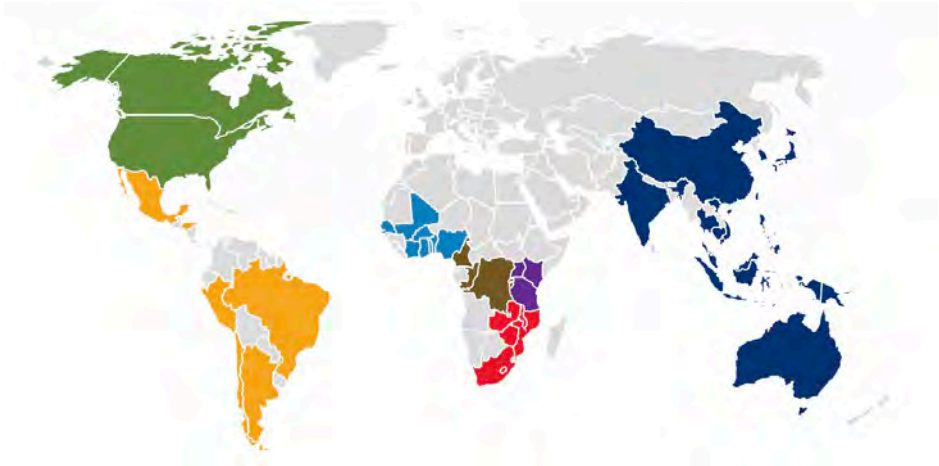
IeDEA Global Cohort Consortium

2023 Research Highlights



Website: iedea.org
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Cohorts and regional principal investigators

- IeDEA Asia-Pacific
  - Annette Sohn, TREAT Asia/amfAR; Matthew Law and Kathy Petoumenos, Kirby Institute
- CCASAnet (Caribbean, Central and South America)
  - Jessica Castilho and Stephany Duda, Vanderbilt University; Pedro Cahn, Fundacion Huesped
- Central Africa IeDEA
  - Kathryn Anastos and Marcel Yotebieng, Albert Einstein College of Medicine; Denis Nash, City University of New York
- East Africa IeDEA
  - Kara Wools-Kaloustian and Constantin Yiannoutsos, Indiana University; Aggrey Semeere, Makerere University
- IeDEA Southern Africa
  - Matthias Egger, University of Bern; Mary-Ann Davies, University of Cape Town
- IeDEA West Africa
  - Antoine Jaquet, University of Bordeaux; Didier Ekouevi, University of Lomé; Ighovwerha Otofokun, Emory University
- NA-ACCORD
  - Richard Moore and Keri Althoff, John Hopkins University

For more information: Aimee Freeman (afreeman@jhu.edu), Annette Sohn (annette.sohn@treatasia.org)

IeDEA

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2023 IeDEA Asia-Pacific Research Highlights

IeDEA

CD4/CD8 Ratio Recovery Among People Living With HIV Starting With First-Line Integrase Strand Transfer Inhibitors: A Prospective Regional Cohort Analysis

- 5529 PLWH enrolled in IeDEA Asia-Pacific adult HIV cohorts who started with triple-ART with at least 1 CD4, CD8, and HIV-1 RNA measurement post- ART were included
  - 80% male, median age 35 years
  - First-line regimen: 65% NNRTI, 19% PI, and 16% INSTI
  - Baseline CD4/CD8 ratio 0.19 (IQR, 0.09–0.33).
- PLWH starting with NNRTI- or PI-based ART had lower CD4/CD8 recovery over 5 years compared with INSTI

Han WM, et al.
J Acquir Immune Defic Syndr. 2023 Feb 1;92(2):180-188. doi: 10.1097/QAI.0000000000003121.

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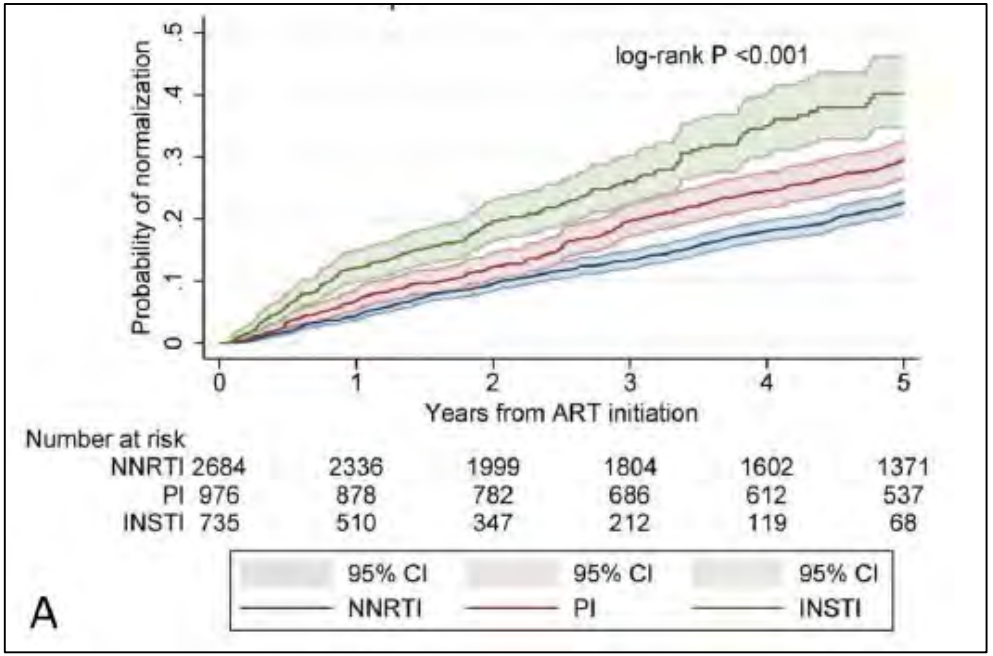
- PLWH started with INSTI had higher odds of achieving CD4/CD8 ratio normalization than NNRTI- or PI-based ART (after adjusting for age, sex, baseline CD4, HIV-1 RNA, HCV, and year of ART initiation).
- <u>Emphasize relative benefits of INSTI-based ART for immune restoration</u>

FIGURE 1. Kaplan–Meier estimates of CD4/CD8 ratio normalization by ART regimen (A)



CD4/CD8 Ratio Recovery Among People Living With HIV Starting With First-Line Integrase Strand Transfer Inhibitors: A Prospective Regional Cohort Analysis. Han WM, et al. J Acquir Immune Defic Syndr. 2023 Feb 1;92(2):180-188. doi: 10.1097/QAI.0000000000003121.

Trends in hepatitis C virus coinfection and its cascade of care among adults living with HIV in Asia between 2010 and 2020

- Assess prevalence of HCV coinfection, trends in the HCV cascade of care, and factors associated with poor HCV outcomes
- 2021 TAHOD-LITE data transfer on >55,000 PLHIV in care @ 11 sites: Cambodia (1), Hong Kong SAR (1), India (2), Indonesia (1), South Korea (1); Thailand (3); Vietnam (2)
- Chronic HCV co-infection defined as testing positive for anti-HCV from 1st January 2010 onwards
- Of 24,421 meeting analysis inclusion criteria (seen at clinic from 2010 onwards and started any ART), 9169 (38%) had an anti-HCV test from 1st January 2010: 971(11%) of these had a positive anti-HCV

Ross J, et al.
PLoS One. 2023 Jun 28;18(6):e0287909. doi: 10.1371/journal.pone.0287909.

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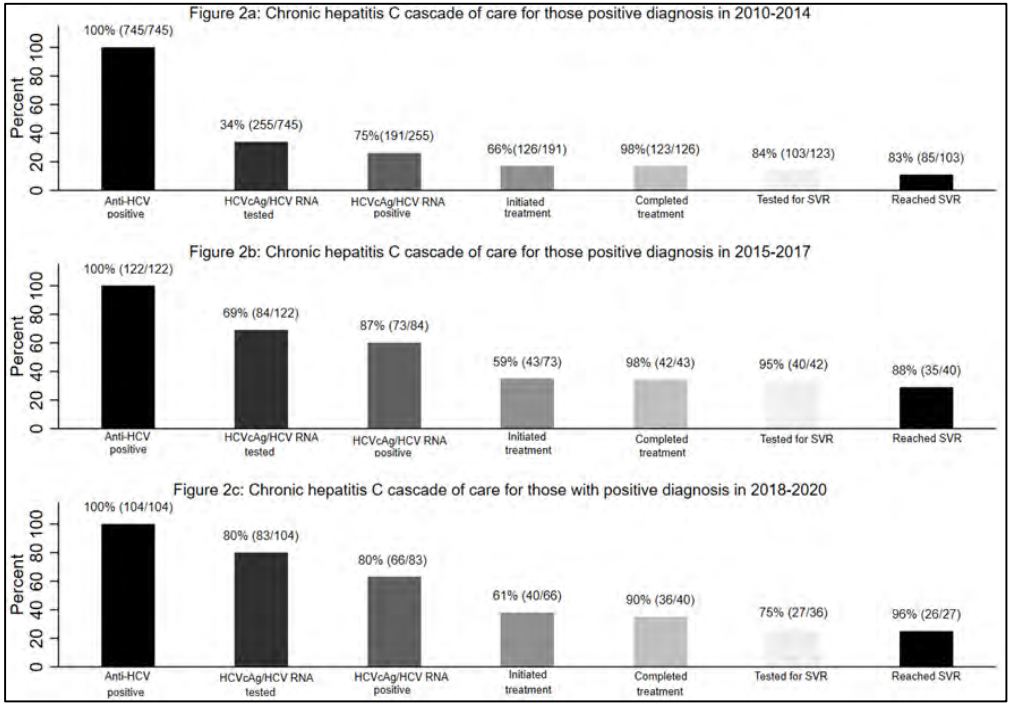
- 2010 to 2020: % pre-HCV treatment testing and achieving SVR increased; HCV treatment initiation decreased
- Later calendar years, HIC sites associated with increased HCV screening, treatment initiation or achieving SVR
- Older age, MSM, IDU, lower CD4 and higher VL associated with reduced HCV screening or treatment



<u>Need to strengthen chronic HCV screening, treatment initiation, and monitoring in the region</u>

Trends in hepatitis C virus coinfection and its cascade of care among adults living with HIV in Asia between 2010 and 2020. Ross J, et al. PLoS One. 2023 Jun 28;18(6):e0287909. doi: 10.1371/journal.pone.0287909.

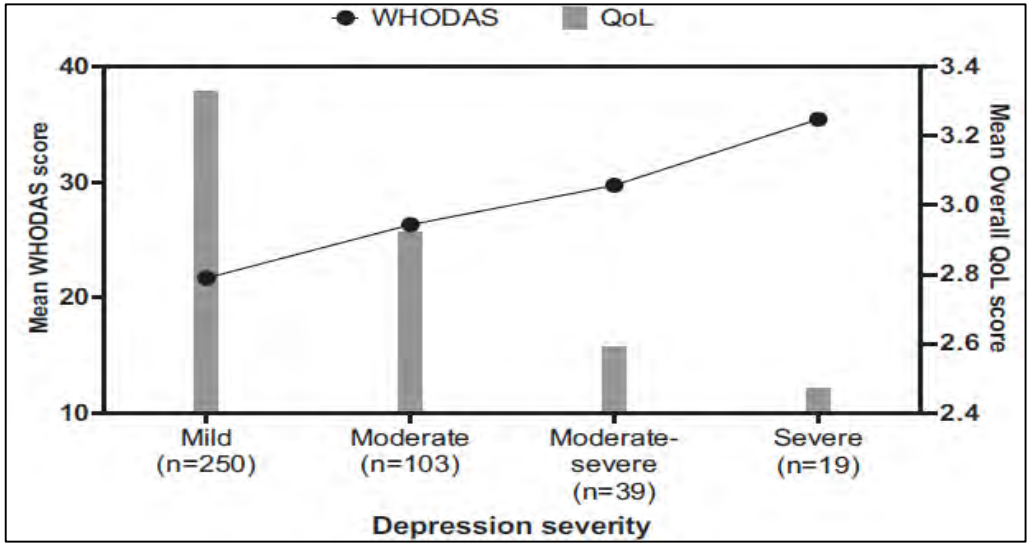
Factors associated with reduced function and quality of life among adult people with HIV with depression and substance use in the Asia-Pacific region

- Explore quality of life, functional ability and associated factors among PWH screening positive for depression and/or SU.
- Cross-sectional study of 864 adult PWH in care at 5 HIV clinical sites: Hong Kong SAR, Philippines, Malaysia, South Korea, Thailand.
- Screening tools: depression - PHQ-9; SU – ASSIST; QoL - WHOQOL-HIV BREF; functional ability - WHODAS 2.0.
  - Among n=753 screening positive for depression or SU, mean WHOQOL-HIV BREF and WHODAS scores indicate greater impairment with increasing depressive symptom severity and SU risk

Rajasuriar R, et al.
AIDS. 2023 Apr 1;37(5):823-835. doi: 10.1097/QAD.0000000000003474. Epub 2022 Dec 29.

- Previous trauma/stress and past mental health diagnosis associated with greater disability and poorer QoL
- Higher CD4 associated with better QoL and functional ability
- <u>Integration of mental health services & interventions addressing disability should be prioritized.</u>

Fig 1b. Trends in mean WHODAS 2.0 and overall QoL scores by depression symptom severity assessed using the PHQ-9 in PWH screened positive for depression in the cohort (n=411)



Factors associated with reduced function and quality of life among adult people with HIV with depression and substance use in the Asia-Pacific region. Rajasuriar R, et al. AIDS. 2023 Apr 1;37(5):823-835. doi: 10.1097/QAD.0000000000003474. Epub 2022 Dec 29.

Disclosure of HIV status and associated clinical outcomes of children and adolescents living with HIV in Asia

- Describe frequency of disclosure and assess effect on ART clinical outcomes, including disease progression, LTFU, and death
- Children and adolescents living with HIV in care at TApHOD sites; aged 6–19 years old; initiated cART between 2008 and 2018; had ≥1 follow-up clinic visit
- Of 1913 children and adolescents (48% female; median age 11.5 years at last clinic visit)
  - 795 (42%) disclosed to about their HIV status at a median age of 12.9 years
  - During follow-up: 11% had disease progression; 3.9% were LTFU; 3.1% died

Sornillo JB, et al.
AIDS Care. 2023 Feb 15:1-10. doi: 10.1080/09540121.2023.2176424.

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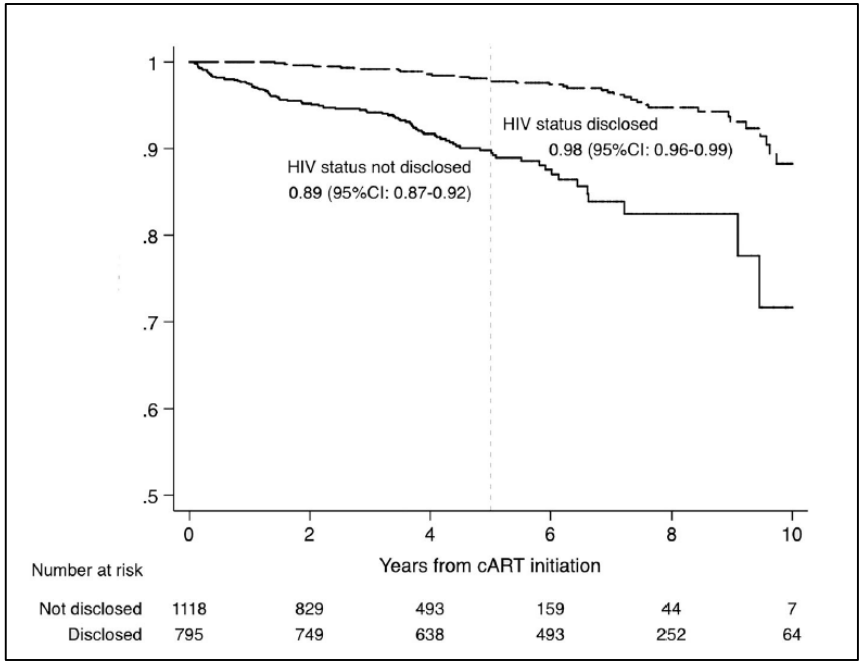
- Lower hazards of disease progression (aHR 0.43 [0.28–0.66]) and death (aHR 0.36 [0.17–0.79]) for disclosed compared to not disclosed to.
- Need to review reasons for delayed disclosure, and to develop interventions to ensure adolescents are informed about their HIV status.

Figure 2. Probability of retention in HIV care by disclosure status in children and adolescents 6–19 years of age after cART initiation in the IeDEA Asia-Pacific cohort ($n = 1913$).



Disclosure of HIV status and associated clinical outcomes of children and adolescents living with HIV in Asia. Sornillo JB, et al. AIDS Care. 2023 Feb 15:1-10. doi: 10.1080/09540121.2023.2176424.

Alcohol use, suicidality and virologic non-suppression among young adults with perinatally acquired HIV in Thailand: a cross-sectional study

- Thai Young adults with perinatally acquired HIV (YA-PHIV) aged 18–25 years at 5 tertiary pediatric HIV care centers in Thailand assessed from November 2020 to July 2021
- Alcohol use (AUDIT), smoking (Fagerstrom Test for Nicotine Dependence), drug/substance use (DAST-10), depression (PHQ-A), anxiety (GAD-7) and QOL (WHO QOL Brief-Thai).
- HIV treatment outcomes extracted from National AIDS Program database

Aurpibul L, et al.
J Int AIDS Soc. 2023 Feb;26(2):e26064. doi: 10.1002/jia2.26064.

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- Of 355 YA-PHIV: 46% male: median age 21.7 years
  - 14% CD4 <200 cells/mm^3 ; 24% HIV-RNA >200 copies/ml
  - 40% sexually active in past 6 months, of whom 61% had 100% condom use
  - 14% harmful alcohol use; 17% current smokers; 11% used drugs/substances
  - 18% moderate to severe depression symptoms; 10% anxiety
- Lower levels of education, harmful alcohol use, and lifetime suicidal attempts associated with non-suppression
- <u>Need for regular screening of alcohol use and mental health, including suicidality, to identify YA-PHIV who need more intensive psychosocial support or referral services</u>

Alcohol use, suicidality and virologic non-suppression among young adults with perinatally acquired HIV in Thailand: a cross-sectional study. Aurpibul L, et al. J Int AIDS Soc. 2023 Feb;26(2):e26064. doi: 10.1002/jia2.26064.

CCASAnet Publication Highlights: 2023

Clinical Infectious Diseases
MAJOR ARTICLE
2023

Cryptococcal Meningitis and Clinical Outcomes in Persons With Human Immunodeficiency Virus: A Global View

Anna K. Person,[1,a] Brenda Crabtree-Ramirez,[2,a] Ahra Kim,[3] Valdiléa Veloso,[4] Fernanda Maruri,[1] Gilles Wandeler,[5] Matthew Fox,[6] Richard Moore,[7] M. John Gill,[8] Darma Imran,[9] Kinh Van Nguyen,[10] Elizabeth Nalitya,[11] Winnie Muyindike,[12] Bryan E. Shepherd,[3] and Catherine C. McGowan[1]

Background: Cryptococcal meningitis (CM) is a major cause of morbidity and mortality in persons with human immunodeficiency virus (HIV; PWH). Little is known about CM outcomes and availability of diagnostic and treatment modalities globally.

Methods: This **retrospective cohort study** investigated cryptococcal meningitis (CM) incidence and all-cause mortality in PWH (518,852) in IeDEA from 1996 to 2017. We estimated incidence using quasi-Poisson models adjusted for sex, age, calendar year, CD4 cell count (CD4), and ART status. Mortality after CM diagnosis was examined using multivariable Cox models. A site survey from 2017 assessed availability of CM diagnostic and treatment modalities.

PMID: 36821489 PMCID: PMC10273391

Results:

3,857 cases of cryptococcal meningitis (CM)

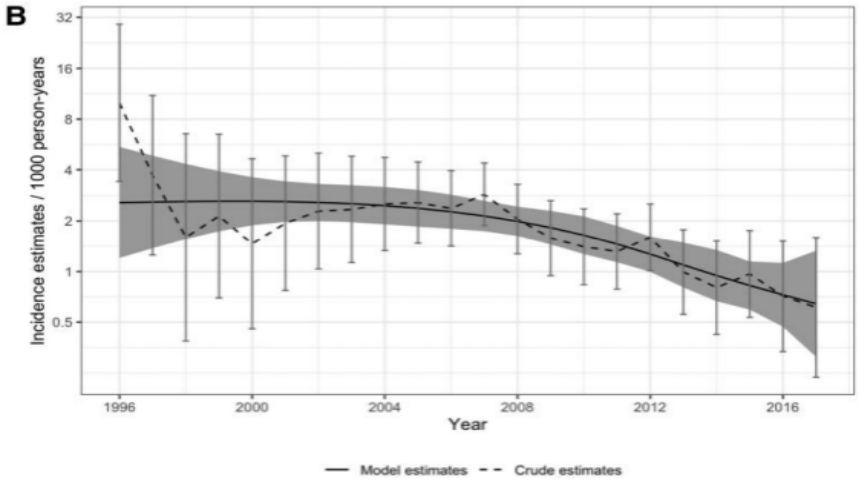
Incidence: 1.54 per 1000 person-years

Mortality at 2.6 years 31.6%

Higher mortality

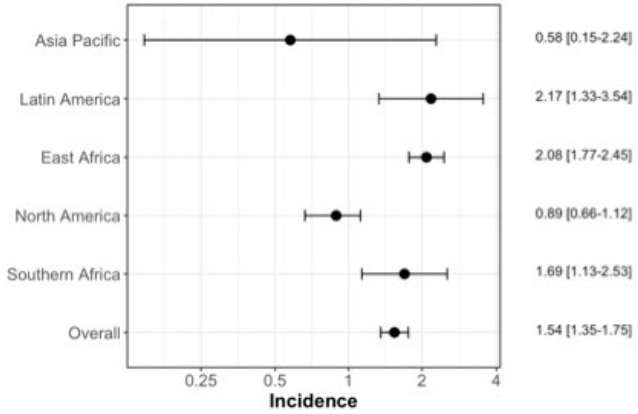
Elderly
CD4 <200 cells/mm3
Diagnosis in the early years of the cohort

Incidence of Cryptococcal Meningitis, at all sites, stratified by years



Results:

Figure 1: Unadjusted incidence of CM diagnosis per 1000-person years (95% CIs) according to region and overall



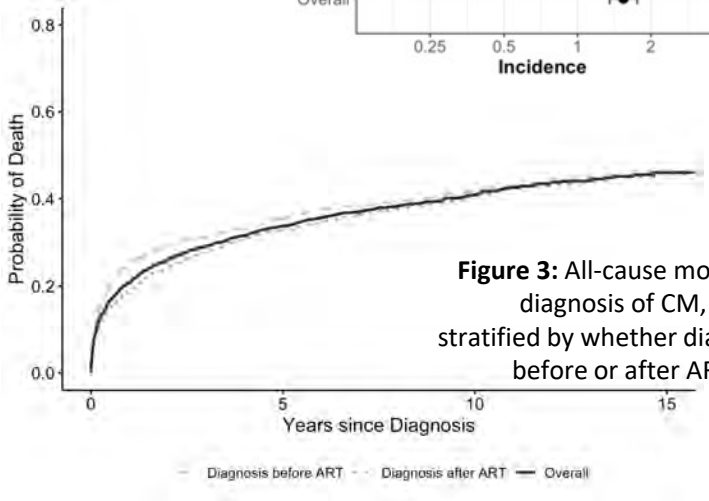


Figure 3: All-cause mortality after diagnosis of CM, overall and stratified by whether diagnosis was before or after ART initiation

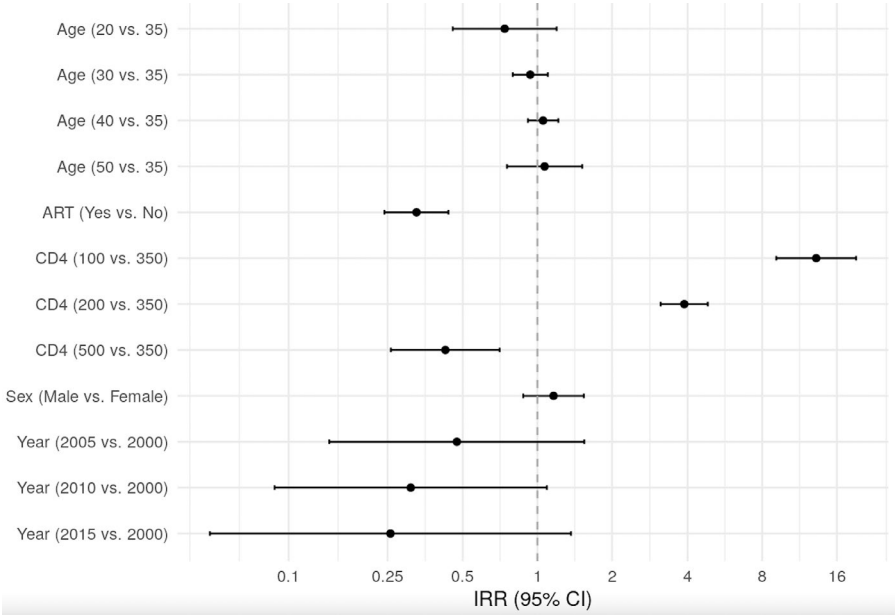


Figure 2: Estimated incidence rate ratio (95% Confidence intervals) of risk factors for cryptococcal meningitis combined across all IeDEA regions, in adjusted analyses

Of the 89 IeDEA sites:

34% had access to Amphotericin B

12% had access to Flucytosine

Conclusions: Mortality after CM diagnosis was high. A substantial portion of CM cases occurred after ART start, though incidence and mortality may be higher than reported due to ascertainment bias. Many sites lacked access to recommended CM treatment.

PMID: 36821489 PMCID: PMC10273391

The Canadian Journal of Statistics
La revue canadienne de statistique

Research Article | Open Access

Optimal multiwave validation of secondary use data with outcome and exposure misclassification

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

First published: 31 March 2023 | https://doi.org/10.1002/cjs.11772

Ran Tao and Bryan E. Shepherd jointly supervised this work.

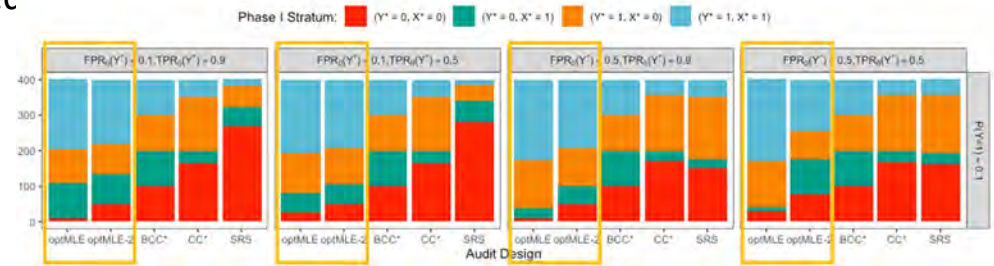
Early View
Online Version of Record
before inclusion in an issue

CCASAnet

Background:

- As the volume of routinely collected data is steadily climbing, researchers are finding more "secondary" uses for them.
- Secondary use data like the observational data used in IeDEA studies are convenient to analyze but expected to be error-prone.
- Data audits can help measure data quality, but they're cost- and time-intensive undertakings.

- While we can't always control how many patients to audit (dictated by funds, time, etc.), we can control which patients to audit.
- This paper describes "optimal" designs to target the most informative patients for the audit to improve the statistical efficiency (i.e., precision) in logistic regression models with error-prone exposure and outcome variables.



Conclusion:

- Our optimal designs are implemented in the `auditDesignR` R package and the Shiny app (image below).
- In simulations, the new design (optMLE-2) outperforms existing ones based on only the original error-prone data (BCC*, CC*) or random sampling (SRS) (Table 1 below).
- The method was illustrated using CCASAnet data to design optimal audits for the analysis of successful TB treatment outcomes and bacteriological confirmation of TB.

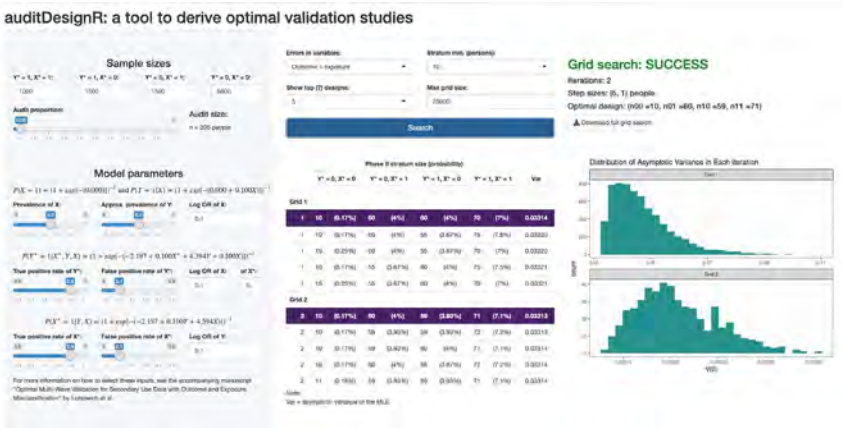


TABLE 1: Simulation results under outcome and exposure misclassification with varied outcome misclassification rates.

Outcome misclassification		optMLE-2				BCC*				CC*				SRS			
$FPR_{\theta_0}(Y^*)$	$TPR_{\theta_0}(Y^*)$	% Bias	SE	RE	RI	% Bias	SE	RE	RI	% Bias	SE	RE	RI	% Bias	SE	RE	RI
$p_{y0} = 0.1$																	
0.1	0.9	−2.85	0.214	1.028	1.015	−4.00	0.254	0.728	0.855	−9.20	0.347	0.391	0.640	−19.4	0.516	0.176	0.459
	0.5	1.11	0.241	0.908	0.960	1.39	0.286	0.643	0.815	−3.98	0.362	0.403	0.679	−17.2	0.512	0.201	0.508
0.5	0.9	−2.99	0.321	0.935	1.017	−3.08	0.409	0.578	0.763	−21.6	0.560	0.308	0.570	−17.7	0.563	0.305	0.552
	0.5	−1.61	0.361	1.067	1.008	−6.31	0.377	0.982	1.004	−10.8	0.512	0.531	0.767	−27.0	0.543	0.472	0.700
$p_{y0} = 0.3$																	
0.1	0.9	1.67	0.190	1.009	0.949	0.34	0.223	0.734	0.855	7.26	0.297	0.413	0.683	−1.46	0.333	0.329	0.569
	0.5	4.83	0.219	1.004	1.049	−0.75	0.226	0.941	1.087	6.54	0.317	0.480	0.723	1.38	0.344	0.406	0.658
0.5	0.9	0.62	0.241	0.924	0.879	−0.27	0.274	0.717	0.814	−7.60	0.386	0.360	0.588	2.02	0.357	0.421	0.626
	0.5	1.73	0.248	0.918	0.957	−0.81	0.240	0.982	1.035	−1.15	0.369	0.416	0.664	−1.01	0.369	0.415	0.675
$p_{y0} = 0.75$																	
0.1	0.9	1.87	0.206	0.917	0.950	0.88	0.227	0.833	0.840	4.11	0.360	0.525	0.585	9.61	0.405	0.467	0.532
	0.5	2.44	0.273	0.978	0.960	3.79	0.303	0.881	0.887	15.8	0.473	0.564	0.573	11.2	0.439	0.608	0.628
0.5	0.9	−3.28	0.248	0.940	0.907	−0.05	0.267	0.873	0.872	0.09	0.390	0.597	0.601	24.4	0.451	0.517	0.530
	0.5	8.79	0.301	1.010	1.030	4.04	0.313	0.974	0.905	6.89	0.465	0.656	0.601	7.05	0.445	0.685	0.699

Note: Exposure misclassification rates were fixed at $FPR_0(X^*) = 0.1$ and $TPR_0(X^*) = 0.9$. The % Bias and SE are, respectively, the empirical percent bias and standard error of the MLE values. RE or RI below 1 indicates an efficiency loss compared to the optMLE design. The grid search successfully located the optMLE and optMLE-2 designs in all and ≥95% of replicates per setting, respectively; across all settings, 162 (1.4%) problematic replicates of the optMLE-2 design were discarded out of 12,000. Fewer than 1% and 5% of the replicates were discarded because of unstable estimates under the SRS, CC*, or BCC* designs when $p_{y0} = 0.1$ and 0.9, respectively. All other entries are based on 1000 replicates.

Lessons learned from over a decade of data audits in international observational HIV cohorts in Latin America and East Africa

Sarah C. Lotspeich[1,2], Bryan E. Shepherd[2], Marion Achieng Kariuki[3], Kara Wools-Kaloustian[4], Catherine C. McGowan[5], Beverly Musick[6], Aggrey Semeere[3], Brenda E. Crabtree Ramírez[7], Denna M. Mkwashapi[8], Carina Cesar[9], Matthew Ssemakadde[10], Daisy Maria Machado[11], Antony Ngeresa[12], Flávia Faleiro Ferreira[13], Jerome Lwali[14], Adias Marcelin[15], Sandra Wagner Cardoso[16], Marco Tulio Luque[17], Larissa Otero[18,19], Claudia P. Cortés[20] and Stephany N. Duda[21]

CCASAnet

and

East Africa IeDEA
INTERNATIONAL EPIDEMIOLOGY DATABASES TO EVALUATE AIDS

J Clin Transl Sci. 2023; 7(1): e245.
Published online 2023 Nov 3. doi: 10.1017/cts.2023.659

- CCASAnet and East Africa IeDEA have over 10 years' experience auditing the observational data drawn from participating HIV clinics to ensure high-quality data for IeDEA analyses.
- During an audit, auditors compared source documentation (e.g., patient charts, electronic health records, laboratory, and pharmacy databases) from selected patient records to the same entries in the research dataset submitted to the network's coordinating center and noted any discrepancies. Findings informed data corrections and re-audits.
- Each network has completed 3 audit cycles. CCASAnet audit cycles took place in 2007–2010, 2012–2014, and 2016–2018; the EA-IeDEA audit cycles were conducted in 2010–2011, 2012–2014, and 2017–2019.
- Audit procedures and technology changed over time, along with improvements in data quality. We described lessons learned and shared eight key recommendations for others.

PMID: 38033704; PMCID: PMC10685260

Core recommendations for implementing data quality audits in observational research networks

R1: Observational research cohorts should **implement data quality audits**, too, not just clinical trials, and audit protocols must be adapted for feasibility in resource-limited settings

R2: Data coordinating centers should **prioritize the first (i.e., "baseline") audit**, as it provides data and workflow insights and can lead to transformations with paper charting or electronic health record use, processes, and staff. In addition, an in-person visit from coordinating center investigators can help establish connections with local investigators and staff.

R3: Subsequent major changes in clinic systems, personnel, or collected study data can introduce errors and should **trigger re-audits**.

R4: **Site personnel should be trained** to understand the data quality assurance process and conduct their own (self-)audits. Creation of site-based data quality programs can build trust, improve attentiveness to data detail and quality, positively impact local data operations, and build capacity for future site-based research.

R5: After establishing trust and stable processes, the coordinating center can implement **lower-cost solutions**, such as self-audits and remote auditing.

R6: The **content of the audits should change over time** to ensure high data quality for the ongoing cohort research. These changes may include auditing different variables or subsets of patients. Also, repeatedly auditing the same content can have diminishing returns.

R7: Paper audit forms should be avoided. **Electronic data capture systems** like REDCap or Excel produce more reusable audit findings that can be used to generate comparisons and summary reports in a timely manner and avoid potential transcription error.

R8: Coordinating centers for multi-national collaborative research consortia should realize that there is no perfect data audit and there are many potential interpretations of audit findings. The **goal is to learn lessons about data** in different contexts and improve quality through collaboration.

PMID: 38033704; PMCID: PMC10685260

SEX DISPARITIES IN THE ROLLOUT OF DOLUTEGRAVIR IN LATIN AMERICA & THE CARIBBEAN

Fernanda F Fonseca[1,2], Paridhi Ranadive[3], Bryan E Shepherd[3], Beatriz Grinsztejn[1], Sandra W Cardoso[1], Valdiléa Veloso[1], Flavia GF Ferreira[4], Maria F Rodríguez[5], Daisy M Machado[6], Vanessa Rouzier[7], Diana Varela[8], Emilia Jalil[1], Jessica L Castilho[3], on behalf of CCASAnet.

[1]Instituto Nacional de Infectologia - Evandro Chagas, Fiocruz, Rio de Janeiro, Brazil, [2]AIDS Healthcare Foundation, USA,[3]Vanderbilt University Medical Center, Nashville, TN, USA, [4]UFMG, Faculdade de Medicina, Belo Horizonte, Brazil, [5]Hospital Clínico San Borja Arriarán, Fundación Arriarán, Santiago, Chile, [6]UNIFESP, Escola Paulista de Medicina, Paulo, Brazil, [7]Groupe Haitien d'Etudes du Sarcome de Kaposi et des Infections Opportunistes, Port-au-Prince, Haiti, [8]Instituto Hondureño de Seguridad Social & Hospital Escuela Universitario, Tegucigalpa, Honduras

OBJECTIVE

We evaluated disparities in DTG uptake in cisgender PWH in Latin America and the Caribbean and impact on HIV viral load, comparing the periods related to the WHO global warning on DTG (2018).

METHODS

Observational data from **CCASAnet** of PWH starting ART after DTG availability for each **site** (Rio de Janeiro, Sao Paulo, Belo Horizonte [Brazil], Santiago [Chile]; Port-au-Prince [Haiti], and Tegucigalpa [Honduras]).

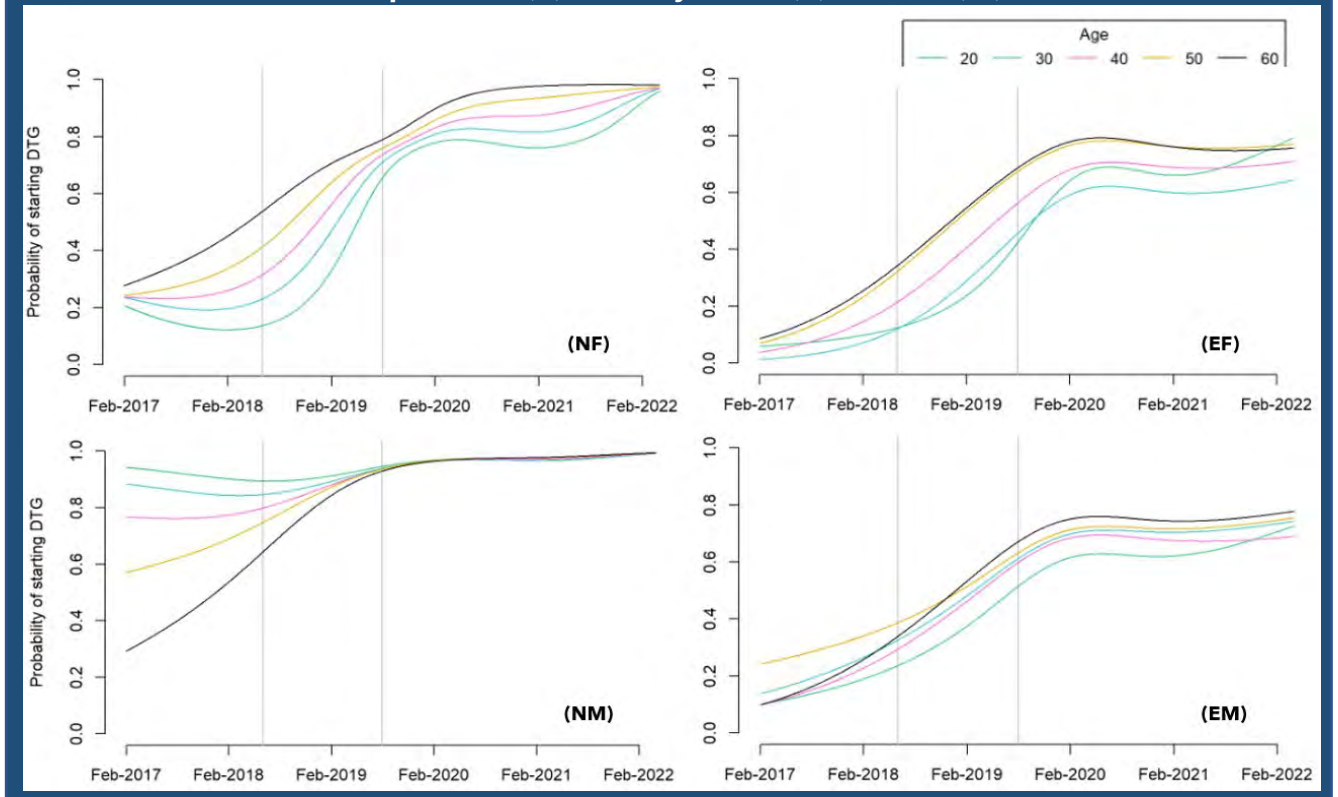
DTG availability dates were Feb/2017 (Brazil); Aug/2019 (Chile), Nov/2018 (Haiti); and Dec/2018 (Honduras).

Calendar Eras of comparison included:
✓**Pre-Warning period** (before May 2018),
✓**During Warning period** (May 2018-July 2019), and
✓**Post-Warning period** (after July 2019)

Outcomes:
1. DTG initiation among ART naïve and among ART experienced PWH
2. Virologic suppression (HIV RNA <50 cps/mL) within one year of ART initiation among ART naïve PWH with ≥1 year of follow-up and VL data.

Statistical Approach for both analyses: Multivariable modified Poisson regression models, adjusting for site, presence of tuberculosis, and sex-age-calendar period 3-way interaction term (ART naïve).For the analysis among ART experienced PWH the models were also adjusted for time updated number of ART prior regimens and HIV VL.

Adjusted probability of DTG initiation by date and age among treatment naïve (N) and experienced (E) -PWH, by female (F) and male (M)



Models for each comparison also adjusted for site and presence of TB.

Fonseca FF, *et al*. SEX DISPARITIES IN THE ROLLOUT OF DOLUTEGRAVIR IN LATIN AMERICA AND THE CARIBBEAN. CROI Conference, 2023, Seattle, USA. **Poster #1057**
https://www.croiconference.org/abstract/sex-disparities-in-the-rollout-of-dolutegravir-in-latin-america-and-the-caribbean/.

DTG initiation among ART naïve PWH

Population: 4622 (1762 female [38%]) PWH initiated ART after local DTG rollout

- 567 (12%) PWH **≥50 years old** (243 female)
- 315 (7%) PWH starting ART **before,** 1195 (26%) **during**, and 3112 (67%) **after the DTG warning**

Outcome: Overall, 3853 (83%) PWH initiated DTG

- Brazil: 1060 (89%), Chile: 373 (50%), Haiti: 2387 (92%), Honduras: 33 (45%).

DTG initiation among ART experienced PWH

Population: 16154 PWH (8051 female [50%]) initiated ART after local DTG rollout

- 2110 (13%) PWH **≥50 years old** (998 female)
- 3151 (20%) PWH starting ART **before,** 10901 (67%) **during**, and 2102 (13%) **after the DTG warning**

Outcome: Overall, 9236 (56%) initiated DTG

- Brazil: 903 (28%), Chile: 135 (15%), Haiti: 8197 (71%), Honduras: 1 (<1%).

Virologic Suppression

Population: 3566 ART-naïve PWH with ≥1 year of follow-up and ≥1 VL test after ART initiation included (female n=1374, 39%), and 2849 (80%) started DTG

Outcome: 2443 (69%) PWH achieved VL suppression.

Compared to starting non-DTG based ART, initiating DTG-based ART use was associated with a higher likelihood of VL suppression (aRR=1.10, 95% CI: 1.04-1.16).

In the **post-DTG warning period**, younger females had a likelihood of VL suppression similar to younger males (aRR=1.04, 95% CI: 0.97 -1.11), which did not change after controlling for DTG use (aRR=1.03, 95% CI: 0.96-1.10).

ADJUSTED RELATIVE RISKS OF STARTING A DTG-BASED REGIMEN AMONG PWH ART-NAÏVE AND ART-EXPERIENCED

	COMPARISON	ART naïve PWH		ART experienced PWH	
		aRR (95%CI)	p-value	aHR (95%CI)	p-value
SEX	16-49 years pre/during-warning: female vs. male	0.75 (0.71-0.80)	<0.001	0.69 (0.66-0.73)	<0.001
SEX	16-49 years post-warning: female vs. male	0.97 (0.95-1.00)	0.03	0.79 (0.70-0.90)	<0.001
SEX	≥50 years pre/during-warning: female vs. male	1.03 (0.91-1.16)	0.64	1.06 (0.99-1.14)	0.089
PERIOD	Female 16-49 years: pre/during vs. post-warning	0.69 (0.65-0.73)	<0.001	1.04 (0.94-1.15)	0.438
PERIOD	Male 16-49 years: pre/during vs. post-warning	0.89 (0.86-0.91)	<0.001	1.19 (1.05-1.36)	0.007
AGE	Female pre/during-warning: 16-49 vs. ≥50 years	0.79 (0.71-0.87)	<0.001	0.59 (0.55-0.63)	<0.001
AGE	Female post-warning: 16-49 years vs. ≥50 years	0.95 (0.92-0.98)	<0.001	0.64 (0.55-0.75)	<0.001
AGE	Male pre/during-warning: 16-49 vs. ≥50 years	1.08 (0.98-1.18)	0.12	0.90 (0.85-0.96)	0.002
AGE	Male post-warning: 16-49 vs. ≥50 years	0.99 (0.97-1.06)	0.63	0.93 (0.92-1.26)	0.367

CONCLUSION

Despite the updated guidelines recommending DTG for all PWH**, younger females in LAC experienced discrepancies in DTG uptake,** potentially impacting long-term treatment outcomes. Assuring sex-equitable access to DTG is urgent needed in the Latin America and the Caribbean.

Fernanda.Fonseca@ahf.org

CCASAnet

Tuberculosis Treatment Outcomes in Brazil: Different Predictors for Each Type of Unsuccessful Outcome

Clinical Infectious Diseases

MAJOR ARTICLE

Felipe Ridolfi,[1,a] Lauren Peetluk,[2,a] Gustavo Amorim,[3] Megan Turner,[4] Marina Figueiredo,[4] Marcelo Cordeiro-Santos,[5,6] Solange Cavalcante,[7,8] Afrânio Kritski,[8] Betina Durovni,[9] Bruno Andrade,[4,10,11,12,13,14,15] Timothy R. Sterling,[4,a] and Valeria Rolla,[1,a] the Regional Prospective Observational Research in Tuberculosis (RePORT)–Brazil Consortium

Clinical Infectious Diseases, Volume 76, Issue 3, 1 February 2023, Pages e930–e937, https://doi.org/10.1093/cid/ciac541

Objective – to evaluate the factors associated with the **different components of unsuccessful TB treatment outcomes** [treatment failure, death, and loss to follow-up (LTFU)]

- updated WHO TB treatment outcome definitions

Eligibility (RePORT-Brazil participants)

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

Biological factors → clinical conditions

- people living with HIV/AIDS (PLHA), anemia, and diabetes

Behavioral factors → substance use - alcohol, drugs, tobacco

- self-report, at baseline
- current, former, and never
- alcohol → CAGE questionnaire > 2
- all drugs were considered
  - marijuana, cocaine, crack, ecstasy, injectable drugs, inhaled solvents, oxycodone, and cocaine paste base

RePORTBrazil
Regional Prospective Observational Research for Tuberculosis

PMID: 35788646 PMCID: PMC10169436

Results

- 915 participants included [19% (n=173) PLHA]

TB treatment outcomes:

- successful 79% (n=727) (cure + treatment completion)
- Unsuccessful 21% (n=188)
  - **118 (13%) LTFU**
  - 44 (5%) treatment failure
  - 26 (3%) death

Conclusions

Different baseline factors → different unsuccessful TB treatment outcomes

Biological factors → death, treatment failure

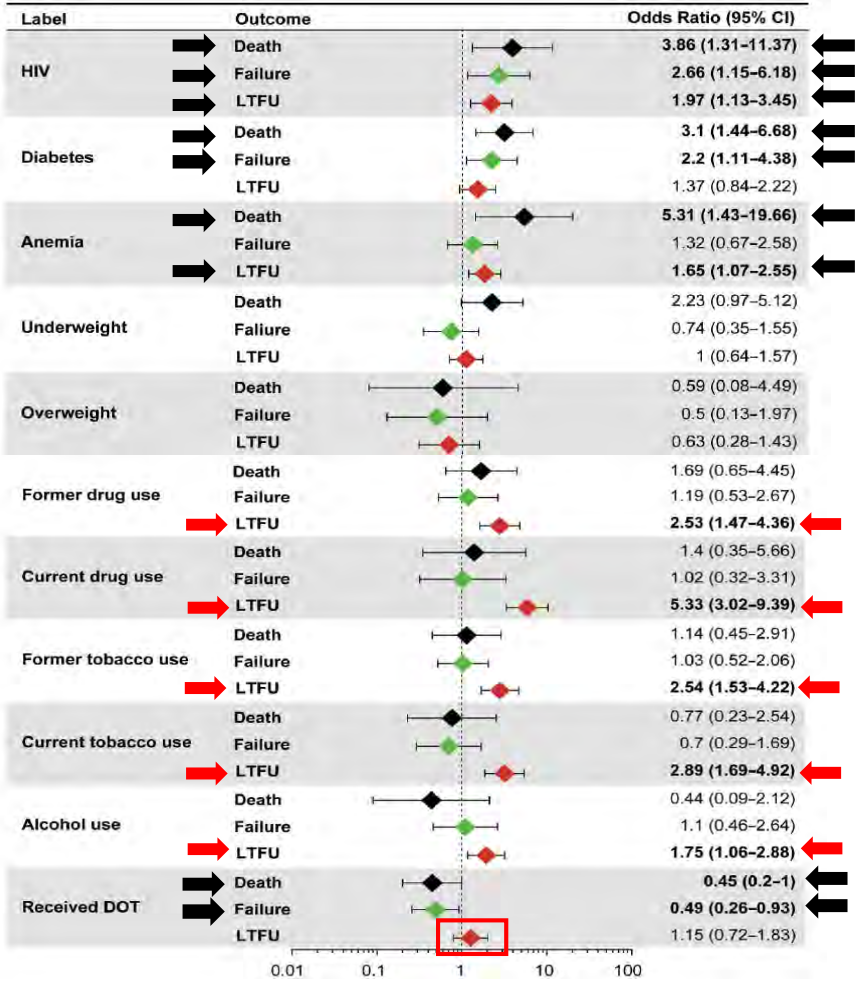
Behavioral factors (substance use) → LTFU

None of the HIV-related factors (CD4 cell count, viral load, or antiretroviral therapy) were associated with unsuccessful outcomes (data not shown)

This study was presented at the Union Conference in Paris – Nov 2023 by Felipe Ridolfi

PMID: 35788646 PMCID: PMC10169436

Figure 1. Coefficient plot. Logistic regression model, using Inverse-probability weighted (IPW) models, of baseline factors associated with the different components of unsuccessful outcomes in tuberculosis (TB) treatment.



Central Africa IeDEA

2023 Research Highlights

Availability of screening and treatment for common mental disorders in HIV clinic settings: data from the global International epidemiology Databases to Evaluate AIDS (IeDEA) Consortium, 2016-2017 and 2020

Parcesepe AM, Stockton M, Remch M, Wester CW, Bernard C, Ross J, Haas AD, Ajeh R, Althoff KN, Enane L, Pape W, Minga A, Kwobah E, Tlali M, Tanuma J, Nsonde D, Freeman A, Duda SN, Nash D, Lancaster K; IeDEA Consortium. *J Int AIDS Soc*. 2023 Aug;26(8):e26147. doi: 10.1002/jia2.26147

AIM:

To describe the reported availability of screening and treatment for depression, anxiety and PTSD at global HIV treatment sites participating in the IeDEA Consortium in 2020 and changes in availability at sites in LMICs between 2016/2017 and 2020.

METHODS:

- **Data:** Used data from 223 sites in 41 countries that completed IeDEA's 2020 site assessment survey, and 68 sites in 27 low- and middle-income countries (LMICs) participating in a 2016/2017 survey on the availability of screening and treatment for mental health disorders
- **Analysis**: Descriptive statistics used to characterize the availability of screening and treatment for mental health disorders, in 2020, and to examine trends over time for LMIC sites participating in both surveys.

Availability of screening and treatment for common mental disorders in HIV clinic settings: data from the global International epidemiology Databases to Evaluate AIDS (IeDEA) Consortium, 2016-2017 and 2020

RESULTS:

- Overall, 50%, 14% and 12% of sites reported screening with a validated instrument for depression, anxiety and PTSD, respectively.
- Screening plus treatment in the form of counselling was available for depression, anxiety and PTSD at 46%, 13% and 11% of sites, respectively.
- Screening plus treatment in the form of medication was available for depression, anxiety and PTSD at 36%, 11% and 8% of sites, respectively.
- Among sites that participated in both surveys, screening for depression was more commonly available in 2020 than 2016/2017 (75% vs. 59%).

Parcesepe AM, Stockton M, Remch M, Wester CW, Bernard C, Ross J, Haas AD, Ajeh R, Althoff KN, Enane L, Pape W, Minga A, Kwobah E, Tlali M, Tanuma J, Nsonde D, Freeman A, Duda SN, Nash D, Lancaster K; IeDEA Consortium. *J Int AIDS Soc*. 2023 Aug;26(8):e26147. doi: 10.1002/jia2.26147

IeDEA

Age-varying associations of depressive symptoms and heavy episodic drinking throughout adulthood among people with HIV and receiving care in Cameroon within a national “treat all” policy

Lancaster KE, Remch M, Edmonds A, Ajeh R, Dzudie A, Adedimeji A, Nash D, Anastos K, Yotebieng M, Yone-Pefura EW, Nsame D, Parcesepe AM. *AIDS Behav*. 2023 Jul;27(7):2070-2078. doi: 10.1007/s10461-022-03939-4.

AIM:

To examine the age-specific effects between depression and heavy episodic drinking (HED) throughout adulthood, and the extent to which these associations differed by gender.

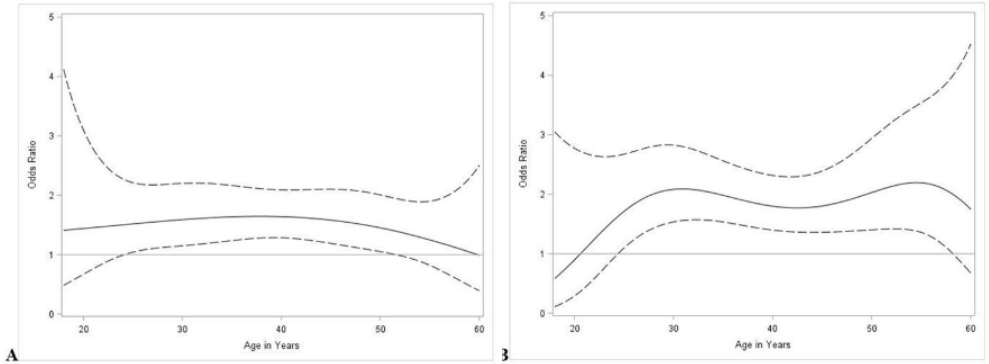
METHODS:

- **Data:** 18-60-year-old patients with HIV who were on antiretroviral therapy (ART) and in care between January 2016 and March 2020 at three HIV clinics in Cameroon. Depressive symptoms were assessed using the two-item Patient Health Questionnaire (PHQ-2) with a score of ≥3 indicating likely major depressive disorder. HED was assessed using data from a locally adapted Alcohol Use Disorder Identification Test (AUDIT)
- **Analysis**: Time-varying effect modeling (TVEM) used to assess longitudinal associations between depressive symptoms and HED.

Age-varying associations of depressive symptoms and heavy episodic drinking throughout adulthood among people with HIV and receiving care in Cameroon within a national “treat all” policy

RESULTS:

- Prevalence of depression and HED were highest at ages 20 and 25, respectively.
- After age 25, the magnitude of the association between depressive symptoms and HED was significant and increased until age 30 (aOR: 1.88, 95% CI: 1.48, 2.39), with associations remaining significant until age 55 (aOR: 1.64, 95% CI: 1.17, 2.29).
- Men (Figure A) had less variability and lower magnitudes of associations between depressive symptoms and HED than women (Figure B).



Time-varying effect modeling showing the association between depressive symptoms and heavy episodic drinking among men (A) and women (B), ages 18 to 60 on antiretroviral treatment living with HIV in Cameroon, 2016–2020

Lancaster KE, Remch M, Edmonds A, Ajeh R, Dzudie A, Adedimeji A, Nash D, Anastos K, Yotebieng M, Yone-Pefura EW, Nsame D, Parcesepe AM. *AIDS Behav*. 2023 Jul;27(7):2070-2078. doi: 10.1007/s10461-022-03939-4.

PrEP Availability Among Health Facilities Participating in the IeDEA Consortium

Kebede S, Brazier E, Freeman AM, Muwonge TR, Choi JY; de Waal R, Poda A, Cesar C, Munyaneza A, Kasozi C, Pasayan MKU; Althoff KN, Shongo A, Low N, Ekouevi D, Veloso VG, Ross J. *AIDS*. 2023 Dec 22. doi: 10.1097/QAD.0000000000003824.

AIMS:

- To describe PrEP drug registration status and availability of PrEP services across HIV care sites participating in the International epidemiology Databases to Evaluate AIDS (IeDEA) research consortium using Site Assessment Surveys conducted in 2014, 2017 and 2020.

METHODS:

- **Data:** Used country-level PrEP drug registration status from the AIDS Vaccine Advocacy Coalition and data from IeDEA's general site assessment surveys conducted in 2014, 2017 and 2020 among participating HIV clinics in seven global regions.
- **Analysis**: Descriptive statistics used to assess PrEP availability reported by IeDEA sites serving adult patients in 2020 and to examine trends in PrEP availability among sites participating in all three surveys.

PrEP Availability Among Health Facilities Participating in the IeDEA Consortium

RESULTS:

- Among 199 sites completing IeDEA's 2020 survey, 161 (81%) reported PrEP was available on site or via referral.
- PrEP availability was highest at sites in North America (29/40; 97%) and East Africa (70/74; 95%) and lowest at sites in Central (10/20; 50%) and West Africa (1/6; 17%).
- PrEP availability was higher among sites in countries where PrEP was officially registered (146/161; 91%) than where it was not (14/32; 44%).
- Availability was higher at health centers (109/120; 90%) and district hospitals (14/16; 88%) compared to regional/teaching hospitals (36/63).
- Among 94 sites that responded to all three surveys, PrEP availability increased from 47% in 2014 to 60% in 2017 and 76% in 2020.

Kebede S, Brazier E, Freeman AM, Muwonge TR, Choi JY; de Waal R, Poda A, Cesar C, Munyaneza A, Kasozi C, Pasayan MKU; Althoff KN, Shongo A, Low N, Ekouevi D, Veloso VG, Ross J. *AIDS*. 2023 Dec 22. doi: 10.1097/QAD.0000000000003824.

Economic costs and cost-effectiveness of conditional cash transfers (CCTs) for the uptake of services for the prevention of vertical transmission in a resource-limited setting

Masiano SP, Kawende B, Ravelomanana NLR, Green TL, Dahman B, Thirumurthy H, Kimmel AD, Yotebieng M. *Soc Sci Med* 2023;320:115684. doi: 10.1016/j.socscimed.2023.115684.

AIMS

- Examine economic costs and cost-effectiveness of CCTs for the uptake of the prevention of mother-to-child transmission (PMTCT) in the Democratic Republic of Congo (DRC)

METHODS

- **Data:** Effectiveness data from randomized, controlled trial of CCTs compared to standard of care (SOC) for PMTCT (Yotebieng 2016). Economic data from international databases, negotiated price lists and the peer-reviewed and grey literature.
- **Analysis**: Costs were from the societal perspective and in 2016 I$. Effectiveness outcomes were PMTCT uptake (accept all PMTCT visits and services) and retention (in HIV care at 6 weeks post-partum). Generalized estimating equations estimated incremental costs and effectiveness (relative risk), with incremental effectiveness the number of women needing CCTs for an additional PMTCT uptake or retention.

Economic costs and cost-effectiveness of conditional cash transfers (CCTs) for the uptake of services for the prevention of vertical transmission in a resource-limited setting

RESULTS

- Mean per person costs were I$516 (CCTs) and I$431 (SOC) for an incremental cost of I$85 (95% CIs: I$59, I$111).
- The cost-effectiveness of CCTs was I$595 (95% CI: I$550, I$638) for an additional woman taking up PMTCT services and I$1028 (95% CI: I$931, I$1125) for an additional woman retained in PMTCT care, compared to SOC.
- CCTs are cost-effective if society is willing to pay at least I$640 (Fig) for an additional woman taking up PMTCT services, with findings robust even in a worst-case cost scenario.

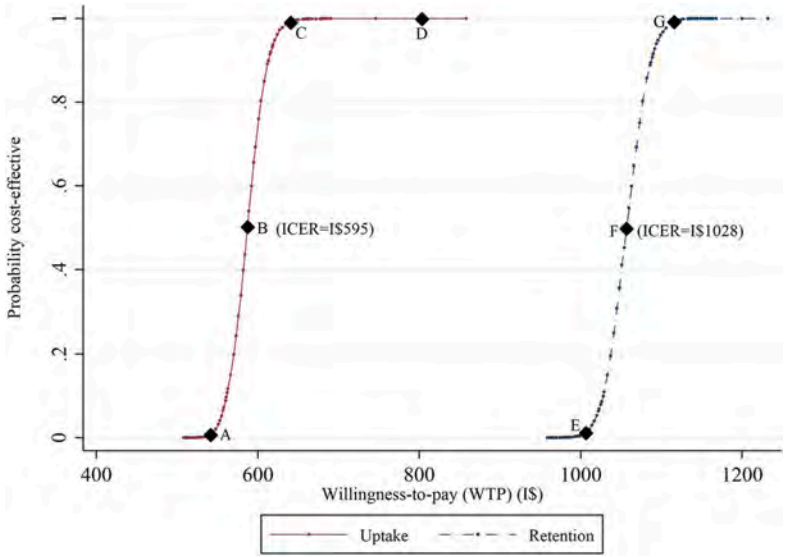


Fig. 2. Cost-effectiveness acceptability curve for conditional cash transfers compared to standard PMTCT care. *ICER, incremental cost-effectiveness ratio; PMTCT, prevention of maternal-to-child transmission.*

Masiano SP, Kawende B, Ravelomanana NLR, Green TL, Dahman B, Thirumurthy H, Kimmel AD, Yotebieng M. *Soc Sci Med* 2023;320:115684. doi: 10.1016/j.socscimed.2023.115684.

Association Between Clinical Encounter Frequency and HIV-Related Stigma Among Newly-Diagnosed People Living with HIV in Rwanda

Hill SE, Zhang C, Remera E, Ingabire C, Umwiza F, Munyaneza A, Muhoza, B, Rwibasira, G, Yotebieng M, Anastos K, Murenzi G, Ross J. *AIDS Behav*. 2023 Dec 19. doi: 10.1007/s10461-023-04226-6.

AIMS:

- To examine whether clinical encounter frequency was associated with change in anticipated, enacted and internalized HIV-related stigma among newly-diagnosed PLHIV living in Kigali, Rwanda.

METHODS:

- **Data:** Newly-diagnosed (within 6 months), adults (≥15 years) PLHIV on ART who enrolled in HIV care at a participating study health center within the 30 days prior to study enrollment.
- **Clinical Encounter Frequency: "**Infrequent encounters" had an average interval between clinical encounters of ≥50 days and "frequent encounters" had an average interval between encounters of <50 days.
- **Stigma Measures:** Anticipated and internalized HIV stigma were measured using the HIV Stigma Framework, Enacted stigma was measured using HIV/AIDS Stigma Instrument.
- **Analysis:** For each type of stigma (anticipated, enacted, and internalized), paired t-tests used to assess change in mean within-group stigma from baseline to 12 months and 6 to 12 months. Bivariate and multivariable linear regression was used to test the association between encounter frequency and mean change in internalized stigma between 6 and 12 months.

Association Between Clinical Encounter Frequency and HIV-Related Stigma Among Newly-Diagnosed People Living with HIV in Rwanda

RESULTS:

- Of 76 participants included in the analysis, 47.4% had infrequent clinical encounters and 52.6% had frequent encounters.
- There was no significant change over time in anticipated (6 to 12 month difference: -0.09; 95% CI: -0.23, 0.06; t=-0.58; p=0.24) or enacted stigma (6 to 12 month difference: 0.02; 95% CI: -0.01, 0.05; t=1.50; p=0.14) among participants with infrequent encounters or those with frequent encounters.
- We observed a significant decrease in the mean internalized stigma score of all participants from baseline to 12 months of -0.75 (95% CI: -0.94,-0.55; t=-7.18; p <0.001) and from 6 months to 12 months of -0.20 (95% CI: -0.35, -0.05; t=-2.55; p=0.01).
- The association between change in internalized stigma and clinical encounter frequency was not significant in bivariate (beta=0.09, 95% CI -0.22 – 0.40, p=0.56) or multivariable regression models adjusted for age, sex, education level, employment status, and baseline quality of life score

Hill SE, Zhang C, Remera E, Ingabire C, Umwiza F, Munyaneza A, Muhoza, B, Rwibasira, G, Yotebieng M, Anastos K, Murenzi G, Ross J. *AIDS Behav*. 2023 Dec 19. doi: 10.1007/s10461-023-04226-6.

East Africa

IeDE

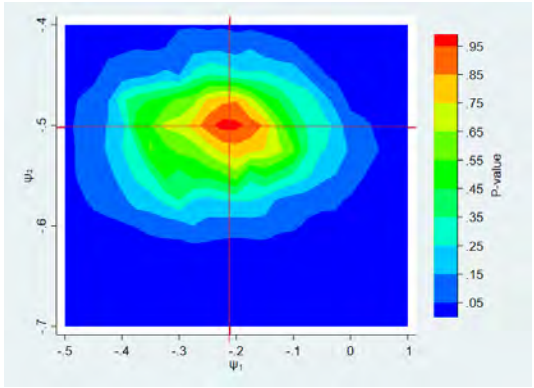
INTERNATIONAL EPIDEMIOLOGY
DATABASES TO EVALUATE AIDS

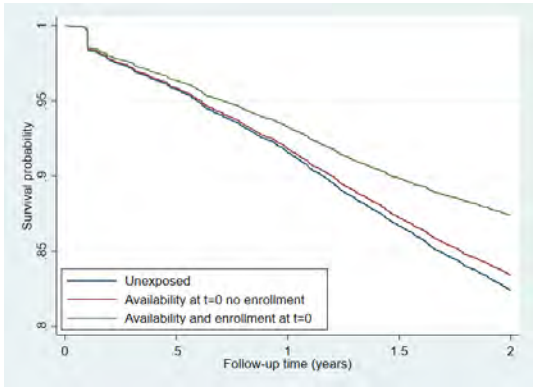
2023 Research Highlights

IeDE

Assessing retention in a program of differentiated care*

- Used a G-estimation approach to make causal inferences about patient attrition (dropout/death) in a program of differentiated care
- Separated the question of program effectiveness into two sub-questions/strategies (vs. no enrollment/exposure to the program):
  - Program available but individual does not enroll
  - Program available and individual enrolls
- Used G-estimation to overcome violations of the positivity assumption (i.e., zero probability of enrollment if program unavailable), which precludes use of IPW methods
- Approach mimics randomization of patients into unexposed, exposed/no enrollment, enrollment.
- Estimates of benefit are measures of the difference between observed and counterfactual survival times assuming randomization.





- The CI for ψ_1, the coefficient associated with program availability includes zero (no difference from unexposed group)
- The CI for ψ_2, the coefficient associated with program enrollment excludes zero (benefit of enrollment is significantly larger than no exposure)
- Benefit is associated with enrollment not mere availability (Figure 1).
- The adjusted survival curves support this assessment (Figure 2).

* Yiannoutsos et al., *Int J Biostatistics*, 2024.

Social support and the effects of the COVID-19 pandemic among a cohort of people living with HIV (PLWH) in Western Kenya

Study design: COVID-19 survey with open ended questions and *Networks* study baseline data.

Setting: Two clinics

- FACES in Kisumu
- AMPATH in Eldoret

Networks cohort

- Completed both COVID-19 surveys in June-July 2020 and May-June 2021
- Patient Health Questionnaire-2 (PHQ-2) was used to measure symptoms of current depression
- Generalized Anxiety Disorder (GAD-2) to assess generalized anxiety disorder symptoms
- Anti retroviral adherence
- Social support (SS)
  - Material
  - Emotional
  - HIV-related
  - Health-related
  - Mental-health related
  - Spiritual/religious
  - Open-ended SS networks

Analysis:

- Quantitative
  - Descriptive - to describe the sample
  - Bivariate to assess demographic and social support factors associated with symptoms of depression and anxiety, and problems related to ARV adherence

- Qualitative
  - Guided by quantative findings
  - content code, categorize, and sort participant answers based on our a priori questions
  - quantified the most frequently mentioned categories of concerns about the pandemic across both years
  - sorted the sample by how participants answered survey questions about their networks (network size, changes)
  - within each category, assessed how participants talked about their networks and forms of support to assess patterns
  - sorted participants by self-reported depression, anxiety, and adherence issues to assess the intersections with their social networks in terms of size, forms of support, and changes over the pandemic

Mburia-Mwalili et al., (2023) PLOS Public Health

Social support and the effects of the COVID-19 pandemic among a cohort of people living with HIV (PLWH) in Western Kenya

Results:

- 174 Networks participants
- 130 completed both COVID-19 surveys in 2020 and 2021
- Mean age 36.6 years: range 20-62 years
- Sex: Female 82 (63.1%).

Quantitative

In 2021, several statistically significant associations between mental health, social support, and network characteristics trends in bivariate analyses were noted (Table 1).

Qualitative

- COVID-19 concerns around infection and safety protocols were most commonly mentioned in both years by nearly half the sample.
- Social networks primarily consisted of family and close ties that endured through the challenges
- Those who said the size of their network had not changed, nearly 20% reported that the forms of support that they give or receive had decreased due to the pandemic.

  "*The people I interact with have remained the same but with very less support compared to the last survey*"

Conclusion

Our findings call for holistic approaches to HIV care that consider the broader political, economic, and social contexts that shape its effectiveness.

Table 1: 2021 COVID-19 survey: social support and other factors associated with depressive symptoms (PHQ-2*)

Characteristic	Second COVID survey May-June 2021 Depression symptoms n = 56 (43.1%)	 No depression symptoms n = 74 (56.9%)	 p-value
Material support			0.0087§
More	8 (14.5)	3 (4.1)	
Same	5 (9.1)	20 (27.0)	
Less	42 (76.4)	51 (68.9)	
Emotional support			0.010§
More	8 (14.5)	3 (4.1)	
Same	8 (14.5)	25 (33.8)	
Less	39 (70.9)	46 (62.2)	
HIV support			0.0010§
More	10 (18.2)	3 (4.1)	
Same	9 (16.4)	31 (41.9)	
Less	36 (65.5)	40 (54.1)	
Health support			0.0027§
More	5 (9.1)	1 (1.4)	
Same	8 (14.5)	28 (37.8)	
Less	42 (76.4)	45 (60.8)	
Mental health support			0.0187§
More	7 (12.7)	3 (4.1)	
Same	10 (18.2)	28 (37.8)	
Less	38 (69.1)	43 (58.1)	
Spiritual support			0.035
More	9 (16.4)	6 (8.1)	
Same	10 (18.2)	28 (37.8)	
Less	36 (65.5)	40 (54.1)	
Marital status			0.026
Married	41 (74.5)	41 (55.4)	
Not married	14 (25.5)	33 (44.6)	
Site			<.0001
FACES (Kisumu)	50 (89.3)	17 (23.0)	
AMPATH (Eldoret)	6 (10.7)	57 (77.0)	

*§ Fishers Exact Test
* Patient Health Questionnaire-2 (PHQ-2)

Mburia-Mwalili et al.,(2023) PLOS Public Health

Mortality among HIV-infected adults on Antiretroviral Therapy in Southern Uganda

Study design:

- A prospective analysis of retrospective data on an adult cohort initiating ART at two clinics within Rakai, Uganda (2014-2018)

- **Data source for tracing:** Files for patients with missed appointments were reviewed to ascertain tracing status by the Outreach Program

Data analysis software: Stata

Outcomes and definitions:

- Primary outcome of interest: Mortality

Statistical methods:

The Frangakis and Rubin method was used to estimate mortality rates adjusted for LTFU with weights

Weights were computed as follows:

LTFU and successfully traced: weight was equal to the proportion of those LTFU divided by those outreached and located

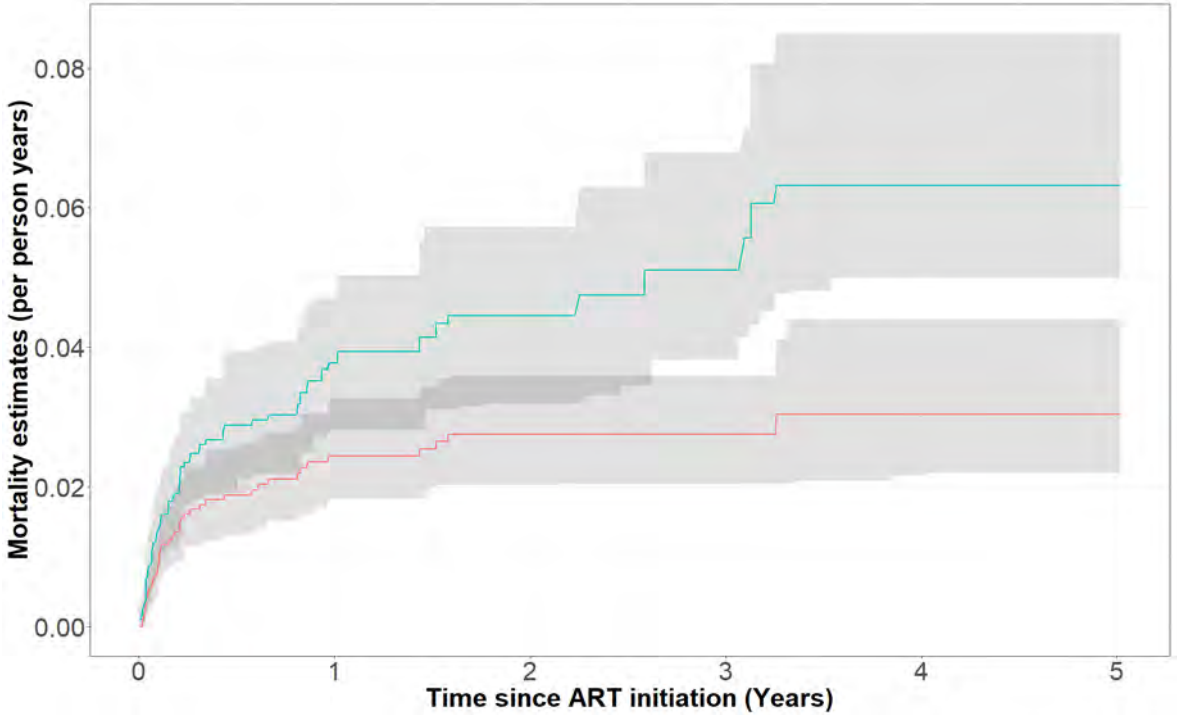
Never LTFU: weight was equal to 1

We used bootstrap and simulation methods for computing 95% confidence Intervals

Dorean Nabukalu et al, JAIDS 2023

East Africa IeDE INTERNATIONAL EPIDEMIOLOGY DATABASES TO EVALUATE AIDS

Mortality among HIV-infected adults on Antiretroviral Therapy in Southern Uganda



- The estimate of mortality rate after tracing (adjusted estimate), was almost 2 times higher than the rate estimated without tracing data (unadjusted estimate)

Figure 1: Unadjusted (red) and adjusted (green) mortality estimates with 95% CI for adult patients living with HIV/AIDS initiated on ART in two RHSP clinics from 2014 to 2018

Dorean Nabukalu et al, JAIDS 2023

East Africa IeDEA
INTERNATIONAL EPIDEMIOLOGY DATABASES TO EVALUATE AIDS

Pre-Switch Regimens Influence the Rate of Weight Gain After Switch to Tenofovir Disoproxil Fumarate, Lamivudine, and Dolutegravir (TLD): Study from East African Cohort.

- It remains unclear whether the increased weight gain seen with INSTI is an off-target drug effect or whether older agents (ie. EFV and TDF) limit natural weight gain.
- Using the AMPATH cohort, we evaluated changes in the rate of weight gain among treatment-experienced, virally suppressed PWH who switched from NNRTI-based regimens to TLD.
- We modeled the weights pre- and post-switch using a two-phase model, and estimated an 18-month excess weight gain by comparing the projected weight to that expected using the pre-switch rate.

18,662 individuals were included in our analysis:

55% switching from EFV and 45% from NVP.

51% were female

Median age: 51 years

Median BMI: 22 kg/m^2

INSTI: Integrase strand transfer inhibitors; EFV: Efavirenz; TDF: Tenofovir Disoproxil Fumarate; PWH: Persons with HIV; AMPATH: Academic Model Providing Access to Healthcare; NNRTI: Non-nucleoside reverse transcriptase inhibitors; NVP: Nevirapine; BMI: Body mass index *(Open Forum Infectious Diseases, Bourgi et al, Dec 2023)*

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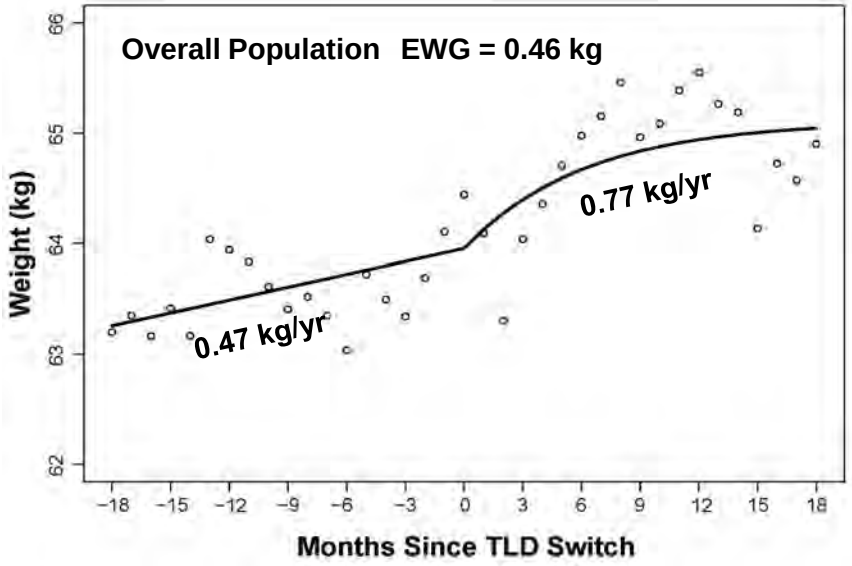
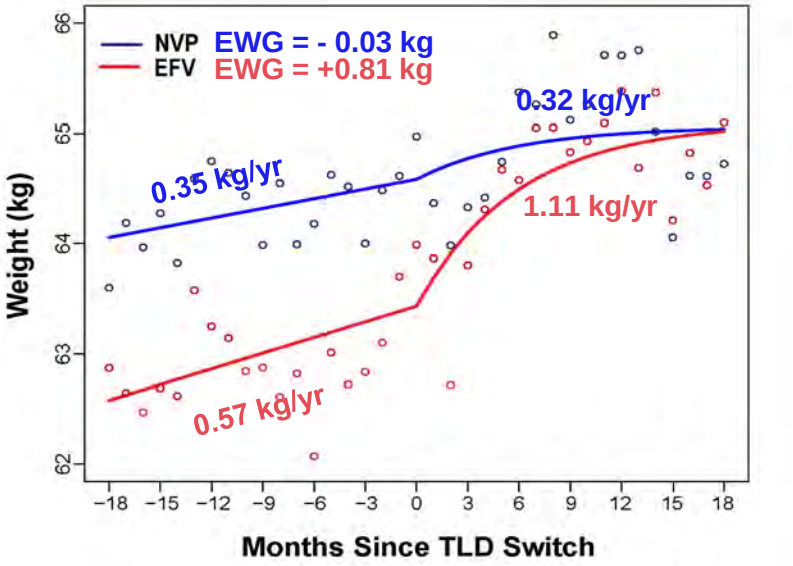
Results and Conclusions:





- ✓ Switching from NNRTI to TLD is associated with a modest increase in the rate of weight gain
- ✓ Pre-switch NNRTI is the key determinant of the amount of weight gain experienced post-switch (EFV >> NVP).

Accepted Manuscript: Bourgi K, Ofner S, Musick B, Wools-Kaloustian K, Humphrey JM, Diero L, Yiannoutsos CT, Gupta SK. Pre-Switch Regimens Influence the Rate of Weight Gain After Switch to Tenofovir Disoproxil Fumarate, Lamivudine, and Dolutegravir (TLD): Study from East African Cohort. **Open Forum Infectious Diseases.** 2023

EFV: Efavirenz; NVP: Nevirapine; EWG: Excess Weight Gain (Difference between projected weight and expected weight using pre-switch rate)

Population-Based Estimates and Predictors of Child and Adolescent Linkage to HIV Care or Death in Western Kenya*

Data Sources and Parent Study

- Home-based counseling and testing (HBCT) data
- AMPATH Medical Record System (AMRS) data
- Outcomes II follow-up study of those children and adolescents (CAs) not identified in AMRS

Setting

- Bunyala, Chulaimbo, and Teso North sub-counties, Western Kenya

Eligibility criteria

- Children and adolescents were eligible for inclusion in our analysis if they were:
  - Younger than 18 years
  - HIV-positive during an HBCT testing visit (either self-reported as prior positive or testing positive at that visit; data were taken from the visit where the child or adolescent was first identified as positive if data from > 1 HBCT visit was available)
  - If they had not enrolled in HIV care before being identified as positive at their first HBCT visit.

Outcomes

- *Time to linkage to care* - time from the first positive HIV result according to HBCT (origin) to the time when a child or adolescent completed a clinical encounter with an HIV care provider as documented in AMRS or identified as linked to care through the Bunyala follow-up study.
- *Time to death* - time from the first positive HIV test result from HBCT (origin) to the time a child or adolescent died as documented in AMRS or as identified in the Bunyala follow-up study.

Analytic methods

- Linkage to care was defined among CAs diagnosed with HIV through AMPATH's HBCT initiative by merging HBCT and AMRS data.
- Using follow-up data from Bunyala, we examined factors associated with linkage or death, using weighted multinomial logistic regression to account for selection bias from double-sampled visits.
- Based on the estimated model, we imputed the trajectory for each person in 3 sub-counties until a simulated linkage or death occurred or until the end of 8 years when an individual was simulated to be censored.

DeLong et al, JAIDS, 2023

*Content on this slide is verbatim from the published paper.

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Population-Based Estimates and Predictors of Child and Adolescent Linkage to HIV Care or Death in Western Kenya

Results

- Of 720 children and adolescents (CAs) in the analytic sample, 68% were between 0 and 9 years and 59% were female.
- Probability of linkage among CAs in the combined 3 sub-counties was 48%–49% at 2 years and 64%–78% at 8 years while probability of death was 13% at 2 years and 19% at 8 years.
- Single or double orphanhood predicted linkage (adjusted odds ratio [aOR]: 2.66, 95% confidence interval [CI]: 1.33 to 5.32) and death (aOR: 9.85 [95% CI: 2.21 to 44.01]).
- Having a mother known to be HIV-positive also predicted linkage (aOR = 1.94, 95% CI: 0.97 to 3.86) and death (aOR: 14.49, 95% CI: 3.32 to 63.19).

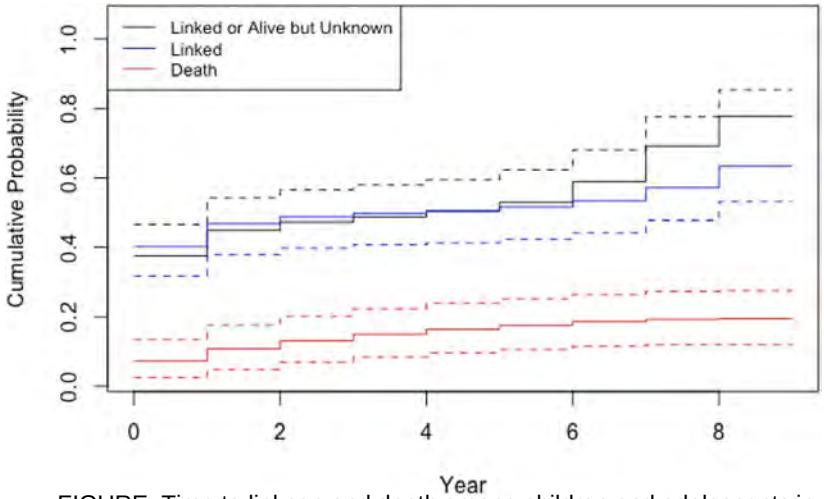

FIGURE. Time to linkage and death among children and adolescents in Bunyala, Teso North, and Chulaimbo sub-counties in western Kenya. The red dashed lines are credible intervals. Blue and black lines indicate that the true linkage probability has more than 95% chance of lying in this range. There is no upper bound for the blue line and no lower bound for the black line. The average lower bound early in the figure may be slightly higher than the higher bound as a result of stochasticity, being imputed separately.

DeLong et al, JAIDS, 2023

*Content on this slide is verbatim from the published paper.

IeDEA Southern Africa

Research highlights 2023

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Hospitalization among infants who initiate antiretroviral therapy (ART) age <3 months

Background

- Routine birth HIV-PCR testing was implemented in 2015 in SA, enabling earlier diagnosis, and a standardised first-line ART regimen was introduced for neonates <4 weeks old
- Shifting to earlier diagnosis and ART start in young infants is expected to reduce morbidity and mortality
- Studies examining hospitalization among infants with HIV in resource-limited settings, in the context of early infant diagnosis and early ART initiation, are limited

Methods

- We identified infants with HIV who started ART at age <3 months in the Western Cape province between 2013-2017
- We used routine electronic data from the Western Cape Provincial Health Data Centre, including hospitalisation and mortality data, from birth until 12 months after ART start
- We also performed medical record reviews of infants who attended 3 tertiary-level facilities for HIV outpatient care, to more closely examine reasons for hospitalisation
- We used mixed-effects Poisson and logistic regression to examine factors associated with hospitalisation (excluding early neonatal admissions at age <7 days), clustered by infant and adjusted for potential confounders: infant sex, previous birth admission or low birthweight, and exposure to infant PMTCT drugs were assigned as potential confounders a priori. CD4% and viral load (VL) at baseline were evaluated as potential mediators in separate models

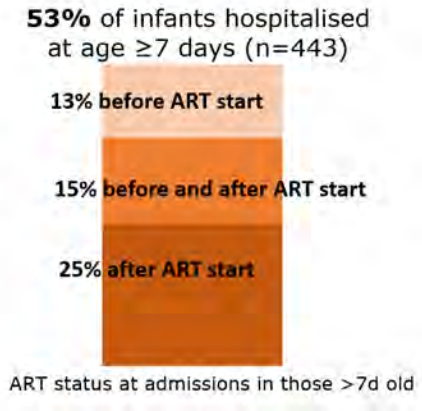
Anderson et al. AIDS. 2023. http://doi.org/10.1097/QAD.0000000000003422

IeDEA

Hospitalization among infants who initiate antiretroviral therapy (ART) age <3 months

Results

- 840 infants initiated ART at age <3 months in the Western Cape (2013-2017)
- Of these, median age at ART initiation decreased from 57 days (IQR 22-74; 2013-2015) to 19 days (IQR 5-54; 2016-2017), after introduction of birth HIV testing 579 infants (69%) were hospitalised; 36% had more than one hospitalization
- Starting ART at older age vs. <1 week was associated with increased hospitalisation rates (at age ≥7 days):
  aIRR (95% CI) 1.86 (1.31-2.64) for age 1-4 weeks
  2.31 (1.62-3.29) for age 5-8 weeks
  2.47 (1.76-3.46) for age 9-12 weeks
- Starting ART at older age vs. <1 week was associated with much higher infectious-cause admission odds:
  aOR (95% CI)* 2.80 (1.27-6.17) for age 1-4 weeks
  16.93 (6.39-44.84) for age 5-8 weeks
  17.80 (6.89-45.99) for age 9-12 weeks
  (*analysis done on 272 patients with detailed folder review data for cause of admission)



Conclusions

- High hospitalisation incidence observed both prior to ART start and after ART start, despite ART start before age 3 months, is concerning
- Later ART start is associated with higher rates of hospitalisation, before and after ART start; the association is partially mediated by higher VLs and lower CD4s at ART start
- Birth testing, early infant diagnosis and early infant ART initiation are important

Anderson et al. AIDS. 2023. http://doi.org/10.1097/QAD.0000000000003422

Cervical precancer and cancer incidence among insured women with and without HIV in South Africa

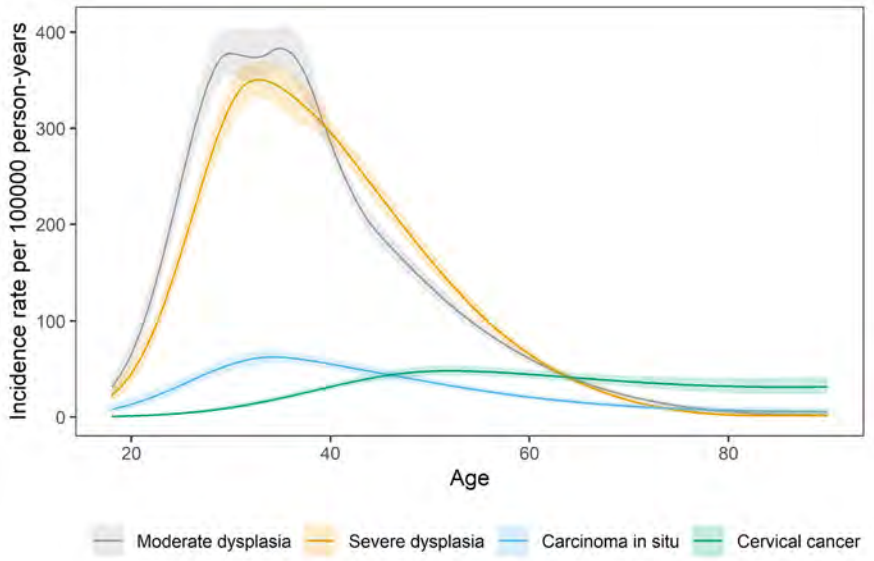


Figure 1. Incidence rate per 100 000 person-years as a function of age, by endpoint of interest. The shaded areas represent 95% confidence intervals.

Methods: We compared cervical precancer and cancer incidence rates between women with and without HIV in South Africa, using reimbursement claims data from a medical insurance scheme from January 2011 to June 2020.

We used Royston-Parmar flexible parametric survival models to estimate cervical precancer and cancer incidence rates as a continuous function of age, stratified by HIV status.

Results (I): Irrespective of HIV status, incidence rates of precancerous cervical lesions were highest among women in their mid-thirties. In contrast, cervical cancer rates increased from the age of 30 years until women reached their fifties (Figure 1).

Fernandez Villalobos et al. Int. J. Cancer. 2024;154:273–283. doi: 10.1002/ijc.34707

Cervical precancer and cancer incidence among insured women with and without HIV in South Africa

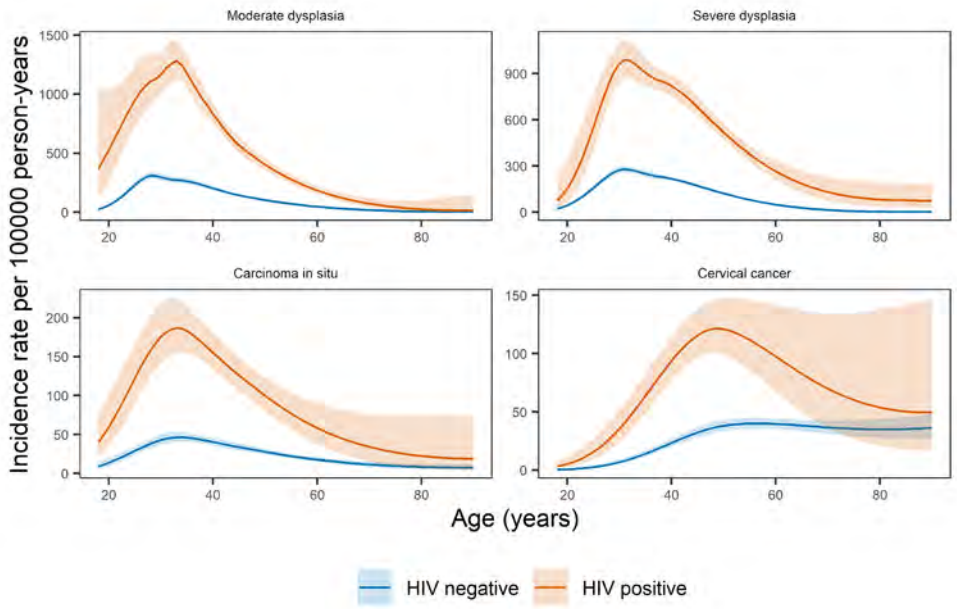


Figure 2. Incidence rate per 100 000 person-years as a function of age and HIV status, by endpoint of interest. The shaded areas represent 95% confidence intervals.

Results (II): Cervical precancer and cancer rates were approximately three times higher among women with HIV than women without HIV (adjusted hazard ratio for cervical cancer: 2.99; 95% confidence interval: 2.40-3.73; Figure 2).

Conclusions: Although the relative contribution of HIV to the incident cancer burden was highest among young women, middle-aged WLWH carried the highest cervical cancer burden in absolute terms.

Analyses of age-specific cervical precancer and cancer rates by HIV status are essential to inform the implementation of targeted cervical cancer prevention policies in regions with a high burden of both HIV and cervical cancer.

Fernandez Villalobos et al. Int. J. Cancer. 2024;154:273–283. doi: 10.1002/ijc.34707

DTG Resist: HIV-1 subtype-specific drug resistance in patients failing Dolutegravir-based first-line, second-line or third-line regimens: multiregional study

Background

- Dolutegravir (DTG) is a second-generation Integrase Strand Transfer Inhibitor (InSTI) recommended by the WHO for 1st, 2nd and 3rd-line Anti-Retroviral Treatment for adults and adolescents.
- Development of DTG resistance is a concern: Pre-existing InSTI resistance, resistance to backbone drugs, or use of DTG as monotherapy is associated with a higher risk of viral failure and/or DTG resistance.

Aims and Methods

1. Determine the patterns and spectrum of InSTI Drug Resistance Mutations (DRMs) in people failing a DTG-based regimen.
   - Prospective recruitment of people living with HIV on any DTG-based ART regimen and developing virologic failure (viral load >1000 copies/mL). Whole genome sequencing is performed on blood samples collected at the time of failure to identify InSTI Drug Resistance Mutations.
   - Data collected from prospective enrollment (prospective arm) will be combined with existing data from South African, North American and European cohorts (retrospective arm).
2. Identify the risk factors for the development of virologic failure and InSTI DRMs.
   - Data from the prospective arm will be linked to the IeDEA routine data for the risk factor analysis (including drug, host and health system factors).
3. Investigate correlations between novel resistance genotypes and phenotypic DTG resistance across HIV-1 subtypes.
   - Phenotypic testing will be done in 100 selected samples to identify the phenotypic relevance of the observed resistance mutations.
   - Novel pathways or mutations relevant for DTG resistance will be investigated by exploratory analyses such as viral Genome-Wide Association Studies (GWAS) or Conjunctive-Bayesian-Networks (CBN)

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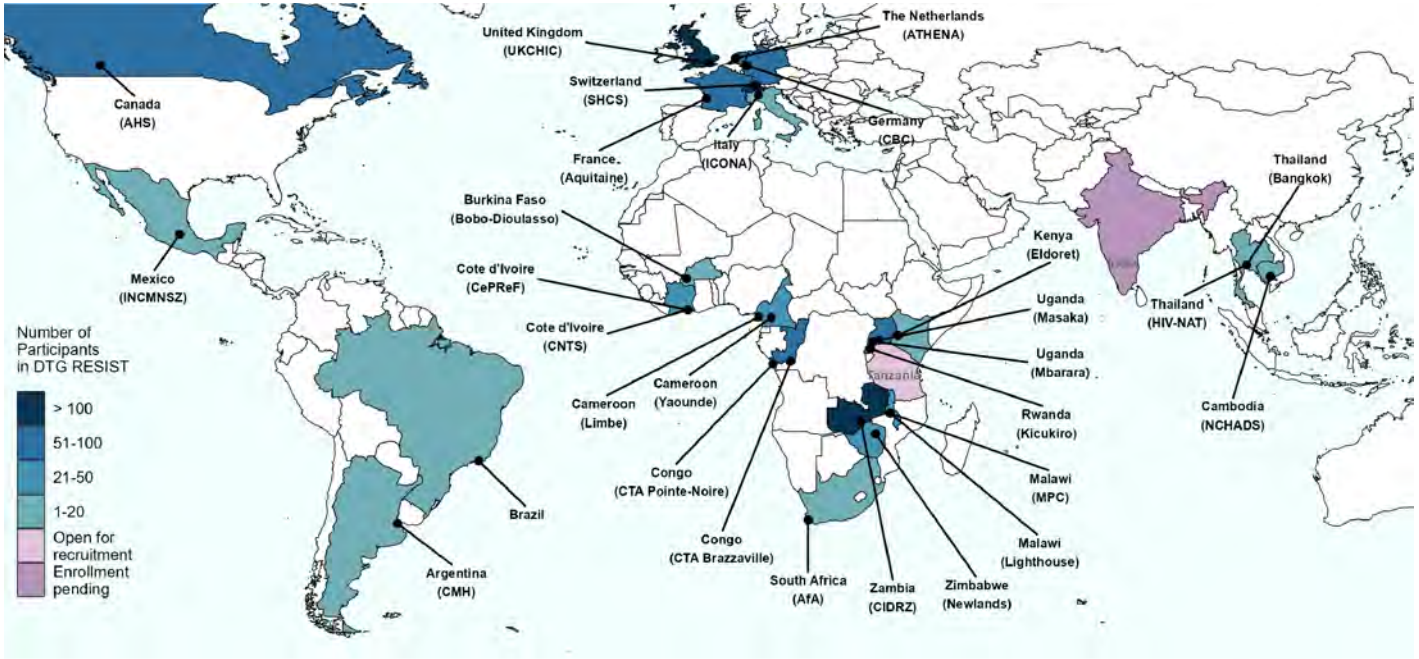
DTG Resist: HIV-1 subtype-specific drug resistance in patients failing dolutegravir-based first-line, second-line or third-line regimens: multiregional study

Data for the DTG Resist study is collected from 24 countries: 8 in the retrospective arm (HIV cohort collaboration), and 16 in the prospective arm, where the recruitment is currently ongoing. 1 country is awaiting ethical approval.



Authorship inequalities in global health research: the IeDEA Southern Africa collaboration

Background

- Research on research has systematically shown gender imbalance in research output worldwide and under-representation of local researchers as authors in studies conducted in global South.
- We assessed authorship inequalities by gender and (income level of) country of affiliation in IeDEA-SA publications.

Methods

- We identified 313 IeDEA-SA publications from years 2007–2020 for the analysis.
- We defined *standardized authorship position* (SAP) as percentiles on the authorship list (first: 0%, last: 100%).
- We used generalized multinomial regression to assess differences in SAP, with focus on comparing first/last vs. central authorship position, by gender and affiliation.

Results

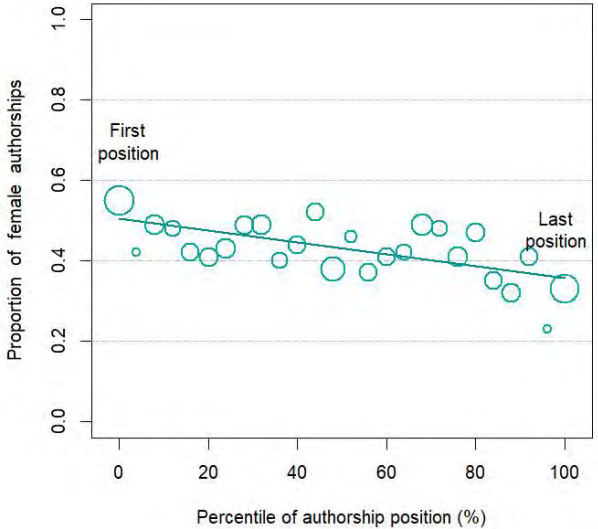
Table: *Characteristics of authors and authorships from 313 articles published by the IeDEA-SA in 2007 to 2020.*

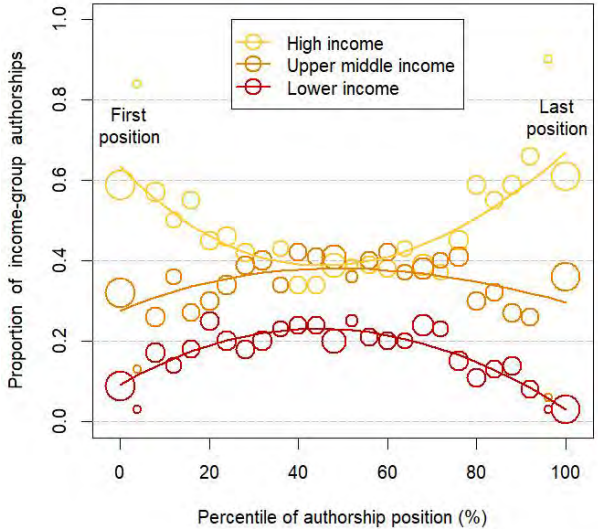
	Authors N (%)	***Author-ships N (%)***	***No. of articles per author Mean (SD)***	***First author-ships N (%)***	***Last author-ships N (%)***
Total	1064	3421	3.2 (8.2)	313	311*
Gender					
Women	547 (51.4%)	1480 (43.3%)	2.7 (6.2)	173 (55.3%)	104 (33.4%)
Men	517 (48.6%)	1941 (56.7%)	3.8 (9.9)	140 (44.7%)	207 (66.6%)
Country of affiliation					
High income	557 (52.3%)	1679 (49.1%)	3.6 (10)	184 (58.8%)	190 (61.1%)
Upper-middle income	275 (25.8%)	1187 (34.7%)	3.5 (7.2)	100 (31.9%)	112 (36%)
Lower income	232 (21.8%)	555 (16.2%)	1.9 (2.5)	29 (9.3%)	9 (2.9%)

Skrivankova VW et al (2023). BMJ Global Health. DOI: 10.1136/bmjgh-2023-013316

Authorship inequalities in global health research: the IeDEA Southern Africa collaboration

Figure: *Proportion of female authorships across the range of standardised authorship position, with a weighted linear regression line (left) and proportion of authorships by country income level with weighted cubic splines (right). The size of the circles is proportional to the number of authorships in each position.*





Women were more likely to publish as first authors, OR = 1.78 (1.09-2.92), and less likely as last authors, OR = 0.59 (0.37-0.94), than men.

LIC authors were less likely to publish as both first authors, OR = 0.30 (0.16-0.57), and last authors, OR = 0.15 (0.06-0.34), than HIC authors.

Conclusions & Outlook

Inequalities in authorship positions by gender and income level should be addressed.

The IeDEA-SA is committed to promote equity in research collaborations, and its authorship guidelines are currently under revision.

IeDEA-SA plans to continue monitoring authorship inequalities in its publications.

Skrivankova VW et al (2023). BMJ Global Health. DOI: 10.1136/bmjgh-2023-013316

Effect of the Friendship Bench intervention on antiretroviral therapy outcomes and mental health symptoms in rural Zimbabwe: A cluster randomized trial

POPULATION

78 Men, 438 Women

Adults living with HIV who screened positive for common mental disorders

Mean age, 45.6 y

INTERVENTION

16 Health facilities (516 participants) randomized

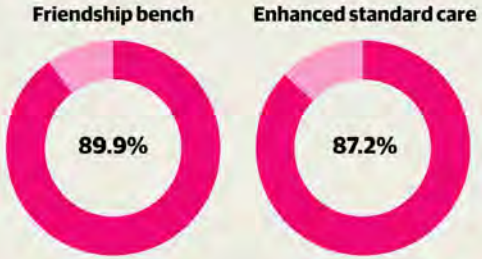
8 Facilities (244 participants)
Friendship Bench
Enhanced standard care care plus 6 weekly counseling sessions by lay workers and peer-led group support

8 Facilities (272 participants)
Enhanced standard care
Nurse-led brief counseling session plus antidepressant prescription and psychiatric care referral as needed

FINDINGS

There was no significant difference between the 2 groups in mean monthly medication adherence between 2-6 mo

Mean monthly medication adherence, 2-6 mo



Unadjusted mean difference, 1.93 percentage points; 95% CI, -1.20 to 5.06 percentage points; P = .23

SETTINGS / LOCATIONS

16 Health facilities in rural Zimbabwe

PRIMARY OUTCOME

Mean monthly medication adherence between 2-6 mo (%), as measured using electronic pillboxes and calculated as the proportion of days that the box was opened the expected number of times based the antiretroviral regimen

Haas AD, Kunzekwenyika C, Manzero J, et al; Friendship Bench ART trial group. Effect of the Friendship Bench intervention on antiretroviral therapy outcomes and mental health symptoms in rural Zimbabwe: a cluster randomized trial. *JAMA Netw Open*. 2023;6(7):e2323205. doi:10.1001/jamanetworkopen.2023.23205

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Effect of the Friendship Bench intervention on antiretroviral therapy outcomes and mental health symptoms in rural Zimbabwe: A cluster randomized trial

Secondary outcomes

- The intervention had no statistically significant effect on viral suppression (viral loads <1000 copies/mL) at 6 and 12 months or on Patient Health Questionnaire (PHQ-9) scores, at 3, 6, 9, and 12 months, a measure of depression symptoms.
- The intervention had a modest effect on Shona Symptom Questionnaire (SSQ-14) scores, a measure of symptoms of depression and anxiety.

West Africa - IeDEA

Research highlights 2023

IeDEA

Effects of the Covid-19 pandemic on ART initiation and access to HIV viral load monitoring in adults living with HIV in West Africa: a regression discontinuity analysis

Jihane Ben Farhat, Thierry Tiendrebeogo, Karen Malateste, Armel Poda, Albert Minga, Eugène Messou, Henri Chenal, Oliver Ezechi, Igho Ofotokun, Didier k. Ekouevi, Fabrice Bonnet, Diana Barger, Antoine Jaquet, ***JAIDS (Ahead of print)***

Introduction

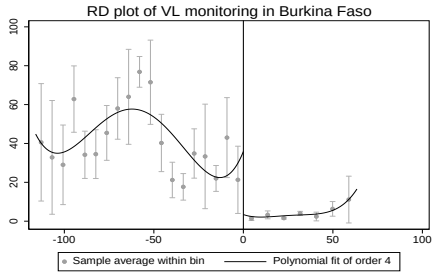
- HIV testing, access to ART and viral suppression remain suboptimal in western and central Africa compared to other regions
- Region with the third highest burden of PLWH in the world, with five countries accounting for approximately 2/3 of all PLWH in the region, including **Côte d'Ivoire** and **Nigeria**
- COVID-19 pandemic and its response have posed several challenges to the global fight to end the HIV pandemic

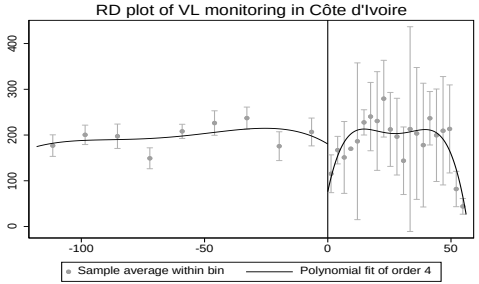
Objective: To document the impact of the COVID-19 pandemic on initial stages of HIV care in West Africa by evaluating the evolution of number of ART initiations and of HIV viral load tests conducted

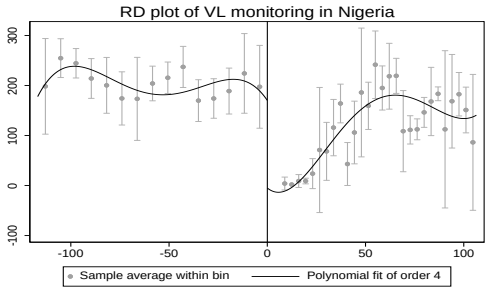
Method: Regression Discontinuity Design (RDD) to estimate changes in the number of ART initiations and HIV VL tests in 5 HIV care programs contributing to the IeDEA West Africa collaboration (CMSDS, CIRBA, CePReF, **Abidjan, Côte d'Ivoire**/ HDJ, **Bobo Dioulasso, Burkina Faso**/NIMR, **Lagos, Nigeria**)

Results

- HIV clinics in two out of three countries in West Africa demonstrated resilience as they successfully maintained access to ART for ALWH despite the challenges imposed by the pandemic
- VL monitoring was significantly disrupted and did not return to pre-pandemic levels one year after in 2021







Conclusion

- Adaptability and effectiveness of HIV programs to mitigate the effects of the crisis in West Africa
- Disruptions to VL testing in these settings raise concerns about the ongoing impact of the pandemic on the availability, quality and comprehensiveness of HIV care
- Importance of closely monitoring the HIV continuum of care in the post-pandemic era to ensure that documented disruptions in services do not have lasting effects on virological and clinical outcomes of ALWHs

Impact of HIV infection on access to cancer care and survival among women with invasive cervical cancer in Côte d'Ivoire: A prospective cohort study

Simon P Boni, Apollinaire Horo, Judith Didi-Kouko-Coulibaly, Aristophane Tanon, Boris K Tchounga, Patrick A Coffie, Jean-Claude Comoe, Raoul D Moh, François Dabis, Innocent Adoubi , Antoine Jaquet. ***Int J Gynaecol Obstet.*** *2023 Nov;163(2):392-401.*

Aim:

To assess the impact of HIV on access to invasive cervical cancer (ICC) care and overall survival (OS) in a time of universal access to ART

Methods

- A cohort of women prospectively diagnosed with ICC was consecutively recruited from 2018 to 2020 in public/private cancer centers
- Logistic and Cox regression models analysis of factors associated with access to cancer care and OS, respectively

Results

- 294 women with ICC aged 50 years (IQR 43–60) were enrolled, including 21.4% of WLHIV, (87% on ART)
- FIGO III-IV stage was less frequent in WLHIV (63.5% vs. 77.1% in HIV-uninfected women; P = 0.029)
- Cancer care was initiated in 124 (42.2%) women (54.0% in WLHIV; 39.0% in HIV-uninfected; P = 0.030).
- Factors independently associated with access to cancer care were FIGO stage I–II ([aOR] 3.58, 95% CI 2.01–6.38) and no treatment by traditional healers prior to ICC diagnosis (aOR 3.69, 95% CI 1.96–6.96)

Results (2)

- The 2-year OS was **37.9% (95% CI 30.0–47.9)**
- HIV status was not predictive of mortality [aHR] 0.98 (95% CI 0.60–1.69)
- An **advanced clinical stage** was the only measured predictor of death (aHR 1.59, 95% CI 1.02–2.47)

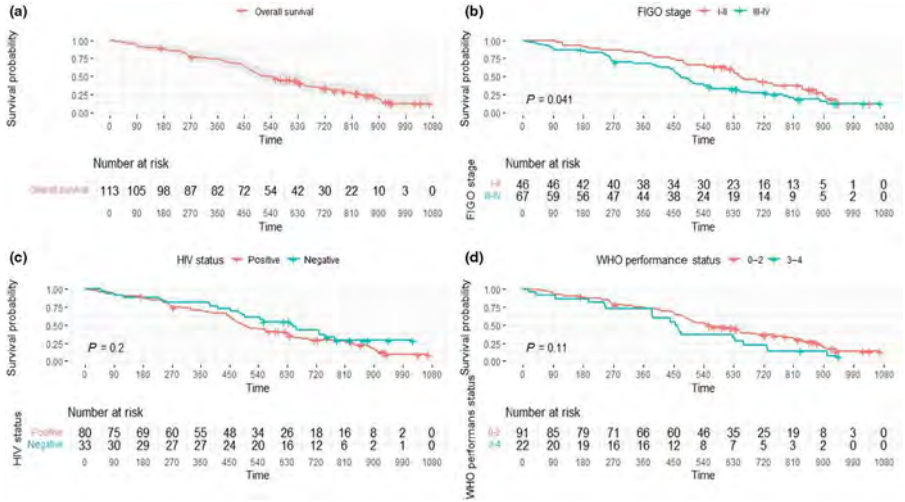


Figure. Overall survival according to HIV status, FIGO stage, and WHO performance status at invasive cervical cancer (ICC) diagnosis among women in Côte d'Ivoire.

- In a time of universal access to ART, HIV infection was not associated with OS among women with ICC in Côte d'Ivoire
- Higher access to cancer care in WLHIV might be mediated by enhanced access to ICC screening services, supporting the need to expand these services to other types of healthcare facilities.

IeDEA

High-risk human papillomavirus distribution according to human immunodeficiency virus status among women with cervical cancer in Abidjan, Côte d'Ivoire, 2018 to 2020

Simon P Boni, Vanessa Tenet, Apollinaire Horo, Daniëlle A M Heideman, Maaike C G Bleeker, Aristophane Tanon, Boston Mian, Isidore D Mohenou, Didier K Ekouevi, Tarik Gheit, Judith Didi-Kouko Coulibaly, Boris K Tchounga, Innocent Adoubi, Gary M Clifford, Antoine Jaquet. ***Int J Cancer*** *2023 [Ahead of print].*

Introduction

As national HPV immunization programs are increasingly being rolled-out across SSA, including Côte d'Ivoire, it is of utmost importance to document HR-HPV vaccine effectiveness at national level and the potential impact of HIV infection

Aim

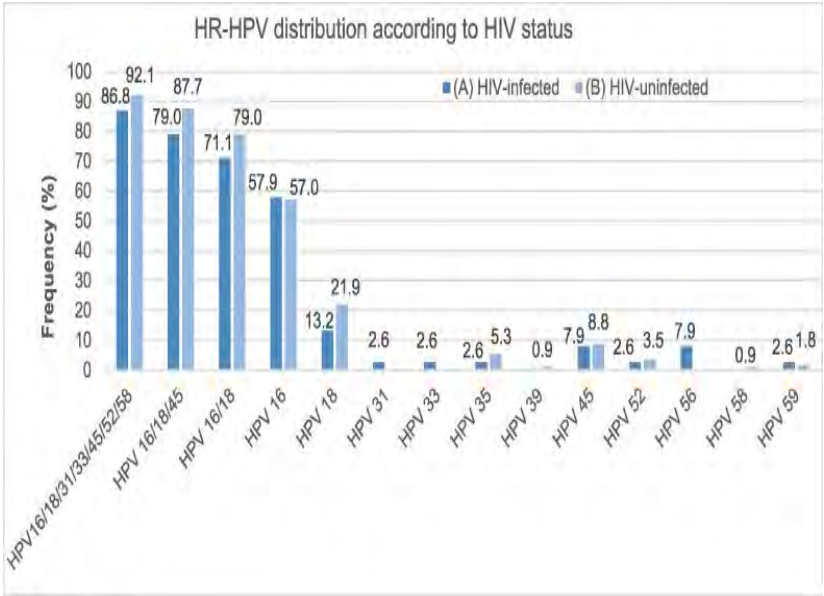
to investigate the HR-HPV distribution in women diagnosed with CC in Côte d'Ivoire, as well as the potential impact of HIV co-infection in a time of universal access to ART

Methods

From July 2018 to June 2020, paraffin-embedded CC specimens diagnosed in Abidjan, were systematically collected and tested for HR-HPV DNA. Type-specific HR-HPV prevalence was compared according to HIV status

Results

- 170 CC specimens analyzed: median age 52 years [IQR: 43.0-60.0]), 25.3% were from WLHIV (median CD4 count : 526 [373-833] cells/mm3; 86% on ART)
- HR-HPV prevalence: 89.4% [95% CI: 84.7-94.1]
- The most prevalent HR-HPV types were HPV16 (57.2%), HPV18 (19.7%), HPV45 (8.6%) and HPV35 (4.6%), with no significant differences according to HIV status
- HPV16/18 : 71.1% [95% CI: 55.9-86.2] in WLHIV vs 78.9% [95% CI: 71.3-86.5] in women without HIV (P = .3)



Conclusions

Major role of HPV16/18 in CC in Côte d'Ivoire, supporting a national/regional scale-up of HPV16/18 vaccination programs regardless of HIV status

Management of depression in people living with HIV/AIDS in Senegal: acceptability, feasibility and benefits of group Interpersonal Therapy

Bernard C, Font H, Ziadeh S, Tine J.M, Diaw A, Ndiaye I, Samba O, Bottai T, Jacquesy L, Verdeli L, Ngom N.F, Dabis F, Seydi M, de Rekeneire N on the behalf of the IeDEA West Africa Cohort Collaboration. ***Global Mental Health****, 2023,10, e36, 1–10*

- **Objective**

To assess the acceptability and feasibility of group Interpersonal Therapy (IPT) combined with a task-shifting approach to treat PLWH with depression in Senegal

- **Methods**

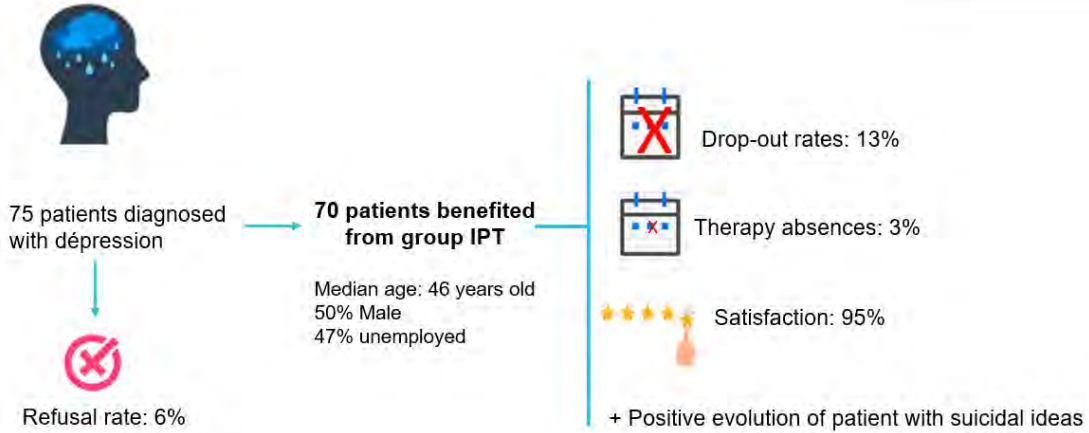
o Screening: PHQ-9 → If score≥5: diagnosis confirmation by a psychiatrist

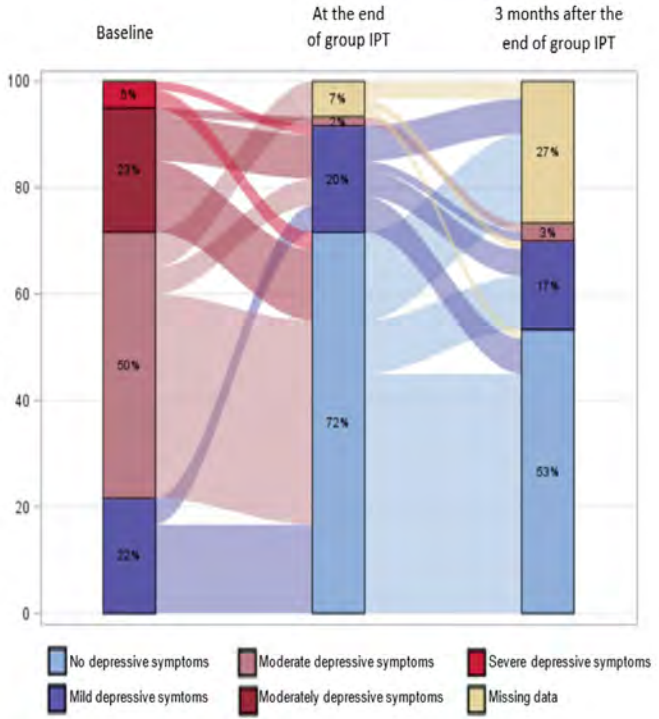
o Application of group IPT: as defined in the WHO manual, administered by social workers or community workers, trained and supervised by an expert trainer

o Assessment of feasibility (refusal rate, percentage of absence) and acceptability (drop-out rate, patients' satisfaction)

o Measure of depressive symptom and disability (WHODAS) improvement between the start, the end of group IPT and 3 month after (paired T-tests, $p<0.05$)

- **Results**





- **Conclusion**

Depressive symptoms and disability improved drastically and sustainably

Group IPT, combined with a task-shifting approach, is well accepted and feasible in a level-3 hospital in Senegal as treatment for depression in PLWH

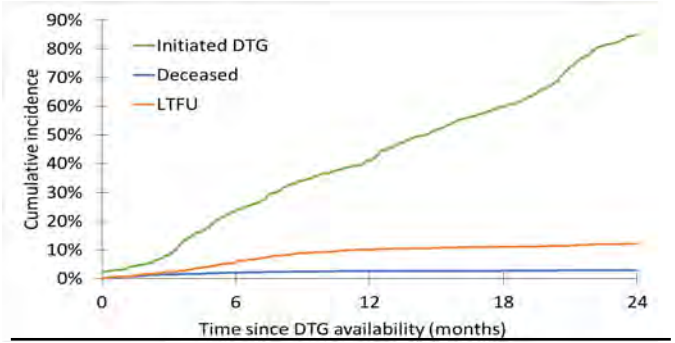
DTG-based ART regimens scale-up in 0-24 year olds living with HIV in West Africa, 2019-2021 (1)

Sophie Desmonde, Agatha David, Karen Malateste, Joycelyne Dame, Sylvie N'Gbeche, Madeleine Amorissani-Folquet, Mariam Sylla, Kouadio Kouakou, Lehila Bagnan Tossa, Elom Takassi, Caroline Yonaba, Valériane Leroy. ***BMJ Global Health*** *(submitted)*

Objective: to document the incidence of initiation of Dolutegravir (DTG)-based antiretroviral therapy (ART) and its determinants in the pediatric West African cohort (pWADA) of IeDEA

Methods

- 3,350 participants seen at least once since 2019
- Cumulative incidence function (CIF) since date of DTG introduction in site and 95%CI
- Cox Frailty model
  - Site heterogeneity (random effect)
  - Baseline: date of DTG introduction in site (or date of ART initiation, whichever came first)
  - Adjusted for sex, baseline age, baseline ART regimen and viral load status



	DTG Cumulative incidence, %	95% CI
6 months	23.6%	[21.6 – 25.6]
12 months	41.3%	[39.0 – 43.6]
18 months	60.0%	[57.7 – 62.3]
24 months	85.1%	[83.3 – 86.6]

In multivariate analyses, DTG transition was associated with :

- **Age and sex:**
  - Less likely in younger children (pediatric formulations unavailable)
  - Boys are more likely to transition to DTG than girls
    - Differences between sex increased with age (in ≥ 15 years, HR: 2.5 [95%CI: 2.1-2.9])

- **Viral suppression:** those failing are less likely to transition
  → Could transition be reserved for clinically stable patients ?

- **Baseline ART regimen:**
  - During the first year, ART naïve children 4x more likely to initiate DTG compared to those on PIs
  - After 12 months of scale-up: "catch-up" effect in those on non PI-based regimens (2 to 3x more likely to initiate DTG compared to those on PIs)
    → Could there be remanent LPV/r in the system before DTG transition?

IeDEA


NA ACCORD
North American
AIDS Cohort Collaboration on Research and Design

Hospital readmissions among persons with HIV in the US and Canada, 2005-2018: A collaboration of cohort studies

Davy-Mendez T*, et al. Journal of Infectious Diseases. 2023 Dec 20;228(12):1669-1708. doi:10.1093/infdis/jiad396.

Background: Hospital readmission trends for persons with HIV (PWH) in North America in the context of policy changes, improved antiretroviral therapy (ART), and aging are not well-known.

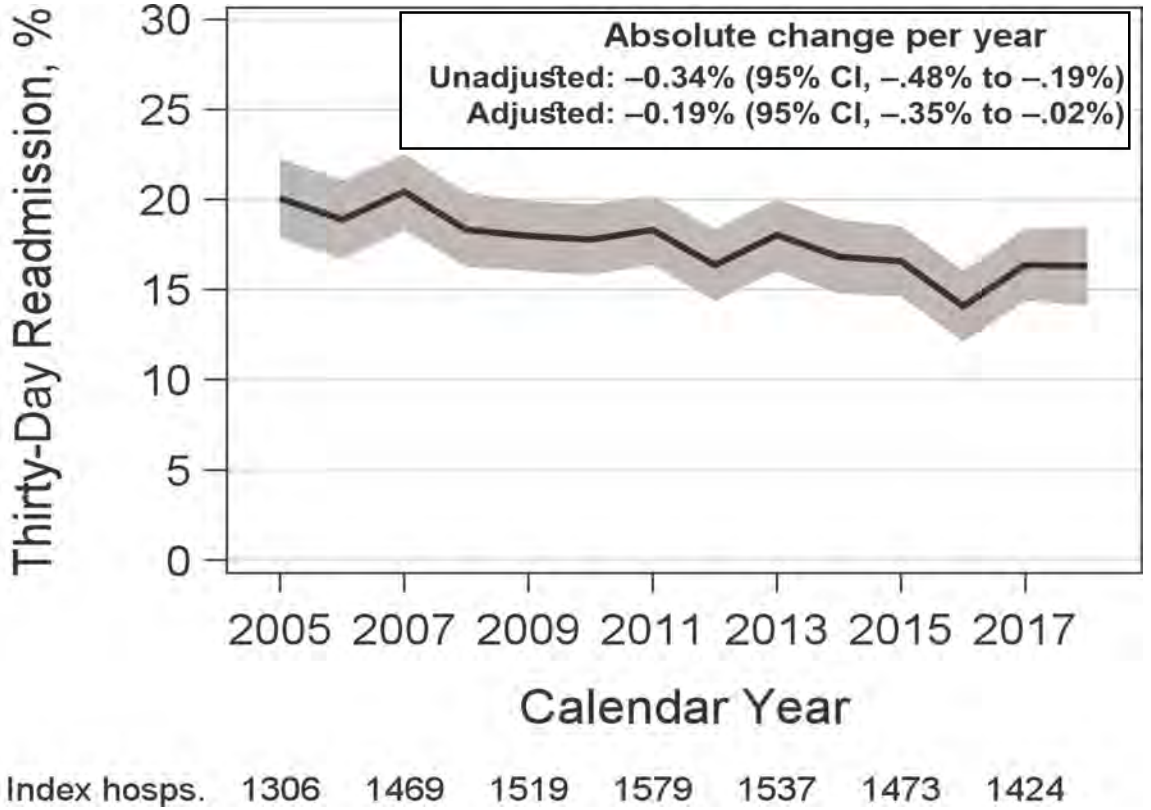
Methods: Using data from the NA-ACCORD, we estimated trends in 30-day hospital readmissions, adjusted for demographics, CD4 count, AIDS history, virologic suppression (<400 copies/mL), and cohort

Results: PWH hospitalized in 2018 versus 2005 had higher median age (54 vs 44 years), CD4 count (469 vs 274 cells/μL), and virologic suppression (83% vs 49%). Unadjusted 30-day readmissions decreased from 20.% (95% CI 18%, 22%) in 2005 to 16% (95% CI 14% ,19%) in 2018. Absolute annual trends were 0.34% reduction in readmissions (95% CI -0.48%, -0.19%) in unadjusted and -0.19% (95% CI -0.35%, -0.02%) in adjusted analyses. By index hospitalization reason, there were significant adjusted decreases only for cardiovascular and psychiatric hospitalizations. Readmission reason was most frequently in the same diagnostic category as the index hospitalization.

Conclusions: Readmissions decreased over 2005-2018 but remained higher than the general population's. Significant decreases after adjusting for CD4 count and virologic suppression suggest that factors alongside improved ART contributed to lower readmissions. Efforts are needed to further prevent readmissions in PWH.

**Davy-Mendez T conducted research in the NA-ACCORD as a pre-doctoral student and post-doctoral fellow. He is currently an Assistant Professor of Medicine at the University of North Carolina - Chapel Hill.*

Figure: Unadjusted probability of 30-day hospital readmission over time (shaded area is 95% CI), with unadjusted and adjusted calendar time trends and 95% CI estimates (inset)



The covariates in the adjusted model are age, gender, race/ethnicity, human immunodeficiency virus (HIV) acquisition risk factor, history of AIDS-defining illness, CD4 count and HIV RNA viral load

Hepatitis B care cascade among people with HIV/HBV coinfection in the NA-ACCORD, 2005-2018

Kim J*, et al. PLoS One 2023; Sep 1;18(9):e029889 doi: 10.1371/journal.pone.0290889

Background: A care cascade is a critical tool for evaluating delivery of care for chronic infections across sequential stages, starting with diagnosis and ending with viral suppression. However, there have been few data describing the hepatitis B virus (HBV) care cascade among people with HIV and HBV coinfection (HIV/HBV).

Methods: A cross-sectional study among people living with HIV/HBV coinfection receiving care between January 1, 2012 and December 31, 2016 within 13 NA-ACCORD clinical cohorts.

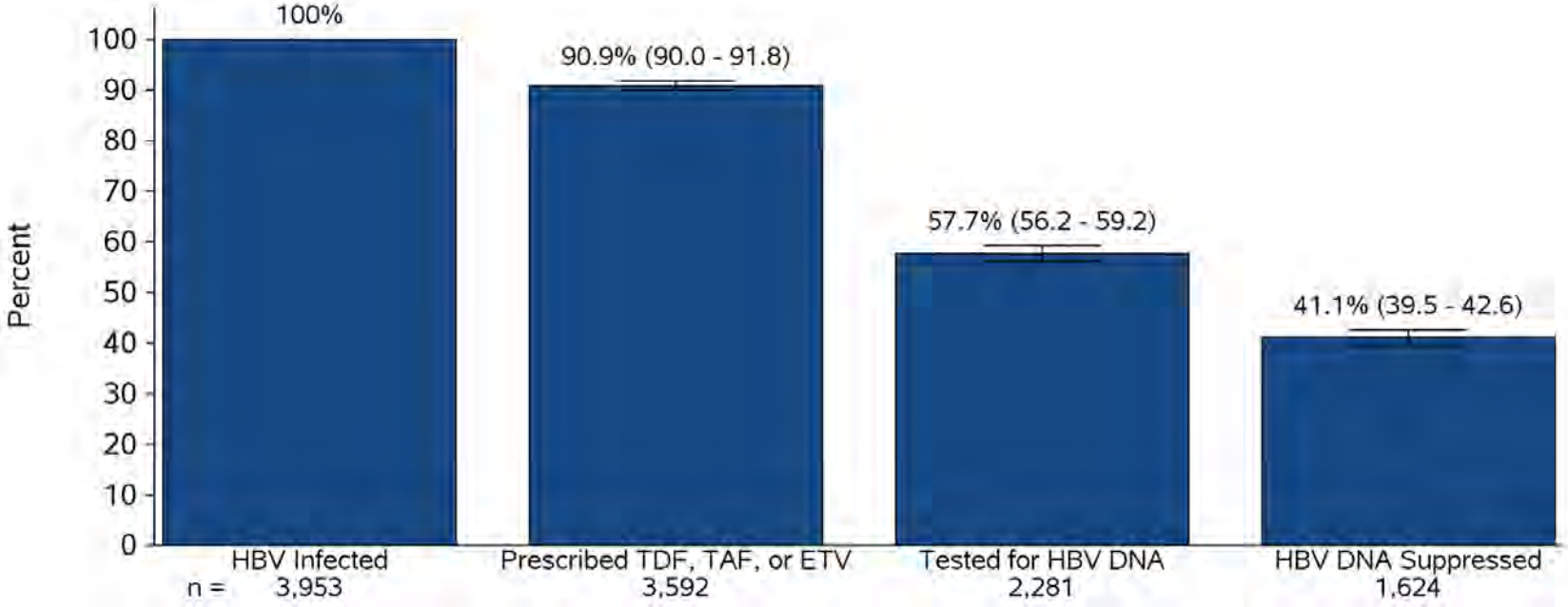
Findings: Among 3,953 persons with laboratory-confirmed HBV (median age, 50 years; 7% female; 44% were Black; 7% were Hispanic),

- 91%, [95% CI 90, 92%] were prescribed tenofovir-based antiretroviral therapy or entecavir along with their antiretroviral therapy regimen
- 55% [95% CI 56, 59%] had HBV DNA measured while on therapy
- 41% [95% CI 40-43%] achieved an undetectable HBV DNA during HBV treatment.

Conclusions: There are significant gaps in measurement of HBV DNA and suppression of HBV viremia among people living with HIV/HBV in the United States and Canada. Periodic evaluation of the HBV care cascade among persons with HIV/HBV will be critical to monitoring success in completion of each step.

**Kim J completed this work as a medical student at Kaiser Permanente Northern California (in partnership with Drexel University College of Medicine and is now a resident physician at UCLA, Los Angeles, California.)*

Figure: Cascade of care among HIV/HBV co-infected persons in the NA-ACCORD, 2012-2016



Abbreviations:
ETV=entecavir
TDF=tenofovir disoproxil fumarate
TAF=tenofovir alafenamide

Optimizing Treatment for Human Immunodeficiency Virus to Improve Clinical Outcomes Using Precision Medicine

Jetsupphasuk M, et al. Am J Epidemiol 2023 Aug 4;192(8):1341-1349.
doi: 10.1093/aje/kwad057.

Background: In first-line ART for HIV, some subgroups of patients may respond better to an efavirenz (EFV)-based regimen than an integrase strand transfer inhibitor (InSTI)-based regimen, or vice versa, due to patient characteristics modifying treatment effects

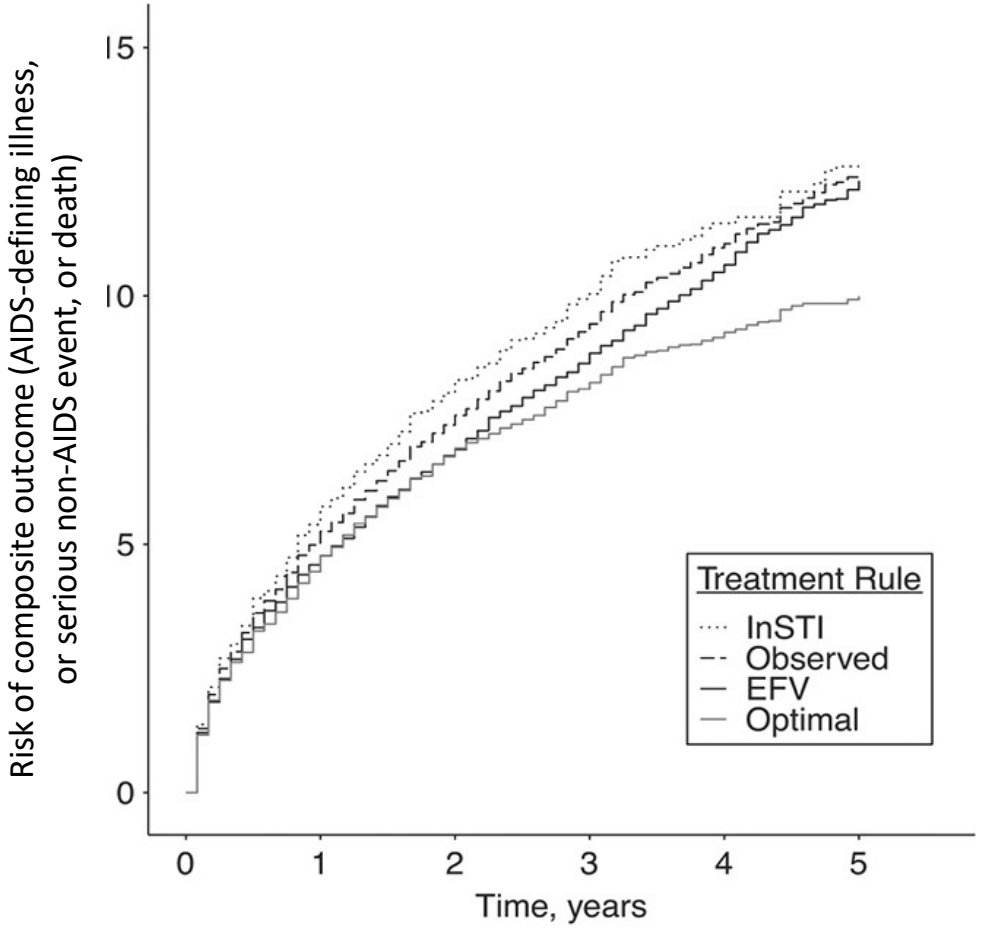
Methods: From 2009–2016, we used statistical methods for precision medicine (i.e., genetic algorithm method with smoothing and augmentation) to estimate an optimal treatment rule resulting in the lowest 5-year risk of the composite outcome of acquired immune deficiency syndrome (AIDS)-defining illnesses, serious non-AIDS events, and all-cause mortality. The treatment rules considered were functions that recommend either an EFV-or InSTI-based regimen conditional on baseline patient characteristics such as demographic information, laboratory results, and health history.

Findings: The estimated 5-year risk under the estimated optimal treatment rule was 10% (95% CI: 9, 11%), corresponding to an absolute risk reduction of

- 2% (95% CI: 1, 4%) risk under the optimal treatment rule when compared with recommending an EFV-based regimen for all patients
- 3% (95% CI: 1, 4%) when compared with recommending an InSTI-based regimen for all patients

Conclusions: Tailoring ART to individual patient characteristics may reduce 5-year risk of the composite outcome compared with assigning all patients the same drug regimen.

Figure: Estimated 5-year cross-validated risk curves when recommending an EFV-based regimen to all patients, an InSTI-based regimen to all patients, according to the observed treatments, and according to the optimal treatment rule, NA-ACCORD 2009-2016.



Evaluating Clinic-Based Interventions to Reduce Racial Differences in Mortality among People with HIV in the US

Zalla LC*, J Infect Dis 2023 Jul 12:jiad263. doi: 10.1093/infdis/jiad263.

Importance: Mortality remains elevated among Black versus White adults receiving HIV care in the United States. We evaluated the effects of hypothetical clinic-based interventions on this mortality gap.

Methods: We computed 3-year mortality under observed treatment patterns among >40 000 Black and >30 000 White adults entering HIV care in the United States from 1996 to 2019. We then used inverse probability weights to impose hypothetical interventions, including immediate treatment and guideline-based follow-up. We considered 2 scenarios: "universal" delivery of interventions to all patients and "focused" delivery of interventions to Black patients while White patients continued to follow observed treatment patterns.

Results: Under observed treatment patterns, 3-year mortality was 8% among White patients and 9% among Black patients, for a difference of 1 percentage point (95% CI, 0.5%, 1.4%).

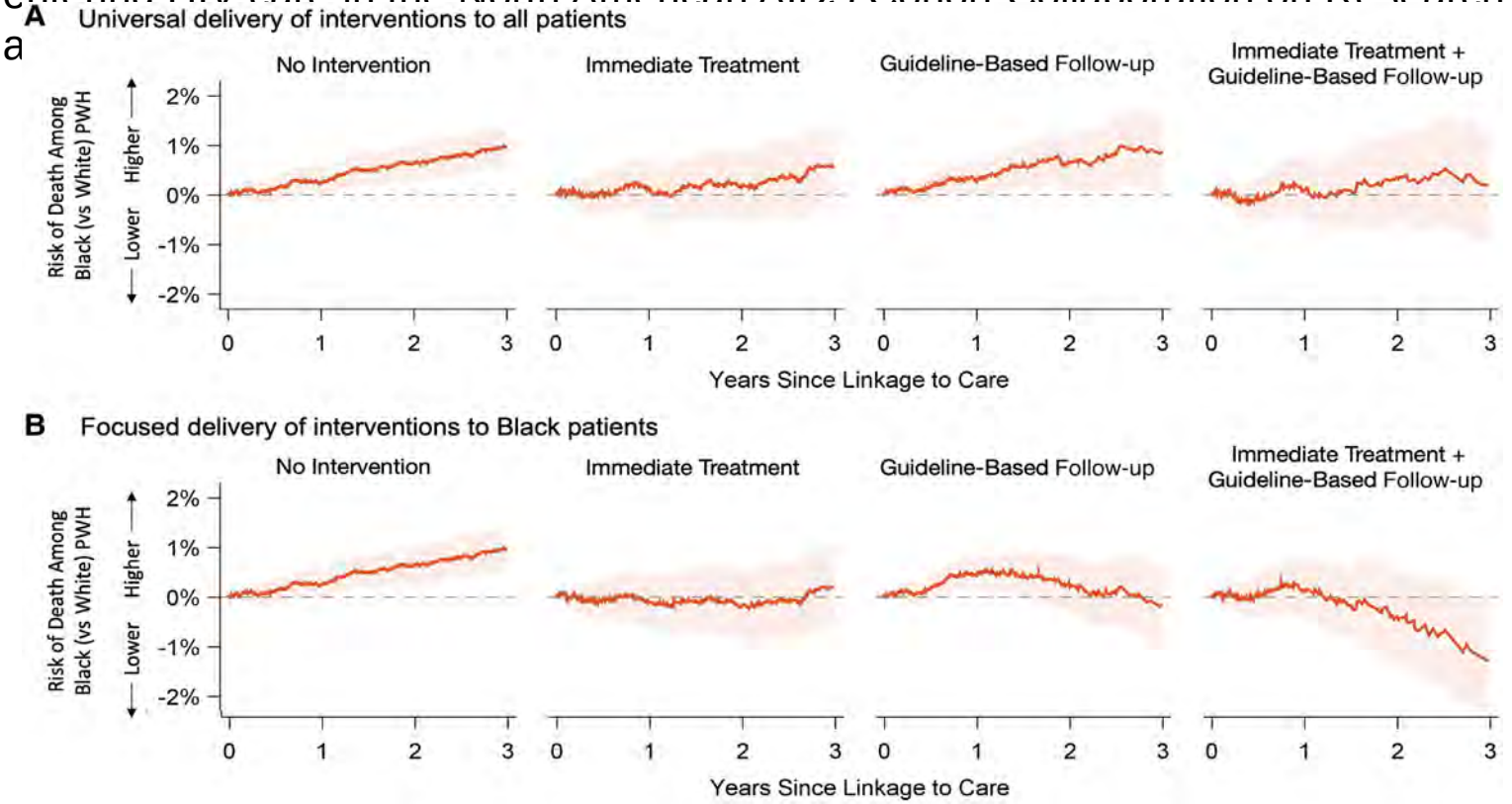
A. Under universal immediate treatment: The difference was reduced to 0.5% (95% CI, −0.4% to 1.3%)
   - Under universal immediate treatment combined with guideline-based follow-up: The difference was reduced to 0.2% (95% CI, −1.0% to 1.4%).

B. Under the focused delivery of both interventions to Black patients while White patients continue to follow observed treatment patterns: The Black–White difference in 3-year mortality was −1.4% (95% CI, −2.3% to −.4%).

Conclusions: Clinical interventions, particularly those focused on enhancing the care of Black patients, could have significantly reduced the mortality gap between Black and White patients entering HIV care from 1996 to 2019

**Zalla LC completed this work as pre-doctoral student (advisor: Jess Edwards, UNC)*

Figure: Absolute differences in 3-year mortality under the observed pattern of care and under hypothetical interventions among Black versus White adults entering HIV care in the North American AIDS Cohort Collaboration on Research a



Effect of Adopting the New Race-Free 2021 CKD-Epi eGFR Creatinine Equation on Racial Differences in Kidney Disease Progression Among People With HIV: An Observational Study

Muiru AN, et al. Clin Infect Dis 2023 Feb 8;76(3):461-468. doi: 10.1093/cid/ciac731.

Importance: The impact of adopting a race-free eGFR creatinine (eGFRcr) equation on racial differences in chronic kidney disease (CKD) progression among people with HIV (PWH) is unknown.

Methods: We defined eGFR stages using the original race-adjusted CKD-EPI eGFRcr equation and the new race-free CKD-EPI eGFRcr equation. We then estimated 5-year probabilities of transitioning from baseline kidney function to more advanced eGFR stages and examined the association of race (Black vs White) with rates of CKD progression using Markov models.

Results: With the race-adjusted eGFRcr equation, Black (n=31,298) vs white participants (n=27,542) had:

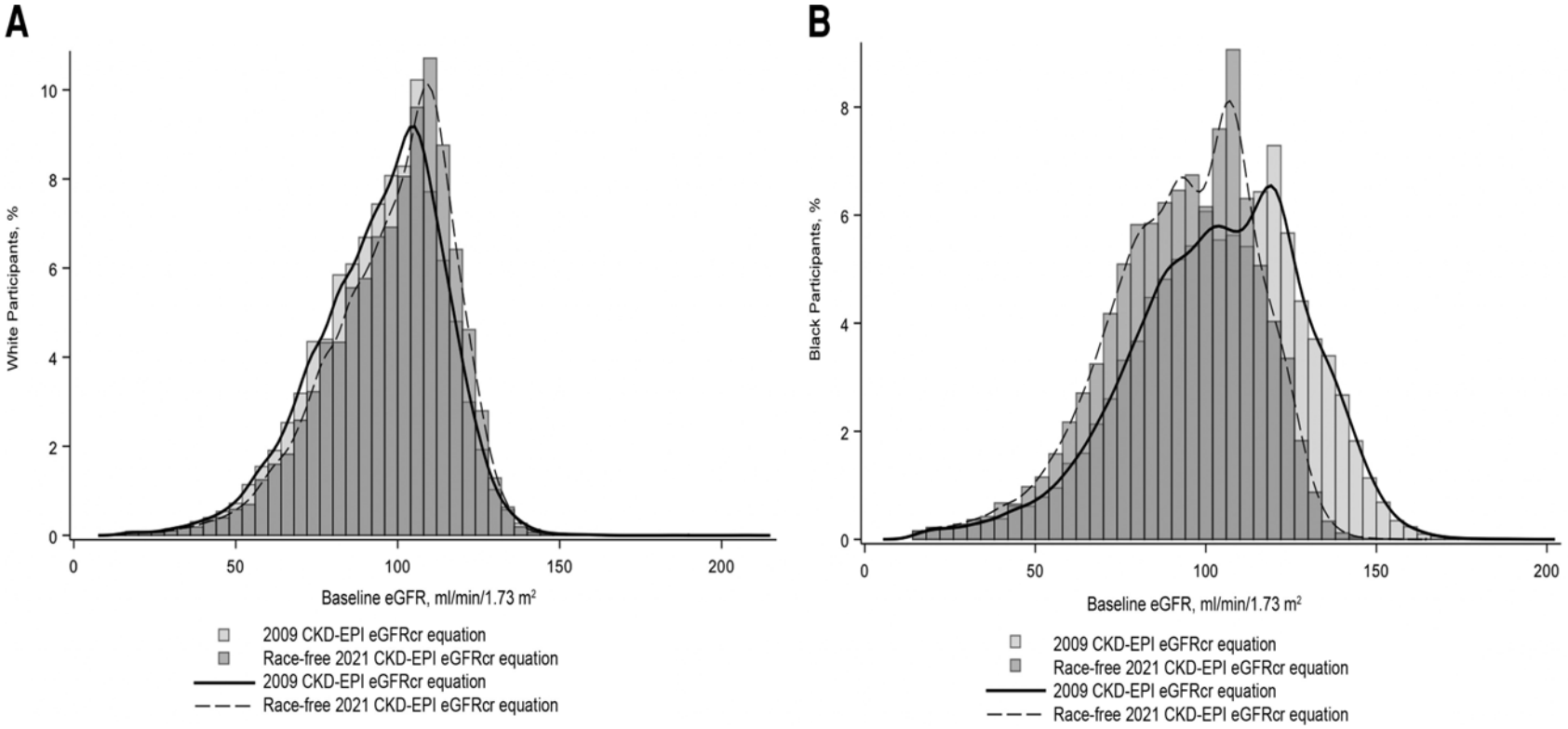
- a 23% lower risk of progressing from eGFR stage 1 to 2 (HR=0.77 [95% CI 0.73, 0.82])
- an equal risk of progressing from stage 2 to 3 (HR=1.00 [95% CI 0.92, 0.07])
- a 3-fold risk of progressing from stage 3 to 4 or 5 (HR=3.06 [95% CI 2.60, 3.62])

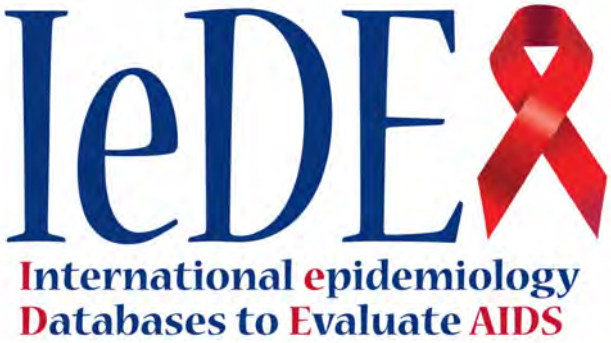
With the race-free eGFRcr equation,

- 16% of Black participants were reclassified into a more severe eGFR stage at baseline
- The reclassified Black individuals had a higher prevalence of CKD risk factors than Black PWH who were not reclassified
- Black participants had a higher risk of disease progression across all eGFR stages than White participants.

Conclusions: The original eGFRcr equation systematically masked a subgroup of Black PWH who are at high-risk of CKD progression. The new race-free eGFRcr equation unmasks these individuals and may allow for earlier detection and management of CKD.

Figure: A, Baseline estimated glomerular filtration rate (eGFR) distribution among white (A) and black (B) participants using the original 2009 Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) eGFR creatinine

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