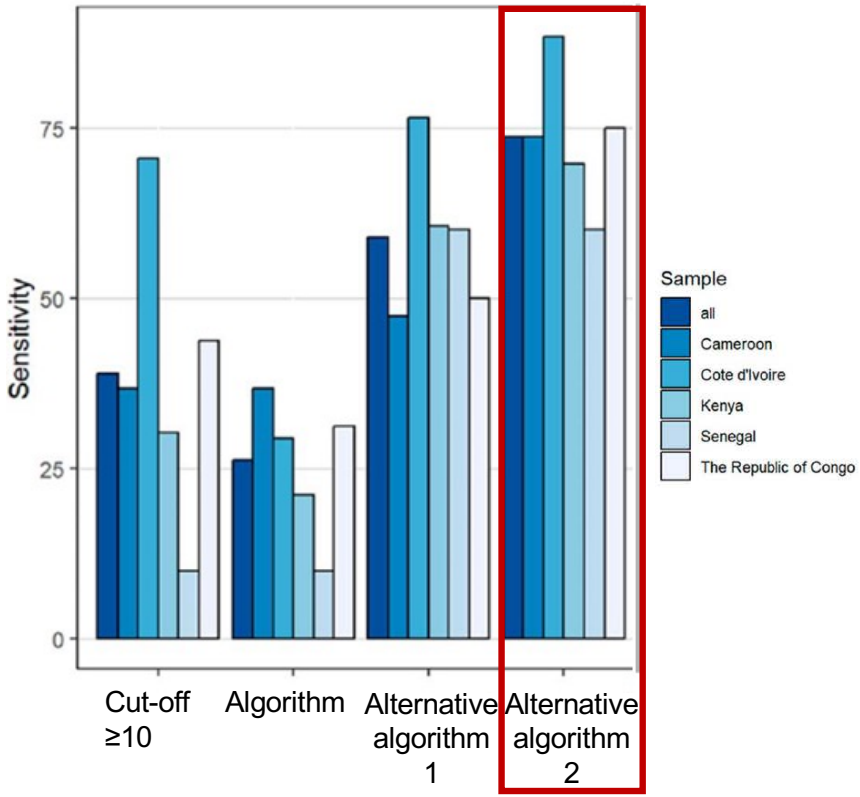
IeDEA

Accuracy of alternative PHQ-9 scoring algorithms to screen for depression in people living with HIV in Sub-Saharan Africa

Main results:

	Cutoff ≥ 10	Algorithm	Alternative Scoring 1	Alternative Scoring 2
Sensitivity	0.39 (0.29; 0.49)	0.26 (0.18; 0.36)	0.59 (0.48; 0.69)	0.74 (0.64; 0.82)
Specificity	0.95 (0.93; 0.96)	0.98 (0.96; 0.99)	0.87 (0.84; 0.90)	0.71 (0.67; 0.75)
Positive predictive value	0.53 (0.41; 0.65)	0.62 (0.46; 0.77)	0.41 (0.32; 0.49)	0.27 (0.22; 0.33)
Negative predictive value	0.91 (0.89; 0.93)	0.9 (0.87; 0.92)	0.93 (0.91; 0.95)	0.95 (0.92; 0.97)
Area under the curve*	0.67 (0.62; 0.72)	0.62 (0.58; 0.67)†	0.73 (0.68; 0.78)†	0.72 (0.68; 0.77)†

Reference: For PHQ-9 scores: AUC for cutoff ≥ 10.
*Comparison of AUC for the different PHQ-9 scores with a reference using for DeLong test.
†$P < 0.005$.



Alternative scoring seem to improve the accuracy of the PHQ-9 in identifying depression and increase reproducibility across different sites

IeDEA

Exploring the sexual and reproductive health knowledge, practices and needs of adolescents living with perinatally acquired HIV in Côte d'Ivoire: a qualitative study

Tisseron *et al.*, Reproductive Health 2024

- Objective: To explore sexual and reproductive health knowledge, practices and needs of adolescents living with HIV in Abidjan, Côte d'Ivoire

- Study design: Exploratory, qualitative study, conducted in 2023 in Côte d'Ivoire including:
  - 26 semi-structured in-depth interviews with adolescents living with HIV (ALHIV) aged 15-19 years, aware of their HIV status and included in the OPTIMISE-AO project
  - One focus group with 5 peer-educators, i.e youth that are involved in the OPTIMISE-AO projects to support and further counsel ALHIV, and ease the communication with the healthcare professionals
- Data collection
  - Interview guide developed with experts in adolescents global health, HIV and SRH research, in collaboration with local healthcare professionals and human science experts in Côte d'Ivoire
  - Questions adapted to each sub-group (male, female, and female who became pregnant), tested with one male and one female adolescent
  - Main topics explored: 1/ Sexual life (first experiences), 2/ Information sources about SRH, 3/Knowledge and use of SRH prevention methods, 4/ Access to SRH services, 5/Pregnancy

Exploring the sexual and reproductive health knowledge, practices and needs of adolescents living with perinatally acquired HIV in Côte d'Ivoire: a qualitative study

Tisseron *et al.*, Reproductive Health 2024

Main results:

- Low level of knowledge in SRH
- Lack of adapted use of SRH prevention tools (condoms, contraceptive methods), sometimes justified by their viral load undetectability
- One-third of female adolescents described experiences of sexual violence
- Difficulties to talk about SRH with the healthcare professionals, even though it is a wish of the adolescents
- Peer-educator could play a major role in supporting adolescents regarding SRH topic, with further training

"I hear that it can cause problems afterwards, you will not be able to have children as you take the injections" (female who became pregnant, 17y)

"I'm undetectable, so I cannot transmit, and then I take pregnon (i.e emergency contraceptive pill)"(female, 18y)

"Well, the first time, I would not say it was rape but it was… […] Well, I told him to wait, that I was not ready, and he said OK. So, I went there from time to time, one day I left, he threw himself on me like that and then he started doing it. (female, 17y)"

"Because our aunties [healthcare providers] have lots of advice to give us, […]; between us, we give each other the wrong advice. So, I prefer the aunties to my friends (female, 16y)"

Metabolic causes of liver disease among adults living with HIV from low- and middle-income countries: a cross-sectional study

Plaisy MK et al. Journal of the International AIDS Society 2024, 27:e26238

❑ **Objectives:**

- ❖ To estimate prevalence of significant liver fibrosis and steatosis, and assess contributing role of metabolic disorders on these liver diseases among adults living with HIV (PWH) on ART in LMICs.

❑ **Methods:**

- ❖ Cross-sectional analysis of data collected at enrollment within the SRN project
- ❖ Study population: PWH aged ≥40 and on ART ≥6months in eight HIV clinics (India, Brazil, Mexico, Rwanda, Kenya, Zambia, Côte d'Ivoire and Togo) across six IeDEA regions
- ❖ Logistic regression models assessed factors associated with liver fibrosis and liver steatosis
- ❖ Levin's formula was used to calculate the population attributable fraction (PAF) of liver fibrosis for infectious and non-infectious condition

IeDEA

❑Results:

- ❖ 2,120 PWH (56% women, median age of 50 (IQR 45-56) years included
- ❖ Overall prevalence of liver fibrosis (7.6% [95% CI, 6.4-8.8]) and steatosis 28% [95% CI, 26-31], with variation between sites/regions
- ❖ **Factors associated with liver fibrosis:**
  - ❖ BMI ≥25 kg/m2, Type 2 diabetes, prolonged exposure to didanosine (table)
  - ❖ Overweight/obesity and T2DM accounted for 41% and 12% of the PAF for liver fibrosis, respectively, while HBsAg and anti-HCV accounted for less than 5%
- ❖ **Factors associated with steatosis**:
  - ❖ Overweight/obesity (aOR 4.25, 95% CI 3.29−5.51), diabetes (aOR 2.06, 95% CI 1.47−2.88), prolonged exposure to stavudine (aOR 1.69, 95% CI 1.27−2.26) and dyslipidaemia (aOR 1.68, 95% CI 1.31−2.16)

- ***Table: Factors associated with liver fibrosis***

Variable		Odds ratio
Sex at birth	Women	Reference
	Men	1.64 (1.11, 2.42)
IeDEA Region	East Africa	Reference
	Asia Pacific	43.03 (8.80, 777.77)
	Central Africa	9.41 (1.97, 168.76)
	CCASAnet	11.40 (2.36, 205.25)
	Southern Africa	8.81 (1.56, 165.41)
	West Africa	8.56 (1.80, 153.27)
Body mass index (kg/m²)	<25	Reference
	≥25	2.45 (1.66, 3.67)
Type 2 Diabetes	No	Reference
	Yes	2.36 (1.53, 3.60)
AST class	<1 ULN	Reference
	≥ULN	3.89 (2.52, 5.96)
Positive HBs Ag	No	Reference
	Yes	1.82 (0.86, 3.55)
Antibody anti-HCV	Negative	Reference
	Positive	1.62 (0.57, 4.06)
AUDIT score	<8	Reference
	≥8	1.07 (0.62, 1.79)
Didanosine cumulative exposure	No or <1 year	Reference
	≥ 1 year	3.40 (1.61, 6.97)

❑ Conclusion:

- ❖ Metabolic disorders were significant risk factors for liver disease in this population
- ❖ Early recognition of metabolic disorders risk factors might be helpful to guide clinical and lifestyle interventions

IeDEA


NA
ACCORD
North American
AIDS Cohort Collaboration on Research and Design

Incidence of non-AIDS defining comorbidities among young adults with perinatally acquired HIV in North America

Haw NJL*, et al. AIDS. 2024 Jul 15;38(9):1366-1374.

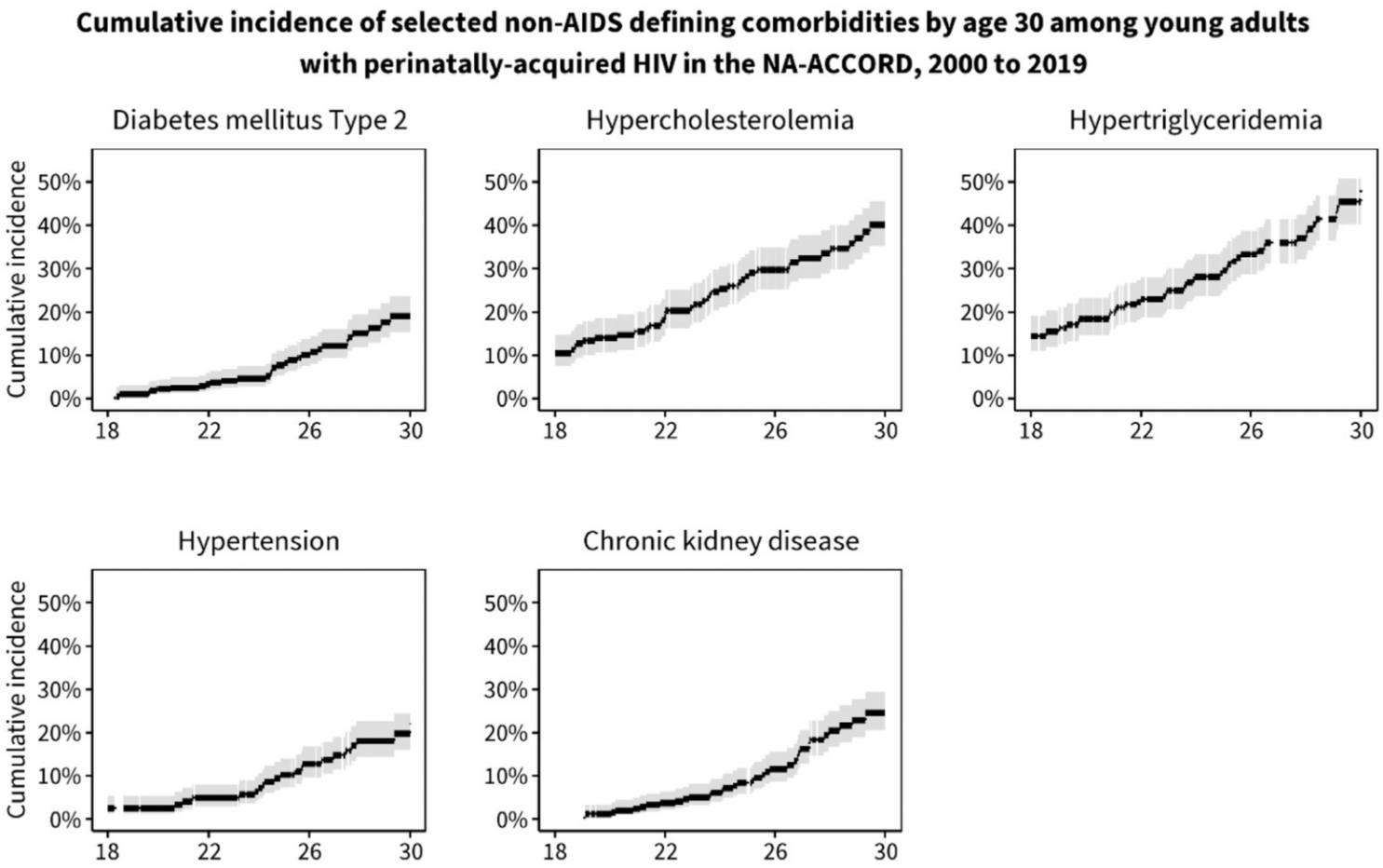
Background: As survival improves among people with HIV (PWH) in North America, the prevalence of non-AIDS defining comorbidities (NADC) continues to increase and people with perinatally acquired HIV (PHIV) may be at risk of earlier onset of NADC compared with people with nonperinatally acquired HIV, given that people with PHIV may experience decades-longer chronic HIV infection and lifetime ART exposure.

Methods: Using data from NA-ACCORD, this study describes the overall and sex- and race-specific incidence of T2DM, dyslipidemia, hypertension, and CKD among young people aged 18–30 years with PHIV who enrolled in continuity HIV care in North America from 2000 to 2019.

Results: Cumulative incidence by age 30 and incidence rates from age 18 to 30 (per 100 person-years) were T2DM: 19%, 2.9; hypercholesterolemia: 40%, 4.6; hypertriglyceridemia: 50%, 5.6; hypertension: 22%, 2.0; and CKD: 25%, 3.3. Non-Black women had the highest incidence of hypercholesterolemia and hypertriglyceridemia, Black adults had the highest hypertension incidence, and Black men had the highest CKD incidence.

Conclusions: There was a high incidence of five chronic comorbidities among people with PHIV. Earlier screening at younger ages might be considered for this unique population to strengthen prevention strategies and initiate treatment in a timely way.

**Dr. Jason Haw conducted research in the NA-ACCORD as a pre-doctoral student with Dr. Katie Lesko, EBC Director. He is currently a Research Associate at Johns Hopkins University.*



Overall cumulative incidence curves of selected non-AIDS defining comorbidities by age 30 among young adults with perinatally acquired HIV in the NA-ACCORD, 2000–2019.

Direct Acting Antiviral use by Atherosclerotic Cardiovascular Disease risk among People with HIV and Hepatitis C Virus in North America

Lang R* et al. 2024 poster presentation at the International Workshop on HIV and Hepatitis Observational Databases (IWHOD)

Background: People with HIV (PWH) are at increased risk of hepatitis C virus (HCV) coinfection and cardiovascular risk increases with aging more dramatically among PWH with HCV compared to those without HCV. We sought to estimate DAA uptake in PWH with HCV in the NA-ACCORD between 2014-2021 and evaluate the association of atherosclerotic cardiovascular disease (ASCVD) risk scores with DAA initiation.

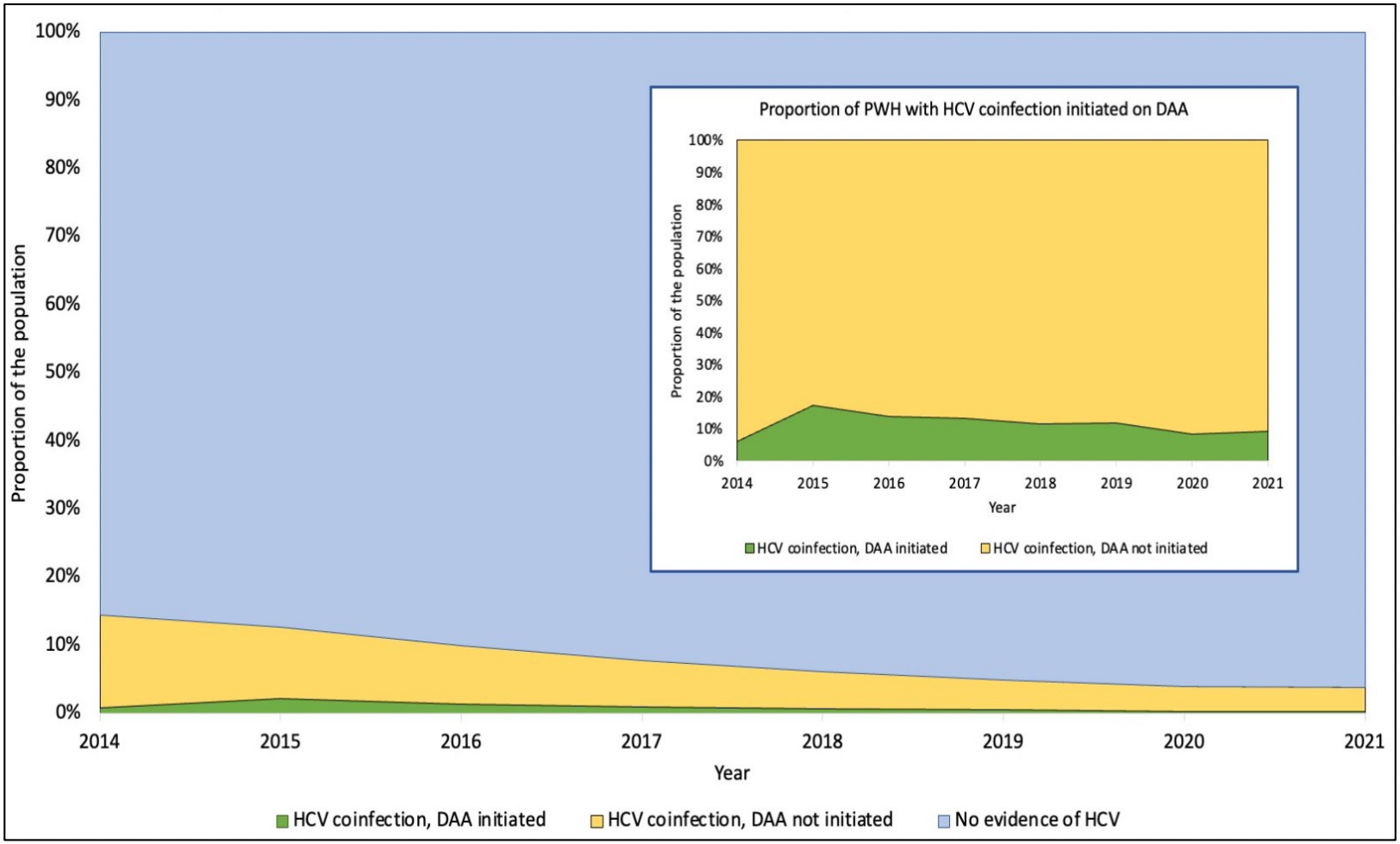
Methods: ASCVD risk score was calculated from age, sex, race, high density lipoprotein, total cholesterol, diabetes, cigarette smoking status, and hypertension or antihypertensive medication use. The proportion of PWH eligible for DAA and the proportion who initiated DAA were examined annually. A discrete time-to-event approach using complementary log-log models estimated crude (HR) and adjusted (aHR) hazard ratios and 95% confidence intervals for DAA initiation by ASCVD risk categories. High: ≥20% Intermediate: 7.5-19.9% Borderline: 5-7.4% Low: <5%

Results: DAA initiation peaked in 2015 with 21% of those eligible initiating, this gradually decreased over time with 10% of those eligible being initiated in 2021. PWH who initiated DAAs were more likely to be 60 years or older (21% vs. 15%), non-Hispanic Black (47% vs 42%), to have hypertension (48% vs 40%), diabetes (14% vs. 11%), chronic kidney disease (16% vs. 12%) and were more likely to have HIV viral suppression at study entry (85% vs 75%).

Conclusions: A treatment gap between those eligible for DAA initiation and those who initiated DAA remained over the study period. In adjusted analysis, increasing ASCVD risk was not associated with DAA initiation among PWH. DAA initiation recommendations do not include consideration of ASCVD risk. Further investigation is needed to identify whether DAA treatment decreases the high CVD risk experienced by HCV coinfected PWH.

**Dr. Raynell Lang conducted research in the NA-ACCORD as a post-doctoral student with Dr. Keri Althoff, mPI. She is currently an Assistant Professor at University of Calgary.*

Proportion of PWH in the NA-ACCORD with evidence of HCV, by DAA initiation between 2014-2021



Recent Kaposi Sarcoma trends in men with HIV: Associations with New to Care at Enrollment Status and Viral Suppression

Coburn S*, et al. Oral presentation at the 2024 International Conference on Malignancies in HIV/AIDS (ICMH)

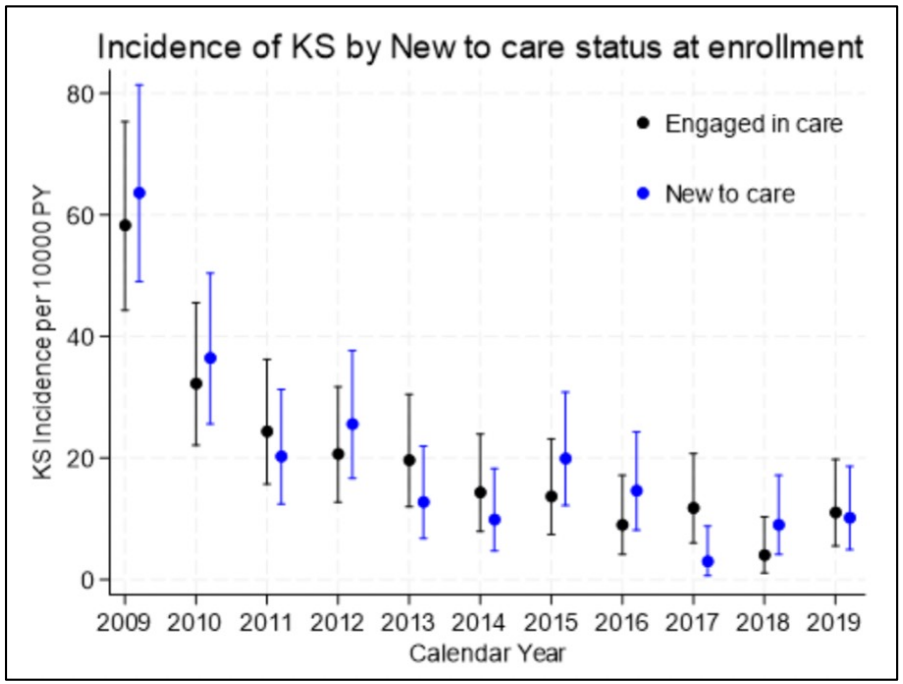
Background: Incidence of Kaposi Sarcoma (KS) sharply declined with effective HIV treatment. Recent studies indicate potential stagnation in this decline among subgroups of people with HIV (PWH). We sought to investigate these potential contributors to persistent KS incidence by evaluating recent trends in KS by new to/re-engaging HIV care and viral suppression status among men with HIV (MWH) in North America.

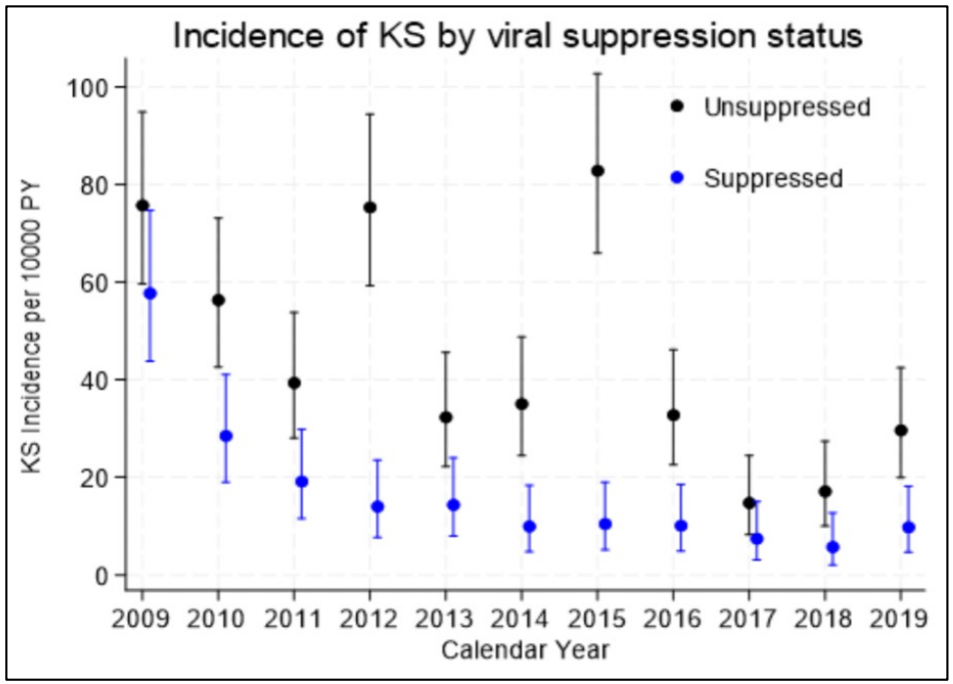
Methods: We estimated annual incidence rates of KS among adult men who enrolled in 2009 or later in NA-ACCORD among cohorts contributing validated cancer diagnoses. We calculated incidence rate ratios (aIRR) with 95% confidence intervals to estimate the association between being new to care or virally un-suppressed and KS incidence. Estimates were mutually adjusted for new to/re-engaging care status, viral suppression status, race/ethnicity, age, and CD4 count at enrollment.

Results: Among 40,090 (167,378 person-years [PY]) MWH, there were 235 KS diagnoses (IR: 14.0 per 10,000 PY). Annual KS rates declined from 31.8 to 7.1 cases per 10,000 PY from 2009 to 2018 but increased to 14.1 cases per 10,000 PY in 2019. Incidence rates were consistently higher among virally unsuppressed versus suppressed men (aIRR 5.0 95% CI 3.7, 6.6). KS rates in virally unsuppressed MWH declined from 122.7 cases to 52.1 cases per 10,000 PY from 2009-2018. KS rates were stable in virally suppressed MWH (4.3- 8.0 per 10,000 PY) but increased in 2019 to 11.6 cases per 10,000 PY.

Conclusions: KS incidence rates were consistently higher in virally unsuppressed MWH, though differences between suppressed and unsuppressed KS rates declined over time. This may indicate that stagnation in KS declines among men are related to poor HIV control; however more research is required to confirm this hypothesis. Increases in KS rates merit continued KS monitoring among PWH already engaged in care.

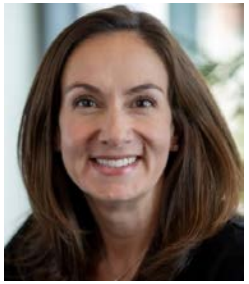
**Dr. Sally Coburn conducted research in the NA-ACCORD as both a pre-doctoral and post-doctoral student with Dr. Keri Althoff, mPI. She is currently an Assistant Scientist at Johns Hopkins University.*


Incidence of KS by New to care status at enrollment
KS Incidence per 10000 PY
0
20
40
60
80
2009
2010
2011
2012
2013
2014
2015
2016
2017
2018
2019
Calendar Year
Engaged in care
New to care


Incidence of KS by viral suppression status
KS Incidence per 10000 PY
0
20
40
60
80
100
2009
2010
2011
2012
2013
2014
2015
2016
2017
2018
2019
Calendar Year
Unsuppressed
Suppressed

The forecasted prevalence of comorbidities and multimorbidity in people with HIV in the United States through the year 2030: A modeling study

Althoff K, et al. PLoS Med. 2024 Jan 12;21(1):e1004325



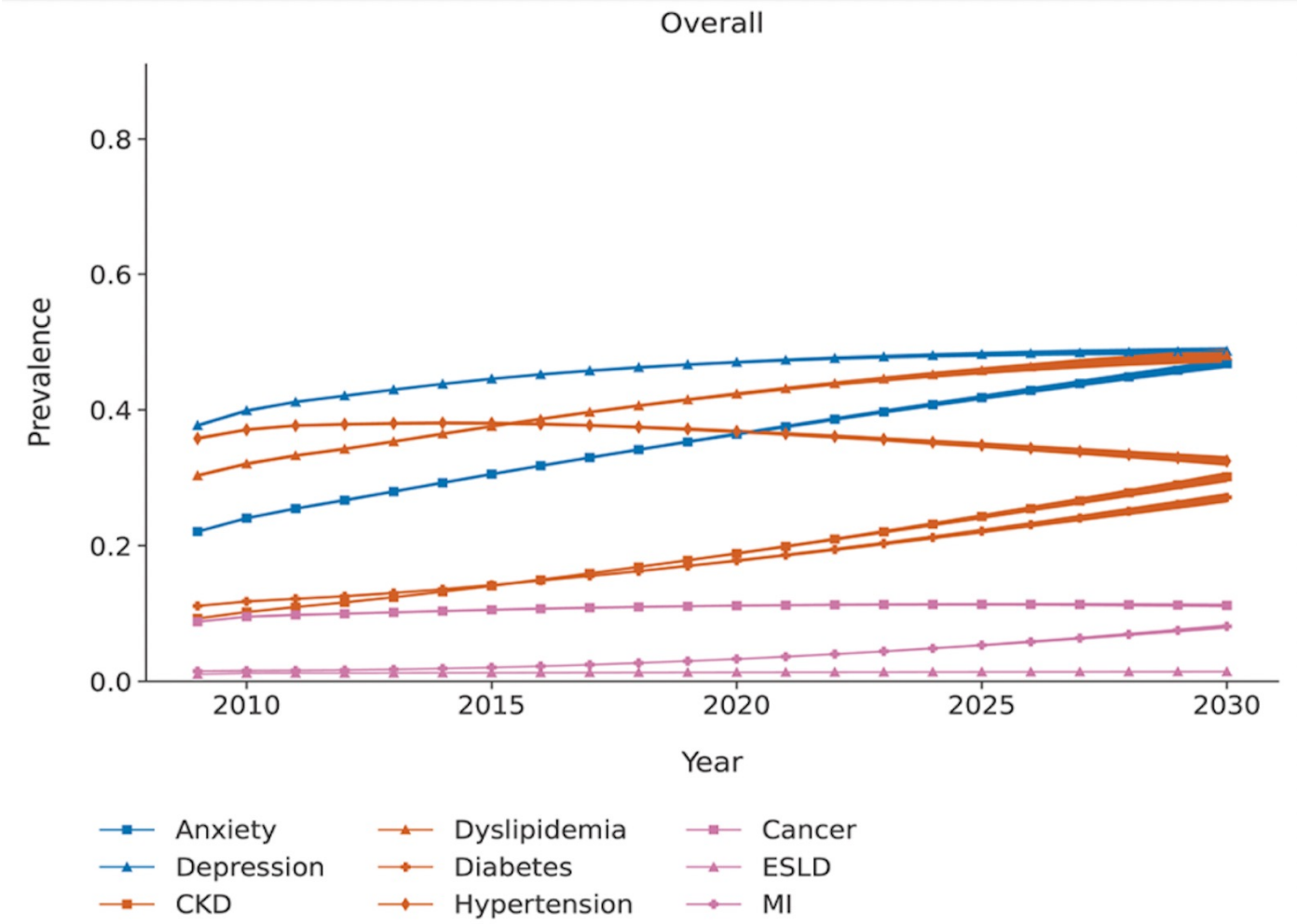
Background: Estimating the medical complexity of people aging with HIV can inform clinical programs and policy to meet future healthcare needs. The objective of our study was to forecast the prevalence of comorbidities and multimorbidity among people with HIV (PWH) using antiretroviral therapy (ART) in the United States (US) through 2030.

Methods: Using the PEARL model-an agent-based simulation of PWH who have initiated ART in the US-the prevalence of anxiety, depression, stage ≥3 chronic kidney disease (CKD), dyslipidemia, diabetes, hypertension, cancer, end-stage liver disease (ESLD), myocardial infarction (MI), and multimorbidity (≥2 mental or physical comorbidities, other than HIV) were forecasted through 2030. Simulations were informed by the US CDC HIV surveillance data of new HIV diagnosis and NA-ACCORD data on risk of comorbidities from 2009 to 2017.

Results: Along with a gradual rise in population size of PWH receiving ART-reaching 908,000 individuals by 2030-PEARL forecasted a surge in prevalence of most comorbidities to 2030. Depression and/or anxiety was high and increased from 60% in 2020 to 64% in 2030. Hypertension decreased while dyslipidemia, diabetes, CKD, and MI increased. There was little change in prevalence of cancer and ESLD. The forecasted multimorbidity among PWH receiving ART increased from 63% in 2020 to 70% in 2030.

Conclusions: The PEARL forecasts suggest a continued rise in comorbidity and multimorbidity prevalence to 2030, marked by heterogeneities across race/ethnicity, gender, and HIV acquisition risk subgroups. HIV clinicians must stay current on the ever-changing comorbidities-specific guidelines to provide guideline-recommended care. HIV clinical directors should ensure linkages to subspecialty care within the clinic or by referral. HIV policy decision-makers must allocate resources and support extended clinical capacity to meet the healthcare needs of people aging with HIV.

Forecasted prevalence of individual comorbidities among PWH using ART overall



The Contribution of Socioeconomic Factors to HIV RNA Suppression in Persons With HIV Engaged in Care in the NA-ACCORD

Chandran A, et al. J Acquir Immune Defic Syndr. 2024 Nov 1;97(3):232-241.

Background: Socioeconomic status (SES) influences well-being among people with HIV (PWH); when individual-level SES information is not available, area-level SES indicators may be a suitable alternative. We hypothesized that (1) select ZIP code-level SES indicators would be associated with viral suppression and (2) accounting for ZIP code-level SES would attenuate racial disparities in viral suppression among PWH.

Methods: NA-ACCORD participants with ≥1 viral load measurement and ≥1 US residential 5-digit ZIP code(s) between 2010 and 2018 were included. In this serial cross-sectional analysis, multivariable logistic regression models were used to quantify the annual association of race and ethnicity with viral suppression, in the presence of SES indicators and sex, hepatitis C status, and age.

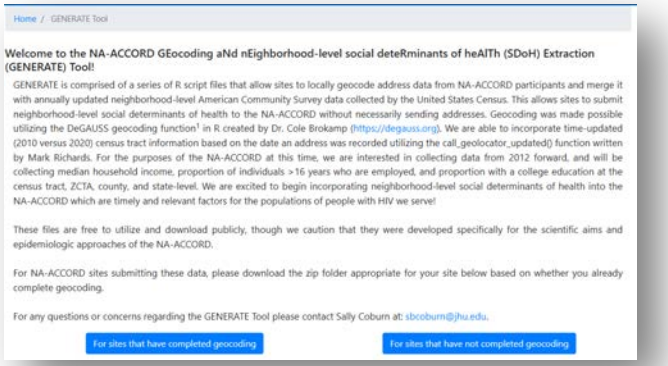
Results: We observed a dose-response relationship between SES factors and viral suppression. Lower income and education were associated with 0.5-0.7-fold annual decreases in odds of viral suppression. We observed racial disparities of approximately 40% decreased odds of viral suppression among non-Hispanic Black compared with non-Hispanic White participants. The disparity persisted but narrowed by 3%-4% when including SES in the models.

Conclusions: ZIP code-based SES was associated with viral suppression, and accounting for SES narrowed racial disparities in viral suppression among PWH in the NA-ACCORD. Inclusion of ZIP code-level indicators of SES as surrogates for individual-level SES should be considered to improve our understanding of the impact of social determinants of health and racial disparities on key outcomes among PWH in North America.

Approach to including SES in studies

"We offer a concrete approach by which the appropriate indicator(s) of SES should be selected when warranted by the research question."

1. "The inclusion of SES in any studies of health disparities should be driven by an ***evidence-derived conceptual framework***."
2. "…we confirmed that the use of ZIP code–level SES resulted in similar outcomes to other studies of individual-level SES and viral suppression, suggesting that ***ZIP code–level SES may be a reasonable surrogate for individual-level SES when individual-level SES measurements are not available***."
3. "…we proposed inserting each ZIP code–level SES indicator into the analytic model ***individually, then in combinations of 2, and then using all 3 as a strategy*** to select ZIP code–level SES indicators when there is no clear choice from previous research.
4. "…changes in the ***magnitude of association with the inclusion of SES <u>and</u> the standard model fit statistics*** can be used to drive optimal model selection."

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