IeDEA Global Cohort Consortium

2019 Research Highlights

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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.

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2019 IeDEA Asia-Pacific Research Highlights
**Trends in mortality among ART-treated HIV-infected adults in the Asia-Pacific region between 1999 and 2017: results from TAHOD and AHOD**

- **Objective:** Investigate incidence of AIDS & non-AIDS deaths, & factors associated with different causes of death (COD) in the Asia-Pacific region in the cART era
- **TREAT Asia (TAHOD) & Australian HIV Observational Database (AHOD) patients on cART between 1999-2017**
- **COD data validated using the CoDe case report form**
- **10,386 patients: 187 AIDS-related deaths, 335 non-AIDS**
- **Incidence rate (IR) during follow-up: AIDS-related 0.28/100 PYS, non-AIDS 0.51/100 PYS**

Decreasing AIDS and non-AIDS–related mortality rates over the past years in the Asia-Pacific region

- From 2003-2007 to 2013-2017: AIDS-related IR fell from 0.51 to 0.09/100 PYS (p <0.001), non-AIDS IR fell from 0.78 to 0.37/100 PYS (p <0.001)
- Higher CD4 associated with reduced hazard for AIDS & non-AIDS mortality
- Diabetes & BMI <18.5 associated with increased hazard for AIDS & non-AIDS mortality
- Non–AIDS mortality at AHOD vs TAHOD LMIC sites: aSHR 1.72, 95% CI, 1.20 to 2.46, (p=0.003); no difference between cohorts for AIDS-related (p=0.834)
The influence of age-associated comorbidities on responses to cART in older people living with HIV

- Objective: Investigate effects of age-associated comorbidities on therapeutic outcomes of cART
- PLHIV age ≥18, in TAHOD between 2003-2015, on cART >6 months
- Comorbidities: hypertension, diabetes, dyslipidaemia, impaired renal function
- Virologic failure: single VL >1000 copies/mL (WHO 2016)
- Immunologic failure: CD4 <250 cells/μL after clinical failure, or two consecutive CD4 <100 within 6m (WHO 2016)

Age-associated comorbidities did not affect virologic outcomes of cART

- 912/5411 patients (17%) with VF: IR 7.72/100 PYS
- Age-related comorbidities not a significant factor for VF (HR 1.31, 95% CI 0.98 to 1.74, p=0.07)
- 391/5621 patients (7%) with immunologic failure: IR 2.75/100 PYS

Patients ≥50 years with comorbidities had a greater rate of immunologic failure vs. patients <50 with comorbidities.
Impact of the frequency of plasma viral load monitoring on treatment outcomes among children with perinatally acquired HIV

- Objective: Determine the impact of annual vs. semi-annual VL monitoring on treatment outcomes
- Aged <18 years, paHIV, enrolled before March 2015, on virally suppressive 1st line NNRTI-based cART
- VS: 2 consecutive VL <400 copies/mL over ≥ 6 months
- Treatment failure: VF (2 consecutive VL >1000), change of ARV class, or death
- 1220 CLWH: 1042 (85%) from annual VL sites (n=6), 178 (15%) from semi-annual VL sites (n=4)

Annual VL monitoring was not associated with an increased risk of treatment failure

- TF in 258 (25%) with annual VL: IR 5.4/100PYS
- TF in 40 (23%) with semi-annual VL: IR 4.3/100PYS
- VL monitoring frequency not associated with TF (aHR: 1.12; 95% CI: 0.80 to 1.59)
Peritransition Outcomes of Southeast Asian Adolescents and Young Adults With HIV Transferring From Pediatric to Adult Care

- Objective: Study clinical & social outcomes of health care transition among Asian adolescents & young adults with HIV (AYHIV)
- AYHIV transferred from pediatric to adult clinic at Malaysia (2), Thailand (3), & Vietnam (1) sites
- Clinical & lab evaluations; completed health, socioeconomic, & transition experience questionnaires
- 93 AYHIV enrolled from Jun 2016-Apr 2017: 56% female, 87% perinatal HIV, median age 20 years

Support strategies for Asian AYHIV must address concerns around HIV disclosure and lack of social support

- Two-thirds in formal education; 43% employed, 43% of females and 35% of males sexually active
- Median ART duration 6.2 yrs; median CD4 601 cells/mm$^3$; 82% had HIV-RNA <40 copies/mL
- In a relationship, shorter post-transition duration, 95% self-reported adherence, & higher CD4 inversely associated with HIV viremia
- Half felt very prepared for transfer to adult care; two-thirds reported needing to keep their HIV a secret; 23%-38% reported never/rarely having someone to confide in
Crystal amphetamine use is common and associated with HIV infection among MSM and TGW in Bangkok, Thailand

• Objectives: (i) Determine amphetamine-type substance (ATS) & drug use patterns, (ii) Evaluate effect of ATS use on HIV incidence, PrEP & ART adherence, and virologic suppression
  ➢ ATS use included crystal meth, ecstasy or oral amphetamine; Problem alcohol use = AUDIT-C score ≥4

• MSM/TG ≥18 years old, presenting to Thai Red Cross Anonymous Clinic for HIV tests surveyed on substance use, sexual risk, HIV status (Jan-Nov 2019)

• 679 MSM and 59 TGW participated

**Factors associated with ATS use among MSM and TGW in Bangkok (n=738)**

<table>
<thead>
<tr>
<th>Factors</th>
<th>Multivariable model</th>
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<tr>
<td></td>
<td>Adj. OR</td>
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<tr>
<td>Age group*</td>
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<tr>
<td>&lt;25 years old</td>
<td>Ref.</td>
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<tr>
<td>≥25 years old</td>
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<td>Paying someone for sex in the past six months*</td>
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<td>No</td>
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<td>Yes</td>
<td>1.26</td>
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<tr>
<td>Receiving money in exchange for sex in the past six months*</td>
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<tr>
<td>Yes</td>
<td>2.22</td>
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<td>Having group sex in the past six months*</td>
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<td>No</td>
<td>Ref.</td>
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<tr>
<td>Yes</td>
<td>3.58</td>
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<tr>
<td>Current tobacco smoking*</td>
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<td>Yes</td>
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<tr>
<td>Problem alcohol use*</td>
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<td>No</td>
<td>Ref.</td>
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<tr>
<td>Yes</td>
<td>2.04</td>
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<tr>
<td>HIV status*</td>
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<tr>
<td>Negative</td>
<td>Ref.</td>
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<tr>
<td>Positive</td>
<td>2.09</td>
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- Tobacco use 18.5%
- Problem alcohol use 26%
- ATS use 17%
  - Crystal meth injection 7%
- Other substance use & sexual practices associated with ATS use
- Need for ATS screening, harm-reduction and treatment interventions
CCASAnet Publication Highlights: 2019
We included data from PLWH ≤18 years of age attending one of six CCASAnet sites in Brazil, Chile, Haiti, Honduras, Mexico, and Peru.

For primary analyses, we compared those with (n=1051) and without TB at enrollment (n=15,987) who were alive and in care 9 months after enrollment.

Prior studies among persons not living with HIV have seen that the risk of mortality is higher among those cured of TB than matched persons who never had TB.

We sought to study whether this was the case in PLWH in Latin America who had completed TB treatment.
TB was associated with higher mortality
  - \( \text{aHR} = 1.57 \) (95% CI 1.25-1.99)
  - Analyses were adjusted for study site, sex, education, age, year of enrollment, and CD4 count

Several sensitivity analyses yielded similar results
  - Limited to those with pulmonary TB,
  - Limited to those who initiated ART in the first 9 months
  - Including ART as time-varying covariate
  - Excluding those who had a second episode of TB >9months

These findings highlight
  - The critical importance of TB prevention in persons with HIV
  - Closer long-term follow-up may be warranted in PLWH with history of TB
• Malnutrition and HIV are two of the main risk factors for TB; both also adversely affect TB treatment outcomes. Previous studies report varying degrees of association between weight change during TB treatment and treatment outcome, but few addressed TB-HIV co-infection.

• **Objectives:** (1) Examine the association between HIV and weight change during first two months of TB treatment, (2) Assess associations of HIV, baseline weight, and weight change in first two months of TB treatment with unsuccessful tuberculosis treatment outcome (treatment failure, TB recurrence, and death)

• Included 547 (n=102, 19% PLWH) culture-confirmed, drug susceptible, pulmonary TB patients enrolled in RePORT-Brazil between June 30, 2015 and May 1, 2018 who received ≥1 dose of standard TB therapy (RZHE) and had two months of follow-up
  – Median age was 37 years [IQR: 26-49], 64% were male

• Among PLWH, median CD4 at baseline was 97 cells/mm³; 36% were on ART prior to TB diagnosis and 28% started ART within 2 weeks of TB diagnosis.
• PLWH gained 1.3 kg less than (95% CI: -2.8-0.1) HIV-negative individuals, adjusted for site, baseline weight, age, sex, smear status, and hemoglobin. Association was more pronounced among PLWH with lower CD4 counts and higher viral loads.

<table>
<thead>
<tr>
<th>Table 3. Cox Proportional Hazards Regression for Predictors of Unsuccessful Treatment Outcome (Death, Treatment Failure, and Tuberculosis Recurrence)</th>
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<tbody>
<tr>
<td>Factor by Population</td>
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<td></td>
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<tr>
<td>Primary analysis population</td>
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<tr>
<td>HIV status</td>
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<td>Positive</td>
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<tr>
<td>Negative</td>
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<tr>
<td>Baseline weight (per 1-kg increase)</td>
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<td>Weight at 2 mo (per 1-kg increase)</td>
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<tr>
<td>Absolute weight change (per 1-kg increase)</td>
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<td>Relative weight change (per 1% increase)</td>
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</table>

• PLWH were 4.8 times more likely (95% CI: 2.1-10.9) to have an unsuccessful TB outcome (death, failure, relapse) than HIV-negative individuals, adjusted for sex and hemoglobin.

• Weight gain was protective for unsuccessful TB outcome. For every 1-kg increase in weight, risk of unsuccessful outcome decreased 12% (HR: 0.88, 95% CI: 0.81-0.95), adjusted for baseline weight, HIV, and sex.

• Mediation analysis suggested that 35% of the effect of HIV on unsuccessful treatment outcome was mediated through weight change.

PMCID: pending
In 2013, the WHO recommended initiating cART in all adults with HIV and CD4 counts > 500.

In 2015, this was updated to recommend cART initiation in all patients with HIV, regardless of CD4 count.

Implementation of these guidelines in real-world settings has not been evaluated in Latin America.

We estimated trends in time from enrolment in care to cART initiation in HIV-positive adults with high CD4 counts in CCASAnet from 2003 to 2017.

We included data from six sites in Brazil, Chile, Honduras, Mexico, Peru.
• Among all patients, median time to cART initiation between 2003 and 2008 was 169 weeks (95% CI: 156 to 180); time to cART initiation decreased to seven weeks (95% CI: 6.4 to 8) between 2015 and 2017 (Figure 1). Among those initiating cART, median time to cART initiation was 4.71 weeks (IQR: 1.43, 9.57) after 2015 (Figure 2).

• However 763 (24%) patients never initiated cART, and of these, 33 (4.3%) were reported as deceased, 481 (63%) were lost to follow-up, and 249 (33%) were administratively censored before initiation.

• Time to cART initiation decreased substantially, roughly following changes in WHO guidelines in this real-world setting in Latin America. However, a high proportion of patients never started cART, compromising retention in care and survival, reinforcing the notion that earlier treatment implementation strategies are needed.
We estimated adjusted attributable risks (AR) and population attributable fractions (PAF) of all-cause mortality for these exposures:

- Presentation to care with advanced HIV (LP)
- ART initiation with advanced HIV (LI) {among those without LP}
- Not initiating ART (NI) {among LP}

The AR is the proportion of deaths that would have been averted if the exposure were eliminated (among the exposed)

The PAF is the proportion of deaths in the entire study population that would have been averted had exposed persons not been exposed.

Late presentation for care and ART initiation with advanced HIV are common in Latin America

We therefore estimated the impact of these conditions on mortality among adults enrolling in care from 2001-2014 at six CCASAnet sites in Argentina, Brazil, Chile, Honduras, Mexico, and Peru.
• Advanced HIV was CD4 <200 cells/µL or AIDS-defining event

• The AR and PAF were derived using predicted probabilities of death from marginal structural models with IPW to reduce confounding and emigrative selection bias

• The AR = \(\frac{p(D|E)-p(D|\bar{E})}{p(D|E)}\)

• The PAF = \(\frac{p(D|E) \times p(E) + p(D|\bar{E}) \times (1-(p(E))) - p(D|\bar{E})}{p(D|E) \times p(E) + p(D|\bar{E}) \times (1-(p(E)))}\)

• Among 9,229 eligible individuals, 56% were LP

• ARs of death at 1, 5, and 10 years post-enrollment:
  • For LP were 86%, 71%, and 58%
  • For LI were 39%, 32%, and 37%

• PAFs of death at 1, 5, and 10 years post-enrollment:
  • For LP were 78%, 58%, and 43%
  • For LI were 20%, 14%, and 15%

• Among LP, ART reduced the mortality hazard by 63%, though 93% of LP started ART; therefore, eliminating NI would only reduce mortality 10%

• Earlier presentation and ART initiation would avert most HIV-related deaths in Latin America
• Source document verification auditing is a procedure for assessing the accuracy and completeness of research data. It can inform activities to improve data quality.
• During 2013-2014, we conducted on-site audits of datasets from nine HIV clinics in CCASAnet and calculated error rates.
• After the audit, some sites were asked to conduct targeted validation of variables with high error rates, resulting in a post-audit dataset.
• To quantify the impact of the audit process, we estimated the times from ART start until death and first AIDS-defining event using the pre-audit data, the audit data, and the post-audit data.
• The overall discrepancy rate between pre-audit and audit data (n = 250) across all audited variables was 17.1%.
• The estimated probability of mortality and an AIDS-defining event over time was higher in the audited data relative to the pre-audit data.
• Among patients represented in both the post-audit and pre-audit cohorts (n = 18,999), AIDS and mortality estimates were also higher in the post-audit data.

Some data changes in the post-audit data may have been independent of the audit process.
Study results and corresponding inferences can be affected by improvements in data quality following data audits.
Central Africa – IeDEA

Research Highlights 2019
Early outcomes after implementation of Treat All in Rwanda: an interrupted time series study


AIMS:

• Estimate the effect of Treat All implementation on timely ART initiation and retention in care.

• Identify predictors of ART initiation and retention in care after Treat All implementation.

METHODS:

• Interrupted time series of patients entering care at IeDEA-affiliated health centers in Rwanda between July 2014 – November 2017.

• Used segmented linear regression models to estimate predicted probability of initiating ART within 30 days of enrollment and six-month retention in care in each month.
RESULTS:

- 34% increase in predicted probability of 30-day ART initiation immediately after Treat All implementation.
- 44% increase in predicted probability of 30-day ART initiation at end of study period from what would have been expected without Treat All.
- No significant change in predicted probability of 6-month retention in care immediately after Treat All implementation and at study end.
- Young PLWH (aged 15-24) 7% less likely to initiate ART within 30 days and 11% less likely to be retained in care.

Proportion of patients initiating ART within 30 days and retained in care at 12 months among new patients in HIV care at 10 Rwandan health centers (N=2885)
Implementation of “Treat All” at adult HIV care and treatment sites in the Global IeDEA Consortium: results from the site assessment survey


**AIMS:** To describe site-level capacity and practice related to HIV care, including the current status of Treat All implementation and the timing of site-level Treat All introduction relative to national guideline adoption.

**METHODS**

- Cross-sectional survey (July-December 2017) of 255 HIV clinics in 44 countries that are actively contributing data to IeDEA consortium.
- Data for 201 adult HIV treatment sites (41 countries) were used to describe the status and timing of site-level introduction of Treat All, as well as site-level practices related to ART initiation.
Implementation of “Treat All” at adult HIV care and treatment sites in the Global IeDEA Consortium: results from the site assessment survey

93% of adult HIV treatment sites (187/201) reported that they currently initiate all patients on ART, irrespective of CD4+ count/WHO stage.

- No significant differences by facility type, urban/rural location, sector (public vs. private), country income, or PEPFAR/Global Fund-support status.

Site-level introduction was earlier at regional/provincial and teaching hospitals (vs. clinic), private sector facilities, and sites located in high-income, non-PEPFAR-supported countries.

- Median year of site-level Treat All introduction ranged from 2011 to 2017 across countries.
Benchmarking “real world” global data on CD4 count at ART initiation against landmark randomized controlled trials shows that early diagnosis and ART initiation following seroconversion are key implementation challenges for the HIV response.

A pre-treatment CD4 count of 350 cells/µL reflects 2.8-3.4 years since seroconversion, on average.

A pre-treatment CD4 count of 500 cells/µL reflects 1-2 years since seroconversion, on average.

Only 25% initiate ART with CD4>500 globally and <50% with CD4>350.
Viral suppression among pregnant and breastfeeding women in routine care in the Kinshasa province: a baseline evaluation of participants in CQI-PMTCT study


AIMS:

1) To estimate the proportion of pregnant and breastfeeding women receiving routine HIV care in maternal and child health (MCH) clinics in the Kinshasa province of the Democratic Republic of Congo with undetectable (<40 copies/ml) or suppressed (<1000 copies/ml) viral load.

2) To assess socio-demographic, clinical and health facility characteristics associated with viral load suppression.

METHODS:

• Between November 2016 and June 2018, all pregnant or breastfeeding women receiving ART care at 105 MCH clinics across 35 health zones in Kinshasa were enrolled and their viral load assessed as part of an ongoing RCT of continuous quality interventions (CQI) on long-term ART outcomes among pregnant and breastfeeding women (NCT03048669).

• Baseline data for 1623 women with viral load testing results were used to estimate undetectable and suppressed viral load and to identify factors associated with viral suppression.
Viral suppression among pregnant and breastfeeding women in routine care in the Kinshasa province: a baseline evaluation of participants in CQI-PMTCT study


RESULTS:
• Only 62% and 53%, respectively, had suppressed (< 1000 copies/mL) and undetectable (<40 copies/mL) viral loads.
• One-third of those on ART for ≥12 months were not virally suppressed.
Impact of universal antiretroviral treatment eligibility on rapid treatment initiation among young adolescents with HIV in SSA


AIM: To examine whether universal antiretroviral treatment (ART) eligibility policies (Treat All) improved rapid ART initiation following care enrollment among 10-14-year-olds in seven sub-Saharan African (SSA) countries.

METHODS:

• Data for 6,912 10-14-year-old patients were used to estimate changes in rapid ART initiation (within 30 days of care enrollment) following adoption of Treat All policies in two groups of countries: Uganda and Zambia (policy adopted in 2013) and Burundi, Democratic Republic of the Congo, Kenya, Malawi, and Rwanda (policy adopted in 2016).

• Regression discontinuity analysis used to estimate effect of Treat All on rapid ART initiation, with enrollment date used as assignment variable, and the date of national Treat All adoption as the discontinuity threshold.
Impact of universal antiretroviral treatment eligibility on rapid treatment initiation among young adolescents with HIV in SSA


RESULTS: National adoption of the “Treat All” recommendation led to large increases in rapid ART initiation among young adolescents, aged 10-14 years.

- In countries adopting the Treat All policy in 2016, there was a 23.4 percentage points (pp) increase (95%CI: 13.9-32.8) in rapid ART initiation.

- There was a smaller increase in rapid ART initiation (11.2pp; 95%CI: 2.5-19.9) in countries adopting pediatric Treat All policies in 2013. However, the rate of increase in rapid ART initiation among 10-14-year-olds in these countries rose appreciably, from 1.5pp per year before Treat All to 7.7pp afterwards.
Semiparametric analysis of competing risks data under missing cause of failure

Background
• Programmatic data to assess HIV care cascade on a system-wide level is difficult because of missing data and lack of statistical methods
• Previous methods address data enhancements to model transition from HIV care to death or disengagement (viewed as “absorbing states” in multi-state models).

Methods
• Develop estimators of state occupation probabilities (valid even under non-Markov situations) (Bakoyannis et al., Stat Sinica, 2019)
• Use patient tracing to develop multi-state models of transition to death or return to care after a “gap” (no longer an absorbing state) (Bakoyannis et al. LiDA, 2020)
• Main challenge: Unknown who has true gap in (is disengaged from) care!
• Solution: Use only patients who were traced to determine a “denominator”
Semiparametric analysis of competing risks data under missing cause of failure

Methods (continued)

• View unreported deaths as outcome misclassification (of death as gap in care) and trace a subset of dropouts to determine misclassification error

• Use prob. of tracing in a (“sieve”) inverse probability weighted (SIPW) estimator of hazard of return to care or death

Results

• SIPW estimator is doubly robust (i.e., either tracing or data augmentation can be wrong and model still consistent)

• Results consistent with recent ad hoc studies (Geng et al., Lancet HIV, 2015, Rebeiro et al., JAIDS 2017): Majority of patients with gap in care return to care

Conclusions

• One more step towards a complete multi-stage model of the HIV care cascade using suitably enhanced programmatic data

• Study limited by unknowns about clinical impact of gaps in care and unstructured transfers (IWHOD 2020 presentation by Thomadakis et al.).
Causal inference when counterfactuals depend on proportion of all subjects exposed

Background

• Most research assumes one subject’s outcome not influenced by another’s.
• The concept of “interference” relaxes that assumption
• Assessing the effect of interference is critical in evaluation of programmatic interventions (implementation science)
• However, operationalizing interference is challenging

Methods

• Miles et al., (Biometrics, 2019) express interference as the effect on a subject’s outcome by the proportion of subjects exposed to the program.
• An example is given from a task-shifting program targeting low-risk patients who are stable on ART.
• Authors use targeted maximum likelihood estimation (TMLE) to estimate both direct (factual) effects and counterfactual effects of a program’s implementation
Causal inference when counterfactuals depend on proportion of all subjects exposed

Results

• (a) Task shifting beneficial in all but one clinic with lowest proportion task shifted
• (b) Counterfactual scenario shifting patients randomly showed no effect)
• (c) Counterfactual scenario with probability of task shifting higher at higher CD4 counts, showed stronger effect with higher proportion task shifted).

Conclusion

• Methodology useful in implementation science and situations where cumulative levels of exposure to a program affect outcomes.
Mortality Among People With HIV Treated for Tuberculosis Based on Positive, Negative, or No Bacteriologic Test Results for Tuberculosis: The IeDEA Consortium

Background

• In resource-limited settings many people are treated for TB empirically in the absence of any TB test.

• It has been shown that people living with HIV (PLWH) treated for TB despite a negative TB bacteriologic test have a higher mortality than those treated for TB with a positive test.

Methods

• Humphrey et al. (final paper *Open Forum Infect Dis, 2020*) used multi-regional IeDEA data on 2019 PLWH treated for TB to compare 12-month mortality among those treated for TB in the absence of a TB test to those treated for TB with either positive or negative TB test results.
Mortality Among People With HIV Treated for Tuberculosis Based on Positive, Negative, or No Bacteriologic Test Results for Tuberculosis: The IeDEA Consortium

Results

• Hazard of death was 56% higher (aHR 1.56, 95% CI 1.08-2.26) among those treated for TB in the absence of any TB test compared to those with positive tests.

• Hazard of death was higher among patients with a negative test compared with those with a positive test but was not statistically significant (aHR, 1.28; 95% CI, 0.91–1.64)

Conclusion

• There is need to scale-up access to TB bacteriologic testing in resource-limited settings

• There is also need to differentiate the true causes of death in the group of people treated for TB without bacteriologic testing.
Real-world use of chemotherapy for KS in a large community-based HIV primary care system in Kenya

Background

• Kaposi’s sarcoma (KS) is one of the most common HIV-associated malignancies in sub-Saharan Africa.
• Worldwide availability of antiretroviral therapy (ART) and chemotherapy in resource-rich settings has improved KS survival.
• Little is known about epidemiology of chemotherapy use for HIV-associated KS in sub-Saharan Africa.

Methods

• Freeman et al. (final paper BMC Cancer, 2020) identified all patients newly diagnosed with HIV-related KS from 2009 to 2012 in the 26-clinic AMPATH network in Kenya.
• Ascertained disease severity at diagnosis, frequency of initiation of chemotherapy, and distribution of chemotherapy regimens used.
• Indications for chemotherapy included AIDS Clinical Trial Group T1 stage and/or “severe” disease defined by WHO KS treatment guidelines.
Real-world use of chemotherapy for KS in a large community-based HIV primary care system in Kenya

Results

• For patients with a chemotherapy indication, cumulative incidence of chemotherapy (death a competing event) was 37% by 1 month and 56% by 1 year.
• Median time from diagnosis to chemotherapy initiation was 25 days (IQR 1–50 days).
• Patients with >3 chemotherapy indications at diagnosis had a 2.30 (95% CI 1.46–3.60) increased risk of chemotherapy initiation within 30 days of diagnosis compared to those with one chemotherapy indication.

Conclusions

• A substantial fraction of KS patients are diagnosed at advanced disease stage.
• Even for patients with chemotherapy indications, nearly half did not receive chemotherapy by one year.
• Liposomal anthracyclines, often used in resource-rich settings, were not first line.
• These findings emphasize challenges in East Africa cancer care, and highlight the need for further advocacy for improved access to higher quality chemotherapy in this setting.
Validation of a self-report adherence measurement tool among a multinational cohort of children living with HIV in Kenya, South Africa and Thailand

Background

• There are limited data on low-cost adherence measurement tools for children living with HIV (CLWH).

Methods

• Vreeman et al. (J Int AIDS Soc, 2019) collected prospective data in a multi-national cohort of children to evaluate a questionnaire for adherence to antiretroviral therapy (ART)

• Child-reported and caregiver-reported adherence scores were contrasted to dichotomized MEMS® and 48-hour treatment interruptions also assessed through MEMS® ("gold standard") as well as viral suppression
Validation of a self-report adherence measurement tool among a multinational cohort of children living with HIV in Kenya, South Africa and Thailand

Results

• Summation score of child and caregiver questionnaire were significantly associated with dichotomized MEMS® adherence and MEMS® 48-hour treatment interruptions, but not with viral suppression

• Child-reported adherence was associated with all three external criteria, while caregiver report was not (Table 5)

Conclusions

• Study provides evidence for a 10-item questionnaire for routine adherence screening in a clinic setting

• Questionnaire performed much better when administered to children rather than their caregivers.
IeDEA Southern Africa
Research Highlights 2019
Characterizing the double-sided cascade of care for adolescents living with HIV transitioning to adulthood across Southern Africa


Background

• Adolescents and young adults living with HIV (AYLH) face transitions in care as they grow older and become responsible for their own health

• In some settings including sub-Saharan Africa, transition to adulthood is not accompanied by physical transfer of care

Aim

• To evaluate gaps in care and viral suppression of AYLH in contexts where adolescents remain at the same facility through to adulthood

Methods

• AYLH <16 years receiving ART in IeDEA-SA sites 2004 to 2017, no history of transferring care

• We evaluated gaps in care and viral suppression in the year before and after their 16th, 18th, 20th, and 22nd birthdays, using different age thresholds as proxies for ‘transition to autonomy’

• We assessed predictors of retention in 12 months post-transition using log-binomial regression models

IeDEA
Characterizing the double-sided cascade of care for adolescents living with HIV transitioning to adulthood across Southern Africa

Results

• We included 5516 AYLH at transition age 16y, 3864 at 18y, 1463 at 20y, & 440 at 22y

• Across all transition-age thresholds, the proportion with no gap in care consistently declined post- when compare to pre-transition (Figure).

• There were no differences in the proportions of patients virally suppressed in either period (Figure)

• Patients were consistently more likely to be retained post-transition if they had no gap in care in the preceding year, across all transition-age thresholds

Conclusions

• Targeted support for AYLH with gaps in care is needed as they take on greater responsibility for their healthcare

• Interventions to increase virologic suppression rates are necessary for all AYLH ageing to adulthood.

Figure: Outcomes across different transition age thresholds
Modelling Antiretroviral drug Resistance In Southern Africa: the MARISA project

1) Construct a model
Compartmental model capturing HIV epidemic in South Africa

2) Calibrate the model
Using different sources of data
- Longitudinal data
- Literature
- Thembisa Model

3) Reproduce HIV epidemic and dynamic of NNRTI resistance

4) Simulate counterfactual scenarios
e.g. earlier switch to 2nd-line regimen

Modelling Antiretroviral drug Resistance In Southern Africa: the MARISA project

- **Counterfactual scenario**: earlier switch to 2\textsuperscript{nd}-line regimen

Increased switching rate
- Black: Baseline model
- Blue: 2*rate
- Red: 5*rate
- Orange: 10*rate

Earlier switch to 2\textsuperscript{nd}-line could have reduced resistance to NNRTI, but not prevented it from emerging.

Earlier antiretroviral therapy initiation and decreasing mortality among HIV-infected infants initiating antiretroviral therapy within 3 months of age in South Africa, 2006-2017

Victoria Iyun MPH1, Karl-Gunter Technau 2, Brian Eley 3, Helena Rabie 4, Andrew Boulle 1,5, Geoffrey Fatti7, Matthias Egger8, Frank Tanser 9, Robin Wood DSC 10, Lee Fairlie 11, Mark F. Cotton 5,13, Mary-Ann Davies 1

• Introduction:
  ➢ Early infant diagnosis of HIV and antiretroviral therapy (ART) have been rapidly scaled-up in South Africa.
  ➢ While the outcomes of infants infected before the availability of early infant diagnosis (EID) and early ART have been described, there is limited data on infants initiating early ART outside research-controlled settings, in the context of improved EID practices and widespread access to ART.
  ➢ We investigated the effect of expanded access to EID and ART on:
    o ART initiation characteristics
    o Outcomes of infants initiating ART (Mortality, loss to follow-up and transfers to other clinics)

• Methods:
  ➢ From nine cohorts within the International epidemiologic Databases to Evaluate AIDS - Southern Africa collaboration, we included infants with HIV initiating ART ≤3 months of age between 2006-2017.
  ➢ We report trends in ART initiation characteristics and the probability of mortality, loss to follow-up (LTFU) and transfer out (TFO) after 6 months on ART.
  ➢ Assessed factors associated with mortality and LTFU.
Findings:

- 1847 infants started ART at a median age of 60 days (interquartile range (IQR) 29-77) and CD4% of 27% (IQR 18%-38%)

- Across ART initiation periods 2006-2009 to 2013-2017, ART initiation age decreased from 68 (IQR 53-81) to 45 days (IQR 7-71) (p<0.001)

- Median CD4% improved from 22% (IQR 15%-34%) to 32% (IQR 22-43) (p<0.001) and the proportion with WHO disease stage declined from 81.6% to 32.7% (p<0.001)

- Overall, 5.0% of infants died, 20.4% became LTFU and 8.5% were TFO by six months on ART.

- Mortality decreased from 10.6% (7.8%-14.4%) in 2006-2009 to 4.6% (3.1%-6.7%) in 2013-2017 (p<0.001)

- LTFU remained similar across calendar periods (p=0.274), with nearly three-quarters of those lost having no follow-up after their ART initiation visit

- Pre-treatment weight-for-age Z-score < -2 was associated with higher mortality.

Conclusions:

- An increasing proportion of infants started ART at younger ages and with less advanced HIV disease over time

- Although mortality was halved from 2010 onwards, mortality remained at 4.1% after 2013.

- Despite earlier ART initiation, the risk of mortality remained high in recent years, suggesting the increasing role of factors beyond ART effectiveness such as prematurity and associated complications, infectious comorbidities and psychosocial characteristics.

Figure: Cumulative incidence functions stratified by calendar period of ART initiation for: (A) Mortality accounting for LTFU and TFO as competing events (B) LTFU accounting for death and TFO as competing events. Plot shows time to LTFU defined as no visit from 4-9 months on treatment.
Drug susceptibility testing and mortality in patients treated for tuberculosis in high-burden countries: a multi-centre cohort study

**Aim:** To compare results of resistance testing done at HIV clinics or TB clinics in low- and middle-income countries with results from phenotypic drug susceptibility testing (DST) done at the Swiss reference laboratory, and examined mortality during TB treatment.

**Methods:**

- Clinical data and *Mtb* isolates from TB patients (≥16 years) stratified by HIV and drug resistance status in 7 countries (figure)
- International Epidemiology Databases to Evaluate AIDS (IeDEA) and collaborating TB clinics

Drug susceptibility testing and mortality in patients treated for tuberculosis in high-burden countries: a multi-centre cohort study

Results:

• DST results were discordant in 20% of patients.

• The accuracy of local DST to detect any resistance was moderate (sensitivity 90.8%, specificity 84.3%).

• Mortality ranged from 6.0% in patients with pan-susceptible TB treated according to WHO guidelines to 57.1% in patients with resistant strains who were under-treated (figure).

• Sex, sputum microscopy and HIV status were not associated with the odds of death.

<table>
<thead>
<tr>
<th>Drug Susceptibility</th>
<th>Adequate Treatment</th>
<th>Over-treatment</th>
<th>Under-treatment</th>
<th>aOR (95% CI)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pan-susceptible</td>
<td>336</td>
<td>20 (6.0)</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Pan-susceptible</td>
<td>23</td>
<td>3 (13.0)</td>
<td></td>
<td>3.31 (0.82-13.45)</td>
</tr>
<tr>
<td>Any resistance</td>
<td>200</td>
<td>36 (18.0)</td>
<td></td>
<td>4.66 (2.16-9.14)</td>
</tr>
<tr>
<td>Any resistance</td>
<td>14</td>
<td>8 (53.1)</td>
<td></td>
<td>19.32 (5.59-66.73)</td>
</tr>
</tbody>
</table>

* adjusted for sex, age, sputum microscopy, and HIV status
** compatible with WHO guidelines
IeDEA West Africa Collaboration

2019 highlighted publications

March 2020
Barriers influencing task-shifting for the management of depression in people living with HIV: a study from West Africa IeDEA cohort collaboration


Objective: to evaluate the barriers that could compromise task shifting in front line health care workers (HCWs) who provide HIV integrated care in West Africa.

Methods

- Cross-sectional survey

- Inclusion Sites:
  - 1 in Dakar, Senegal
  - 3 in Abidjan, Cote d’Ivoire

- Participants:
  - Doctors (incl. residents)
  - Nurses, caregivers
  - Lay workers (incl. rediators)
  - Pharmacists (incl. assistants)

+ Determinants of poor responses: logistic regressions
Results

- 168 respondents (76 nurses, 53 medical doctors, 23 lay workers, 16 pharmacists)
- Median age: 40 years old / 44% men

<table>
<thead>
<tr>
<th>Knowledge</th>
<th>Attitudes / Practices</th>
</tr>
</thead>
<tbody>
<tr>
<td>High % of good answers (74.2%) (global score), particularly HIV &amp; Depression score (90%)</td>
<td>Low social distance (70.8%)</td>
</tr>
<tr>
<td>BUT Lower scores:</td>
<td>Low professional barriers (69.6%)</td>
</tr>
<tr>
<td>• in participants other than doctors (p&lt;0.0001)</td>
<td>BUT:</td>
</tr>
<tr>
<td>• concerning symptoms (72%) and causes (60%)</td>
<td>&gt;50% considered diagnosis and management needed to be left to a specialist</td>
</tr>
<tr>
<td>Limited access to a depression training (32.7%) = main factor associated to low knowledge scores</td>
<td>Interested on being trained: 82.1%</td>
</tr>
<tr>
<td></td>
<td>Interest involvement in therapeutic sessions: 89.9%</td>
</tr>
</tbody>
</table>

Conclusion:
To guarantee the success of task-shifting + to increase the confidence of professionals in their skills to be active in depression care: **improve the access to specific training on depression** considering screening, management, but also perceptions and attitudes, as some barriers subsist.
Assessment of the scale-up of cervical cancer screening in Abidjan stratified by HIV status

Objective
To report the successes and challenges of scaling up a population-based cervical cancer (CC) screening program from HIV clinics to various healthcare facilities in Abidjan, Côte d'Ivoire.

Methods
- Retrospective analysis of characteristics, outcomes, and follow-up of women attending an initial CC screening visit in Abidjan between January 2010 and December 2014
- Data from the 2014 population census were used to estimate screening coverage

Results
- 16 169 women attending an initial CC screening with 1616 (10.0%) positive VIA test
- 848 women eligible for immediate cryotherapy, 618 (72.9%) underwent “see-and-treat”
- 1-year follow-up rate after cryotherapy was 23.1% (143/618), higher among women with HIV (111/362, 30.7%) than among other women (32/256, 12.5%) ($P=0.001$)

Conclusion
- Despite successful expansion of CC screening from HIV clinics to other facilities, the estimated screening coverage of the targeted population remained low
- Follow-up of positively screened and treated women is a major challenge that would benefit from an innovative information system
Coverage of cervical cancer screening in Abidjam-Dabou, Côte d'Ivoire 2014: 1.2% (95% CI 0.6–3.1)
Cervical cancer screening uptake and correlates among HIV-infected women: a cross-sectional survey in Côte d’Ivoire, West Africa
Boris Tchounga, Simon Pierre Boni, Jean Jacques Koffi, Apollinaire G Horo, Aristophage Tanon, Eugene Messou, Serge-Olivier Koule, Innocent Adoubi, Didier K Ekouevi, Antoine Jaquet
BMJ Open. 2019 Aug 30;9(8):e029882

Objective
Estimate the coverage of cervical cancer screening and associated factors among WLHIV attending HIV clinics part of IeDEA West Africa in Abidjan, Côte d’Ivoire

Methods
- Cross-sectional survey conducted from May to August 2017 in the four highest volume urban HIV clinics of government’s or NGO’s sector in Côte d’Ivoire
- WLHIV, aged 25–55 years, followed since at least 1 year sampled
- Standardised questionnaire administered to each participant to collect information on cervical cancer screening uptake and its correlates

Results
- 1991 WLHIV were included in the study, aged in median 42 years (IQR 37–47)
- 1913 (96.1%) had ever heard about cervical cancer and 1444 (72.5%) had been offered cervical cancer screening
- 1188 reported a personal history of cervical cancer screening for an overall coverage of 59.7% (95% CI 57.6 - 62.0).
Factors associated with uptake to cervical cancer screening among women living with HIV

<table>
<thead>
<tr>
<th>Variables</th>
<th>Uni variable model</th>
<th>Multivariable model (final)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n/N</td>
<td>aOR (CI 95%)</td>
</tr>
<tr>
<td>Age (years)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;45</td>
<td>747/1293</td>
<td>1</td>
</tr>
<tr>
<td>≥45</td>
<td>441/698</td>
<td>1.3 (1.0 – 1.5)</td>
</tr>
<tr>
<td>Educational level</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No formal / primary level</td>
<td>568/1057</td>
<td>1</td>
</tr>
<tr>
<td>Secondary level</td>
<td>430/679</td>
<td>1.5 (1.2 – 1.8)</td>
</tr>
<tr>
<td>University</td>
<td>190/255</td>
<td>2.5 (1.8 – 3.4)</td>
</tr>
<tr>
<td>Information on CC</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Informed elsewhere</td>
<td>135/535</td>
<td>1</td>
</tr>
<tr>
<td>Informed in usual HIV clinic</td>
<td>1,053/1456</td>
<td>7.7 (6.2 – 9.7)</td>
</tr>
<tr>
<td>Clarity of information on screening</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not clear for me</td>
<td>341/820</td>
<td>1</td>
</tr>
<tr>
<td>Very clear for me</td>
<td>847/1171</td>
<td>4.0 (3.0 – 4.4)</td>
</tr>
<tr>
<td>Knowing HIV as a risk factor</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>631/1172</td>
<td>1</td>
</tr>
<tr>
<td>Yes</td>
<td>557/819</td>
<td>1.8 (1.5 – 2.2)</td>
</tr>
</tbody>
</table>

Conclusion
- Initiatives to support cervical cancer screening in HIV care programs resulted in effective access to more than half of the WLHIV in Abidjan
- Efforts are still needed to provide universal access to cervical cancer screening, especially among socioeconomically disadvantaged WLHIV.
Age-stratified mortality differentials among ART-treated adolescents and youth aged 10-24 years with perinatally-acquired versus non-perinatally acquired HIV in the IeDEA collaboration (MR136)

Desmonde et al; preliminary results presented at IWHOD 2019

- **Objective:** to provide mortality differentials for adolescents and youth with perinatally (YPHIV) vs non perinatally acquired HIV (YNPHIV), by region and sex during the periods of 10-14, 15-19 and 20-24 years. Use these data to contribute to Spectrum model mortality estimates in adults > 15 years.

- **Methods**
  - Study population: 104,846 participants who initiated ART in an IeDEA program between 2004-2016
  - Proxy for perinatal infection: enrolled < 10 years
  - Post-ART mortality rates per 100 person-years of follow-up
  - Negative binomial regression model
    - Mortality rate ratios YNPHIV vs YPHIV stratified by age, region and sex
    - Adjusted for time-varying age, sex, CD4 count at ART initiation (<350 cells/µL, ≥350 cells/µL, unknown) and time on ART (<12 months, ≥12 months).
Publication # 4: Adolescents (IeDEA West Africa MR lead)

Age-stratified mortality differentials among ART-treated adolescents and youth aged 10-24 years with perinatally-acquired versus non-perinatally acquired HIV in the IeDEA collaboration (MR136)

Desmonde et al.; preliminary results presented at IWHOD 2019

• Results

- Significantly higher mortality rates in YNPHIV vs YPHIV in 10-14 years and 15-19 years
- Higher RR in males compared to females
- Mortality rates were comparable in YNPHIV and YPHIV at the ages 20-24 years.
Publication # 5: Children

Growth in the first 5 years after antiretroviral therapy initiation among HIV-infected children in the IeDEA West African Pediatric Cohort


- **Objective:** to describe growth evolution and associated factors in the first 5 years on ART among HIV-infected children enrolled IeDEA pWADA.

- **Methods**
  - Study population: HIV-infected children <10 yrs from the pWADA cohort, enrolled until 2016, with at least one anthropometric data within the first 5 years on ART (weight and height)
  - Statistical analysis:
    - Linear mixed models for each anthropometric indicator (WAZ, HAZ and WHZ/BAZ), with spline term to take into account bimodal trajectories.
Publication # 5: Children

Growth in the first 5 years after antiretroviral therapy initiation among HIV-infected children in the IeDEA West African Pediatric Cohort

• High prevalence of malnutrition among at ART initiation

• Weight and height gains following ART initiation, weight gains in the first 12 months ++, constant height increase over 5 years.

• Part of the population remains malnourished even after 5 years on ART

<table>
<thead>
<tr>
<th>Months after ART init</th>
<th>0</th>
<th>12</th>
<th>24</th>
<th>36</th>
<th>48</th>
<th>60</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>3195</td>
<td>2045</td>
<td>1578</td>
<td>1287</td>
<td>1026</td>
<td>438</td>
</tr>
<tr>
<td>% Underweight</td>
<td>55.7</td>
<td>26.8</td>
<td>21.9</td>
<td>20.7</td>
<td>19.7</td>
<td>19.2</td>
</tr>
<tr>
<td>% Stunted</td>
<td>50.2</td>
<td>37.9</td>
<td>25.7</td>
<td>20.7</td>
<td>17.3</td>
<td>16.4</td>
</tr>
<tr>
<td>% Wasted</td>
<td>39.7</td>
<td>12.8</td>
<td>12.7</td>
<td>12.2</td>
<td>14.8</td>
<td>13.7</td>
</tr>
<tr>
<td>% Malnourished overall</td>
<td>68.7</td>
<td>47.7</td>
<td>37.6</td>
<td>33.8</td>
<td>32.8</td>
<td>30.1</td>
</tr>
</tbody>
</table>
NA-ACCORD
2019 Research Highlights
Determinants of Liver Complications Among HIV/Hepatitis B Virus-Coinfected Patients

• **BACKGROUND**: Hepatitis B virus (HBV) infection is a leading cause of end-stage liver disease (ESLD) and hepatocellular carcinoma (HCC) in HIV. Factors contributing to the high rates of liver complications among HIV/HBV-coinfected individuals remain unknown.

• **METHODS**: Validated diagnoses of ESLD and HCC from 1996-2010 in the US and Canada. Multivariable Cox regression used to examine adjusted hazard ratios [aHRs with 95% CIs] of first occurrence of ESLD or HCC associated with hypothesized determinants and with increasing durations of HIV suppression (≤500 copies/mL).

• **RESULTS**: Among 3573 HIV/HBV patients with 13,790 person-years of follow-up, 111 liver complications occurred (incidence rate = 8.0 [95% CI: 6.6 to 9.7] events/1000 person-years).

• **Rates of liver complication were increased with:**
  - non-black/non-Hispanic race [aHR = 1.76 (1.13-2.74)],
  - diabetes mellitus [aHR = 2.07 (1.20-3.57)],
  - lower time-updated CD4 cell count [<200 cells/mm: aHR = 2.59 (1.36-4.91); 201-499 cells/mm: aHR = 1.75 (1.01-3.06) versus ≥500 cells/mm],
  - heavy alcohol use [aHR = 1.58 (1.04-2.39)], higher FIB-4 at start of follow-up [>3.25: aHR = 9.79 (5.73-16.74); 1.45-3.25: aHR = 3.20 (1.87-5.47) versus FIB-4 <1.45].

• **HIV suppression for ≥6 months was associated with lower liver complication rates compared with those with unsuppressed HIV [aHR = 0.56 (0.35-0.91)].

**CONCLUSIONS:** Non-black/non-Hispanic race, diabetes, lower CD4 cell count, heavy alcohol use, and advanced liver fibrosis were determinants of liver complications among HIV/HBV patients. Sustained HIV suppression should be a focus for HIV/HBV-coinfected patients to reduce the risks of ESLD/HCC.
Characterizing the Human Immunodeficiency Virus Care Continuum Among Transgender Women and Cisgender Women and Men in Clinical Care: A Retrospective Time-series Analysis.

• **BACKGROUND:** Prior studies suggest that transgender women (TW) with human immunodeficiency virus (HIV) are less likely to be virally suppressed than cisgender women (CW) and cisgender men (CM). However, prior data are limited by small sample sizes and cross-sectional designs.

• **METHODS:** We analyzed annual HIV care continuum outcomes by gender status from January 2001 through December 2015 among adults (aged ≥18 years). Outcomes were retention in care and viral suppression. Retention in care was defined according to the US HRSA criteria. The last HIV RNA measurement was used in the calendar year for an individual. P values for trends in the outcomes over a calendar year were estimated using a log-binomial model with generalized estimating equations (GEE) and a continuous variable for calendar year.

• **RESULTS:** The study population included TW (n = 396), CW (n = 14 094), and CM (n = 101 667). TW had lower proportions retained in care than CW and CM (P < .01). Estimates of retention in care were consistently lower in TW, with little change over time within each group. TW and CW had similar proportions virally suppressed over time (TW, 36% in 2001 and 80% in 2015; CW, 35% in 2001 and 83% in 2015) and were lower than CM (41% in 2001 and 87% in 2015). These differences did not reach statistical significance after adjusting for age, race, HIV risk group, and cohort.

• **CONCLUSIONS:** TW experience challenges with retention in HIV care. However, TW who are engaged in care achieve viral suppression that is comparable to that of CW and CM of similar age, race, and HIV risk group suggesting that additional research is needed to understand care engagement disparities.

**Theme Discussion CROI 2020:**
Progression through the HIV Care Continuum for transgender women in the NA-ACCORD (Katie Lesko)

Proportion with HIV RNA suppression (≤200 copies/mL), by gender status, in the NA-ACCORD, 2001–2015.
Association of immunosuppression and HIV viraemia with non-Hodgkin lymphoma risk overall and by subtype in people living with HIV in Canada and the USA

• **BACKGROUND**: Research is needed to better understand relations between immunosuppression and HIV viraemia and risk for non-Hodgkin lymphoma, a common cancer in people living with HIV. We aimed to identify key CD4 count and HIV RNA (viral load) predictors of risk for non-Hodgkin lymphoma, overall and by subtype.

• **METHODS**: We studied people living with HIV during 1996-2014 the US and Canada. To determine key independent predictors of risk for non-Hodgkin lymphoma, we assessed associations with time-updated recent, past, cumulative, and nadir or peak measures of CD4 count and viral load, using demographics-adjusted, cohort-stratified Cox models. We compared models using Akaike's information criterion.

• **RESULTS**: Of 102 131 people living with HIV during the study period, 712 people developed non-Hodgkin lymphoma.

• The key independent predictors of risk for overall non-Hodgkin lymphoma were:
  - Recent CD4 count (ie, lagged by 6 months; <50 cells per μL vs ≥500 cells per μL, hazard ratio [HR] 3·2, 95% CI 2·2-4·7)
  - Average viral load during a 3-year window lagged by 6 months (cumulative measure; ≥100 000 copies per mL vs ≤500 copies per mL, HR 9·6, 95% CI 6·5-14·0).
Association of immunosuppression and HIV viraemia with non-Hodgkin lymphoma risk overall and by subtype in people living with HIV in Canada and the USA

• RESULTS (Cont): The key independent predictors of diffuse large B-cell lymphoma:
  - Recent CD4 count <50 cells per μL vs ≥500 cells per μL, HR 2·4, 95% CI 1·4-4·2
  - Average viral load ≥100 000 copies per mL vs ≤500 copies per mL, HR 7·5, 95% CI 4·5-12·7.

• Recent CD4 count was the sole key predictor of risk for CNS non-Hodgkin lymphoma (<50 cells per μL vs ≥500 cells per μL, HR 426·3, 95% CI 58·1-3126·4)

• Proportion of time viral load was greater than 500 copies/mL during the 3-year window was the sole key predictor for Burkitt lymphoma (100% vs 0%, HR 41·1, 95% CI 9·1-186·6)

• Conclusions: Both recent immunosuppression and prolonged HIV viraemia have important independent roles in the development of non-Hodgkin lymphoma, with likely subtype heterogeneity. Early and sustained ART to decrease HIV replication, dampen B-cell activation, and restore overall immune function is crucial for preventing non-Hodgkin lymphoma
The Effect of Initiating INSTI-based vs. NNRTI-based Antiretroviral Therapy on Progression to Diabetes among North American Persons in HIV Care
Rebeiro PF, et al. IDWeek 2019, Abstract # _

• **BACKGROUND**: INSTI-based ART has been implicated in greater weight gain than other regimens in PLWH. There is little evidence about INSTIs’ role in serious clinical outcomes proximal to weight gain ~ for example, incident diabetes. We therefore examined the impact of initial ART regimen class/drug on incident diabetes mellitus (DM) in the NA-ACCORD.

• **METHODS**: Selected treatment-naïve adults initiating INSTI-, PI-, or NNRTI-based ART from 2007-2016. the outcome of incident DM defined as HgA1c >6.5%, diabetes-specific medication, or DM diagnosis along with diabetes-related medication. Follow-Up was from ART initiation until incident DM, virologic failure, regimen core switch, cohort close, death or loss to follow-up (≥12 months with no contact before cohort close).

• Competing risks regression to obtain marginal Cumulative Incidence Functions for incident DM by ART class and drug. Death before DM was a competing risk. Stratified Cox proportional hazards regression to obtain adjusted Hazard Ratios (aHRs) and 95% confidence intervals (CI) for incident DM by ART class and drug. Adjusted for age, sex, race, HIV risk group, Year of ART initiation, weight, CD4, HIV-1 RNA.
CONCLUSIONS: Initiating INSTI- or PI-vs. NNRTI-based regimens may confer increased risk of DM, though risk is heterogeneous among INSTIs. Future directions include mediation analyses of direct vs. indirect effects of ART to determine if elevated risk observed in these analyses is attributable to weight gain on the regimen.
Life expectancy disparities among adults with HIV in the United States and Canada: The impact of a reduction in drug- and alcohol-related deaths using the Lives Saved Simulation (LISSO) Model

• **Background:** Improvements in life expectancy among persons with HIV (PWH) receiving ART in the US and Canada may be different among key populations and comparison groups. Given the differences in substance use among key population sand comparison groups, the current opioid epidemic, drug- and alcohol-related deaths maybe contributing to the disparities in life expectancy. We sought to determine if disparities in life expectancy at age 20 exists among key pupations and their comparison groups in three time periods (2004-7, 2008-11, 2012-15), and estimate the potential increase in expected life expectancy with a simulated 20% reduction in drug- and alcohol-related deaths.

• **Methods:** Drug and alcohol related deaths were identified in cohorts submitting NDI Plus matching or death certificate information using ICD-9 and -10 codes identified by the NCHS and a free text search in the cause of death data submitted from physician report and/or outreach to the decedent's family. We built an agent-based simulation (LISSO) model using individual-level data from the NA-ACCORD, including the age at death for those who were randomly “saved.” Those saved experienced the mortality rate of their peers in subsequent years.
Conclusions:

- Disparities persist in LE in Black (vs. White) MSM and IDU (vs non-IDU). White women had a stunted increase in LE and Black women’s LE exceed White women’s LE in the most recent period (2012-2015).

- A 20% reduction in drug- and alcohol-related mortality would have the greatest life expectancy benefit for Black MSM, White women, and IDUs. Our findings suggest that preventing drug- and alcohol-related deaths among PWH could narrow life expectancy disparities among some key populations, and their comparison groups with HIV, but other causes of death must be addressed.