Cohorts and regional principal investigators

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  - Kara Wools-Kaloustian and Constantin Yiannoutsos, Indiana University; Aggrey Semeere, Makerere University

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- **IeDEA West Africa**
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- **NA-ACCORD**
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• This work is solely the responsibility of the authors and does not necessarily represent the official views of any of the institutions mentioned above.

• Regional acknowledgements of site investigators, cohorts, study teams and administrators, data managers, and coordinating and data centers are available at: https://www.iedea.org/resources/
2021 IeDEA Asia-Pacific
Research Highlights
Global estimates of viral suppression in children and adolescents and adults on antiretroviral therapy adjusted for missing viral load measurements: a multiregional, retrospective cohort study in 31 countries

- Retrospective cohort study: 7 IeDEA regions; individuals initiating ART between Jan 2010 - Dec 2019
- 21,594 children/adolescents from 106 sites, 22 countries
- 255,662 adults from 143 sites, 30 countries
- Intention to treat (ITT) approach: Include all PLHIV who started ART, with or without viral load (VL) outcomes
- Adjusted approach: Accounted for missing VL measurements among transferred, LTFU, or in follow-up without VL testing

Proportion of children and adults with HIV viral suppression (VS) at years 1, 2, and 3 following ART initiation

- Adults with HIV are approaching global target of 95% VS, but substantial efforts are still needed to reach the VS target for children and adolescents.

Virological failure and HIV drug resistance among adults living with HIV on second-line antiretroviral therapy in the Asia-Pacific

• Cross-sectional: Adult PLHIV on second-line ART for ≥6 months; HIV VL and genotypic resistance tests collected or conducted Jul 2015 - May 2017, 12 Asia-Pacific sites

• Virological failure (VF) defined as VL >1000 copies/mL + 2nd VL >1000 within 3–6 months

• N=1378: 74% male; 93% on boosted PI 2nd-line; median duration on 2nd-line 3 years; median CD4 count at 2nd-line switch 103 cells/μL

• 101 (7%) with VF and 41 (41%) with resistance data
  ➢ 80% had ≥1 NNRTI RAM, 63% ≥1 NRTI RAM, and 35% ≥1 PI RAM

Factors associated with VF in patients on second-line ART (multivariate analysis)

<table>
<thead>
<tr>
<th></th>
<th>OR</th>
<th>95% CI</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at switch to 2nd line ART (years)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤30</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>31-40</td>
<td></td>
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<td>41-50</td>
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<td></td>
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<tr>
<td>Female</td>
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</tr>
<tr>
<td>HIV mode of exposure</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heterosexual contact</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>MSM</td>
<td>0.29</td>
<td>(0.10-0.83)</td>
<td>0.020</td>
</tr>
<tr>
<td>Injecting drug use</td>
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<td>(0.08-0.60)</td>
<td>0.003</td>
</tr>
<tr>
<td>Other/Unknown</td>
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<td>(0.14-1.09)</td>
<td>0.073</td>
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<tr>
<td>CD4 at switch to 2nd line (cells/μL)</td>
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<tr>
<td>≤50</td>
<td>1</td>
<td></td>
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<tr>
<td>51-100</td>
<td>0.97</td>
<td>(0.50-1.86)</td>
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<tr>
<td>101-200</td>
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<td>(0.22-1.03)</td>
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<tr>
<td>&gt;200</td>
<td>0.36</td>
<td>(0.17-0.77)</td>
<td>0.008</td>
</tr>
</tbody>
</table>

- Low proportions with VF and significant RAMs reflect durability of current 2nd-line regimens
- Broader scale-up of routine VL monitoring and enhanced adherence support needed before substantial HIV DR emerges, which would lead to costly resistance testing and 3rd-line ART

Viral hepatitis cascade of care among adults living with HIV in Asia-Pacific

- Retrospective cohort study: to (i) identify prevalence of HBV and HCV among adult PLHIV, and (ii) report the viral hepatitis treatment cascade of care
- 22,340 adult PLHIV enrolled in the TAHOD-LITE observational cohort, on cART, and in follow-up between 2010-2019
  - Viral hepatitis co-infection: ever tested positive for HBV surface antigen (HBsAg) or anti-HCV (HCVAb)
- 8612 (39%) had an HBsAg test: 672 (8%) positive
- 8231 (37%) had an HCVAb test: 779 (9%) positive

Low rates of HBV and HCV screening and viral load monitoring, and suboptimal proportions initiating treatment suggest need for improved access to viral hepatitis testing and treatment for PLHIV in the region.

Viral hepatitis cascade of care among adults living with HIV in Asia-Pacific.
Integration of mental health services into HIV healthcare facilities among Thai adolescents and young adults living with HIV

• Prospective cohort: (i) assess burden of depression, anxiety and suicidality using PHQ-9 and GAD-7; and (ii) determine impact of integrated mental health/HIV services on treatment outcomes

• 150 HIV-positive (AYHIV) and 150 HIV-negative adolescents and young adults 15-25 years of age enrolled between Feb-Apr 2018

• AYHIV at enrolment: 17 (11%) with significant depressive symptoms; 11 (7%) with significant anxiety symptoms; 21 (14%) with suicidal ideation – not substantially different from HIV-negative youth
• After referral to psychiatric care: 13% of AYHIV had confirmed mental health disorder
• 1 year later: 42% had resolution of serious symptoms; 26% had improved PHQ-9 and GAD-7 scores
• Mental health screening and referral services can and should be scaled up for AYHIV

Pediatric disclosure of HIV status and effect on mortality and LTFU among children and adolescents living with HIV in Asia

- Retrospective cohort study: (i) describe frequency of HIV disclosure in children and adolescents, (ii) assess effect of disclosed status on ART clinical outcomes
- Inclusion criteria: 6-19 years old; initiated cART between Jan 2008 - Dec 2018; initiated cART at ≥12 months before database closure; had ≥1 clinic visit between ages 6–19
- N=1,913: 48% female
- 42% disclosed; median age at disclosure 13 years

Probability of retention in care by disclosure status

- Those who had been disclosed to had lower proportion of death (0.9% vs. 4.7%) and similar proportion of LTFU (3.9% vs. 3.9%) compared to those who were not disclosed to.

- Probability of retention in care at 5 years: 98% disclosed vs. 89% not disclosed (p <0.001)

- Disclosure and its impacts need to be better addressed in pediatric HIV clinics in the region.

CCASAnet Publication Highlights: 2022
Methods:

Longitudinal analyses of children (aged ≤18yo) switching to 2nd-line ART in cohorts from Brazil, Haiti, & Honduras, 1998-2018, to examine cumulative incidences and relative hazards (using competing risks methods and Cox models) of:

- Virologic failure while on second-line ART (a VL >1000 copies/mL or 2 consecutive measurements ≥400 but <1000 copies/mL)
- Loss to follow-up (most recent clinic visit that was >12 months before the database close)
- Major ART regimen change (switch of ≥2 ARVs in the initial regimen, the addition of ≥2 ARVs to the initial regimen, switch to a regimen with >3 active ARVs, or substitution of single drug that was different from the initial drug class)
- All-cause mortality

Background:

- Little is known about long-term outcomes of children living with HIV in Latin America
- Few studies have examined antiretroviral therapy (ART) regimen switches in the years after the introduction of ART in this population
Results:

- 672 children starting second-line ART were included.
- Three years after starting second-line ART, the cumulative incidence of loss to follow-up was 0.14 (95% CI: 0.11 to 0.17) (Figure, A), of death was 0.10 (95% CI: 0.08 to 0.13) (Figure, B), and of major regimen change was 0.19 (95% CI: 0.15 to 0.22) (Figure, C).
- Of those changing regimens, 35% were due to failure and 11% due to toxicities/side effects.
- Among the 312 children with viral load data, the cumulative incidence of virologic failure at 3 years was 0.62 (95% CI: 0.56 to 0.68), (Figure, D).
- Time to virologic failure and regimen change were uncorrelated (rank correlation -0.001; 95% CI: -0.18 to 0.17).

Conclusions:

- Poor outcomes after starting second-line ART in Latin America were common.
- The high incidence of virologic failure and its poor correlation with changing regimens was particularly worrisome.
- Additional efforts are needed to ensure children receive optimal ART regimens.
Methods:

Longitudinal analyses of WLWH aged ≥16yo enrolling in cohorts from Brazil, Chile, Honduras, & Peru, 2000-2017, to examine HIV outcomes at 12 months after pregnancy outcome:

- **Retention in care:** ≥2 visits, ≥3 months apart
- **Virological suppression:** HIV-1 RNA viral load <200 copies/mL

Background:

- HIV incidence among women of reproductive age and vertical HIV transmission rates remain high in Latin America
- We quantified HIV care continuum barriers & outcomes among pregnant women living with HIV (WLWH) in Latin America
Results:

- Among 579 WLWH, median postpartum follow-up was 4.34 years (IQR 1.91, 7.35); 459 (79%) were HIV-diagnosed before pregnancy confirmation, 445 (77%) were retained in care, and 259 (45%) were virologically suppressed at 12 months postpartum.
- Cumulative incidence of LTFU was 21% by 12 months and 40% by five years postpartum (Figure).
- Those HIV-diagnosed during pregnancy vs. those HIV-diagnosed before had lower odds of both:
  - Retention (aOR = 0.58, 95% CI: 0.35 to 0.97), Table 2
  - Virological suppression (aOR = 0.50, 95% CI: 0.31 to 0.82), Table 4

Conclusions:

- HIV diagnosis during pregnancy was associated with poorer 12-month retention and virological suppression.
- Young women should be tested and linked to HIV care earlier to narrow these disparities.
In a multicenter prospective cohort study from Brazil (RePORT-Brazil, n=643), diabetes was associated with an increased risk of unfavorable treatment outcomes, including mortality, in pulmonary tuberculosis patients. These observations were confirmed in the Brazilian National Disease Notification System (SINAN, n=20989) during the same period.
**Method:** Univariate and multivariate models were performed to evaluate associations between glycemic status and TB treatment outcomes.

**Results:**
- Diabetes, but not prediabetes, was associated with unfavorable outcomes in the RePORT-Brazil and SINAN cohorts.
- Furthermore, diabetes was associated with high risk of death (during TB treatment) in both RePORT-Brazil (aRR:2.16, p=0.040) and SINAN (aRR:1.93, p= 0.001).

**Conclusion:** Diabetes was associated with an increased risk of unfavorable outcomes and mortality in Brazilian PWTB. Interventions to improve tuberculosis treatment outcomes in persons with diabetes are needed.

**PMID:** 34651642

**Adjustment variables:** Dysglycemia or DM or , PDM, Hb (g/dL) smoking, alcohol, illicit drug, abnormal X-ray, HIV status. Plus :Prior TB and, male sex for SINAN
A Clinical Prediction Model for Unsuccessful Pulmonary Tuberculosis Treatment Outcomes

Lauren S. Peetles,1,2, Peter F. Rebeiro,3, Felipe M. Ribeiro,1 Bruno B. Andrade1,3,4, Marcelo Cordeiro-Santos,3,4, Adriano Kritski,1,2, Betina Durvoi,1, Solange Calvacante,6,7, Marina C. Figueiredo,7, David W. Hass1,2,6, Dandan Liu2,6, Valeria C. Rolla,6,4, and Timothy R. Sterling2,6, on behalf of the Regional Prospective Observational Research in Tuberculosis (RePORT)-Brazil Network

Methods:

- **Background:** Clinical prediction models can inform treatment strategies to improve outcomes. Systematic review of existing TB outcome prediction models showed high amounts of bias due to poor reporting and limited statistical rigor.

- **Objective:** Develop and internally validate a prediction model for unsuccessful pulmonary TB treatment outcomes.

- **Study population:** 944 RePORT-Brazil participants with culture-confirmed, drug-susceptible, pulmonary TB who started anti-TB therapy.

- **Outcome:** Unsuccessful TB treatment outcome, including death, treatment failure, and loss to follow-up.

- **Candidate predictors:** Baseline variables selected *a priori* using literature review and clinical input.

**PMID:** 34214166
Results:

- 191 (20%) of 944 participants had an unsuccessful TB treatment outcome
- Final model included seven baseline predictors: hemoglobin, HIV, drug use, diabetes, age, years of education, and tobacco use
- Model demonstrated good performance
  - **Discrimination**: c-statistic = 0.77 (95% CI: 0.73-0.80); internally validated c-statistic: 0.75 (95% CI: 0.71-0.78)
  - **Calibration** indicates predicted risks correlate well with observed risks at predicted risks <40%. Internally-validated calibration intercept and slope of -0.12 and 0.89, respectively
- Predicted risks can be calculated with nomogram or online calculator
- **Decision curve analysis** indicates that risk-based intervention should be considered when the cost-benefit ratio of the intervention is between 1:9 and 2:3 or when the risk threshold at which intervention is would be employed is between 11% and 41%

Conclusion: Using information readily available at treatment initiation, the prediction model performed well in this population. Model may inform future efforts to improve TB treatment outcomes with risk-based interventions

PMID: 34214166
Nonparametric estimation of Spearman’s rank correlation with bivariate survival data

Svetlana K. Eden¹ | Chun Li² | Bryan E. Shepherd¹

Background:

• Interest in assessing the correlation between two right-censored variables, such as times from ART initiation to viral failure and to regimen change.
• Challenging because do not see times to events for many observations.
• We developed new rank correlation statistics and applied to CCASAnet data.
New Methods:
1. Spearman’s correlation in a restricted region (e.g., within first 10 years)
2. Spearman’s correlation with those censored beyond observation window assigned highest rank
Both methods make no distributional assumptions, have nice statistical properties, and do well in simulations.

Application to CCASAnet:
• 6691 Adults initiating ART
• Rank correlation within first 10 yrs
  • 0.26 (95% CI 0.17, 0.36)
• Rank correlation assigning highest ranks to censored beyond follow-up
  • 0.35 (95% CI 0.27, 0.44)
• Suggests moderate correlation
• Method applied in another CCASAnet publication highlighted earlier
  • Somerville et al. (2021) JAIDS.
Central Africa IeDEA

2021 Research Highlights
Comparison of cohort characteristics in Central Africa IeDEA and Demographic Health Surveys: Rwanda and Burundi


**AIMS:**

• To examine the representativeness of the Central Africa IeDEA (CA-IeDEA) cohorts in Rwanda and Burundi.

**METHODS:** Compared distributions of key sociodemographic and clinical characteristics (age, marital status, BMI, pregnancy status) by sex among urban PLWH.

• Datasets: a) longitudinal CA-IeDEA data abstracted from medical records and b) cross-sectional Demographic and Health Surveys (DHS) using probabilistic sampling.

• Multiple comparable timepoints.

• 2-proportion z-tests, with and without proxy for engagement in care.

• Cohen’s h effect size (does not take sample size into account).
Comparison of cohort characteristics in Central Africa IeDEA and Demographic Health Surveys: Rwanda and Burundi

RESULTS:

• **Rwanda:** CA-IeDEA cohort and DHS populations similar in age and marital status for men and women.

• **Burundi:** Women similar in age and marital status, but CA-IeDEA cohort had more younger and single men, possibly because of site-level outreach to sexual minority populations.

• **Both countries:** CA-IeDEA cohorts had higher proportion of underweight individuals, suggesting that symptomatic individuals more likely to access care at IeDEA sites in these settings.

Disparities in dolutegravir uptake affecting females of reproductive age with HIV in low- and middle-income countries after initial concerns about teratogenicity


AIM:

• To describe disparities in dolutegravir (DTG) uptake by sex and age-group in low- and middle-income countries after an initial 2018 Safety Signal implicating DTG exposure at conception in infant neural tube defects and the subsequent WHO 2019 recommendation of DTG for all adults and adolescents living with HIV.

METHODS:

• Cumulative incidence of DTG uptake (i.e., newly initiating ART with DTG or switching to DTG from another regimen) among patients aged ≥16 years who received HIV care from January 2017 through March 2020.
Disparities in dolutegravir uptake affecting females of reproductive age with HIV in low- and middle-income countries after initial concerns about teratogenicity

RESULTS:

• Sample included 134,672 patients from Brazil, Cambodia, Democratic Republic of the Congo, Haiti, Kenya, Lesotho, Mozambique, Rwanda, Tanzania, Uganda, and Zimbabwe.

• 52% of patients were females of reproductive age (i.e., 16-49 years).

• Disparities in uptake by sex and age group emerged after the 2018 Safety Signal and persisted after the WHO recommended DTG-containing ART for all people living with HIV, including women and girls regardless of age and contraception.

Hypertension among people living with HIV/AIDS in Cameroon: A cross-sectional analysis from CA-IeDEA


**AIMS:**

- To examine the prevalence and predictors of HTN among PLWH attending three large clinics in Cameroon

**METHODS:**

- Cross-sectional study
- Inclusion: All non-pregnant PLWH ≥20 years who received care between 2016 and 2019 at one of the three CA-IeDEA sites in Cameroon.
- HTN definition: Blood pressure (BP) ≥ 140/90 mm Hg or self-reported use of BP lowering medication
Hypertension among people living with HIV/AIDS in Cameroon: A cross-sectional analysis from CA-IeDEA

RESULTS:

• Among 9,839 eligible PLWH, 25.0% had prevalent HTN, with only 1.1% on treatment, and 21.4% of those on treatment having controlled HTN.

• Median age (47.4 vs. 40.5 years), self-reported duration of HIV infection (5.1 vs 2.8 years), duration of ART exposure (4.7 vs 2.3 years), and CD4 count (408 vs 359 cell/mm3) were higher in hypertensives than non-hypertensives (all p<0.001).

• Age and body mass index (BMI) were independently associated with higher prevalent HTN risk.

• PLWH starting ART had a 30% lower risk of prevalent HTN, but this advantage disappeared after a cumulative 2-year exposure to ART.

Mental health and initiation of antiretroviral treatment at enrolment into HIV care in Cameroon under a national “treat all” policy: a cross-sectional analysis


AIMS:
1) To estimate the prevalence of same-day ART initiation at enrollment into HIV care and;
2) To estimate the relationship between mental health symptoms and same-day ART initiation at enrollment into HIV care among a cohort of PLWH in Cameroon.

METHODS:
• In person interviews w/426 individuals initiating HIV care at 3 clinics in Cameroon
• Measures: ART initiation at enrollment into care (same day vs. non-same day); depressive symptoms (PHQ-9 score>9); anxiety symptoms (GAD-7 scores>9); PTSD symptoms (PCL5 scores>30); harmful drinking (AUDIT scores>15); any mental health disorder symptoms; any mental health or substance use disorder symptoms; age; gender
• Analyses: Separate multivariable log-binomial regression models used to estimate association between mental health symptoms and ART initiation at enrollment controlling for age, gender, and clinic
Mental health and initiation of antiretroviral treatment at enrolment into HIV care in Cameroon under a national “treat all” policy: a cross-sectional analysis

RESULTS:

- 365/420 (87%) initiated ART the same day they enrolled into HIV care; 75% of others initiated ART w/in 7 days of enrollment into HIV care
- 20% report depressive symptoms; 15% PTSD; 12% anxiety; 13% harmful alcohol use
- Prevalence of delayed ART initiation among individuals with symptoms of depression, anxiety, or PTSD was **1.9 (95% CI 1.2, 3.1)** times the prevalence among those without
- Prevalence of delayed ART initiation among individuals with symptoms of depression, anxiety, PTSD, or harmful alcohol use was **1.7 (95% CI 1.0, 2.7)** times the prevalence among those without symptoms of any of these disorders
- Specifically, depression (**aPR: 1.7; 95% CI: 1.1, 2.7**) and PTSD (**aPR: 1.8; 95% CI: 1.2, 2.9**) were significantly associated with delayed ART initiation after adjustment
- After adjustment, anxiety and harmful alcohol use were not meaningfully associated with delayed ART initiation

Effects of national adoption of Treat-All guidelines on pre-ART CD4 testing and viral load monitoring after ART initiation: A regression discontinuity analysis


AIMS:
• To examine trends in pre-ART CD4 testing and viral load (VL) monitoring at 6 months after ART initiation (+/- 2 months) after national adoption of Treat All policies.

METHODS:
• Sharp regression discontinuity in time (RDiT) design used to estimate effect of Treat All adoption among ART-naïve patients enrolling in HIV care between 2006 and 2018.
• Patients’ date of enrollment in HIV care used as the exposure assignment (i.e., “running variable”), with date of national Treat All adoption as a threshold or cut-off value. Local linear estimation within data-driven bandwidths used to estimate causal effects of Treat All on laboratory monitoring.
• Analyses stratified by age group (adults ≥20y, adolescents 10-19y, and children <10y) and country income level, defined as low/lower-middle income countries (L/LMICs) and high/upper-middle income countries (H/UMICs), using World Bank income classification (2017).
Effects of national adoption of Treat-All guidelines on pre-ART CD4 testing and viral load monitoring after ART initiation: A regression discontinuity analysis

RESULTS:

• 547,837 ART-naïve patients enrolled in HIV care during 2006-2018 at 225 clinics in 26 countries where Treat-All policies were adopted, including 492,9890 with sufficient follow-up time for VL monitoring.

• Treat-All adoption led to an immediate decrease in pre-ART CD4 testing among adults in L/LMICs (-8.9 percentage points [pp]; 95% CI: -11.0, -6.8), and a small increase in in H/UMICs, (+1.6pp; 95% CI: 0.2, 3.0), with no changes among adolescents or children.

• In L/LMICs, VL monitoring after ART initiation was low among all patients just before Treat-All and there was no immediate change at Treat-All adoption. In H/UMICs, VL monitoring increased among adults immediately after Treat-All adoption (+2.9pp; 95% CI: 0.5, 5.4), with no change among adolescents or children.

East Africa
International Epidemiology Databases to Evaluate AIDS

2021 Research Highlights
Feasibility of Rapid Case Ascertainment for Cancer in East Africa: An Investigation of Community-Representative Kaposi Sarcoma in the Era of Antiretroviral Therapy

Introduction:

• Rapid case ascertainment (RCA) is the thorough research-level evaluation of a patient shortly following diagnosis of a particular condition.
• We sought to evaluate the feasibility of performing RCA for patients among a community-representative sample of new diagnoses of KS in East Africa.
• We describe the methods required, the successes, and limitations of the process.

Methods:

• Identified newly diagnosed KS among HIV-infected adults (≥18 years) at one of three primary care networks in East Africa using
  ➢ querying of the HIV clinic EMR
  ➢ regular manual review of records at the histopathology laboratory and relevant clinic venues
  ➢ receipt of sporadic notification by field clinicians.
• Once potential cases identified: study team verified eligibility for RCA and attempted to perform a detailed clinical and laboratory evaluation.
• We estimated feasibility as the pace of RCA performance after health system diagnosis of KS, accommodating death as a competing event using the Aalen-Johansen estimator.

Semeere et al, In press Cancer Epidemiology 2021
Results

- 593 patients with suspected new KS, 171 were ineligible
- Of the 422, RCA was performed within 1 month for 56% and within 3 months for 65% (95% CI: 59 to 70%)
- Non-performance reasons: death (47%), inability to contact (44%), refusal/unsuitable consent (8.3%), relocation (0.7%)

Determinants of finding patients diagnosed with Kaposi’s sarcoma to perform rapid case ascertainment within 90 days of health system diagnosis at three clinical sites in sub-Saharan Africa.

<table>
<thead>
<tr>
<th>Determinant</th>
<th>Unadjusted Risk Ratio (95% CI)</th>
<th>P value</th>
<th>Adjusted Risk Ratio (95% CI)</th>
<th>P value</th>
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</thead>
<tbody>
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<td>0.44</td>
<td>1.00 (0.99 to 1.011)</td>
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</tr>
<tr>
<td>Women</td>
<td>Ref.</td>
<td></td>
<td>Ref.</td>
<td></td>
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<tr>
<td>Men</td>
<td>0.98 (0.84 to 1.13)</td>
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<tr>
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<td>1.4 (1.2 to 1.5)</td>
<td>&lt;0.001</td>
<td>1.5 (1.3 to 1.7)</td>
<td>&lt;0.001</td>
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<td>Mbarara-RRH, Uganda</td>
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<td>0.003</td>
<td>0.88 (0.70 to 1.1)</td>
<td>0.27</td>
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<td>Mode of identification of patient</td>
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<td>Clinician Notification</td>
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<tr>
<td>Electronic Medical Records</td>
<td>0.59 (0.40 to 0.89)</td>
<td>0.012</td>
<td>0.57 (0.39 to 0.85)</td>
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<td>Pathology Laboratory Records</td>
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<td>0.004</td>
<td>0.88 (0.73 to 1.1)</td>
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<td>0.003</td>
<td>0.080 (0.012 to 0.54)</td>
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<tr>
<td>Medical Ward</td>
<td>0.61 (0.40 to 0.92)</td>
<td>0.019</td>
<td>0.55 (0.39 to 0.79)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Conclusion

- RCA is feasible for the investigation of community-representative KS in East Africa
Social, economic, and health effects of the COVID-19 pandemic on adolescents retained in or recently disengaged from HIV care in Kenya

Introduction

• Adolescents living with HIV (ALHIV, ages 10-19) may be particularly vulnerable to widespread disruptions during the COVID-19 pandemic

Methods

• We assessed a range of effects of the pandemic on ALHIV in western Kenya, and whether effects were greater for ALHIV with recent loss to program (LTP)
• Recruited to parent study at 3 sites in western Kenya from February 2019–September 2020:
  - ALHIV retained in care
  - ALHIV LTP and traced in the community
• Phone interviews July 2020–January 2021 assessed pandemic effects on: financial and food security, healthcare access and behaviors, and mental health

Enane LA et al, PLOS ONE 2021
Results
• Phone surveys with 334 ALHIV or their caregivers (275 retained and 59 LTP):
  ➢ A greater proportion of LTP ALHIV were no longer engaged in school (45.8% vs. 36.4%, p=0.017)
  ➢ Over a third (120, 35.9%) lost income
  ➢ 135 (40.4%) did not have enough food some (121, 36.2%) or most (14, 4.2%) of the time
  ➢ 99.4% of ALHIV had ART with them; 6.3% missed at least one dose in past 7 days

Conclusions
• The COVID-19 pandemic has had devastating socioeconomic effects for Kenyan ALHIV and their households.
  ➢ Sustained ART access, adherence may signal resilience and strengths of ALHIV, care programs
  ➢ There is a critical need to support ALHIV during this crisis

Enane LA et al, PLOS ONE 2021
Pregnancies among women living with HIV using contraceptives and antiretroviral therapy in western Kenya: a retrospective, cohort study

• Intro: Preventing unintended pregnancies is paramount for women living with HIV
  ➢ Efavirenz-containing ART reduces contraceptive implant effectiveness
• Some uncertainty around electronic medical records (EMR) quality
• Methods: Conducted a 3-phase sampling study from 2011 to 2015:
  ➢ 1st phase: EMR, with retrospective cohort
  ➢ 2nd phase: manual chart review for randomly-selected subsample
  ➢ 3rd phase: telephone interview for purposively-selected subsample
• Estimated adjusted incidence rate ratios (aIRR) with Poisson regression with inverse probability weights and generalized raking

Patel RC et al. BMC Medicine. 2021
• Results:
  - 85,324 women contributed 170,845 women-years (w-y) in EMR
  - 5080 in chart review and 1285 in telephone interviews

<table>
<thead>
<tr>
<th>Comparison groups</th>
<th>aIRR (95% CI) for EMR only</th>
<th>aIRR (95% CI) for all 3 phases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Among implant users</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Efavirenz vs. nevirapine</td>
<td>1.9 (1.6, 2.4)</td>
<td>3.2 (1.8, 5.7)</td>
</tr>
<tr>
<td>Among efavirenz users</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DMPA¹ vs. implant</td>
<td>1.8 (1.5, 2.1)</td>
<td>2.4 (1.0, 6.1)</td>
</tr>
</tbody>
</table>

¹DMPA=depomedroxyprogesterone acetate

• Conclusions:
  - pregnancy rates higher with efavirenz and implants but comparable to other leading contraceptives
  - 3-phase sampling method is innovative tool for EMR robustness

Patel RC et al. BMC Medicine. 2021
Outcomes of Retained and Disengaged Pregnant Women Living with HIV in Uganda

Introduction

• Disengagement from HIV care among pregnant women living with HIV may lead to unfavorable outcomes such as Mother to Child Transmission (MTCT)

• HIV transmission rates are likely to be underestimated if women and infants who are lost to follow-up (LTFU) are not accounted for

Methods

• Study conducted July 2017-July 2018 at six public Kampala City Council Authority (KCCA) clinics in Uganda

• Women disengaged from PMTCT were traced through community outreach

• Maternal and infant outcomes were compared between disengaged and retained women

  ➢ Disengaged (DW) = not attended 6-week post-partum visit by 10 weeks after estimated date of delivery
  ➢ DW were matched with retained women (RW) by age and duration on ART
  ➢ DW categorized into two groups; women who delivering in care and those disengaged before delivery

Kiragga AN et al, *PLOS ONE* 2021
Results

- 734 women (349 DW and 375 RW) screened
- Community Tracing was successful for 160 (44.6%) DW who were matched with 162 RW
- Among DW successfully traced and vital status obtained, 52 (32.5%) transferred to another health facility
- The majority of DW (99; 71.7%) delivered after they had disengaged from care
- HIV Viral load suppression and disclosure of HIV status to spouses, was higher among RW
- MTCT of HIV was higher among women who disengaged from care

Conclusion

- Pregnant and breastfeeding WLWHIV who disengage from care are difficult to trace in urban
- Many have detectable viral loads, leading to the potential for an increased risk of MTCT
- Efforts to reduce disengagement from care remain critical for elimination of MTCT of HIV

Kiragga AN et al, PLOS ONE 2021

Figure 1: HIV Outcomes among retained and disengaged women
A method for semiparametric regression of disengagement from care and death under incomplete event ascertainment and interval-censored event times

Introduction
• The analysis of disengagement from care and death in AMPATH is complicated due to the following reasons
  ➢ Unknown exact event times (interval censoring).
  ➢ Incomplete death ascertainment
• Ignoring these issues leads to bias and invalid conclusions.

Methods
• We addressed this issue by developing an Augmented Inverse Probability Estimator (AIPW)
• The method can be implemented using the new ciregic_aipw function in the R package intccr.

Park et al, Biostatistics 2021, Online ahead of print
Table 1. Covariate effects on the cumulative incidence function of disengagement from care and death.

<table>
<thead>
<tr>
<th>Covariate</th>
<th>Disengagement</th>
<th>Death</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Naïve complete case analysis</td>
<td>Proposed AIPW approach</td>
</tr>
<tr>
<td>Gender</td>
<td>(\hat{\beta}) (p-value)</td>
<td>(\hat{\beta}) (p-value)</td>
</tr>
<tr>
<td>M vs F</td>
<td>(\cdot.155 &lt;.001)</td>
<td>(-.054 &lt;.001)</td>
</tr>
<tr>
<td>CD4 at ART initiation per 100 cells/µl</td>
<td>(\cdot.029 &lt;.001)</td>
<td>(\cdot.227 &lt;.001)</td>
</tr>
<tr>
<td>Age at ART initiation per 10 years</td>
<td>(\cdot.256 &lt;.001)</td>
<td>(\cdot.075 (.036))</td>
</tr>
</tbody>
</table>

• **Conclusion:** The proposed method provides **trustworthy estimates** of key outcomes under **incomplete event ascertainment** and **interval censoring**.

Park et al, *Biostatistics* 2021, *Online ahead of print*
IeDEA Southern Africa
Achieving consistency in measures of HIV-1 viral suppression across countries: derivation of an adjustment based on international antiretroviral treatment cohort data

- Different countries have used different viral suppression thresholds when reporting progress towards viral suppression targets, which limits comparability.

- We aim to develop a simple formula for adjusting reported levels of viral suppression at different thresholds to be consistent with the definition currently used by UNAIDS (<1000 RNA copies/ml) or other definitions.

- The formula was estimated by fitting different statistical models to viral load data from the IeDEA and ART-CC collaborations.

- The figure shows the effect of applying this formula in a hypothetical country that reports viral suppression of 80% at a threshold of <200 RNA copies/ml. The predicted level of suppression at <1000 copies is 88.3% (95% CI: 85.5-90.6%).
Variations in the characteristics and outcomes of children living with HIV following universal ART in sub-Saharan Africa (2006–17): a retrospective cohort study

- Outcomes from 32,221 CLHIV initiating ART at ≤5 years in sub-Saharan Africa, from 45 paediatric sites in 16 low-income (N=11,510), lower-middle-income (N=8252), and upper-middle-income (N=12,459) countries.

- Overall we found:
  - a progressive decrease in the prevalence of advanced disease characteristics (underweight and severe immune suppression) at ART initiation.
  - significant decline in mortality over time, with substantial variations across country income groups.
  - 1 in 5 children continue to be lost to follow-up.

- There is a need to increase focus on tailored approaches for improved paediatric HIV programme uptake of early infant diagnosis, early ART initiation, linkage to care and retention in care for CLHIV, particularly in low-income and lower-middle-income countries.

Novel approach to estimate tuberculosis transmission in primary care clinics in sub-Saharan Africa: protocol of a prospective study

- We describe a novel and rapid study design to assess risk factors for airborne TB transmission at primary care clinics in high-burden settings.

- We will collect environmental data such as indoor CO₂ levels, relative humidity, frequency of coughs, and presence of *Mtb* DNA in the air, as well as patient data over 4 weeks at a primary care clinic in Cape Town, South Africa (Figure).

- We will calculate rebreathed air volume based on people density and CO₂ levels and develop a mathematical model to estimate the risk of TB transmission.
Estimating Tuberculosis Transmission Risks in a Primary Care Clinic in South Africa: Modeling of Environmental and Clinical Data

- We studied TB transmission at a primary care clinic in South Africa using patient and environmental data.

- We collected patient movements, cough frequency, and clinical data, and measured indoor carbon dioxide (CO2) levels, relative humidity, and \textit{Mtb} genomes in the air.

- We found an increased presence of \textit{Mtb} DNA in the air of 32\% (95\% credible interval, 7\%–63\%) per 100 additional young adults (aged 15–29 years) and 1\% (0–2\%) more \textit{Mtb} DNA per 10\% increase of relative humidity (Figure).

- Estimated cumulative transmission risks for patients attending the clinic monthly for at least 1 hour range between 9\% and 29\%.

**Figure**: Patient and environmental factors associated with \textit{Mtb} genome copies in the air, presented as standardized risk ratio from a multivariate analysis.

We examined outcomes PLHIV defined as LTFU in 2014-2017 at 8 ART programs in Southern Africa by checking medical records and by tracing.

- **3,256 participants**
  - 385 (12%) wrongly categorized as LTFU
  - 577 (17%) with missing contact details

- **2,294 PLHIV traced**
  - 768 (34%) alive and in care, including 385 (17%) silent transfers
  - 528 (23%) alive without care or unknown care
  - 252 (11%) died

- Overall, the status of 1,323 (41% of 3,256) PLHIV remained unknown

Results were heterogeneous across sites.

**Figure: Vital status and care outcomes among traced PLHIV**
Figure: Adjusted hazard ratios for cancer incidence with associated 95% confidence intervals, per 100 decrease of CD4 cell count.

The models assumed a linear relationship between CD4 cell count (time-updated, lagged 12 months) and the log-hazard of the cancer, while adjusting for sex, calendar year, and diagnosis of other cancers. The cancers are ranked in decreasing order of their adjusted hazard ratios.

EBV=Epstein-Barr virus; HPV=human papillomavirus.
Immunodeficiency and Cancer in 3.5 Million People Living with HIV: the South African HIV Cancer Match Study

Main findings

• The association between lower CD4 cell counts and higher cancer incidence rates was strongest for conjunctival cancer (adjusted hazard ratio [aHR] per 100 CD4 cells/µl decrease: 1.46, 95% confidence interval [CI] 1.38-1.54), Kaposi sarcoma (aHR 1.23, 95% CI 1.20-1.26), and non-Hodgkin lymphoma (aHR 1.18, 95% CI 1.14-1.22).

• Among infection-unrelated cancers, lower CD4 cell counts were associated with higher incidence rates of oesophageal cancer (aHR 1.06, 95 CI 1.00-1.11), but not breast, lung, or prostate cancer.

Conclusions

• Lower CD4 cell counts were associated with an increased risk of developing various infection-related cancers among people living with HIV.

• Reducing HIV-induced immunodeficiency may be a potent cancer prevention strategy among PLWH in sub-Saharan Africa, a region heavily burdened by cancers attributable to infections.

West Africa - IeDEA

Research highlights 2021
Objective: To describe the growth evolution and the immune response of adolescents with perinatal HIV (APH) across adolescence

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

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

<table>
<thead>
<tr>
<th><strong>Variables</strong> (median [IQR] or %)</th>
<th><strong>Total</strong></th>
<th><strong>North Am and Europe</strong></th>
<th><strong>South and Central Am</strong></th>
<th><strong>South and SE Asia</strong></th>
<th><strong>West and Central Afr</strong></th>
<th><strong>East and Southern Afr</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at ART initiation (years)</td>
<td>6.9 [4.4-8.5]</td>
<td>2.4 [0.6-5.7]</td>
<td>4.3 [2.0-6.7]</td>
<td>5.5 [3.4-7.4]</td>
<td>7.5 [5.7-8.8]</td>
<td>7.5 [5.7-8.8]</td>
</tr>
<tr>
<td>Stunting at 10y</td>
<td>28%</td>
<td>6%</td>
<td>17%</td>
<td>39%</td>
<td>22%</td>
<td>33%</td>
</tr>
</tbody>
</table>
Growth and CD4 patterns of adolescents living with perinatally acquired HIV worldwide, a CIPHER cohort collaboration analysis

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

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

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

**Objective**: to document HIV disclosure frequency and process; and to assess the association of HIV disclosure with the 24-month health outcomes among of adolescents with perinatal HIV APHIV

**Study population**: ART-treated APHIV aged 10–19 years, included in HIV care before the age of 10 years in Abidjan, and Lomé

**Variable of interest**: full HIV disclosure assessed at baseline, and over the 24-month follow-up period

**Outcome**: favorable combined 24-month outcome = none of these classifying criteria:
- Death, or progression to AIDS clinical stage
- CD4 count decrease >10% compared to baseline
- Detectable viral load >50 copies/mL
- Lost-to-follow-up: last visit >6 months at the database closure

<table>
<thead>
<tr>
<th></th>
<th>Total, N=209 (%)</th>
<th>Abidjan, N=108 (%)</th>
<th>Lomé, N=101 (%)</th>
<th>P Value(^{(1)})</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female sex</td>
<td>54.6</td>
<td>58.3</td>
<td>50.5</td>
<td>0.25</td>
</tr>
<tr>
<td>Full HIV-disclosure</td>
<td>41.6</td>
<td>57.4</td>
<td>24.8</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>AIDS WHO clinical stage</td>
<td>17.2</td>
<td>2.8</td>
<td>32.7</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>ART regimen</td>
<td></td>
<td></td>
<td></td>
<td>0.48</td>
</tr>
<tr>
<td>2 NRTI+1NNRTI</td>
<td>81.2</td>
<td>83.0</td>
<td>79.2</td>
<td></td>
</tr>
<tr>
<td>2 NRTI+1PI</td>
<td>18.8</td>
<td>17.0</td>
<td>20.8</td>
<td></td>
</tr>
<tr>
<td>Median CD4/mm(^{3})</td>
<td>521</td>
<td>540</td>
<td>484</td>
<td>0.71(^{(2)})</td>
</tr>
<tr>
<td>Median age at inclusion</td>
<td>13</td>
<td>14</td>
<td>12</td>
<td>0.01(^{(2)})</td>
</tr>
<tr>
<td>Median ART duration</td>
<td>6</td>
<td>9</td>
<td>5</td>
<td>&lt;0.01(^{(2)})</td>
</tr>
</tbody>
</table>

\(^{(1)}\) Chi2 test; \(^{(2)}\) Wilcoxon-Mann-Whitney test. ART: Antiretroviral therapy
Correlates of a favorable combined 24-month health outcome, 2015-2017

At 24 months:
- 74% fully HIV-disclosed (psychologist and parents mainly involved in disclosure process)
- 55% had an unfavorable outcome (2.9% died, 3.3% reached the AIDS WHO Stage, 36.3% had a CD4 count decrease > 10%, 34.9% had a detectable viral load)

<table>
<thead>
<tr>
<th>HIV Site*Disclosure (Interaction)</th>
<th>aOR (95% CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abidjan (Ref: HIV not disclosed)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HIV disclosed ≤ 2years</td>
<td>0.34 (0.06-1.92)</td>
<td>0.22</td>
</tr>
<tr>
<td>HIV disclosed &gt;2years</td>
<td>1.44 (0.53-3.87)</td>
<td>0.47</td>
</tr>
<tr>
<td>Lomé (Ref: HIV not disclosed)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HIV disclosed ≤ 2years</td>
<td>0.30 (0.87-1.04)</td>
<td>0.05</td>
</tr>
<tr>
<td>HIV disclosed &gt;2years</td>
<td>0.21 (0.05-0.84)</td>
<td>0.03</td>
</tr>
</tbody>
</table>

- Sex female (ref: males) | 0.76 (0.41-1.41) | 0.39    |
- No access to piped drinking water (ref: Yes) | 0.60 (0.25-1.45) | 0.26    |
- Rural Residential (ref: Urban) | 0.64 (0.23-1.81) | 0.40    |

- Living with (ref: Both parents)
  - Only one parent | 0.99 (0.45-2.15) | 0.98    |
  - Other family member | 0.56 (0.24-1.29) | 0.17    |

- ART duration in years, median [IQR] | 0.98 (0.89-1.09) | 0.52    |

aOR: adjusted Odds Ratio
Cerebral alterations in West African adults with and without HIV aged ≥50: An MRI study


**Objectives:** To describe brain alterations in people living with HIV aged above 50 years old, receiving antiretroviral treatment (ART) and living in Senegal compared to HIV-negative subjects

**Methods**
- Cross-sectional study
- Inclusion Site: Fann National University Hospital in Dakar, Senegal
- PLVIH aged ≥50 and on ART ≥6months
- Magnetic Resonance Imagering – 3 Tesla at the radiology service at the Principal Hospital, in Dakar
- MRI evaluation: Global atrophy (3D-T1) + White Matter Hyperintensities (FLAIR)

**Characteristics of the sample**
- 20 HIV adults vs 26 non-HIV adults
- Comparable socio-demographic and clinical characteristics
- 43.5% aged ≥60 years
- Female: 58.7%
- Hypertension: 28.3%
- Alcohol or drug consumption <2%
Cerebral alterations in West African adults with and without HIV aged >50: An MRI study

Results

- **Prevalence** [Confidence interval 95%]

<table>
<thead>
<tr>
<th></th>
<th>Non-HIV adults</th>
<th>HIV adults</th>
<th>p</th>
<th>Whole sample</th>
</tr>
</thead>
<tbody>
<tr>
<td>Global atrophy</td>
<td>11.5% [0.0 - 23.8%]</td>
<td>30% [9.9 - 50.1%]</td>
<td>0.15</td>
<td>19.6% [8.1 - 31.1%]</td>
</tr>
<tr>
<td>White Matter Hyperintensities (WMH)</td>
<td>34.6% [16.3 - 52.9%]</td>
<td>25% [6.0 - 43.9%]</td>
<td>0.54</td>
<td>30.4% [17.1 - 43.7%]</td>
</tr>
</tbody>
</table>

  **No significant effect of HIV status on atrophy or WMH**

- **Associated factors** (multivariable analyses, backward selection)

  In the whole sample:

  - Global atrophy
    - Unemployment (p=0.02)
    - Hypertension (p=0.03)
  - WMH
    - Age ≥ 60 (p=0.02)

Conclusion:

- Atrophy / WMH: high prevalence among older people living in West Africa, without a clear HIV impact
- Need to describe cardiovascular disease’s impact on the brain in this population
- Main study limitation: small sample size

*As brain MRI studies are critical to better understand cognitive and emotional outcomes, we encourage those studies in older PLHIV in West Africa*
Objective:
To document the association between chronic viral hepatitis, HIV infection and Non-Hodgkin Lymphomas in Côte d’Ivoire and Senegal

Methods:
- A case-control study was conducted in referral hospitals of Abidjan (Cote d’Ivoire) and Dakar (Senegal)
- Cases of NHL were matched with controls on age, gender and participating site
- The diagnosis of NHL relied on the combination of a first local pathological examination confirmed by a centrally-based diagnosis completed with immunohistochemistry (IHC)
- HIV, HBV and HCV serology tests were systematically performed (prior any chemotherapy)
- A conditional logistic regression model estimated the associations by the Odds Ratio (OR) with their 95% confidence interval (CI)
Results

- Enrollment of NHL cases in Abidjan and Dakar (2017-2020)
  
  150 participants eligible for a confirmatory diagnosis with IHC
  22% excluded based on IHC
  117 patients enrolled with confirmed NHL based on IHC

- Factors associated with NHL in Abidjan and Dakar (2017-2020)

<table>
<thead>
<tr>
<th></th>
<th>n/N</th>
<th>aOR (95% CI)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anti-HIV antibody</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>100/321</td>
<td>1</td>
<td>0.002</td>
</tr>
<tr>
<td>Positive</td>
<td>17/30</td>
<td>3.32 (1.54-7.16)</td>
<td>0.002</td>
</tr>
<tr>
<td>HBs antigen</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>102/320</td>
<td>1</td>
<td>0.03</td>
</tr>
<tr>
<td>Positive</td>
<td>15/31</td>
<td>2.23 (1.05-4.75)</td>
<td>0.03</td>
</tr>
<tr>
<td>Anti-HBc antibody</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>40/114</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Positive</td>
<td>77/237</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Anti-HCV antibody</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>108/337</td>
<td>1</td>
<td>0.008</td>
</tr>
<tr>
<td>Positive</td>
<td>9/14</td>
<td>4.82 (1.52-15.29)</td>
<td>0.008</td>
</tr>
</tbody>
</table>

Conclusion

Chronic viral hepatitis B and C were independently associated with NHL in West Africa

- Timely preventive measures against HBV infection and access to curative anti-HCV treatment might prevent a significant number of NHL
Human papilloma viruses infection among adolescent females perinatally infected with HIV in Côte d'Ivoire


Objective

• This study aimed to describe the HPV prevalence and correlates among adolescent females with perinatally acquired HIV eligible to HPV vaccination

Methods

• Cross-sectional study conducted from April to June 2016, in the four major pediatric HIV clinics of Abidjan
• Prior to the administration of HPV immunization, all females with HIV aged 11-16 years were proposed to participate
• A dedicated questionnaire was administered to assess sexual activity and gynecological hygiene practices followed by a gynecological examination and a cervico-vaginal swab collection
• HPV genotype identification performed using the Anyplex™ II HPV28 Detection (Seegene)
Results

- Among the 250 participants, the median age was 13 years [11-14]
- HPV prevalence was 3.6% [1.6-6.7]
- 77.8% of HPV-infected females harboring at least one oncogenic HPV

Conclusion

- Prevalent HPV infections were identified in this population of females with HIV eligible to HPV vaccination and were associated to vaginal toilet
- Genital hygiene practices and sexual education should be promoted in this high-risk population to prevent the acquisition of oncogenic HPV

Factors associated with the presence of HPV among adolescent females with HIV

<table>
<thead>
<tr>
<th>Factors</th>
<th>aOR</th>
<th>(95% IC)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>1.6</td>
<td>[0.7; 3.7]</td>
<td>0.240</td>
</tr>
<tr>
<td>Education level</td>
<td>0.8</td>
<td>[0.2; 4.4]</td>
<td>0.840</td>
</tr>
<tr>
<td>Vaginal cleansing</td>
<td>8.3</td>
<td>[1.6; 41.4]</td>
<td>0.009</td>
</tr>
<tr>
<td>Sexually active</td>
<td>3.1</td>
<td>[0.2; 37.2]</td>
<td>0.380</td>
</tr>
<tr>
<td>Initial CD4 count</td>
<td>1.0</td>
<td>[1.0; 1.0]</td>
<td>0.384</td>
</tr>
<tr>
<td>Clinical stage</td>
<td>0.9</td>
<td>[0.4; 2.5]</td>
<td>0.900</td>
</tr>
</tbody>
</table>
Virologic outcomes among adults with HIV using integrase inhibitor-based antiretroviral therapy.

**Background:** Integrase strand transfer inhibitor (InSTI)-based regimens have been recommended as first-line antiretroviral therapy (ART) for adults with HIV. But data on long-term effects of InSTI-based regimens on virologic outcomes remain limited. Here we examined whether InSTI improved long-term virologic outcomes compared with efavirenz (EFV).

**Methods:** We included adults from the North American AIDS Cohort Collaboration on Research and Design who initiated their first ART regimen containing either InSTI or EFV (exposures) between 2009 and 2016. We estimated differences in the proportion virologically suppressed (outcome) up to 7 years of follow-up in observational intention-to-treat and per-protocol analyses.

*Lu H* completed this work as a PhD-trainee (mentor: Steve Cole, UNC)
Results: Of 15318 participants, 5519 (36%) initiated an InSTI-based regimen and 9799 (64%) initiated the EFV-based regimen. In observational intention-to-treat analysis, 81.3% of patients in the InSTI group and 67.3% in the EFV group experienced virologic suppression at 3 months after ART initiation, corresponding to a difference of 14.0% (95% CI 12.4-15.6). At 1 year after ART initiation, the proportion virologically suppressed was 89.5% in the InSTI group and 90.2% in the EFV group, corresponding to a difference of -0.7% (95% CI -2.1 to 0.8). At 7 years, the proportion virologically suppressed was 94.5% in the InSTI group and 92.5% in the EFV group, corresponding to a difference of 2.0% (95% CI -7.3 to 11.3). The observational per-protocol results were similar to intention-to-treat analyses.

Conclusions: Although InSTI-based initial ART regimens had more rapid virologic response than EFV-based regimens, the long-term virologic effect was similar. Our findings may inform guidelines regarding preferred initial regimens for HIV treatment.

**Objective:** To project the future age distribution of people with HIV using antiretroviral therapy (ART) in the US, under expected trends in HIV diagnosis and survival (baseline scenario) and achieving the Ending the HIV Epidemic (EHE) goals of a 75% reduction in HIV diagnoses from 2020-25 and sustaining levels to 2030 (EHE75% scenario).

**Design:** An agent-based simulation model with mathematical functions estimated from North American AIDS Cohort Collaboration on Research and Design data and parameters from the US Centers for Disease Control and Prevention's annual HIV surveillance reports.

**Methods:** The PEARL (ProjEcting Age, multimoRbidity, and poLypharmacy in adults with HIV) model simulated individuals in 15 subgroups of sex-and-HIV acquisition risk and race/ethnicity. Simulation outcomes from the baseline scenario are compared with outcomes from the EHE75% scenario.
**Results:** Under the baseline scenario, PEARL projects a substantial increase in number of ART-users over time, reaching a population of 909,638 [95% uncertainty range (UR): 878,449-946,513] by 2030. The overall median age increased from 50 years (y) in 2020 to 52y in 2030, with 23% of ART-users age ≥65y in 2030. Under the EHE75% scenario, the projected number of ART-users was 718,348 [703,044-737,817] (median age=56y) in 2030, with a 70% relative reduction in ART-users <30y and a 4% relative reduction in ART-users age ≥65y compared to baseline, and persistent heterogeneities in projected numbers by sex-and-HIV acquisition risk group and race/ethnicity.

**Conclusions:** Our results provide important guidance for the critical task of preparing healthcare systems to meet the impending demand of the US population aging with HIV.
Mortality among persons entering HIV care compared to the general US population: an observational study.

**Background:** Understanding advances in the care and treatment of adults with HIV as well as remaining gaps requires comparing differences in mortality between persons entering care for HIV and the general population. Our objective was to assess the extent to which mortality among persons entering HIV care in the United States is elevated over mortality among matched persons in the general U.S. population and trends in this difference over time.

**Participants:** 82,766 adults entering HIV clinical care between 1999 and 2017 and a subset of the U.S. population matched on calendar time, age, sex, race/ethnicity, and county using U.S. mortality and population data compiled by the National Center for Health Statistics.

**Measurements:** Five-year all-cause mortality, estimated using the Kaplan-Meier estimator of the survival function.
Results: Overall 5-year mortality among persons entering HIV care was 10.6%, and mortality among the matched U.S. population was 2.9%, for a difference of 7.7 (95% CI, 7.4 to 7.9) percentage points. This difference decreased over time, from 11.1 percentage points among those entering care between 1999 and 2004 to 2.7 percentage points among those entering care between 2011 and 2017.

Conclusion: Mortality among persons entering HIV care decreased dramatically between 1999 and 2017, although those entering care remained at modestly higher risk for death in the years after starting care than comparable persons in the general U.S. population, suggesting that some factors (e.g. treatment discontinuation or disengagement from care) may influence the effectiveness of care.

**Background:** Studies suggest lower risk of breast cancer in women with HIV versus without HIV. These estimates may be biased by lower life expectancy and younger age distribution of women with HIV. Our analysis evaluated this bias and characterized secular trends in breast cancer among women with HIV initiating antiretroviral therapy. We hypothesized breast cancer risk would increase over time as mortality decreased.

**Setting:** Women with HIV prescribed antiretroviral therapy in the North American AIDS Cohort Collaboration on Research and Design (NA-ACCORD) from 1997 through 2016.

**Methods:** We estimated breast cancer hazard (cause-specific hazard ratios) and cumulative incidence accounting for competing risks (subdistribution hazard ratios) to assess changes in breast cancer risk over time. This was assessed overall (1997-2016) and within/across calendar periods. Analyses were adjusted for race/ethnicity and inverse probability weighted for cohort. Cumulative incidence was graphically assessed by calendar period and race/ethnicity.

*Coburn S* completed this work as a PhD-trainee (mentor: Keri Althoff, JHU)
**Results:** We observed 11,587 women during 1997-2016, contributing 63 incident breast cancer diagnoses and 1,353 deaths [73,445 person-years (median follow-up = 4.5 years)]. Breast cancer cumulative incidence was 3.2% for 1997-2016. We observed no secular trends in breast cancer hazard or cumulative incidence. There were annual declines in the hazard and cumulative incidence of death (cause-specific hazard ratios and subdistribution hazard ratios: 0.89, 95% confidence interval: 0.87 to 0.91) which remained within and across calendar periods.

**Conclusions:** These findings contradict the hypothesis of increasing breast cancer risk with declining mortality over time among women with HIV, suggesting limited impact of changing mortality on breast cancer risk. Additional inquiry is merited as survival improves among women with HIV.

**Legend:** Cumulative incidence of breast cancer over age by calendar period (A) and race/ethnicity (B) (N=11,587), NA-ACCORD, 1997-2016. *Truncated at age 80 due to limited person-years (<100 person-years).*
COVID-19 infections post-vaccination by HIV status in the US

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**Importance:** Recommendations for additional doses of COVID vaccine are restricted to people with HIV who have advanced disease or unsuppressed HIV viral load. Understanding SARS-CoV-2 infection risk post-vaccination among PWH is essential for informing vaccination guidelines. Our objective was to estimate the risk of breakthrough infections among fully vaccinated people with (PWH) and without (PWoH) HIV in the US.

**Design, setting, and participants:** The Corona-Infectious-Virus Epidemiology Team (CIVET)-II cohort collaboration consists of 4 longitudinal cohorts from integrated health systems and academic health centers. Each cohort identified individuals ≥18 years old, in-care, and fully vaccinated for COVID-19 through 30 June 2021. PWH were matched to PWoH on date fully vaccinated, age group, race/ethnicity, and sex at birth. Incidence rates per 1,000 person-years and cumulative incidence of breakthrough infections with 95% confidence intervals were estimated by HIV status. Cox proportional hazards models estimated adjusted hazard ratios (aHR) of breakthrough infections by HIV status adjusting for demographic factors, prior COVID-19 illness, vaccine type (BNT162b2, [Pfizer], mRNA-1273 [Moderna], Jansen Ad26.COV2.S [J&J]), calendar time, and cohort. Risk factors for breakthroughs among PWH, were also investigated.

**Outcome:** COVID-19 breakthrough infections, defined as laboratory evidence of SARS-CoV-2 infection or COVID-19 diagnosis after an individual was fully vaccinated, stratified by HIV infection status.

*Coburn S and Lang R completed this work as post-doctoral fellows (mentor: Keri Althoff, JHU)*
**Results:** Among 109,599 individuals (31,840 PWH and 77,759 PWoH), the rate of breakthrough infections was higher in PWH versus PWoH: 44 [41, 48] vs. 31 [29, 33] per 1,000 person-years. Cumulative incidence (Figure on left) at 210 days after date fully vaccinated was low, albeit higher in PWH versus PWoH overall (2.8% versus 2.1%, log-rank p<0.001, risk difference=0.7% [0.4%, 1.0%]) and within each vaccine type. Breakthrough infection risk was 41% higher in PWH versus PWoH (aHR=1.41 [1.28, 1.56]). Among PWH, younger age (18-24 versus 45-54), history of COVID-19 prior to fully vaccinated date, and J&J vaccination (versus Pfizer) were associated with increased risk of breakthroughs. There was no association of breakthrough with HIV viral load suppression or CD4 count among PWH (Figure on right).

**Conclusions:** COVID-19 vaccination is effective against infection with SARS-CoV-2 strains circulating through 30 Sept 2021. PWH have an increased risk of breakthrough infections compared to PWoH emphasizing the importance of additional vaccine doses for all PWH.