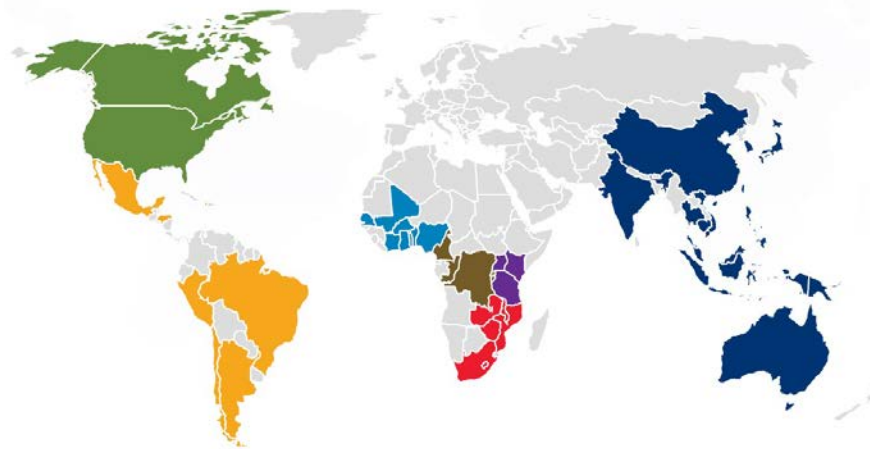


# leDEA Global Cohort Consortium

## *2022 Research Highlights*



Website: [iedea.org](http://iedea.org)  
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# Acknowledgements

- The International Epidemiology Databases to Evaluate AIDS (IeDEA) is supported by the U.S. National Institutes of Health's National Institute of Allergy and Infectious Diseases, the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development, the National Cancer Institute, the National Institute of Mental Health, the National Institute on Drug Abuse, the National Heart, Lung, and Blood Institute, the National Institute on Alcohol Abuse and Alcoholism, the National Institute of Diabetes and Digestive and Kidney Diseases, the Fogarty International Center, and the National Library of Medicine: **Asia-Pacific**, U01AI069907; **CCASAnet**, U01AI069923; **Central Africa**, U01AI096299; **East Africa**, U01AI069911; **NA-ACCORD**, U01AI069918; **Southern Africa**, U01AI069924; **West Africa**, U01AI069919.
- This work is solely the responsibility of the authors and does not necessarily represent the official views of any of the institutions mentioned above.
- 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/funding-acknowledgements/>

# 2022 IeDEA Asia-Pacific Research Highlights



## Virological failure and treatment switch after ART initiation among PLHIV with and without routine VL monitoring in Asia

- Assess association between routine VL testing and viral failure (VF) during 1<sup>st</sup>-line ART, and factors associated with switching to 2<sup>nd</sup>-line ART
- PLHIV  $\geq 18$  years initiating ART between 2003-2021 at 21 TAHOD sites
- Routine VL at site = median number VL tests  $\geq 0.80$  per patient per year; VF = VL  $\geq 1000$  copies/ml
- Of 6277 PLHIV: 48% from 11 routine VL sites; 52% from 10 non-routine VL sites
  - Median age 35 (30–42) years; 68% male; 91% started NNRTI ART
  - 1021 had subsequent VF: rate 2.15 (95%CI 2.02–2.29) per 100 PY
  - 817 switched to 2nd line: rate 1.44 (95%CI 1.35–1.54) per 100 PY

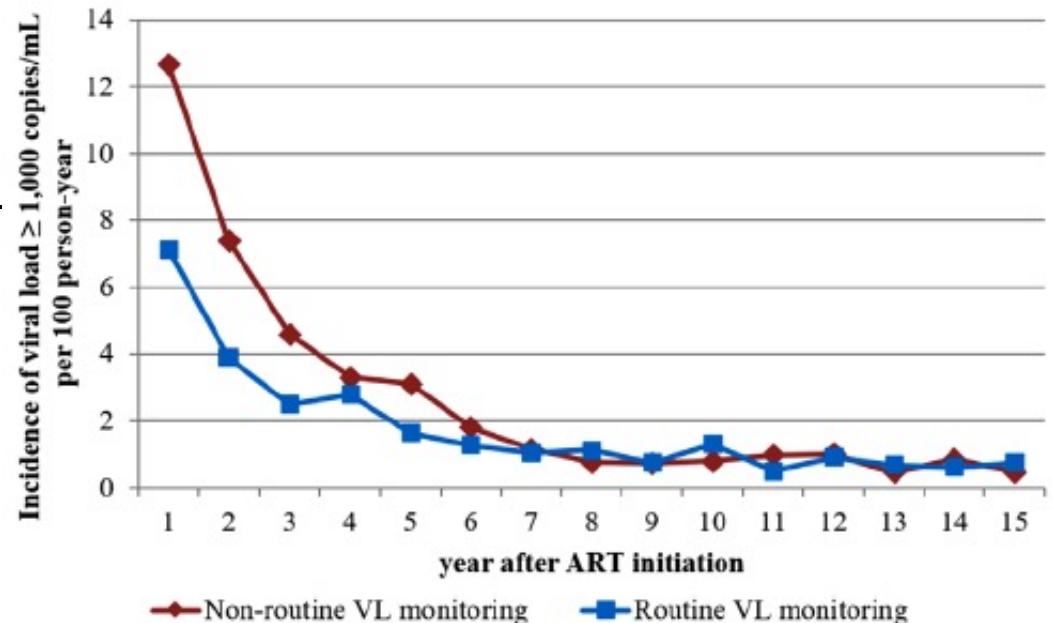
Teeraananchai S, et al.

J Int AIDS Soc. 2022 Aug;25(8):e25989. doi: 10.1002/jia2.25989.



- VF more frequent at non-routine vs routine VL sites: aIRR 2.85 (95%CI 2.27–3.59)
- Higher risk of switching at routine vs. non-routine VL sites: aSHR 1.78 (95%CI 1.17–2.71)
- PLHIV from non-routine VL sites had higher incidence of persistent VF and a low switching rate, reflecting possible under-utilized VL testing

**Incidence of VF after ART initiation during first-line therapy**



Virological failure and treatment switch after ART initiation among people living with HIV with and without routine viral load monitoring in Asia. Teeraananchai S, et al. J Int AIDS Soc. 2022 Aug;25(8):e25989.

## Mortality after loss to follow-up: a linkage study of people living with HIV in Thailand and Malaysia

- Assess survival outcomes among PLHIV lost to follow-up (LTFU) in Thailand and Malaysia
- Data linkages to national death registry or HIV database done in 2020 for 489 PLHIV LTFU while in care at 2 sites in Malaysia and 4 in Thailand
- LTFU = having no documented clinical contact in previous year, excluding transfers and deaths
- 151 (31%) deaths after being LTFU: mortality rate 4.89 per 100 PY

Jiamsakul A, et al.

J Acquir Immune Defic Syndr. 2022 Aug 15. doi: 10.1097/QAI.0000000000003067.



- Risk factors for mortality after LTFU:
  - Older age (41–50 years, HR 1.99, 95%CI 1.08 to 3.68; >50 years, HR 4.93, 95%CI 2.63 to 9.22; vs. age  $\leq$ 30 years)
  - Receiving NRTI + PI (HR 1.87, 95%CI 1.22 to 2.85 vs. NRTI+NNRTI)
  - Positive HCV Ab (HR 2.25, 95%CI 1.40 to 3.62)
  - Previous AIDS illness (HR 1.45, 95%CI 1.03 to 2.05)
- Improved survival associated with higher CD4 count: CD4 351–500 cells/mL, HR 0.40 (95%CI 0.21–0.76) vs. CD4  $\leq$ 200 cells/mL
- About one-third of PLHIV LTFU died while out of care, emphasizing importance of efforts to re-engage PLHIV after LTFU, and ensure access to ongoing ART

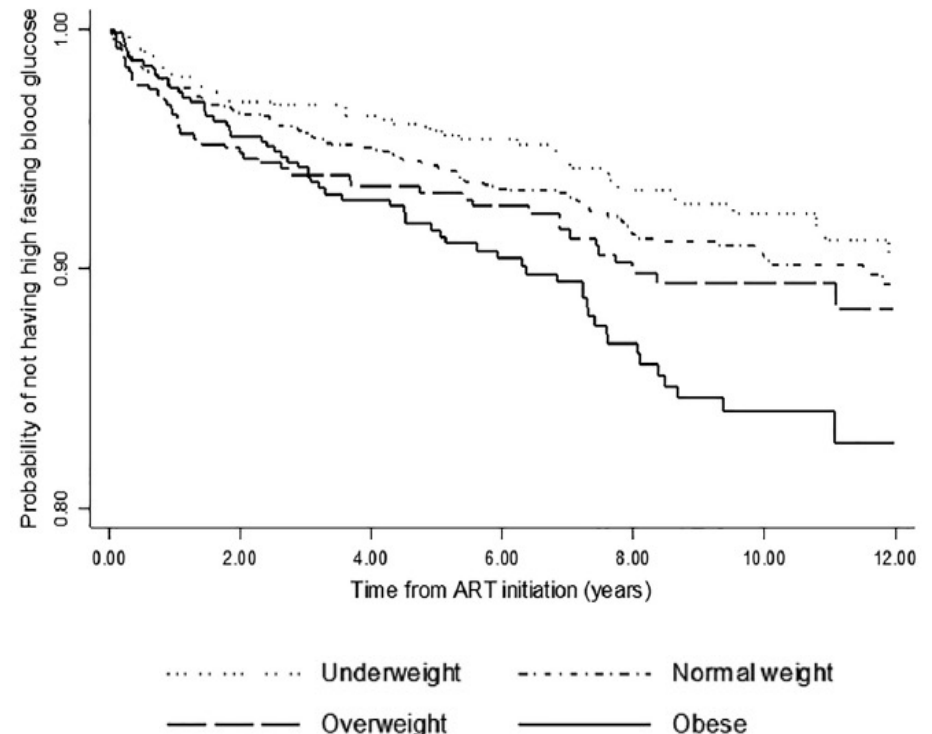


## BMI as a predictor of high fasting blood glucose among PLHIV in the Asia-Pacific region

- Investigate incidence and factors associated with high fasting blood glucose (FBG) among PLHIV in the Asia-Pacific
- PLHIV enrolled in TAHOD from 2003 to 2019, receiving ART, and without prior TB
  - Asian BMI classification: underweight ( $<18.5$  kg/m<sup>2</sup>), normal (18.5–22.9 kg/m<sup>2</sup>), overweight (23–24.9 kg/m<sup>2</sup>), and obese ( $\geq 25$  kg/m<sup>2</sup>)
  - High FBG = a single post-ART FBG measurement  $\geq 126$  mg/dL
- 3939 PLHIV: 63% male; median age at ART initiation 34 years; 50% normal BMI, 23% underweight, 13% overweight, and 14% obese

- 8% had high FBG: incidence 1.14 per 100 PY
- High FBG associated with:
  - Obese vs. normal weight, HR 1.79; 95%CI 1.31–2.44 (p <0.001)
  - Older age vs ≤30 years: 31–40 years, HR 1.47; 95%CI 1.08–2.01; 41–50 years, HR 2.03; 95%CI 1.42–2.90; ≥51 years, HR 3.19; 95%CI 2.17–4.69, (p <0.001)
- Obese PLHIV at increased risk of high FBG; regular monitoring needed as PLHIV age

**Kaplan–Meier curves of PLHIV by Asian BMI classification**



BMI as a predictor of high fasting blood glucose among people living with HIV in the Asia-Pacific region. Khuon D, et al. HIV Med. 2022 Jun 24. doi: 10.1111/hiv.13351.

## Prevalence and risks of depression and substance use among adults living with HIV in the Asia-Pacific region

- Cross-sectional study to assess prevalence and risk factors for depression and substance use (SU)
- PLHIV  $\geq 18$  years attending routine clinical visits @ 5 sites (China; Malaysia; Philippines; South Korea; Thailand) from Jul 2019 - Jun 2020
- Data collection: PHQ-9 (depression); ASSIST (SU); study questionnaire (e.g., income, stressors); medical records (e.g., HIV data)
- N=864: 88% male; median age 39 years; 53% acquired HIV via male-to-male sex; 97% on ART; 67% had available VL and  $<1000$  copies/mL

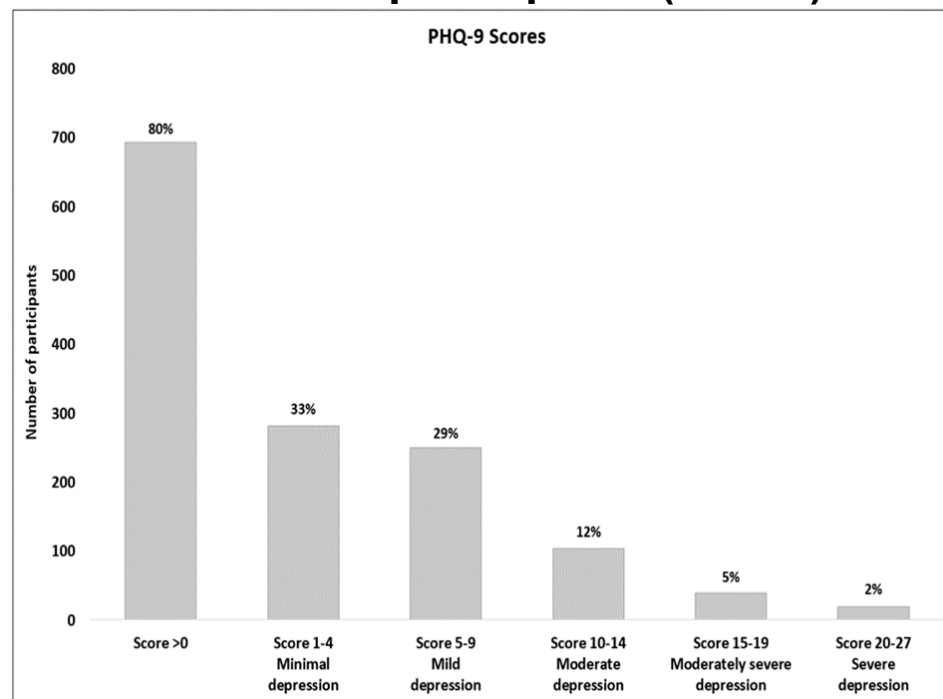
Ross JL, et al.

AIDS Behav. 2022 Dec;26(12):3862-3877. doi: 10.1007/s10461-022-03714-5. Epub 2022 Jun 6.



- 19% had moderate-to-severe depressive symptoms; 80% ever used  $\geq 1$  substance.
- Moderate-to-severe depressive symptoms associated with:
  - Younger age, lower income, suboptimal ART adherence
- Moderate-to-high risk SU in 62% of users, associated with:
  - Younger age, male, stressors, suboptimal ART adherence

### PHQ-9 scores and severity classification of participants (N=864)



Need for improved integration & access to MSD services in HIV clinical settings

Prevalence and risks of depression and substance use among adults living with HIV in the Asia-Pacific region. Ross JL, et al. AIDS Behav. 2022 Dec;26(12):3862-3877.



## Long-term post-transition outcomes of adolescents and young adults living with perinatally and non-perinatally acquired HIV (AYHIV) in Southeast Asia

- Assess factors associated with clinical, social, and behavioral outcomes after transition from pediatric to adult HIV care
- AYHIV in Malaysia, Thailand, and Vietnam followed from 2017-2019 with annual clinical assessments and lab testing
- 93 AYHIV: 60% female; 94% acquired HIV perinatally; 81% Thai; median age 20 years; median follow-up time 94 weeks
- @ wk 96: 77% suppressed VL; 39% recent alcohol use; 49% sexually active, 17% moderate depression (PHQ-9  $\geq 9$ ); 13% suicidal ideation

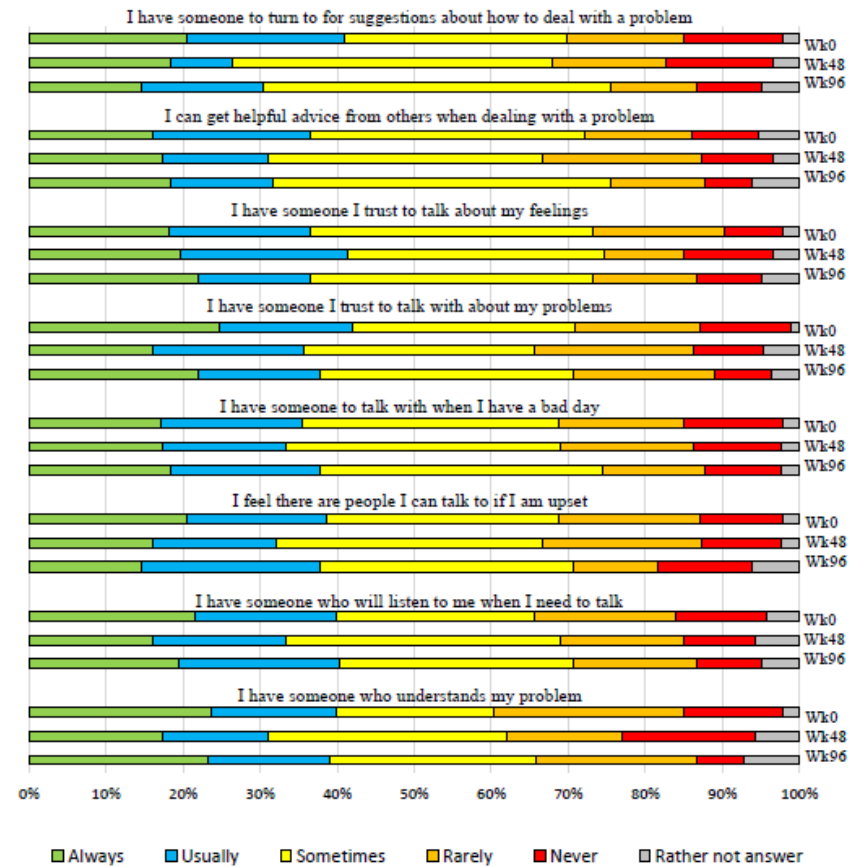
Sohn AH, et al.

J Adolesc Health. 2022 Dec 17:S1054-139X(22)00720-0. doi: 10.1016/j.jadohealth.2022.10.021.



- HIV viremia associated with:
  - <90% ART adherence (aIRR 2.2), CD4 count <500 cells/mm<sup>3</sup> (aIRR 4.75), and being on NNRTI (vs. PI, aIRR 2.71)
  - Having trusted person to talk with was protective (vs. never, aIRR 0.41)
- Indications of social isolation and mental health problems after transition could hinder HIV infection control and social independence progress.

### Social relationship questionnaire responses



Long-term post-transition outcomes of adolescents and young adults living with perinatally and non-perinatally acquired HIV in Southeast Asia. Sohn AH, et al. J Adolesc Health. 2022 Dec 17:S1054-139X(22)00720-0. doi: 10.1016/j.jadohealth.2022.10.021.



# CCASAnet Publication Highlights: 2022



## Site-Level Comprehensiveness of Care Is Associated with Individual Clinical Retention Among Adults Living with HIV in International Epidemiology Databases to Evaluate AIDS, a Global HIV Cohort Collaboration, 2000–2016

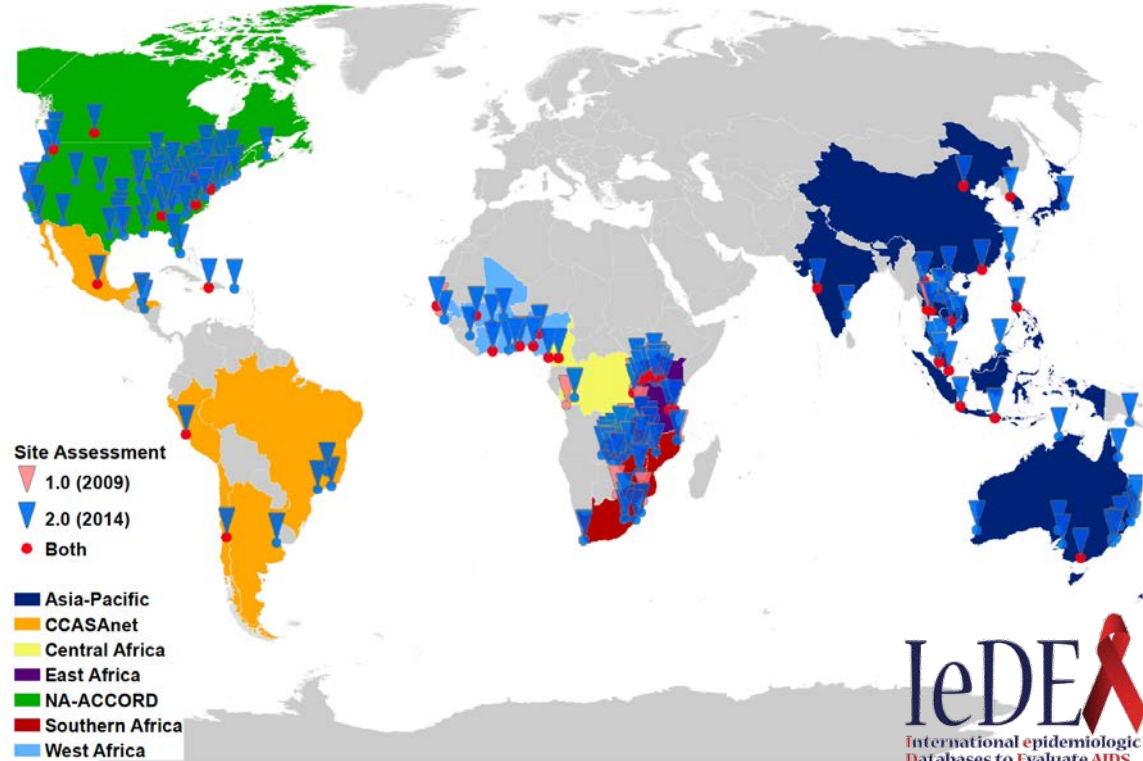
Paul Y. Wada, MD,<sup>1</sup> Ahra Kim, MPH,<sup>1</sup> Karu Jayatilake, PhD,<sup>1</sup> Stephany N. Duda, PhD,<sup>1</sup> Yao Abo, MD, MPH,<sup>2</sup> Keri N. Althoff, PhD,<sup>3</sup> Morna Cornell, PhD, MPH,<sup>4</sup> Beverly Musick, MS,<sup>5</sup> Steve Brown,<sup>5</sup> Annette H. Sohn, MD,<sup>6</sup> Yu Jiun Chan, MD, PhD,<sup>7</sup> Kara K. Wools-Kaloustian, MD,<sup>5</sup> Denis Nash, PhD, MPH,<sup>8</sup> Constantin T. Yiannoutsos, PhD, MS,<sup>9</sup> Carina Cesar, MD,<sup>10</sup> Catherine C. McGowan, MD,<sup>1</sup> and Peter F. Rebeiro, PhD, MHS, MS,<sup>1</sup>  
on behalf of the International Epidemiology Databases to Evaluate AIDS (IeDEA)\*

### Methods:

- Site data was measured in IeDEA site assessments 1.0 (2000–2009) and 2.0 (2010–2016)
- Each site received a comprehensiveness score (1=present, 0=absent), with tallies ranging from 0 to 7: cART adherence measures, nutritional support, PMTCT services, CD4+ testing, TB screening, HIV-related prevention services, & community tracing
- We obtained individual-level cohort data for adults with  $\geq 1$  visit from 2000 to 2016 at sites responding to either assessment
- Person-time was recorded annually, with RIC defined as completing two visits  $\geq 90$  days apart in each calendar year.
- Multivariable modified Poisson regression clustered by site yielded risk ratios and predicted probabilities for individual RIC by comprehensiveness

### Background & Objective:

- Retention in care (RIC) reduces HIV transmission and associated morbidity and mortality
- Comprehensiveness of services has been recommended as a metric to assess the quality of care in HIV programs
- We therefore examined whether delivery of comprehensive services at the site level influenced individual RIC within IeDEA





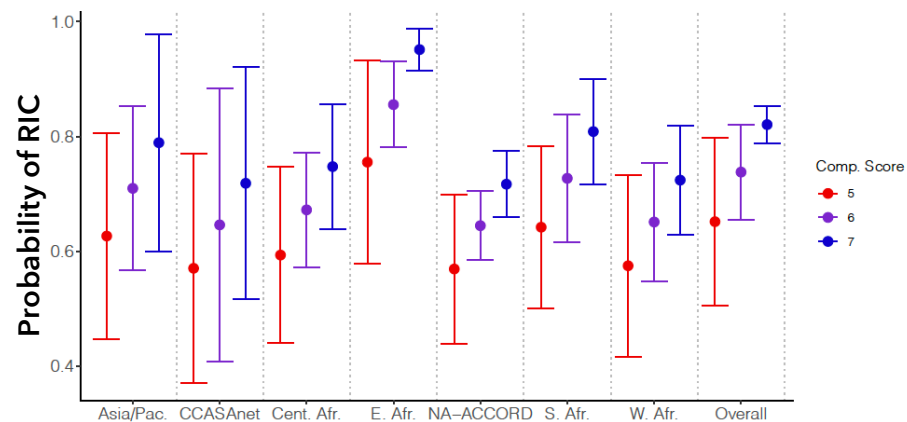
## Results:

- We observed 347,060 individuals in care at 122 sites with 1,619,558 person-years of follow-up
- 69.8% of person-time was retained in care, varying by region from 53.8% (Asia-Pacific) to 82.7% (East Africa)
- RIC improved by about 2% per year from 2000 to 2016 ( $p=0.012$ )
- Every site provided CD4+ count testing, and >90% of individuals received care at sites that provided combination antiretroviral therapy adherence measures, PMTCT, TB screening, HIV-related prevention, and community tracing services
- In adjusted models, individuals at sites with more comprehensive services had higher probabilities of RIC (0.71, 0.74, and 0.83 for scores 5, 6, and 7, respectively;  $p = 0.019$ )

## Conclusion:

- Within leDEA, greater site-level comprehensiveness of services was associated with improved individual RIC
- Much work remains in exploring this relationship, which may inform HIV clinical practice and health systems planning

Characteristic	N, total p-y	Not retained, <sup>a</sup> N=488,731 p-y	Retained, <sup>a</sup> N=1,130,827 p-y	p Value, test statistic
leDEA region	1,619,558			<0.0001, <sup>b</sup> $\chi^2_6=89316.12$
Asia-Pacific	84,846	39,223 (46.2)	45,623 (53.8)	
CCASAnet	216,331	87,286 (40.3)	129,045 (59.7)	
Central Africa	71,467	25,472 (35.6)	45,995 (64.4)	
East Africa	631,725	109,222 (17.3)	522,503 (82.7)	
NA-ACCORD	224,208	83,197 (37.1)	141,011 (62.9)	
Southern Africa	108,264	31,868 (29.4)	76,396 (70.6)	
West Africa	282,717	112,463 (39.8)	170,254 (60.2)	
Comprehensiveness <sup>c</sup>	1,619,558			<0.0001, <sup>b</sup> $\chi^2_4=64821.15$
3	38,946	7,357 (18.9)	31,589 (81.1)	
4	83,364	43,373 (52.0)	39,991 (48.0)	
5	103,729	51,748 (49.9)	51,981 (50.1)	
6	426,158	153,824 (36.1)	272,334 (63.9)	
7	967,361	232,429 (24.0)	734,932 (76.0)	
cART adherence	1,619,558			<0.0001, <sup>b</sup> $\chi^2_1=2358.80$
No	85,537	32,158 (37.6)	53,379 (62.4)	
Yes	1,534,021	456,573 (29.8)	1,077,448 (70.2)	
Nutritional support	1,619,558			<0.0001, <sup>b</sup> $\chi^2_1=19292.42$
No	479,070	181,600 (37.9)	297,470 (62.1)	
Yes	1,140,488	307,131 (26.9)	833,357 (73.1)	
PMTCT	1,619,558			<0.0001, <sup>b</sup> $\chi^2_1=1346.58$
No	112,744	39,478 (35.0)	73,266 (65.0)	
Yes	1,506,814	449,253 (29.8)	1,057,561 (70.2)	
CD4 testing	1,619,558			N/A
No		0 (0)	0 (0)	
Yes	1,619,558	488,731 (30.2)	1,130,827 (69.8)	
TB screening	1,619,558			<0.01, <sup>b</sup> $\chi^2_1=1572.87$
No	146,108	50,728 (34.7)	95,380 (65.3)	
Yes	1,473,450	438,003 (29.7)	1,035,447 (70.3)	
HIV prevention	1,619,558			<0.0001, <sup>b</sup> $\chi^2_1=9739.14$
No	19,463	12,155 (62.5)	7,308 (37.5)	
Yes	1,600,095	476,576 (29.8)	1,123,519 (70.2)	
Community outreach	1,619,558			<0.0001, <sup>b</sup> $\chi^2_1=47165.35$
No	196,570	196,570 (51.3)	99,999 (48.7)	
Yes	1,422,988	387,983 (27.3)	1,035,005 (72.7)	



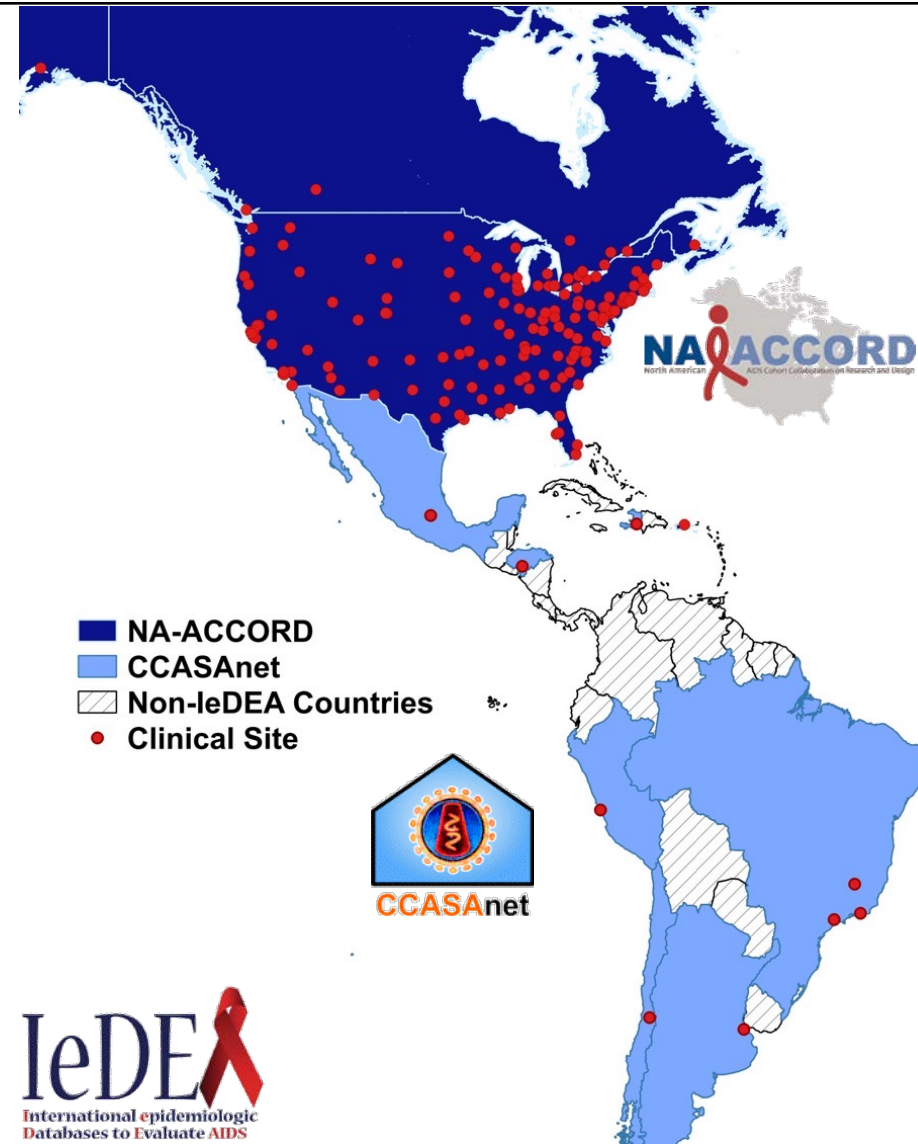
## Weight gain post-ART in HIV+ Latinos/as differs in the USA, Haiti, and Latin America

Lara E. Coelho,<sup>a,\*</sup> Cathy A. Jenkins,<sup>b</sup> Bryan E. Shepherd,<sup>b</sup> Jean W. Pape,<sup>c</sup> Fernando Mejia Cordero,<sup>d</sup> Denis Padgett,<sup>e</sup> Brenda Crabtree Ramirez,<sup>f</sup> Beatriz Grinsztejn,<sup>g</sup> Keri N. Althoff,<sup>g</sup> John R. Koethe,<sup>h</sup> Vincent C. Marconi,<sup>i</sup> Phyllis C. Tien,<sup>j</sup> Amanda L. Willig,<sup>k</sup> Richard D. Moore,<sup>g</sup> Jessica L. Castillo,<sup>h</sup> Jonathan Colasanti,<sup>i</sup> Heidi M. Crane,<sup>l</sup> M. John Gill,<sup>m</sup> Michael A. Horberg,<sup>n</sup> Angel Mayor,<sup>o</sup> Michael J. Silverberg,<sup>p</sup> Catherine McGowan,<sup>h</sup> and Peter F. Rebeiro,<sup>b,h</sup> on behalf of the North American AIDS Collaboration on Research and Design (NA-ACCORD) and the Caribbean, Central and South America network for HIV epidemiology (CCASAnet) of the International epidemiology Databases to Evaluate AIDS (IeDEA)

**Background:** Obesity prevalence has steadily increased in the world for the past half century. However, prevalence and trends vary between countries and can be associated with cultural and environmental contexts. In persons with HIV (PWH), obesity prevalence is also on the rise; furthermore, factors associated with HIV infection progression and antiretroviral therapy have been implicated in weight gain and obesity incidence.

**Objective:** Evaluate weight and BMI trajectories over time, as well as probabilities of becoming overweight or obese, in PWH initiating ART across 5 countries in Latin America and the US.

**Methods:** A longitudinal study of weight and BMI trajectories between 2000 and 2018 for PWH initiating ART in cohorts from Brazil, Honduras, Mexico, Peru, Haiti (within CCASAnet), and the US (within NA-ACCORD).



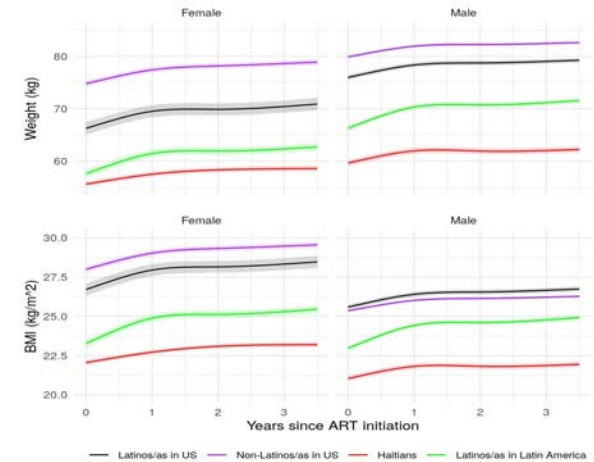
## Results

- PWH substantially gained weight after ART initiation in both North and Latin America.
- Weight and BMI trajectories after ART initiation differed in Haitians, Latinos/as in Latin America and in Latinos/as and non-Latinos/as in the US.
- Latinos (males) in Latin America had the greatest probability of becoming overweight/obese and of becoming obese post ART initiation.
- Latinas (females) in the US had the greatest probability of becoming overweight/obese while non-Latinas in the US had the greatest probability of becoming obese.

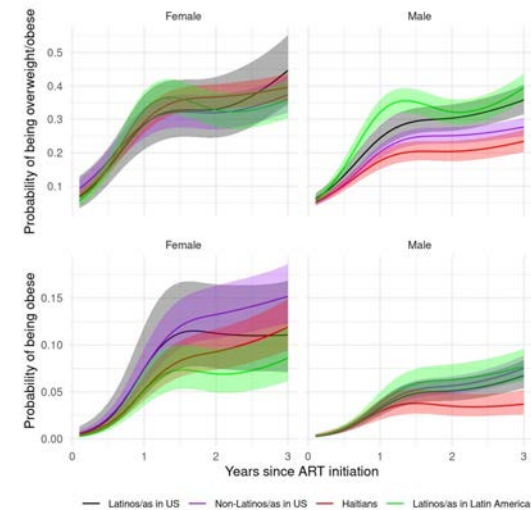
## Conclusion

- In the Americas, PWH gain substantial weight after ART initiation. Despite environmental and cultural differences, PWH in Latin America, Haiti and Latinos and non-Latinos in the US share similar BMI trajectories on ART and high probabilities of becoming overweight and obese over time.

## Weight and BMI trajectories



## Probabilities being overweight and obese



# Clinical effects of durability of immunosuppression in virologically suppressed ART-initiating persons with HIV in Latin America. A retrospective cohort study

Yanink Caro-Vega,<sup>a</sup> Peter F. Rebeiro,<sup>b</sup> Bryan E. Shepherd,<sup>b</sup> Pablo F. Belaunzarán-Zamudio,<sup>a</sup> Brenda Crabtree-Ramirez,<sup>a</sup> Carina Cesar,<sup>c</sup> Paula Mendes Luz,<sup>d</sup> Claudia P. Cortes,<sup>e</sup> Denis Padget,<sup>f</sup> Eduardo Gotuzzo,<sup>g</sup> Catherine C. McGowan,<sup>b</sup> and Juan G. Sierra-Madero<sup>a\*</sup>

**Background:** Clinical outcomes are rarely studied in people living with HIV (PWH) who are virologically suppressed but have incomplete CD4 recovery.

**Aim:** To explore whether time living with severe immunosuppression predicts clinical outcomes better than baseline or time-updated CD4.

## Methods:

- We estimated the association between cumulative percentage of time with CD4 <200 cells/ $\mu$ L during viral suppression (VS) (%t<sub>CD4<200</sub>), and mortality and comorbidities during 2000-2019.
- We used data from the CCASAnet cohort, updated in April 2020 (Argentina, Brazil, Chile, Honduras, Mexico, and Peru)
- We included PWH ( $\geq 18$  years) initiating ART between 2000-2017, with documented VS during the first 12 months of ART initiation and followed up until 2019
- Follow-up from 1<sup>st</sup> date of VS until virologic failure, death, LTFU



Lancet Reg Health Am. 2022  
April ; 8: .

doi:10.1016/j.lana.2021.100175.

<https://pubmed.ncbi.nlm.nih.gov/35602655>

## Outcomes:

1. Death; 2. ADE or SNADE; 3. any event (death, ADE or SNADE); 4. SNADE

- *Deaths were those reported  $\leq 365$  days after the last viral load <200 copies/mL available*
- *SNADE: non-AIDS-defining cancers, cardiovascular, liver and renal disease diagnoses*

## Statistical Analyses:

- We used Cox models to estimate the risk of event using these time-varying predictors: %t<sub>CD4<200</sub>, time-updated CD4 count, and both predictors together
- We fit similar Cox models to estimate the risk of each of our outcomes
- For ADE/SNADE or SNADE, death is a competing risk; people who died were censored at the time of death, and these models are therefore estimating cause-specific hazards

**Results:**

- 8,362 patients included; 51% had CD4<200 at ART initiation
- Patients starting ART with CD4<200 cells/ $\mu$ L had a median of 38% (IQR: 0 – 100%) of the time with CD4<200 cells/ $\mu$ L at 12 months after first VS, 16% (IQR: 0 – 57%) at 24 months, and 10% (IQR:0 – 28%) at 48 months
- PWH virologically suppressed on ART that were severely immunosuppressed with greater percentage of time had a significantly increased risk of mortality (27%; 95%CI: 19%-35%) and of serious non-AIDS-defining events (11%; 95%CI: 7%-14%) even after adjusting for time-updated CD4 counts

**Conclusion:**

- The association between higher cumulative percentage of time with low CD4 counts and poor outcomes of mortality and clinical events suggest that these patients require better screening for early diagnoses of comorbidities and perhaps different prophylactic practices, even if they remain virologically suppressed

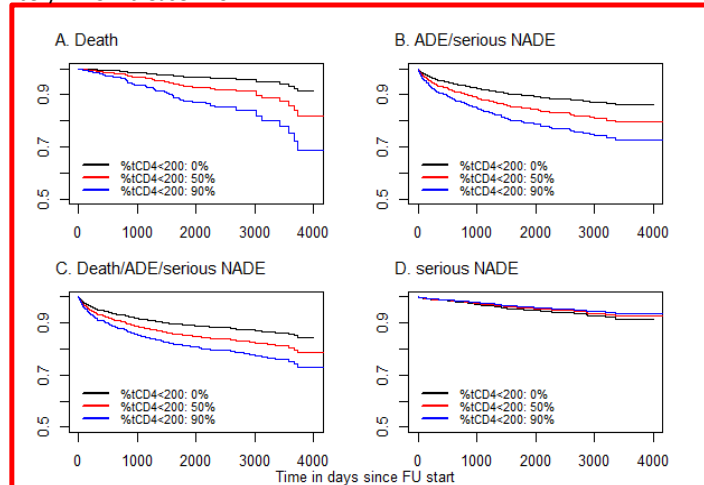
	Exposure & Covariates	Death		ADE or SNADE		Any event	
		HR	95% CI	HR	95% CI	HR	95% CI
Model including percentage of time CD4<200	Percentage of time with CD4<200 15% vs 0%	1.27	1.19 – 1.35	1.13	1.09 – 1.17	1.15	1.07 – 1.14
	90% vs 0%	4.13	2.82 – 6.04	2.12	1.72 – 2.63	1.83	1.52 – 2.21
Model including both percentage of time CD4<200 & time-updated CD4 count	Percentage of time with CD4<200 15% vs 0%	1.05	0.97 – 1.14	1.09	1.05 – 1.14	1.08	1.04 – 1.12
	90% vs 0%	1.36	0.86 – 2.16	1.70	1.33 – 2.16	1.60	1.29 – 1.99
	Time-updated CD4 count 350 vs 200	0.51	0.42 – 0.61	0.85	0.79 – 0.93	0.92	0.85 – 0.98
	500 vs 200	0.26	0.18 – 0.37	0.73	0.61 – 0.86	0.84	0.73 – 0.97

**Table 1:** Adjusted hazard ratios (HR) for death, AIDS-defining events, & serious non-AIDS-defining events using models with %t<sub>CD4<200</sub> & both predictors

**Table 1 Notes:** All the models include probable HIV acquisition risk, education level, CD4 at ART initiation group, calendar year of follow-up start, and are stratified by site. Models with ADE and SNADE in the outcome excluded the Honduras site.

1. Percentage of time with CD4<200 was included in models as a continuous variable; the values 15%, and 90% were compared to 0% to improve interpretation of the associations.

2. Similarly, updated CD4 count was also included in models as a continuous variable; the values 350 and 500 were compared to 200 for interpretation. These can be thought of as the adjusted relative hazards for a 150 (350 vs.200) and 300 (500 vs. 200) cell/mm3 increase in CD4



**Figure 1.** Survival probability for death, AIDS-defining and/or serious non-AIDS defining events by percentage of time with CD4 <200

# The Effect of Diabetes and Prediabetes on *Mycobacterium tuberculosis* Transmission to Close Contacts

The Journal of Infectious Diseases

MAJOR ARTICLE

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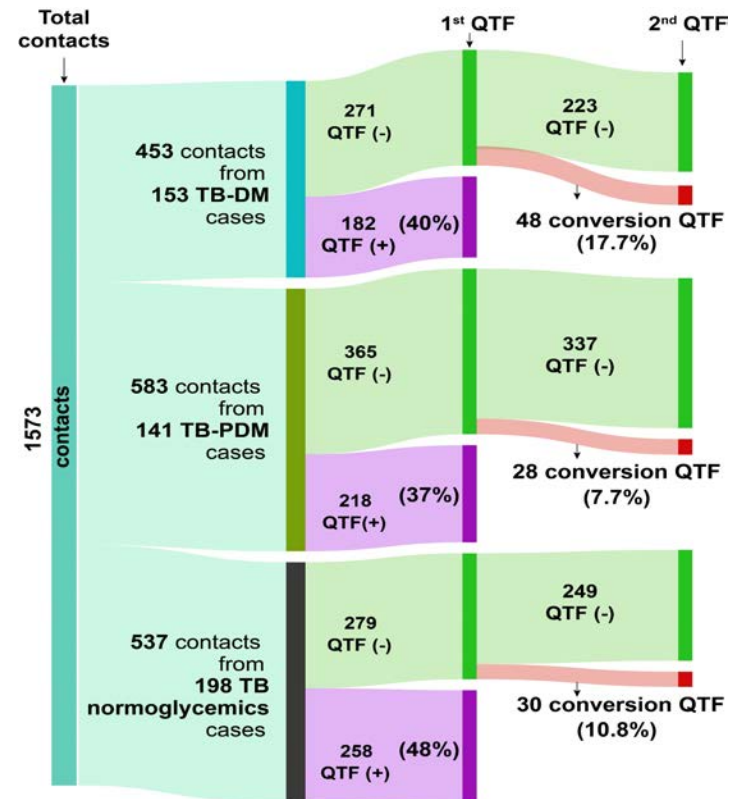
IDSA  
Infectious Diseases Society of America

hivma  
hiv medicine association

OXFORD

Although diabetes mellitus (DM) is associated with an increased risk of developing active disease once infected with *M. tuberculosis*, the effect of DM on *M. tuberculosis* transmission has not been evaluated.

- This was a multicenter prospective observational cohort study (RePORT-Brazil) of individuals  $\geq 18$  years old with culture-confirmed pulmonary tuberculosis and their close contacts.
- Close contacts were defined as having  $\geq 4$  hours of contact/week with the tuberculosis index case at any time in the previous 6 months
- The sample size was 1573 close tuberculosis contacts:
  - 537 close contacts of 198 normoglycemic persons with TB
  - 1036 contacts of 294 TB-dysglycemic cases
  - DM = 153 and pre-diabetes (PDM) = 141



## Methods:

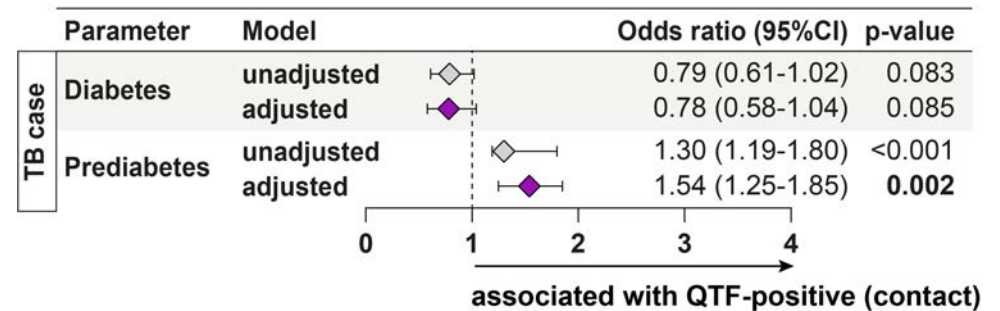
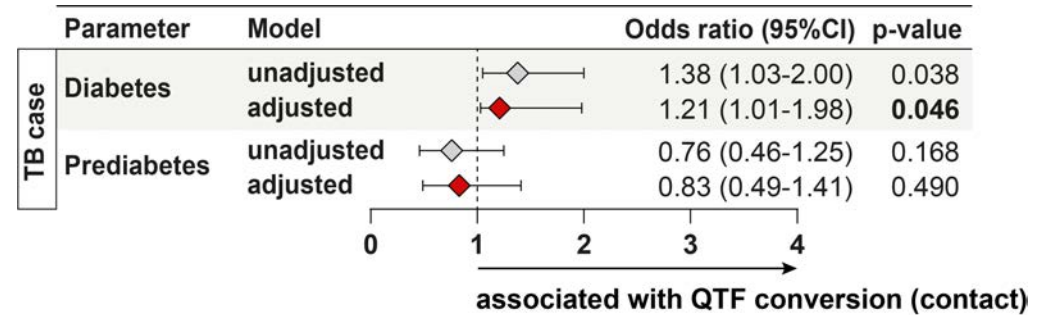
Contacts were investigated at baseline and 6 months after enrollment. QuantiFERON (QTF) positivity at baseline and conversion (from negative to positive at month 6) were compared according to glycemic status (DM and preDM) of persons with TB.

## Results:

– Multivariable analyses demonstrated that **DM**, persistent cough, AFB-positive, and pulmonary cavities in the TB source cases were associated with QTF conversion

- **PreDM**, AFB-positive, pulmonary cavities, and having secondhand smoke exposure in TB index cases were independently associated with QTF-positive in contacts at baseline.

**Conclusion:** This study demonstrated that dysglycemic TB patients were at increased risk of transmitting Mtb to close contacts in a well-characterized, large, multi-center cohort in Brazil.

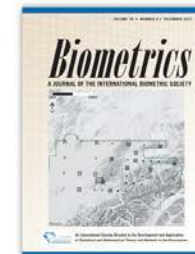


*Adjusted for HIV, secondhand smoke exposure, persistent cough, AFB-positive, abnormal x-ray (TB cases) and age (years), smoking and diabetes (contacts).*

## Efficient odds ratio estimation under two-phase sampling using error-prone data from a multi-national HIV research cohort

Sarah C. Lotspeich  Bryan E. Shepherd, Gustavo G. C. Amorim, Pamela A. Shaw, Ran Tao

First published: 02 July 2021 | <https://doi.org/10.1111/biom.13512>



[Volume 78, Issue 4](#)

December 2022

Pages 1674-1685



References



Related



Information

### Background:

- There are concerns about data quality with the use of routinely collected observational data such as that used in leDEA studies.
- Data quality can be assessed via chart reviews/data audits of subsamples of the data.
- Data audit information can be used in analyses to improve estimation.
- This paper describes a new approach to combine original and audit data in logistic regression models with error-prone exposure and outcome variables.



- In simulations, the new method (SMLE) outperforms analyses that only use the original error-prone data (Naive), analyses that only use the audited data (CC), and analyses that use inverse probability weighting of the audit data (HT). The new approach also has some advantages (and disadvantages) versus a doubly robust method (Raking).
- The method was illustrated using CCASAnet data looking at risk factors associated with having an AIDS defining event (ADE) within 2 years of ART initiation; lower CD4 and prior AIDS were associate with ADE using the new method (Table 5 below).

TABLE 5 log OR estimates and 95% confidence intervals from the analysis of the CCASAnet dataset

Covariate	Naive		CC		HT		Raking		SMLE	
	log OR	95% CI	log OR	95% CI	log OR	95% CI	log OR	95% CI	log OR	95% CI
$\sqrt{CD4/10}$	-0.280	(-0.343, -0.217)	-0.688	(-1.164, -0.212)	-0.755	(-1.154, -0.356)	-0.620	(-0.922, -0.318)	-0.482	(-0.725, -0.240)
AIDS	1.543	(1.317, 1.770)	0.243	(-1.166, 1.653)	0.579	(-0.850, 2.009)	0.093	(-1.131, 1.318)	1.388	(0.582, 2.194)
Site: A	-1.399	(-1.755, -1.042)	-0.396	(-2.433, 1.642)	-0.357	(-2.601, 1.887)	-0.289	(-1.945, 1.368)	1.129	(0.278, 1.980)
Site: C	0.409	(0.154, 0.664)	0.561	(-1.368, 2.491)	0.658	(-1.447, 2.764)	0.543	(-1.099, 2.184)	0.184	(0.003, 0.365)
Site: D	-0.991	(-1.412, -0.570)	-2.416	(-5.027, 0.194)	-2.638	(-5.015, -0.261)	-2.548	(-5.226, 0.131)	-1.225	(-2.394, -0.056)
Site: E	-0.225	(-0.581, 0.131)	-0.688	(-3.353, 1.976)	-0.686	(-3.615, 2.244)	-0.542	(-2.855, 1.772)	-0.732	(-1.725, 0.260)
Male	0.073	(-0.169, 0.316)	-0.728	(-2.330, 0.874)	-0.823	(-2.395, 0.749)	-1.195	(-2.669, 0.280)	-0.703	(-1.933, 0.527)
Age/10 years	0.014	(-0.091, 0.119)	0.354	(-0.296, 1.003)	0.310	(-0.315, 0.935)	0.223	(-0.311, 0.756)	-0.690	(-1.644, 0.263)
Year of ART	-0.023	(-0.051, 0.006)	0.092	(-0.144, 0.327)	0.155	(-0.206, 0.516)	0.081	(-0.134, 0.297)	-0.508	(-1.225, 0.210)

Note. 95% CI is the 95% confidence interval.



# Central Africa IeDEA



2022 Research Highlights

# Same-Day Antiretroviral Therapy Initiation as a Predictor of Loss to Follow-up and Viral Suppression Among People With Human Immunodeficiency Virus in Sub-Saharan Africa

Ross J, Brazier E, Fatti G, Jaquet A, Tanon A, Haas AD, Diero L, Castelnuovo B, Yiannoutsos CT, Nash D, Anastos KM, Yotebieng M. Clin Infect Dis. 2023 Jan 6;76(1):39-47. <https://doi.org/10.1093/cid/ciac759>

## AIMS:

- To examine the association between same-day ART initiation and both loss to follow-up (LTFU) and viral suppression among patients enrolled in HIV care at IeDEA clinics in 11 African countries.

## METHODS:

- **Data:** ART-naïve adult PLHIV from sites participating in the International epidemiology Databases to Evaluate AIDS consortium (IeDEA) who enrolled in care after Treat-All implementation and prior to January 2019.
- **Analysis:** Multivariable Cox regression used to estimate the association between same-day ART initiation and loss to follow-up, and Poisson regression to estimate the association between same-day ART initiation and 6-month viral suppression.

# Same-Day Antiretroviral Therapy Initiation as a Predictor of Loss to Follow-up and Viral Suppression Among People With Human Immunodeficiency Virus in Sub-Saharan Africa

## RESULTS:

- Among 29,017 patients from 63 sites, 18,584 (64.0%) initiated ART on the day of enrollment.
- Same-day ART initiation was less likely among those with advanced HIV disease versus early-stage disease.
- Loss to follow-up was significantly lower among those initiating ART  $\geq 1$  day of enrollment, compared with same-day ART initiators (20.6% vs 27.7%; adjusted hazard ratio 0.66, 95% CI 0.57-0.76).
- No difference in viral suppression was observed by time to ART initiation (adjusted rate ratio 1.00, 95% CI 0.98-1.02).

# Clinical and programmatic outcomes of HIV-exposed infants enrolled in care at geographically diverse clinics, 1997-2021: A cohort study

Edmonds A, Brazier E, Musick BS, Yotebieng M, Humphrey J, Abuogi LL, Adedimeji A, Keiser O, Msukwa M, Carlucci JG, Maia M, Pinto JA, Leroy V, Davies MA, Wools-Kaloustian KK; leDEA. *PLoS Med.* 2022 Sep 15;19(9):e1004089. doi: [10.1371/journal.pmed.1004089](https://doi.org/10.1371/journal.pmed.1004089).

## AIMS:

- Describe characteristics of HIV-exposed infants and their mothers
- Estimate the cumulative incidences of 4 primary outcomes – DNA PCR testing, loss to follow-up (LTFU), HIV diagnosis, and death – through 24 months of age among HIV-exposed infants
- Assess associations of antiretroviral therapy (ART) during pregnancy, preterm birth, small for gestational age, low birth weight, and calendar time with the primary outcomes

## METHODS:

- **Data:** Infants were eligible if they were documented as having a mother with HIV and if they enrolled in care (i.e., first database entry) at <18 months of age.
- **Analysis:** Descriptive statistics were used to characterize HIV-exposed infants and their mothers; cumulative incidence functions, accounting for competing risks, were estimated via proportional subdistribution hazard models.

# Clinical and programmatic outcomes of HIV-exposed infants enrolled in care at geographically diverse clinics, 1997-2021: A cohort study

## RESULTS:

- >82,000 HIV-exposed infants born over a 25-year period at 198 clinics providing routine HIV services in 10 countries were included.
- There were improvements over time in maternal ART use during pregnancy, along with decreases in HIV diagnosis and death among HIV-exposed infants.
- Cumulative incidences of DNA PCR testing, LTFU, HIV diagnosis, and death through 24 months of age varied widely across regions, however, infant retention at 2 years remained suboptimal and did not exceed 60% in any period in any region.

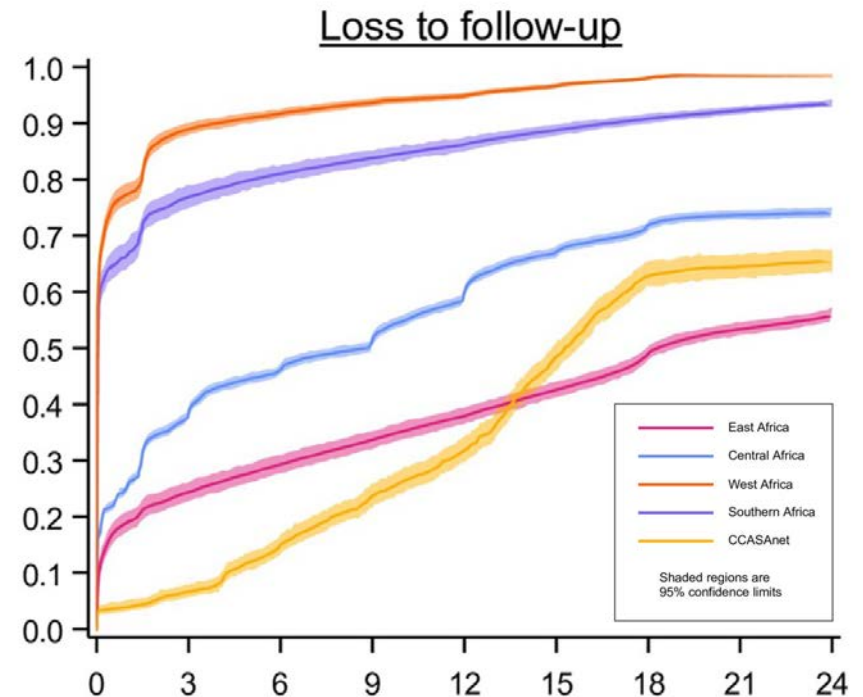


Fig 1. Cumulative incidences of DNA PCR testing, LTFU, HIV diagnosis, and death through 24 months of age among HIV-exposed infants in the IeDEA consortium and Umoyo+, by region, 1997-2020. CCASAnet, Caribbean, Central, and South America network for HIV epidemiology; IeDEA, International epidemiology Databases to Evaluate AIDS; LTFU, loss to follow-up.

# Viral Load Status Before Switching to Dolutegravir-Containing Antiretroviral Therapy and Associations With Human Immunodeficiency Virus Treatment Outcomes in Sub-Saharan Africa

Romo ML, Edwards JK, Semeere AS, Musick BS, Urassa M, Odhiambo F, Diero L, Kasozi C, Murenzi G, Lelo P, Wyka K, Kelvin EA, Sohn AH, Wools-Kaloustian KK, Nash D; International epidemiology Databases to Evaluate AIDS (IeDEA). Clin Infect Dis. 2022 Sep 10;75(4):630-637. doi: [10.1093/cid/ciab1006](https://doi.org/10.1093/cid/ciab1006).

## AIMS:

- To describe viral load (VL) testing status among patients who switched to dolutegravir (DTG) and examine associations with subsequent HIV treatment outcomes while on DTG

## METHODS:

- **Data:** Patients at IeDEA sites in CA and EA who were aged  $\geq 16$  years at the time of HIV care enrollment who switched to a DTG-containing regimen from a nevirapine- or efavirenz-containing regimen from July 2017 through February 2020, started ART  $\geq 6$  months before switching, and had  $\geq 6$  months of possible follow-up after switching
- **Analysis:** Multivariable cause-specific hazards regression used to estimate the association of the most recent VL test in the 12 months before switching with subsequent treatment outcomes.

# Viral Load Status Before Switching to Dolutegravir-Containing Antiretroviral Therapy and Associations With Human Immunodeficiency Virus Treatment Outcomes in Sub-Saharan Africa

## RESULTS:

- 36,393 patients at 37 sites in 5 countries (Democratic Republic of the Congo, Kenya, Rwanda, Tanzania, Uganda) switched to a dolutegravir-containing regimen from July 2017 through February 2020, with a median follow-up of approximately 11 months.
- Compared with those who switched with a VL <200 copies/mL, patients without a recent VL test or with a preswitch VL  $\geq 1000$  copies/mL had significantly increased hazards of
  - Incident VL  $\geq 1000$  copies/mL without evidence of resuppression (adjusted hazard ratio [aHR], 2.89; 95% confidence interval [CI], 1.99–4.19 and aHR, 6.60; 95% CI, 4.36–9.99, respectively)
  - Pulmonary tuberculosis or a World Health Organization clinical stage 4 event (aHR, 4.78; 95% CI, 2.77–8.24 and aHR, 13.97; 95% CI, 6.62–29.50, respectively).



# COVID-19 associated changes in HIV service delivery over time in Central Africa: Results from facility surveys during the first and second waves of the pandemic

Rogers A, Brazier E, Dzudie A, Adedimeji A, Yotebieng M, Muhoza B, Twizere C, Lelo P, Nsonde D, Mafoua A, Munyaneza A, Gateretse P, Diafouka M, Murenzi G, Niyongabo T, Anastos K, Nash D. *PLoS One*. 2022 Nov 30;17(11):e0275429. doi: [10.1371/journal.pone.0275429](https://doi.org/10.1371/journal.pone.0275429).

## AIMS:

- To document changes in HIV care associated with the COVID-19 pandemic at selected clinics in Central Africa, along with clinic-level strategies for minimizing disruptions in HIV care and treatment for people with HIV (PWH).

## METHODS:

- **Data:** A 51-item questionnaire on COVID-19 pandemic-associated changes in HIV service delivery was completed by clinicians involved in HIV care at 21 clinics in five countries participating in Central Africa International epidemiology Databases to Evaluate AIDS (CA-IeDEA). The survey was completed at two timepoints: June-July 2020 and October 2020 to February 2021.
- **Analysis:** Descriptive statistics were used to characterize changes in HIV care and related services.

# COVID-19 associated changes in HIV service delivery over time in Central Africa: Results from facility surveys during the first and second waves of the pandemic

## RESULTS:

- While 81% of sites reported at least one negative consequence of COVID-19 for clinic operations during the first survey, none reported suspending antiretroviral therapy (ART) initiation services for new patients, and 24% reported adopting telemedicine.
- In the follow-up survey, fewer sites (48%) reported at least one disruption to clinic operations, and more sites reported mitigation strategies, including expanding rapid ART initiation services and providing extra supplies of ART medications to reduce visit frequency.
- In the follow-up survey, more sites, especially in Rwanda, reported stockouts of commodities, including HIV and viral load testing and HIV pre-exposure prophylaxis.
- More than one-fifth of sites reported stockouts of second- or third-line ART at each survey timepoint.

# Depressive Symptoms, Gender, Disclosure, and HIV Care Stage Among People Living with HIV in Cameroon

Parcesepe AM, Remch M, Dzudie A, Ajeh R, Nash D, Anastos K, Yotebieng M, Adedimeji A, Pefura-Yone E, Lancaster K. *AIDS Behav.* 2022 Mar;26(3):651-661. doi: [10.1007/s10461-021-03425-3](https://doi.org/10.1007/s10461-021-03425-3).

## AIMS:

- To estimate the prevalence of depressive symptoms across three stages of HIV care: those not yet on antiretroviral therapy (ART), recent ART initiators (ART initiation  $\leq$  30 days prior), and ART users (ART initiation  $>$  30 days prior) and to examine whether disclosure or gender modified the relationship between HIV care stage and depressive symptoms.

## METHODS:

- **Data:** Cross-sectional data from 12,507 PLWH at enrollment into leDEA Cameroon between 2016-2020. Recent depressive symptoms were assessed using the Patient Health Questionnaire-2 (PHQ-2), with a score  $\geq 3$  considered indicative of depressive symptoms
- **Analysis:** Adjusted prevalence differences of depressive symptoms were estimated using binomial regression to compare recent ART initiators and ART users. Disclosure and gender were examined as effect measure modifiers of the relationship between HIV care stage and depressive symptoms.

## Depressive Symptoms, Gender, Disclosure, and HIV Care Stage Among People Living with HIV in Cameroon.

### RESULTS:

- The prevalence of depressive symptoms was 11.9%, 22.0%, and 8.7% among PLWH not yet on ART, recent ART initiators, and ART users, respectively.
- Among ART users, the prevalence of depressive symptoms decreased with time since ART initiation. The prevalence of depressive symptoms was 17.7%, 9.5% and 8.0% among participants who had initiated between 31 days and less than 6 months ago, from 6 to 12 months prior, and more than 12 months prior.
- ART users had significantly lower prevalence of depressive symptoms compared to recent ART initiators (aPD - 0.09 [95% CI - 0.11, - 0.08]).
- Neither gender nor HIV disclosure modified the effect measure of the relationship between HIV care stage and depressive symptoms.

**East Africa**

**I e D E**

INTERNATIONAL EPIDEMIOLOGY  
DATABASES TO EVALUATE AIDS



**2022 Research Highlights**

IeDE 

# Evaluation of four chemotherapy regimens for treatment of advanced AIDS-associated KS

## Background/Methods

- Kaposi sarcoma (KS) is a substantial contributor to mortality in resource-limited settings
- Projected clinical & economic outcomes for PLWH & advanced KS initiating chemo:
  - Oral etoposide (etoposide)
  - Bleomycin-vincristine
  - Paclitaxel
  - Pegylated liposomal doxorubicin (PLD)
- Projected/calculated for each regimen:
  - Life expectancy
  - Incremental cost-effectiveness ratios (ICERs; the difference in life expectancy divided by the difference in lifetime costs between strategies)

## Results (1)

### Base-case model results

Chemotherapy regimen	Undiscounted per-person life expectancy	Discounted per-person life expectancy	Discounted per-person lifetime cost	ICER (\$/YLS)
<b>Base-case</b>				
Etoposide	6.8	5.0	\$2,340	-
Bleomycin-vincristine	11.2	7.4	\$3,180	350
Paclitaxel	15.4	9.9	\$4,150	<b>380</b>
PLD	16.0	10.3	\$4,830	2,080
<b>PLD price reduction scenario (44% price reduction from \$180 to \$100 per cycle)</b>				
PLD	16.0	10.3	\$4,440	<b>890</b>

**Abbreviations:** PLD: pegylated liposomal doxorubicin; ICER: incremental cost-effectiveness ratio; YLS: year-of-life-saved  
 Costs reported in 2019 USD  
 Cost-effectiveness threshold: \$910/YLS; bolded ICERs are cost-effective at this threshold

- Paclitaxel improves projected life expectancy, is cost-effective, and should be standard of care now
- PLD could be cost-effective with a 44% price reduction

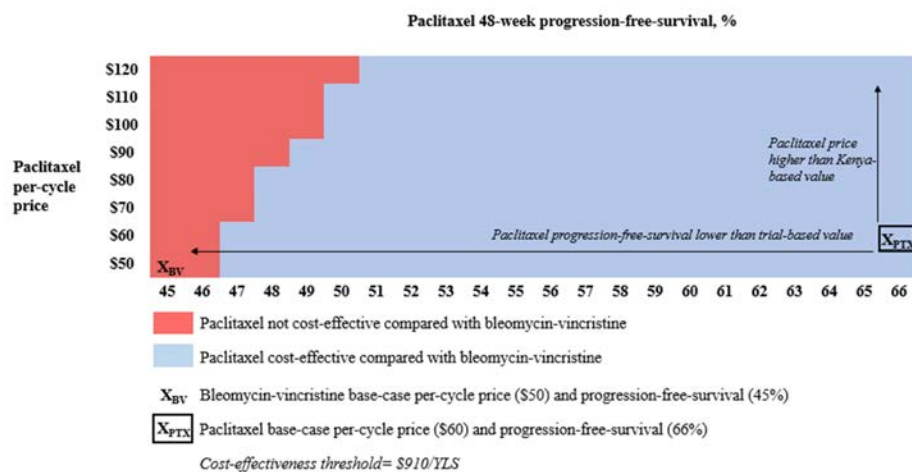
*Freeman et al, Lancet Global Health 2022*



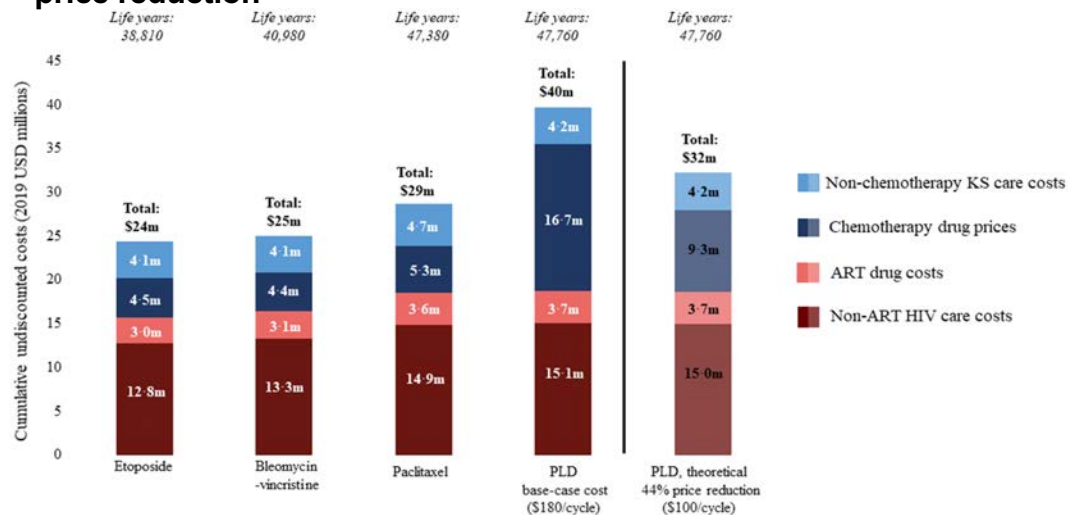
# Regimens for treatment of advanced AIDS-associated KS

## Results (2) and Conclusions

**Figure 1. Two-way sensitivity analysis of paclitaxel progression-free-survival and price: paclitaxel vs. bleomycin-vincristine**



**Figure 2. Budget impact analysis of etoposide, bleomycin vincristine, paclitaxel, PLD, and PLD with 44% price reduction**



- Paclitaxel would save ~6,400 years of life and cost an additional \$4 million over five years compared with bleomycin-vincristine; the majority of this increase is HIV-related due to improved survival
- PLD would cost an additional \$15 million compared to paclitaxel at current price, but would cost an additional \$7 million with 44% cost reduction

Freeman et al, *Lancet Global Health* 2022



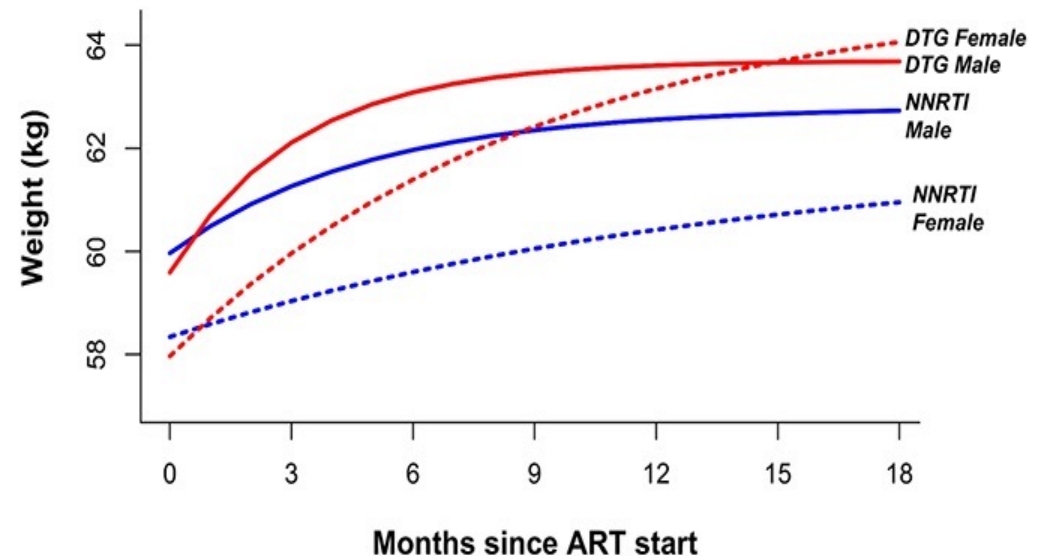
# Weight Gain Among Treatment-Naïve PWH Receiving DTG in AMPATH

## Background/Methods

- Studies have linked integrase strand transfer inhibitors (INSTI) with increased weight gain
- ART naïve first treatment regimen 1/2015 – 9/2018
- DTG vs. nonnucleoside reverse transcriptase inhibitors (NNRTI)
- modelled weight changes over time
- Logistic regression models were constructed to evaluate the association between different variables with extreme increase in body mass index ( $\geq 10\%$  increase)

## Results

Figure 1: Changes in Weight Over Time by sex and regimen





# Weight Gain Among Treatment-Naïve PWH Receiving DTG in AMPATH

## Results (2) and Conclusions

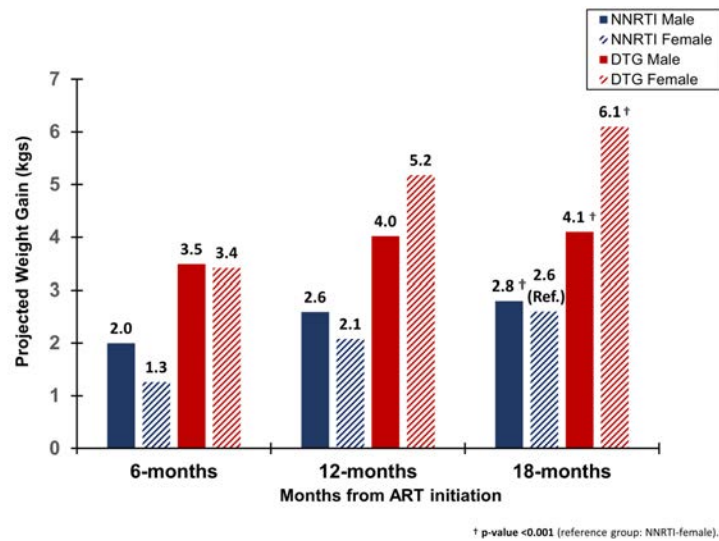


Figure 2: Projected weight gain by sex and treatment regimen

Study confirms higher weight gain with DTG-based regimens compared with traditional ART

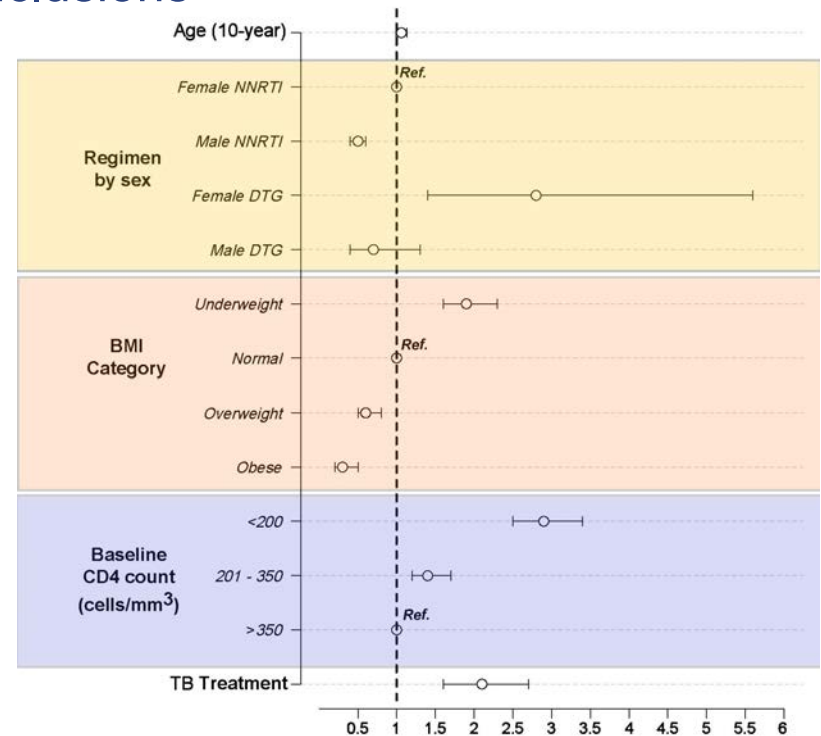


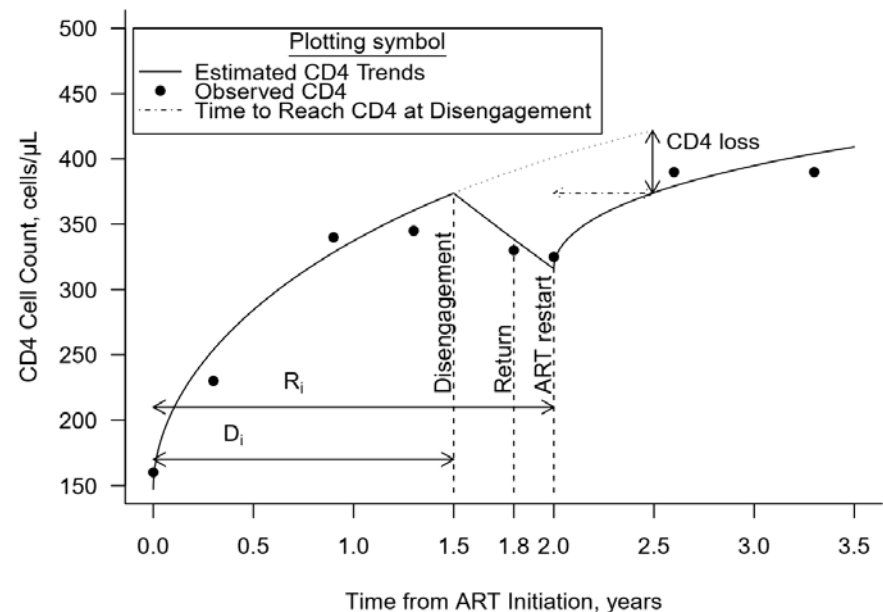
Figure 3: Adjusted hazard of extreme weight gain

# The effect of HIV treatment interruption on subsequent immunologic response\*

## Background/Methods

- Immunologic response after ART restart following care interruption is not well studied
- Data from individuals in East Africa leDEA who return to care after transient disengagement were included
- CD4 data before and during disengagement from care and after ART re-initiation were modeled by a linear mixed model (LMM) with two subject-specific knots placed at the time of disengagement from care and treatment re-initiation

Figure 1. Graphical representation of the model



# The effect of HIV treatment interruption on subsequent immunologic response\*

## Results and Conclusions

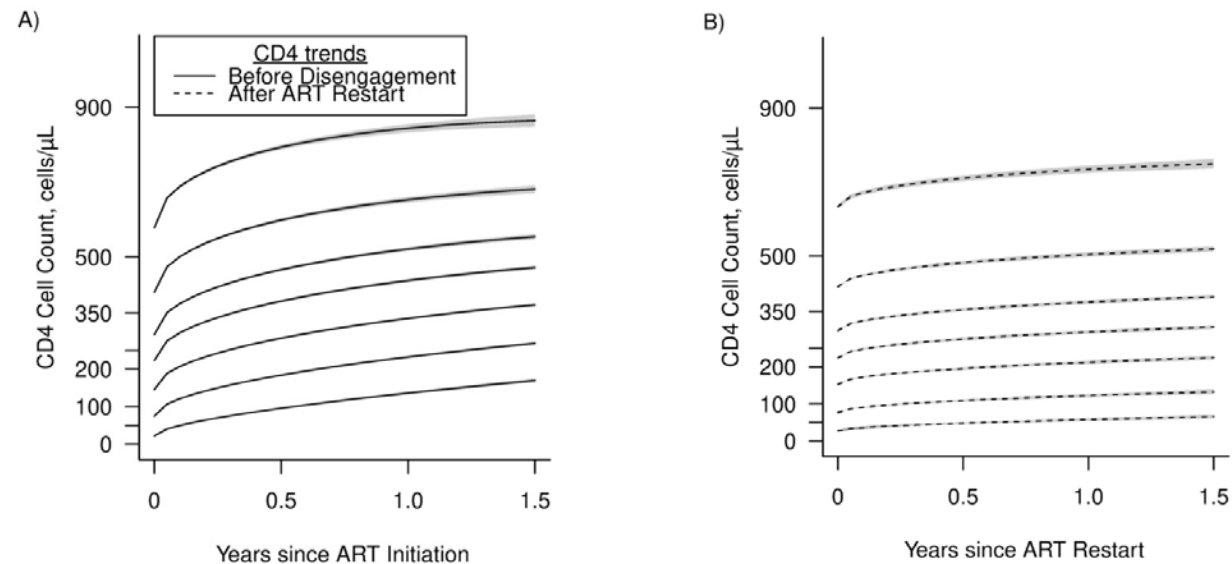


Figure 2: CD4 trends before care disengagement and after ART restart conditioning on baseline CD4 intervals

- CD4 increase after initial ART initiation substantially higher, even after performing various sensitivity analyses
- Given that poorer CD4 restoration is associated with increased mortality/morbidity, specific interventions targeting at better retention are urgently required

*Thomadakis et al, American Journal of Epidemiology 2022*

# Retention in care and viral suppression in the PMTCT continuum at a large referral facility in western Kenya

## Methods

### Eligibility criteria:

- Woman living with HIV (WLHIV)
- $\geq 1$  visit at site during pregnancy 2015-2019
- Delivery date  $\leq 18$  months before database closure in 2019
- All infants born to eligible WLHIV

### Outcomes:

- Retention in care (attending clinic +/- 90 days of 4 time points: delivery, and 6, 12 and 18 months postpartum)
- Gap in care: missing any scheduled visit by  $> 30$  days, within periods delineated by above time points
- viral suppression (VS)  $< 1000$  copies/mL, during pregnancy and postpartum

### Analytic methods:

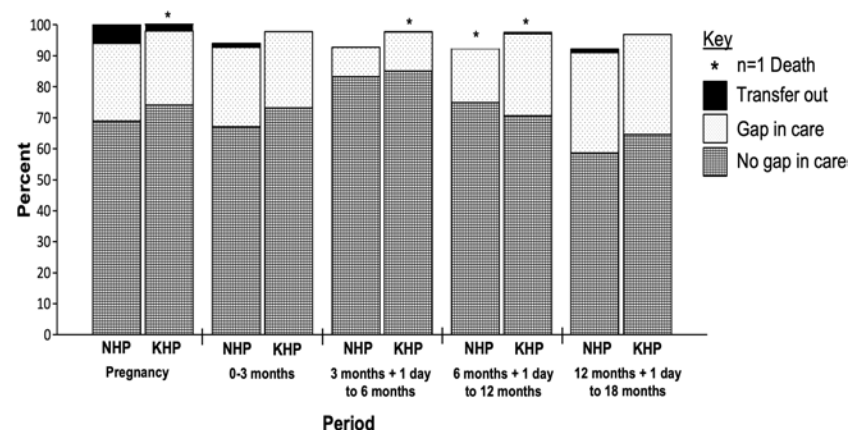
- Group stratification:
  - Newly HIV-positive (NHP; enrolled in HIV care during pregnancy)
  - Known HIV-positive (KHP; enrolled in HIV care before pregnancy)
- Semiparametric proportional odds regression for interval-censored competing risk data to analyze cumulative incidence of VS from 2 weeks to 18 months post-delivery, and  $\geq 6$  months post-ART initiation

*Humphrey et al, AIDS and Behavior, 2022*

## Retention in care and viral suppression in the PMTCT continuum at a large referral facility in western Kenya Results

- 856 pregnant WLHIV
    - 167 (20%) NHP
    - 689 (80%) KHP
  - 698 infants with  $\geq 1$  HIV test results from birth through 18 months postpartum
    - 1.9% HIV positive
    - 40–65% lacked an HIV test result at each of the 6 week and 6-, 12- and 18-month time points
  - Retention declined over time and was higher among KHPs compared to NHPs
- Gaps in care 10-32% across postpartum periods and highest during 12-18 months postpartum
  - Viral Suppression (VS)
    - Pregnancy: 88% among KHPs
    - Postpartum: 88% among KHPs, 93% among NHPs
  - Competing risk model for time to VS after delivery
    - adjusted odds of VS increased by 18% for each additional year of age
    - NHP status not associated with VS or death/LTFU

Characteristic	Total n=856	New HIV- Positive n=167	Known HIV- Positive n=689	P-value
Postpartum retention in care				
6 months	749 (88%)	116 (70%)	633 (92%)	<0.001
12 months	727 (85%)	112 (67%)	615 (89%)	<0.001
18 months	661 (77%)	88 (53%)	573 (83%)	<0.001



*Humphrey et al, AIDS and Behavior, 2022*

# Clinical and programmatic outcomes of HIV-exposed infants enrolled in care at geographically diverse clinics, 1997-2021: A cohort study

## Background/Methods

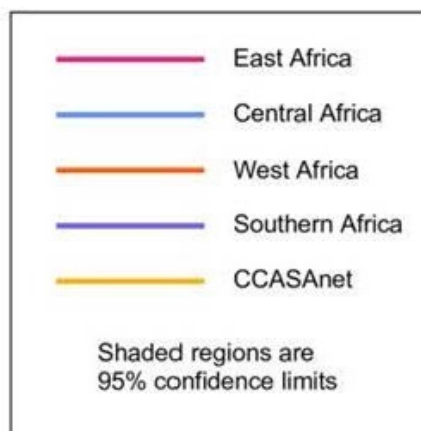
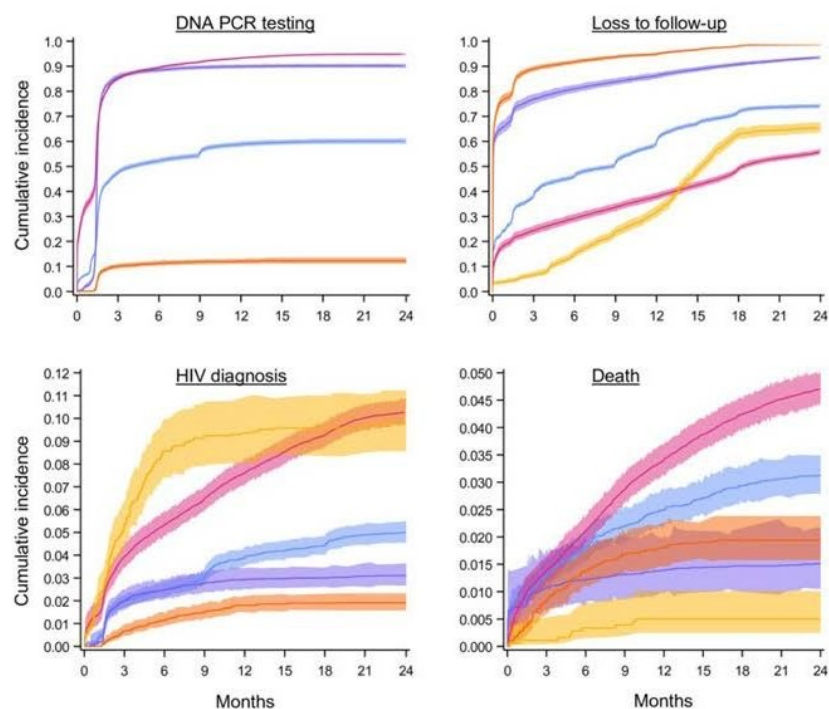
- Although 1.3 million women with HIV give birth annually, care and outcomes for HIV-exposed infants remain incompletely understood
- HIV-exposed infants were eligible for this retrospective cohort analysis if enrolled at <18 months at 198 clinics in 10 countries across 5 leDEA regions
- estimated cumulative incidences of DNA PCR testing, loss to follow-up (LTFU), HIV diagnosis, and death through 24 months of age using proportional subdistribution hazard models accounting for competing risks.
  - Competing risks were transfer, care withdrawal, and confirmation of negative HIV status, along with LTFU and death, when not the outcome of interest
- In CA and EA, associations between maternal/infant characteristics and each outcome were qualified

## Results (1)

- 82,067 infants (47,300 EA, 10,699 CA, 6,503 WA, 15,770 SA, 1,795 CCASAnet) born 1997-2021
- Maternal ART range 65.6% (CCASAnet) to 89.5% (EA), with improvements in all regions over time
- 24-month cumulative incidence for all outcomes varied widely across regions (See Figure)
- Although infant retention did not improve, HIV diagnosis and death decreased over time, and in EA, the cumulative incidence of HIV diagnosis decreased substantially, declining to 2.9% (95% CL, 1.5%, 5.4%) in 2020
- Maternal ART was associated with:
  - Decreased infant mortality
    - EA 0.65 sdHR; 95% CL, 0.47, 0.91
    - CA 0.51 sdHR; 95% CL, 0.36, 0.74
  - Decreased Infant HIV diagnosis
    - EA sdHR, 0.40; 95% CL, 0.31, 0.50
    - CA sdHR, 0.41; 95% CL, 0.31, 0.54

*Edmonds et al, PLoS Med, 2022*

## Clinical and programmatic outcomes of HIV-exposed infants Results and Conclusions



There was marked regional and temporal heterogeneity in clinical and programmatic outcomes, however infant LTFU was high across all regions and time periods

*Edmonds et al, PLoS Med, 2022*



# IeDEA Southern Africa

Research highlights 2022



# Ongoing high prevalence of severe immune suppression among children in South Africa

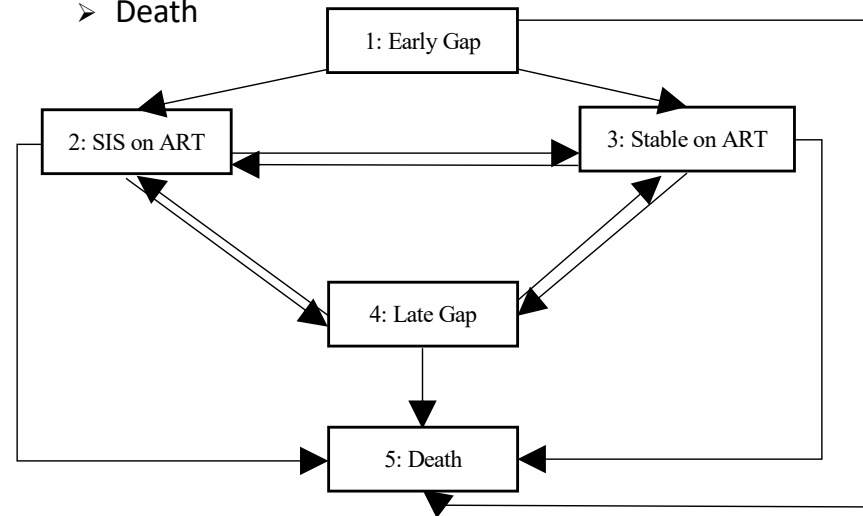
## Background

- Following rapid improvements in HIV programmes, children are now starting antiretroviral therapy (ART) younger and healthier
- Sustained retention and adherence to ART is especially challenging, and it is possible that severe immune suppression (SIS) will be increasingly seen among those on ART
- We describe SIS at ART start and on ART between 2007-2020, using data from 3 leDEA cohorts from South Africa

## Methods

- Inclusion criteria:
  - Children aged <5 years with a CD4 measure at ART start and  $\geq 1$  subsequent measure
  - $\geq 9$  months of follow-up between ART start and database closure (Oct 2018 – Mar 2021)
- A multistate model was used to estimate transition probabilities between 5 states based on CD4 measures after ART start.

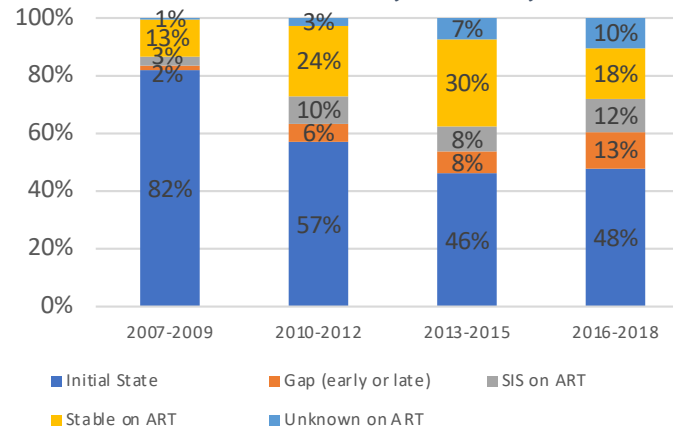
- Defined a Gap in care: >9 months without a recorded visit
- We defined five states:
  - SIS on ART: according to the WHO 2006 definition for SIS
  - Stable on ART: not SIS
  - Early Gap: gap commencing <9 months of ART start
  - Late Gap: gap commencing  $\geq 9$  months on ART
  - Death



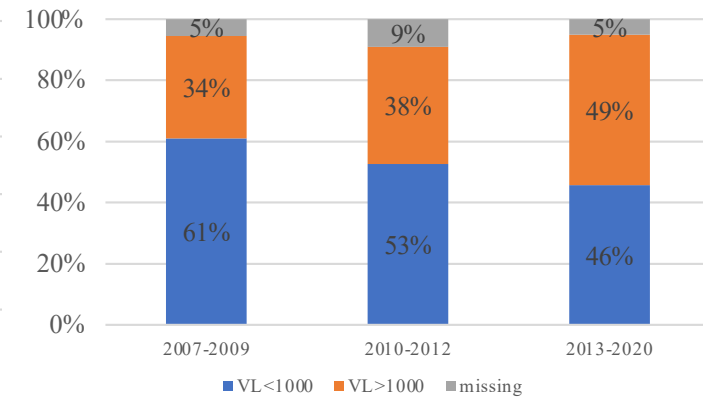
## Results

- Among 2536 children, 70% had SIS at ART start, 36% experienced SIS on ART. An increasing proportion were age <1 year at ART initiation
- Increasingly SIS on ART occurred following a gap, in those with SIS on ART for >1 year and following a period of unknown immune status
- Our multi-state model found:
  - Later year of ART initiation associated with reduced transition from SIS to Stable
  - Infants and those starting ART with SIS more likely to transition from Stable to SIS
  - Viraemia strongly predicted death from both the on ART states

Prior state to SIS on ART by calendar year



Viraemic status at SIS by year of ART start



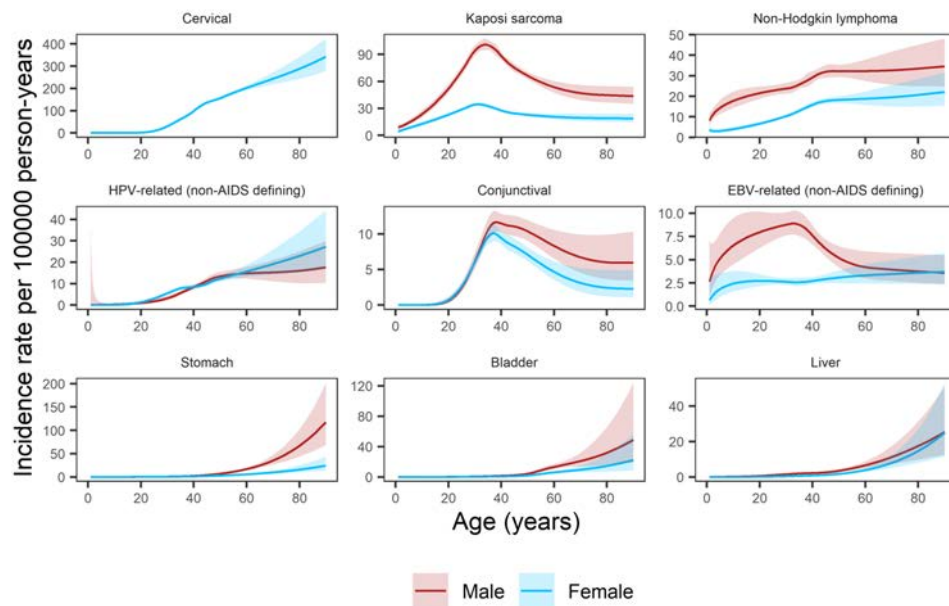
Characteristic	2007-2009	2010-2012	2013-2020	Total	
<b>Total</b>	1114	762	660	2536	
<b>Age at ART start (years)</b>	<b>Median (IQR)</b>	<b>1.27 (0.5-2.7)</b>	<b>1.10 (0.4-2.6)</b>	<b>0.79 (0.2-1.8)</b>	<b>1.10 (0.4-2.4)</b>
0-1	473 (42.5%)	367 (48.2%)	366 (55.5%)	1206 (47.6%)	
<b>Immune status at ART start</b>	<b>Severely Immune Suppressed</b>	<b>805 (72.3%)</b>	<b>509 (66.8%)</b>	<b>448 (67.9%)</b>	<b>1762 (69.5%)</b>
<b>Viraemic during follow-up</b>	565 (50.7%)	419 (55.0%)	378 (57.3%)	1362 (53.7%)	
<b>SIS during follow-up</b>	436 (39.1%)	250 (32.8%)	241 (36.5%)	927 (36.6%)	

## Conclusion

- Increasingly SIS occurred among ART-experienced children. Those starting ART with SIS and during infancy remain especially vulnerable to SIS once on treatment.
- Managing ART in these children may be more complex and reducing AIDS-related mortality further is likely to remain challenging

# Age and Cancer in 5.2 Million People with HIV: the South African HIV Cancer Match Study

**Figure 1:** Incidence rates per 100,000 person-years (solid lines) as a function of age and sex for infection-related cancers. The shaded areas represent 95% confidence intervals.



## Methods

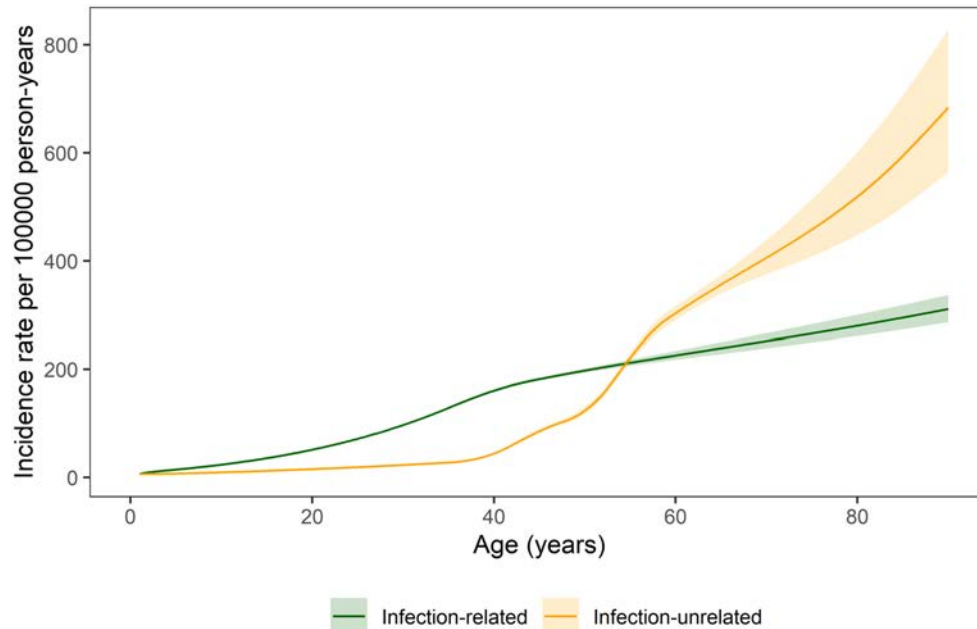
We used data from the South African HIV Cancer Match (SAM) study, a nationwide cohort of people with HIV (PWH) to examine the association between age and cancer risk and estimate age-specific cancer rates in male and female PWH in South Africa.

## Results

The incidence rates of most types of infection-related cancers increased with older age. However, the rates of Kaposi sarcoma and conjunctival cancer peaked in middle-aged people with HIV ([Figure 1](#)).

## Age and Cancer in 5.2 Million People with HIV: the South African HIV Cancer Match Study

**Figure 2:** Incidence rates per 100,000 person-years (solid lines) as a function of age for any infection-related and any infection-unrelated cancers. The shaded areas represent 95% confidence intervals.



The risk of an infection-related cancer remained higher than that of an infection-unrelated cancer until the age of 54 years. Most cancer diagnoses in people with HIV above the age of 54 were infection-unrelated (Figure 2).

### Conclusions

As people with HIV in South Africa become older, prevention and early detection of infection-unrelated cancers will become increasingly important.

Prevention strategies for infection-related cancers remain essential to reduce cancer burden in young and middle-aged people with HIV in South Africa.

# Life-years lost associated with mental illness: a cohort study of beneficiaries of a South African medical insurance scheme

## Background

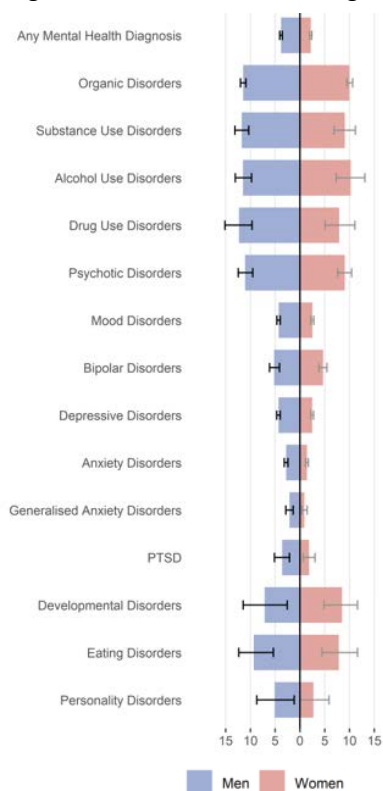
- Mental illness ranks among the top ten leading causes of disease burden in South Africa, with an estimated lifetime prevalence of 30%.
- In high-income countries, studies have shown that people with illnesses have more than double the mortality rates compared to the general population.
- However, evidence of this excess mortality from low- and middle- income settings is scarce.

## Methods

- We analysed the reimbursement claims and vital registration data of beneficiaries from a large South African medical insurance scheme. We used ICD-10 diagnoses (F00-F99) as indicators of mental illness.
- We estimated the life-years lost (LYL) associated with various types of mental illnesses. The LYL measures the average difference in life expectancy among people with mental health diagnoses starting at the age of the diagnosis, compared to people of the same age without a mental health diagnosis.
- We computed LYL for men and women separately, and disaggregated the LYL by cause of death (natural, unnatural, unknown).

# Life-years lost associated with mental illness: a cohort study of beneficiaries of a South African medical insurance scheme

**Figure:** Life-years lost among people who received mental health diagnoses compared with the people of the same sex and age without a mental health diagnosis.



## Results

- Of 1,070,183 beneficiaries, 282,926 (26.4%) received a mental health diagnosis (men: 22.1%, women: 30.5%). The most common types of disorders were anxiety disorders (16.6%) and mood disorders (14.6%).
- The LYL associated with any disorder was 3.83 (95% CI 3.58-4.10) in men and 2.19 (95% CI 1.97-2.41) in women. The LYL varied by type of disorder (**Figure**).
- In men, 3.42 (95% CI 3.17-3.70) of the 3.83 LYL were attributable to natural causes and 0.45 (95% CI 0.32-0.59) to unnatural causes. In women, 1.94 (95% CI 1.73-2.15) of the 2.19 LYL were attributable to natural causes and 0.22 (95% CI 0.15-0.28) to unnatural causes.

## Conclusion

- Our study demonstrates a considerable burden of premature death among people with mental illness, primarily attributable to death from natural causes.
- People diagnosed with eating, developmental, psychotic, substance use, and organic mental disorders are at the highest risk of premature death.
- A similar study combining data from NA-ACCORD and from a South African HIV care program is in the works (SA263).

# Diagnosis and treatment of opioid-related disorders in a South African private sector medical insurance scheme: a cohort study

## Background

- The use of opioids is increasing globally, but data from low- and middle-income countries on opioid related mental and behavioural disorders are scarce.
- We examined the incidence of opioid-related disorders, opioid agonist use, and excess mortality among persons with opioid-related disorders in South Africa's private healthcare sector

## Methods

We analysed longitudinal data of beneficiaries ( $\geq 11$  years) of a South African medical insurance scheme using reimbursement claims from Jan 1, 2011, to Jul 1, 2020. Beneficiaries were classified as having an opioid-related disorder if they received an opioid agonist (buprenorphine or methadone) or an ICD-10 diagnosis for harmful opioid use (F11.1), opioid dependence or withdrawal (F11.2-4), or an unspecified or other opioid-related disorder (F11.0, F11.5-9).

We calculated adjusted hazard ratios (aHR) for factors associated with opioid-related disorders, estimated the cumulative incidence of opioid agonist use after receiving an ICD-10 diagnosis for opioid dependence or withdrawal, and examined excess mortality among beneficiaries with opioid-related disorders.

## Results

Of the 1,251,458 beneficiaries, 1286 (0.1%) had opioid-related disorders. Men, young adults in their twenties, and beneficiaries with co-morbid mental health or other substance use disorders were at increased risk of opioid-related disorders. The incidence of opioid-related disorders increased by 12% (95% CI 9%-15%) per year. The cumulative incidence of opioid agonist use was 18.0% (95% CI 14.0-22.4) 3 years after diagnosis. Opioid-related disorders were associated with an increased risk of mortality (aHR 2.28, 95% CI 1.84-2.82). Opioid-related disorders were associated with a 7.8-year shorter life expectancy

Table 1: Characteristics of beneficiaries with and without opioid-related disorder.

Participant characteristics	Persons with opioid related disorders N=1,286 (0.1)	Persons without opioid related disorders N=1,250,172 (99.9)	Total N=1,251,458 (100.0)
Male	810 (63.0)	601,610 (48.1)	602,420 (48.1)
Female	476 (37.0)	648,562 (51.9)	649,038 (51.9)
Median age	32 (21-47)	33 (21-47)	33 (21-47)
Mental health diagnosis	894 (69.5)	311,003 (24.9)	311,897 (24.9)
Substance use disorder diagnosis (excl. ICD-10 F11)	404 (31.4)	7,456 (0.6)	7,860 (0.6)
Infectious diseases	151 (11.7)	89,429 (7.2)	89,580 (7.2)

Tlali M et al. (2022). *The International Journal on Drug Policy*, 109, S. 103853. <http://doi.org/10.1016/j.drugpo.2022.103853>

Table 2: Hazard ratios for mortality in persons with opioid-related disorders.

Analyses	Unadjusted HR (95% CI)	Adjusted analyses		
		Model 1	Model 2	Model 3
		aHR (95% CI)	aHR (95% CI)	aHR (95% CI)
Opioid-related disorders	2.13 (1.72-2.63)	2.28 (1.84-2.82)	1.67 (1.35-2.06)	
Harmful use	2.29 (1.19-4.39)			2.45 (1.27-4.74)
Dependence or withdrawal	1.60 (1.06-2.41)			2.44 (1.60-3.72)
Unspecified or other F11 code	2.38 (1.58-3.59)			1.35 (0.89-2.03)
Opioid agonist use	2.81 (2.09-3.77)			3.06 (2.26-4.15)

Table 3: Excess life-years lost associated with opioid-related disorders for natural, unnatural and all causes of death.

Sex	Excess life-years lost (95% confidence intervals)		
	All-cause	Natural deaths	Unnatural deaths
Men	7.81 (3.20-12.25)	8.38 (3.84-12.72)	-0.57 (-1.54-1.56)
Women	7.83 (3.14-11.90)	7.52 (2.64-11.90)	0.31 (-0.33-1.62)

## Conclusion

The incidence of people diagnosed with or treated for an opioid-related disorder in the private sector is increasing rapidly. People with opioid-related disorders are a vulnerable population with substantial psychiatric comorbidity who often die prematurely. Evidence-based management of opioid-related disorders is urgently needed to improve the health outcomes of people with opioid-related disorders.





# DTG Switch: Virologic failure after routine switching to DTG-based first line ART in Malawi and Zambia

## Background

WHO recommends Dolutegravir (DTG) as part of first-line antiretroviral therapy (ART).

Concern: *Development of DTG resistance*

- Existing NRTI mutations could increase the risk of selection for DTG resistance
- Ideally, only suppressed patients should be switched – however, routine viral load (VL) monitoring often not available

## Methods

Compare risk of virologic failure (VF; VL>400 c/ml) at 1 year after switching to DTG-based regimen, between participants with and without VF at baseline (time of switch).

- Prospective cohort: Participants (18+y, first-line ART) recruited at time of routine switch to DTG\*.
- Two ART programs with different switching policies:

ART program	Switching to DTG *	Enrolment period
Malawi (Lighthouse Trust)	Irrespective of VL	2019-2020
Zambia (CIDRZ Lusaka)	Only if last VL<1000 c/mL	2020-2021

\* Eligibility for switching to a DTG based regimen follows the national guidelines for the clinical management of HIV

# DTG Switch: Virologic failure after routine switching to DTG-based first line ART in Malawi and Zambia

## Results

**Table:** Virologic outcomes of PLWH at 1 year after routine switching to DTG-based first-line ART

	VL available at 1Y		VL missing at 1Y <sup>b</sup>	Total N
	VL < 400 copies/ml N	VL ≥ 400 copies/ml N (%) <sup>a</sup>	N (%) <sup>b</sup>	
Malawi				1388
VL < 400 at BL	1036	29 (2.7%)	247 (18.8%)	1312
VL ≥ 400 at BL	43	13 (23.2%)	20 (26.3%)	76
<b>RR (95% CI)</b>	<b>8.6 (4.7 to 15.5)</b>			
P	<0.0001			
Zambia				1411
VL < 400 at BL	1258	24 (1.9%)	87 (6.4%)	1369
VL ≥ 400 at BL	38	1 (2.6%)	3 (7.1%)	42
<b>RR (95% CI)</b>	<b>1.4 (0.19 to 9.9)</b>			
P	0.75			

## Conclusion

The Malawi data indicates that PLWH **switching with unsuppressed VL** have a **substantially higher risk of VF** at 1 year than PLWH with suppressed VL at the time of the switch.

The Zambian policy of only switching patients who were virologically suppressed at the last routine VL **may reduce this risk.**

VL, viral load; BL, baseline; 1Y, 1-year follow-up; RR, relative risk; CI, confidence interval; P, P-value  
a; denominator is the number of patients with VL measurement at 1Y.  
b; denominator is the number of patients with VL measurement at BL (Total N).

# West Africa - leDEA



Research highlights 2022

## Growth and CD4 patterns of adolescents living with perinatally acquired HIV worldwide, a CIPHER cohort collaboration analysis

*Jesson et al. J Int AIDS Soc. 2022 Mar;25(3):e25871*

**Objective:** To describe the growth evolution and the immune response of adolescents with perinatal HIV (APH) across adolescence

**Study population:** APH on ART before 10 years of age, with available data on height/CD4, living in sub-Saharan Africa, North America and Europe, Asia-Pacific and South and Central America

**Statistical methods:** Linear mixed models for Height-for-Age Z-score and CD4 count evolution between 10 and 19 years of age.

Growth analysis:  
N = 20 939

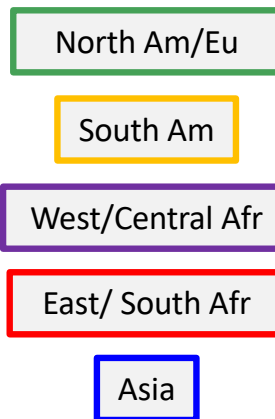
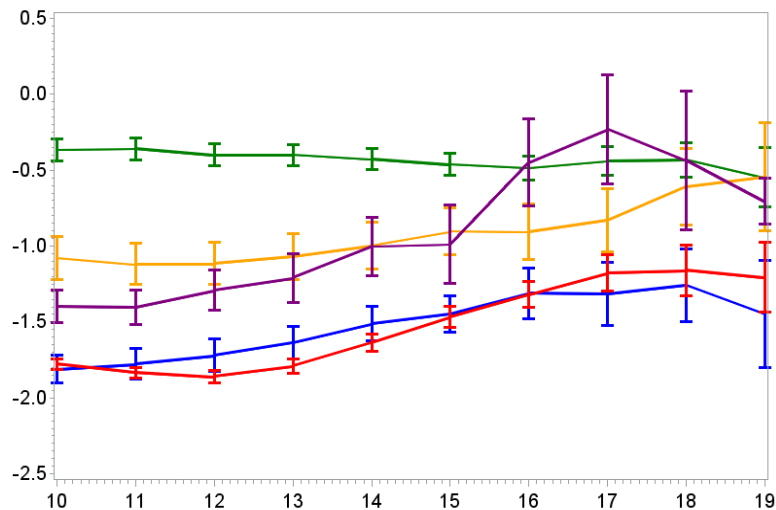
CD4 analysis:  
N= 19 557

50% Females

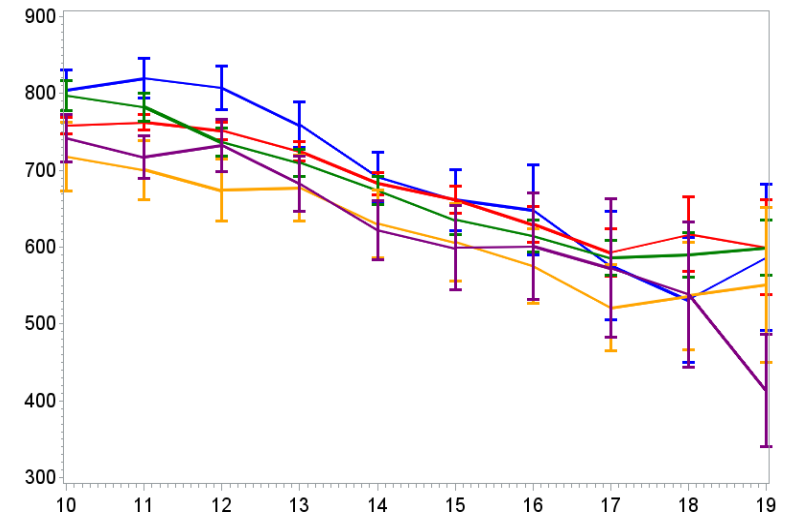
Variables (median [IQR] or %)	Total	North Am and Europe	South and Central Am	South and SE Asia	West and Central Afr	East and Southern Afr
Age at ART initiation (years)	6.9 [4.4-8.5]	2.4 [0.6-5.7]	4.3 [2.0-6.7]	5.5 [3.4-7.4]	7.5 [5.7-8.8]	7.5 [5.7-8.8]
Stunting at 10y	28%	6%	17%	39%	22%	33%
CD4 count (cell/mL) at 10y†	731 [491-998]	750 [522-1010]	683 [438-960]	779 [557-1014]	678 [452-950]	722 [480-1000]

## Growth and CD4 patterns of adolescents living with perinatally acquired HIV worldwide, a CIPHER cohort collaboration analysis

Height-for-age Z-scores, females



CD4 count, females



Growth patterns differed by sex and region. Higher HAZ overall for high-income regions, may be related to earlier access to care and lower malnutrition risk.

CD4 patterns were not sex- or region-specific. A small decline was observed between 10 and 19 years of age, and needs to be further investigated

Late ART initiation, with severe stunting and low CD4 count at age 10 can lead to high prevalence of stunting and immunodeficiency during adolescence, which are difficult to reverse

# WEIGHT GAIN FOLLOWING SWITCH TO DOLUTEGRAVIR AMONG ADULT HIV COHORTS IN WEST AFRICA

*Tiendrebeogo et al, CROI 2023*

## □ Background

- ❖ Most countries have transitioned to Dolutegravir (DTG)-based regimens as first-line antiretroviral therapy
- ❖ Documented adverse metabolic effects from developed countries contrast with limited information from resource-limited settings

□ **Objective:** To explore changes in body weight before and after switch to a DTG-based regimen and assess the association between switch to DTG and significant weight gain ( $\geq 10\%$  increase) over a 12-month period in adults living with HIV (ALHIV) on ART in West Africa

## □ Methods

- ❖ **Main analysis:** ALHIV with documented switch to DTG-based ART during 2019-2021, in care  $\geq 36$  months at the date of switch with  $\geq 1$  weight measure during the 24-months pre-switch & 12-months post-switch period. Weight change was estimated with a linear mixed model within P1 & P2, stratified by body mass index (BMI) class
- ❖ **Secondary analysis:** Multivariate logistic regression with random effect were used to compare significant weight gain ( $\geq 10\%$ ) in ALHIV on ART, prior and after the date of DTG introduction (site level dependent) between ALHIV who switched to DTG and those who did not at the date of database closure (control group).

## Weight gain following switch to dolutegravir – Results

### □ Main analysis:

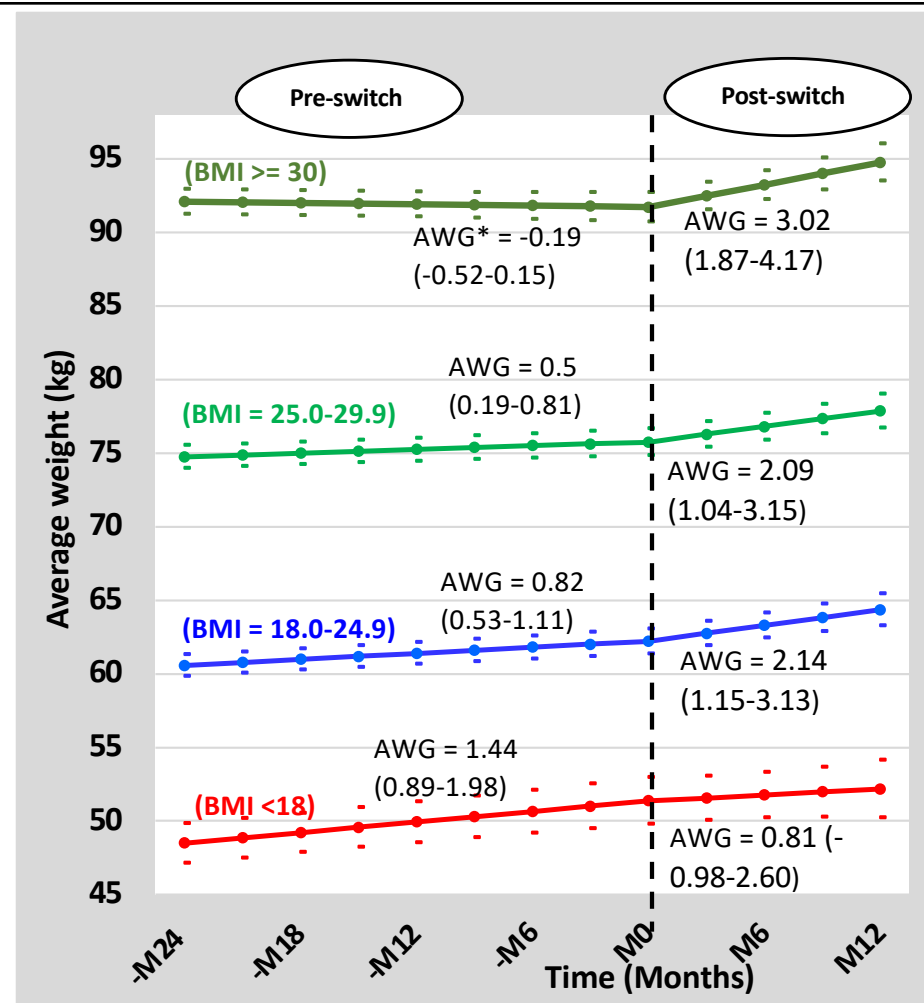
- ❖ 5,294 ALHIV (27% men) included
- ❖ Mainly switches from NNRTIs (83%) and PI-based (15%) ART
- ❖ Average Weight Gain was not significant in underweight patients, increased significantly in normal weight, overweight and obese ALHIV during post switch period

### □ Secondary analysis

- ❖ 3,458 ALHIV (1795 switchers & 1664 controls) included
- ❖ Adjusted for sex, age and baseline ART regimen, switching to DTG was associated with weight gain  $\geq 10\%$  (aOR=1.77 95%CI=[1.38; 2.26])

### Conclusions

- ❖ Twelve-month DTG exposure was associated with a significant weight gain, particularly among those with a high BMI.
- ❖ Close monitoring of weight and metabolic profile should be supported to characterize long-term health impact of DTG.
- ❖ Alternative ART regimen may be considered in individual with or at-risk for cardiometabolic disorders



\* AWG (Average Weight Gain) unit = kg/year (95%CI)  
Final model was adjusted on sex, age, BMI at month 24 pre-switch and treatment line (1st,  $\geq 2$ nd line)

## Sexual and reproductive health of adolescents living with HIV in pediatric care programs in Abidjan : Structured provision of care and perceptions of health care workers in 2019.

*Revegue MHDT et al. Rev Epidemiol Sante Publique. 2022 Aug;70(4):163-176.*

**Objective:** To assess the offer in terms of sexual and reproductive health (SRH) services in HIV pediatric care programs in Côte d'Ivoire for adolescents living with HIV (ALHIV)

**Mixed methods, study conducted in 2019 in 3 clinical care centers:**

**1/** Quantitative inventory of SRH services available within the programs, with assessment of their adaptation and integration into HIV care services, by direct observation and discussion with professionals

Main results of the inventory:

- **Not enough SRH professionals:** Each center followed between 114 to 309 ALHIV in 2019. One to two midwives were available in each center, one center had a gynecologist.
- **SRH needs were insufficiently covered:** Condom distribution was occasional, focus group on SRH prevention was conducted monthly/quarterly with psychologists. Hormonal contraception was not available.
- **Barriers for SRH-based care:** ALHIV<18 years needed the consent of a parent/tutor to have access to benefit from care.



## Sexual and reproductive health of adolescents living with HIV in pediatric care programs in Abidjan : Structured provision of care and perceptions of health care workers in 2019.

2/ Qualitative, semi-structured interviews, with 14 healthcare professionals (physicians, nurses, midwife, psychologist, counsellor) about their perceptions of SRH needs and care for ALHIV

### Main results of the interviews with healthcare professionals:

- Several **socio-cultural and organizational barriers**, according to different actors
  - ALHIV: feel they are too young, fear/shame to disclose sexual activity
  - Parents:, highly taboo subject, negative reaction in case of SRH information delivered to ALHIV
  - Healthcare professionals: have personal opinions and lack of training on SRH questions, several against contraception for female adolescents
  - Structural: overworked professionals, no dedicated spaces to develop activities around SRH prevention and counselling
- Perceptions that **ALHIV frequently engaged in risky unprotected sexual behaviors**
- **Levers of action to optimize SRH services:**
  - Promote safe and timely HIV serostatus disclosure to ALHIV (<12 years)
  - Offer specific training of healthcare professionals, support parents with focus groups
  - Adapt SRH counseling & services according to the age of ALHIV

## Barriers to Early Diagnosis of Cervical Cancer in Côte d'Ivoire : A mixed-method study

*Plaisy et al, BMC Women's Health (accepted)*

### Context & Aim:

- In many developing countries, Cervical cancer (CC) is usually associated with poor survival related to an advanced disease at diagnosis
- In a context of limited access to screening services, there is little information about factors associated with advanced CC stages
- **The study's aim was to determine barriers to early diagnosis of CC in Côte d'Ivoire**

### Methods:

- **Design:** Mixed cross-sectional study (quantitative and qualitative)
- **Study population:** Women diagnosed with CC between July 2018 and June 2019 through the cancer registry of Abidjan project
- **In-depth semi-structured interviews** among a subset of these women and six healthcare providers to further document barriers to early diagnosis of CC
- **Data Analyses:** Univariable and multivariable logistic regression (quantitative data) ; thematic analysis technique triangulated with quantitative data (qualitative data)

## Barriers to Early Diagnosis of Cervical Cancer in Côte d'Ivoire : A mixed-method study

### Quantitative findings

Factors associated with advanced cervical cancer, Côte d'Ivoire, 2019, (n=95)

	Multivariable analysis	
	OR (95% CI)	P value
<b>HIV-uninfected status vs HIV-infected status</b>	<b>5.4 [1.6 – 17.7]</b>	<b>0.006</b>
<b>No health insurance vs having health Insurance)</b>	<b>3.1[2.0 – 85.5]</b>	<b>0.007</b>
No prior knowledge about cervical cancer vs (prior knowledge)	2.1 [0.7 – 6.3]	0.16
Direct attendance at specialized facilities vs referenced	7.1 [1.1 – 44.0]	0.01

### Qualitative findings

- Lack of patient information and awareness about CC and screening by healthcare providers (HP)
- Inadequate knowledge of the signs and symptoms of CC among HP
- Inadequate awareness and screening campaigns

### Conclusion

- Aside an increased access to efficient CC screening services in developing settings, access to health insurance and integrated care program appears to be a key determinant of early diagnosis of CC

## Factors associated with verbal fluency in older adults living with HIV in West Africa: A longitudinal study

*Bernard C, et al. Trop Med Int Health, [ahead of print]*

- **Objective:**

To evaluate the factors associated with verbal fluency\* in older people living with HIV (PLHIV) in West Africa

- **Methods**

- Longitudinal study
- Inclusion sites: one in Senegal and two in Cote d'Ivoire
- PLVIH aged  $\geq 60$  and on ART  $\geq 6$  months
- Cognitive evaluation at baseline and 2 years later (Isaacs Set Test – 60 sec)
- Associated factors: using multivariate linear regression models

\*a cognitive function which *declines in aging and HIV infection and is related to lower quality of life*

# Factors associated with verbal fluency in older adults living with HIV in West Africa: A longitudinal study

## • Results

▪ At baseline: 97 PLHIV      Median age: 64  
Female: 45.4%    Low educational level: 54.6%  
Hypertension: 49.5%

▪ 2-year follow-up: 41 PLHIV

Performance median annual change: -0,9 (IQR: -2,7; 1,8)

## • Conclusions

- Main factors: usual socio-demographic data
- Factors specifically associated with decline: marital status and hypertension
- No association with HIV-related factors

→ Factors associated with verbal fluency decline were remediable in older West African PLHIV  
→ Interventions on cardio-metabolic health are highly recommended to prevent cognitive disorders in PLHIV

### 1. Factors associated with performance at baseline

	$\beta$	F	p-value
Age <sup>a</sup>	-0.8	8.5	0.005
Low educational level	7.0	10.1	0.002
Female	-8.3	14.0	0.0003

### 2. Factors associated with annual change

	$\beta$	F	p-value
Age <sup>a</sup>	0.3	4.3	0.05
Low educational level			
Female	2.0	4.3	0.05
Living alone	-2.2	4.4	0.04
Hypertension	-2.0	5.6	0.03



**NA-ACCORD**

North American

AIDS Cohort Collaboration on Research and Design

## Association of Race and Ethnicity With Initial Prescription of Antiretroviral Therapy Among People With HIV in the US

Zalla LC\*, et al. JAMA. 2023;329(1):52-62. doi:10.1001/jama.2022.23617

CROI 2023 poster #876

**Background:** INSTIs were approved for use in 2007 in the U.S. and were initially used for PWH who were unable to suppress HIV RNA using other regimens. The regimen has been demonstrated to be effective with minimal side effects.

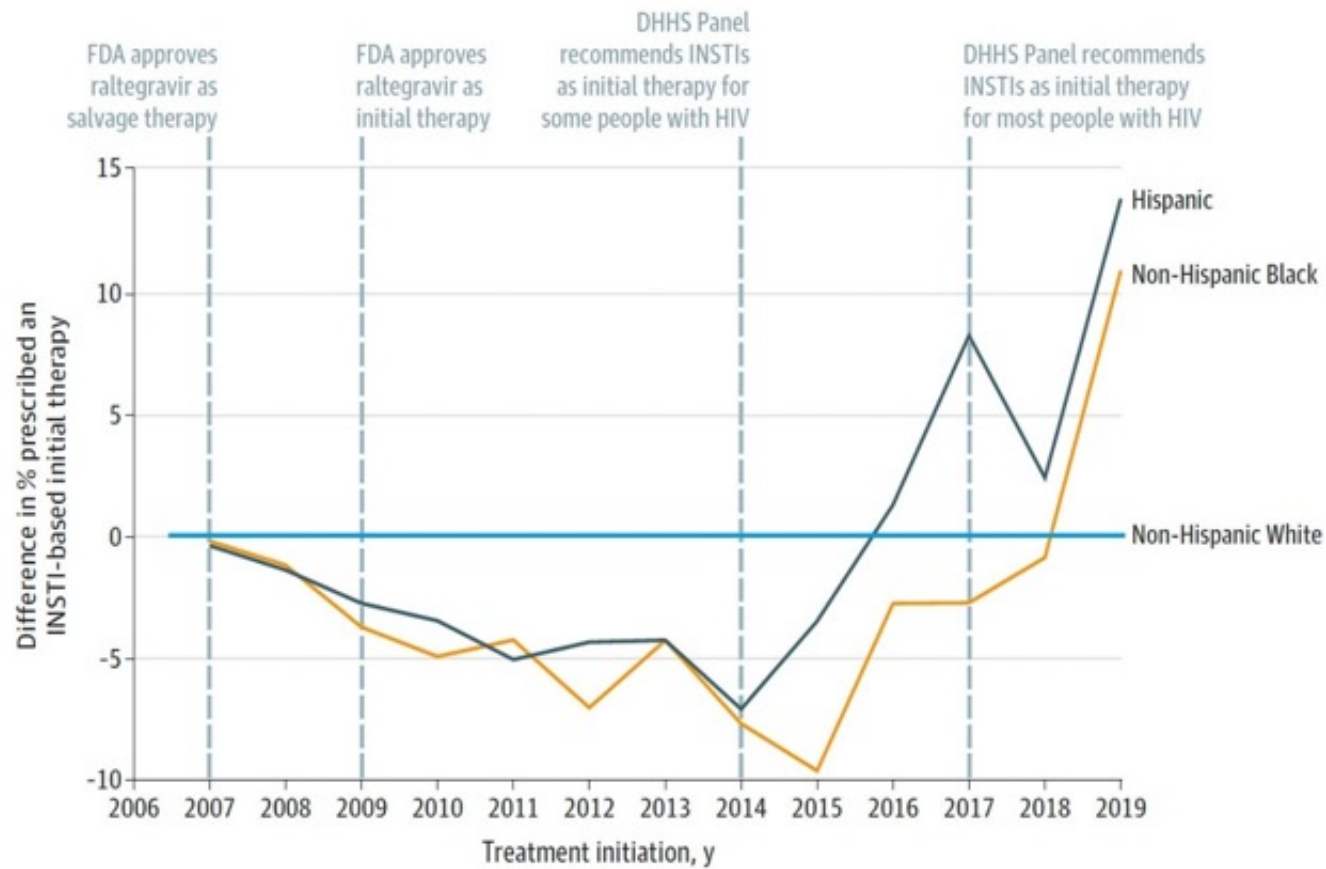
**Methods:** Using data from the NA-ACCORD, we estimated the difference in percent of Black and Hispanic patients (relative to White patients) who were [prescribed an INSTI-containing initial ART regimen](#) by year of ART initiation

**Results:** Although data demonstrated INSTIs were at least as effective as other regimens and had fewer side effects, we found that [Black and Hispanic individuals initiating antiretroviral therapy were less likely to be prescribed INSTIs than their White counterparts from 2007 to 2014](#) (Black vs. White absolute difference=-5% [95% CI -7, -4]; and Hispanic vs. White absolute difference=-5% [95% CI -7, -3]). However, the [racial and ethnicity disparities narrowed after INSTIs became guideline recommended in 2014](#). By 2018, 90% of Black patients (95% CI: 88%, 92%), 93% of Hispanic patients (95% CI: 89%, 97%), and 91% of White patients (95% CI: 87%, 94%) starting antiretroviral therapy were prescribed INSTIs. (see Figure depicted on next page).

**Conclusions:** [New treatments can exacerbate health disparities if only those with power and privilege are able to access the new treatments.](#) The findings demonstrate how guidelines can narrow health disparities.

*\*Zalla LC completed this work as part of her doctoral thesis (mentor: Jessie Edwards, UNC)*

**Figure:** Difference in Percent of Black and Hispanic Patient Relative to White Patient Prescribed an INSTI-Containing Initial ART Regimen by year at Treatment Initiation, 2007-2019





## The prevalence of mental health disorders in people with HIV and the effects on the HIV care continuum, 2008-2018

Lang R\*, et al. AIDS . 2023 Feb 1;37(2):259-269. doi: 10.1097/QAD.0000000000003420.

**Background:** At the introduction of ART, estimates of 12-month prevalence of MHDs among PWH in the U.S. found nearly half of PWH screened positive for one or more of: major depression, dysthymia, generalized anxiety disorder, or panic attacks. Studies have reported the prevalence of major depression, anxiety, bipolar disorder (BD), and schizophrenia are more common among PWH compared to the general population.

**Methods:** We described the prevalence of diagnosed depression, anxiety, bipolar disorder, and schizophrenia in PWH in the NA-ACCORD, and the differences in HIV care continuum outcomes in those with and without mental health disorders (MHDs) from 2008-2018.

**Findings:** The prevalence of MHDs was high among the 122,896 PWH in the NA-ACCORD; 67,643 (55.1%) were diagnosed with one or more mental health disorders (39% with depressive disorders, 28% with anxiety disorders, 10% with bipolar disorder, and 5% with schizophrenia) and 24% were mental health multimorbid. Those who were mental health multimorbidity had a 2% higher prevalence of retention in care (aPR=1.02 [95% CI 1.02, 1.02]). (see Figure on next slide). Those with bipolar disorder or mental health multimorbidity ( $\geq 2$  MHDs) were less likely to be virally suppressed than those without these conditions (aPR=0.99 [95% CI 0.98, 0.99] comparing those with vs. without bipolar disorder; aPR=0.99 [95% CI 0.99, 1.00] comparing those with vs. without mental health multimorbidity).

**Conclusions:** Although the definitions of depression, anxiety, bipolar disorder, and schizophrenia relied on clinical diagnoses, mental health treatment information and hospitalization are also available to assess severity. Measuring mental health disorders bolsters the NA-ACCORD's research platform for mental health outcomes and the role of mental health in aging with HIV, the HIV care continuum, and other questions relevant to the modern treatment era. Many NA-ACCORD HIV clinical cohorts offer on-site mental healthcare; the findings suggest low barriers to mental health care within HIV clinics may be important for retention in care.

*\*Lang R completed this work as post-doctoral fellows (mentor: Keri Althoff, JHU)*



## CD4/CD8 Ratio and Cancer Risk Among Adults With HIV

Castilho JL, et. al. J Natl Cancer Inst. 2022 Jun 13;114(6):854-862. doi: 10.1093/jnci/djac053.

**Background:** Independent of CD4 cell count, a low CD4/CD8 ratio in PWH is associated with deleterious immune senescence, activation, and inflammation, which may contribute to carcinogenesis and excess cancer risk.

**Methods:** We examined [whether low CD4/CD8 ratios predicted cancer](#) among PWH in the U.S. and Canada using data from the NA-ACCORD. There were 5628 incident cancers among 83,893 PWH. These included lung cancer (n = 755), Kaposi sarcoma (n = 501), non-Hodgkin lymphoma (n = 497), and anal cancer (n = 439).

**Findings:** The overall median 6-month lagged CD4/CD8 ratio was 0.52 (interquartile range = 0.30-0.82). Compared with a 6-month lagged CD4/CD8 of 0.80, [a CD4/CD8 of 0.30 was associated with increased risk of any incident cancer](#) (adjusted hazard ratio = 1.24 [95% confidence interval = 1.14 to 1.35]). The [CD4/CD8 ratio was also inversely associated with non-Hodgkin lymphoma, Kaposi sarcoma, lung cancer, anal cancer, and colorectal cancer in adjusted analyses](#) (all 2-sided P < .05). Results were similar using 12-, 18-, and 24-month lagged CD4/CD8 values. (see Figure on next slide)

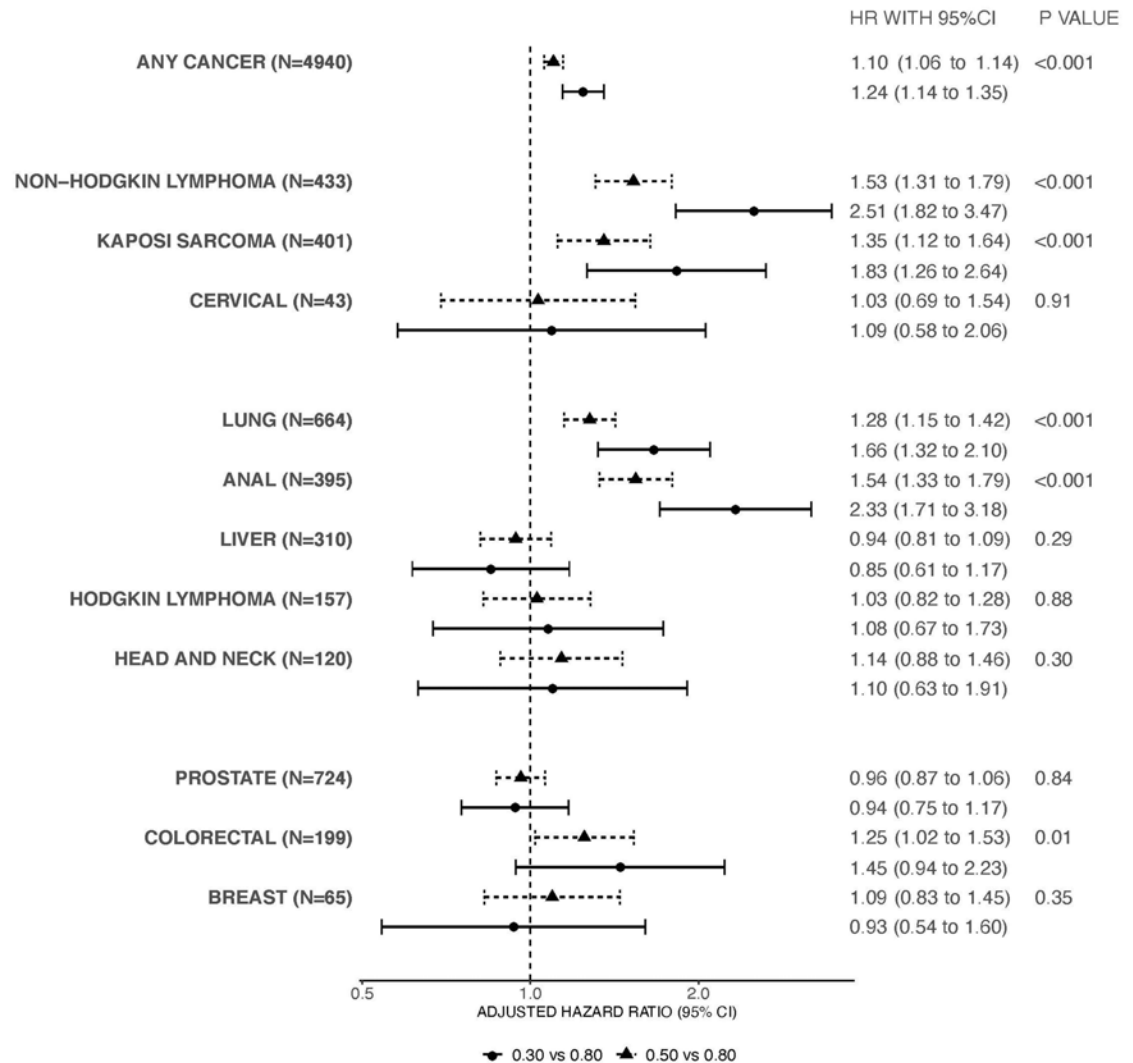
**Conclusions:** A low [CD4/CD8 ratio up to 24 months before cancer diagnosis was independently associated with increased cancer risk in PWH](#) and may serve as a clinical biomarker.

**Figure:** Adjusted hazard ratios (HR) and 95% confidence interval (CI) for cancer risk comparing the 6-month lagged, time-varying CD4/CD8 ratio values.

*Circles represent the adjusted hazard ratio comparing: CD4/CD8 value of 0.30 vs 0.80*

*Triangles represent the adjusted hazard ratio comparing: CD4/CD8 value of 0.50 vs 0.80*

*The error bars represent the 95% confidence intervals. Wald statistic was used to calculate P values (2-sided)*

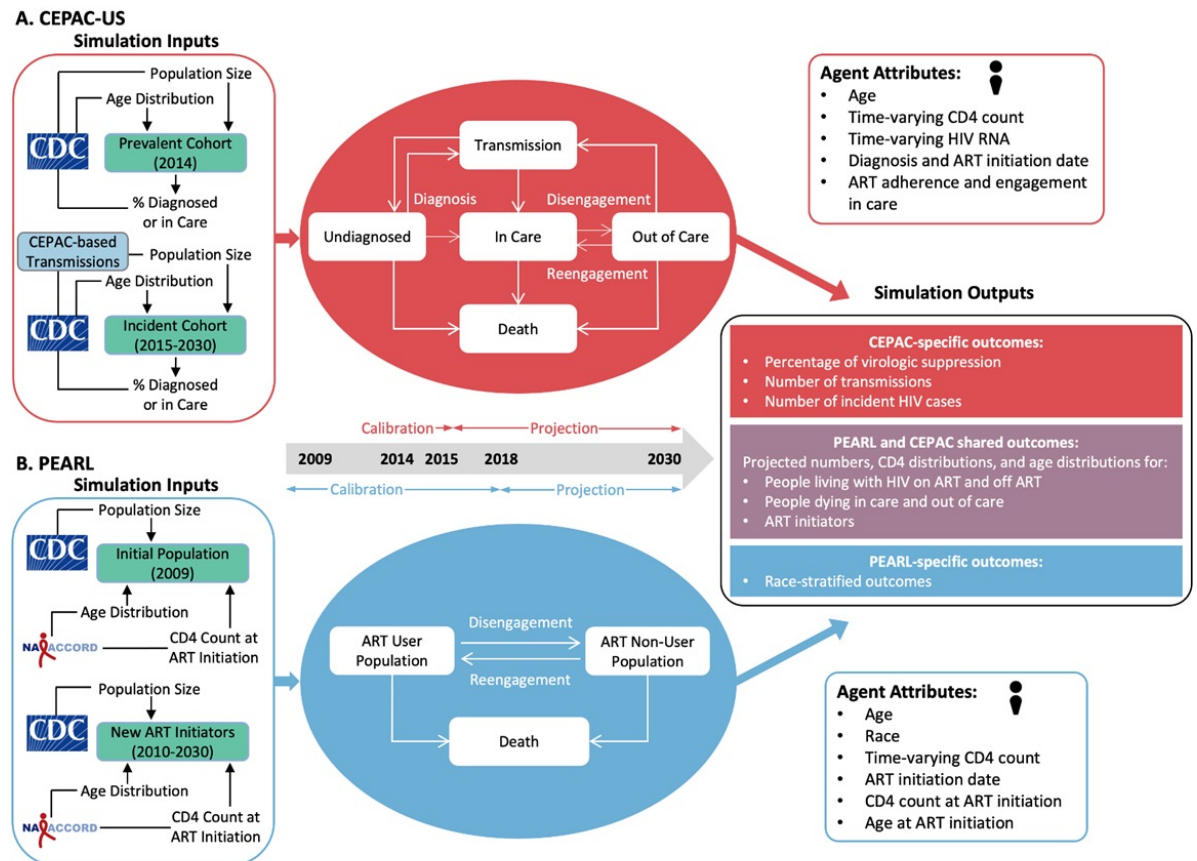


# The projected number of men who have sex with men with HIV in the US: comparing the PEARL and CEPAC-US models

Hyle EP, et al. J Infect Dis. 2023;227(3):412-422.

**Background:** Men who have sex with men (MSM) on antiretroviral therapy (ART) are at risk for multimorbidity as life expectancy increases. **Simulation models** can project population sizes and age distributions to assist with health policy planning.

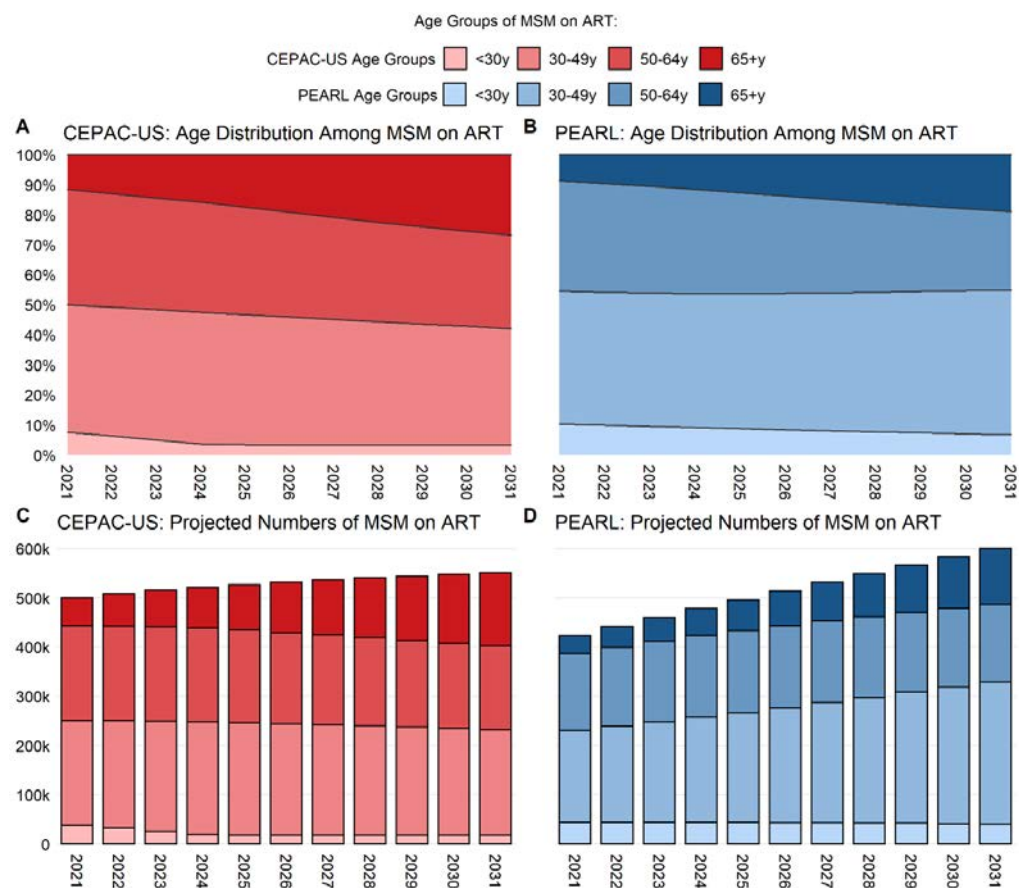
**Methods:** We populated the CEPAC-US model with CDC data to project the HIV epidemic among MSM in the United States. The PEARL model was predominantly informed by NA-ACCORD data (2009-2017). We compared projected population sizes and age distributions of MSM receiving ART (2021-2031) and investigated how parameters and assumptions affected results.



**Results:** We projected an aging and increasing population of MSM on ART: CEPAC-US, mean age 48.6 (SD 13.7) years in 2021 versus 53.9 (SD 15.0) years in 2031; PEARL, 46.7 (SD 13.2) years versus 49.2 (SD 14.6) years. We projected 548,800 MSM on ART (147,020 ≥65 years) in 2031 (CEPAC-US) and 599 410 (113,400 ≥65 years) (PEARL). Compared with PEARL, CEPAC-US projected a smaller population of MSM on ART by 2031 and a slower increase in population size, driven by higher estimates of disengagement in care and mortality.

**Conclusions:** Findings from two structurally distinct microsimulation models suggest that the MSM population receiving ART in the United States will increase and age over the next decade. Subgroup-specific data regarding engagement in care and mortality can improve projections and inform health care policy planning.

**Figure:** The projected age distribution, age, and numbers of MSM on ART from the CEPAC-US and PEARL models (2021-2031).



# Severe Illness after post-vaccination COVID-19 breakthrough by HIV status in the US

Lang R\*, Humes E et. al. for the Corona-Infectious-Virus Epidemiology Team (CIVETs) of the NA-ACCORD of IeDEA doi: <https://doi.org/10.1001/jamanetworkopen.2022.36397>

**Importance:** Understanding the severity of postvaccination SARS-CoV-2 (ie, COVID-19) breakthrough illness among people with HIV (PWH) can inform vaccine guidelines and risk-reduction recommendations. The objective of our study was to [estimate the rate and risk of severe breakthrough illness among vaccinated PWH and people without HIV \(PWoH\) who experience a breakthrough infection.](#)

**Design, setting, and participants:** In this cohort study, the Corona-Infectious-Virus Epidemiology Team (CIVET-II) collaboration included adults (aged  $\geq 18$  years) with HIV who were receiving care and were fully vaccinated by June 30, 2021, along with PWoH matched according to date fully vaccinated, age group, race, ethnicity, and sex from [4 US integrated health systems and academic centers.](#) Those with postvaccination COVID-19 breakthrough before December 31, 2021, were eligible.

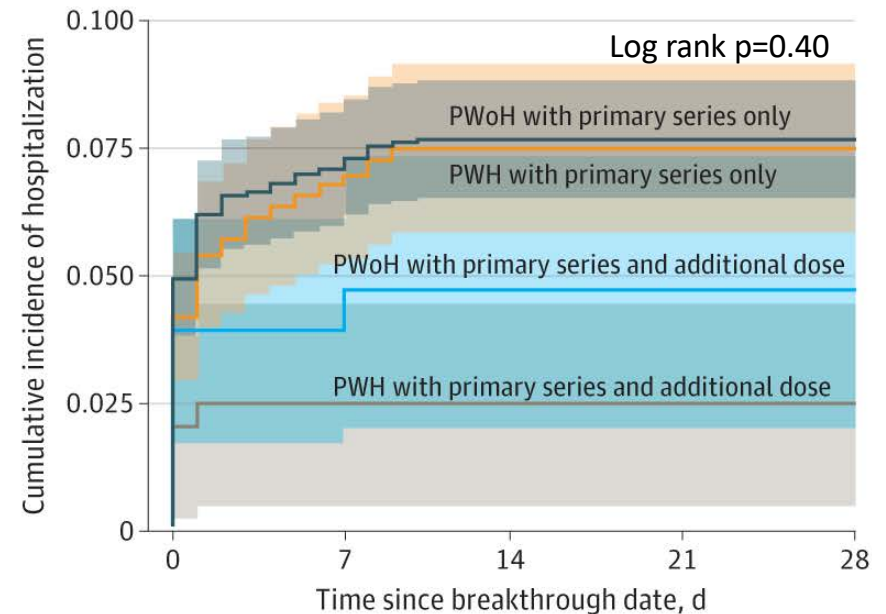
**Outcome:** [Severe COVID-19 breakthrough illness](#), defined as hospitalization within 28 days after a breakthrough SARS-CoV-2 infection with a primary or secondary COVID-19 discharge diagnosis

*\*Lang R completed this work as post-doctoral fellows (mentor: Keri Althoff, JHU)*

**Results:** Among 3649 patients with breakthrough COVID-19 (1241 PWH and 2408 PWOH), most were aged 55 years or older (2182 patients [59.8%]) and male (3244 patients [88.9%]). The cumulative incidence of severe illness in the first 28 days was low and comparable between PWOH and PWH (7.3% vs 6.7%; risk difference, -0.67%; 95% CI, -2.58% to 1.23%). The risk of severe breakthrough illness was 59% higher in PWH with CD4 cell counts less than 350 cells/ $\mu$ L compared with PWOH (aHR, 1.59; 95% CI, 0.99 to 2.46;  $P = .049$ , Table). Among 249 hospitalized patients, 24 (9.6%) were mechanically ventilated and 20 (8.0%) died, with no difference by HIV status.

**Conclusions:** In this cohort study, the risk of severe COVID-19 breakthrough illness within 28 days of a breakthrough infection was low among vaccinated PWH and PWOH. PWH with moderate or severe immune suppression had a higher risk of severe breakthrough infection and should be included in groups prioritized for additional vaccine doses and risk-reduction strategies.

**Figure:** Cumulative Incidence of Severe COVID-19 Breakthrough Illness by HIV Status and vaccine doses



**Table:** Relative risk of severe illness after breakthrough infection

	Crude Hazard Ratio	Adjusted Hazard Ratio
PWOH	Ref	Ref
PWH and CD4 <350	<b>2.00 (1.26, 3.02)</b>	<b>1.59 (0.99, 2.46)*</b>
PWH and CD4 $\geq$ 350	<b>0.70 (0.50-0.97)</b>	0.95 (0.67, 1.32)



# IeDE

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