Acknowledgements

This report would not be possible without the hard work and dedication of the investigators, research coordinators, and administrative support staff who make up AMPATH’s research community. We appreciate all their contributions to this report. AMPATH’s co-directors of research, Professors Winstone Nyandiko and Rachel Vreeman deserve special recognition for their constant support in the development of this report. Their leadership continues to strengthen the Research Program.

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Shawn Grinter
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Please visit the AMPATH Research Program website to learn how our research programs are helping improve the health of the Kenyan people.

www.medicine.iu.edu/ampathresearch
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Overview

The AMPATH Research Program has continued steady growth in the first half of 2016. In the first six months, the cumulative total of direct research and training grants awarded to the program exceeded US$ 100 million – an important milestone. The National Institutes of Health in the United States continued to be the largest sponsor of research and training grants at AMPATH and nearly all of the new awards reported this year were from NIH sources.

AMPATH investigators continued to publish at a steady rate with nearly 23 publications appearing in peer reviewed journals. While this is down from the same period last year, it is consistent with the average over the previous 5 years. New publication submissions also continued at a normal rate with more than 55 manuscripts, abstracts, posters, and articles to the Publications Committee in the first 6 months of 2016.

Grants

In the first part of this year, investigators reported nearly US$ 4.5 million in new awards. This increased AMPATH’s cumulative total of research direct awards to over US$100 million since the start of the program (See Figure 1).

![FIGURE 1: AMPATH Research & Training Grants Awarded by Year (Cumulative Total Direct Costs in US$)](image-url)
During this period, around 96 percent of new awards reported were from various institutes in the NIH (See Figure 2).

This continues trends from previous periods with the NIH as the largest sponsor of research grants at AMPATH (See Figure 3).
Publications

AMPATH investigators continued to publish at a consistent rate though they published fewer publications than during the same period last year. However, last year was a record year for the number of publications produced and the current period is more consistent with averages from the previous 5 years. In total, 22 manuscripts from AMPATH investigators appeared in peer reviewed journals (See Figure 4). A bibliography of publications from the first half of 2016 is included at the end of this report.

In addition, AMPATH investigators were actively involved in preparing publications for submission to a wide range of professional conferences and journals. The AMPATH Publications Committee, which reviews all publications produced from AMPATH research projects, reviewed a total of 62 draft publications during this period.

FIGURE 4: Number of AMPATH Research Publications since 1998 (n=423)
## Study Reports

The following reports were provided by AMPATH investigators and their study teams and cover the period of January 1 – June 30, 2016.

<table>
<thead>
<tr>
<th>Study Title</th>
<th><strong>A Formative Study to Develop Culturally Valid Psychosocial Assessment Tools and Interventions to Promote Family Well-Being in Kenya</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Principal Investigator(s)</td>
<td>Eve Puffer, Duke University</td>
</tr>
<tr>
<td>Co-Investigator(s)</td>
<td>David Ayuku, Moi University</td>
</tr>
<tr>
<td>Working Group(s)</td>
<td>SSRN</td>
</tr>
<tr>
<td>Description</td>
<td>The purpose of this study is to assess family functioning and children’s psychosocial well-being in a Kenyan context in order to develop culturally tailored measures and family-based intervention approaches. Many measures of child well-being, mental health, and behavior were developed in the West and are inappropriate or insufficient for use in Kenya. The same is true for measures of family well-being. Culturally tailored measures are needed to assess important aspects of family relationships, such as communication, conflict, and parenting. Such measures will be useful in identifying children and families who are in need of treatment and in measuring the impact of interventions for children and families to identify which treatments work best. We will use a variety of methods to develop assessment tools to measure family functioning and mental health. These will include focus groups with community members (both youth and adults), community leaders, and people already working in the field of mental health in the communities. Methods will also involve questionnaires and observational measures, in which family and child behaviors are directly observed and assessed. A family-based intervention to address psychosocial concerns will be developed using a community-based participatory approach.</td>
</tr>
<tr>
<td>Site(s)</td>
<td>Moi’s Bridge Health Centre</td>
</tr>
<tr>
<td>Project Period</td>
<td>5/28/2013 - 4/16/2016</td>
</tr>
<tr>
<td>Funding Status</td>
<td>Funded – Grand Challenges Canada &amp; Johnson and Johnson</td>
</tr>
<tr>
<td>Direct Award (USD)</td>
<td>$129,000</td>
</tr>
<tr>
<td>Update</td>
<td>We are continuing to validate the measures of family functioning in mental health, focusing on the Pioneer location. This includes administering surveys, in-depth interviews, and observational measures to a diverse sample of families. We are currently collecting data on a small scale to conduct an interim analysis of data to refine measures in preparation for the possible larger validity study we have been planning. The validity study will be done in order to determine whether the survey measure which is currently being pilot tested accurately predicts diagnosis of both family functioning issues and mental health status of individuals within a family. We are in the final stages of completing the pilot study of a family therapy intervention for families struggling with interpersonal conflict and who have an adolescent child with behavioral or emotional concerns. This has been funded through Professor David Ayuku’s funding from Grand</td>
</tr>
</tbody>
</table>
Challenges Canada. For this project, we trained community-based lay counselors, who were then supervised by medical psychology students at Moi. This collaborative model has proven feasible and acceptable, contributing to the well-being of communities and to the education of these students. As part of this study, we piloted a mobile-phone based tool to support the counselors in the field. Preliminary pilot results are promising, and full analysis will be conducted in the coming months following completion of treatment and data collection.

**Future Plans**

We will continue the validity study as described above, with the goal of completing the small-sample (20 families) study and completing data analysis to refine measures. We will complete the intervention pilot study and conduct data analysis to inform the next phase of implementation. *Note related to protocol updates: We have had amendments since the approved protocol but I was not able to upload additional documents.*

**Publication(s)**


<table>
<thead>
<tr>
<th>Study Title</th>
<th>A Stage 2 Cognitive Behavioral Trial, Reduce Alcohol First in Kenya Intervention (RAFIKI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Principal Investigator(s)</td>
<td>Rebecca Papas, Brown University</td>
</tr>
<tr>
<td>Co-Investigator(s)</td>
<td>B. Gakinya, Moi University</td>
</tr>
<tr>
<td>Working Group(s)</td>
<td>AMWG, SSRN</td>
</tr>
<tr>
<td>Description</td>
<td>This study will determine whether a group cognitive-behavioral therapy intervention that demonstrates preliminary evidence of reducing alcohol use among HIV-infected outpatients in western Kenya is effective when compared against a group health education intervention in a large sample over a longer period of time. It will be delivered by paraprofessionals, individuals with limited professional training. This approach is consistent with successful cost-effective models of service delivery in resource-limited settings in which paraprofessionals (e.g., clinical officers, traditional birth attendants and peer counselors) are trained.</td>
</tr>
<tr>
<td>Site(s)</td>
<td>Endebess Sub-District Hospital Moi's Bridge Health Centre</td>
</tr>
<tr>
<td>Funding Status</td>
<td>Funded – NIH - National Institute on Alcohol Abuse and Alcoholism (NIAAA)</td>
</tr>
<tr>
<td>Direct Award (USD)</td>
<td>$2,268,832</td>
</tr>
<tr>
<td>Update</td>
<td>Over the last six months we've been conducting follow-ups on the participants and so far we've done the final follow-ups for up to cohort 21. Data cleaning is ongoing and preliminary analysis has begun.</td>
</tr>
<tr>
<td>Future Plans</td>
<td>We plan to finish with all follow-ups and begin conducting initial analysis</td>
</tr>
<tr>
<td>Publication(s)</td>
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| Study Title | A5225/HiFLAC Protocol - A Phase I/II Dose-Finding Study of High-Dose Fluconazole Treatment in AIDS-Associated Cryptococcal Meningitis |
| Principal Investigator(s) | Abraham Siika, Moi University |
| Co-Investigator(s) | David Lagat, Moi University |
| Working Group(s) | AMWG, SSRN |

| Description | A5225/HiFLAC is a phase I/II dose escalation and validation study of the safety, tolerability, and therapeutic effect of an induction-consolidation strategy of high-dose fluconazole alone for the treatment of cryptococcal meningitis (CM) in HIV-infected participants. The study will proceed in two stages. In Stage 1, Dose Escalation, up to three induction doses of fluconazole will be tested in sequentially enrolled cohorts. Stage 2, Dose Validation, will not open until the maximum tolerated dose (MTD) of fluconazole has been identified in Stage 1. In Stage 2, induction doses of fluconazole that are found to be safe in Stage 1 will be tested in simultaneously enrolled cohorts. In each stage, participants will be randomized at entry into Step 1. Over the course of the study, participants will register to subsequent steps (Steps 2-4) based on their initial randomization and/or their response to treatment. The study steps are: Step 1: Induction therapy with either high dose fluconazole or ampho B; Step 2: Induction following early ampho B intolerance (only for participants randomized to ampho B treatment in Step 1) (fluconazole at 400-800 mg daily); Step 3: Consolidation therapy (fluconazole 400 mg daily); and Step 4: Maintenance therapy (fluconazole 200 mg daily). |
| Site(s) | MTRHMoi's Bridge Health Centre |
| Funding Status | Funded – |
| Direct Award (USD) | Not Reported |

| Update | Enrollment pause was lifted in April 2016 and the site is now actively screening potential participants to be enrolled into this study. Stage 2 was open following release of version 3.0 of the protocol already submitted to and approved by IREC. There are currently 7 participants enrolled into the study for stage 2 at the Eldoret site. |
| Future Plans | The site plans to continue with recruitment of participants into this study. Currently there are only 7 slots remaining and the study will soon be closed to accrual. |

<table>
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<tr>
<th>Publication(s)</th>
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| Study Title | A5263 'A Randomized Comparison of Three Regimens of Chemotherapy with Compatible Antiretroviral Therapy for Treatment of Advanced AIDS-KS in Resource-Limited Settings' |
| Principal Investigator(s) | Abraham Siika, Moi University |
### Study Title

**A5264/AMC067  A Randomized Evaluation of Antiretroviral Therapy Alone or with Delayed Chemotherapy versus Antiretroviral Therapy with Immediate Adjunctive Chemotherapy for Treatment of Limited Stage AIDS-KS in Resource-Limited Settings (REACT-KS)**

### Principal Investigator(s)

Abraham Siika, Moi University

### Co-Investigator(s)

AMWG, SSRN

### Working Group(s)

AMWG, SSRN

### Description

A5264/AMC 067 is a phase III, open-label, prospective, randomized study stratified by CD4+ lymphocyte cell count and antiretroviral therapy (ART) history. The study will compare the KS tumor outcomes of ART alone or with delayed Etoposide (ET) to ART with immediate ET, for initial treatment of limited stage AIDS-KS in chemotherapy and radiation treatment naïve HIV-1 infected participants who are currently not receiving ART.
<table>
<thead>
<tr>
<th><strong>Direct Award (USD)</strong></th>
<th>[Not Reported]</th>
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<tbody>
<tr>
<td><strong>Update</strong></td>
<td>The DSMB met on 10 March 2016 to review safety and efficacy data from the A5264 study. The DSMB recommended that enrolment and randomization to A5264 should be stopped because the study is unlikely to answer the research question concerning the effects of immediate versus delayed etoposide on the planned primary endpoint. The DSMB stated that the reason for stopping the study is futility, not safety. The protocol team has recommended that participants who are currently enrolled in A5264 should continue study treatments and follow-up per the current protocol. At Eldoret, a total of 17 participants had been enrolled into the study at the time of the enrolment closure.</td>
</tr>
<tr>
<td><strong>Future Plans</strong></td>
<td>Continue with follow up of active participants.</td>
</tr>
<tr>
<td><strong>Publication(s)</strong></td>
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</table>

<table>
<thead>
<tr>
<th><strong>Study Title</strong></th>
<th><strong>A5273 'Multicenter Study of Options for Second-Line Effective Combination Therapy (SELECT)'</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Principal Investigator(s)</strong></td>
<td>Abraham Siika, Moi University</td>
</tr>
<tr>
<td><strong>Co-Investigator(s)</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Working Group(s)</strong></td>
<td>AMWG, SSRN</td>
</tr>
<tr>
<td><strong>Description</strong></td>
<td>A5273 is a phase III, dual-arm, open-label, randomized, non-inferiority study for participants who are on a failing non-nucleoside reverse transcriptase inhibitor (NNRTI)-containing first-line regimen. The study will evaluate the difference in virologic failure rate between two treatment arms: lopinavir/ritonavir plus raltegravir (LPV/r + RAL) and LPV/r plus best available nucleos(t)ide reverse transcriptase inhibitors (NRTIs). The NRTIs to be used will be specified by the site prior to randomization. The primary objective for this study will be to determine whether the combination of LPV/r + RAL is associated with virologic efficacy that is non-inferior to that achieved with LPV/r + best-available NRTIs by 48 weeks of follow-up.</td>
</tr>
<tr>
<td><strong>Site(s)</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Project Period</strong></td>
<td>1/22/2013 - 10/3/2016</td>
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<tr>
<td><strong>Funding Status</strong></td>
<td>Funded – NIH - AIDS Clinical Trials Group (ACTG)</td>
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<tr>
<td><strong>Direct Award (USD)</strong></td>
<td>Not Reported</td>
</tr>
<tr>
<td><strong>Update</strong></td>
<td>The study is closed to follow up and a letter notifying the local IRB of study closure was submitted in September 2014. Acknowledgements of study closure was received from both IREC and Pharmacy and Poisons Boards Expert Committee on Clinical Trials (ECCT)</td>
</tr>
<tr>
<td><strong>Future Plans</strong></td>
<td>Continue with data analysis.</td>
</tr>
<tr>
<td><strong>Publication(s)</strong></td>
<td>Raltegravir in second-line antiretroviral therapy in resource-limited settings (SELECT): a randomised, phase 3, non-inferiority study  Alberto M La Rosa, MD , Linda J Harrison, MSc , Babafemi Taiwo, MBBS , Carole L Wallis, PhD , Lu Zheng, PhD , Peter Kim, MD ,</td>
</tr>
<tr>
<td>Study Title</td>
<td>A5274/REMEMBER Reducing Early Mortality and Early Morbidity by Empiric Tuberculosis Treatment Regimens'</td>
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<td>--------------------------------------------------------------------------------------------------</td>
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<tr>
<td>Principal Investigator(s)</td>
<td>Abraham Siika, Moi University</td>
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<tr>
<td>Co-Investigator(s)</td>
<td>AMWG, SSRN</td>
</tr>
<tr>
<td>Working Group(s)</td>
<td></td>
</tr>
<tr>
<td>Description</td>
<td>In this randomized, open-label, phase IV strategy trial, participants from resource-limited settings (RLS) who present with advanced HIV disease and no probable or confirmed tuberculosis (TB), as defined in the current ACTG diagnosis appendix, and who are initiating antiretroviral treatment (ART) will be randomized to one of two strategy arms: immediate, empiric TB treatment (public health approach) or local standard of care TB treatment (individualized approach). The primary endpoint is survival status in the two arms 24 weeks after randomization. AIDS progression (any new WHO Stage 3 or 4 condition), virologic and CD4+ cell response, HIV and TB drug resistance, AND safety and tolerability of, and adherence to HIV and TB drugs will be evaluated, as will the cost-effectiveness of the two strategies. The primary objective is to compare survival probabilities between the two study arms 24 weeks after randomization.</td>
</tr>
<tr>
<td>Site(s)</td>
<td></td>
</tr>
<tr>
<td>Project Period</td>
<td>10/1/2012 - 12/31/2016</td>
</tr>
<tr>
<td>Funding Status</td>
<td>Funded – NIH - AIDS Clinical Trials Group (ACTG)</td>
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<tr>
<td>Direct Award (USD)</td>
<td>Not Reported</td>
</tr>
<tr>
<td>Update</td>
<td>A5274/REMEMBER study was closed to follow-up on May 3, 2016 after the last participant completed the final on-study visit.</td>
</tr>
<tr>
<td>Future Plans</td>
<td>A5274 protocol team to continue with data analysis.</td>
</tr>
<tr>
<td>Publication(s)</td>
<td></td>
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</table>

<table>
<thead>
<tr>
<th>Study Title</th>
<th>A5288 'Management Using the Latest Technologies in Resource-limited Settings to Optimize Combination Therapy After Viral Failure (MULTI-OCTAVE)'</th>
</tr>
</thead>
<tbody>
<tr>
<td>Principal Investigator(s)</td>
<td>Abraham Siika, Moi University</td>
</tr>
<tr>
<td>Co-Investigator(s)</td>
<td>AMWG, SSRN</td>
</tr>
<tr>
<td>Working Group(s)</td>
<td></td>
</tr>
<tr>
<td>Description</td>
<td>A5288 is an open-label phase IV, prospective interventional, strategy study in resource-limited settings (RLS) for HIV-infected participants with triple-class experience or</td>
</tr>
</tbody>
</table>
resistance to [nucleoside reverse transcriptase inhibitors (NRTIs), non-NRTIs (NNRTIs), and protease inhibitors (PIs)] and who are failing their current regimen. The use of novel agents and contemporary management tools that include standard genotyping, plasma viral load (VL) monitoring will be evaluated. The screening genotype results and antiretroviral (ARV) history will be used to allocate potential participants to one of the four cohorts and for selection of ARV regimen for each potential participant. At sites where feasible and relevant (including MTRH) the study will also conduct an adherence study. This will be a randomized comparison of cell phone-based adherence intervention plus local standard-of-care adherence procedures (CPI+SOC) versus the SOC adherence procedures. The primary objective of the study is to use novel agents and contemporary management tools, including standard genotyping to select an appropriate third-line regimen, interventions to improve adherence and plasma viral load (VL) monitoring, in order to achieve a ≥ 65% rate of virologic control at 48 weeks of follow-up.

<table>
<thead>
<tr>
<th>Site(s)</th>
<th>Project Period</th>
<th>Funding Status</th>
<th>Direct Award (USD)</th>
<th>Update</th>
<th>Future Plans</th>
<th>Publication(s)</th>
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<tr>
<td></td>
<td>12/18/2013 - 12/31/2015</td>
<td>Funded – NIH - AIDS Clinical Trials Group (ACTG)</td>
<td>Not Reported</td>
<td>Follow up of active participants is ongoing and no major challenges were experienced.</td>
<td>Continue with follow up of active participants as per protocol.</td>
<td>Divergent ARV Resistance at Screening for ACTG A5288 Study of 3rd-Line ART in RLS Carole L. Wallis, Beatriz Grinsztejn, Saran Vardhanabhuti, Raquel V. Viana, Robert A. Salata, Peter Mugyenyi, Catherine Godfrey, Michael D. Hughes, Ann Collier, John W. Mellors.</td>
</tr>
</tbody>
</table>

### Study Title

**A5290**  
*A Randomized, Phase 2b Study of a Double-Dose Lopinavir/Ritonavir-Based Antiretroviral Regimen with Rifampin-Based Tuberculosis Treatment versus a Standard-Dose Lopinavir/Ritonavir-Based Antiretroviral Regimen with Rifabutin-Based Tuberculosis Tre*

### Principal Investigator(s)

Abraham Siika, Moi University

### Co-Investigator(s)

Fatuma Some, Moi University

### Working Group(s)

TBWG

### Description

A5290 is a prospective, randomized (1:1:1), open-label, phase 2b study comparing three lopinavir/ritonavir (LPV/r)-based antiretroviral (ARV) regimens among participants in high tuberculosis (TB) endemic resource-constrained settings undergoing treatment for confirmed or probable TB and requiring protease inhibitor (PI)-based antiretroviral therapy (ART). A two accrual period design will be used, including a full pharmacokinetic (PK) and safety evaluation to be conducted when 54-60 participants enrolled during the accrual period 1 have completed 28 days of ARV treatment and day 12 ± 2 (after initiation of ART) drug levels are available (an early interim PK and safety evaluation will also be completed when 10-12 participants per arm have completed 28 days of ARV treatment.
and day 12 ± 2 drug levels are available). Primary Objective: To compare rates of virologic suppression to < 400 copies/mL at 48 weeks for the two standard dose LPV/r and RBT arms versus the double-dose LPV/r and RIF arm.

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<thead>
<tr>
<th>Site(s)</th>
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<tbody>
<tr>
<td>Project Period</td>
<td>5/13/2015 - 11/30/2018</td>
</tr>
<tr>
<td>Funding Status</td>
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</tr>
<tr>
<td>Direct Award (USD)</td>
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Update

A5290 study was closed to accrual on February 16, 2016 with a total of 71/60 participants enrolled during the first accrual period. The ‘over enrollment’ was necessitated by missing or unevaluable samples for some participants. At Moi University Clinical Research Centre, 9 participants were enrolled into Accrual period 1. The study as a whole is now closed to accrual. The second accrual period will not be opened due to feasibility concerns.

Future Plans

Follow up of active participants will continue over the next 6 months.

Study Title

AMPATH - Oncology Institute: HPV and Cervical Cancer in Kenyan Women with HIV/AIDS

Principal Investigator(s)

Patrick Loehrer, Indiana University - Purdue University in Indianapolis (IUPUI)
Darron Brown, Indiana University - Purdue University in Indianapolis (IUPUI)

Co-Investigator(s)

Omenge, Orango, Kaaria, Alice, Cu-Uvin, Susan

Working Group(s)

ORWG

Description

The core objective of this project is to better understand the natural history of oncogenic HPV infections in HIV-infected Kenyan women, and to identify potentially modifiable (and non-modifiable) factors that are associated with progression of oncogenic HPV infection to clinical disease, including cervical cancer. Our central hypothesis is that the incidence, persistence, and spectrum of HPV are all substantially greater in HIV-infected versus non-HIV-infected Kenyan women, and that this explains a higher incidence of cervical neoplasia in HIV-infected populations. We further hypothesize that these and other modifiable factors (such as concurrent STIs, sexual behaviors, nutrition, and environment) disproportionately and adversely impact outcomes of local therapies such as cryotherapy and Loop Electrosurgical Excision Procedure (LEEP) in HIV-infected women. The specific aims of this AMPATH-Oncology Institute are to:

1. Expand the capabilities and expertise of the current laboratories and biobanking capabilities in Kenya through AMPATH and the Kenya Medical Research Institute (KEMRI)
2. Identify potentially modifiable behavioral and biological factors that are associated with the duration of infection with oncogenic HPV and cervical dysplasia in HIV-infected and non-HIV-infected women from western Kenya
3. Assess the risk factors associated with the short and long term results of cryotherapy and LEEP in VIA-positive (including LEEP-eligible) HIV-infected and non-HIV-infected women in western Kenya
4. Provide biostatistical and data management support for proposed projects in this application
for future pilot projects, and 5. To establish a sustainable, multi-institutional and transdisciplinary mentoring program fostering the development of new cancer researchers in Kenya

**Site(s)**
Moi Teaching and Referral Hospital, Center for Global Health Research - KEMRI at Kisumu City, Kenya

**Project Period**
9/19/2014 - 8/31/2019

**Funding Status**
Funded – NIH - National Cancer Institute (NCI)

**Direct Award (USD)**
$2,132,402

**Update**
A total of 187 women have been recruited into the study for Project 1, with 96 being HIV-infected and 91 HIV-uninfected. This enrollment represents approximately 85% of our planned total of 220 Kenyan women. Women have begun returning for follow-up quarterly visits as well. Project 2 Summary: 54 clients have been recruited into the study across 2 study sites. This accrual is lower than expected and we are opening a third clinic to increase opportunities for enrollment. All specimens from these women on both projects are banked at present, awaiting transport to the KEMRI laboratory for HPV analysis. Translational Biology Core: All specimens collected to this date (cervical, anal and vaginal swabs, sera, and oral rinses) have been processed and stored at -80°C. Cervical biopsies obtained during the study period are currently being stored in the Department of Pathology at MTRH. All samples have been logged and periodic inventories of specimens have been performed. The TBC has purchased a separate freezer that is dedicated to this study and will be part of the Biobank. Testing on cervical and vaginal swabs on stored samples for Neisseria gonorrhoea and Chlamydia trachomatis has begun. Data regarding these results has been stored within the RedCap databases developed specifically for Projects 1 and 2. Whole blood samples used for HIV viral load and CD4 count testing are processed and tested in real time and this data has been entered and stored in the RedCap databases. Investigators from USOM who have experience using the Roche Linear Array HPV Genotyping Test (Drs. Darron Brown and Aaron Ermel) with a technician experienced in using this assay (Brahim Qadadri, MS) visited KEMRI in November of 2015 to teach and adapt the assay for use in their laboratory. Members of the laboratory at KEMRI have performed preliminary assays on control specimens for which HPV typing results were known and successfully amplified and detected HPV types on these specimens. In summary: We have demonstrated the capability to collect and store specimens from the AMPATH-Oncology laboratories. We have also established a RedCap data base which will host data obtained from this trial. We have established a successful and vibrant mentoring core to which we have had a number of applicants and they have given informal presentations to the leadership of the U54 team. We have developed a working relationship between two research organizations in Kenya: AMPATH Oncology and KEMRI.

**Future Plans**
We plan to continue to accrue patients as outlined in the protocol. We have downsized estimates for project 2 because of apparent decreasing incidence of invasive lesions in this population, but we will also expand our coverage to rural sites within the AMPATH catchment area. We will have another face to face meeting in Eldoret in August, 2016 with senior Leadership (Loehrer, Omenge, Moormann) and local staff and mentees. We also plan to have a meeting of our Internal Advisory Board at that time. AMPATH-
Oncology is planning on hosting the 2017 U54 consortium meeting in early 2017. This will provide further opportunities to exchange ideas and identify potential solutions towards common problems observed with our fellow U54 awardees.

Publication(s)
IU Simon Cancer Center Cancer Research Day May 2016 - Poster Session

Study Title
Analysis of ICU Admissions and Outcomes at the Moi Teaching and Referral Hospital Intensive Care Unit

Principal Investigator(s)
Peter Kussin, Duke University

Co-Investigator(s)
Wangari Waweru-Siika, Moi Teaching and Referral Hospital

Working Group(s)
AMWG

Description
This study aims to explore the outcomes and mortality of patients admitted to the intensive care unit (ICU) at Moi Teaching and Referral Hospital by conducting a retrospective chart review of all patients admitted during 2011 through 2015. We aim to describe the demographic and clinical characteristics of these patients, evaluate specific procedures performed while patients are admitted to the ICU, investigate microbiological lab data specifically surrounding sepsis, and to establish the general cost of a hospital stay at MTRH. The overall goal is to develop a strong foundational data set that can be used to evaluate future clinical interventions. Furthermore, we intend for the prospective arm of this study, which is completely tablet-based, to serve as one step closer to the first electronic medical record for inpatient care at MTRH.

Site(s)
Moi Teaching and Referral Hospital

Project Period
10/26/2015 - 6/1/2016

Funding Status
Unfunded –

Direct Award (USD)

Update
Rationale: The burden of critical care is greatest in resource-limited countries (RLCs) where mortality increases as gross national income decreases. To date, intensive care unit (ICU) outcomes have not been reported in Kenya. Given the commitment of the Ministry of Health to expand ICU care across the country, such analysis is timely. Objectives: To examine ICU mortality at Moi Teaching and Referral Hospital (MTRH); to identify risk factors associated with higher mortality; to validate the use of Mortality Probability Model-II (MPM-II). Methods: A retrospective observational cohort study of 450 patients admitted to the ICU from January 1, 2013 to April 5, 2015. Data was collected on demographics, admission diagnoses, interventions, and cost. Measurements and Main Results: Of 671 admitted patients, 450 charts were analyzed. Median age was 29 years. Most patients were male (61%) and ≥18 years old (70%). Diagnoses and interventions associated with the highest odds of mortality were Burns with > 10% body-surface-area (O.R. 9.95, p-value 0.0071), Acute Stroke (6.90, 0.0003), Sepsis (4.03, 0.0001), Intracranial Hemorrhage (3.06, 0.0149), Acute Renal Failure (2.41, 0.0229), Vasopressor use (8.76, <0.0001), and Mechanical Ventilation (4.80, <0.0001). Overall ICU-mortality was 53.6%. Median cost per hospitalization was $1146. Area under receiver operating characteristic (ROC) curve for MPM-II discrimination was 0.78 (95% CI, 0.72 - 0.82) and Hosmer-
Lemeshow Chi-square statistic was 151.15 (p-value < 0.001) for calibration. Conclusions: ICU mortality of 53.6% is the highest reported in sub-Saharan Africa. This suggests the need for targeted interventions to manage high-risk diagnoses and better triage protocols to improve ICU outcomes in Kenya. The MPM-II has poor calibration and does not adequately predict mortality in this population.

**Future Plans**
1. submit manuscript on general outcomes
2. submit manuscript on outcome of traumatic brain injury in cohort
3. complete analysis of pediatric outcomes
4. consider creation of site specific model of mortality
5. consider prospective continuation of this study

**Publication(s)**
1. Presentation by Hussain Lalani MSIV and Doris Duke International fellow at Doris Duke Fellowship Meeting may 2016

**Study Title**
Assessing Neurodevelopmental Delays in Children Born to HIV-infected Mothers in Western Kenya: A Pilot Study

**Principal Investigator(s)**
Megan McHenry, Indiana University

**Co-Investigator(s)**
Eren Oyungu, Moi University

**Working Group(s)**
PRWG

**Description**
With the success of preventing mother-to-child HIV transmission and improving infrastructure for HIV care, fewer children born to HIV-infected mothers are infected themselves. Those who are infected are increasingly able to access appropriate care, which transforms HIV from a fatal disease to a chronic illness. Despite these advances, the children of HIV-infected mothers are more likely to have neurodevelopmental delays (NDDs) than HIV-unexposed children. The mean scores on motor and cognitive testing of children born to HIV-infected mothers are consistently below population means. Moreover, despite controlling for prematurity and low birth weight, HIV-infected infants - particularly those with early HIV-seropositive conversion, worse disease stage, and higher viral loads -- fare much worse developmentally than their uninfected peers. In addition, HIV-exposed, yet uninfected children in resource-limited settings (RLS) also appear to have lower global developmental scores and increased deficits in language and behavior. In sub-Saharan Africa, where over 90% of HIV-infected children live and HIV is most prevalent in women, the risk of this population not reaching its full developmental potential could affect quality of life, educational achievement, and earning potential. While it is clear that these children are at a significantly increased risk for NDDs compared to the general population, current data on the risks of both HIV exposure and perinatal antiretroviral therapy (ART) exposure on children's neurodevelopment are limited and heterogeneous. Thus, it is unclear to what extent exposure to either antiretroviral medications or to the virus itself, or infection with HIV, may impact neurodevelopment. To further complicate the picture, developmental risk factors, such as malnutrition and orphan-hood, disproportionately affect children born to HIV-infected mothers. With limited access to primary care, children in RLS do not undergo routine, age-appropriate developmental screening and thus are less likely to access any available interventions in these settings. Data from a retrospective chart review within the comprehensive Academic Model Providing Access To Healthcare (AMPATH) clinical care system in
western Kenya, where HIV-exposed children are followed relatively closely, still show that only 10% of pediatric encounters have a documented clinician assessment of development, even though it is a standard element of the clinical encounter form. Currently, little is known about the training and experience of healthcare providers to assess for delays and to refer to available resources for interventions within specific communities in resource-limited, highly HIV-impacted settings. How clinicians or caregivers perceive children with NDDs and their beliefs surrounding these conditions, particularly for children born to HIV-infected mothers, are not known. Few developmental screening tools have been developed or adapted for RLS, and existing screening tools may be too lengthy for practical use in busy, overwhelmed healthcare systems. In order to make gains in how to screen and refer children appropriately for NDDs, further research is needed regarding how these delays are understood and discussed among child caregivers and clinicians. Determining these perceptions and assessing potential developmental screening instruments for this setting are crucial first steps to improve identification of NDDs in children born to HIV-infected mothers and to develop sustainable interventions appropriate for this setting. 

Study Objectives: The objective of the research proposed is to understand caregiver and clinical providers' perceptions of NDDs, including screening for NDDs and their treatment, for children in western Kenya to guide future design of a brief, culturally appropriate screening tool for NDDs. Specific Aims: To meet this objective, we will undertake the following specific aims: 1. We will utilize qualitative methods to determine the perceived etiology, manifestations, and intervention options for child NDDs from the perspectives of clinical staff and caregivers of HIV-infected and HIV-exposed children in Kenya. 2. We will develop brief, candidate neurodevelopmental screening questions that are clinically relevant and culturally acceptable by utilizing developmental assessments validated in other settings and incorporating contextual caregiver and clinicians' perspectives. 3. We will evaluate the feasibility of implementing a validation study to examine NDD screening methods in a pilot sample of children under three years of age born to HIV-infected mothers.

Site(s)
Kitale District Hospital, MTRH, Port Victoria Sub-District Hospital, Turbo Health Centre, Webuye District Hospital

Project Period
1/1/2016 - 12/30/2016

Funding Status
Funded – Indiana University - Center for AIDS Research

Direct Award (USD)
$8,500

Update
We have completed all of the caregiver and clinical provider interviews. We are getting them transcribed and translated currently. We are only able to do Phase one of the study at this time due to funding.

Future Plans
I hope that we'll be able to analyze the transcripts, write up the results, and publish them over the next 6 months.

Publication(s)

Study Title
Biomarkers of Vincristine Toxicity in Kenyan Children

Principal Investigator(s)
Jodi Skiles, Indiana University
### Project Description

**Co-Investigator(s)**
F. Njuguna, Moi University

**Working Group(s)**
ORWG, PRWG

**Description**
This study evaluates the presence of peripheral neuropathy induced by Vincristine in Kenyan children receiving chemotherapy. The main purpose is to assess whether the genetic makeup of each child (particular the genotype of CYP3A5) influences drug exposure and subsequent vincristine toxicity.

**Site(s)**
Moi Teaching and Referral Hospital

**Project Period**

**Funding Status**
Funded – NIH

**Direct Award (USD)**
$8,743

**Update**
The first of the manuscripts that will result from this work was submitted to NEJM in May 2014. It received good comments, but was ultimately rejected. It was then resubmitted to Journal of Clinical Oncology where it received constructive feedback and the request for the planned 2nd manuscript to be submitted to support the methodology used in this paper. The 2nd manuscript was completed and submitted to Journal of Chromatography B where it received constructive feedback but was also ultimately rejected. We are in the process of running additional experiments to allow us to adequately respond to reviewer comments prior to resubmission to a new journal. Once it is accepted for publication, the original manuscript will be re-submitted to Pediatric Blood and Cancer. Publication of the 2 manuscripts referred to above.

**Future Plans**
Publication of the 2 manuscripts referred to above

### Study Title
**Bridging Income Generation with Group Integrated Care (BIGPIC)**

**Principal Investigator(s)**
Rajesh Vedanthan, Mount Sinai School of Medicine
Jemimah Kamano, Moi University

**Co-Investigator(s)**
Pastakia, Sonak Naanyu, Violet Chesoli, Cleophas Andama, Benjamin Fuster, Valentin Horowitz, Carol Manyara, Simon Menya, Diana

**Working Group(s)**
AMWG, CVMD

**Description**
The objective of this proposal is to utilize a trans disciplinary implementation research approach to address the challenge of reducing CVD risk in low-resource settings. The research aims at integration of group medical visits and microfinance with the additional social network characteristics. **Aim 1:** Identify the contextual factors, facilitators, and barriers that may impact integration of group medical visits and microfinance for CVD risk reduction, using a combination of qualitative research methods: 1) baraza; and 2) focus group discussions among individuals with diabetes or at increased risk for diabetes, microfinance group members, and rural health workers. Then develop a contextually and culturally appropriate integrated group medical visit-microfinance model. **Aim 2:** Evaluate...
the effectiveness of group medical visits and microfinance groups for CVD risk reduction among individuals with diabetes or at increased risk for diabetes, by conducting a four-arm cluster randomized trial comparing: 1) usual clinical care; 2) usual clinical care plus microfinance groups only; 3) group medical visits only (no microfinance); and 4) group medical visits integrated into microfinance groups. Aim 3: Evaluate the incremental cost-effectiveness of each intervention arm of the trial.

Site(s)
Bumala A Health Centre, Bumala B Health Centre, Chulaimbo Sub-District Hospital, Endebess Sub-District Hospital, Kapsera District Hospital, Khunyaung Sub-District Hospital, Matayas Health Centre, Moi's Bridge Health Centre, Saboti Sub-District Hospital

Project Period
4/1/2015 - 4/1/2015

Funding Status
Funded – NIH

Direct Award (USD)
$2,478,465

Update
Marked progress has been made on this study project during the period of January 1, 2016 thru June 30, 2016. Below is a delineation of progress, key outcomes and accomplishments by category.

Administrative:
• Year two NIH grant renewal and Moi IREC approval sought and obtained
• Capacity building of the study personnel with specialized and targeted training ongoing
• Faculty and study team visits to Eldoret, Kenya for the purposes of site monitoring, capacity building, and training is ongoing

Aim 1:
• Qualitative data analysis of all the mabaraza and FGDs for Aim 1 is ongoing
• Protocol finalized and approved by IREC and IRB
• Contextually and culturally appropriate integrated and group medical visit-microfinance model developed through a series of design meetings (5 meetings)
• Acceptability focus group discussions carried out with patients, clinicians and microfinance group members (8 sessions in total were carried out)

Aim 2:
• Randomization scheme has been completed
• Discussion ongoing with AMPATH Chronic Disease Management Program, AMPATH Community Strategy Initiative, and AMPATH Safety Net Program, to coordinate the initiation of the cluster randomized trial
• Operational details of enrollment, data entry, and data management ongoing

Aim 3:
• Costing questionnaire survey instrument has been drafted and in the process of being finalized
• Potential Challenges and Actions Taken to Resolve/Address Challenges:
  • Participant recruitment may pose to be a challenge for the formation of groups for GMVs and MF groups

Future Plans
Overall: Finalize methods manuscript and submit for publication
Aim 1: Complete content analysis of mabaraza and FGD transcripts Submit qualitative findings for conference presentation Draft manuscript
Aim 1.1: Finalize integrated and GMV-MF
model through design team meeting that will be carried out (2 sessions) Analyze all the transcripts from acceptability and pilot FGDs and subsequently submit abstracts and draft a manuscript. Aim 2: Finalize programming of the costing questionnaire Testing of costing and social network survey to ensure that it is ready for administering to study participants within the appropriate time period Finalize the hiring process and training of clinicians and field staff who will be involved in the group medical visit-microfinance intervention Finalize development and implementation of a data management plan in order to avoid future data management issues Initiate enrollment in final quarter of 2016

Publication(s)

Study Title

Can integration of effective family planning services into Anticoagulation Management Services (AMS) improve uptake?

Principal Investigator(s)

Astrid Christoffersen-Deb, University of Toronto

Co-Investigator(s)

Imran Manji, Moi Teaching and Referral Hospital

Working Group(s)

PHPC WG

Description

The purpose of the study is to evaluate whether integration of family planning education and free, on-site provision of all reversible family planning methods in Anticoagulation Monitoring Service (AMS) Clinic can improve uptake of long-acting reversible contraception (LARC; specifically intrauterine contraceptive devices (IUCDs) and contraceptive implants) in this high-risk population. Our hypothesis is that implementation of an educational intervention emphasizing long-acting reversible contraception (LARC) combined with free on-site provision of LARC within Anticoagulation Monitoring Service (AMS) can improve uptake of these methods by 250% in this population. Our objectives are to: 1) Determine whether integration of education about and free provision of highly effective long-acting reversible contraceptive methods within Anticoagulation Monitoring Services (AMS) is feasible. 2) Determine whether integration of education about and free provision of highly effective long-acting reversible contraceptive methods within Anticoagulation Monitoring Services (AMS) can improve uptake of long-acting reversible contraceptive methods (IUCDs and contraceptive implants). 3) Determine whether integration of education about and free provision of highly effective long-acting reversible contraceptive methods within an Anticoagulation Monitoring Services (AMS) Clinic can prevent unplanned pregnancies. In order to evaluate these objectives we will provide the intervention and follow the participants for the following 1 year time period. At 3-month, 6-month, and 12-month follow-up we will evaluate whether they are using any method of family planning and whether they have experienced subsequent unplanned pregnancies. This data will be compared to the same group of women prior to implementation of the education intervention and free, on-site provision of all reversible contraceptive methods.

Site(s)

Moi Teaching and Referral Hospital

Project Period

4/20/2015 - 8/31/2016

Funding Status

Unfunded –
Direct Award (USD)

Update

We had four major challenges encountered at each step of the project cycle. The program initiation was initially behind schedule due to the challenges faced in the logistics of coordinating its various multi-step components, and adapting them to the local context. We have so far faced 2 challenges under project evaluation. Initially, child development assessments were planned to take place at baseline, midpoint and endpoint. We learned during the baseline assessments that we would not be likely to show program impact due to the long-term, complex nature of these assessments. We therefore decided to abandon the midpoint assessments and complement the neurodevelopmental assessments with the addition of measurement of parental behaviour and stress at both baseline and endpoint.

Future Plans

Over the next six months, we will analyze the three month follow-up data available for 186 participants. We plan to submit a manuscript with this three month follow-up data to a peer-reviewed journal. We aim to finish the six month follow-up data collection by September 2016 and the twelve month follow-up by March 2017. We will continue to conduct data analysis over time to evaluate our primary outcome of increased use of Tier 1 contraceptive methods. We will also plan to submit a manuscript with our final data to a peer-reviewed journal.

Publication(s)

Study Title

Chama Cha Mama Toto: Evaluating A Peer Support Mechanism To Improve Maternal And Infant Health

Principal Investigator(s)

Astrid Christoffersen-Deb, University of Toronto

Co-Investigator(s)

Julia Songok, Moi University

Working Group(s)

PHPC WG

Description

Chama cha Mama Toto are mother-child groups tailored to the needs of mothers and their children living in rural areas of western Kenya. The study is being performed in two phases. Phase I of the study sort to show the effectiveness of Chamas in Bunyala Sub-county, in enhancing women, child health and child development. This Phase ended in August 2014 paving way for Phase II. Phase II entailed the integration of a positive parenting curriculum into Chamas known as Malezi Mema Parenting Programme in February 2016. The programme was adapted from the South African 'Sinovuyo Parenting programme' in consultation with Jamie McLaren Lachman. This is the first time that the adapted Sinovuyo Parenting program is being implemented in a real-world setting at scale rather than in a research program. The curriculum comprises of 18 topics that address the key main areas of parenting. The curriculum is divided into two main sections. Section 1 provides mothers with knowledge on positive parenting while section 2 provides mothers with ways of managing maternal stress, alternative methods of dealing with difficult behaviour in children as opposed to harsh punishment and helping children through stressful situations. The sessions are delivered in a Chama using a collaborative approach with the guidance of trained CHVs. The sessions are also supervised by 'Malaikas' who consist of program assistants who have been trained in supervision. The parents are led
through a discussion that involves group discussions/ brainstorm, role plays, exercises, song, dance and a homework practice to go and implement what they learned and give feedback in the next session. This second phase aims to validate the integration of parenting curriculum into Chama cha Mama Toto Program. The study also seeks to show the effectiveness of peer support mechanisms in improving maternal confidence and esteem, to alleviate maternal stress, to reduce incidence of harsh parenting, to change the attitude towards punishment in Bunyala Sub- County and to determine the acceptability of the program among Chama women, their partners, and the community at large.

Site(s)  
Mukhobola Health Centre, Osieko Dispensary, Port Victoria Sub-District HospitalRwambua Dispensary, Rugunga Dispensary, Not at facilities, but located in the community units attached to the facilities.

Project Period  
5/1/2015 - 10/31/2016

Funding Status  
Funded – Grand Challenges Canada

Direct Award (USD)  
$250,000

Update  
The project has accomplished a great number of activities. Baseline data collection for both the intervention and the control group began in August 2015 and run up to mid January 2016. This was done concurrently with the identification of a good parenting curriculum, editing, adaptation and finally translation of the curriculum into the Kenyan context adaptation of the curriculum and translation. Training of CHVs and supervisors was done in January. The curriculum was officially launched in Chamas in February 2016 with two sessions being delivered every month. Supervisions are also ongoing everytime Chamas meet to ensure the program is delivered with fidelity. The team also conducted interviews with mothers in April to supplement the information gathered during baseline. This data is meant to be baseline for maternal stress levels, attitudes towards harsh parenting and current behaviour correction practiced by mothers. We also recently conducted FGDs in Bunyala involving mothers in Chamas and also partners to assess reaction, uptake and acceptability of the program in the community.

Future Plans  
We plan on continuing with session delivering for the next 3 months. If the schedule goes on as planned, the curriculum will be done by end of October 2016. Supervisions are also going to be taking place for the purposes of monitoring and evaluation. We also anticipate to begin endpoint data collection which will entail child assessments, mothers interviews on child development, mothers interviews on parenting and maternal stress and FGDs in October.

Publication(s)  
Study Title  
Childhood Leukemia in Kenya Identified Through Malaria Slide Review

Principal Investigator(s)  
Terry Vik, Indiana University

Co-Investigator(s)  
F. Njuguna, Moi University

Working Group(s)  
ORWG, PRWG
### Description

The aim of this study is to improve the case detection rate of leukemia by retrospectively reviewing blood smears done for malaria screening to identify children with leukemia in defined population cohorts. If the case detection rate can be improved by utilizing a common and well established procedure, then there is potential to identify children, refer them earlier for treatment and save lives.

### Site(s)

Moi's Bridge Health Centre

### Project Period

7/1/2012 - 6/30/2015

### Funding Status

Funded – Alex's Lemonade Stand Foundation

### Direct Award (USD)

$200,000

### Update

The DNA analysis has been completed for nearly 200 slides. The results are being analyzed. Over 20 cases of leukemia have been confirmed by the genetic testing. Two manuscripts are in preparation.

### Future Plans

Complete the manuscripts and submit for publication after review by co-authors and the publications committee.

### Publication(s)

**Study Title**

Community perceptions and perceived needs of street-connected children and youth in Eldoret Kenya: a qualitative investigation

**Principal Investigator(s)**

Lonnie Embleton, University of Toronto

**Co-Investigator(s)**

David Ayuku, Moi University

**Working Group(s)**

None

**Description**

Very little research exists that explores public perceptions and reactions to street-connected children and youth in low- and middle-income settings and how this impacts the care and services they receive; and no one has explored this topic to date in our setting. Moreover, no one has investigated street-connected youth's opinions and perceptions of their treatment by the public and their needs in relation to the provision of healthcare and services in Eldoret. Gathering youth’s opinions and perspectives on their treatment and care will assist with the design and development of services and interventions for this vulnerable population. When youth are involved in the design and development of programs they are more likely to uptake services and seek care that is responsive to their needs. Similarly, exploring the opinions and perspectives of local policymakers, community members, and healthcare providers concerning street-connected children and youth, which influence their decision-making (ethical or unethical) in regards to the provision of programs, services, treatment, support, and care for this population is vital to reduce the harms associated with street-involvement. Gathering this data represents the first step in designing and developing effective evidenced-based interventions and policies, in a community-based participatory manner, which are responsive to the perspectives of street-connected children and youth and community members within the local social-cultural context. **SPECIFIC AIMS**

**AIM 1:**

Explore and describe the perceptions of community members across different social
strata about the causes, characters, and needs of street-connected youth in Eldoret, Kenya. **AIM 2:** Describe the experiences of street-connected youth in Eldoret, Kenya, aged 15-24, with stigma and discrimination on the streets and when accessing services and healthcare. **AIM 3:** Elucidate ideas concerning appropriate service delivery and care for street-connected youth in Eldoret, Kenya from community members across different social strata. 3.1) Identify street-connected youth’s opinions on what will assist or facilitate access to healthcare and specifically explore their needs in relation to HIV prevention.

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<tr>
<td>Update</td>
<td>This project received ethics approval from IREC and is under review at the University of Toronto REB.</td>
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<tr>
<td>Future Plans</td>
<td>Over the next 6 months it is expected we will receive approval from the University of Toronto REB and collect the data for this project.</td>
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**Study Title**

Developing and Assessing a Community-Based Model of Antiretroviral Care

**Principal Investigator(s)**

Abraham Siika, Moi University

**Co-Investigator(s)**

Kara-Wools Kaloustian, Indiana University

**Working Group(s)**

TBWG

**Description**

ART Co-ops study will develop and assess an alternative care model that is established on the platform of a HIV-infected peer-group (ART Co-op) and facilitated by community health workers (CHWs). This model of care is intended to decentralize ART services and bring them closer to the patients. Specifically, we will: 1. Develop an acceptable and sustainable model for extending HIV care and treatment into the community. 2. Perform a pilot study comparing the outcomes of patients enrolled in the ART Co-ops program to those receiving standard of care. 3. Determine the cost savings and cost effectiveness of ART Co-ops.

| Site(s)                      |                                   |
|------------------------------|                                   |
| Project Period               | 2/9/2015 - 2/9/2017                |
| Funding Status               | Funded – Centers for Disease Control and Prevention (CDC) |
| Direct Award (USD)           | $924,042                           |
| Update                       | 1. The study completed data collection and analysis for specific aim 1 (FGD's and Interviews), specific aim 1 data analysis informed the protocol and amendments were recommended. 2. One (1) study clinical officer was employed 3. Four (4) CHW's were |
4. The clinical officer and CHW's were trained on Good Clinical Practise (GCP) by FHI 360 in January 2016. They also attended the comprehensive ART management Training offered by AMPATH Training Institute in February 2016. 5. A team from CDC (sponsor) visited the site as from the 2nd - 5th February 2016 to assess the study readiness for specific aims 2,3 & 4. They gave recommendations which have since been implemented. 6. Creation of the study database and programming of study data collection forms was initiated. 7. CHW's were trained on community strategy in April 2016.

Future Plans

1. Identify study eligible patients and enroll for specific aims 2,3 & 4. 2. Establish and manage ART Co-op groups. 3. Follow-up of enrolled patients in Co-op groups.

Publication(s)

**Effect of free maternity care on maternal and fetal outcomes of preeclampsia/eclampsia at a teaching hospital in Western Kenya: A retrospective chart review.**

Astrid Christoffersen-Deb, University of Toronto

PHARMCR WG

The aim of this study is to determine the incidence of diagnosis and treatment of pre-eclampsia and eclampsia at MTRH. We will measure the maternal and neonatal outcomes in women with these diagnoses. We will evaluate the data in order to determine areas for improvement in our diagnosis and management of pre-eclampsia/eclampsia in order to decrease maternal and neonatal morbidity and mortality at MTRH. Finally, we would like to evaluate the effect free maternal care has played in the measured incidence and outcomes of pre-eclampsia and eclampsia at our institution. Specifically, we will: 1. Determine and compare the incidences of pre-eclampsia within our institution in the year before and the year after the initiation of free maternal care in June, 2013 2. Evaluate the maternal and neonatal outcomes, including major causes of morbidity and mortality in each group. Again we will compare these before and after the initiation of free maternal care in June, 2013. 3. Evaluate the risk factors for adverse maternal and neonatal outcomes 4. Evaluate the adherence of treatment in our facility in accordance with World Health Organization standards, again comparing treatment before and after the initiation of free maternity care in June, 2013. The data for this study is collected using a comprehensive 100-item data collection form, including patient demographics, symptomatology, documented clinical signs and laboratory results, delivery details, and maternal and neonatal outcomes.
Update

The data team did analysis of the data collected on The baseline results from a sample size of 95 mother child pairs in the intervention arm indicated that 26 children (27.5%) delayed in growth and development as compared to 6 children (21.4%) from a sample size of 28 mother-child pairs in the control group p = 0.53. Attitude towards punishment in a Likert scale of 0-4 was 2.9 ±0.17 in the intervention group compared to 3.3 ± 0.22 in the control group p=0.36. Mean parental stress in a Likert scale of 0-4 was 3.9 ± 0.5 in the intervention group and 3.9 ± 0.3 in the control group p = 0.79. The mean number of instances of harsh punishment was 0.5 ± 0.42 in the intervention group compared to 0.8 ± 0.65 in the unexposed group p = 0.009.

Future Plans

Due to a dramatic difference in the number of files that had maternal deaths, 12 after free maternity care and 1 before, and having found that a significant number of patient files could not be retrieved, we have made an amendment that will allow us to pull all maternal mortality files so as to identify any records that may have been missed in the initial file retrieval. After obtaining IREC approval we will retrieve and review all maternal mortality files. We also plan on completing data analysis and complete writing the manuscript.

Publication(s)

<table>
<thead>
<tr>
<th>Study Title</th>
<th>Engaging Street Youth in HIV Interventions (EASY)</th>
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</thead>
<tbody>
<tr>
<td>Principal Investigator(s)</td>
<td>Paula Braitstein, University of Toronto</td>
</tr>
<tr>
<td>Co-Investigator(s)</td>
<td>David Ayuku, Moi University</td>
</tr>
<tr>
<td>Working Group(s)</td>
<td>PRWG</td>
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<tr>
<td>Description</td>
<td>This is an 18-month project funded by the Canadian Institutes for Health Research (CIHR) aiming to identify, adapt, and pilot interventions to engage street-connected children and youth (SCY) into HIV prevention, care and treatment. The first stage requires a comprehensive literature review identifying potential interventions from the literature; the second stage requires narrowing down the possible selection of interventions by their feasibility, cost, ethics, and potential effectiveness; and the third stage is to pilot and evaluate 2-3 interventions.</td>
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<tr>
<td>Site(s)</td>
<td>MTRH</td>
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<tr>
<td>Project Period</td>
<td>4/1/2016 - 9/30/2017</td>
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<tr>
<td>Funding Status</td>
<td>Funded – Canadian Institutes of Health Research</td>
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<tr>
<td>Direct Award (USD)</td>
<td>$150,000 Canadian</td>
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<tr>
<td>Update</td>
<td>A comprehensive literature review has been done to identify about 31 possible interventions, these interventions have been discussed through several meetings and conference calls and have been narrowed down to about 5 possible interventions. A Start-Up Meeting for the Project has been held and a Job Advertisement has been posted seeking to hire a Senior Research Assistant so as to facilitate smooth implementation of the Project.</td>
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<tr>
<td>Future Plans</td>
<td>Costing of the shortlisted interventions, and piloting of the top choices.</td>
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<tr>
<td>Publication(s)</td>
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<tr>
<td><strong>Study Title</strong></td>
<td><strong>Enhancing Training for Implementation Research in Chronic Disease: CITE/Kenya</strong></td>
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<tr>
<td><strong>Principal Investigator(s)</strong></td>
<td>Tom Inui, Indiana University</td>
</tr>
<tr>
<td><strong>Co-Investigator(s)</strong></td>
<td>Paul Ayuo, Moi University</td>
</tr>
<tr>
<td><strong>Working Group(s)</strong></td>
<td>AMWG</td>
</tr>
<tr>
<td><strong>Description</strong></td>
<td>An innovative clinical and implementation research training program for Kenyan investigators, one built on the foundation of the highly successful and mature clinical and implementation research core curriculum for young investigators within our IUSM CTSI, will be developed. This program will attract graduate trainees nominated by faculty at Moi University schools of medicine, public health, dentistry, nursing, and possibly young faculty from health-related behavioral and social science programs at Moi. This curriculum will be presided over by seasoned Eldoret-based investigators from the AMPATH research network (especially Dr. Thomas Inui and his 5 co-directors of the AMPATH Field Research program). Trainees who complete the core curriculum will be eligible to compete for resources to propose and conduct research in an implementation research practicum under the supervision of a tailored mentorship panel populated by Moi and international faculty. This research will focus upon a chronic disease of importance to the health of the populations in Western Kenya and will contribute to the improvement of health care processes, including village-based processes, medical and psycho-social services, and integration of care for chronic conditions within the MOH delivery system. The 'laboratory' for this research will be the AMPATH-MOH chronic disease program. The training program will build on the successful AMPATH multi-disciplinary and multi-institutional research foundation already in place, supported by AMPATH’s remarkable e-Health infrastructure. This program's graduate training will enable Kenyans to acquire knowledge and skills in health systems and implementation research, enhance their capacity to promote continuous improvement of health care, inform health policy, and acquire leadership and management skills needed to develop, manage and improve chronic disease control programs. The ultimate aim of this proposal is to prepare Moi health professionals to serve as effective change agents and scientific leaders in Kenya's evolving system of care.</td>
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<tr>
<td><strong>Site(s)</strong></td>
<td>Moi's Bridge Health Centre</td>
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<tr>
<td><strong>Project Period</strong></td>
<td>10/1/2012 - 9/30/2016</td>
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<td><strong>Funding Status</strong></td>
<td>Funded – NIH - Fogarty International Center (FIC)</td>
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<td><strong>Direct Award (USD)</strong></td>
<td>$862,970</td>
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<tr>
<td><strong>Update</strong></td>
<td>Drs Inui and Litzelman traveled to Eldoret in March 2016 to hear presentations from all D43 fellows. While all fellows are making good progress, IREC approval delays were delaying project closure. Individual meetings were held to plan practicum project closure processes that should make it possible for the fellows to report on project final results by</td>
</tr>
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</table>
September 2016. Drs Siika and Ayuo have agreed that Dr. Litzelman should assume PI responsibilities for the continued activities of this training grant after Dr. Inui's formal retirement June 30, 2016.

**Future Plans**

Dr. Litzelman, Siika and Ayuo should preside over practicum project final result reports and plans for publication/dissemination of findings in September 2016.

**Publication(s)**

**Study Title**

Evaluation of the growth and development of young children of HIV-infected mothers in western Kenya.

**Principal Investigator(s)**

Megan McHenry (maiden name: Uhl), Indiana University

**Co-Investigator(s)**

**Working Group(s)**

PRWG

**Description**

Children under five years of age are at significant risk for mortality in resource-limited settings. One in nine children in sub-Saharan Africa die before they reach five years of age. Approximately 45% of child deaths are related to poor growth and malnutrition. Children born to HIV-infected mothers are at increased risk for stunting, wasting, and being underweight, and children with HIV and AIDS are even more likely to be malnourished. Without treatment, 50% of HIV-infected and 7% of HIV-exposed, but uninfected infants will die before two years of age. My long-term research goal is to provide evidence to improve the nutritional status and, in turn, decrease under-5 mortality for children born to HIV-infected women in resource-limited settings. As access to HIV care expands and we push towards the Millennium Development Goal of reducing child mortality, we must address the risks faced by young children exposed to or infected with HIV. The Academic Model Providing Access To Healthcare (AMPATH) in Kenya provides an ideal setting in which to evaluate the growth and development of this vulnerable population, and to explore effective interventions to improve their health. AMPATH is a long-standing, academic partnership, created between the Moi University School of Medicine, Moi Teaching and Referral Hospital, and the Indiana University School of Medicine, that provides care for over 15,000 HIV-infected and HIV-exposed children, one of the world's largest pediatric HIV cohorts. Few current data focus on the best strategies to foster the growth and development of HIV-exposed and HIV-infected children under five years of age and living in resource-limited settings. The objective of this study is to evaluate the growth and development of young children of HIV-infected mothers in western Kenya, with attention to identifying areas to target for future interventions. We plan to accomplish our research objective by pursuing the following four specific aims:  

**Aim 1:** Evaluate the changes in anthropometrics over time for children under the age of five who are born to HIV-infected mothers enrolled in AMPATH clinics. Hypothesis: Among those enrolled in AMPATH, HIV-infected children will have lower Z-scores for measured anthropometrics (WAZ, HAZ, WHZ) than HIV-exposed children.  

**Aim 2:** Determine factors associated with poor weight gain in this population of children. Hypothesis: Factors such as being orphaned, being HIV-infected, having developmental delays, having been hospitalized, and lower immunization rates will be associated with lower Z-scores for measured anthropometrics in both HIV-exposed and
HIV-infected children under 5. Aim 3: Evaluate the rates at which clinical providers detect failure-to-thrive in children under 5 years during routine AMPATH clinic visits. Hypothesis: Clinical providers will have low rates of identifying failure-to-thrive as a problem for children under-five requiring follow-up. Aim 4: Describe the mortality rates and rates of losses to follow-up in this population. Hypothesis 4a: Mortality rates will be higher among those children who are HIV-infected and malnourished. Hypothesis 4b: Losses to follow-up are more common among HIV-exposed children compared to HIV-infected children. Rates of those lost to follow-up for both groups will be <20%, which is generally considered acceptable in research studies.

Site(s)  
Project Period  
Funding Status  
Direct Award (USD)  
Update  

<table>
<thead>
<tr>
<th>Site(s)</th>
<th>Project Period</th>
<th>Funding Status</th>
<th>Direct Award (USD)</th>
<th>Update</th>
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<tbody>
<tr>
<td></td>
<td>7/1/2015 - 6/30/2017</td>
<td>Unfunded –</td>
<td></td>
<td>We performed some of our preliminary analyses on the data set from September 2014. We were able to submit our preliminary results to the AIDS conference and Pediatric HIV workshop in South Africa. It was accepted for oral abstract presentation at the AIDS conference and in the abstract book for the Pediatric HIV workshop. We’ve since mapped at the rest of the analyses that we’ll want for the manuscript and are awaiting the data from the most recent data pull in December 2015. Here are the results included in the abstract being presented: Data from 13,925 children born to HIV-infected mothers were included. 51.7% (n=7197) female, 2.67% (n=373) double orphans, 69.2% (n=9639) HEU, 14.75% (n=2054) HIV-infected, and 16.0% (n=2232) without confirmatory HIV testing during study period. Mean age at HIV diagnosis was 2.04±1.53years. Mean weight-for-age Z score (WFAZ) was -0.68 ±1.45. 32.8% (n=4561) WFAZ -2 to -3 (moderately underweight) and 14.4% (n=2014) WFAZ &lt;-3 (severely underweight) during the study period. Mean height-for-age Z score (HFAZ) was -1.38±1.92. 46.7% (n=6506) HFAZ -2 to -3 (moderately stunted) and 25.0% (n=3488) HFAZ &lt;-3 (severely stunted). Mean weight-for-height Z score (WFHZ) was 0.35±2.09. 17.5% (n=3044) WFHZ -2 to -3 (moderately wasted) and 13.1% (n=2295) WFHZ &lt; -3 (severely wasted). When comparing z-score by age between HIV-infected and HEU children, a statistically significant difference was found for HFAZ (p-value=0.000), WFAZ (p-value=0.000), WFHZ (p-value=0.000). When comparing z-scores by age between male and female children, a difference was found for HFAZ (p-value=0.028). For those with a HIV-infected sibling, the HIV-infected children in this study were more likely to have WFAZ&lt;-2 (OR: 1.167; 95%CI: 1.042-1.307), while HEU were less likely (OR:0.932; 95%CI: 0.970-0.998). HEU were more likely to have WFAZ&lt;-2 if they were orphaned (OR 1.189; 95%CI: 1.001-1.413) and enrolled in clinic at a later age (OR 3.212; 95%CI: 3.012-3.425), with each year of delayed enrollment increasing risk of WFAZ&lt;-2 by 17% (OR:1.167; p-value&lt;0.001). HEU were more likely to have WFHZ &lt;-2 if they were enrolled in clinic at a later age (OR: 1.502; 95%CI: 1.328-1.697). There were no significant correlations between HIV-infected children’s WFHZ and orphan status, age of clinic enrollment, and presence of an HIV-infected sibling. We are hoping to get the newest data pull from December 2015, so that we can run our analyses on it and write up the final manuscript. We are struggling to get this data. However, once we do, we’ll be able to get the manuscript out.</td>
</tr>
<tr>
<td>Study Title</td>
<td>Factors associated with adolescent pregnancy, antenatal care attendance, and linkage to both HIV and antenatal care for those participating in Home-Based Counseling and Testing in Western Kenya</td>
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<tr>
<td>Principal Investigator(s)</td>
<td>Katherine MacDonald, Indiana University</td>
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<td>Co-Investigator(s)</td>
<td>Edith Apondi, Moi Teaching and Referral Hospital</td>
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<td>Working Group(s)</td>
<td>PRWG, RHWG</td>
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<tr>
<td>Description</td>
<td>This study is a sub-analysis of the adolescent population who were selected in the study 'HIV Prevalence and Antenatal Care Attendance among Pregnant Women in a Large Home-Based HIV Counseling and Testing Program in Western Kenya' by Ndege et al. We will focus on examining factors associated with pregnancy, ANC attendance, and enrollment in HIV and antenatal care. This cross sectional retrospective study can facilitate identifying adolescents who are at risk of becoming pregnant and yet less likely to receive antenatal care. Most importantly the study could identify factors associated with poor linkage to HIV and ANC care, and could uncover an opportunity to identify pregnant adolescents who are unknowingly living with HIV by utilizing the home-based counseling and testing (HBCT) platform. We aim to describe the adolescents who participated in HBCT, and determine associated socioeconomic and health factors related to pregnancy, ANC attendance, HIV infection and enrollment in HIV and ANC care.</td>
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<tr>
<td>Site(s)</td>
<td>Burnt Forest, Chulaimbo, Kapsaret, Port Victoria, and Teso communities (not health centre or hospital based)</td>
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<td>Project Period</td>
<td>7/12/2016 - 8/22/2016</td>
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<tr>
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<tr>
<td>Direct Award (USD)</td>
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<tr>
<td>Update</td>
<td>Currently, we are waiting for the data set analysis.</td>
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<tr>
<td>Future Plans</td>
<td>In the next six months, we hope to finish the data analysis, submit an abstract for the Society of Adolescent Health and Medicine conference, and write a manuscript.</td>
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<tr>
<td>Publication(s)</td>
<td>FLTR Evaluation</td>
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<tr>
<td>Study Title</td>
<td>FLTR Evaluation</td>
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<tr>
<td>Principal Investigator(s)</td>
<td>Paula Braitstein, University of Toronto</td>
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<tr>
<td>Co-Investigator(s)</td>
<td>Sylvester Kimaiyo, Moi University</td>
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<tr>
<td>Working Group(s)</td>
<td>AMWG, PHPC WG</td>
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<tr>
<td>Description</td>
<td>The FLTR evaluation aims to evaluate the core aspects of the HIV prevention-care continuum, using a combination of quantitative and qualitative methods. We investigate issues related to Finding, Linking, Treating, and Retaining people living with HIV in AMPATH catchments, involving behavioral scientists, biostatisticians, epidemiologists, among others.</td>
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<td>Site(s)</td>
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<tr>
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<tr>
<td>Update</td>
<td>Much of the focus at the moment is creating FLTR datasets for Bunyala, Chulaimbo, and Teso catchments which will become incredibly rich datasets to evaluate the successes and weaknesses in the HIV care cascade. Please see other updates for more details on this (outcomes study, Pathways to Better Health). In addition we are pursuing several specific analyses including:</td>
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<td>- Adolescent pregnancy, HIV and uptake of ANC and HIV care in home-based testing (led by Katherine MacDonald)</td>
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<td></td>
<td>- Incidence and risk factors for adolescent pregnancies in young women living with HIV in AMPATH (led by Heather Millar)</td>
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<td></td>
<td>- The impact of peers and pharmacy technicians on reporting and management of ART toxicity (led by Sonak Pastakia)</td>
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<td>- ART toxicity in HIV-infected children (led by Beatrice Jakait)</td>
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<td>- Impact of Care Navigators on linkage to care (led by Becky Genberg)</td>
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<td></td>
<td>- Impact of Peer Navigators on HIV testing and uptake of care among street-connected children and youth (led by Paula Braitstein)</td>
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<td>- We are participating in a global meta-analysis if the outcomes of persons lost to follow-up from HIV care (led by Matthias Egger in Bern, Switzerland)</td>
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<td>- Spatial distribution of persons failed to link to HIV care (led by Cici Bauer)</td>
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<td>- State Space Models to describe the HIV care cascade (led by Joseph Hogan)</td>
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<td>- Impact of point of entry on mortality and retention in care (led by Becky Genberg)</td>
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<td></td>
<td>- Qualitative investigation of the reasons why people fail to link to care (led by Juddy Wachira)</td>
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<td>- Qualitative investigation of patient-provider communication (led by Juddy Wachira)</td>
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<td></td>
<td>- Qualitative investigation of the acceptability and impact of the Care Navigators and Peer Navigators (led by Juddy Wachira)</td>
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<tr>
<td>Future Plans</td>
<td>We hope over the next six months to have produced FLTR datasets for Bunyala, Chulaimbo, and Teso. We intend to apply for NIH funding to do more outcomes evaluation of those failed to link to care, those who linked to care but became lost to</td>
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</table>
follow-up, the viral loads on a random sample of the HIV-positives, and HIV incidence among a random sample of HIV-negatives. We intend to publish updated linkage and engagement data for Bunyala, and complete several of the papers listed above.

### Study Title

**Group B streptococcus colonization among antenatal women: Prevalence and Antibiotic Susceptibility at Moi Teaching and Referral Hospital**

### Principal Investigator(s)

Saudah Farooqui, Moi University

### Co-Investigator(s)

Astrid Christoffersen-Deb, University of Toronto

### Working Group(s)

PHPC WG

### Description

This project is being done in Moi Teaching and Referral Hospital in the antenatal clinic. Based on studies performed in developed countries, approximately 10%-30% of pregnant women are colonized with GBS (Group B Streptococcus) in the vagina or rectum. GBS sepsis is a leading cause of maternal and perinatal morbidity and mortality and one of the most common causes of neonatal sepsis throughout the world. A rectovaginal swab is done on all pregnant women who fit our inclusion criteria and the culture is done in Lancet lab. Our main objectives are: 1. To determine the prevalence of GBS colonization among pregnant women seeking antenatal care in MCH at MTRH. 2. To determine the antibiotic susceptibility profile in pregnant women attending antenatal clinic at MTRH. 3. To determine feasibility of a screen and treat program at MTRH.

### Site(s)

Project Period: 5/5/2015 - 10/30/2015

### Funding Status

Unfunded –

### Update

The other challenge was location of the control group. The original list was generated from ANC clinics in selected health facilities back in 2012 in phase 1. By the time the assessment team were going back to locate them in order to conduct baseline assessment, a substantial number of them could not be traced. Some had relocated due to floods and in search of better livelihoods, one mother and one child had died, some children had outgrown the assessment tool. Others had joined Chamas after seeing the benefits fellow mothers who were in Chamas had accrued. We therefore only managed to get a control list of 28 mother-child pairs, which is lower than expected. The team then embarked on performing new sample size calculations to determine how many more controls we would need to perform a focused interview on to see an effect. In addition, we will be performing baseline and endpoint interviews to evaluate change in the intervention group. This will provide us comparison data without requiring a control group.

### Future Plans

We hope to present and defend our thesis before the Moi University School of Medicine and have the article for publication ready once we are through with our defence.
### Publication(s)

<table>
<thead>
<tr>
<th>Study Title</th>
<th>Principal Investigator(s)</th>
<th>Co-Investigator(s)</th>
<th>Working Group(s)</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>HI-Train: Health Informatics Training and Research in East Africa for Improved Health Care</td>
<td>Abraham Siika, Moi University</td>
<td>Martin Were, Indiana University</td>
<td>TBWG</td>
<td>With increased deployment of eHealth systems, comes the need for an appropriate health information technology workforce. This workforce includes: (a) Local level: Health IT professionals, eHealth specialized programmers, data managers, implementation managers, support specialists and reporting personnel; (b) Institutional level: chief medical information officers; and health information management specialists, (c) administrative: regional and national eHealth coordinators and eHealth monitoring and evaluation specialists, and (d) Other: health information privacy and security specialists and HI researchers. End users, institutional managers and policy makers also need to be appropriately trained on the relevant eHealth systems. Alarmingly, most sub-Saharan countries remain woefully unprepared to systematically train an adequate workforce to support the eHealth systems already being deployed. Countries like Uganda and Kenya recognize an emergent need for national strategies to build health informatics human capacity. These countries have appropriately developed national eHealth capacity-building strategies Implementing the strategies however requires direct leadership by Higher Education Institutions in the relevant countries. The urgency for sustainable mechanisms to increase HI workforce and research capacity in developing countries is self-evident. This goal can only be realized by having enough faculty members from developing countries fully trained in Health Informatics. These staff faculty can then be part of a well-functioning and high quality HI program moving forward. Recognizing this need, and the multidisciplinary competencies needed for HI training and research, our team identified partner institutions with complementary capabilities to support advanced Health Informatics training in East Africa for our project. Aims 1) Provide post-graduate (Masters and PhD) level training in Health Informatics and research. The focus will be on post-graduate training for health professionals and computer science personnel to help them become HI faculty at their institutions. 2) Increase number of women and marginalized populations in faculty-level training in Health Informatics and research at the LMIC higher education institutions. 3) Improve the quality and quantity of Health Informatics research conducted primarily by re-searchers based in the LMIC countries in collaboration with our Northern partners. 4) Provide model curricula, educational programs and approaches for faculty-level health informatics training that can be emulated by regional higher education institutions.</td>
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<th>Site(s)</th>
<th>Project Period</th>
<th>Funding Status</th>
<th>Direct Award (USD)</th>
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## Update

### Future Plans

The project intends to support a few students from the new cohort of Masters applicants for the the Health Informatics programs at Makerere and Moi Universities beginning in August and September 2016 respectively. Various activities have been planned for the 2016/2017 period including to facilitate various programming hackathons, workshops and conferences. More focus will also be on gender mainstreaming initiatives. The first group of students will finalize their course work and be able to start their research work in order to finalize by September 2017. Examinations are scheduled for 12th to 23rd September 2016. The new students to undertake common courses. PhD students to begin studies at University of Bergen in January 2016.

### Publication(s)

Abstracts for the NASCOP M&E workshop held at Kenya School of Monetary studies as follows  Kasiiti, Noah Applicability of fingerprint technology for unique patient matching in health care settings  Savai, Simon .Integrating a robust mobile application to KenyaEMR Balugaba, Bonny .Cost evaluation of Electronic Medical Records Implementations in Kenya.

## Study Title

**HIV-1 Drug Resistance in Different Subtypes**

### Principal Investigator(s)

Rami Kantor, Brown University

### Co-Investigator(s)

Lameck Diero, Moi University

### Working Group(s)

AMWG

### Description

Examine drug resistance upon tenofovir-containing first line antiretroviral therapy in multiple subtypes in western Kenya using different analyates.

### Site(s)

- Project Period: 5/12/2012 - 7/31/2015

### Funding Status

Funded – NIH - National Institute of Allergy and Infectious Diseases (NIAID)

### Direct Award (USD)

$98,168

### Update

Future Plans

Data analyses are ongoing to finalize dissemination.

Publication(s)


Study Title

IeDEA Comprehensive Adherence Measure for Pediatrics (ICAMP)

Principal Investigator(s)

Rachel Vreeman, Indiana University

Co-Investigator(s)

Winstone Nyandiko, Moi University

Working Group(s)

PRWG

Description

The primary objective of the proposed study is to validate an adherence questionnaire for pediatric and adolescent patients at 3 IeDEA sites using electronic dose monitors (Medication Event Monitoring Systems®, or 'MEMS', MWV/AARDEX, Switzerland) as external criterion for adherence. While the adherence questionnaire (known as the Comprehensive Adherence Measure for Pediatrics - Short Form, or 'CAMP-SF') has been previously validated in a large, urban referral site at AMPATH in the East Africa IeDEA region, re-validation is warranted to ensure external and internal validity is upheld across...
resource-limited sites. In conducting this validation study, we will also collect valuable, detailed prospective data on adherence to ART among this sample of HIV-infected children and adolescents using electronic dose monitoring. The study has the following specific aims and hypotheses:  Specific Aim 1: Validate a 10-item adherence questionnaire for routine use as an adherence measurement tool in resource-limited settings. Hypothesis 1a: Adherence estimates from the CAMP-SF will be reliable and valid across 3 IeDEA sites in East Africa, Southern Africa and Asia-Pacific when compared with MEMS electronic dosing data. Specific Aim 2: Describe pediatric adherence to ART prospectively over 6 months using electronic dose monitoring (i.e., MEMS) and the CAMP-SF among a sample of HIV-infected children and adolescents at 3 IeDEA sites. Hypothesis 2a: Rates of adherence to ART will be similar for children across different IeDEA sites. Hypothesis 2b: More pediatric non-adherence will be reported during prospective evaluation using the CAMP-SF than in existing rates reported in IeDEA datasets for children. Specific Aim 3: Evaluate factors associated with adherence among a sample of HIV-infected children and adolescents at 3 IeDEA sites. Hypothesis 3a: Risk of medication non-adherence is increased among older children, children with lower disease stages, children with higher CD4 counts, children with a higher medication burden, and orphaned children. Hypothesis 3b: Sites will differ in factors that may influence adherence, including number of children initiating ART; availability of nutritional support, adherence support, disclosure support, and pediatric formulations; and routine use of standardized adherence measures. Specific Aim 4: Assess evidence of the impact of ART non-adherence on clinical outcomes such as treatment failure and mortality, and programmatic factors such as loss-to-follow up. Hypothesis 4a: Medication non-adherence by MEMS is associated with increased risk of changing to second-line antiretroviral medications. Hypothesis 4b: Medication non-adherence by MEMS is associated with increased risk of mortality. Hypothesis 4c: Medication non-adherence by MEMS is associated with high risk of loss to follow-up.

### Site(s)

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<th>Site(s)</th>
<th>Funding Status</th>
<th>Direct Award (USD)</th>
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| 8/1/2014 - 7/31/2016 | funded - NIH - national institute of allergy and infectious diseases (niaid) | $171,257 | All three IeDEA study sites - Busia clinic at AMPATH (Kenya), HIV-NAT clinic (Bangkok, Thailand) and Rahima Moosa Mother Child Hospital (Johannesburg, South Africa) - have completed 6 months of study follow-up and data collection with approximately 100 pediatric patients and their caregivers at each site. The HIV-NAT site completed study follow up and data collection in February 2016. These data were used in an abstract that was submitted and accepted for a poster presentation at the 8th International Workshop on HIV Pediatrics being held ahead of the AIDS 2016 conference in Durban, South Africa. The HIV-NAT team from Thailand is presenting preliminary findings, in which we found evidence that the questionnaire items developed at our site in Kenya were performing well in detecting non-adherence among Thai patients. In January, Mr. Scanlon made a site visit to Bangkok to oversee study wrap up and moving the data to the analysis team at Indiana University. In the past month, both the Busia site in Kenya and the site in South Africa finished study follow-up and data collection. These data are now in the process of being cleaned and moved to Indiana University for data analysis, which will be...
undertaken over the next few months. In mid-July, Dr. Vreeman and Mr. Scanlon visited with the team in Johannesburg to oversee the conclusion of the study and transitioning data to Indiana University. The data from the Busia site is already with the Indiana University biostatistics team and is in the early stages of analysis.

**Future Plans**

Over the next six months, data cleaning and analysis will be completed. Data will be analyzed by-site to test the validity of the questionnaire at each site, and will be compiled for cross-site validation as well. The data cleaning and analysis process will require continued contact with the various site teams through weekly phone calls in which data cleaning, analysis and other relevant matters will be discussed. In addition, by the end of 2016 we aim to have a manuscript drafted and ready for submission for a peer-reviewed journal on the results of this study.

**Publication(s)**

Accepted as a poster presentation at the 8th International Workshop on HIV Pediatrics, held July 15-16 in Durban, South Africa. Validation of Adherence Questionnaire Items for HIV-Infected Children and Adolescents in Thailand Authors: Torsak Bunupuradah1, Stephen Kerr1, Michael L. Scanlon2, Wanzhu Tu2, James E. Slaven2, SiwanartÂ Thammasala1, SararatÂ Chanthaburanun1, Rachel C. Vreeman2,3 Author affiliations: 1HIV-NAT, Thai Red Cross AIDS Research Centre, Bangkok, Thailand; 2Indiana University School of Medicine, Indianapolis, Indiana; 3Academic Model Providing Access to Healthcare (AMPATH), Eldoret, Kenya

**Study Title**

Incidence of and risk factors for toxicity among HIV-infected children receiving cART: Findings from a large observational cohort in western Kenya

**Principal Investigator(s)**

Beatrice Jakait, Moi Teaching and Referral Hospital

**Co-Investigator(s)**

Paula Braitstein, University of Toronto

**Working Group(s)**

PRWG

**Description**

This is a retrospective study whose aim is to find out the incidence of adverse drugs reactions in children and the factors associated with it in children on antiretroviral therapy in AMPATH.

**Site(s)**

All Sites

**Project Period**

12/16/2014 - 9/15/2016

**Funding Status**

Unfunded –

**Direct Award (USD)**

In the last six months data collection has been completed. Data review has been done and the manuscript is being written. Preliminary findings show that there is a very low incidence of adverse drug reactions in children on antiretroviral therapy. The factors associated with adverse drug reactions include older age at the time of ART start, being on a Zidovudine based compared to a Stavudine based regimen, being on an Efavirenz based relative to a Nevirapine or Lopinavir based regimen and attending an urban clinic.

**Future Plans**

In the next six months the manuscript should be written and sent out for publication
### Study Title

**Innovative public-private partnership to target subsidized antimalarials in the retail sector**

### Principal Investigator(s)

Wendy Prudhomme, Duke University

### Co-Investigator(s)

Diana Menya, Moi University

### Working Group(s)

PHARMCR WG

### Description

In most malaria-endemic countries, a large fraction of fevers are treated in the informal health sector where diagnostic testing is uncommon and effective drugs are expensive. For many families, particularly in rural areas, the first source of treatment for fevers are retail medicine outlets such as chemists, pharmacists and small, unregulated medicine shops. These retail outlets, also referred to as the 'informal health sector', are more accessible than formal health services, but effective drugs are expensive and most clients purchase cheaper, ineffective therapies to which high levels of resistance exist. The Global Fund piloted a drug subsidy called the Affordable Medicines Facility - malaria (AMFm) to reduce the prices of effective, high quality ACTs in the private sector. AMFm was launched in 2010 and provided quality-assured ACTs to wholesale markets at substantially reduced prices in seven pilot countries, including Kenya. $339 million dollars were earmarked for subsidies and 155.8 million doses were delivered in the first 18 months of the program (ICF International, 2012). Prices of subsidized ACTs in most pilot countries dropped below that of cheaper, ineffective drugs and substantial cost savings were seen by the end consumer. In Kenya, the retail market share of ACTs increased from 12% to 61% in the first 18 months of the program (Tougher et al., 2012). However, there is concern that dramatically lowering the price of ACTs opened the door to over-treatment and overuse of ACTs. The overall objective of this study is to evaluate the public health impact of targeted antimalarial subsidies through scale-up by determining the community-wide effects of targeting an antimalarial subsidy through a partnership between CHVs and the private retail sector. Cluster-randomized design was used to assign community units to either an intervention or control arm. The study is being carried out in two sub-counties in Western Kenya (Bungoma East and Kiminini) with similar malaria burden but different access to health services. Community Units (CUs) in each sub-county were the clustered and randomized. There are 32 CUs in total across both sub-counties, 20 in Bungoma East and 12 in Kiminini. Half of the community units in each study area (10 in Bungoma East sub-county and 6 in Kiminini) were randomly allocated to the intervention and the remainder of the community units to the comparison arm. In the intervention arm a conditional subsidy is offered in the form of a voucher providing for the purchase of a WHO-qualified ACT at a reduced, fixed price to those with a positive malaria test that can be redeemed at a local drug retailer, while individuals in the comparison arm only receive standard community health volunteer (CHV) visits. Cross-sectional household surveying at pre-intervention, and 6 months, 12 months, and 18 months post-baseline will be used to determine any change in the percent of fevers that are tested for malaria and the effect of testing on subsequent drug purchasing decisions. The primary hypothesis to be tested is that offering a fixed-price voucher that reduces the cost for ACT purchase in the retail sector conditional on a positive malaria test (targeted subsidy) can improve uptake of testing for malaria and will increase the proportion of
fevers tested for malaria before treatment. The primary outcome of this study is to compare the percent of fevers that receive a malaria test from any source between the intervention and control arms. The secondary outcomes of this study will also be measured and compared between intervention and control arms. The main secondary outcome is the percent of all ACTs used that were taken by people with a malaria positive test. Additional secondary outcomes are: the percent of all ACTs used that were taken by people without a test, the percent of those with a positive test who got an ACT, and the percent of those with a negative test who got an ACT.

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**Update**

Testing: After six months of intervention, we recorded a total of 11,802 fevers that were tested for malaria, with a positivity and negativity rate of 25% and 75% respectively. 79% of the positive cases redeemed their vouchers for a qualified ACT at a discount in a nearby study enrolled shop at the communities. (source: quarterly report to MOH)

6th Month cross-sectional follow up survey results: Between February and April 2016, we carried out the first 6th month cross-sectional follow up survey, (August 2015 - January 2016). A random sample of households in all study areas (both intervention and comparison CUs) were contacted and asked about any fever or illness in the last one month. Any household with a reported illness was enrolled and asked questions about the actions taken for that illness. The percent of households with recent fever ranged from 36% to 49% indicating a high burden of acute febrile illness. Nearly half of all respondents self-medicate with drugs purchased over the counter as their first action. Many of these individuals go on to visit a health facility later. Between 44-51% of individuals had a malaria test, and three-quarters reported they had a positive test. The proportion of individuals taking AL after a negative test or without having a test was very high (68-86% and 73-82%, respectively). More than 95% of all households reported owning an ITN in all areas.

CHVs Activities: To ensure quality CHVs performance on Malaria testing and data capture, we continued carrying out monthly supervision. We have experience a minimal drop in the number of Community Health Volunteers working with us to provide free malaria test from 271 to 266.

**Future Plans**

On 11th July 2016 we started the 12th month cross-sectional follow up survey. We plan to compare the results with both baseline and the 6th Month survey to determine any change in the percent of fevers that are tested for malaria and the effect of testing on subsequent drug purchasing decisions.

**Publication(s)**

Submitted 5 abstracts for ASTMH 2016 Annual Meeting scheduled for November 13-17, Atlanta, GA, U.S.. The Abstracts were reviewed by the AMPATH publication committee.

**Study Title**

IU Health Cardiovascular Research Biobanking Project

**Principal Investigator(s)**

Tom Inui, Indiana University
Atrial fibrillation is the most common sustained arrhythmia in high-income countries. Recent insights have been made with regard to the genetic variations that may predispose an individual to developing atrial fibrillation. There has long been observed a disproportionately low prevalence of atrial fibrillation among Africans and African-American compared to people of European descent. Whether mutations in the genes known to cause atrial fibrillation are also causing AF among Kenyan patients with this disorder is unknown. Identification of the frequency of mutations in these genes in patients with atrial fibrillation in Kenya may shed light into the causal pathways of atrial fibrillation in this population. Using a case-control (1:2) research design in a Kenyan population with atrial fibrillation, we propose to perform mutational analysis of the coding sequence and flanking splice sites of the KCNQ1, KCNJ2, KCNE2 and KCNA5 genes known to be mutated in familial and lone atrial fibrillation in patients from high-income countries. A thorough phenotyping protocol will be employed which will include clinical assessment, a medical history, echocardiography and electrocardiography. Genetic material will be collected, stored and processed in Eldoret as the first initiative of the Genetic Biorepository Initiative (PI: Inui, Co-PI: Emonyi) and subsequently shipped for analysis of specific alleles at Indiana University. Using a convenience sample of approximately 140 patients with atrial fibrillation and 140 controls, we will demonstrate the frequency of pathological mutations in the aforementioned genes and provide a thorough clinical description of patients with atrial fibrillation including echocardiographic descriptions and the burden of other comorbid illnesses.

Over the past six months, echocardiographic interpretation was completed by Duke investigators. A clinical descriptive poster and a manuscript are under review for submission to an international Fogarty research meeting and a peer-reviewed journal, respectively. Preliminary genomic analyses are now completed but being validated.

We expect an acceptance of the clinical manuscript that describes risk factors for, and prognosis of, atrial fibrillation in Kenya. It should also be possible to write and submit a manuscript that integrates genomic and clinical data.
### Working Group(s)

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<td>AMWG</td>
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This project is focused on identifying the individual, psychosocial, and structural barriers to timely linkage and retention. This project has three specific aims:

1. **To comprehensively describe linkage and retention to HIV care following home-based counseling and testing by examining time from testing to linkage and the socioeconomic, demographic and structural determinants of linking to care.** We will conduct retrospective and multilevel analyses using existing de-identified clinical and facility-level data collected within AMPATH, defining linkage to care as the completion of an initial HIV clinical encounter with a provider following testing. We will also examine factors that predict retention in HIV care over time.

2. **To characterize the psychosocial and structural facilitators and barriers to linkage and retention to care following positive HIV diagnosis through HBCT and PITC.** We will conduct a qualitative study to examine the psychosocial factors inhibiting or motivating linkage to care, experiences in accessing care, and factors that promote or interrupt retention among those who tested positive via HBCT or PITC. We will also collect data from clinicians and community health workers to examine how features of the healthcare system facilitate or constrain linkage and retention to care.

3. **To develop and implement a feasibility study of a pilot psychosocial intervention aimed at increasing linkage to care among individuals testing positive for HIV.** The content of this intervention pilot will be informed by the results of Aims 1 and 2. The first aim of this study involves secondary analysis of data collected during home-based counseling and testing linked to medical records data. This data will include information collected as part of routine testing procedures and care, for those who successfully linked to care. AIM 2 will employ qualitative approaches to identify barrier and facilitators to linkage and retention. AIM 3 will include information collected as part of routine care, for those who successfully linked to care. Specifically, medical record reviews at baseline and post-intervention.

### Site(s)

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<td>6/4/2012 - 12/20/2013</td>
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### Funding Status

**Funded – NIH** - National Institute of Mental Health (NIMH)
**Funded – NIAID** - National Institute of Allergy and Infectious Diseases (NIAID)

### Direct Award (USD)

$152,806

### Update

During this year of the project we continued data collection to meet the objectives of the second aim of the study. We conducted qualitative research to characterize the psychosocial and structural facilitators and barriers to linkage and retention to care following positive HIV diagnosis through home-based counseling and testing from the perspective of 'adults who linked to care' and 'adults who did not link to care'. 30 in-depth interviews were carried out between the months of July and August 2015 in three different AMPATH sites (Mukhobola (Rural), Port Victoria (Semi-urban) and Busia (Urban)) with AMPATH patients who linked to care following an HIV-positive test result through HCT/PHCT. We conducted an additional n=20 interviews to complete data collection among adults who linked to care. For this phase of the project, all the interviews were conducted in Swahili. Transcription and translation to English of these interviews took place for a period of four months; September 2015 to December 2015. Data Quality Monitoring of the transcribed and translated interviews was carried out for a period of two months: from January 2015 to February 2015. Beginning in mid-April of 2016, we also
conducted 30 in-depth interviews with adults who did not link to care following an HIV-positive test result through home-based counseling and testing in the Bunyala region of western Kenya. We have also made progress on the geospatial analyses as part of Aim 1 of this project. We have successfully cleaned and mapped the HCT data from Bunyala and are expecting to complete spatial analysis by December of this year.

Future Plans

During the next phase of the project, we will complete the ongoing analysis of key informants (data previously collected and reported during last year’s progress report). We have completed the coding of the data from n=60 interviews with health care providers in the western Kenyan region and will continue to analyze this data over the rest of the calendar year. In addition we will complete transcription and translation on the adults who did/did not link to care study and we will begin the process of analyzing the data by creating a codebook and coding the data. We expect to begin this process in September of 2016.

Publication(s)


Study Title

Nurse Management of Hypertension Care in Rural Western Kenya

Principal Investigator(s)

Rajesh Vedanthan, Mount Sinai School of Medicine

Co-Investigator(s)

Sylvester Kimaiyo, Moi University

Working Group(s)

AMWG, CVMD

Description

This project aims to evaluate barriers and facilitators to nurse management of hypertensive patients in rural western Kenya, using a qualitative research approach. The four specific aims for attaining this objective are: Aim 1: To evaluate facilitators and barriers to nurse-based management of hypertensive patients in rural western Kenya. This will be accomplished by conducting a rapid assessment procedure involving key informant interviews, focus group discussions, and field observations. Aim 2: To develop and evaluate an innovative smartphone-based DEcision Support and Integrated REcord-keeping (DESIRE) tool utilizing a participatory, iterative, human-centered design process, to assist nurses taking care of hypertensive patients. We will evaluate the usability and feasibility of the DESIRE tool using qualitative methods (e.g. think-aloud, mock patient encounters, semi-structured interviews, and focus groups). Aim 3: To conduct an impact evaluation of a pilot program for nurse-based management of hypertension to be implemented by AMPATH, by performing secondary analysis of routine clinical data collected by AMPATH. The primary outcome measure will be change in systolic blood pressure in hypertensive patients assigned to nurse-based management after one year. Aim 4: To estimate the nurse workforce requirements for stable, long-term treatment of hypertension throughout western Kenya, using a needs-based workforce estimation model.
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<td>Funding Status</td>
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<tr>
<td>Direct Award (USD)</td>
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<td>Update</td>
<td>Notable progress has been made from January 1, 2016 through June 30, 2016 as delineated below: Administrative: Capacity building and mentoring of study personnel with specialized and targeted training is ongoing. Advisory Committee and Study Oversight meetings conducted. Aim 1: Manuscript published. Aim 2: Data collection using the DESIRE tool is ongoing. Patient perspectives on mHealth nearly complete. 4 focus group discussions (FGDs) conducted. 2 key informant interviews (KIIs) conducted. All sessions conducted to-date have been transcribed and translated. To-date, 39 participants (19 male, 20 female) have been enrolled. Aim 3: All data collection activities and data entry complete. Data cleaning ongoing. Poster presented at ACC 2016. Aim 4: All data collection activities and data entry complete. Content analysis complete. Model development complete. Manuscript in preparation. Papers/publications/posters: Manuscript: Vedanthan, Rajesh et al. 'Barriers and Facilitators to Nurse Management Of Hypertension: A Qualitative Analysis From Western Kenya'. Ethnicity &amp; Disease 26.3 (2016): 315. Poster: Kumar, Anirudh et al. 'Effect of Nurse-Based Management of Hypertension In Rural Western Kenya'. Presented at ACC April, 2016. Challenges: Aim 2 study recruitment has been difficult for the following reasons: 1. Tracing participants is difficult due to the absence of working telephone numbers and/or other contact information. 2. Certain participants are elderly, and unable to meet the demands of participation in the study project. Male participation has been difficult because there is a higher rate of female patients attending clinic visits. Implementation of the DESIRE took a longer than anticipated since participants had limited prior exposure to the use of tablets. The following actions have been taken to resolve and/or address these challenges: To resolve issues with patient recruitment, the team has worked closely with the AMPATH's CDM team to locate participants.</td>
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<td>Future Plans</td>
<td>Next Steps: Aim 2: Complete evaluation of the DESIRE tool. Complete participant enrollment. Complete transcription/translation/content analysis. Submit abstracts with reported findings to professional conferences. Aim 3: Complete final data analyses. Finalize manuscript and submit for publication. Aim 4: Finalize manuscript and submit for publication.</td>
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<tr>
<td>Study Title</td>
<td>Optimizing Linkage and Retention to Hypertension Care in Rural Kenya</td>
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<tr>
<td>Principal Investigator(s)</td>
<td>Valentin Fuster, Mount Sinai School of Medicine</td>
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Co-Investigator(s) Jemima Kamano, Moi University

Working Group(s) AMWG, CVMD

Description Hypertension awareness, treatment, and control rates are low in most regions of the world. A critical component of hypertension management is to facilitate sustained access of affected individuals to effective clinical services. In partnership with the Government of Kenya, the Academic Model Providing Access to Healthcare (AMPATH) Partnership is expanding its clinical scope of work in rural western Kenya to include hypertension and other chronic diseases. However, linking and retaining individuals with elevated blood pressure to the clinical care program has been difficult. To address this challenge, we propose to develop and evaluate innovative community-based strategies and initiatives supported by mobile technology. The objective of this project is to utilize a multi-disciplinary implementation research approach to address the challenge of linking and retaining hypertensive individuals to a hypertension management program. The central hypothesis is: community health workers (CHWs), equipped with a tailored behavioral communication strategy and a smartphone-based tool linked to an electronic health record, can increase linkage and retention of hypertensive individuals to a hypertension care program and thereby significantly reduce blood pressure among these patients. We further hypothesize that these interventions will be cost-effective. To test these hypotheses and achieve the overall objectives, we will pursue the following specific aims: Aim 1: Identify the facilitators and barriers to linking and retaining individuals with high blood pressure to a hypertension care delivery program, using a combination of qualitative research methods: 1) baraza (traditional community gathering) form of inquiry; 2) focus group discussions among individuals with elevated blood pressure during home-based testing; and 3) focus group discussions among CHWs. Subsidiary Aim 1.1: Using identified facilitators and barriers, develop a tailored behavioral communication strategy guided by the Health Belief Model modified by incorporating emotional elements for the CHWs to use with hypertensive patients, focusing on regular and timely attendance at hypertension clinic. We will test the communication strategy for face and content validity using focus group discussions with CHWs and individuals with elevated blood pressure. Subsidiary Aim 1.2: Using identified facilitators and barriers, develop a smartphone-based tool linked to the AMPATH Medical Record System (AMRS) to be used by CHWs to optimize linkage and retention of hypertensive patients to the care program, and evaluate the usability and feasibility of this tool using think-aloud technique, mock patient encounters, focus group discussions, and participant observation. Aim 2: Evaluate the effectiveness of CHWs equipped with a tailored behavioral communication strategy and a smartphone-based tool in improving linkage and reducing blood pressure among hypertensive patients, by conducting a cluster randomized trial comparing: 1) usual care (CHWs with standard training on recruitment of individuals with any chronic condition); 2) CHWs with an additional tailored behavioral communication strategy; and 3) CHWs with a tailored behavioral communication strategy an also equipped with smartphone-based tool linked to the AMRS. The co-primary outcome measures will be: 1) documented linkage to care following home-based testing, and 2) one year change in systolic blood pressure among hypertensive individuals. Aim 3: Evaluate the incremental cost-effectiveness of each intervention arm of the cluster randomized trial. Cost effectiveness will be presented both in terms of costs per unit decrease in blood pressure and in terms of costs per reductions in cardiovascular disease (CVD) risk by extrapolating one-year blood pressure reductions to CVD risk reductions based on the
QRISK2-2011 CVD risk calculator specific for Black African populations. This research will generate innovative and productive solutions to the expanding global problem of hypertension, and will add to existing knowledge on scalable and sustainable strategies for effectively managing hypertension and other chronic diseases in low- and middle-income countries.

**Site(s)**

**Project Period**  
5/4/2012 - 3/31/2017

**Funding Status**  
Funded – NIH - National Heart, Lung, and Blood Institute (NHLBI)

**Direct Award (USD)**  
$2,104,519

**Update**

Notable progress has been made from January 1, 2016 through June 30, 2016 as delineated below:

**Administrative:**  
- Year five NIH grant renewal and Moi IREC approval sought and obtained
- Capacity building of the study personnel with specialized and targeted training ongoing
- Data Safety and Monitoring Board (DSMB) conference call held on February 26, 2016
- Faculty and study team visits to Eldoret, Kenya for the purposes of site monitoring, capacity building, and training is ongoing

**Aim 1:**  
- Primary qualitative manuscript 'Barriers Influencing Linkage to Hypertension Care in Kenya: Qualitative Analysis from the LARK Hypertension Study': published in the Journal of General Internal Medicine (JGIM)
- Secondary qualitative manuscript in preparation
- Content validity analyses complete
- Content validity manuscript in preparation

**Subsidiary Aim 1.1:**  
- Study databases/servers (Virtual Machine, AMRS & Redcap) launched
- Smartphone-based assessment tools and MUzima-based data collection tool (both linkage and retention) developed and launched

**Aim 2:**  
- Rollout of the smartphone-based tool implemented in all eight (8) of the clusters/community units of the tech-based arm
- Community Health Workers (CHWs) in the tech-based arms received intensive training on smartphone use, device management, app/software use, and troubleshooting
- Follow-up training was provided to CHWs and Community Health Extension Workers (CHEWs) at the time of study rollout for each community unit
- Total of 8 community units, 120 CHWs and 9 CHEWs

**Enrollment:**  
- Initiated in April of 2014
- Cessation of participant enrollment took place in the first quarter of the 2016 following the attainment of our target enrollment numbers
- Cumulative enrollment: N= 1,508

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<tr>
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<th>Males</th>
<th>Females</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Usual Arm</td>
<td>181</td>
<td>304</td>
<td>485</td>
</tr>
<tr>
<td>Paper-based</td>
<td>226</td>
<td>292</td>
<td>518</td>
</tr>
<tr>
<td>Tech Arm</td>
<td>269</td>
<td>505</td>
<td>865</td>
</tr>
<tr>
<td>Total</td>
<td>643</td>
<td>865</td>
<td>1,508</td>
</tr>
</tbody>
</table>

**Assessment Tool:**  
- As of July 20, 2016, a total of 200 behavioral assessment tools have been administered by CHWs
- Web-based data entry of paper behavioral assessment tools ongoing
- Data Management
- Data management protocol developed and in use
- SAS script and concept dictionary developed and in use
- Data cleaning ongoing
- Process Evaluation
- 40 Objective Structured Clinical Examinations (OSCEs) conducted out of a targeted of 40
- 6 sets of Focus Group Discussions (FGDs) with CHWs completed
- 8 sets of FGD with patients with hypertension completed
- Written tests and usability testing embedded in process evaluation
- Data entry of OSCEs and transcription of FGDs completed (April, 2016)
- Statistical analysis of process evaluation outcomes (OSCEs data, written test and
transcripts) resulted in the preparation of two posters/abstracts—Knowledge Retention and Skill Retention. Both presented at the World Congress of Cardiology Conference (April, 2016) o A one day training took place across the three arms of the study with a narrative on: 1) The LARK study, 2) Hypertension, 3) Behavioral assessment tools and communication strategy, and 4) Motivational interviewing. Tech-arm CHWs received additional one day training on smartphone. Aim 3 (cost-effectiveness analysis): Administration of 12-month f/u costing questionnaire was scaled up with special emphasis on real-time data entry. Data entry of paper costing questionnaires is challenging due to missing variables. Preliminary analysis ongoing. 12 months costing follow-up for the costing questionnaire is ongoing. o To-date a total of 336 participants have completed their 12-month follow-up. See table below for more details.

<table>
<thead>
<tr>
<th>Arm Type</th>
<th>Males</th>
<th>Females</th>
<th>Total</th>
<th>Usual Arm</th>
<th>Paper-based</th>
<th>99</th>
<th>73</th>
<th>172</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tech Arm</td>
<td>11</td>
<td>13</td>
<td>24</td>
<td>112</td>
<td>112</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>TOTAL</td>
<td>195</td>
<td>141</td>
<td>336</td>
<td>195</td>
<td>195</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Papers/publications/posters:
- Qualitative manuscript #1 published by Journal of General Internal Medicine. "Barriers Influencing Linkage to Hypertension Care in Kenya: Qualitative Analysis from the LARK Hypertension Study"; PMID 26728782.
- Qualitative manuscript #2 in advanced stages of preparation. "Perceptions of the Role of Community Health Workers in Hypertension Management: A Qualitative Study from Rural Kenya." Abstract presentation at the World Congress of Cardiology Conference, June 2016.
- 'Hypertension Knowledge Retention Among Community Health Workers in Rural Western Kenya: Process Evaluation of the LARK Hypertension Study' Abstract presentation at the World Congress of Cardiology Conference, June 2016.
- 'Fidelity of Hypertension-Related Skills Among Rural Western Kenya Community Health Workers: Process Evaluation of the LARK Hypertension Study' Content Validity manuscript in preparation.
- 'Development and Validation of a Behavioral Assessment Tool to Optimize Linkage and Retention to Hypertension Care in Kenya: LARK Hypertension Study' Challenges: Data management: Data management and data cleaning has been challenging and time-consuming, due to multiple data streams (paper-based costing questionnaires to be entered with tablet-based data entry platform, paper-based behavioral assessment tools to be entered with web-based data entry platform, tablet-based costing questionnaires, smartphone-based behavioral assessment tools, and AMRS database). Duplicate AMRS ID numbers has been very challenging.
- Identification of errors during routine data querying has been significant.
- Data entry: Completion of retrospective data entry has experienced delays due to missing data on paper forms. Procurement: Procurement delays due to extensive and time-consuming administrative procedures.
- Difficulty in tracing participants for 12 months follow-up marked with pronounced working distance to the household, competing roles by the study participant limiting possibility of getting the participants at their households, adverse weather conditions like rain among others.
- CHWs at times are not pro-active in their study implementation which in turn deters study progress. The following actions have been take to resolve and/or address these challenges: Follow-up visits: We have worked closely with the AMPATH Chronic Disease Team to align follow-up visits with scheduled clinic days to capture as many participants as possible. We have engaged CHWs to track non-linked/non-retained participants. We have organized 'repeat screening' events to invite and attract non-
linked/non-retained participants. We are supplementing the above activities with home-based visits as necessary.

- **Data Management:**
  - We have worked closely with our Data Coordinating Center team (data manager, biostatisticians, and informatics) to streamline the process of merging and cleaning the dataset.
  - We have instituted weekly data management calls to address and resolve data management issues.
  - We have programmed skip logic and entry limits into all electronic data entry systems, in order to minimize errors in the data.
  - We have transitioned to full electronic data entry.
  - We have created a Standard Operating Procedures document that covers all aspects of data collection, data entry, data management, and data cleaning.
  - Reconciliation of AMRS ID numbers at 12-month f/u visit
  - Timely resolution of errors in the error queue

- **Data Entry:**
  - We have worked closely with the AMPATH Chronic Disease Team to facilitate data entry.
  - We have engaged in ongoing discussions with CDM team and research staff to attempt to recover missing data at baseline.
  - Completion of any pending BA tools at 12-month f/u visit
  - Procurement: We have worked closely with the AMPATH Research and Sponsored Projects Office to try and streamline the procurement processes as much as possible.

**Future Plans**

- Complete 12-month costing follow-up aligned with BA administration, usability and feasibility administration have been indicated.
- Scale up utilization of data management protocol aimed at realizing data integrity, aligned with continuous data cleaning, matching and merging among other scope of work related to data.
- Continue error resolution/prevention and identification of the missing variables.
- Continue capacity building: Study personnel to be considered for any future trainings/workshops.
- Continue with abstracts, posters and manuscripts preparation and submissions.
- Plan for Global Alliance for Chronic Diseases (GACD) Annual Scientific meeting/conference scheduled for October, 2016 in Sydney, Australia.

**Publication(s)**

1. Fidelity of Hypertension-Related Skills Among Rural Western Kenya Community Health Workers: Process Evaluation of the LARK Hypertension Study
2. Hypertension Knowledge Retention Among Community Health Workers in Rural Western Kenya: Process Evaluation of the LARK Hypertension Study
3. Barriers Influencing Linkage to Hypertension Care in Kenya: Qualitative Analysis from the LARK Hypertension Study

**Study Title**

Pathways to better health

**Principal Investigator(s)**

Paula Braitstein, University of Toronto

**Co-Investigator(s)**

**Working Group(s)**

PHPC WG

**Description**

The goal of this study is to merge together data from the home-based HIV counseling and testing program with HIV care and treatment data from the AMRS.

**Site(s)**

The catchments of Bunyala, Teso, and Chulaimbo

**Project Period**

1/4/2016 - 10/31/2016
### Funding Status

Funded – Regenstrief Institute

### Direct Award (USD)

$45,000

### Update

We have so far only been able to link data from the original home-based HIV counseling and testing (HBCT), Perpetual Home-based HIV counseling and testing (PHCT) and AMRS data for those who are HIV-positive. Unfortunately the patient matching module of the AMRS is still not working so we are not able to do the HIV-negatives because there are too many of them to review manually. So we have focused on creating unique patient records for the positives whether from HBCT, PHCT, and AMRS to identify linkage rates and to create population-based datasets of people living with HIV in these catchments.

### Future Plans

We expect the process to be complete by the end of August. We will seek additional funding from the National Institutes of Health to conduct more prospective work to identify the outcomes of people who, according to our data merging, did not link to care, and the outcomes of people who linked to care but became LTFU. We are hoping we can get enough funds to do random sampling of the positives to obtain viral loads on them and so get the community and population viral loads in these catchments, as well as random sampling of the HIV-negatives in HBCT/PHCT to estimate HIV incidence in these catchments. We are already working on an updated linkage and engagement in care paper for Bunyala because we have found that actual linkage rates are much higher than we previously reported.

### Publication(s)

**Study Title**

**Patient-Centered Disclosure Intervention for HIV-Infected Children, Helping AMPATH Disclose Information and Talk about HIV Infection (HADITHI)**

**Principal Investigator(s)**

Rachel Vreeman, Indiana University

**Co-Investigator(s)**

W. Nyandiko, Moi University

**Working Group(s)**

SSRN, PRWG

**Description**

The purpose of this study is to assess the effect of a patient- and family-centered intervention guiding disclosure to HIV-infected Kenyan children using a randomized trial comparing the intervention to routine care. The primary endpoint will be probability of disclosure among children, with secondary endpoints of adherence, clinical outcomes, psychological distress and social outcomes. Phase One, which will last 6 months, focuses on cultural adaptation of the intervention materials through intensive patient participation, including focus groups and cognitive interviewing; selecting narrative components; and training dedicated disclosure counselors. Phase Two consists of a randomized design to examine whether the culturally adapted, multi-component HADITHI intervention increases the prevalence of disclosure to HIV-infected children in western Kenya compared to children receiving usual care. HIV-infected children ages 10-15 years who are enrolled in HIV care within the eight selected AMPATH clinics in western Kenya will be eligible for study enrollment and have a comprehensive patient assessment every 6 months for 2 years.

**Site(s)**

Moi's Bridge Health Centre
### Project Period
9/1/2012 - 9/1/2016

### Funding Status
Funded – NIH - National Institute of Mental Health (NIMH)

### Direct Award (USD)
$1,886,804

### Update
Phase 1: The first phase of the HADITHI study was a qualitative inquiry into the experiences of HIV-infected adolescents and caregivers of HIV-infected children with HIV disclosure to children in terms of their beliefs, practices and preferences. Dissemination of early findings are proceeding. Phase 2: Phase 2 of the HADITHI study aimed to evaluate the impact of clinic-level disclosure intervention that involves multiple counseling components, including peer support groups and individual counseling. All 286 patients were recruited for Phase 2, and data collection for all active participants in the 24 months of patient follow-up has been completed. Month 24 assessments included blood samples for viral load testing and hair sampling for ARV concentrations, in addition to the multiple measures of adherence, depression, behavioral symptoms, stigma, quality of life, and social functioning. In the last six months, focus group discussions, surveys and participant follow up was conducted for a total of 49 participants for the body safety book tool for HADITHI. Data preparation for key analysis is ongoing. The HADITHI counselling materials created during the study includes counseling pamphlets, disclosure and stigma videos, an animation tool, which was created using cross-cultural adaptation techniques continued to be used in most clinics. Hair samples were transported to the USA to evaluate drug level concentration, as well as compile evaluations assessing the feasibility and validity of this type of testing in our population.

### Future Plans
Over the next 6 months, we plan to start key data analysis and Complete end of September 2016, Prepare analyses for main outcomes for manuscripts and conference presentations by December 2016 and Implement the HADITHI counseling tools in AMPATH clinics for helping disclosure practices with pediatric patients

### Publication(s)

### Study Title
**Pharmacovigilance in a Resource-Limited Setting: Approaches to Targeted Spontaneous Reporting for Suspected Adverse Drug Reactions to Antiretroviral Treatment**

### Principal Investigator(s)
Paula Braitstein, University of Toronto

### Co-Investigator(s)
B Jakait, Moi Teaching and Referral Hospital

### Working Group(s)

### Description
Little is known about the toxicity profile of combination antiretroviral treatment (cART) in African populations where genetic differences, co-morbidities, and malnutrition together may influence the adverse reactions of cART in this population. The purpose of this project is to evaluate the feasibility and effectiveness of five approaches to Targeted Spontaneous Reporting (TSR) for documenting SADR in the resource constrained clinical
setting in western Kenya. The approaches include; TSR 1: The completion of the Kenya National Suspected Adverse Drug Reaction form for patients with a change or discontinuation in their cART. These forms are then forwarded on to the National pharmacovigilance (PV) office at the Pharmacy and Poisons Board (PPB) in Nairobi. TSR 2: Use of routinely-used clinical encounter forms that have been enhanced to specifically collect a relatively small amount of SADR data to be collected by the provider seeing the patient during the clinical visit. TSR 3 and TSR 4: Involve conducting in-depth interviews on 1,000 patients receiving cART treatment to prompt patients about SADR and their impact on patient adherence and quality of life. Patients undergoing interviews are randomly assigned to be interviewed by an HIV peer (TSR 3) or a pharmacy personnel (TSR 4) who will have received the same training for the project. The interviews will be conducted over 12 months or a maximum of 12 scheduled clinical visit (Whichever comes first). TSR 5: Use of data routinely captured in the pharmacy when clinicians substitute or change a patient’s regimen, including documentation if such an event occurred on the prescription form and the cause of the event (i.e. toxicity, treatment failure, TB drug interaction, pregnancy, other).

<table>
<thead>
<tr>
<th>Site(s)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Project Period</td>
<td>10/1/2012 - 12/31/2013</td>
</tr>
<tr>
<td>Funding Status</td>
<td>Funded – World Health Organization (WHO)</td>
</tr>
<tr>
<td>Direct Award (USD)</td>
<td>$162,000</td>
</tr>
</tbody>
</table>

Accomplishments The project was able to target and collect SADRs from a large population of patients. Under the patient interviews the project enrolled 844 participants in to the study. Among these were 344 pregnant women and children, a population considered special and whose data on SADR attributable to ART has not been largely studied especially in resource limited settings. Challenges We had challenges with the recruitment and enrolment of children and adolescents who were on ART but had not been disclosed to their HIV status beyond their knowledge of ‘being sick’. With the high prevalence of HIV among adolescents, strategies should be put in place to provide support for parents and guardians to disclose to children and adolescents. There was also a huge challenge with incomplete data even after combining multiple sources of data, that is, the pharmacy data and patients’ electronic medical records (EMRs), to fill the national pharmacovigilance forms (TSR 1). Therefore a point person or department is required to compile patient data, follow up on patients and submit the forms. Preliminary findings A majority of the ART treatment changes were attributed to SADRs and this was easily identified through the prescription forms (TSR 5). Hence, programs should invest more in the pharmacovigilance to facilitate the identification of SADRs which may impact on ART adherence. This may be through peer- based TSR models as we noted the close personal interaction between the peers (TSR 3), due to shared experience, provided an avenue to identify and deal with issues like non-adherence, food -insecurity, stigma especially for patients starting ART and family and social challenges that the patients encountered. Hence this attribute may be used in the identification of SADRs, the improvement of linkage and retention in care and the promotion of adherence.

Future Plans Currently, we are in the process of analyzing the patient data collected with Redcap and
AMPATH Research Program Office  

AMRS. We plan to publish on this data later this year. We are however planning to submit a publication on the lessons learnt in implementing the five TSR approaches to the publication committee before the end of July, 2016.

<table>
<thead>
<tr>
<th>Study Title</th>
<th>Point in Time (PIT) Count of Street Children in Eldoret</th>
</tr>
</thead>
<tbody>
<tr>
<td>Principal Investigator(s)</td>
<td>Paula Braitstein, University of Toronto</td>
</tr>
<tr>
<td>Co-Investigator(s)</td>
<td>David Ayuku, Moi University</td>
</tr>
<tr>
<td>Working Group(s)</td>
<td>PRWG</td>
</tr>
<tr>
<td>Description</td>
<td>This is a one-time project funded by the Canadian Institutes for Health Research (CIHR) and aims at counting all the street children and youth in Eldoret Town and its Peri-urban areas namely; Langas, Huruma, Kapsoya, Town Bases; California, Juakali, Mangula, Asiz and Eastleigh. Counting will be facilitated using Fingerprint Scanners and related supplies, HIV and First Aid Services will be provided. The count will take place over a seven day period. The aims of the project are to determine whether counting street children in a low-income setting is feasible using PIT count techniques, used in homeless populations successfully in Canada and the United States, estimate the number of street-connected children and youth in Eldoret, and estimate HIV prevalence among them.</td>
</tr>
<tr>
<td>Site(s)</td>
<td>MTRH</td>
</tr>
<tr>
<td>Project Period</td>
<td>5/1/2016 - 12/31/2016</td>
</tr>
<tr>
<td>Funding Status</td>
<td>Funded – Canadian Institutes of Health Research</td>
</tr>
<tr>
<td>Direct Award (USD)</td>
<td>$35,000 Canadian</td>
</tr>
<tr>
<td>Update</td>
<td>A Start-Up Meeting for this project was held on 14th April 2016 and planning meetings have been held. Sensitization of the County Commissioner and the County Children's Officer has been done. Street Barrack Leaders have also been sensitized on the Project. Staff and Volunteers undertaking the exercise have been identified and a Sensitization Meeting for them is underway. Tentative dates for the Count has been set for early September 2016.</td>
</tr>
<tr>
<td>Future Plans</td>
<td>We intend to actually do the count, and write the paper. This will provide important preliminary data for a NIH implementation research project to find, link, treat and retain HIV-infected street children and youth.</td>
</tr>
<tr>
<td>Publication(s)</td>
<td></td>
</tr>
</tbody>
</table>

Study Title | 'Point of Care CD4 testing for people who fail to engage in care after testing HIV positive'. |
| Principal Investigator(s) | Paula Braitstein, University of Toronto |
### Co-Investigator(s)
Samson Ndege, Moi University

### Working Group(s)
AMWG

### Description
This supplement responds to unique aspects of Specific Aim 1 of the East Africa-International epidemiological Databases to Evaluate AIDS (IeDEA) grant, which seeks to 'Determine the short and long-term outcomes of adults and children along the entire spectrum of HIV care.' Our broad aim is to inform and evaluate the implementation of AMPATH's HIV treatment and prevention work by fully characterizing the cascade of HIV care in population-based settings and identifying gaps and opportunities for improvement. The primary objective of this study is to characterize the outcomes of HIV-positive adults who did not engage with HIV care following the catchment-wide HBCT campaign held from Dec 2009-Feb 2011 in Bunyala.

### Site(s)

### Project Period
2/2/2015 - 2/1/2016

### Funding Status
Funded – NIH

### Direct Award (USD)
$62,432

### Update
In the last six months we have completed data collection for the initial n=120 individuals who had tested HIV-positive during HCT and not linked to care in the Bunyala region according to the AMRS data. We have confirmed that of those 120 randomly selected individuals, a total of 22 (18%) were deceased. We were able to contact 73 individuals to assess their engagement in HIV care. Of the 73, 58 (79%) reported that they had ever sought HIV care, with the majority (n=43, 74%) reportedly seeking care from AMPATH. For the n=66 individuals who provided a sample for point-of-care CD4 testing, the median CD4 count was 462 cells/mm3.

### Future Plans
Over the next month we will clean and analyze the data from the initial n=120 individuals who were randomly selected. We are also continuing fieldwork to identify n=62 additional people in the Bunyala region. We aim to collect outcomes and CD4 testing on this group which represents 10% of those who had linked to care following testing and were then lost-to-follow-up. Additionally, we will also be submitting an amendment to IREC to contact additional samples in Teso and Chulaimbo of individuals who tested positive during PHCT and did not link to care.

### Publication(s)

#### Study Title
Prevalence and Impact of Alcohol Use in Patients Enrolling in HIV Care

#### Principal Investigator(s)
Kara Wools-Kaloustian, Indiana University

#### Co-Investigator(s)
Lameck Diero, Moi University

#### Working Group(s)
AMWG, SSRN

#### Description
Though drug use (including inhalant use) is an increasing problem in East Africa, alcohol remains the most common substance of abuse in our populations. There are limited data
on the impact of alcohol use on immune reconstitution, adherence and retention in care within sub-Saharan African HIV-infected populations. Given the high rates of food insecurity and resulting malnutrition, the impact of alcohol use on clinical outcomes in HIV-infected individuals in East Africa may be more profound than that seen in North America. Further exploration of the prevalence of and impact of alcohol use on the outcomes of HIV-infected individuals in sub-Saharan Africa is needed in order to inform HIV-care and treatment programs and assess the need for systems adaptation targeted towards identifying and intervening in individuals with alcohol addiction issues.

### Study Title

**Randomized, Phase II Trial of CHOP vs. Oral Chemotherapy with Concomitant Antiretroviral Therapy in Patients with HIV-associated Lymphoma in Sub-Saharan Africa**

### Principal Investigator(s)

Naftali Busakhala, Moi University

### Co-Investigator(s)

Evangeline Njiru, Moi Teaching and Referral Hospital

### Working Group(s)

ORWG

### Description

Patients will be randomized to one of two treatment arms: either standard, intravenously delivered CHOP, delivered over six 3-week cycles or oral chemotherapy delivered over three 6-week cycles. Formal assessment of objective response (complete response [CR]/partial response [PR]/stable disease [SD]) will be performed following cycle 6 for CHOP and following cycle three for the oral regimen, and the patient will then be followed for relapse and survival. Patients found to have progressive disease (PD) at any time will come off study and receive the local standard of care treatment for their disease.
<table>
<thead>
<tr>
<th>Funding Status</th>
<th>Funded – NIH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Direct Award (USD)</td>
<td>USD 4,764 + 8% indirect costs per patient enrolled in the Treatment Segment for non-CT-related costs plus the actual cost of CT scans.</td>
</tr>
<tr>
<td>Update</td>
<td>There were delays in importation of study drugs, delays in procurement of study insurance and delays in getting an MOU signed with the laboratory at Kericho</td>
</tr>
<tr>
<td>Future Plans</td>
<td>We have imported most of the study supplies and we have signed an MOU with the Kericho laboratory</td>
</tr>
</tbody>
</table>

### Study Title: Rapid Case Ascertainment (RCA) to evaluate Kaposi’s sarcoma at the Academic Model Providing Access to Healthcare (AMPATH) clinics, Eldoret, Kenya

<table>
<thead>
<tr>
<th>Principal Investigator(s)</th>
<th>Naftali Busakhala, Moi University</th>
</tr>
</thead>
<tbody>
<tr>
<td>Co-Investigator(s)</td>
<td>ORWG</td>
</tr>
<tr>
<td>Working Group(s)</td>
<td>ORWG</td>
</tr>
<tr>
<td>Description</td>
<td>The Rapid Case Ascertainment (RCA) Kaposi’s sarcoma (KS) study will swiftly and thoroughly evaluate patients with a new diagnosis of KS in order to confirm diagnosis, initiate treatment and facilitate research into why the patients developed the KS. Therefore the study will recruit newly diagnosed KS patients and will look at clinical and demographic factors to determine why individuals developed KS.</td>
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<tr>
<td>Site(s)</td>
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<td>Project Period</td>
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<td>Funding Status</td>
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<td>Direct Award (USD)</td>
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<td>Update</td>
<td>Setting up the study by piloting of study questionnaires and reviewing of data collection.</td>
</tr>
<tr>
<td>Future Plans</td>
<td>We intend to begin to recruit study participants.</td>
</tr>
<tr>
<td>Publication(s)</td>
<td></td>
</tr>
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</table>

### Study Title: REALITY 'Reduction of EARly mortalITY in HIV-infected adults and children starting antiretroviral therapy'

<table>
<thead>
<tr>
<th>Principal Investigator(s)</th>
<th>Kara Wools-Kaloustian, Indiana University</th>
</tr>
</thead>
<tbody>
<tr>
<td>Co-Investigator(s)</td>
<td>Abraham Siika, Moi University</td>
</tr>
<tr>
<td>Working Group(s)</td>
<td>AMWG</td>
</tr>
<tr>
<td>Description</td>
<td>A 2x2x2 open-label factorial multi-centre trial, conducted in 9 centres in 4 countries</td>
</tr>
</tbody>
</table>
AMPATH Research Program Office

( Kenya, Malawi, Uganda, Zimbabwe). Study participants will be 1800 HIV-infected patients including adults, adolescents and children aged 5 years or older with low CD4 counts about to initiate combination antiretroviral therapy (ART). There will be Three methods to reduce early mortality following ART initiation (i) increasing the potency of ART with a 12 week induction period using 4 antiretroviral drugs from 3 classes (ii) augmented prophylaxis against opportunistic/bacterial infections and helminths for 12 weeks (iii) macronutrient intervention using ready-to-use supplementary food for 12 weeks. Each intervention will be compared with standard of care, which in previously untreated patients presenting late with very low CD4 counts is to initiate ART with 3 drugs from 2 classes, together with cotrimoxazole prophylaxis and macronutrient intervention only for those with low BMI (or low weight-for-height/mid-upper arm circumference in children). The primary objective of the trial is to identify effective, safe and acceptable interventions to reduce early mortality (all-cause) in HIV-infected adults, adolescents, and older children (5 years or more) initiating ART.

Site(s)  
Project Period  
8/1/2013 - 8/1/2017  
Funding Status  
Funded – Medical Research Council  
Direct Award (USD)  
Update  
At the Eldoret site, a total of 208 participants were enrolled (195 adults and 13 children) before the study was closed to accrual/enrolment. All the participants have already completed study treatment and follow up. The study is now closed to follow up.

Future Plans  
Continue with data analysis and dissemination of study findings.

Publication(s)  

Study Title  
SAFI (Stigma in AIDS Family Inventory) Validation Study

Principal Investigator(s)  
Rachel Vreeman, Indiana University

Co-Investigator(s)  
Winstone Nyandiko, Moi University

Working Group(s)  
PRWG
**Description**

For families raising HIV-infected children in resource-limited settings, HIV/AIDS-related stigma shapes every aspect of the children’s HIV management, from daily adherence to medication to decisions about pediatric HIV disclosure. We do not know the most effective strategies to reduce stigma for HIV-infected children and their families in resource-limited settings nor how to measure its effects on physical, emotional, or social outcomes. We want to learn more about how stigma affects families. As part of the HADITHI study, SAFI aims to develop and test a reliable, valid instrument to measure HIV/AIDS stigma as perceived, enacted, and internalized by Kenyan families with HIV-infected children. The specific aims for the SAFI validation study are to:  

**Aim 1:** Identify and modify H/A stigma questionnaire items for maximum reliability and content validity to measure perceived, enacted and internalized H/A stigma among Kenyan families with HIV-infected children.  

**Aim 2:** Assess the validity of the measures of perceived, enacted and internalized H/A stigma compared to independent construct measures including pediatric adherence to therapy and children’s physical, psychological and social outcomes.  

**Aim 3:** Examine whether disclosure of a child’s HIV status to the child reduces perceived, enacted, or internalized stigma for families with disclosed children compared to families with non-disclosed children. We thus propose assembling, adapting, and then validating measurement items for assessing the relevant domains of H/A stigma experienced by HIV-infected children and their caregivers in sub-Saharan Africa.

**Site(s)**

**Project Period**  
12/17/2013 - 11/30/2015

**Funding Status**  
Funded – NIH - National Institute of Mental Health (NIMH)

**Direct Award (USD)**  
$567,828

**Update**

The specific aims for the SAFI(Stigma in AIDS Family Inventory) validation study are: Aim 1: Identify and modify HIV/AIDS stigma questionnaire items for maximum reliability and content validity to measure perceived, enacted and internalized HIV/A stigma among Kenyan families with HIV-infected children. Aim 2: Assess the validity of the measures of perceived, enacted and internalized H/A stigma compared to independent construct measures including pediatric adherence to therapy and children’s physical, psychological and social outcomes. Aim 3: Examine whether disclosure of a child’s HIV status reduces perceived, enacted, or internalized stigma for families with disclosed children compared to families with non-disclosed children. No modifications have been made to the specific aims as stated in the original proposals. We have ongoing Institutional Review Board and local ethics committee approval for the aims. Data that was collected through the SAFI study to provide a comprehensive and validated family HIV/AIDS-related stigma measure for assessing HIV/AIDS (H/A) stigma in western Kenya, including perceived, enacted and internalized stigma is being prepared for analysis. Stigma videos have been developed and are ready for use in the community and AMPATH clinics.

**Future Plans**

In the next 6 months, we plan to complete the analysis of data collected from the HADITHI cohort of families to assess the validity of the HIV/AIDS Stigma questionnaire measures of family stigma compared to independent construct measures including medication adherence, and children’s clinical, psychological, and social outcomes. We also plan to implement the stigma films as educational and moving tools to help reduce the
**Publication(s)**


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**Study Title**

**Tablet Computer-Based Disclosure Counseling for HIV-Infected Adolescents and their Families: A Pilot Study of Perspectives from Providers**

**Principal Investigator(s)**

Megan McHenry (maiden: Uhl), Indiana University

**Co-Investigator(s)**

PRWG

**Working Group(s)**

**Description**

The objective of this study is to evaluate a pilot project using Google tablet computers for disclosure-related counseling with HIV-infected children and their caregivers in three AMPATH clinics. Google Nexus 7 Android tablets donated to the IU-AMPATH Android Program will be loaded with materials developed as part of the ongoing HADITHI disclosure intervention trial (PIs: Nyandiko and Vreeman) and includes educational materials on HIV and disclosure, counseling-based activities, and video narratives sharing experiences of HIV and disclosure. A plan was in place prior to this proposal of this study to implement the tablet computers in these clinic sites regardless of whether the benefits or hindrances of these devices are measured. This study is focused on understanding how this implementation affects the healthcare provider's disclosure practice or perspectives. The healthcare providers (HCPs) targeted in this study will include all healthcare workers who handle children in the clinics of study. This would include a clinical officer, nurse, counselor, social worker, or other similar position. Our central hypothesis is that AMPATH HCPs will find these tablet computers usable and helpful as a tool in disclosure counseling. The long-term goal of this study is to provide evidence to better support adolescents through the disclosure process and increase the number of adolescents who know their HIV status. We plan to accomplish our research objective by achieving the following specific aims: Aim 1: Describe current disclosure practices and barriers to disclosure at three clinics (Bumala, Busia, and Port Victoria) in Western Kenya through interviews with key clinic staff. Aim 2: Compare the prevalence of disclosure at these clinics for HIV-infected adolescents (10 to 14 years) before and after the introduction of the tablet computers using disclosure status data collected through AMRS. Aim 3: Evaluate provider acceptability and usability of the tablet computers for disclosure counseling through surveys, cognitive interviews, and focus group discussions. Sub-aim 3a: Describe any changes in providers' knowledge, comfort, and attitudes regarding disclosure after the introduction of the tablet computers.

**Site(s)**

Bumala A Health Centre Bumala B Health Centre Busia District Hospital Port Victoria Sub-District Hospital

**Project Period**

2/13/2015 - 8/19/2016

**Funding Status**

Unfunded –
### Direct Award (USD)

**Update**

Although our initial data collection was wrapped up, we submitted an amendment in order to give one more additional survey to the clinical providers who completed Phase 2 (those who used the tablet computers for disclosure education). We also conducted focus group discussions with the adolescents at the clinic to understand their experience with the tablet computers as a resource for disclosure. The additional survey for the clinical providers will help us understand the sustained effects, in any, that the tablets computers were able to provide, as the most recent follow up with the providers was in November 2015. The perspectives gained from the adolescents in the focus groups will help us get greater understanding of the impact the tablets may have had in the clinic. Our findings thus far are as follows: 21 healthcare providers participated (8 clinical officers, 5 nurses, 8 social support staff). The proportion of participants, in regards to gender and clinical roles, was similar among each of the clinics (p-values 1.00 and 0.654, respectively). Most believed caregivers should disclose their children's status to them, with healthcare providers offering encouragement and answering children's questions. Major perceived barriers for caregivers to disclose were lack of parental HIV knowledge and stigma. Surveys indicated tablets were used during 75% or more of clinic encounters by 67% (14/21) of providers one month after tablet distribution, and 85% (18/21) at the end of the study. Provider comfort with disclosure increased significantly between the first and third surveys (p-value=0.039). This increased comfort was persistent during the study period (p-value 0.024 between 1st and 4th survey, p-value of 0.027 between 1st and 5th survey). Although it did not reach statistical significance, males seem to indicate that the tablet was more helpful in their discussion of HIV disclosure counseling compared to females (p-value=0.051). At follow-up, all (n=21) providers reported tablets improved clinical disclosure process. Many (n=16) reported child participation and adherence improved and children increasingly attended clinic specifically to watch tablet disclosure videos. Providers reported caregivers and children began initiating dialogue about critical issues such as medication adherence after watching the disclosure videos. Additionally, all (n=21) reported reviewing materials during their free time, in particular outside of work, to increase their own knowledge and comfort with disclosure. No technical issues were reported.

### Future Plans

We will complete the amendment activities by next week. We hope to analyze that data and complete the manuscript for publication within the next 6 months.

### Publication(s)


### Study Title

Taking to the Streets: a Mixed-Methods Systematic Review of the Reasons Children and Youth Become Street-Involved

### Principal Investigator(s)

Lonnie Embleton, Moi University

### Co-Investigator(s)

Paula Braitstein, Indiana University
### Working Group(s)

**PRWG**

### Description

A wide variety of reasons children take to the streets to work or live have been cited in the literature; yet there lacks any compiled data on this topic by geographic region. It is suspected the dynamics that drive children to the streets are quite diverse and vary between high income and low-to-middle income countries. This systematic review aims to identify similarities and differences internationally for children living or working on the streets. In turn this literature should help identify future research needs as well as policy changes to best suit the needs for the millions of children worldwide before or after they turn to the streets as a way of survival. Overall objective To compile and critically analyze the literature regarding reasons why children and youth, aged <1-24, turn to the streets as a way to survive in order inform public health research and policy, while identifying gaps in knowledge and evaluating the strength of existing evidence. Specific Aim To describe the reasons children and youth become street-involved in both high and low to middle income countries including but not limited to: differences between street connected children in resource-constrained and very-high income settings, children on and of the street and males and females for street-involvement and the age they start living on the streets. Specific Questions: 1. What are the reasons children and youth come to the street both from quantitative and qualitative literature and are the reasons between the two methodologies similar or different? 2. What are the differences in reasons between children on the street versus of the street for coming to the streets? (if able to distinguish based on reporting) 3. What are the differences between children/youth in high versus low/middle income countries? 4. What are the differences between genders?

### Site(s)

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<th>8/1/2013 - 5/1/2014</th>
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### Funding Status

Unfunded –

### Direct Award (USD)

This review has been published in JAMA pediatrics.

### Future Plans

No more work will occur on this study. This study is closed.

### Publication(s)


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### Study Title

The IU Simon Cancer Center (IUSCC) AMPATH-Oncology Institute (AOI): An Exemplar of Care for the Developing World and a Population-Based Research Environment for IUSCC

### Principal Investigator(s)

Tom Inui, Indiana University

### Co-Investigator(s)

Naftali Busakhala, Moi University

### Working Group(s)

ORWG
Kenya, like much of the developing world, is rapidly undergoing an 'epidemiologic transition' from a health scene dominated by infectious diseases to one in which the major causes of death and disability are cancer and other chronic diseases. Under these circumstances, applying science to the management and control of cancer has become as relevant to Kenya as it is in the United States. Similarly, what is learned about the prevention and treatment of cancer in the developing world literally has direct relevance to care in the United States. Cancer care and attendant research in Kenya, whose population is the most genetically diverse in the world, will catalyze the discovery of new genes of importance to our fight against cancer, new genomic predictors of cancer, and new genetic variants that predict response to therapy. Recognizing both emerging threats to population health and potential for advancing care and science, the IU Simon Cancer Center (IUSCC) and the IU-Kenya AMPATH Program have been actively pursuing resources to respond. The focus of the partnership is to develop a sustainable and comprehensive academic clinical care program that will serve the citizens of western Kenya, and in the process, create a unique program of international collaboration for patients with, or at risk for, malignancies. The mission of the AMPATH Oncology Institute (AOI) is to be the premier cancer program in Sub-Saharan Africa, noted for excellence in cancer prevention, treatment and palliative care. AOI activities will directly contribute to advances in cancer care, accelerate discoveries in the biology and treatment of cancer, and provide support for the IU Simon Cancer Center's quest to become a federally designated Comprehensive Care Center. Naftali Busakhala will characterize the awareness, beliefs, attitudes and behaviors of women coming to AMPATH's clinician breast exam screening as volunteers, comparing these beliefs to those of a community-based sample of women. He will also characterize the yield of the AMPATH screening program, the kinds of cancers detected, and the quality of care achievable in Western Kenya at present, with comparison against an international standard of care. Chite Asirwa will similarly characterize the awareness, beliefs, attitudes and behaviors of a community-based sample of women, comparing their beliefs to those of their husbands, often a key influence on behavior in traditional societies. Taken together these two studies should reveal a great deal about how to influence women's behaviors and encourage participation in the only breast cancer screening program available presently - clinician examination. Both of these studies will use the BCAM (Breast Cancer Awareness Measure), a survey tool developed in Great Britain. We have worked carefully through the standard BCAM to sort questions into theoretically sound domains, using the Health Belief Model as a framework. Violet Naanyu will be conducting field testing and focus groups to do a culturally appropriate Kiswahili version.

MTRH Mosoriot Rural Health Training Centre Turbo Health Centre Webuye District Hospital Kapsokorony

10/1/2011 - 6/30/2016

Funded – Walther Cancer Foundation

$1,200,000

In the past six months, all six planned manuscripts from this study were finally accepted for publication in peer-reviewed journals. Only one manuscript, while accepted for publication, is yet to be printed. The study closed for any enrollment activities at the end of December, 2015.
Future Plans

A final report to the Walther Cancer Foundation must be submitted by August 31, 2016.

Publication(s)


Study Title

The Production and Reproduction of Kinship in CCIs in Uasin Gishu County

Principal Investigator(s)

Michael Callaghan, University of Toronto

Co-Investigator(s)
<table>
<thead>
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<th>PRWG</th>
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<tr>
<td><strong>Description</strong></td>
<td>This is a qualitative social science project that seeks to explore how residents of Charitable Children's Institutions (CCIs; including orphanages) produce and understand kinship relations. Based on a structural-functionalist theoretical orientation, we hypothesize that when children move to CCIs, they will create new fictive kin relationships. We hope to map these relations and explore the directionality of things like authority and hierarchy, and to understand the sorts of privileges and obligations inherent in these relationships. We will conduct a series of open-ended, semi-structured interviews with current and former residents and staff of CCIs in Uasin Gishu county, Eldoret. Our survey instrument is designed to elicit information about the nature of kin networks at the CCI, and how traditional life milestones (such as marriage or coming of age) are manifest in these networks. We will also ask residents to draw kinship diagrams to better visualize their relationship networks. The data will be analyzed with an emphasis on functionalism and symbolic anthropology.</td>
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<td><strong>Direct Award (USD)</strong></td>
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<tr>
<td><strong>Update</strong></td>
<td>Since January, the protocols and instruments have been designed and circulated for feedback among team members. Ethics clearance has been submitted too.</td>
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<tr>
<td><strong>Future Plans</strong></td>
<td>We hope to start research as soon as possible after receiving clearance. Before the end of the year, we hope to complete all data collection and analysis and to have made significant progress on writing up the results.</td>
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| Study Title | **The Role of Faith Leaders Towards Promotion of Home Based HIV Counseling, Testing and Linkage to Treatment Program Around Kisumu, Kenya** |
| Principal Investigator(s) | Eunice Kamaara, Moi University |
| Co-Investigator(s) | Amy Nunn, Brown University |
| Working Group(s) | SSRN |
| **Description** | |
| **Site(s)** | |
| **Project Period** | 11/1/2014 - 10/30/2015 |
| **Funding Status** | Funded – Brown University - Center For AIDS Research |
| **Direct Award (USD)** | $25,000 |
| **Update** | Over the last 6 months, we have done further analysis of our data and drafted two paper |
for publication. We also plan to explore possibilities for further research on the basis of our study finding.

**Future Plans**

We plan to publish the two papers ad to close the project in September 2017.

**Publication(s)**

<table>
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<tr>
<th>Study Title</th>
<th>The Role of PD-1 Pathway and Tissue Microenvironment in HIV-Kaposi Sarcoma and Endemic Kaposi Sarcoma Cohort in Western Kenya</th>
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<tr>
<td>Principal Investigator(s)</td>
<td>Patrick Loehrer, Indiana University</td>
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<tr>
<td>Co-Investigator(s)</td>
<td>Asirwa Chite, Indiana University</td>
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<tr>
<td>Working Group(s)</td>
<td>ORWG</td>
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**Description**

Even before the HIV pandemic, equatorial Africa had among of the highest KS incidences in the world. In this area, 'endemic KS' (the term given to the HIV-unassociated form of KS) was manifested primarily as indolent localized disease in men and represented 4 to 10% of adult cancers. Although sub-Saharan Africa was already a hotbed for KS, the clinical manifestations and impact of the disease dramatically changed with the onset of the HIV epidemic in the 1980's when the incidence of KS and other HIV associated malignancies exploded. The advent of anti-retroviral therapy (ART) improved prognosis of HIV-associated KS, but survival remains unacceptably poor in low to middle income countries (LMIC). A recent Cochrane review on late stage KS showed that in 6 studies in which chemotherapy was added to HAART, no survival benefit was seen above that of ART therapy alone nor amongst the different types of chemotherapy. Endemic KS, while less likely to progress to visceral disease, leaves patients with profound functional disabilities often requiring treatment. Because this population is HIV negative, ART is not used. Research that leads to a better understanding of the biology of KS must be explored to provide alternative therapies to ART and standard chemotherapy. Based upon preliminary data from UCSF which supports the role of PD1 pathway and tissue microenvironment in KS, we propose to conduct a prospective analysis on two patient cohorts. Cohort 1: KS in HIV-infected subjects who have failed at least one KS-directed chemotherapeutic intervention; and Cohort 2: KS in HIV-negative patients (i.e. endemic KS) who have failed at least one KS-directed chemotherapeutic intervention.

**Site(s)**

**Project Period**

10/1/2015 - 9/30/2018

**Funding Status**

Funded – NIH - National Cancer Institute (NCI)

**Direct Award (USD)**

$158,406

**Update**

We do anticipate a carry forward balance. Due to the delayed approval of the IRB, we will be requesting a carryover balance of $185,836 to complete the proposed aims. The goal of this supplement is to stimulate HIV malignancy research via support of collaborative pilot projects in NCI-designated Cancer Centers (CC) and low and middle income countries (LMICs), per World Bank classification. Findings from this collaboration could potentially improve cancer control, prevention and treatment strategies in the US and the LMIC.
The Indiana University Melvin and Bren Simon Cancer Center agrees to complete the aim described in the supplement. These aims include:

**Aim 1:** To define the microenvironment of KS tissue from two cohorts of KS patients from Western Kenya using multi-parameter flow cytometry. **Aim 2:** To fully characterize subjects by clinical stage and extent of KS, functionality, level of lymphedema, CD4 counts, viral load and past responses to therapy. **Aim 3:** To correlate the data on clinical presentation, prior response and PD1 to identify specific phenotypes for future clinical trials. **Aim 4:** To mentor at least 3 scientists from LMIC by pairing with faculty from IUSCC and UCSF through this project to enhance the research workforce within Kenya. **Summary of Accomplishments.** None to date. Obtain all necessary IRB/IREC Approvals and informed consents (enclosed) Protocol No: 1603358685 Site: Indiana University Simon Cancer Center PI: Patrick J Loehrer, Sr, M.D. Date of IU IRB approval of the protocol: Approved June 09, 2016 Date of IREC approval 001605: April 8, 2016 Subcontract sent to UCSF for final execution 7/14/2016 Subcontract sent to Moi for final execution 7.217.2016

**Obstacles Encountered:**
1) There was delay in submission to the IU IRB until the protocol was reviewed and approved by the IREC (IRB of Moi Teaching and Referral Hospital) which was finally approved on April 8th, 2016. 2) We had concerns from the IU IRB that questioned our application for an exempt from DSMB. They initially felt that punch biopsy required a DSMC. We had some difficulty explaining that this represents standard of care in Kenya and we eventually convinced them. 3) They also questioned whether the IUSCC SRC needed to review which we also resolved. 4) The provisional approval wished to have the IREC approval sent to them, which we have done. 5) All of the above have been taken care of and we received full IRB approval on June 09, 2016.

**Future Plans**

**Future Tasks:**
1) Now that the study has recently been approved, we will need to approve the subcontract with University of California-San Francisco and Moi University. Dr. Chite Asirwa will serve as the local PI with assistance from Dr. Evangeline Njiru. 2) Once the subcontracts are in place, we can begin to accrue patients. We expect rapid accrual given the high incidence in dermal manifestations of KS at MTRH.

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**Publication(s)**

**Study Title**
Validation of Spirometry Prediction Equations in Western Kenya

**Principal Investigator(s)**
Peter Kussin, Duke University

**Co-Investigator(s)**
David Lagat, Moi University

**Working Group(s)**
AMWG

**Description**
This is a cross-sectional study of healthy adult Kenyans living in and around Eldoret. The purpose of the study is to validate a set of spirometry prediction equations for the local population. Adults age 18 years and older who are HIV negative, with no history of chronic cardiac or pulmonary disease and with <5 pack year smoking history are eligible for participation. Specific Aim: Determine pulmonary function reference equations that can accurately predict normal spirometric values in a Kenyan population. 1A: Statistically compare phenotypically normal Kenyan spirometric profiles with values obtained from published pulmonary function reference equations to determine the most
Vincristine Optimization in Kenyan Children with Cancer

Jodi Skiles, Indiana University - Purdue University in Indianapolis (IUPUI)

Festus Njuguna, Moi University

ORWG, PRWG

In resource-limited settings, access to chemotherapeutic agents is confined to a few therapies. Vincristine (VCR) is a mainstay in such settings due to its low cost and lack of myelosuppression, however, little is known regarding its disposition and true optimal dosing, especially in the pediatric population. Negative clinical outcomes, such as serious side effects due to drug overdosing or lack of efficacy due to sub-therapeutic dosing, may result. VCR is associated with highly variable cumulative dose-dependent peripheral neuropathy (VIPN). While pediatric oncology patients in the U.S. who receive VCR experience significant VIPN and excellent disease outcomes, Kenyan children with cancer who receive VCR experience little to no VIPN, highlighting the opportunity for optimization of VCR in this population. While there are clearly multiple factors that contribute to poor disease outcomes in Kenya, suboptimal dosing of VCR is the piece we aim to address in this study. The biological basis for the minimal VIPN we have observed in Kenyan children is uncertain but includes such things as genetic differences in VCR pharmacologic pathways as well as genetic variability in susceptibility to neuropathy. This gap in knowledge provides a clear opportunity to optimize use of this medication in Kenyan children with cancer and evaluate genetic associations with VIPN in order to personalize this medication for individual children once VCR dosing is augmented.

Preliminary data has shown that Kenyan children with cancer (n=100) experience minimal VIPN. Despite the negligible neuropathy observed, subclinical VIPN can be detected using a very detailed, non-invasive assessment tool that we developed for detecting even very minor toxicity. Utilization of this tool in Kenyan children allowed us to identify an association between VIPN severity, CYP3A5 genetic polymorphisms, and an individual's ability to metabolize VCR, such that children with an allelic variant of CYP3A5 that results...
in a high VCR metabolizer phenotype experience less VIPN. Variability in VCR response and toxicity may be particularly significant within Africa, where human genetic variability is greatest, and where ~90% of Kenyans patients were fast VCR metabolizers. In one recent study, pharmacokinetic (PK) variability was linked to overall survival in children with acute lymphoblastic leukemia (ALL), such that children with faster VCR clearance had a greater chance of relapse. If VCR disposition, response, and neurotoxicity are linked, it may be possible to optimize dosing based on easily obtained knowledge of genetic polymorphisms responsible for disposition and subsequent neurotoxicity variability. This research is of particular importance in Africa, where VCR is one of few available anticancer drugs and is used in the treatment of over half of all cancer patients. Furthermore, given that most Kenyan children are CYP3A5 high expressers and thus VCR fast metabolizers, they may tolerate and benefit from higher doses of vincristine than are conventionally used in the U.S. and Africa. This proposed prospective study will be conducted in two parts, which will both enroll pediatric patients age 1-18 years with newly diagnosed acute lymphoblastic leukemia or nephroblastoma. Part I will be a VCR dose escalation phase (in combination with routine multi-agent chemotherapy) to determine the maximum tolerated dose of VCR in a population of Kenyan children with cancer. Part II will be utilize the maximum tolerated dose of vincristine determined from Part I in place of the standard dose of VCR in combination with routine multi-agent chemotherapeutic protocols. DNA and pharmacokinetic samples will be collected on all subjects to allow determination of biomarkers of development of VIPN. Subjects will be monitored closely for development of toxicity with laboratory assessments as well as detailed neuropathy assessments. The specific aims (SA) for this proposal are as follows: SA1: To determine the maximum tolerated dose (MTD) of VCR administered in conjunction with conventional chemotherapy in cohorts of Kenyan children with ALL or Wilms tumor receiving VCR as part of their anti-cancer treatment. SA2: To validate our pilot study findings and to further evaluate the association between common or functional variants in genes in the vinca alkaloid pharmacologic pathway and across the human genome with VCR PK, VIPN, and disease response in the same populations as SA1. SA3: To further develop our pharmacologic prediction model of VIPN describing associations between pharmacogenetic, pharmacokinetic, and clinical biomarkers and carefully characterized VIPN in the same population of patients as SA1. SA4: To evaluate the validity and reliability of several chemotherapy-induced peripheral neuropathy (CIPN) measurement approaches when used to quantify neuropathy and associated neuropathic pain in Kenyan children receiving vincristine.

2/3/2014 - 1/31/2018

Funded – NIH - National Cancer Institute (NCI) NIH - Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD)

$103,254

This study commenced in February 2014 and 31 subjects were enrolled and enrollment to Phase I is now complete. Based on our data, Dose level 2 is the maximum tolerated dose. Data analysis is ongoing with hopeful submission of a manuscript in the next 6 months. It is unlikely that Phase II of this study will be completed due to ongoing issues with abandonment of care in this population making it difficult to draw any meaningful
conclusions about whether the dose escalation schema has any impact on outcomes/survival.

**Future Plans**
Submission of a manuscript with hopeful (but unlikely) identification of funding to complete Phase II of this study. Conversations ongoing with the Amsterdam team about how/if to pursue Phase II.

**Publication(s)**
IeDEA 10 Year Progress Report

East Africa International Epidemiologic Database to Evaluate AIDS (IeDEA) Year 10 Science Report

August 1, 2015- July 31, 2016

Kara Wools-Kaloustian M.D. M.S.
Director, Division of Infectious Diseases
Professor of Medicine
David H. Jacobs Scholar of Infectious Diseases
Indiana University School of Medicine
Co-PI East African IeDEA

Constantin T. Yiannoutsos, Ph.D.
Professor of Biostatistics
Indiana University School of Public Health
Richard M. Fairbanks School of Public Health
Department of Biostatistics
Indiana University
Co-PI East African IeDEA

Grant Number: U01AI069911
June 6, 2016
Specific Aims:
No change in specific aims from the last report.

A. Studies and Results

B1. Infrastructure:

Composition and structure of the consortium
The consortium consists of ten active HIV-treatment programs (Kenya-2, Tanzania-4, Uganda-4), five U.S. universities and University of Toronto. The composition of the consortium is outlined in Table 1. An investigator from each institution sits on the Executive Committee, which continues to meet every two months in order to address administrative issues within the consortium. The scientific agenda is currently being addressed through working group conference calls (i.e. KS, Cervical Cancer, TB, Hepatitis, Congenital Abnormalities, Pediatrics, NIDA (Alcohol Study)). The Data Core continues to meet every four weeks in order to discuss issues related to the development of site-level master data sets as well as analysis data sets for individual concept proposals. The Statistics and Methodology Core is composed of Professors Yiannoutsos (IU) and Glidden (UCSF) along with Drs. Maya Petersen (Berkeley), Ann Mwangi (Moi) and Agnes Kiragga (Makerere). Members of this committee continue to meet (via phone, e-mail or in person) on an ad hoc basis to address specific analyses.

Regulatory:
The dates of original approvals and continuing reviews outlined in Table 1. Projects with prospective data collection are submitted and receive approvals separate from those for the primary consortium.

Development and support of an EMRS infrastructure:
All clinical sites contributing data to the consortium have stable electronic medical records systems (EMRS). An OpenMRS platform is utilized at all sites except Kisesa and IDI. Rakai has newly transitioned to OpenMRS express under the Ugandan national program. All sites have functional EMRS and have not had significant issues over the last year.

Regional Data Center:
During the past year the Regional Data Center has received data from the Rakai and the FACES sites. Processing of the data from Rakai was completed at the end of April. Processing of the FACES data is complete with the exception of the cervical cancer screening data which was submitted at the end of May. The current composition of the Regional Database is outlined in Table 2. The Regional Data Center continues to receive and process data requests from the consortium investigators and has generated analysis data sets for fifteen concept proposals and has updated existing analysis data sets for seven other proposals. The list of data requests, their concept numbers, and status can be found in Appendix 1-Project Tracking Table (links to the original concept sheets can be found in the tracking document on the EA-IeDEA website www.iedea-ea.org).
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<th>Country</th>
<th>Site</th>
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<th>Original Approval</th>
<th>Latest Continuing Review Approval</th>
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<td>AMPATH</td>
<td>Moi University College of Health Sciences (MU/CHS) &amp; Moi Teaching and Referral Hospital (MT&amp;RH)</td>
<td>20 Jun 2006</td>
<td>28 Oct 2015</td>
<td>27 Oct 2016-</td>
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<td>Mbarara University ISS Clinic (NIDA Study)</td>
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<td>2 June 2015</td>
<td>30 May 2016</td>
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<td>New York University</td>
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Table 2: Patient Enrollment as of 28 March 2015

<table>
<thead>
<tr>
<th>Country</th>
<th>Program /Site</th>
<th>Adults Enrolled No.</th>
<th>Adults Receiving ART No. (%</th>
<th>Children Enrolled No.</th>
<th>Children HIV Infected No. (%</th>
<th>Children Receiving ART No. (%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kenya</td>
<td>AMPATH</td>
<td>142,670</td>
<td>102,407 (71.8)</td>
<td>44,173 (85.0)</td>
<td>26,492 (60.0)</td>
<td>19,649 (74.2)</td>
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<td></td>
<td>FACES</td>
<td>24,866</td>
<td>17,878 (71.9)</td>
<td>2,782 (5.4)</td>
<td>1,352 (48.6)</td>
<td>984 (72.8)</td>
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<tr>
<td>Uganda</td>
<td>Masaka</td>
<td>21,547</td>
<td>15,446 (71.7)</td>
<td>2,246 (4.3)</td>
<td>2,163 (96.3)</td>
<td>1,578 (73.0)</td>
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<tr>
<td></td>
<td>Mbarara (UCSF)</td>
<td>24,975</td>
<td>14,137 (56.6)</td>
<td>80 (0.2)</td>
<td>80 (100.0)</td>
<td>33 (41.3)</td>
</tr>
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<td></td>
<td>IDI</td>
<td>29,380</td>
<td>15,525 (52.8)</td>
<td>151 (0.5)</td>
<td>8 (100.0)</td>
<td>0 (0.0)</td>
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<tr>
<td></td>
<td>Rakai</td>
<td>6,538</td>
<td>3,087 (47.2)</td>
<td>516 (1.0)</td>
<td>516 (100.0)</td>
<td>216 (41.9)</td>
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<tr>
<td>Tanzania</td>
<td>Morogoro</td>
<td>9,271</td>
<td>6,159 (66.4)</td>
<td>1,033 (2.0)</td>
<td>991 (95.9)</td>
<td>677 (68.3)</td>
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<td>ORCI</td>
<td>1,589</td>
<td>1,425 (89.7)</td>
<td>49 (0.1)</td>
<td>49 (100.0)</td>
<td>37 (75.5)</td>
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<td>Tumbi</td>
<td>9,115</td>
<td>4,802 (52.7)</td>
<td>913 (1.8)</td>
<td>889 (97.4)</td>
<td>520 (58.5)</td>
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<td>Kisesa</td>
<td>2,356</td>
<td>1,503 (63.8)</td>
<td>146 (0.3)</td>
<td>143 (97.9)</td>
<td>107 (74.8)</td>
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<tr>
<td>TOTAL</td>
<td></td>
<td>272,307</td>
<td>182,369 (67.0)</td>
<td>51,946 (16.0)</td>
<td>32,683 (62.9)</td>
<td>23,801 (72.8)</td>
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</tbody>
</table>

Education and Training:

In the past year, Agnes Kiragga, a doctoral candidate at Makerere University in Kampala, Uganda, co-mentored by Dr. Yiannoutos, continues to be employed as a senior statistical analyst at the Infectious Diseases Institute (IDI) in Kampala Uganda and is partially supported by EA-IeDEA. She has produced two papers (see next section) from her thesis in collaboration with Professor Yiannoutos and Dr. Judith Lok, Associate Professor at the Department of Biostatistics at Harvard University School of Public Health and one additional paper is in submission at the JIAS. A Biostatistics intern, Mr. Philani Mpofu, originally from Zimbabwe, holder of a baccalaureate degree in statistics from Vassar University, was partially supported by IeDEA funds over the past year has been accepted as a doctoral candidate in the Department of Biostatistics at Indiana University. Mr. Mpofu has completed one analysis, concerning the evolution of TB incidence over the first decade of ART scale-up in EA-IeDEA, which was published in JAIDS earlier this year. He is working on a number of projects as part of his doctoral studies, which are related to the causal effect of ART on TB incidence in East Africa (also see below). Mr. Mpofu will be mentored by Dr. Yiannoutos during his PhD training. Mr. Joseph Nondi, an EA-IeDEA scholarship recipient, completed his MSc degree in statistics at Kilimanjaro Christian Medical Center (KCMC) in Tanzania, with funding from EA-IeDEA. Mr. Nondi is employed at the National AIDS Control Programme in Dar es Salaam. In his role as the coordinator of the CTC Tanzanian AIDS database, he serves as a critical link between IeDEA and this enormous national resource. A supplement proposal, assessing the impact of point-of-care CD4 testing in the country, based on data gleaned from the national database, serves, in addition to its epidemiological value, as a proof of concept for using a virtually untapped resource to address important research questions in that country. This project is currently under regulatory review in Tanzania. Another student mentored by Dr. Yiannoutos at the University of Athens, Elisavet Syriopoulou has generated a paper in collaboration with EA-IeDEA personnel and Dr. Lok, which is under submission at the JIAS. Ms. Syriopoulou has since secured an internship in Denmark and is currently a research assistant at Lancaster University in the UK. The work was presented by Dr. Lok at the Spring Meeting of the International Biometric Society East North Atlantic Region (ENAR) held in March 2016 in Austin, TX. One of Dr. Yiannoutos’ current mentees, Mr. Kyriakos Kouvelakis also at the University of Athens, is analyzing data from the European EuroCoord Collaboration to provide mortality estimates from HIV-infected patient in to the UNAIDS for their 2017 version of the Spectrum software in collaboration with Professor Giota Touloumi at the Division of Hygiene and Epidemiology at the University of Athens.

Dr. Kara Wools-Kaloustian and Professor Yiannoutos co-advised a doctoral student who received her PhD in the summer of 2015, Dr. Samiha Sarwat, within the Department of Biostatistics at the Indiana University
Fairbanks School of Public Health. Dr. Sarwat’s research was sponsored by the Clinical and Translational Sciences Institute (Indiana CTSI) to develop methodology to address patterns in weight evolution among patients starting ART (Concept15). A multi-regional manuscript is in preparation, from Dr. Sarwat’s thesis, involves over two million longitudinal weight measurements on almost 200,000 adult patients from five IeDEA regions. Dr. Nash and Dr. Yiannoutsos mentored Mr. Eduardo, a doctoral degree holder from Columbia University Mailman School of Public Health, who used EA-IeDEA data to complete his thesis (Concept 14). Dr. Eduardo successfully defended his dissertation in the fall of 2015 and at least one manuscripts from this work is close to final form2. Dr. Wools-Kaloustian and Dr. Yiannoutsos were co-mentors with Dr. Braithwaite for Dr. Jason Kessler’s K-08 application entitled “Optimizing retention in care among HIV infected alcohol misusers in East Africa”. This application proposed the utilization of data from the East African IeDEA cohort to refine models that assess the impact of various retention strategies directed toward alcohol misusers. A paper related to the impact of early outreach on re-engagement in care, in collaboration with Dr. Peter Rebeiro of Vanderbilt University and CCASAnet is in the final stages of preparation.

Dr. Aggrey Semeere is being mentored by Dr. Jeffrey Martin and works directly with Dr. Martin on all aspects of the research related to Kaposi’s sarcoma (KS) that is being conducted in East Africa IeDEA. Trained originally as a clinician, Dr. Semeere underwent formal training in epidemiology and biostatistics in the Master’s Degree Program in Clinical Research at UCSF and has recently returned to a post-doctoral fellowship position at the Infectious Diseases Institute (IDI) in Kampala. He is currently in the second year of a five year fellowship supported by NIH U54 CA190153, an award that leverages IeDEA infrastructure at both the IDI and AMPATH. All of Dr. Semeere’s field work is being conducted within the auspices of IeDEA including his leadership of projects concerning the incidence of KS in the ART era (Concept 37), and survival following KS diagnosis in the ART. He is also assuming administrative leadership of several aspects of the KS work, including chairing consortium-wide conference calls. Dr. Semeere exemplifies what can be achieved through dedication to a long-term rigorous training and mentoring plan.

Dr. Suzanne Goodrich, under Dr. Wools-Kaloustian’s mentorship, is working with IeDEA biostatisticians to analyze and report the findings from the NIDA-sponsored supplement looking at the impact of alcohol use on retention in care. In addition, Dr. Wools-Kaloustian continues to provide informal mentorship to a number of clinician-investigators as they develop their concept sheets and manuscripts.

Development of epidemiologic and statistical methods:

The East Africa IeDEA Consortium has continued to develop statistical methods to address frequently encountered biases in the estimation of various aspects or characteristics of the patients who contribute data to our analyses. The focus of the statistical research efforts of our region has consistently been in the adjustment of estimates based on loss to follow-up and the resulting unrepresentativeness of the dropout population by the patient population still in care, a core assumption of all routinely used statistical methods. East Africa IeDEA investigators have made critical contributions in this area, starting with important papers in the use of double sampling techniques that take advantage of the availability of patient outreach data in some of our sites3-6. We have also been the first to carefully delineate the subtle differences between loss to follow-up, disengagement from care and retention and connection to care 7. In this past year we continued these efforts by publishing several manuscripts that were directly informed by our double-sampling methodology, either through mainline IeDEA funds or databases generated through targeted supplements to the grant.

Adjustment by double sampling on mortality and longitudinal measures:

Dr. Agnes Kiragga, published one manuscript in 2014 related to mortality estimation adjustment after taking into consideration data from double sampling of patients who were lost to follow-up 6 and adjustment of longitudinal measurements (specifically CD4 total lymphocyte counts) collected over time, by the fact that sicker patients (and thus those with lower CD4 count, are more likely to die, drop out and to be disengaged from care. This non-random removal of these patients from the populations entering in the usual estimation of average CD4 counts at the program level, results in a dramatic overestimation of CD4 counts over time and, by
extension, misleads stakeholders and decision makers in their effort to monitor and evaluate HIV care and treatment programs. Dr. Kiragga published a second manuscript on this issue. We have expanded these efforts for the case of longitudinally collected dichotomous (yes/no) and ordinal (e.g., low, medium, high) outcomes. These methods were applied in the estimation of adherence levels among patients initiating ART in East Africa. Usually adherence is measured solely on patients who continue to participate in care and treatment and do not take into consideration the possibly non-random nature of patient dropout and death which is likely related to the level of adherence while the patient was still receiving care. Figure 1 shows the difference between this routine (naïve) estimation of self-reported adherence rates (left panel) and the adjusted ones after death and dropout, and the resulting lower rates of treatment access, have been taken into consideration (right panel). Developing these methods formed the core of a master’s thesis in biostatistics by Elisavet Syriopoulou. A presentation of these methods, which included adjustments for both longitudinal measures (i.e., CD4 counts and adherence levels) was made at the most recent conference of the International Biometric Society, East North Atlantic Region, by Dr. Judith Lok.

As was the case with respect to CD4 counts, levels of adherence, even under the best case scenario of self-report, are likely to be significantly overestimated even under conservative assumptions of treatment access among patients who have dropped out of care.

**Double sampling and competing risks**

A new research emphasis in the region is the development of methods which exploit data available from double sampling of dropouts to make adjustments for competing risk data. Such data arise frequently when one event (e.g., death) precludes observation of another (e.g., loss to follow-up, treatment modification, pregnancy, etc.). If, as is usually the case, mortality is underestimated, then estimates of the cumulative incidence of the competing event will be biased, frequently in an unexpected manner. Simulations carried out in the region are shown in Figures 2 (for the case where death is misclassified by under-reporting but not disengagement from care) and Figure 3, where both competing risks of death and disengagement from care have been misclassified (Figure 3). This paper has been published in PLoS ONE by Dr. Giorgios Bakoyannis and...
Constantin Yiannoutsos. More recent work by Dr. Bakoyiannis, Zhang and Yiannoutsos, received the ENAR Regional Advisory Board (RAB) Poster Award at the 2016 Spring Meeting of ENAR in Austin, TX for his poster entitled "A maximum profile pseudolikelihood estimator for the proportional cause-specific hazards model under outcome misclassification." The work was based on data collected in EA-IeDEA and an NIH biostatistics methods grant led by Dr. Constantine Frangakis at Johns Hopkins University.

A paper, in collaboration between Drs. Bakoyiannis, Yiannoutsos, along with Dr. Menggang Yu from the University of Wisconsin, attempts to quantify the impact of death under-reporting (and resulting “misclassification” of the death endpoint as loss to follow-up) when trying to estimate the cumulative incidence of these two semi-competing events was submitted to the Scandinavian Journal of Statistics. By “semi-competing” we mean that LTFU does not preclude death, however without patient outreach the outcome of death after LTFU cannot be observed. Death, however, always prevents the observation of loss to follow-up.

These results show that, while the rate of LTFU is slightly overestimated in the naïve analyses (because of unreported deaths), patient mortality is drastically underestimated (because of misclassification of a large majority of deaths as LTFU). While these results are largely in line with previous reports, none of those methods took into account the competing risk of loss to follow-up in the estimation.

“New user” methods

Dr. Martin’s team continues to use an approach called “New User” methodology, described in the Year 9 Progress Report, to assess the impact of ART on incident KS.

Contributions to the Global IeDEA Consortium:

Dr. Rachel Vreeman continues to serve as chairperson of the Pediatric Working Group and Dr. Jeff Martin continues to serve as the co-Chair of the Cancer Working Group. Ms. Beverly Musick continues to serve as the chairperson for the Data Harmonization Working Group. Dr. Constantin Yiannoutsos was recently elected chair of the new Strategic Data Working Group.

New Administrative Supplement to Enhance Data Infrastructure:

Automation of data extraction from OpenMRS

This supplement entitled titled “Automation of data extraction from OpenMRS” with activities led by Ms. Musick was described in our Year 9 Annual Report.

Concept #86: BD2K EA IeDEA regional consortium-Facilitating multi-regional collaboration by extending the IeDEA Data Exchange Standard
This project has two primary goals. Aim 1 is to extend the IeDEA-DES to include new tables, variables, definitions for HIV-related data that have been identified as high priority by the NIH and international partners like the UNAIDS and the WHO. We have selected the following topics for extension: data on pregnancy, child development, adolescent care transition, disclosure of HIV status, infectious diseases other than HIV (e.g., tuberculosis, malaria), non-communicable diseases (e.g., diabetes, cancer), and related medication and laboratory values. The project team consisting of clinicians, informaticians, epidemiologists, and data managers from four IeDEA regions, NIH, and HICDEP has had multiple teleconferences and one face-to-face meeting in February. A preliminary draft of the extended variables has been circulated and presented at the IeDEA Network Meeting in Boston. The team has received feedback and has near-final definitions for all topics except child development which should be completed by the end of June.

Aim 2 is to define a set of data quality checks for the new tables and variables, and implement these checks as R scripts to allow regional data managers to easily assess completeness and internal consistency of their data. Preliminary data checks were discussed at the face-to-face meeting in February and work is underway to program these new checks into R scripts.

B2. Scientific Productivity:

Please note that all East African Concept Sheets may be accessed through the Project Tracking Document which can be accessed at https://www.iedea-ea.org (Password Required but will be provided on request)

Aim 1: Determine the short and long-term outcomes of adults and children along the entire spectrum of HIV care and examine patient and site-level factors associated with these outcomes.

Project 1.1 Describe the multi-level determinants of late ART-initiation in adults and children.

This project is being addressed by Concept 39 “Characteristics of patients at enrollment into HIV care and outcomes prior to therapeutic ART eligibility or initiation in the IeDEA East Africa cohort” initiated by Dr. Elul. The statistical analysis for this project was completed by Dr. George Bakoyannis, a Post-Doctoral Fellow supervised by Professor Yiannoutsos. A manuscript is in preparation, and it is anticipated that it will be submitted for publication during the summer of 2016

Project 1.2 Investigate the incidence and determinants of treatment-limiting adverse events (AE) among ART-treated populations in East Africa.

As previously noted, due to funding constraints this project could not be initiated as outlined in the original grant application. A modification of this project was submitted and funded as a supplement. In addition, a WHO-funded project which relies on in-kind support from East African IeDEA also addresses these specific aims. These projects are taking place at the AMPATH site in Eldoret, Kenya:

Administrative Supplement: “Building off the HIV Platform: Extension of Pharmacovigilance to Populations with Tuberculosis or Malignancies”.

Tuberculosis Pharmacovigilance: Clinicians utilized the new TB encounter forms with the supplemental pharmacovigilance section from January 2013 to June 2013. In the six months of data collection, approximately 800 encounter forms were completed. The preliminary results of this project were presented in the Year 9 Progress Report. Discussions concerning the complexity in calculating incidence rates occurred in February 2016 between statisticians and investigators and these analyses will be available in 2016 with a subsequent manuscript anticipated in 2016 as well. In the interim, a lead investigator from the Kenyan study team was appointed as the pharmacist in charge of the Moi Teaching and Referral Hospital Tuberculosis Clinic
where this study took place. This transition will facilitate more detailed investigations of this unique population in subsequent IeDEA projects.

**Oncology Pharmacovigilance:** The Oncology pharmacovigilance forms were used at the AMPATH Eldoret and Chulaimbo Clinics. The forms were completed by pharmacology technologists, pharmacists, and other staff during the clinical care of the patient. Adverse Drug Reactions (ADRs)/Symptoms reported from January 2012 – December 2012 were compared to the number of ADRs/Symptoms reported from January 2013 to July 2013. Preliminary results of this project were presented in the Year 9 Progress Report. Final dataset development and analysis is in progress. We anticipate that a manuscript will be ready for submission by December 2016.

**WHO/Gates funded grant:**

"Pharmacovigilance & Toxicity Documentation in the Context of Antiretroviral treatment-threatening: Comparative Evaluation of 4 Strategies in a Resource- constrained setting".

The objectives and preliminary results of this project were outlined in the Year 9 Progress Report. As noted in that report completion of the "Kenya National Suspected Adverse Drug Reaction" (SADR) form for patients with a change or discontinuation in their ART was one of the objectives. Though data collection for this study has been completed, serious adverse event reporting has continued in order to ensure that Kenya is able to evaluate ART associated SADRs. Moi Teaching and Referral Hospital (MTRH-AMPATH) remains the largest contributor of SADR data on ART to the Poison’s and Pharmacy Board (PPB) in Kenya. Analysis is on-going for this project and should be completed in 2016.

**Project 1.3 Clinic and Patient-level determinants of durability of first-line ART regimen and time from first-line failure to second-line ART initiation in children in the international IeDEA cohort.**

This project is **Concept 40** “Clinic and Patient-level determinants of durability of first-line regimen and time from first-line failure to second-line ART initiation in children in the International IeDEA Cohort” a multi-regional project led by Dr. Wools-Kaloustian. A description of this project was included in the Year 9 Progress Report. The Analyses have been re-run on an updated dataset and contextual variables were added to the analysis. A draft manuscript will be ready for circulation by August 2016.

**Project 1.4 Preventing 200,000 HIV infections in East Africa through better use of existing resources: a simulation modeling approach.**

Model design and debugging and attributable publications were reported in the Year 9 Progress Report.

**Other projects that fall within Specific Aim 1:**

There are a number of other projects that fall under the umbrella of Specific Aim 1

**Concept 13:** “Models of patient outreach and their associated rates of loss to follow-up in the East African IeDEA consortium”

This project is led by Dr. Braitstein and has been renamed “**Facility-level factors influencing retention of patients in HIV care in East Africa**”13. This paper was revised and resubmitted to PlosOne and is currently under re-review. The abstract is outlined below:

Losses to follow-up (LTFU) remain an important programmatic challenge. While numerous patient-level factors have been associated with LTFU, less is known about facility-level factors. Data from the East African
International epidemiologic Databases to Evaluate AIDS (EA-IeDEA) Consortium was used to identify facility-level factors associated with LTFU in Kenya, Tanzania and Uganda. Patients were defined as LTFU if they had no visit within 12 months of the study endpoint for pre-ART patients or 6 months for patients on ART. Adjusting for patient factors, shared frailty proportional hazard models were used to identify the facility-level factors associated with LTFU for the pre- and post-ART periods. Data from 77,362 patients and 29 facilities were analyzed. Median age at enrolment was 36.0 years (Interquartile Range: 30.1, 43.1), 63.9% were women and 58.3% initiated ART. Rates (95% Confidence Interval) of LTFU were 25.1 (24.7-25.6) and 16.7 (16.3-17.2) per 100 person-years in the pre-ART and post-ART periods, respectively. Facility-level factors associated with increased LTFU included secondary-level care, HIV RNA PCR turnaround time >14 days, and no onsite availability of CD4 testing. Increased LTFU was also observed when no nutritional treatment was provided (pre-ART only), when TB patients were treated within the HIV program (pre-ART only), and when the facility was open ≤4 mornings per week (ART only). Our findings suggest that facility-based strategies such as point of care laboratory testing and separate clinic spaces for TB patients may improve retention.

Concept 14: “Factors associated with CD4 count and ART initiation and their relationship to survival”

This project is led by Dr. Eduard Eduardo under the direction of Drs. Nash and Yiannoutsos, was described in the Year 9 Progress Report. Three analyses were finalized as part of Mr. Eduardo’s PhD dissertation: 1) Association between site active screening and patient CD4 cell count at ART initiation, 2) Association between site active screening entry points and patient CD4 cell count at ART initiation, and 3) Association between site active screening entry point and patient survival. The key finding for Analysis 1 is that mean patient CD4 cell count at ART initiation does not differ materially between sites with and without active screening; While informative, publication of these data are not currently being prioritized. A manuscript developed from the second analysis is in the late stages of development and we anticipate that it will be submitted for publication in 2016. The main finding from Analysis 2 is that sites with active screening entry points have higher patient CD4 cell counts at ART initiation than sites without active screening entry points. Preliminary results from Analysis 3 were reported in the Year 9 Progress Report.

Concept 19: “Estimates and correlates of pediatric ART adherence”

This concept is led by Dr. Vreeman. The project and its preliminary results were described in the Year 9 Progress Report. An updated analysis was completed and the manuscript revisions are circulating among the co-authors and it is anticipated that the final manuscript will be submitted for publication in mid-summer 2016. Dr. Vreeman and the analytic team plan to employ similar modeling for the global pediatric ART adherence analyses that will be undertaken in 2016.

Concept 20: “Adolescent Care in East Africa”

This project has been transitioned from Dr. Gisore to Dr. Apondi, another Pediatrician at AMPATH. Revisions to these analyses have been made by Dr. Mwangi and reviewed by Dr. Yiannoutsos. A very preliminary draft manuscript was circulated to co-authors for review and comments have been returned to the primary author. We anticipate that a manuscript will be ready for submission by the end of 2016.

Concept 25: “Sub-optimal CD4 reconstitution among patients on antiretroviral therapy in the developed and developing countries; Frequency and patterns, determinants and clinical significance”

This project is led by Drs. Easterbrook at the WHO and Damalie Nakanjako, Agnes Kiragga at the Infectious Diseases Institute. A manuscript entitled “Frequency and impact of suboptimal immune recovery on first-line antiretroviral therapy within the International epidemiologic Databases to Evaluate AIDS-EA African Cohort”14 was e-published in AIDS. 2016 Mar 8.

Concept 27: “Predicators and factors associated with treatment failure among HIV-infected children on ARVs”
This project is led by Dr. Irene Marete, a pediatrician at AMPATH. The final analysis has been completed by Dr. Mwangi and a preliminary draft of the manuscript has been developed by Dr. Marete and circulated to the co-authors. We anticipate that a manuscript will be ready for submission by the end of 2016.

**Concept 32:** “Revising mortality estimates and predictors of mortality among HIV-infected children in western Kenya”

This project is led by Drs. Paula Braitstein and Ann Mwangi. As has previously been shown, the true mortality rate among adult HIV-infected patients in care depends heavily on knowing the mortality rate of patients who have fallen out of care. This is equally true of pediatric patients and in 2010 and 2015 we published our findings from having traced random samples of HIV-infected and exposed children. We are now working on revising pediatric mortality estimates. Our intended timeline is to have an abstract ready for submission to the CROI and/or IWHOD 2017 meetings.

**Concept 33:** “What is the capacity for the Conduct of adverse event/toxicity monitoring in resource-constrained settings?”

This is a multi-regional analysis led by Dr. Braitstein that resulted in the manuscript “Targeted Spontaneous Reporting: Scoping opportunities to conduct routine pharmacovigilance for antiretroviral treatment on an international scale” that was accepted for publication by the journal, Drug Safety.

**Concept 42:** “The incidence of first-line ART failure and incidence and determinants of initiation of second-line ART in adults meeting local criteria for first-line failure”

This project is led by Dr. Suzanne Goodrich. A manuscript entitled “The incidence of first-line ART failure and the incidence and determinants of initiation of second-line ART in adults in the East African IeDEA cohort” is in development and expected to be submitted for publication in summer 2016. The updated analysis assesses 89,601 patients (64% female; median age 36.7 (IQR 30.8-43.9) years; median CD4 count 128 (IQR 54-202) cells/µL) from 84 sites. 20,039 patients failed by ≥1 criterion with cumulative incidence of first-line ART failure by all definitions at 1, 3, 5 and 7 years of was 8.6% (95% CI: 8.4-8.8), 21.7% (95% CI: 21.4-22.0) and 28.8% (95% CI: 28.4-29.2) respectively. Virologic monitoring accounted for the fewest failures (1.5%) and lowest change in regimen (CIR) over time due to poor accessibility to testing at most sites while immunologic monitoring accounted for the most failures (12.3%) and the highest CIR after 3 years but similar CIR to clinical monitoring in years 1-3. Change to second-line ART was made in 2,545 patients. Virologic failure resulted in the highest rates of ART change at one year (CIR 0.435) compared to clinical and immunological failure (CIR 0.064 and 0.105 respectively) and the fewest deaths and loss-to-follow-up (LTFU). The hazard of change to second-line decreases with each one year increase in patient age, each one cell increase in CD4 count and decreases with WHO stage III/IV classification. Facility-level factors influencing the hazard of first-line failure or change to second-line ART are still under analysis.

**Concept 45:** “Clinical characteristics and outcomes of adolescents attending HIV clinics in IeDEA East Africa”.

This project is led by Dr. Nuwagaba-Biribonwoha, Columbia University and ICAP, and is supported by Dr. Kiragga at IDI. Revision of datasets are in process as it a revision of the analysis and it is anticipated that the statistical analysis will be completed during the summer of 2016 and a manuscript will be submitted by the end of 2016.

**Concept 53:** “Switching of ART to second- and third-line regimens: a global view”

This is a multi-regional concept led by Dr. Egger of the Southern African Region.
The manuscript entitled “Monitoring and Switching of Antiretroviral Therapy in sub-Saharan Africa: Collaborative Analysis” was published in Lancet-HIV16.

**Concept 54:** “Treatment outcomes on first-line, second-line and third-line ART: a global view”

This is a multi-regional concept led by Dr. Egger of the Southern African Region. The East African data was transferred in May, 2013.

**Concept 56:** “HIV among adults aged 50 years and older over the continuum of care (testing and diagnosis, clinic registration and ART initiation) in East Africa: characteristics treatment outcomes, co-morbidities, and ART toxicities”

This project is led by Dr. Easterbrook. Analysis datasets for this project were finalized in October 2013 and statistical analyses have been completed and are in the process of being reviewed with the intention of finalizing all analyses during the summer of 2016 and having a manuscript completed for submission by the end of 2016.

**Concept 58:** “Adherence to antiretroviral therapy (ART) for HIV-infected children and adolescents followed in Global IeDEA sites”

This is a multi-regional analysis led by Dr. Vreeman. A description of this project was provided in the Year 9 Progress Report. An abstract entitled “Models of support for disclosure of HIV status to infected children and adolescents in resource-limited settings” was accepted for poster presentation at IWHOD 201617. An abstract entitled “Adherence Measurement and Support Services for HIV-infected Children and Adolescents Followed in Global Sites of the International Epidemiologic Databases to Evaluate AIDS (IeDEA)” with the site-level descriptions was accepted for a poster presentation at the 21st International AIDS Conference 17, as well as an abstract within the abstract book for the International Pediatric HIV Workshop in Durban, South Africa. Patient-level data have been submitted, processed and fully cleaned from Central Africa, CCASAnet, Asia-Pacific, and East Africa. Clean-up queries have been sent to Southern Africa and we are awaiting response and revised datasets. West Africa has completed the site surveys but will not be participating in the patient-level portion as no adherence data are available within the region. We hope to have all patient-level data ready for analysis by June 2016, to have analyses completed by the end of 2016, and manuscript submitted for review in early 2017.

**Concept 62:** “2014 Update of concept-Immunodeficiency at the start of ART: a global view”

This is a multi-regional analysis led by Southern Africa. The manuscript “Immunodeficiency at the start of ART in children: A global view” led by Mary-Ann Davies is currently being circulated to co-authors and it is anticipated that it will be submitted for publication in the summer of 2016.

**Concept 63:** “Disparities in the overall and cause-specific mortality between HIV-positive women from Europe, North America and sub-Saharan Africa”

This is a multi-regional analysis led by Dr. Julia del Amo. East African IeDEA submitted data for this project in November 2015.

**Supplement for HIV/AIDS implementation science in PEPFAR:** “Engagement in care among HIV-infected patients in resource limited settings: A Protocol for Assessing the Magnitude of and Reasons for Failure to Engage in Care among HIV-infected Patients in the East Africa International Epidemiologic Databases to Evaluate AIDS (IeDEA) Consortium”

This is Concept 52 and is led by Drs. Geng and Martin at UCSF. All data collection is complete and data analysis and manuscript preparation are underway. In the past year, two manuscripts were published: “Patient-
reported factors associated with reengagement among HIV-infected patients disengaged from care in East Africa” in *AIDS*; and “Retention in Care and Patient-Reported Reasons for Undocumented Transfer or Stopping Care Among HIV-Infected Patients on Antiretroviral Therapy in Eastern Africa: Application of a Sampling-Based Approach” in *Clinical Infectious Diseases*. Another analysis entitled “Structural, psychological and clinic-based barriers to re-engagement among patients lost to follow-up from HIV care in Eastern Africa” was presented in abstract form.

**Supplement from NIDA Concept #81:** “Prevalence and Impact of Alcohol Use in Patients Enrolling in HIV Care: An East African International Epidemiologic Databases to Evaluate AIDS (IeDEA-EA) Project”

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Hazardous drinkers (25%)</th>
<th>Non-hazardous drinkers (75%)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>125/193 (65%)</td>
<td>173/572 (30%)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Married</td>
<td>89/136 (65%)</td>
<td>272/414 (66%)</td>
<td>0.9559</td>
</tr>
<tr>
<td>HIV status disclosed</td>
<td>77/135 (57%)</td>
<td>191/342 (56%)</td>
<td>0.8136</td>
</tr>
<tr>
<td>WHO Stage III/IV</td>
<td>34/176 (19%)</td>
<td>76/515 (15%)</td>
<td>0.1534</td>
</tr>
</tbody>
</table>

**At 6-month follow-up**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Hazardous drinkers (25%)</th>
<th>Non-hazardous drinkers (75%)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LTFU and tracked</td>
<td>51/193 (26%)</td>
<td>129/572 (23%)</td>
<td>0.2728</td>
</tr>
<tr>
<td>In care elsewhere</td>
<td>21/40 (53%)</td>
<td>52/99 (53%)</td>
<td>0.9978</td>
</tr>
<tr>
<td>Not in care</td>
<td>16/40 (40%)</td>
<td>38/99 (38%)</td>
<td>0.8595</td>
</tr>
<tr>
<td>Died</td>
<td>3/40 (8%)</td>
<td>9/99 (9%)</td>
<td>&gt;0.9999</td>
</tr>
</tbody>
</table>

**Table 4: Age and CD4 count at enrollment**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Hazardous Drinkers</th>
<th>Non-Hazardous Drinkers</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>At Enrollment</td>
<td>N</td>
<td>Mean</td>
<td>Median</td>
</tr>
<tr>
<td>Age</td>
<td>193</td>
<td>35</td>
<td>33</td>
</tr>
<tr>
<td>CD4 Count</td>
<td>114</td>
<td>372</td>
<td>344</td>
</tr>
</tbody>
</table>

This project is led by Drs. Wools-Kaloustian and Goodrich. This project was described in the Year 9 Progress report and data collection was completed in Year 9. Data analysis for Aim 2 is underway and a manuscript is expected to be complete by June 2016. Data analysis for Aims 1 and 3 will be complete by mid-2016. An abstract entitled “Prevalence of hazardous alcohol use, characteristics and retention in care of adults newly enrolling in HIV care in the East Africa IeDEA cohort” was submitted to IAS but was not accepted for presentation. It was however accepted as a poster at the University of Nairobi HIV/AIDS Collaborative Meeting in January 2016. Initial results showed that of the 765 patients (39% male) analyzed at 3 EA-IeDEA consortium sites, 25% had AUDIT scores consistent with hazardous drinking and 75% with non-hazardous drinking. Significantly, males were 65% of hazardous drinkers but only 30% of non-hazardous drinkers. There was no significant difference in marital status, HIV disclosure, WHO stage III/IV at enrollment, distribution of CD4 count or being LTFU between the two groups. Among patients LTFU who were successfully tracked, there were no significant differences in their care status.
Collaborations with international organizations within specific aim 1:

World Health Organization:

The East Africa IeDEA Consortium has also actively participated in discussions with the World Health Organization (WHO) for support of the WHO Strategic Information (SI) initiative. Discussions with the WHO were initiated by Dr. Matthias Egger from the IeDEA Southern Africa region and five projects of mutual interest between the IeDEA Collaboration and the WHO have been identified. The East Africa region is supporting the Southern Africa region in East Africa’s area of expertise, Retention in Care, by providing the WHO with corrected estimates of retention in care, based on work completed as part of an administrative supplement assessing the rates of retention in care by five sites within the East Africa IeDEA Collaboration. It should be noted, that East Africa is the only region with available data on retention in care after patients are lost to a program (through data collected as part of the aforementioned supplement plus data available from patient outreach performed as part of routine care in 2 sites within the region). Experience with retention in care and results from the administrative supplement have resulted in a major paper describing the estimated mortality in the region (see Figure 3 from this paper). As shown in Figure 4 below, mortality is substantially under-reported in the region resulting in a number of frequently unanticipated biases well beyond those related to underestimation of mortality. These results suggest that extreme caution has to be exercised when attempting to estimate mortality data under high rates of loss to follow-up. We have worked closely with Dr. Denis Nash from Central Africa to address estimates of retention in care prior to ART initiation in all IeDEA regions to use our expertise with outcome misclassification (see Bakoyannis and Yiannoutsos, PLoS ONE, 2015) to augment these analyses, since our method is closely relevant to under-reporting of the competing events of death and/or disengagement from care prior to ART initiation when retention in care and ART start are the ultimate endpoints to be estimated.

Having these data available is the only way to inform WHO’s “90-90-90” initiative (90% of all people living with HIV will know their HIV status, 90% of all people with diagnosed HIV infection will receive sustained antiretroviral therapy and 90% of all people receiving antiretroviral therapy will have viral suppression by 2020). The definition of the above initiative, requires that 90% of people with HIV will be receiving antiretroviral therapy somewhere, which implies that individuals who have left one program but are receiving treatment elsewhere (and, unless they have formally transferred, they are lost to follow-up with respect to this program), are still retained in care and are part of the 90% on sustained antiretroviral therapy envisioned by the WHO. Thus, if, as it has been suggested, retention in care is defined as loss to program (or, conversely, as retention in care at the original treatment program), the rate of retention will be underestimated, possibly significantly. The East Africa IeDEA region has led the way in undertaking ground-breaking research in delineating the frequently inadequately understood difference between loss to follow-up (or loss to program), retention in care and engagement in care (the latter two terms being similar but focusing on the program and on the patient respectively).
A related issue, identified as an area of mutual interest by the WHO and IeDEA, is long-term survival of HIV-infected patients. Again, this is an area where the East Africa IeDEA Regional Consortium will contribute significantly, as correct estimation of survival (“long-term” or otherwise) is a function (complement) of mortality, and thus requires complete ascertainment of death among HIV patients. Short of that, mathematical corrections must be applied based either on speculation (sensitivity analysis) or data external to the study. The East Africa IeDEA Consortium has developed a number of methods to correct for the incomplete ascertainment of death, due to the high rate of loss to program observed in our region, most recently resulting in a statistical publication22 (see Figure 6).

UNAIDS:

UNAIDS periodically issues a new version of their software Spectrum, (http://www.unaids.org/en/dataanalysis/datatools/spectrumep2013), which generates estimates of various characteristics of the epidemic (there are several examples of country-level reports in the above web site). Dr. Yiannoutsos and Ms. Musick have previously worked closely with other IeDEA regions and the UNAIDS to provide inputs for the Spectrum software, with respect to mortality of HIV-infected adults. The result of the original collaboration, which involved all seven IeDEA regions in Africa, North and South America and Asia Pacific, plus the Collaboration of Observational HIV Epidemiological Research in Europe (COHERE) and EuroSIDA in Europe, culminated in a major article in the Journal of Sexually Transmitted Infections23. UNAIDS approached IeDEA for a similar effort with respect to HIV-related mortality in pediatric and adolescent populations around the world. The request was made in early fall of 2014 for the release of the new version of the Spectrum software in early 2015. The East Africa Regional Data Center was able to leverage the experience and analytical software that was created for the 2012 adult Spectrum analyses, plus an existing multi-regional concept proposal, submitted by Dr. Annette Sohn, of the IeDEA Asia Pacific region, which endeavors to assess, among other issues, pediatric and adolescent mortality. The East Africa Regional Data Center collected data from five of the six participating regions (West, Central and East Africa, plus South America and the Caribbean and Asia Pacific) and provided the analysis files to Dr. Mary-Ann Davies at the Southern Africa IeDEA region so that she could perform the same analyses with Southern Africa IeDEA Data. Mortality estimates resulting from these analyses were submitted to the Futures Institute (now Avenir Health), which compiles these data for the new Spectrum implementation. A white paper summarizing the results from the five regional data analyzed by Dr. Yiannoutsos was created. A manuscript, under the lead of Dr. Sohn is in development. Some of the results of the analyses provided by Drs. Yiannoutsos and Davies were summarized by Dr. Mary Mahy of the UNAIDS Evidence, Strategy and Results Department, in a meeting organized by the Collaborative Initiative for Paediatric HIV Education and Research (CIPHER) at the conclusion of the 18th International Workshop for HIV Observational Cohorts (IWHOD) in Catania Sicily in 2015 and have been incorporated in a subsequent report by the UNAIDS. This report, which revised downward, by 40%, the fast-track target of the number of children that will need ART within the next five years.

The first paper from this effort, under preparation with analytical support by by Drs. Yiannoutsos and Davies, deals with mortality in infants and pre-teen children (ages 0-9 years) is in preparation and may be included in a UNAIDS-sponsored supplement to be published in AIDS, or proposed as a stand-alone publication. A second paper, which addresses mortality in adolescents and young adults (ages 10-19 years) is also contemplated.

In 2015 UNAIDS requested an update of the worldwide mortality estimates for the 2016 revision of the Spectrum software. IeDEA responded and took advantage of software which had been developed by Drs. Leigh Johnson, Andrew Boule of SA-IeDEA and Yiannoutsos of EA-IeDEA and used data available from the retention in care projects undertaken earlier in the year within the scope of the IeDEA-WHO collaboration, to produce estimates of mortality from 6 of the 7 IeDEA regions (North America being the only region not included in this analysis). This work, which was led by Nanina Anderegg of the University of Bern and SA-IeDEA and Dr. Yiannoutsos of EA-IeDEA, resulted in international mortality estimates which will be used in the 2016 version of the Spectrum. The estimates are using a similar methodology as in 2012 to adjust for death under-reporting, which was based on inflation factors resulting from vital-registry linkage data in the Republic of South
Africa (and, in EA-IeDEA, patient tracing), will be published in a UNAIDS-sponsored supplement in the journal AIDS.

UNAIDS is in discussions with Dr. Yiannoutsos and Bakoyannis from EA-IeDEA for methodological work to improve the mortality estimates which will be incorporated into the 2017 version of the Spectrum software. A major upgrade in the new version is methodology which will be able to incorporate CD4 counts after ART initiation (a critical need as follow-up on patients around the world is expanding) and which will be able to take into account death under-reporting. Dr. Yiannoutsos gave a preliminary report at the UNAIDS Reference Group meeting in London, UK in October, 2015, providing a first proposal for a method that would handle these requirements. A second, improved method was presented by Drs. Yiannoutsos and Bakoyannis at the meeting of the Measurement and Surveillance of HIV Epidemics (MeSH) Consortium, a Gates-funded organization based in the London School of Hygiene and Tropical Medicine, which is supporting the work. More recently, work was presented by Drs. Bakoyannis and Yiannoutsos at the most recent IWHOD Conference in Budapest, Hungary and at the most recent UNAIDS Reference Group meeting in Geneva. The methodology, which is based on an adjusted multi-state Markov model (which corresponds to the structure of the Spectrum software) and which addresses the issue of death under-reporting while taking into account longitudinal CD4 in the definition of the transition states, was approved by the Group and will form the core of the mortality estimation methodology of the new version in 2017. Dr. Yiannoutsos is putting together a multi-regional concept proposal for approval by the IeDEA EC, to elicit data from all IeDEA regions for this project. A paper from the work presented at IWHOD and multiple papers involving the methodology development are in progress.

CIPHER:

Dr. Wools-Kaloustian continues to work with the Collaborative Initiative for Paediatric HIV Education and Research (CIPHER) to complete two projects: “Duration of first-line antiretroviral regimens in children: a global perspective” (Concept 59) on which she serves as the scientific Co-Chair and “Global epidemiology of adolescents with perinatal HIV-infection” (Concept 61). Dr. Vreeman is also working with the CIPHER analyses and has been asked to be the scientific co-chair for a new CIPHER concept, “Outcomes associated with second-line antiretroviral regimens in children: A global perspective.” In the last year, Dr. Vreeman has been invited to serve on the CIPHER steering committee, as well as the scientific organizing committee for the International HIV Pediatrics Workshop and the organizing committee for the 2nd Adolescent Transition Workshop (all of which are IAS/CIPHER-sponsored.)

Analytic datasets have now been completed for the Duration of First-line and the Adolescent concepts. Data Analysis is currently underway at the CIPHER affiliated data centres.

Administrative Supplements initiated 2014-2015

“Prospective validation of an adherence monitoring tool among HIV-infected children and adolescents at IeDEA sites-ICAMP”

This is a multi-regional project led by Dr. Vreeman from the East Africa Region was described in detail in the Year 9 Progress Report. This project is referred to as the IeDEA Comprehensive Adherence Measure for Pediatrics (ICAMP).

In the last year, all sites (Busia Health Clinic, AMPATH, Busia Kenya; HIV-NAT Clinic, TREAT Asia Network, Bangkok, Thailand and; Empilweni Services Research Unit, Rahima Moosa Mother and Child Hospital Johannesburg, South Africa) recruited cohorts of approximately 110 children for comprehensive adherence measurement in the validation study. The Thai site has finished 6 months of follow-up for their cohort, including collection of MEMS data, adherence questionnaire data, viral loads, and clinical database extraction. An abstract describing the adherence among this cohort alone is being prepared for submission to the
International Pediatric HIV Workshop. The Kenya site has only two assessments remaining before the cohort will finish their 6 months of follow-up. All data have been entered into the study REDCap database as the study has progressed, and the cohort’s data are anticipated to be ready for analysis within the next 6 weeks. The South Africa site had delays in the IRB approval process which led to delays in project initiation, but they have now recruited all of their participants, and their 6 months of follow-up will conclude in June of 2016. The ICAMP study aims to have study participant follow-up finished by July of 2016, with datasets ready for analysis by September of 2016.

“Point of Care CD4 testing for people who fail to engage in care after testing HIV positive”

This supplement is led by Dr. Paula Braitstein. This study was described in detail in the Year 9 Progress Report. This project has been delayed due a change in the USAID testing paradigm. Under current USAID policy, the focus on HIV testing has moved from the community back to the clinic. As such USAID refuses to allow any HIV counselors to do home-based counseling and testing. As a consequence, individuals who were trained and had started tracing in the community, were moved out of the community and into facilities to increase testing rates. As such, we had to hire three additional HIV counselors (through other funds we purchased a third point-of-care CD4 testing machine so have added a third counselor), through the county of Busia. However, the County Health Coordinator wanted the original counselors (who had been moved to facility testing) to do the tracing because they were more knowledgeable about the community and much less likely to accidentally disclose someone’s HIV status. This required official and documented swapping of staff between the USAID AMPATHplus program and the study. As of this report, we have two counselors in place and have started tracing again.

“Implementation of Causal Modeling Technology to Assess and Improve the Effects of Antiviral Therapy in Children”

This project is led by Joseph W. Hogan, ScD at Brown University and head of biostatistical research at AMPATH. This project was described in detail in the Year 9 Progress Report. The team used a large subset of the AMPATH data to develop the methods for this project. The EA-IeDEA dataset is in process and will be delivered by June 20, 2016.

**Concepts Initiated 2014-2015**

**Concept 66: "Developing global surveillance estimates for perinatally infected adolescents on antiretroviral therapy transitioning to adulthood"** SPECTRUM (See Collaborations with international organizations within specific aim 1)
The above results, produced by Dr. Yiannoutsos, correspond to preliminary work on this concept and were completed in January 2015. Figure 5 above is from a presentation by Dr. Mary Mahy, Epidemiology Consultant at the UNAIDS, presented at the meeting of Collaborative Initiative for Pediatric HIV Education and Research (CIPHER) at the periphery of the most recent IWHOD conference.

As noted previously, two manuscripts summarizing the mortality among infants and small children (ages 0-9 years of age) and pre-teen and adolescents (ages 10-19 years of age) are in preparation under the coordination of Dr. Annette Sohn of the Asia Pacific region. We expect that the first of these will be submitted by mid-summer 2016.

**Concept 67: “SiZER maps to investigate significant features of weight changes in HIV-infected patients”**

This “spin-off” paper from **Concept 15** addresses whether d4T-based regimens at ART initiation are associated with shorter-term weight change compared to non-d4T-based regimens. This analysis, done as part of Dr. Sarwat’s doctoral dissertation, is described in detail in the Year 9 Progress Report. The analysis is complete and it is anticipated that a manuscript will be completed for submission in 2016.

**Concept 68: "Changes in the comprehensiveness of care provided at HIV care and treatment programs in the IeDEA collaboration from 2009 to 2014."**

This multi-regional proposal led by Cristin Quinn with the INCC was describe in detail in the Year 9 Progress Report. East Africa IeDEA has not received a recent update on the progress of this manuscript.

**Projects Initiated 2015-2016**

**A Qualitative study of bottlenecks in access to HIV care and treatment in Kisesa, Tanzania Study**

This study is led by J. Waymoi and M. Urassa at Kisesa. The overall aim of this study is to explore HIV patients’ interactions with health services in the Kisesa cohort study area in Tanzania, in the context of a larger multi-country study taking place in seven HIV community cohort sites in the ALPHA network in Eastern and Southern sub-Saharan Africa, to understand how differences in HIV programs influence patients use of these
services and their health outcomes. The community cohort studies contributing to the ALPHA network offer a unique opportunity to understand the importance of context in influencing attrition through the cascade, and ultimately differences in mortality in relation to service use. Not only is the network able to trace infections, diagnoses, contact with treatment services and deaths occurring in the surveillance populations, the cohort and linked clinic data also enable sampling frames to be developed that can identify and trace those who have lost contact with the HIV care services altogether, including the families of infected individuals who have died.

This study utilized a qualitative approach to investigate how differences in HIV policy and program implementation influence the health care-seeking experiences of people living with HIV through the continuum of HIV care in Eastern and Southern Africa. This research complements ALPHA's ongoing work on HIV-related mortality estimates through the cascade within the HDSS, as well as the policy and practice reviews being conducted within each HDSS site.

The qualitative design involved in-depth interviews and seeded focus group discussions with people living with HIV/AIDS (PLHA). Specifically, in-depth interviews were conducted with: PLHA, health health workers and families of the deceased. Seeded group discussions were conducted with PLHA diagnosed but not initiated on ART. Analysis of data was done with the aid of NVIVO software.

Data collection and transcription is complete. Data translation is largely complete with 46 out of the 51 interviews translated and the remaining six undergoing translation. Final report is expected the end of June 2016. An abstract from this project entitled Understanding the relationship between couple dynamics and engagement with HIV care services: Insights from a qualitative study in a rural Tanzania setting was accepted as a poster at IAS 2016.

**Concept 70** "Age-, CD4-, and viral load-stratified rates of opportunistic infections and mortality in youth ages 0-24: Descriptive analyses and derivation of inputs for simulation models"

This is a multi-regional concept being led by Ms. S. Desmonde of West Africa. East Africa IeDEA is updating the datasets for this project and continues to work closely with Ms. Desmonde with regard to data interpretation. The group meets on a monthly basis and has received data from all regions. They are in the process of harmonizing and preparing analysis datasets. In order to obtain more information about the completeness of the OI data obtained, they have submitted a brief supplemental site-level questionnaire to the regional data managers. Preliminary analyses are already underway with analysis datasets expected to be ready by early August 2016.

**Concept 74:** “Empirical evaluation of propensity score matching utilizing IeDEA observational cohort data evaluating 48-week treatment outcomes among ART-treated adults”

This is a multi-regional concept being led by Dr. Rutherford with the INCC. The dataset from East African IeDEA has been delivered for analysis. Preliminary analyses have been conducted which resulted in an oral presentation titled “Comparison of 48- and 96-week outcomes in adults initiating tenofovir + lamivudine/emtricitabine + efavirenz and those initiating two other nucleoside reverse transcriptase inhibitors + efavirenz using propensity-score matched IeDEA observational cohort data and data from randomised controlled trials” at IWHOD in April 2016.

**Concept 76: IeDEA-WHO Collaboration: Global analysis of delays from ART eligibility to antiretroviral treatment initiation among adults**

This is a multi-regional concept being led by Dr. Nash with analytical assistance from Dr. Yiannoutsos. This analysis has been completed and has informed the 2015 WHO guidelines and resulted in two IWHOD 2016 abstracts: 1) “Cumulative incidence of ART initiation at the original clinic of enrolment: An analysis of IeDEA network data from 241 clinics in 28 countries, 2004-2014” for a poster presentation 2) “Loss to clinic prior to
ART initiation among patients enrolling in HIV care in the IeDEA network, 2004-2014” for an oral presentation. The IeDEA consortium is currently in the midst of discussions about how best to move forward with manuscript development for this concept.

**Concept 80: Increases in Regimen Durability Associated with the Introduction of Tenofovir in Adults on standard first-line ART in the International IeDEA Cohort**

This is a multi-regional concept led by Dr. Brennan. The analysis has been completed and has resulted in a poster presentation at IWHOD 2016, “Have changes in WHO guidelines led to more stable first-line treatment in sub-Saharan Africa?” and a manuscript submitted to AIDS in May 2016 entitled “Has phasing out stavudine in accordance with changes in WHO guidelines led to a decrease in single-drug substitutions in first-line ART in sub-Saharan Africa?”

**Concept 82: Update of mortality estimates of HIV-infected patients for Spectrum is a multiregional concept being led by Dr. Yiannoutsos**

Refer to section “UNAIDS” on Page 11 for a detailed description of this project.

**Concept 82A: Adjusting for incomplete failure ascertainment in joint models: A multiple imputation approach**

This is a multiregional concept being led by Dr. Yiannoutsos. A first attempt to incorporate longitudinal measurements was presented in the October 2015 meeting of the UNAIDS Reference Group by Dr. Yiannoutsos. This involves a joint model of longitudinal CD4 count and a survival model. The novelty of the approach is that the survival model includes imputed vital status information on the patients who have not been outreached, produced by a model constructed on similar (in terms of various measurements obtained prior to dropout) patients who disengaged from care and were subsequently traced within the community. The results given in the two figures below (which come from Dr. Bakoyannis most recent IWHOD presentation).

Multiple imputation is a way to straightforwardly incorporate external evidence obtained from patient outreach into the estimation method. The results presented in Figure 6 shows how patient risk can be differentiated by incorporating interim results (such as CD4 count after ART initiation) into the calculations and confirms the impact of unreported death in the estimation of mortality.

**Concept 82B: Adjusting for incomplete failure ascertainment in multi-state markov models**

This multiregional project is being led by Drs. Bakoyannis and Yiannoutsos and was presented in the most recent UNAIDS Reference Group meeting held in Geneva Switzerland in May 2016. This work uses multiple
imputation and a novel approach to semi-parametric (i.e., Cox) modeling to both incorporate the evidence from external (double-sample/patient outreach) data and address computational issues inherent in multi-state modeling. The two following tables drive home the point of both the revision that is being effected by correct information and the outputs from the models.

In Figure 7, note the direction of the bias in mortality estimation and estimation of disengagement from care (a critical aspect of the 90-90-90 UNAIDS/WHO guidelines). The observed data analysis hopelessly underestimates true mortality and over-estimates disengagement from care (because many unreported deaths are misclassified as disengagements), while complete-case analysis dramatically underestimates disengagement from care (because many true disengagements are classified as censored observations).

![Figure 7](image)

**Figure 7.** Transition probabilities of mortality (left panel) and disengagement from care (right panel). Red line is the naïve (unadjusted estimator based on only available data); black is the proposed estimator and dashed black curve is the estimator resulting from considering all known deaths into the model (complete-case analysis).

**Concept 83:** Statistical designs and methods for double-sampling for HIV/AIDS Studies

This project is being led by Drs. Bakoyannis and Yiannoutsos. This is an umbrella concept for a number of modeling approaches to incorporate external data into the modeling of interval-censored data, survival analysis and the analysis of competing risk data. A number of papers are under development both within IU and by Dr. Frangakis at Hopkins and numerous papers will be developed over the next 12-24 months.

**Concept 85:** Models of support for disclosure of HIV status to infected children and adolescents in resource-limited settings

This is a multi-regional concept being led by Drs. Vreeman, Arrivé and Ayaya. The objective of this concept was to describe current policies and available interventions to support disclosure of HIV status in pediatric HIV care across the global regions of IeDEA. An online site assessment survey was conducted across the sites caring for children using a standardized questionnaire administered to the sites through the REDCap platform (http://project-redcap.org/) within the multiregional survey about adherence and support services for children and adolescents. The results were presented as a poster at the 2016 IWHOD meeting in Budapest, Hungary. The team is planning to draft a manuscript describing these findings within the next 4 months.
In the findings from across the sites surveyed, which included 180 sites in 31 countries, the clinics were caring for a median of 162 children each (inter quartile range [IQR]=81-351) in the past 12 months. Almost all the sites (98%) reported offering disclosure counseling services. Disclosure resources and procedures varied across regions: specific staff training on counseling for disclosure was done in 72% to 96% of sites, a protocol for disclosure of HIV status to children was available in 14% to 71% of sites, and HIV disclosure status was collected routinely in 50% to 91%. 83% of the sites had at least 3 of the services described above available.

Among the 53 sites (29%) with a formal disclosure protocol, 32 designed it locally and 21 borrowed/adapted from various external sources including 4 from WHO guidelines and 5 from Ministry of Health National ART treatment guidelines and 12 from isolated sources. Disclosure counselling was more often provided by counsellors (87%), but also by nurses (77%), physicians (74%), social workers (68%) or other clinicians (65%). It was offered to both caregivers and children in 92% of the 177 sites. An age for disclosure of HIV status to children was recommended in 79 (44%) of the sites, with recommendations to start at a median of 7 years [IQR:6-9] and end at a median of 14 years [IQR: 12-14]. Caregivers were involved in the disclosure process in 95% of the sites, and counsellors in 87%. 143 sites (79%) are routinely collecting disclosure status.

**Concept 87: Evaluating Global HIV Prevention, Care and Treatment Services available for Children in IeDEA regions (Pediatric site assessment 2.0)**

Dr. Vreeman is leading the multiregional evaluation of the services available for children and adolescents across the IeDEA regions in pediatric site assessment 2.0 in partnership with Dr. Lindegren and the analytic team from Vanderbilt University. In 2009, we assessed available services at sites caring for pediatric patients in 6 global regions of the International Epidemiologic Database to Evaluate AIDS (IeDEA) consortium. Between September 2014 and January 2015, we repeated this assessment, using a web-based survey across IeDEA regions. The surveys asked about facility characteristics and capacity to deliver WHO-recommended pediatric HIV prevention, care, and treatment services. From the site-level data, we created a measure of comprehensiveness of available pediatric care services based on the WHO’s current 9 categories of essential services. In the subset of sites with data from both 2009 and 2014, we evaluated trends in service delivery capacity.

The initial pediatric site assessment findings sought to describe trends in site capacity and comprehensiveness of services among global pediatric HIV care programs between 2009 and 2014. Clinical staff from 172 pediatric sites in 45 countries completed the 2014-2015 site survey. The available services in 2014 varied across regions and sites overall; only 40% of sites provided HIV counseling and testing, whereas 99% offered adherence counseling. Overall, 35% of sites (n=61) offered comprehensive services (8-9 essential services out of 9), while 55% (n=94) offered 5-7 essential services and 10% (n=17) offered only 3-5. In the 2014 survey, the median comprehensiveness score across all of the sites was 7.0 (IQR 6.0-8.0), a significant increase from the median of 6.0 (IQR 4.2-6.0) in 2009 (p<0.001), and the magnitude of change varied by region (p<0.001). The two WHO essential services with most varied provision across global regions were 1) HIV counseling and testing and 2) both CD4 and HIV viral load testing. This global survey demonstrates significant gains in the comprehensiveness of services available for HIV-infected children worldwide, while identifying gaps to target resources.

While the team has received and analyzed the site-level survey findings, they are currently in the process of requesting patient-level variables to examine in comparison with the comprehensiveness of services. Though rejected from IWHOD and the Adolescent Transitions meeting, the 2.0 peds site assessment data have been compiled into an abstract for AIDS 2016 and the Pediatric HIV Workshop30.

**Concept 88: Association between clinic-level factors and individual retention, engagement, and loss to follow up following ART initiation in the IeDEA collaboration from 2009-2014.**
This is a multiregional concept being led by Drs. Riebero and Duda. Details of this project can be found in the Global IeDEA Concept circulated by Dr. Riebero and approved by the EC. The East African Region is in the process of creating a dataset for this analysis and it is anticipated these data will be available at the end of June.

**Concept 89: Pregnancy rates among HIV+ women using various combinations of ART and contraception**

This is a single site concept being conducted with data from AMPATH and led by Dr. Patel. The goal of this concept is to investigate contraceptive failure rates in women taking ART with a particular interest in the interaction between EFV and depo-provera. Final analysis datasets were delivered on 6/8/2016.

**Aim 2: Assess the penetrance and outcomes of PMTCT strategies.**

**Project 2.1: Automating the linkages between mother and infant records.**

Details of this project are outlined in the Year 9 Progress Report. **Concept 69** “ART and congenital anomalies- a systematic review of mother baby data on association of ART and congenital anomalies in Western Kenya” was developed to analyze the data for this project. This concept is being led by Dr. Apondi a Pediatrician at AMPATH and was describe in detail in the Year 9 Progress Report. The dataset for this project is being developed and will be finalized now that the updated Pediatric Data have been submitted to EA IeDEA from FACES. A data analyst will be assigned to this project within the next month.

**Project 2.2: PMTCT program evaluation following the introduction of the 2010 WHO guidelines.**

This project was dropped in Year 9.

**Project 2.3: Long-term outcomes of women exposed to intermittent antiretroviral regimens for PMTCT.**

This project is being addressed under **Concept 35**: The impact of intermittent 3-drug pMTCT on long term outcomes of women initiated on ART for treatment” and is led by Dr. Wools-Kaloustian. After the WHO introduced the 90-90-90 goals it was felt that further pursuit of this analysis would not add value to the literature so this project was dropped.

**Other projects that fall within Specific Aim 2:**

**Concept 8:** “Incidence and determinants of pregnancy in women enrolled in care and treatment programs in East Africa”

This project is led by Dr. Elul. The analyses for this concept have been completed and a manuscript entitled “Untangling the relationship between antiretroviral therapy use and incident pregnancy: Data from 47,313 HIV-positive women in East Africa was accepted for publication by JAIDS in 2016.”

**Concept 46:** “PEPFAR: Programmatic and Clinical HIV Treatment Outcomes in Pregnancy”

This analysis led by Drs. Holmes, Yiannoutsos and Wools-Kaloustian, represents a multi-year collaboration between East Africa IeDEA and the President’s Emergency Plan for AIDS Relief (PEPFAR). The analyses for this project were completed in May 2016. This concept resulted in an oral presentation at IWHOD 2016 titled, “Increased prevalence of pregnancy and comparative risk of program attrition among individuals starting HIV treatment in Africa” in 2016. In addition a draft manuscript has been developed and submission to Lancet HIV is anticipated in July 2016.
This analysis involves 156,474 HIV-infected adults initiating ART between 2004 and 2014, 104,791 (67.0%) of whom were women. Of these, 72,776 (69.4%) were never observed to have a pregnancy (never-pregnant women), and 32,015 (30.6%) were pregnant at least once during follow-up (ever pregnant women). Among women who were ever pregnant, 19,130 (59.8%) were pregnant at ART initiation.

Overall, there was no significant difference in the cumulative incidence of program attrition over two years between pregnant women starting ART and non-pregnant women. However, among women starting ART while healthy (WHO Stage 1 or 2), pregnant women experienced a 9.6% cumulative incidence of program attrition at 6 months, compared to 6.5% in non-pregnant women (absolute difference 3.1% 95% confidence interval – CI – 2.6%-3.6%), a difference that increased by two years of follow-up (Figure 8). By contrast, among women starting ART with advanced disease (WHO stage 3 or 4), pregnant women had lower 6-month attrition rates (8.4%) compared to non-pregnant women (14.4%) (absolute difference 6.0%, 95% CI 4.7%-7.2%).

Aim 3: Monitor the translation of evidence into practice for managing co-infections with an emphasis on Tuberculosis (TB).

Due to the complexities of the TB Treatment programs at AMPATH and Mbarara no significant progress has been made on this project beyond that outlined in the Year 9 Annual Report.

Other projects that fall within Specific Aim 3:

Concept 4: “Impact of HIV-TB integration on TB incidence among persons receiving HIV-care and treatment in East Africa”

This project was initially led by Dr. Tsiouris at Columbia University and then transitioned to Ms. Suzue Saito working under the direction of Dr. Batya Elul. This analysis resulted in a publication in JAIDS entitled, “Declining Tuberculosis Incidence among People Receiving HIV Care and Treatment Services in East Africa, 2007-2012”.
Multi-regional Project: “Collection of key tuberculosis (TB) variables in ART programs within the IeDEA consortium: diagnostics, treatment and risk factors for incident TB”

This multi-regional project is being led by Drs. Pettit and Sterling from CCASAnet. Four programs within East Africa took part in this project including: AMPATH, Kenya; Masaka Hospital, Uganda; Kisesa Clinic, Mwanza, Tanzania; and Tumbi Regional Hospital, Kibaha, Tanzania. A number of concept sheets utilizing these data have been developed and are listed below. The patient level data needed to complete these analyses were sent from East African IeDEA on Jan 8, 2016.

- **Concept 71**: “Diagnosis and Treatment of TB HIV co-infected children” is led by Marie Ballif from the IeDEA-Southern Africa. This analysis resulted in the poster entitled “TB Treatment Outcomes for HIV/TB co-Infected Children in Resource-Limited Countries” at CROI 2016.  

- **Concept 72**: “Management of tuberculosis in HIV-infected pregnant women” is led by Marie Ballif.

- **Concept 78**: “Evaluation of Xpert MTB/RIF implementation among HIV programs in the IeDEA Consortium” is led by Kate Clouse. It has resulted in an oral presentation “Low implementation of Xpert MTB/RIF among HIV/TB co-Infected adults,” at the 46th Union Conference on Lung Health, in December 2015.

- **Concept 79**: Collection of key Tuberculosis (TB) variables in ART Programs within the IeDEA consortium: diagnostics, treatment and risk factors for the incident TB. This project is led by April Pettit.

- **Concept 97**: “Diagnosis, treatment and outcomes of extra-pulmonary Tuberculosis in HIV-co-infected adults and children led by Marie Ballif is a recently approved concept.

- **Concept 98**: “Description and outcomes of HIV-infected patients treated for tuberculosis without microbiological confirmation in HIV care programs within the IeDEA Consortium” led by Dr. S. Goodrich is a recently approved concept.

Multi-regional Project: “Impact of HIV infection on the population genomics of drug-resistant Mycobacterium tuberculosis: insights from macro-evolutionary analyses”

This project is led by the IeDEA Southern African Region. East Africa has completed enrollment, Redcap data entry and has shipped all specimens to Switzerland.

Administrative Supplement:

Multi-regional Project: “Liver Disease in HIV program survey”

This is a multiregional project led by Gilles Wandeler representing the West and Southern Africa Regions. Details of this project were outlined in the Year 9 Progress Report. This project is also detailed in Concept 73. Two East African sites participated in the chart review (IDI, AMPATH) and seven sites completed the site survey (IDI, AMPATH, Morogoro, ORCI, Kisesa, FACES, Mbarara). All data from EA have been transferred to Southern Africa for analysis. This concept has resulted in two posters 1) “Changes in Viral Hepatitis Screening Practices over Time in African HIV Cohorts” presented at CROI 2016 and 2) The HIV/AIDS Department Hepatitis Programme presentation at the WHO Testing guideline Meeting in Oct 2015.

Aim 4: Determine the prevalence, incidence, determinants and outcomes of malignancies in East Africa with a focus on Kaposi’s sarcoma and cervical cancer.

**Project 4.1: Epidemiology of Kaposi’s sarcoma (KS) in the ART era**

Details of this project are outlined in the Year 9 Progress Report. In summary under the auspices of this project, KS biopsy services have been established at AMPATH, Mbarara, IDI, and Masaka. By helping to confirm the diagnoses of KS, we have been able to facilitate the conduct of translational research of the etiology of the cancer. Specifically, Dr. Helen Byakwaga of Uganda, who is mentored by Dr. Martin, has
identified an association between two heretofore unstudied biomarkers with KS. She found that activity of the enzyme indoleamine 2,3-dioxygenase (IDO), as measured by plasma kynurenine/tryptophan ratio, in a publication in *JAIDS* \(^{38}\), as well as plasma levels of the high mobility group box 1 (HMGB1) protein (in abstract form) are both associated with occurrence of KS.

Having firm KS diagnoses has also made it possible for us to formally study the accuracy of clinical diagnosis as well as the incidence in of East Africa, with a level of accuracy and precision that has rarely been performed in the region \(^{39-41}\). It also allowed for a qualitative study of reasons why patients with KS became lost to follow-up, these data were presented at the 15th International Conference on Malignancies in AIDS and Other Acquired Immunodeficiencies \(^{42}\).

**NCI Supplement:** “Survival among HIV-infected individuals with Kaposi’s Sarcoma in Sub-Saharan Africa in the era of potent antiretroviral therapy”.

Details of this project led by Drs. J. Martin and S. Aggrey are outlined in the Year 9 Progress Report and Concept 84. In summary, three groups of HIV-infected adults receiving care, were identified at each of the participating programs. The first group included patients with newly diagnosed KS while not yet on ART, and this group was compared to: a) patients with newly diagnosed tuberculosis or cryptococcosis while not yet on ART (“Serious OI group”); and b) patients first meeting eligibility for ART by CD4 count criteria but with no prior WHO Stage III/IV diagnosis (“CD4 group”). Patients were followed until death or administrative database closure. Among those LTFU (defined as absent from clinic for at least 3 months since expected return date at the time of database closure), all those in the KS group were tracked in the community to update vital status as well as a random 15% sample of the Serious OI and CD4 groups. Outcomes among the random sample of patients tracked were incorporated via probability weights into subsequent analyses. Results of these analyses were presented at the 15th International conference on Malignancies in AIDS and Other Acquired Immunodeficiencies \(^{43}\). “Pitfalls of practicing cancer epidemiology in resource-limited settings: the case of survival and loss to follow-up after a diagnosis of Kaposi’s sarcoma in five countries across sub-Saharan Africa” was published in BMC cancer in 2016 \(^{44}\). Two other analyses emanating from this project were also presented in the past year. The first was an investigation as to how fast antiretroviral therapy is started after diagnosis of KS \(^{45}\), and the second was a study of the barriers to retention to care after KS diagnosis \(^{46}\).

**Project 4.2:** “Assess the prevalence and determinants of high-grade cervical dysplasia and cervical cancer as well as compare treatment modalities”.

This project is currently being led by Dr. Wools-Kaloustian and Dr. Omenge. **Concept 100** “Rates of Cervical Cancer Screening Uptake and Predictors of VIA Positivity among Women in a Rural Western Kenya” is currently being circulated in the East African has been developed and approved and a formal data request has been submitted to AMPATH for these data. The FACES data have been received and our summer intern Josh Love is processing these data under the supervision of Ms. Musick.

**Other projects that fall within Specific Aim 4:**

**Concept 57:** “African Network for Cervical Cancer Screening and Treatment”

This is a multi-regional concept initiated in collaboration with the CFARs led jointly by Dr. Wools-Kaloustian from East African IeDEA and Dr. Cu-Uvan from the Inter-CFAR collaboration on HIV-Research in women resulted in a publication in the Journal of Lower Genital Tract Disease in early 2016 entitled “An Insight into Cervical Cancer Screening and Treatment Capacity in Sub-Saharan Africa” \(^{47}\).
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The following bibliography includes AMPATH research publications that were published between January 1, and June 30, 2016. A complete bibliography of AMPATH research publications published since 1989 along with full text articles is available online through the AMPATH Research Member Access Portal, www.medicine.iu.edu/ampathresearch/member-access.


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