SEMI ANNUAL RESEARCH REPORT

January – June 2014

Acknowledgements

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www.medicine.iu.edu/ampathresearch

Contents

Overview

The start of the New Year brought steady growth to the AMPATH Research program. This report includes updates from more than 60 research studies active in the AMPATH catchment area. A number of new studies started work in the first half of 2014 adding nearly US$ 3.15 million in new awards to AMPATH's research portfolio.

AMPATH investigators produced more than 25 peer reviewed publications in the first six months of 2014 – more than reported in the same period last year. Participation in national and international research conferences continues to be strong and efforts continue to disseminate key research findings to policy makers around the world.

The following report includes updates from research studies at AMPATH along with brief updates on the status of funding for research and publications produced in the first 6 months of 2014. It was compiled with the assistance of AMPATH investigators, research coordinators, and assistants from more than 15 institutions in Kenya and North America. We begin the report with a brief summary of AMPATH research funding awarded in 2014 and continue with a description of the publications produced during the year. We conclude with brief project updates provided by AMPATH investigators and listed alphabetically by the study title.

Please visit the AMPATH Research Network Website to download a copy of this and past reports, www.medicine.iu.edu/ampathresearch.

Grants

Since the start of 2014 less than half a dozen new studies have been reported. However, these new studies have been awarded nearly US$3.15 million in direct costs. All of these new awards were made by the NIH and most of these new awards support research in oncology and non-communicable diseases. The addition of these awards brings the total level of program direct awards to more than US$ 86.5 million since the program received its first research award in 1998 (See Figures 1-3).

Publications

AMPATH investigators published 25 manuscripts in peer reviewed journals during the first half of this year. This continues previous trends and has increased the total number of publications to 314 (See Figure 4). A bibliography of publications for the first 6 months of 2014 is included at the end of this report.

In addition, the AMPATH Publications Committee, which reviews all publications produced from AMPATH research projects, reviewed a total of 79 draft publications. Around 39 percent of the publications reviewed were abstracts and 11 percent were poster presentations presented at professional conferences. Manuscript submissions (47 percent) made-up most of the remaining publications submitted for review (See Figure 5).

Research Project Updates

Study Title	**A Stage 2 Cognitive Behavioral Trial, Reduce Alcohol First in Kenya Intervention (RAFIKI)**
Principal Investigator(s)	Rebecca Papas, Indiana University B. Gakinya, Moi University
Co-Investigator(s)	Maisto, S. Martino, S. Baliddawa, J. Sidle, J. Hogan, J. Carroll, K.
Working Group(s)	Adult (Primary) Behavioral (Secondary)
Description	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.
Site(s)	Iten District Hospital, Moi Teaching and Referral Hospital (MTRH), Turbo Health Centre, Webuye District Hospital
Project Period	11/1/2011 – 8/31/2016
Funding Status	Funded – NIH - National Institute on Alcohol Abuse and Alcoholism (NIAAA)
Direct Award (USD)	$2,268,832
Update	The 5-year RAFIKI RCT, which examines the efficacy of a group Cognitive Behavioral Therapy (CBT) intervention to reduce alcohol use when compared against a group health education intervention, finished its second year of recruitment in June 2014. We have randomized 361 total participants, and have completed recruitment and intervention for cohorts 1-12. In the January-June 2014 reporting period, we recruited and randomized 100 participants. Recruitment and retention are progressing within expectations according to our NIH specific aims. We have had no immediately reportable serious adverse events during the course of this study.
Future Plans	Continue the positive work already being done, while focusing on maintaining strong recruitment numbers.
Publication(s)	

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)	John Sidle, Indiana University Abraham Siika, Moi University
Co-Investigator(s)	Lagat, D.
Working Group(s)	Adult (Primary) Basic (Secondary)
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 subsequents 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)	Moi Teaching and Referral Hospital (MTRH)
Project Period	5/18/2011 – 12/31/2013
Funding Status	Funded – NIH - National Institute of Allergy and Infectious Diseases (NIAID)
Direct Award (USD)	Not Reported
Update	Stage 1 of the protocol was closed to accrual. A total of 96 participants were accrued in all participating sites. Stage 1 data was reviewed for safety and a new protocol amendment released. Version 3.0 of the protocol will allow opening of stage 2 of the study. Submission to IREC was made and the site is awaiting feedback.
Future Plans	17 participants have been enrolled into the study since the beginning. The protocol is on paused status until all required approvals are obtained for version 3.0.
Publication(s)	

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)	Busakhala, N. Njiru, E.
Working Group(s)	Adult (Primary) Basic (Secondary)
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 na- HIV-1 infected participants who are currently not receiving ART
Site(s)	Moi Teaching and Referral Hospital (MTRH)
Project Period	11/28/2012 – 6/30/2014
Funding Status	Funded – NIH - National Institute of Allergy and Infectious Diseases (NIAID) , NIH - National Cancer Institute (NCI), NIH - National Institute of Dental and Craniofacial Research (NIDCR)
Direct Award (USD)	Not Reported
Update	The study is progressing well even though getting patients who meet the inclusion /exclusion criteria is challenging. The site is therefore trying to recruit from locations with high KS prevalence and where KS can be diagnosed early.
Future Plans	A total of 12 participants have been enrolled since the study was opened to accrual at our site.
Publication(s)	

Study Title	**A5265 A Phase III, Open-Label, Randomized, Assessment-Blinded Clinical Trial to Compare the Safety and Efficacy of Topical Gentian Violet to that of Nystatin Oral Suspension for the Treatment of Oropharyngeal Candidiasis in HIV-1 Infected Participants in Non-U.S. Settings**
Principal Investigator(s)	Abraham Siika, Moi University
Co-Investigator(s)	Lagat, D.

Working Group(s)	Adult (Primary) Basic (Secondary)
Description	A5265 is a phase III, open-label, randomized, assessment-blinded clinical trial in non-U.S. sites to compare the safety and efficacy of topical gentian violet (GV) to that of oral nystatin.Therapy will be considered as failed if participants have no clinical improvement (assessed by severity and extent of pseudomembranous candidiasis) during either treatment regimen. Evaluation of signs and symptoms of oral candidiasis (OC) will be done by an evaluator who is blinded to treatment assignment. Quantification of colony forming units (CFUs) of Candida species (spp.) and assessment of the emergence of resistance will be performed using an oropharyngeal swab and a second specimen from oral rinse/throat wash will be collected and stored for future testing.
Site(s)	Moi Teaching and Referral Hospital (MTRH)
Project Period	2/1/2012 – 12/31/2012
Funding Status	Funded – NIH - National Institute of Allergy and Infectious Diseases (NIAID) , NIH - National Institute of Dental and Craniofacial Research (NIDCR)
Direct Award (USD)	Not Reported
Update	A5265 protocol was closed to follow-up in January 2014 because the last participant completed the study on December 12, 2012 and the sponsor decided not to re-open the study due to study feasibility of the proposed re-design.
Future Plans	The study is closed to follow up and therefore no further plans are underway.
Publication(s)	

Study Title	**Chama Cha Mamatoto: Evaluating a Peer Support Mechanism to Improve Maternal and Infant Health**
Principal Investigator(s)	Julia Songok, Moi University Astrid Christoffersen-Deb, University of Toronto
Co-Investigator(s)	Ruhl Laura Fazen Louis
Working Group(s)	Reproductive (Primary) Pediatrics (Secondary)
Description	This project seeks to address a critical fourth delay that sustains high rates of maternal and neonatal mortality in western Kenya: the delay in a community's accountability to its mothers and infants. Community health workers will form groups in the community and educate them twice a month on medical and social topics. In addition, there will be financial component called GISE that enables women to save money and hence cater for their health and other needs. The primary aim of the study is to evaluate: (1) Impact (2) Accountability and (3) Sustainability of chamas in improving uptake of community based maternal and infant health services.

Site(s)	Saboti Sub-District Hospital
Project Period	12/1/2011 – 4/12/2014
Funding Status	Funded – Grand Challenges Canada
Direct Award (USD)	$248,000
Update	Over the last 6 months, there has been a lot of activity involving quantitative and qualitative data collection. Four focus group discussions were held one with each of the following groups;- Chama women, Non Chama women, Provincial administration officials combined with Providers and CHVs facilitating Chamas Quantitative data was also collected for both intervention group and control groups and preliminary analysis ongoing.
Future Plans	Data fully analyzed.
Publication(s)	

Study Title	**Anticoagulation Project**
Principal Investigator(s)	Sonak Pastakia, Purdue University Imran Manji, Moi University
Co-Investigator(s)	Schellhase, Ellen Jakait, Beatrice Akwanalo, Constantine Karwa, Rakhi Saina, Collins Nabwire, Mercy Kanyi, John Maina, Mercy
Working Group(s)	Adult (Primary)
Description	A comprehensive pharmacist run anticoagulation care management system customized to a resource constrained setting has been created and implemented. The primary interventional element of this program is the creation of an organized system for INR monitoring of patients requiring anticoagulation with warfarin.
Site(s)	Moi Teaching and Referral Hospital (MTRH), Webuye District Hospital
Project Period	12/1/2008 – 12/31/2017
Funding Status	Funded – Purdue University College of Pharmacy, Indiana Hemophilia and Thrombosis Center (IHTC), Celgene Corporation
Direct Award (USD)	$100,000
Update	Over the last six months the clinic has grown to enrol over 1000 patients with about 800 active patients being managed currently. Sustainability continues to remain a challenge

	with human resource and supplies being the major drivers of cost.
Future Plans	It is hoped that some of the staff costs will be taken up by MTRH so as to ensure continued running of this lifesaving service. We also anticipate piloting of a new mobile based medical records system. We are also in the advanced stages of preparing a manuscript describing the dynamics of venous thromboembolism in the presence of HIV.
Publication(s)	

Study Title	**Biomarkers of Vincristine Toxicity in Kenyan Children**
Principal Investigator(s)	Jodi Skiles, Indiana University F. Njuguna, Moi University
Co-Investigator(s)	
Working Group(s)	Oncology (Primary) Pediatrics (Secondary)
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 (MTRH)
Project Period	6/23/2011 – 6/30/2014
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 has been resubmitted to Journal of Clinical Oncology and is currently under consideration there. The other manuscripts are still in progress but are anticipated to be submitted within the next quarter.
Future Plans	Submission/acceptance of 2 additional manuscripts
Publication(s)	

Study Title	**Building Competencies through Bilateral International Exchanges-Using Qualitative Methods to Measure the Impact on Pediatric Residents from Host and Visiting Countries in Professionalism, Communication and Systems-Based Care**
Principal Investigator(s)	Debra Litzelman, Indiana University Samuel Ayaya, Moi University

Co-Investigator(s)	Umoren, R. Woodward, J. Vreeman, R. Palmer, M. Stelzner, S. Lorant, D. Riner, M.
Working Group(s)	Pediatrics (Primary)
Description	This study uses focus groups to assess the impact of resident exchange project on participating residents from Indiana University School of Medicine (IUSOM), Moi University School of Medicine (MUSM), and Universidad Autonoma del Estado de Hidalgo Health Sciences Campus (UAEH) particularly related competencies in professionalism, communication, systems based practice, and practice based learning and improvement.
Site(s)	Moi Teaching and Referral Hospital (MTRH)
Project Period	11/27/2007 – 6/30/2014
Funding Status	Funded – Indiana University - Office of Research in Medical Education
Direct Award (USD)	Not Reported
Update	No additional study data collected.
Future Plans	Analysis of study data
Publication(s)	

Study Title	**Cervical Cancer See and Treat: How Best to Follow-up**
Principal Investigator(s)	Susan Cu-Uvin, Indiana University E. Omenge, Moi University
Co-Investigator(s)	Mabeya, H. Washington, S. Itsura, P.
Working Group(s)	Oncology (Primary) Reproductive (Secondary)
Description	This is a cross sectional study involving 660 HIV-infected women attending 4 AMPATH-CCSPP (Cervical cancer Screening and Prevention Program) sites who have undergone VIA and cryotherapy >6 months for cervical dysplasia. Demographic information as well as a full medical history will be obtained. They will undergo a gynecologic examination. Women with suspected frank cervical cancer or current genital tract infection will not be enrolled and will be referred for standard of care. Women with genital tract infection will undergo syndromic treatment and will be eligible to be enrolled 3 weeks after treatment if they have cleared the infection. During the gyn exam, the following will be done for all study participants: VIA, conventional Pap smear, endocervical cytobrush for HPV typing.

	All women with positive VIA result will undergo colposcopy and biopsy at the next available colpo/biopsy clinic day. Those with negative VIA result will return in 4-6 weeks to receive the results of their Pap smear and HPV typing. If either the Pap smear or HPV typing is abnormal, they will undergo colposcopy with biopsy on the next available colpo/biopsy clinic day. Women with negative VIA, PAP smear and HPV will follow standard of care that is annual screening with VIA. Histological diagnosis will be the gold standard. Women will be asked several questions regarding their experience.
Site(s)	Chulaimbo Sub-District Hospital, Moi Teaching and Referral Hospital (MTRH), Mosoriot Rural Health Training Centre, Turbo Health Centre
Project Period	9/1/2011 – 6/30/2013
Funding Status	Funded – Other
Direct Award (USD)	$252,146
Update	The study was closed for recruitment on June 30, 2013. The study is currently at Manuscript writing. An abstracted entitled Visual Inspection With Acetic Acid (VIA) Agrees Reasonably Well With Pap Smear and HR HPV Typing for Follow-up After VIA/Cryotherapy in HIV-infected Women' was accepted and presented during CROI 2014 held at Boston, USA between 3rd and 6th March 2014. This study is now closed.
Future Plans	Study is now closed.
Publication(s)	The abstarct presented resulting from this study is 'Visual Inspection With Acetic Acid (VIA) Agrees Reasonably Well With Pap Smear and HR HPV Typing for Follow-up AfterVIA/Cryotherapy in HIV-infected Women'. The Authors were; E. OMENGE., T. Liu, P Its

Study Title	**Childhood Leukemia in Kenya Identified Through Malaria Slide Review**
Principal Investigator(s)	Terry Vik, Indiana University F. Njuguna, Moi University
Co-Investigator(s)	Skiles, J. Moormann, A.
Working Group(s)	Oncology (Primary) Pediatrics (Secondary)
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)	Kitale District Hospital, Moi Teaching and Referral Hospital (MTRH), Turbo Health Centre
Project Period	7/1/2012 – 12/31/2014

Funding Status	Funded – Alex's Lemonade Stand Foundation
Direct Award (USD)	$200,000
Update	We have completed slide collections at our two study sites. We have reviewed a total of 30,000 slides so far and have about 6,000 more slides to review. We have identified about 1-2% of slides as suspicious for leukemia and have confirmed a few cases as positive for leukemia by review of cases and medical records. Data analysis is ongoing. We are planning a prospective study to use this slide screening technique for early referral of possible cases of leukemia.
Future Plans	We have asked for a 6 month no cost extension for our study to complete review of slides collected for the study. We will finalize the review in this study period. We will present the results of the study at a poster for the Society International Oncology Paediatric (SIOP) meeting in October.
Publication(s)	Festus Njuguna, Jodi Skiles, Ann Moormann Robin Mukhwana and Terry A Vik. *Estimating The Incidence Of Acute Leukemia In Children In Western Kenya By Review Of Malaria Blood Smears: A Pilot And Feasibility Study*. Abstract submitted to SIOP meeting in Toron

Study Title	**Computerized Counseling to Promote Positive Prevention and HIV Health in Kenya (CARE+ Kenya)**
Principal Investigator(s)	Ann Kurth, New York University Abraham Siika, Moi University
Co-Investigator(s)	John Sidle Joyce Baliddawa David Ayuku
Working Group(s)	Adult (Primary) Behavioral (Secondary)
Description	The specific aims of this project are: 1. Adapt a theoretically driven computerized counseling intervention (CARE+ Kenya) for use in Western Kenya (1st 18 months). 2.1.A. Conduct interviews with up to 25 HIV-positive urban and up to 25 rural men and women patients from the Academic Model Providing Access to Healthcare (AMPATH) to understand HIV and computer training needs. Conduct two staff focus groups (n~16) to assess positive prevention and ART adherence support practices, beliefs about patient computer use and training needs. 2.1.B. Using above, modify intervention content,translate and record audio files into local Kiswahili, and adapt skill-building videos on 'positive health' (prevention, disclosure, ART adherence, reproductive health, etc.). 2.1.C. Conduct iterative software usability testing with 10 urban and 10 rural patients (n=20) and 8 staff. Perform three day test-retest reliability assessment to establish psychometric performance of measures. 2.2 RCT. Establish biological and behavioral efficacy of a longitudinal HIV computerized counseling intervention in Kenya ('CARE+Kenya') (Months 18-42). 2.2.A. Longitudinal RCT in an urban and a rural clinic. Randomly assign HIV-positive adults with missed ART doses on self-report, pharmacy refill or pill counts; or unprotected sex in last 6 months, >1 partner in last year, or sexually

	transmitted infection (STI) in last 3 years; to intervention (n=125) or risk-assessment control (n=125) for baseline, 3, 6, and 9 month sessions. HIV transmission risk will be measured by self-reported unprotected sex with HIV-negative/unknown partner, and trends in C. trachomatis, N. gonorrhoeae, T. vaginalis. ART adherence will be measured by HIV-1 viral load at 0, 6, 9 months, and at all time points, by electronic monitoring, pharmacy refill, self-report, and clinic attendance. 2.3 Establish cost-effectiveness of computerized counseling in Kenya (Months 1-48). 2.3.A. Follow patients at the two clinics to evaluate standard of care counseling messages and collect patient time-spent data (n=100, at baseline), to determine unmet patient counseling need. 2.3.B. Economically evaluate CARE+Kenya. If RCT shows the intervention reduces viral load and transmission risks, we will use a Bernoulli transmission dynamics model to estimate number of secondary HIV infections prevented; then create a cost-effectiveness model to calculate 2 incremental cost-effectiveness ratios: 1) cost/HIV infection averted, and 2) cost/disability adjusted life year (DALY) saved. 2.3.C. If CARE+ Kenya is efficacious and efficient, we will develop a proposal for a cluster-randomized trial to assess translational effectiveness of CARE+ Kenya throughout the AMPATH system. 4.0 Specific CARE Study Aim 4 : Explore the ethical issues affecting participants who used the computerized counseling tool in the HIV/AIDS clinical setting for both rural and urban clinics during the RCT. 4.0 A. We will look specifically at issues surrounding privacy of information for computerized tools, and the effect of computerized counseling on the ethical practice of care. 4.0 B. We will target 102 patients in both the clinics, including 55 participants enrolled from MTRH and 47 participants enrolled from Burnt Forest. We will employ a descriptive and explanatory research design. 5.0 Specific CARE Study Aim 5 : Implement the CARE+ Tool in the real-world clinic setting at MTRH clinics to gain experience with logistics and usefulness of the tool outside the more controlled RCT environment. 5.0 A. Our experiences from this implementation period will inform development of larger applications to NIH and foundations for more widespread implementation of the tool throughout AMPATH clinics following the study.
Site(s)	Moi Teaching and Referral Hospital (MTRH)
Project Period	8/14/2009 – 6/30/2014
Funding Status	Funded – NIH - National Institute of Mental Health (NIMH)
Direct Award (USD)	$1,810,361
Update	ACCOMPLISHMENTS: We finalized recruitment in the No Cost Extension period in April 2014. Study participant recruitment for the No Cost Extension began late last year i.e. on the 5th November 2013. Unlike RCT, participants were being recruited from the three AMPATH sites (Module 1, 2 and 3). Our modes of referrals were by providers, Psychosocial department, Pharmacy as well as self-referral. Participants' logs were stored on whether a patient was individual/self referral or provider referral. As of April 2014, we had recruited a total of 114 clients = 22 males and 92 females. Of the 114 recruited, Intimate Partner Violence (IPV) cases were 30, Suicidal tendencies were 34 and finally severe depression cases were 13. All those being identified were first referred for assessment at Psychosocial department. If Psychosocial deemed necessary, they referred those to further services as needed. All those with issues of IPV were also referred to Ampath legal department for further action. After assessment, descriptive reports were done and a referral copy was given back to Psychosocial department and another one to

	CARE Plus Study. For cases like Depression and Suicidal, the participants were first referred for assessment at Psychosocial department then referred to the MTRH mental health department for further treatment where necessary. After assessment, reports were compiled and a copy given back to CARE Plus for archive purposes. For AIM 4 of the study, we enrolled 50 participants from MTRH and 45 from Burnt Forest. Currently the FGDs and Patient Interviews recordings are being transcribed before coding begins. We will employ a descriptive and explanatory research design. Over the past six months of recruitment, we faced the following challenges; CHALLENGES: 1. Minimum cooperation from AMPATH staff: Overall, cooperation from the health care providers and frontline health workers was minimum when referring participants to the study area e.g. lack of incentives, the idea that the study was 'taking away' their source of income among others. 2. Minimum cooperation from AMPATH patients: Generally, majority of our participants were very reluctant to sit through the entire computer session due to time limits and lack of incentives despite study staff explaining that since this was not anymore a study but rather a real world implementation phase. As a real world implementation, we were not reimbursing them for their time like we did during the RCT phase. 3. Infrastructure: Migration of standalone databases from the study settings into the larger Ampath infrastructure became a challenge for the staff. A lot of time and resources were used to figure out the step-by-step, which in turn lead to wastage of valuable time for the no-cost-extension.
Future Plans	The study officially came to an end on June 30, 2014. We are currently working on the close-out procedures at both AMPATH and NYU to comply with NIH regulations.
Publication(s)	

Study Title	**Cross-Cultural Histories of Family Care-Giving to AIDS Orphans in Western Kenya**
Principal Investigator(s)	Jeanette Dickerson-Putman, Indiana University - Purdue University in Indianapolis (IUPUI) H. Maithya, Moi University
Co-Investigator(s)	
Working Group(s)	Behaviroal (Primary) Pediatrics (Secondary)
Description	The overall goal of the project is to complete an anthropological and clinic-based study that seeks to understand the history of the care-giving experiences of primary providers of care-giving to AIDS orphans in Kenya among two different cultural groups served by the same AMPATH support program.
Site(s)	Chulaimbo Sub-District Hospital, Mosoriot Rural Health Training Centre
Project Period	9/1/2009 – 5/30/2014
Funding Status	Funded – IUPUI - Research Support Funds
Direct Award (USD)	$35,000

Update	The Kenyan members of the research team have not been in regular contact with Dickerson-Putman for almost a year. As a result Dickerson-Putman can not provide a current Biosketch or Citi results test for the Co-Principal Investigator Maithya. The code book for the Mosoriot research site was completed in 2013 and Dickerson-Putman decided in the Spring of 2014 to go forward with the data analysis of the Mosoriot data on her own.
Future Plans	Dickerson-Putman hopes to make good progress on the analysis of the Mosoriot data.
Publication(s)	

Study Title	**Diabetes Mellitus and Glucose Intolerance in HIV Patients in Western Kenya**
Principal Investigator(s)	Jane Carter, Moi University N. Kirui, Moi University
Co-Investigator(s)	Kamano, J. Diero, L. Chege, P. Pastakia, S. Gardner, A. Mwangi, A.
Working Group(s)	TB (Primary) Cardiovascular (Secondary)
Description	The goal of this study is to determine the association between diabetes mellitus, glucose intolerance, and HIV among HIV positive patients in Western Kenya. In this study, we propose that HIV and ART use increases the risk of diabetes mellitus and glucose intolerance among HIV patients in Western Kenya.
Site(s)	Moi Teaching and Referral Hospital (MTRH), Webuye District Hospital
Project Period	9/3/2012 – 8/31/2015
Funding Status	Unfunded
Direct Award (USD)	
Update	No Update Provided
Future Plans	No Update Provided
Publication(s)	

Study Title	**Drug Resistance in HIV Infected Children after Failure of Prevention of Mother to Child Transmission in Western Kenya**
Principal Investigator(s)	Winstone Nyandiko, Moi University Rami Kantor, Brown University
Co-Investigator(s)	Vreeman, R. Songok, J. Diero, L. Kosgei, R. Ayaya, S.
Working Group(s)	Pediatrics (Primary) Reproductive (Secondary)
Description	The project seeks to determine the proportion of children getting HIV infected despite interventions of pMTCT, and the type, if any, of antiretroviral drug resistance in those children who get HIV infected after failure of pMTCT.
Site(s)	Kitale District Hospital, Matayos Health Centre, Moi Teaching and Referral Hospital (modules 1-4), Turbo Health Centre, Webuye District Hospital
Project Period	5/3/2011 – 4/10/2015
Funding Status	Funded – AITRP Grant-Brown University
Direct Award (USD)	$20,000
Update	We have not enrolled any study participant since the last update .We have had challenges in getting eligible patients to be recruited. This is due to few children turning positive after undergoing the PMTCT intervention within AMPATH.This is as a result of a vibrant PMTCT program within AMPATH. We have so far enrolled a total of fourteen patients into the study up to date. None of the study participants has either withdrawn or defaulted. The study is still open to enrolment.
Future Plans	We are still hoping that we shall be able to get eligible participants for us to improve on the rate of recruitment.
Publication(s)	Manuscript is under development. Abstract submitted to AIDS conference in Australia this year.

Study Title	**EARNEST: A Randomised Controlled Trial to Evaluate Options for Second-line Therapy in Patients Failing a First-line 2NRTI+ NNRTI Regimen in Africa**
Principal Investigator(s)	Abraham Siika, Moi University Kara Wools-Kaloustian, Indiana University
Co-Investigator(s)	Mabeya, H. Washington, S.

	Itsura, P.
Working Group(s)	Adult (Primary)
Description	EARNEST is a three arm parallel group, open-label, multi-centre, randomised controlled trial. 1200 patients will be included who are HIV-infected adults who have taken a first-line NNRTI-based regimen continuously for a total period of at least 12 months, and developed treatment failure defined by modified WHO 2010 criteria as one of the following: New WHO Stage 4 event (with CD4 < 200 cells/mm3 and viral load (VL) > 400 copies/ml); CD4 < 100 cells/mm3, or CD4 fall to pre-treatment baseline or below, or CD4 < 200 cells/mm3 X 2 with previous CD4 > 400 cells/mm3 (with VL > 400 copies/ml); VL > 5,000 copies/ml; 2 The trial aims to determine whether, in patients failing a first-line NRTI and NNRTI-containing regimen 1. bPI plus raltegravir (an integrase inhibitor) is superior to standard of care (bPI plus 2 new NRTIs) in achieving good HIV disease control at 96 weeks after randomisation. 2. bPI monotherapy is non-inferior to standard of care in achieving good HIV disease control at 96 weeks after randomisation
Site(s)	Moi Teaching and Referral Hospital (MTRH)
Project Period	2/9/2011 – 12/31/2014
Funding Status	Funded – European & Developing Countries Clinical Trials Partnership (EDCTP), Medical Research Council, Instituto de Salud Carlos III, Irish Aid, Swedish International Development Cooperation Agency (SIDA)
Direct Award (USD)	Not Reported
Update	The study was closed to follow up in January 2014 and all participants were transitioned to primary care provider AMPATH. All participants who were receiving raltegravir continued to be given study provided raltegravir until August 2014 after which they continue with AMPATH program provided drugs.
Future Plans	The study is closed to follow up therefore no specific plans for the next 6 months.
Publication(s)	

Study Title	**Enhancing Training for Implementation Research in Chronic Disease: CITE/Kenya**
Principal Investigator(s)	Tom Inui, Indiana University Paul Ayuo, Moi University
Co-Investigator(s)	Siika, A. Litzelman, D.
Working Group(s)	Adult (Primary)
Description	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.
Site(s)	Moi Teaching and Referral Hospital (MTRH)
Project Period	10/1/2012 – 9/30/2016
Funding Status	Funded – NIH - Fogarty International Center (FIC)
Direct Award (USD)	$862,970
Update	Cohort 1 trainees have completed protocols for their practicum research projects, now under review in research working groups and IREC. Cohort 2 trainees completed the core curriculum seminars in Eldoret. All current trainees presented plans for their research in a half-day Work-in-Progress session open to faculty and attended by the D43 Oversight Committee (Drs. Ayuo, Siika, Litzelman, Tierney, Inui, and Kroenke) in Eldoret. The Oversight Committee met to discuss trainee progress and program directions. All trainees were felt to be on track and pursuing worthy research directions.
Future Plans	A Cohort 3 has been selected and needs to be matriculated in core curriculum seminars. Attempts should be made to integrate D43 core into the core curriculum for Moi registrars. A discussion of moving the D43 in the direction of a degree program in implementation research should take place.
Publication(s)	

Study Title	**Evaluating Handheld Clinical Decision Support Tools to Improve Community-Based Delivery of Reproductive and Pediatric Health Services**
Principal Investigator(s)	Julia Songok, Moi University Astrid Christoffersen-Deb, University of Toronto
Co-Investigator(s)	1. Louis Fazen 2. Dr Laura Ruhl
Working Group(s)	Reproductive (Primary)
Description	The primary aim is to evaluate the effectiveness of a handheld CDS system in a cluster randomized-controlled trial among 89 community health workers (CHWs) in Kosirai district over a 4-month enrollment period. By using data collected on the existing CHW Initial Encounter Form and interfacing with AMPATH's electronic medical record system, we will identify and categorize women according to well-defined antenatal risk criteria and deliver patient-specific 'Smart Forms' to each pregnant woman served by enrolled CHWs. This research has four objectives: 1) Evaluate comparatively the effectiveness of handheld CDS to improve community-based health service delivery 2) Evaluate the effectiveness of incorporating patient-specific multimedia Information, Education and Communication (IEC) materials into Smart Forms for generating behavior change among clients 3) Determine the cost-effectiveness of a CDS Smart Forms system employed by CHWs and 4) Assess qualitatively the process of implementation of the Smart Forms system, including the technical specifications, human capacity requirements, and acceptability among providers and clients.
Site(s)	Mt. Elgon District Hospital
Project Period	1/12/2011 – 3/12/2014
Funding Status	Funded – Grand Challenges Canada
Direct Award (USD)	$97,361
Update	Over the last six months, Qualitative data was collected through four focus group discussions. Two with community health volunteers and two with women. In addition, Key informant interviews were also conducted with, Public Health Officers, Community Health Extension Workers and Clinical Officers. Quantitative data was collected from CDS Smart Forms on ODK for Intervention group and Electronic forms on ODK for control group. All data has been collected so far
Future Plans	Complete data analysis of the project
Publication(s)	

Study Title	**Evaluation of A Comprehensive Strategy to Measure Pediatric Adherence to Antiretroviral Therapy (CAMP study)**
Principal Investigator(s)	Rachel Vreeman, Indiana University Winstone Nyandiko, Moi University
Co-Investigator(s)	Inui, T. Tierney, W. Tu, W. Marrero, D. Ayaya, S. Blaschke, T. Arpadi, S. Caroll, A. Bell, D.
Working Group(s)	Pediatrics (Primary)
Description	The primary objective of this study is to develop and test a reliable, valid instrument to measure pediatric ART adherence for children ages 0 to 14 years in western Kenya and to evaluate which administration strategy yields the most accurate information about children's ART adherence. We will pursue the following four specific aims: Aim 1: Develop a reliable, valid comprehensive pediatric ART adherence measurement questionnaire (CAMP - Comprehensive ART Measure for Pediatrics); Aim 2: Develop a reliable, valid, short-form version of the pediatric ART adherence measurement tool (SF-CAMP) for use as an adherence screening measure in busy clinical care environments; Aim 3: Evaluate the field readiness, implementation feasibility, and clinical utility of CAMP and SF-CAMP within the AMPATH HIV clinical care system in western Kenya; and Aim 4: Evaluate the reliability and validity of this measurement tool in a clinic-based care setting compared to a home?based care setting.
Site(s)	Moi Teaching and Referral Hospital (MTRH)
Project Period	9/11/2009 – 2/28/2014
Funding Status	Funded – NIH - National Institute of Mental Health (NIMH), PEPFAR - United States President's Emergency Plan for AIDS Relief - Public Health Evaluation (PHE)
Direct Award (USD)	$1,336,011
Update	Recruitment and patient assessments are complete for the CAMP study. In the past 6 months, we have continued work in data collection, cleaning, and analyses as part of Phase 2, Phase 3, and Phase 5 of the study. Phase 2: The objective of Phase 2 was to validate an adherence questionnaire using multiple measures of adherence. The questionnaire has been developed and validated in Phase 2, and underwent re-validation in Phase 3. Two manuscripts that describe the validation of adherence questionnaire items from Phase 2 are currently under review at the Journal of the International AIDS Society and AIDS & Behavior. We found that several adherence questionnaire items performed well for adherence assessment (against our other measures of adherence: MEMS, CD4) and the items most correlated with adherence were included in a 'short-

	form' version for testing in Phase 3. Currently, we are working on two further analyses with the Phase 2 data. First, we are using our detailed MEMS adherence data and drug concentration samples to develop a pharmacokinetic algorithm of nevirapine and efavirez dosing. Second, we are working on cleaning the data related to pill counts, which we will then analyze against our other measures of adherence. We are also conducting a supplemental Phase 2 non-adherence study, which will be a retrospective study to investigate clinical characteristics and outcomes among a sub-group of non-adherence Phase 2 patients. Consent has been obtained, and data extraction from patients' charts is ongoing. Phase 3: The objective of Phase 3 was to revalidate the adherence questionnaire items tested in Phase 2 in a clinical setting with clinicians administering a short-form of the adherence questionnaire. Data has been collected and is now being cleaned within the AMPATH RedCAP database. After data cleaning and preparation are complete, analyses will include comparing performance of the adherence items against each other (i.e., patient response to adherence question to clinician versus study staff) and against MEMS. Phase 5: The objective of Phase 5 was to investigate whether adherence questionnaire items performed differently in a home versus a clinic setting. These data have been collected, and in the past 6 months we have been working to clean the data and prepare them for analyses. The data cleaning process has taken longer than expected due to challenges with the database. These have been resolved and the data are now undergoing preliminary analyses.
Future Plans	Over the next 6 months, we aim to • complete analyses related to the NVP and EFV dosing algorithm and pill count data for Phase 2 • write up these results of the dosing algorithm and pill count analyses and submit them to JAIDS • complete data extraction and begin preliminary data analyses for the Phase 2 non-adherence sub-study • complete analyses for Phase 3 and to write up the results for submission to prominent AIDS journal • complete analyses for Phase 5
Publication(s)	Vreeman RC, Nyandiko WM, Liu H, Tu W, Scanlon ML, Slaven JE, Ayaya SO, Inui TS. Evaluation of a comprehensive antiretroviral therapy measure for pediatrics. AIDS & Behavior - UNDER REVIEW Vreeman RC, Nyandiko WM, Liu H, Tu W, Scanlon ML, Slaven JE, Ay

Study Title	**Feasibility Intervention Trial of Two Types of Improved Cook Stoves in Three Developing Countries**
Principal Investigator(s)	Diana Menya, Moi University Jaime Miranda, Universidad Peruana Cayetano Heredia, Lima, Peru
Co-Investigator(s)	Checkley, W. Carter, J. Ogaro, F. Diero, L. Mwangi, A.
Working Group(s)	Public Health (Primary) Cardiovascular (Secondary)

Description	This is a multi-center community-based feasibility trial in which improved cook stoves with a chimney will be installed in 40 rural households of women aged 20 to 49 years at each of the three sites. All households will have a baseline observational period of 4 months in which outcome, environmental, and behavioral data will be collected longitudinally. Thereafter, 20 households will be randomly assigned to receive a commercially-available, improved cook stove with a chimney or a locally-constructed improved cook stove with a chimney. Behavioral, compliance, outcome and exposure data will be collected longitudinally for 4 months. Exposure assessments will include particulate matter and carbon monoxide. Respiratory outcome assessments will include spirometry, carboxyhemoglobin, exhaled nitric oxide and diffusing capacity of the lung for carbon monoxide. At the end of the 4 month period, households that received the Envirofit improved cook stoves will have their cook stoves switched with the locally-constructed improved cook stoves and vice versa, and all households will be followed for another 4 months. At the end of the year, all participants will be asked which cook stove they prefer and will be asked provide information on preferences, practices, and use patterns that influenced their final choice.?
Site(s)	Burnt Forest, Ndanai Sub-Location
Project Period	7/1/2011 – 6/30/2014
Funding Status	Funded – NIH - National Heart, Lung, and Blood Institute (NHLBI)
Direct Award (USD)	$76,239
Update	Period 2 follow-up completed in January 2014, Period 3 follow-up started in February 2014; follow-up completed in May 2014. A total of 44 participants followed up to completion. 1 participant dropped out of the study.
Future Plans	Administrative study close out in progress.
Publication(s)	

Study Title	**Health Facility Incentives to Improve Adherence to Malaria Diagnostic Test Results**
Principal Investigator(s)	Wendy O'Meara, Duke University Diana Menya, Moi University
Co-Investigator(s)	Armstrong, J. Manji, I.
Working Group(s)	Public Health (Primary)
Description	Global investments in controlling malaria have led to some exciting reductions in the burden of malaria. In some areas, malaria-related deaths have dropped by more than 90 percent. As malaria transmission declines, a greater fraction of pediatric fevers are from other causes. However, these fevers continue to be treated as malaria, often despite the availability of diagnostic testing. In a typical rural health facility in Kenya, more than 90

	percent of febrile patients are prescribed an antimalarial when no diagnostic tests are available. Even when microscopy or rapid diagnostic tests (RDTs) are available, between 50-80 percent of patients with a negative test are nonetheless prescribed antimalarials. Inappropriately treated fevers in children can lead to serious consequences for the patient and can accelerate the spread of drug resistance. In addition to the risk to patients, overuse of antimalarials also puts a financial strain on the government health system. This project aims to test an innovative, sustainable financial incentive designed to reduce the number of non-malarial fevers that are treated inappropriately with antimalarial drugs. This study will test a financial incentive targeted at the health facility to determine if it improves adherence to diagnostic results and clinical protocols. Eighteen rural health facilities in western Kenya will be enrolled and randomly allocated to one of two arms. We will compare the effectiveness of clinical and technical training in diagnosis of malaria alone (Arm 1) to training plus financial incentives linked to prescription practices (Arm 2) in improving diagnosis and treatment of malaria and non-malaria fevers. The practice of prescribing antimalarials to patients with a negative diagnostic will be compared between facilities with and without the incentive structure. Secondary outcomes will include sensitivity and specificity of routine microscopy at health centers, use of alternative treatments for slide negative fevers, and frequency of stock-outs of antimalarial drugs. This project will be conducted in collaboration with Kenya's Division of Malaria Control and avenues to roll-out the intervention, if successful, will be actively explored.
Site(s)	
Project Period	4/1/2012 – 3/31/2014
Funding Status	Funded – NIH
Direct Award (USD)	$250,000
Update	Dissemination of study findings was done in April, both at health facility level and the national level with representatives from Malaria Control Unit being present. The study is now closed out.
Future Plans	Not Applicable
Publication(s)	

Study Title	**Improving Diabetes Management and Cardiovascular Risk Factors Through Diabetes Peer Group Education in Western Kenya**
Principal Investigator(s)	Sonak Pastakia, Purdue University Gerald Bloomfield, Duke University
Co-Investigator(s)	Joseph Egger
Working Group(s)	Cardiovascular (Primary) Adult (Secondary)

Description	This project will seek to assess the hypothesis that diabetes education through peer support groups in western Kenya will be feasible and significantly improve diabetes knowledge-base and diabetes control in comparison to routine care.
Site(s)	Moi Teaching and Referral Hospital (MTRH), Ziwa Sub-District Hospital
Project Period	2/1/2012 – 12/31/2013
Funding Status	Funded – NIH - Fogarty International Center (FIC), NIH - National Heart, Lung, and Blood Institute (NHLBI), Duke Global Health Institute
Direct Award (USD)	$15,000
Update	Data collection finished. Data analysis and manuscript near final stage.
Future Plans	Publish
Publication(s)	

Study Title	**Indiana University-Moi University Academic Research Ethics Partnership**
Principal Investigator(s)	Eric Meslin, Indiana University David Ayuku, Moi University
Co-Investigator(s)	Were, E.
Working Group(s)	Bioethics (Primary)
Description	The IU-Moi AREP is funded for five years with a $1.25 million grant from the Fogarty International Center at the National Institutes of Health to establish a new research ethics training partnership with colleagues at Moi University in Eldoret, Kenya. IU-Moi AREP is a curriculum development and training initiative that builds on longlasting partnerships and collaborations in East Africa. IU-Moi AREP has developed two Masters' degree programs:one at Indiana University-Purdue University Indianapolis and one at Moi University in Eldoret, Kenya.These graduate programs have common overlapping components,joint advisory committes,shared dissemination plans and harmonized evaluation strategies. Both programs include a curriculum involving required core courses, electives and a practicum experience, part of which is taken at the counterpart university. Besides, each IU-Moi AREP partner convenes an annual Teaching Skills in International Research Ethics(TaSkR) workshop to provide training to approximately 40 faculty and students each year.
Site(s)	Moi Teaching and Referral Hospital (MTRH), Moi University
Project Period	5/31/2012 – 5/31/2017
Funding Status	Funded – NIH - Fogarty International Center (FIC)
Direct Award (USD)	$1,250,000

Update	TaSkR VI The sixth annual Teaching Skills in International Research Ethics (TaSkR VI) was held in Eldoret, Kenya from 19-21 February. The theme for the workshop was 'Genomics and Biobanking' and attracted 118 participants from Africa and North America. The key note address on 'Informed Consent in the Era of Biobanking' was delivered by Prof. Isaac Mwase. Other topics presented include Genomics and Tissue Banks, Biological Material Storage and Transfer-IREC Experience, KEMRI Research Review Process, New Developments in Biobanking Governance, Community Views on Breast Cancer and Tissue Donation, Community Engagement and Informed Consent, Ethical, Social and Cultural Program for Global Health Program Lessons, Quality Assurance in Teaching Research Ethics. Moi University was represented by Prof. David Ayuku, Prof. Edwin Were, Prof. Joseph Kahiga and Prof. Eunice Kamaara. Planning for the next workshop, TaSkR VII, which will be held in Indianapolis in the spring of 2015 has commenced. It is hoped that the workshop can be opened up to non-IU researchers, institutions and organizations. MSc. Intl. Health Research Ethics Students (Moi) As of June 2014, 40 students are enrolled in the MHSc. Program and are at various stages of completion. It is expected that 5 students will be completing their MHSc. in 2014. MA in Philosophy (International Research Ethics Concentration) Indianapolis As of June 2014, 3 students have been enrolled in the MA program: 1 has graduated, 1 is scheduled graduate in 2014, and 1 is scheduled graduate in 2015. We had one student from IU complete their practicum at Moi University in Eldoret from May 1 to June 6, 2014.
Future Plans	We are expecting five students from Moi University come to Indianapolis for their practicum. The practicum will be from October 6 to November 14. A formal selection criteria for this group was developed and applied to the eleven (11) concept papers submitted. Of these, five (5) were selected. Plans are underway to schedule their activities and match them with mentors from IU. As with other practicum experiences in the past, this group will attend core lectures as per the NIH Responsible Conduct of Research Topics. These include conflict of interest, human and animal subjects, safe laboratory practices, mentor/mentee relationships, collaborative research (including with industry), peer review, data acquisition/management, research misconduct, authorship/publication, social responsibility, and contemporary issues in biomedical research. They also attend the two day Research Coordinator Education Program aimed at introducing participants 'to critically important concepts, requirements, and practical aspects of coordinating research studies across all types of clinical research.' They will audit three courses here on campus: PHL555 - Ethical and Policy Issues in International Research Ethics by Dr. Eric Meslin, PHL547 - Foundations of Bioethics by Dr. Peter Schwarz, and M504 - Introduction to Research Ethics by Dr. Kimberly Quaid. In addition to this, there will be talks on the IU-Kenya Partnership, Office of International Affairs, the Regenstrief Institute, the IU Simon Cancer Center and AMPATH. They will also visit Eli Lilly, the Hall Center for Law and Health at the IU McKinney School of Law, and the IU Biobank. The students will present their research in a Work in Progress session in November at the IU Center for Bioethics. Moi plans on having a short course this November or December. Through these short courses in the past, some participants gained interest and enrolled in the masters program at Moi.
Publication(s)	Ndebele P, Wassenaar D, Benatar S, Fleischer T, Kruger M, Adebamowo C, Kass N, Meslin EM, Hyder. A Research Ethics capacity building in Sub-Saharan Africa: A review of NIH Fogarty-Funded programs 2000-2012. Journal of Empirical Research in Human Researc

Study Title	**IU Health Cardiovascular Research Biobanking Project**
Principal Investigator(s)	Tom Inui, Indiana University Sylvester Kimaiyo, Moi University
Co-Investigator(s)	Bloomfield, G.
Working Group(s)	Adult (Primary) Cardiovascular (Secondary)
Description	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.
Site(s)	Moi Teaching and Referral Hospital (MTRH)
Project Period	4/30/2012 – 4/28/2017
Funding Status	Funded – IU Health
Direct Award (USD)	$1,060,000
Update	Over the interval December 2013 through June, 2014 the enrollment of all patients was completed for a total cohort size of 290 patients, including 70 with valvular and another 70 with nonvalvular atrial fibrillation. Clinical, laboratory, echocardiographic and ekg data were completed on these cases and is undergoing cleaning.
Future Plans	In the next six months, packed white blood cell pellets should be shipped from the AMPATH reference lab to genomics labs at IU. Next gen analyses, including new genes of relevance to myocardial membrane stability are to be explored for their association with atrial fibrillation risk.

Publication(s)	Presentation: Bloomfield G. 'Cardiovascular Disease in sub-Saharan Africa: An Academic Model for Countering the Epidemic' 11-Dec-13 Krannert Institute of Cardiology at Indiana University Grand Rounds, Indianapolis IN Presentation: Temu, TM. 'Genetic
Study Title	**Linkage and Retention to Care in Western Kenya Following HIV Testing**
Principal Investigator(s)	Becky Genberg, Brown University Juddy Wachira, Moi University
Co-Investigator(s)	Braitstein, Paula Naanyu, Violet Rachlis, Beth
Working Group(s)	Adult (Primary)
Description	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)	
Project Period	6/4/2012 – 12/20/2013
Funding Status	Funded – NIH - National Institute of Mental Health (NIMH), NIH - National Institute of Allergy and Infectious Diseases (NIAID), NIH
Direct Award (USD)	$152,806

Update	We recently received continuing approval from both the Brown IRB and IREC through August 2015. In terms of the first Aim of this study, we are continuing to work on the merging of linkage data from HCT and AMRS in additional catchment areas. We have complete and clean data from Bunyala and presented this data at the 9th International Conference on HIV Treatment and Prevention Adherence in June 2014. Additional abstracts will be submitted to the Treatment as Prevention (TasP) Summit which will take place in September 2014. In terms of our retention work, we are continuing analyses regarding retention in care among patients currently enrolled in care in AMPATH. Several different analyses include: 1) an examination of outcomes among a randomly sampled group of patients lost-to-follow-up, 2) an analysis of retention in care depending on point of entry (e.g., HCT, VCT, PITC), and 3) an examination of gaps in care among patients currently enrolled in AMPATH. We are also working on qualitative analyses related to retention, including an analysis of the facility and individual barriers to linkage and retention in care among patients currently enrolled in AMPATH clinics.
Future Plans	In terms of the second Aim of this study, we are scheduled to begin the first round of qualitative data collection with health care professionals in September 2014. The goal of this study is to understand the factors that are important to explain linkage and retention in care from the provider's perspective and to understand their attitudes regarding patient-provider relationships and adherence. We are also completing an evaluation of the care navigators program currently in place at MTRH and expect this to be complete by the end of the calendar year. In January 2015 we will begin the next round of qualitative data collection with patients who tested positive through HCT and did not link to care after testing.
Publication(s)	Genberg BL, Naanyu V, Wachira J, Hogan J, Braitstein P. Population-based estimates of engagement in the continuum of HIV care in western Kenya: From HIV testing to retention. Oral presentation at: The 9th International Conference on HIV Treatment and Prevention

Study Title	**MESA Malaria Prevention Study (MPS)**
Principal Investigator(s)	Wendy O'Meara, Duke University A. Obala, Moi University
Co-Investigator(s)	Mangeni, J. Menya, D.
Working Group(s)	Public Health (Primary)
Description	International efforts to scale up malaria control have achieved considerable success and have pointed toward the possibility of global malaria eradication. Achieving the long-term goal of eradication requires effective implementation of current tools, development of new technologies, and ongoing surveillance of the successes and failures of both. As malaria transmission declines and becomes increasingly heterogeneous, a finer-grained picture of malaria burden and intervention efficacy is required. In Kenya, considerable reductions in malaria morbidity and mortality have been reported, but success has not been uniform. In Bungoma East district in western Kenya, data suggest that control efforts

	have not had the expected impact; despite the fact that Insecticide Treated Net (ITN) ownership exceeds 70%, malaria infection and morbidity remain high. The observation that malaria burden has not responded to control measures suggests a breakdown in effectiveness of ITN, but not due simply to ownership, a common measure of 'coverage'. Breakdown in prevention of malaria may be due to a number of different factors in addition to coverage, including improper use and low adherence by households, changing vector populations and reduced susceptibility of the vector. In the first phase of the proposed project, this study will seek to answer the question of why malaria morbidity has remained alarmingly high in an area with high coverage of effective interventions. We will use the efficacy decay framework to quantify barriers to effective prevention. In the second phase, the lessons from phase 1 will be applied to developing a tool that can generate local, timely information in a cost-effective manner to identify and address barriers to elimination. Specific Aim 1: Quantify the efficacy decay at each step using case-control methodology. We will use a case control study to estimate the relative contribution of each step in the efficacy decay of ITNs to malaria prevention in an area where coverage is high but malaria burden has remained resistant to control measures. Specific Aim 2: Develop a rapid assessment tool that can be implemented at sentinel health facilities to identify local bottlenecks to malaria elimination. Based on the results of the efficacy decay analysis, we will develop a tool that can be used by community health workers to identify local barriers to effective prevention and stimulate local solutions.
Site(s)	Webuye District Hospital
Project Period	1/1/2013 – 9/30/2014
Funding Status	Funded – Malaria Eradication Scientific Alliance (MESA)
Direct Award (USD)	$197,500
Update	We have finished enrolling for the case control study and the mosquito trapping. We are analyzing data and developing a rapid assessment tool based on our findings. We will begin training CHWs in the next month.
Future Plans	We will train CHWs to use the rapid assessment tool and validate the tool as a means to identify breakdown in malaria prevention.
Publication(s)	

Study Title	**Modified Directly Observed Antiretroviral Therapy (M-DART): An intensive, nurse-directed, home-centered, treatment strategy to reduce mortality and loss to follow-up in high-risk HIV-infected patients initiating antiretroviral therapy**
Principal Investigator(s)	Abraham Siika, Moi University Kara Wools-kaloustian, Indiana University
Co-Investigator(s)	Murage,T. Thirumurthy,H. Goodrich,S.
Working Group(s)	Adult (Primary)

Description	M-DART study is a randomized clinical trial comparing the effectiveness of a home-based modified directly observed antiretroviral (ART) treatment strategy to clinic-based standard of care in patients with HIV/AIDS in Port Victoria,Busia,Chulaimbo,Kitale and Khunyangu,Kenya.The aim is to reduce both mortality and the number of patients lost to follow-up after ART therapy is initiated.In addition to these important objective outcomes,it also seeks to determine if M-DART can contribute to an increased quality of life for patients and help to diminish HIV related stigma.
Site(s)	Chebiemit District Hospital, Huruma Sub-District Hospital, Kitale District Hospital, Matayos Health Centre, Saboti Sub-District Hospital
Project Period	8/1/2011 – 3/31/2014
Funding Status	Funded – PEPFAR - United States President's Emergency Plan for AIDS Relief - Public Health Evaluation (PHE)
Direct Award (USD)	$825,501
Update	-The last patient completed study follow-up in January 10th 2014. -Study closed out in March 31st 2014. -Data cleaning was done and missing data retrieved. -Preparation of data for analysis.
Future Plans	Complete data analysis -Publish
Publication(s)	

Study Title	**Nurse Management of Hypertension Care in Rural Western Kenya**
Principal Investigator(s)	Rajesh Vedanthan, Mount Sinai School of Medicine Sylvester Kimaiyo, Moi University
Co-Investigator(s)	
Working Group(s)	Adult (Primary) Cardiovascular (Secondary)
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.
Site(s)	Mosoriot Rural Health Training Centre, Turbo Health Centre
Project Period	9/17/2011 – 7/30/2016
Funding Status	Funded – NIH - Fogarty International Center (FIC)
Direct Award (USD)	$675,543
Update	For Aim 1 activities, all transcripts finalized and translated, coding was completed in Atlas software and content analysis was completed for 13 key informant interviews and focus group discussion transcripts. Poster was presented at World Congress of Cardiology in Melbourne in May 2014. Manuscript is now in preparation. For Aim 2 activities, usability testing focus group discussion have been completed, feasibility testing semi-structured interviews have been completed (2 program staff; 3 nurses), feasibility testing focus group discussion has been completed, content analysis has been completed, consultative feedback was provided to AMPATH Chronic Disease Management Team. For Aim 3 activities, data entry has been initiated and the Study Oversight Committee has been assembled, and preliminary statistical analyses is ongoing. Dr. Vedanthan was invited to be a panelist at Consortium of Universities for Global Health Annual Conference, 'Leveraging HIV infrastructure to confront NCDs'. For Aim 4 activities, a detailed protocol for collection of workforce estimation model inputs has been finalized and approved by all ethical review boards. The research activities on Aim 4 has been initiated.
Future Plans	Over the next 6-12 months, I hope to complete the following activities pertaining to each of the study aims: Aim 1: submit further abstracts to professional conferences (Sept-Nov 2014) and complete manuscript. Aim 2: Complete manuscript. Aim 3: ensure data entry is completed, ensure accuracy and cleaning of data, conduct preliminary analyses, submit abstracts to professional conferences Aim 4: conduct data collection activities for needs and capacity and perform data analysis. Complete estimation model and run with inputs from data collection. Submit abstracts to professional conferences.
Publication(s)	Vedanthan R, Kamano JH, Horowitz CR, Ascheim D, Velazquez EJ, Kimaiyo S, Fuster V. Nurse Management of Hypertension in Rural Western Kenya: Implementation Research to Optimize Delivery. Annals of Global Health 2014; 80: 5-12. PMID: 24751560
Study Title	**Optimizing Linkage and Retention to Hypertension Care in Rural Kenya**
Principal Investigator(s)	Valentin Fuster, Mount Sinai School of Medicine Jemima Kamano, Moi University
Co-Investigator(s)	Fuster, V.

	Horowitz, C. Were, M. Inui, T. Hogan, J. Velazquez, E. Bloomfield, G. Naanyu, V. Menya, D. Kimaiyo, S. Akwanalo, C.
Working Group(s)	Adult (Primary) Cardiovascular (Secondary)
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)	Mosoriot Rural Health Training Centre, Turbo Health Centre
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	We have hired two additional Research Assistants to assist with the project. Qualitative work for Aim 1 was completed conducted under the supervision and direction of Violet Naanyu. We have also published a manuscript in Trials Journal in April 2014 (see reference below). Subsidiary Aim 1.1 Behavioral assessment tools and communication strategy (both Swahili and English Versions) were developed by the design team and finalized based on input from the LARK study team and content validity testing. The documents have been approved by IREC/IRB and are currently utilized in linkage and retention of Hypertensive patients to care program. Subsidiary Aim 1.2 Concepts for the Behavioral assessment tool is been generated by the Developers team which will pave way for programming function. Video clips are ongoing and will be finalized within the next month. Usability and Feasibility protocol have been completed. Aim 2 Enrollment/Roll-out update: Roll-out process is ongoing having randomized the 24 Community Units (CU) into three arms encompassing 1). Usual care arm, 2). Paper-based/Motivational Interviewing arm and 3). Smartphone/Motivational Interviewing arm. Each arm is constituted with 8 CUs. We have completed roll-out of the study in usual care arm and we are mid-way in paper-based/motivational interviewing arm. As of June 2014, a total of 168 participants have been enrolled. Aim 3: Cost Effectiveness The costing questionnaire has been developed and content validity completed. The paper-based content has been rolled out aligned with the above sated study arms. The electronic version is yet to be completed. Research data base (Redcap/Virtual Machine server) have been secured.
Future Plans	Subsidiary Aim 1.2 Concepts for the Behavioral assessment tool and programming to be finalized, this will pave way for smartphone training tentatively as from 20th August, 2014. Aim 2 Roll out update: Completion of the roll-out process to be done in paper-based/motivational interviewing arm before Smartphone/Motivational Interviewing arm

	which is projected to be initiated mid August 2014. Aim 3: Cost Effectiveness The electronic version of costing questionnaire to be completed before August 1, 2014 and the data will be dowloaded from the tablets for data collection as well as data entry.
Publication(s)	Author names: Rajesh Vedanthan, Jemima H Kamano, Violet Naanyu, Allison K Delong, Martin C Were, Eric A Finkelstein, Diana Menya, Constantine O Akwanalo, Gerald S Bloomfield, Cynthia A Binanay, Eric J Velazquez, Joseph W Hogan, Carol R Horowitz, Thomas

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 W. Nyandiko, Moi University
Co-Investigator(s)	Marete, I. Inui, T. Mwangi, A. Hogan, J. MC Henry, M.
Working Group(s)	Pediatrics (Primary) Behavioral (Secondary)
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)	Burnt Forest, Chulaimbo Sub-District Hospital, Khunyangu Sub-District Hospital, Kitale District Hospital, Moi Teaching and Referral Hospital (MTRH), Mosoriot Rural Health Training Centre, Turbo Health Centre, Webuye District Hospital
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	In the past 6 months, analyses have been complete and disseminated for Phase 1 of the HADITHI study, and patient assessments and data collection is ongoing for Phase 2. Phase 1: Phase 1 of the HADITHI study involved conducting focus group discussions with Kenyan caregivers to elicit their perspectives on disclosure of HIV status to children are complete, and in the past 6 months we have completed these qualitative analyses and presented the findings at 3 major international conferences: the Pediatric Academic Societies, 6th International Workshops on Pediatric HIV, and the International AIDS Society meetings. Findings from these publications have been well received, as many of our colleagues working in pediatric settings around the world struggle with how best to support adolescents and caregivers through the disclosure process. Phase 2: Phase 2 of the HADITHI study aims to evaluate the impact of a clinic-level disclosure intervention that involves multiple components, including peer support and counseling training. All 276 patients have been recruited for Phase 2, and data collection is ongoing. Data have been collected for the first 3 evaluations (baseline, 6 months, and 12 months), and data entry is ongoing for these evaluations. We have had some challenges with data entry, but these are being resolved as we continue to work with our data manager to review and update our data entry protocols to ensure efficient and high quality data entry. Another major accomplishment in the past 6 months is that our disclosure videos for use in peer support and counseling groups have been loaded on to computer tablets for counselors to use at the intervention sites. We worked with an Indiana University Purdue University-Indianapolis informatics team to create a HADITHI app for Google Nexus tablets that were donated to the study through the Google for Good Project. The counselors are currently being trained in the use of the tablets for counseling activities, which will become an important intervention component for evaluation
Future Plans	Over the next 6 months, we plan to: • complete Phase 2 12-month evaluations with study participants and begin 18-month evaluations • implement the use of Google Nexus tablets at intervention clinics for: 1. showing HADITHI disclosure videos and for accessing other disclosure-related materials; and, 2. weekly audio reflections from counselors that document counseling sessions • work with adolescents from AMPATH who have been through previous AMPATH peer support programs to reform the HADITHI intervention peer support group curriculum • conduct 2 or more group counseling session at all of the intervention clinics • conduct preliminary analyses on baseline characteristics of study participants and write up the results for submission to a special issue on disclosure in AIDS Care
Publication(s)	1. Vreeman RC, Scanlon ML, Klein CE, McAteer CI, McHenry MS, Inui TS, Marete I, Nyandiko WM. 'Disclosure of HIV Status to Infected Children: Perspectives from Caregivers in Western Kenya.' Presented at Pediatric Academic Societies meeting, Vancouver, BC.

Study Title	**Prevalence and Impact of Alcohol Use in Patients Enrolling in HIV Care**
Principal Investigator(s)	Kara Wools-Kaloustian, Indiana University Lameck Diero, Moi University
Co-Investigator(s)	Judith Hahn

	Jayne Kulzer Suzanne Goodrich Lameck Diero Mwebesa Bosco Bwana Patrick Oyaro Maurice Aluda
Working Group(s)	Adult (Primary) Behavioral (Secondary)
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.
Site(s)	Moi Teaching and Referral Hospital (MTRH)
Project Period	6/3/2013 – 7/31/2014
Funding Status	Funded – NIH - National Institute on Drug Abuse (NIDA)
Direct Award (USD)	$36,000
Update	The total enrollment number 277 from Modules 2 and 3 of MTRH clinics. During the last six months we have been able to follow-up and do 147 six-month CD4 counts Follow-up of LTFU: - A total of LTFU patients were 133, where were transfers out 50(16 among those who transferred to another study within the program), 18 were deceased, and 7 were double enrollments. Challenges One major challenge has been participants transferring to out to non-AMPATH sites, The second challenge has been participants missing out on test due to lack of CD4 tubes' Last but not least is follow up of Lost to follow up participants has been a challenge because scanty locator information and most phone numbers are no longer in use.
Future Plans	Continue tracking those who are lost to follow up, through phone and where possible home visit.
Publication(s)	

Study Title	**REACH Informatics Center of Excellence**
Principal Investigator(s)	Paul Biondich, Indiana University Abraham Siika, Moi University
Co-Investigator(s)	Braitstein, P.

	Diero, L. Sidle, J. Downs, S. Hogan, J. Kroenke, K. Mamlin, B. Meslin, E. Nyandiko, W. O'Meara, W. Palakal, M. Rotich, J. Shen, C. Vreeman, R. Were, M. Wools-Kaloustian, K. Yia
Working Group(s)	Adult (Primary)
Description	The project is a collaboration between Indiana and Moi Universities and the global leadership of the Regenstrief Institute. Theprogram will: 1. Provide post?doctoral informatics training to faculty at Moi University and Moi Teaching and Referral Hospital to implement and use health information technology to enhance research and improve health care quality, efficiency and outcomes. 2. Support the training of East Africans so as to support the development, implementation, maintenance, evolution and use electronic health records (EHRs) in low-income countries through didactic and mentored practicum training
Site(s)	Moi Teaching and Referral Hospital (MTRH)
Project Period	6/1/2009 – 6/30/2014
Funding Status	Funded – NIH - Fogarty International Center (FIC)
Direct Award (USD)	$945,464
Update	Fellowship programme. • The 4th Fellowship student is still continuing with his studies. He completed his 1st year of studies and now embarking on finalizing the online courses before finalizing the program in August 2014. He was not able to secure a project within the AMPATH research programmes. • The 5th Fellow is back in Eldoret after a one year study at Indiana. He is now engaged in various Health informatics projects and programmes as well as finalizing his online courses. He intends to complete his Masters in Health Informatics in July 2015. Short courses • Data Management training was held on 11th to 13th February 2014 and attended by 8 participants from KEMRI FACES, TASO Uganda, Poison's Board Kenya and Medical Practitioners Board Kenya. • Kenya EMR Mentors workshop was held on 12th May 2014 and attended by 24 participants from North Rift region in Kenya. • The OpenMRS Implementation workshop was held on 13th to 15th May 2014 and attended by 11 participants from Uasin Gishu County Government, KEMRI CDC, and Lwala Alliance • On-going mentorship on EMR Implementation with KEMRI FACES/CDC/CGHR, Uasin Gishu County Hospitals and Lwala

	Community Alliance
Future Plans	The main grant period has ended. The short courses Health Informatics training programme will continue without grant support. The following short courses are scheduled in the next six months; 1. Research Data Management 2. Mobile Application Development for Healthcare data collection 3. OpenMRS Implementation workshops 4. EMR system Development 5. Data Analysis and reporting 6. EMR systems Data Collection tools and design
Publication(s)	

Study Title	**Street Youth's Perspectives on Sexual Health in Western Kenya**
Principal Investigator(s)	Paula Braitstein, Indiana University David Ayuku, Moi University
Co-Investigator(s)	Naanyu, V. Ott, M. Wachira, J. Embleton, L. Kamanda, A. Winston, S.
Working Group(s)	Pediatrics (Primary)
Description	This is a qualitative study that aims to provide a preliminary understanding of sex from the perspective of street youth. Specifically, we will examine the language, types and functions of sexual behaviors among Kenyan street youth aged 11-24 years. The study has three main aims which include: 1. AIM 1: Describe the self-reported sexual terminology and behaviors of street youth aged 11-24 years, including terminology for and examples of sexual violence. 2. AIM 2: Describe the self-reported understanding among street youth about official non-vernacular words, including sex, rape/sexual assault, abuse, sexual abuse, consensual sex, non-consensual sex, and the sexual behaviors that may or may not characterize each. 3. AIM 3: Describe the role of sex among street youth including initiation rites and transactional sex. The study findings are hoped to inform and improve the design of sexual health interventions geared towards reducing the associated morbidity rates in this region.
Site(s)	
Project Period	8/1/2013 – 6/30/2014
Funding Status	Funded – NIH
Direct Award (USD)	Not Reported
Update	Two manuscripts: 1) 'Mshefa': The initiation of homeless or runaway children into the street community in western Kenya 2) 'Once you join the streets you will have to do it': sexual practices of street children and youth in western Kenya, have been developed and will be forwarded to the AMPATH publication committee by August 2014 for review,

	before being submitted to various journals for publication. Two additional manuscripts are currently been developed. We hope to complete these manuscripts by October 2014.
Future Plans	We hope to have published at least four manuscripts by the next 6 months.
Publication(s)	

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 Naftali Busakhala, Moi University
Co-Investigator(s)	Asirwa, C.
Working Group(s)	Oncology (Primary)
Description	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.
Site(s)	Mosoriot Rural Health Training Centre, Turbo Health Centre, Kapsakwony
Project Period	10/1/2011 – 7/1/2014
Funding Status	Funded – Walther Cancer Foundation
Direct Award (USD)	$1,200,000
Update	Three protocols are open - two focused on breast cancer prevention research and the third on cervical cancer prevention. The first two protocols (PI: Busakhala and Asirwa) have concluded data-gathering and analysis activities. The third protocol (PI: Omenge) focuses on women's opinions about screening and aggressive early treatment of cervical cancer. The Omenge protocol finished enrolling 2712 participants (women surveyed at Moi Teaching and Referral Maternal and Child Health, Webuye District Hospital and Turbo Health Center) June 27, 2014. A fourth proposal was developed to launch and assess the effectiveness of an educational program for women attending clinical breast exam screening events. Current analyses reveal conclusive evidence of significant learning as a result of exposure to this session. We now believe we know what body of information can inform and motivate women to seek screening for early-stage breast cancer and at least one powerful way to deliver this information (small group dialogue).
Future Plans	Over the next 6 months, effort must be focused on summarizing research results for publication. Emerging publications are summarized as follows: 1. Refining a questionnaire to assess breast cancer knowledge and barriers to screening in Kenya: Psychometric Assessment of the BCAM. To describe the validity and reliability of BCAM in western Kenya. Wachira. Completed awaiting submission 2. Barriers to uptake of breast cancer screening in Kenya. Use the open-ended BCAM text data to describe perceptions of barriers. Wachira. Submitted to EAMJ 3. Impact of an educational tool on levels of breast cancer awareness. A report of the impact of an educational intervention. Kisuya. Preparation nearing completion 4. Levels of breast cancer awareness in women volunteering for clinical breast examination as well as a comparison of findings from screening examination volunteers (Busakhala) and community women (Asirwa data). Combined data from the Walther breast cancer surveys. Busakhala and Asirwa Early draft circulated from screening volunteer data 5. Qualitative (Descriptive BCAM Verbatim responses) of lay perceptions of breast cancer in western Kenya A description of BCAM verbatim/qualitative data. Naanyu Preparation underway, partial draft circulated. 6. Factors associated with uptake of cervical cancer screening among women seeking care at gynecology clinics in western Kenya. Analysis of screening-focused from Omenge's protocol Omenge. Envisioned, pending analysis results 7. Predictors of uptake of cervical cancer treatment among women with abnormal visual inspection with acetic acid (VIA) and not eligible for cryotherapy. Analysis of treatment-focused data. Omenge/ Envisioned, pending analysis results

Publication(s)	Busakhala, N. Outcomes of screen-detected breast cancer in western Kenya. 2013 National Cancer Institute Directors Meeting, Lyon, France. July 10, 2013. -- Wachira J, Chite AF, Naanyu, V, Busakhala N, Kisuya J, Keter A, Mwangi A, Inui T and The Wa
Study Title	**A Formative Study to Develop Culturally Valid Psychosocial Assessment Tools and Interventions to Promote Family Well-Being in Kenya**
Principal Investigator(s)	Eve Puffer, Duke University David Ayuku, Moi University
Co-Investigator(s)	
Working Group(s)	Pediatrics (Primary) Behavioral (Secondary)
Description	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.
Site(s)	Mihuu Community, Webuye; Burnt Forest Community; Pioneer Community
Project Period	5/28/2013 – 1/30/2014
Funding Status	Funded – Duke Global Health Institute, Johnson and Johnson
Direct Award (USD)	$29,500
Update	Analysis of previous focus group qualitative data about community perceptions of family functioning, relationships, and communication was completed. This analysis informed the creation of a survey measure of family functioning and individual mental health that is currently being pilot tested in Pioneer communities with potential activities in Burnt Forest and Webuye communities as well. This is to prepare for the quantitative validation of the survey.
Future Plans	The validity portion of the study will include both survey administration as well as in-depth interviews and observations with families in these areas. 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. Following the validity study we plan to begin the family therapy intervention pilot informed by community advisory committees. The family therapy intervention will address issues raised in the focus group qualitative data in order to make the intervention culturally relevant for peri-urban and rural communities in Kenya.
Publication(s)	

Study Title	**Sexual Health Risks and HIV and STI Prevalence Among Street Involved Youth in Western Kenya**
Principal Investigator(s)	Paula Braitstein, Indiana University
Co-Investigator(s)	Amon Chirchir Susanna Winston David Ayuku E Jane Carter Winstone Nyandiko
Working Group(s)	Pediatrics (Primary) Behavioral (Secondary)
Description	This is a cross sectional study characterizing the sexual health risks, behaviors and outcomes in street-involved youth in Eldoret. The specific aims of this study are to: 1) characterize the sexual risk behaviors (including age of sexual debut, age discrepancy of partners, exchange/survival sex, number of partners, and condom use) of the street youth in Eldoret; 2) determine the prevalence of and risk factors for sexual abuse and assault of street youth; 3) assess access to reproductive health care for street youth in Eldoret, and 4) determine the prevalence of and risk factors for HIV and STIs among street youth. The study population will consist of street-involved youth ages 12-21 in Eldoret, Kenya, with a goal of enrolling 200 youth. Subjects will participate in a structured interview to complete a questionnaire regarding street life and sexual health, and undergo STI screening tests (blood tests for HSV-2Ab and syphilis, self-collected gential and rectal swabs for chlamydia, gonorrhea, trichomonaisis) and HIV counseling and testing. Data analysis will include descriptive statistics for demographics, sexual behaviors and risk factors. We will use multivariable logistic regression analyses to identify independently associated demographics, risk factors (sexual abuse, drug use, lack of access to healthcare) and specific risk behaviors, with STI and HIV infections
Site(s)	Moi Teaching and Referral Hospital (MTRH), OSCAR Clinic, Berur
Project Period	9/1/2011 – 7/1/2014
Funding Status	Funded – Brown University - Center For AIDS Research, Brown Framework in Global Health
Direct Award (USD)	$40,000

Update	Manuscript is under review.
Future Plans	Hope to have manuscript published.
Publication(s)	

Study Title	**Accuracy of Oral HIV Self-tests in Kenya**
Principal Investigator(s)	Ann Kurth, New York University Abraham Siika, Moi University
Co-Investigator(s)	Were, Edwin Naanyu, Violet Emonyi, Wilfred
Working Group(s)	Adult (Primary) Basic (Secondary)
Description	Knowledge of HIV status is key to earlier access to HIV treatment and prevention services. In resource limited settings such as in sub-Saharan Africa, the shortage of health care workers has been identified as a barrier in the effort to scale up HIV prevention and treatment service. Given the public health implications of unknown HIV status, availability of self-testing for rapid scale up of HIV testing is compelling; increasing awareness of HIV status is an important step towards reducing HIV transmission and enabling antiretroviral therapy (ART) that reduces mortality as well as secondary HIV transmission. Performance and accuracy parameters of HIV self-testing (HST) will be determined. We hypothesize: Aim 1: Kenyan populations can accurately determine their oral fluid (OF) HST results (expected sensitivity of ?96% and specificity of 99%) Aim 2: OF HST will be acceptable and feasible (?95% say HST is acceptable/easy to use) Aim 3: The proportion of those who are preliminary positives (confirmed by ELISA), who are referred to care, will attend clinic within one month post HST confirmed result will be the same or higher levels as seen in those who test through regular VCT (AMPATH EHR anonymous data).
Site(s)	Moi Teaching and Referral Hospital (MTRH)
Project Period	7/1/2013 – 2/28/2014
Funding Status	Funded – International Initiative for Impact Evaluation (3ie)
Direct Award (USD)	$76,358
Update	Study Main Outcomes for Aims 1-3 are summarized below: Prevalence: We show here prevalence of HIV infection based on staff finger stick (FS) results, since staff FS results were equivalent to the ELISA laboratory blood test (sensitivity and specificity both 100%) and available for all participants. A total of 35 of 239 participants were positive for HIV infection, indicating prevalence of just under 15% (0.146; 95% CI: 0.107 - 0.197). Sensitivity and Specificity: Determination of the accuracy of oral fluid (OF) HIV self-testing (HST) was based on comparison with the ELISA blood test and staff FS rapid HIV testing. Among the 239 OF HIV self-testing results, 36 (15.1%; 95% CI: 11.1% - 20.1%) were invalid. Among the invalid OF HST results, only one participant was from the videotaped cohort;

	invalid results were more likely among participants not videotaped, but this difference was not statistically significant (OR = 3.60; p = 0.3251 by Fisher's Exact Test). Invalid results were excluded from analysis of accuracy. Among 29 participants with positive ELISA results, 3 false negatives were observed for OF HST (Sensitivity = .897; 95% CI: 0.726 - 0.978). Among 49 participants with negative ELISA results, 1 false positive was observed for OF HST (Specificity = 0.980; 95% CI: 0.891 - 0.999). Among 29 participants with positive staff FS results, 3 false negatives were observed for OF HST (Sensitivity = .897; 95% CI: 0.726 - 0.978). Among 174 participants with negative staff FS results, one false positive was observed for OF HST (Specificity = 0.994; 95% CI: 0.968 - 0.999). All participants positive by FS were confirmed by ELISA, which identified exactly the same people as having HIV infection. However, only a sample of negatives was confirmed by ELISA, hence the slight difference in specificity. Negative and positive predictive values for OF HST relative to ELISA and staff FS results were estimated as well. Among 51 participants with a negative OF HST result, 48 were also negative by ELISA (NPV = 0.941; 95% CI: 0.838 - 0.988). Among 27 participants with a positive OF HST result, 26 were also positive by ELISA (PPV = 0.963; CI: 0.810 - 0.999). Among 176 participants with a negative OF HST result, 173 were also negative by staff FS (NPV = 0.983; 95% CI: 0.951 - 0.996). Among 27 participants with a positive OF HST result, 26 were also positive by staff FS (PPV = 0.963; CI: 0.810 - 0.999). HST Acceptability: Almost all said that use of the HST was acceptable (94%) and confidence in the ability to perform and interpret the self-test appeared to increase with exposure to actually doing the test. Most participants (94%) said that they would use a self-test in the future. Linkage to Care: All those confirmed to be HIV-positive were informed of the HIV result and actively referred to HIV care at AMPATH facilities. One Month Phone Call Follow-up Survey: One-month post diagnosis, staff made follow-up phone calls to all confirmed HIV+s regarding care utilization (n=35). Ninety-one percent completed one month follow-up (32/35). There were 2 lost to follow-up (non-working contact numbers) and 1 deceased because of traffic accident unrelated to the study. Seventy-eight percent (25/32) self-reported that they accessed HIV services. Among those who did not access HIV services (7/32), reasons included, not ready to go (n=2), not satisfied with results (n=1), did not want people to see them at the clinic (n=1), no reason for not accessing care (n=1) and other (n=2). When we reviewed the medical records to confirm linkage to care, only 11 participants of the 25 who self-reported they accessed HIV care services actually sought care. However, one participant who previously reported they did not access HIV services did seek care. This 38% (12/32) linkage compares to 46% linkage in AMPATH HBCT (n=178 HIV+ Port Victoria program data). Implications of our findings include: (1) Clear interest in, and good acceptability of, HIV self-testing (HST) among the general population. HST may particularly reach men and at risk people within the broader adult population. (2) General population adults can conduct the HIV self-test. Sensitivity was reasonable, though lower than expected or perhaps, ideal. Strategies to increase sensitivity/predictive value should be considered in any HST roll-out. (3) If HST is rolled out in Kenya, there will be need for clear instructions and possibly, user training in some form. (4) The need for OF self-tests to be confirmed will have health system implications.
Future Plans	Study concluded 2/28/2014. IREC IRB study closure approval dated 14th July 2014.
Publication(s)	Kurth AE, Cleland CM, Chhun N, Sidle JE, Were E, Naanyu V, Emonyi W, Macharia SM, Sang E, and Siika AM, 'Oral HIV Self-testing Accuracy, Acceptability, and Feasibility in a General Population in Kenya.' In Review, JAIDS.

Study Title	**Mortality Among Street Connected Children and Youth in Eldoret, Kenya: a Retrospective Chart Review**
Principal Investigator(s)	Lonnie Embleton, Moi University Paula Braitstein, Indiana University
Co-Investigator(s)	Ayuku David Kamanda Allan Makori Dominic Nalyanya
Working Group(s)	Pediatrics (Primary)
Description	There are increasing reports of deaths among street connected children and youth in Eldoret, Kenya. A number of deaths have been documented by a community advocate since January 2010 and brought to the attention of our research team as a major concern. It is known that many of these children and youth engage in high risk behaviours, such as substance use, transactional sex, are subject to physical and sexual violence, perform hazardous labour and in general have harsh living conditions on the streets, all of which heighten their risk for death. It is suspected that many of the reported deaths among this population are preventable and require the urgent attention of service providers and policymakers to implement programs and services to decrease mortality in this marginalized population. In light of the increased reports of death among this vulnerable population in Eldoret, Kenya, this present proposal seeks to perform a case-series review of deaths among street connected children and youth through a retrospective chart review at Moi Teaching and Referral Hospital (MTRH). This proposal seeks to ascertain cause of death and HIV status from MTRH and mortuary records for known deaths among street connected children and youth aged less than 25 who have passed away from January 2010-December 2013 in and out of the hospital. Currently there are no reports in the literature concerning mortality among street connected children and youth in sub-Saharan Africa; yet it is vital to understand the causes of death in this population in order to prevent unnecessary deaths. This case series in Eldoret, Kenya will provide valuable preliminary data and insight into the causes of mortality among street connected children and youth. Ascertaining causes of death will assist local service providers and policymakers to target key public health areas to decrease mortality. Aim 1. To estimate the number of deaths that have occurred among street children and youth aged 0 to <25 years, in and out of hospital, in Eldoret Kenya between January 2010 and December 2013. Aim 2. To determine the causes of death among street children and youth aged 0 to <25, utilizing hospital and mortuary records from MTRH, in Eldoret Kenya between January 2010 and December 2013. Aim 3. To determine the HIV status of deceased street children and youth aged 0 to <25, utilizing hospital and mortuary records from MTRH, in Eldoret Kenya between January 2010 and December 2013.
Site(s)	Moi Teaching and Referral Hospital (MTRH)
Project Period	10/30/2013 – 4/30/2014
Funding Status	Unfunded –

Direct Award (USD)	
Update	We completed data collection, analysis, and submitted a manuscript at BMC Research Notes. The following is an excerpt of our findings and their relevance to AMPATH: We performed a retrospective chart review of reported deaths among street-connected children and youth (SCCY) in Eldoret, Kenya to describe causes of death and determine the number of deaths attributable to HIV. We extracted data on deaths occurring from October 2009 to April 2014 from Moi Teaching and Referral Hospital (MTRH) and Academic Model Providing Access to Healthcare (AMPATH) records. In total there were 53 recorded deaths, 40% of whom were aged ≤18 years. A third of males died due to homicide (33%) and over a quarter due to accidental injuries (30%) while the majority of females died from natural causes (75%). HIV (suspected or confirmed) was the underlying cause of death for 40% of cases and over half for females (55%). This retrospective case series concerning mortality among street connected children and youth in Eldoret, Kenya highlights important gaps in adolescent HIV care, specifically among vulnerable and highly marginalized populations. We identified that 23% of the deceased were HIV-positive (confirmed with AMPATH records) and in combination with those suspected HIV-positive (verbal autopsy or death due to PCP/PTB) this rises to 43%. Of the HIV-positive cases with AMPATH records, 5 were receiving regular care and ART, while the remaining cases never returned after an initial visit, had no CD4 count documented and had not initiated ART. These findings suggest a potentially hidden epidemic of HIV among street connected children and youth and may indicate a low uptake of and retention in care after testing HIV-positve. There is a need to augment HIV care for street youth and other vulnerable adolescent populations and AMPATH should consider creating a dedicated HIV and sexual health clinic for vulnerable and marginalized adolescents. :
Future Plans	Publication of paper related to findings
Publication(s)	Mortality among street-connected children and youth in western Kenya: a retrospective case series Authors: Embleton L, Ayuku D, Makori D, Kamanda A, Braitstein P Under review at BMC Research Notes

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 Paula Braitstein, Indiana University
Co-Investigator(s)	Ayuku David
Working Group(s)	Pediatrics (Primary)
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)	Moi Teaching and Referral Hospital (MTRH)
Project Period	8/1/2013 – 5/1/2014
Funding Status	Unfunded –
Direct Award (USD)	
Update	This systematic review is in the data extraction and data study quality evaluation phase. In total we have included 53 quantitative papers looking at the reasons that children and youth become street-involved in low-, middle-, and high-income countries.
Future Plans	In the next 6 months, we plan to complete data extraction and assessing study quality. As well we aim to complete analysis, manuscript development and submit the paper for publication.
Publication(s)	

Study Title	**Inhalants and the Pathway to HIV Infection Among Street Youth in Western Kenya**
Principal Investigator(s)	Paula Braitstein, Indiana University David Ayuku, Moi University
Co-Investigator(s)	Atwoli, L Ayaya, S Ott, M Marshall, B Hogan, J Auerswald, C Kwena, Z Bukusu, E

Working Group(s)	Pediatrics (Primary)
Description	This proposal is under review at NIDA. Our long-term goal is to develop innovative, evidenced-based, developmentally-appropriate interventions that build resilience, promote health, prevent substance use, and reduce health-related risks among street-involved adolescents (SIA). The objective of this ground-breaking application is to describe the epidemiology of volatile substance misuse (VSM) and HIV among SIA in an HIV endemic region, and determine whether and how VSM increases their risk of HIV acquisition. Our central hypothesis is that those who use VS will be at higher risk of acquiring HIV compared to those who do not. To achieve our objectives, we will enroll a quasi-random sample of 800 HIV-negative adolescents aged 12-18 years living full-time on the streets of 3 cities in western Kenya and follow them for 48 months, collecting self-reported data on HIV risk behaviors and other relevant data while conducting HIV testing at baseline and every 6 months. Our specific aims (SA) are to: SA1: Characterize the epidemiology of VSM and other substance use among SIA in the region. SA1A: Determine the prevalence of VSM and other substance use at baseline and investigate its relationship to baseline environmental (city of enrolment), social network (involvement of an adult in their life, network diversity), mental health (post-traumatic stress, depression), and resilience characteristics (participation in religious or community activities). SA1B: Estimate the distribution of time to first VS use among non-users at baseline, and identify baseline determinants of initiation, cessation and relapse during follow-up. SA1C: Evaluate the longitudinal determinants of VS initiation, cessation and relapse including environmental, social network, mental health, poly-substance use, and resilience characteristics. SA2: Estimate the effect of VSM on HIV risk and HIV incidence, independently and in the context of poly-substance use (PSU). SA2A: Determine the relationship between VSM, PSU, and prevalence of HIV risk behaviors at baseline. SA2B: Estimate the effect of baseline VSM and PSU on changes in HIV risk behaviors during follow-up. SA2C: Estimate the effect of baseline and longitudinal measures of VSM on HIV incidence at 3 and 5 years of follow-up. SA2D: Investigate the degree to which the total effect of VSM on HIV incidence is mediated by initiation of or changes in poly-substance use and HIV risk behaviors. A key secondary sub-aim will be to describe uptake of and retention in care among HIV-infected participants.
Site(s)	Moi Teaching and Referral Hospital (modules 1-4), Nakuru and Kisumu
Project Period	9/1/2014 – 9/1/2018
Funding Status	Unfunded –
Direct Award (USD)	
Update	This proposal was unfunded. We are aiming to retool it into an HIV specific cohort looking at prevalence, incidence and uptake of care among street youth for submission to NIAID (Dec 2014).
Future Plans	Submit to NIAID
Publication(s)	

Study Title	**SAFI (Stigma in AIDS Family Inventory) Validation Study**
Principal Investigator(s)	Rachel Vreeman, Indiana University Winstone Nyandiko, Moi University
Co-Investigator(s)	Irene Marete Hai Liu Violet Naanyu
Working Group(s)	Pediatrics (Primary)
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)	Burnt Forest, Chulaimbo Sub-District Hospital, Khunyangu Sub-District Hospital, Kitale District Hospital, Moi Teaching and Referral Hospital (MTRH), Mosoriot Rural Health Training Centre, Turbo Health Centre, Webuye District Hospital
Project Period	12/17/2013 – 11/30/2015
Funding Status	Funded – NIH - National Institute of Mental Health (NIMH)
Direct Award (USD)	$567,828
Update	Since January, we have successfully conducted 10 focus groups at 3 representative clinics, with a total of 95 participants. Participants were asked questions regarding perceived, enacted and internalized H/A stigma. Translation and transcription of the group discussions has been completed, and coding of the transcripts is underway. We will also generate a comprehensive set of stigma measurement items for reliability and validity testing using existing data, patient input from the focus group discussions, and cross-cultural test adaptation. To this end, we are conducting a systematic review to compile items used to measure pediatric and caregiver H/A stigma in other settings. The review is

	well underway, with data now being extracted from the systematically identified studies.
Future Plans	For the SAFI revision, in the next 4 months, we will complete the qualitative analysis of the focus group discussions on H/A stigma, we will complete the systematic review, and we will compile, modify, and implement the potential H/A stigma measurement items in the assessments for the HADITHI cohort. We will use the HADITHI cohort of families to assess the validity of the questionnaire measures of family stigma compared to independent construct measures including medication adherence, and children's clinical, psychological, and social outcomes. The data collected through the SAFI revision will enable us to assemble a comprehensive family H/A stigma measure with maximum reliability and validity for assessing all relevant domains of stigma, including perceived, enacted and internalized stigma, and for use with all members of the family unit.
Publication(s)	

Study Title	**HIV-1 Drug Resistance in Different Subtypes**
Principal Investigator(s)	Rami Kantor, Brown University Lameck Diero, Moi University
Co-Investigator(s)	Nathan Buziba Wilfred Emonyi
Working Group(s)	Adult (Primary) Basic (Secondary)
Description	Examine drug resistance upon tenofovir-containing first line antiretroviral therapy in multiple subtypes in western Kenya using different analyates.
Site(s)	Moi Teaching and Referral Hospital (MTRH)
Project Period	5/12/2012 – 2/20/2014
Funding Status	Funded – NIH - National Institute of Allergy and Infectious Diseases (NIAID)
Direct Award (USD)	$98,168
Update	Samples successfully received and laboratory assays being finalized.
Future Plans	Finalizing lab assays; data analysis; preparation of abstracts and papers.
Publication(s)	

Study Title	**Antiretroviral Treatment Failure and Drug Resistance in HIV-infected Patients on Second Line Regimens in Western Kenya**
Principal Investigator(s)	Rami Kantor, Brown University Lameck Diero, Moi University
Co-Investigator(s)	Nathan Buziba

	Wildred Emonyi
Working Group(s)	Adult (Primary) Basic (Secondary)
Description	To determine prevalence and correlates of second line virological failures, research patterns and implications of drug resistance and examine predictors of drug resistance evolution in patients failing second line antiretroviral therapy in western Kenya.
Site(s)	Moi Teaching and Referral Hospital (MTRH)
Project Period	6/30/2011 – 2/20/2014
Funding Status	Funded – Brown University - Center For AIDS Research
Direct Award (USD)	$225,220
Update	Study presented in 2014 CROI. Laboratory analysis finalized for current papers. 2 papers in preparation. Laboratory analyses for additional genes.
Future Plans	Finalize papers publication. Continue laboratory assays for additional genes and more sensitive assays.
Publication(s)	As above.

Study Title	**Treatment Outcomes of Childhood Cancer in Western Kenya**
Principal Investigator(s)	Jodi Skiles, Indiana University - Purdue University in Indianapolis (IUPUI) Festus Njuguna, Moi University
Co-Investigator(s)	Hugo Martin Saskia Mostert Terry Vik Floor Abbink Gertjan Kaspers Gilbert Olbara Floor Abbink
Working Group(s)	Oncology (Primary) Pediatrics (Secondary)
Description	While basic epidemiologic information in on childhood cancer in Western Kenya has been recently reported, little is known about outcomes of cancer treatment in this population. This is a major pitfall in improving the care and cure for children in this part of the world. Our study aims to provide a retrospective review of childhood cancer treatment outcomes in Western Kenya since implementation of standard treatment protocols in 2009. This retrospective analysis of childhood malignancies and treatment outcomes in Western Kenya will be carried out using information from patients seen at the Moi Teaching and Referral Hospital. Patients who were first seen at the hospital between 1st January 2009 and 31st December 2013 will be included. All children up to 18 years of age will be included. Information on patient demographics, diagnosis, treatment provided and

	treatment outcomes will be collected from the patients' medical records.
Site(s)	Moi Teaching and Referral Hospital (MTRH)
Project Period	9/16/2013 – 12/31/2014
Funding Status	Unfunded –
Direct Award (USD)	
Update	Data collection is now complete and data cleaning and analysis is now underway.
Future Plans	Completion of data analysis with a goal to have a manuscript draft compiled and (hopefully) submitted.
Publication(s)	

Study Title	**Evaluation of HIV Drug Resistance Prevalence and Consequences in the Setting of the Recent Political Crisis in Kenya**
Principal Investigator(s)	Rami Kantor, Brown University Lameck Diero, Moi University
Co-Investigator(s)	Nathan Buziba Wilfred Emonyi
Working Group(s)	Adult (Primary) Basic (Secondary)
Description	Determine and compare prevalence of virological failure and drug resistance at the time of post-crisis resumption of care, in Kenyan patients with and without crisis-induced antiretroviral treatment interruption.
Site(s)	Burnt Forest, Turbo Health Centre
Project Period	11/24/2009 – 2/20/2014
Funding Status	Funded – NIH - National Institute of Allergy and Infectious Diseases (NIAID) , Friendship Foundation
Direct Award (USD)	$54,652
Update	Paper published.
Future Plans	Additional resistance analyses and publication.
Publication(s)	M Mann, L Diero, E Kemboi, F Mambo, W Injera, A DeLong, L Schreier, K Wools Kaloustian, N Buziba, R Kantor. Unplanned Antiretroviral Treatment Interruptions Induced by the Kenyan Post-Election Crisis are Associated with HIV virologic Failure. Journal of A

Study Title	**HIV-1 Genotypic Diversity and Drug Resistance in Western Kenya**
Principal Investigator(s)	Rami Kantor, Brown University Lameck Diero, Moi University
Co-Investigator(s)	Nathan Buziba Wilfred Emonyi
Working Group(s)	Adult (Primary) Basic (Secondary)
Description	Identify circulating HIV-1 subtypes and recombinant forms, determine genotypic background in drug-na persons and determine drug resistance in persons failing antiretroviral thearpy in western Kenya, using multiple testing analytes.
Site(s)	Moi Teaching and Referral Hospital (MTRH)
Project Period	5/17/2006 – 2/20/2014
Funding Status	Funded – Brown University - Center For AIDS Research, Rhode Island Foundation
Direct Award (USD)	$40,000
Update	Study presented at the 23rd International HIV Drug Resistance Workshop in Berlin Gernany in June 2014. Paper under revision for the Journal of International AIDS Society.
Future Plans	Finalize paper publication. Analysis of additional HIV genes and more sensitive resistance assays.
Publication(s)	As above.

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
Co-Investigator(s)	Naftali Wisindi Busakhala Evangeline Wawira Njiru
Working Group(s)	Adult (Primary) Basic (Secondary)
Description	This is an ACTG prospective, randomized, active-controlled clinical trial in which participants will be randomized 1:1:1 to oral etoposide (ET) plus antiretroviral therapy (ART), bleomycin and vincristine (BV) plus ART, or paclitaxel (PTX) plus ART. The primary objective will be to compare the clinical efficacy of two regimens, oral ET plus ART and BV plus ART, to PTX plus ART for initial treatment of advanced stage AIDS-KS.
Site(s)	Moi Teaching and Referral Hospital (MTRH)

Project Period	4/1/2014 – 2/28/2021
Funding Status	Funded – NIH - AIDS Clinical Trials Group (ACTG), NIH - National Cancer Institute (NCI), NIH - National Institute of Dental and Craniofacial Research (NIDCR)
Direct Award (USD)	Not Reported
Update	The study was amended and all approvals were obtained for protocol version 2.0. Study drugs are now on site and we are working on requesting for site activation for us to begin screening and enrolling participants.
Future Plans	We plan to screen and enroll participants into the study soon after receiving site activation letter from ACTG.
Publication(s)	

Study Title	**A5273 'Multicenter Study of Options for Second-Line Effective Combination Therapy (SELECT)'**
Principal Investigator(s)	Abraham Siika, Moi University
Co-Investigator(s)	Faraj Some
Working Group(s)	Adult (Primary) Basic (Secondary)
Description	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.
Site(s)	Moi Teaching and Referral Hospital (MTRH)
Project Period	1/22/2013 – 10/3/2016
Funding Status	Funded – NIH - AIDS Clinical Trials Group (ACTG)
Direct Award (USD)	Not Reported
Update	The initial recruitment target for A5273 was 600 patients. However enrolment was halted in September 2013 due to preliminary findings of other similar international studies. The EARNEST study was a large study that was conducted in Africa for second-line therapy, which included three therapy arms. The results from the comparison of the Aluvia + 2NRTIs and Aluvia + raltegravir arms are particularly relevant for A5273. Although the study included very different endpoints, the results showed that the raltegravir arm was not superior to the nucleoside arm. These findings, along with the findings of the

	SECOND-LINE study, spurred the A5273 study team to update the sample size estimates and power calculations. The new analysis demonstrated that enrollment could be stopped without compromising the ability to address the primary objective of the study.
Future Plans	Once approval of protocol version 2.0 is received, all active participants will be exited and transitioned to primary care provider, AMPATH. The plan is that participants should be exited starting October 2014.
Publication(s)	

Study Title	**A5274/REMEMBER Reducing Early Mortality and Early Morbidity by Empiric Tuberculosis Treatment Regimens '**
Principal Investigator(s)	Abraham Siika, Moi University
Co-Investigator(s)	David K Lagat
Working Group(s)	Adult (Primary) Basic (Secondary)
Description	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.
Site(s)	Moi Teaching and Referral Hospital (MTRH)
Project Period	10/10/2012 – 12/31/2016
Funding Status	Funded – NIH - AIDS Clinical Trials Group (ACTG)
Direct Award (USD)	Not Reported
Update	This study is now closed to accrual. A total of 70 participants were recruited at the Eldoret site out of the international number of 851.
Future Plans	The next 6 months will be a period of follow up of the already enrolled participants. During this period, it is expected that some of the participants will start exiting the study.
Publication(s)	

Study Title	**A5288 'Management Using the Latest Technologies in Resource-limited Settings to Optimize Combination Therapy After Viral Failure (MULTI-OCTAVE)'**
Principal Investigator(s)	Abraham Siika, Moi University
Co-Investigator(s)	Beatrice Wangari Ndege
Working Group(s)	Adult (Primary) Basic (Secondary)
Description	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 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
Site(s)	Moi Teaching and Referral Hospital (MTRH)
Project Period	12/18/2013 – 12/31/2015
Funding Status	Funded – NIH - AIDS Clinical Trials Group (ACTG)
Direct Award (USD)	Not Reported
Update	So far a total of 5 participants have been enrolled and follow up is going on well. All required screening lab results have been received for two additional participants who should be enrolled in the next few weeks. The main challenge is the duration it takes from screening to enrollment, which can take up to 3 months.
Future Plans	We plan to actively screen and enroll participants into the study and follow up active ones too.
Publication(s)	

Study Title	**SEE and LEEP by trained nurses: Task sharing in cervical cancer screening**
Principal Investigator(s)	Barry Rosen, University of Toronto Philip Tonui, Moi University
Co-Investigator(s)	0
Working Group(s)	Oncology (Primary) Reproductive (Secondary)
Description	We propose a 'See and LEEP' strategy in rural Kenya to provide a point-of-need service for women with a positive cancer screen. LEEP is highly effective at treating pre-malignant disease, has low morbidity and can be used in a low-resource setting. Using a 'See and Treat' strategy we have noted that 30% of women treated with cryotherapy continue to have precancerous cervical lesions or worse, and 35% of women with an abnormal VIA screen never return for further care. We can do better. Using a nurse-led model of care, we can provide access to more effective treatment (LEEP) at the point-of-need to reduce the burden of cervical cancer.
Site(s)	Moi Teaching and Referral Hospital (modules 1-4), Webuye District Hospital
Project Period	10/1/2013 – 3/31/2015
Funding Status	Funded – Grand Challenges Canada
Direct Award (USD)	$100,000
Update	Between January and June 2014, the project made the following progress. Secured approval from the the Nursing Council of Kenya to train four nurses (on colposcopy and LEEP (NCK/R/2013 of 21/3/2014). These four nurses will train other nurses. Ethics approval was secured from MTRH/MUCHS (IREC/2014/236 of 22/4/2014) and U of T (Protocol ID 30276 of 3/7/2014). The first training of nurses is planned shortly.
Future Plans	An initial 2 day training-of-trainers (TFT) training of four nurses is planned for 28th and 29th August 2014. Further training and mentoring of the nurses will be done between Sept and Dec 2014 We are planning to start data collection in Jan 2015.
Publication(s)	

Study Title	**TB Reach**
Principal Investigator(s)	E Jane Carter, Brown University Nathan Buziba, Moi University
Co-Investigator(s)	Dr Wilfred Injera
Working Group(s)	TB (Primary) Pediatrics (Secondary)
Description	The aim of the TB Reach grants from the Stop TB Partnership at WHO is to reach those

	who have no access to TB diagnosis. We have been awarded a Wave 2 grant and then a Wave 2 year 2 grant. We have 4 aims in our present grant. 1.) To use our intensified case finding model with cough monitors to perform community based awareness and screening for TB. 2.) To roll out GenXpert for smear negative TB suspects within reach of our Xpert sites. We expand the reach of the site but the development of a sputum transport system with the Xpert site as the hub of the system. 3.) To provide a TB Screening package for all children under 5 years of age living in a smear positive household to increase screening and access to both TB diagnosis and IPT for prevention and 4.) To provide TB screening for new patients in District Hospitals using the cough monitor model of Moi Teaching and Referral Hospital.
Site(s)	Angurai Health Centre
Project Period	7/1/2013 – 12/31/2014
Funding Status	Funded – World Health Organization (WHO)
Direct Award (USD)	$803,472
Update	In aim 1 we are presently in 188 sites across Western, North Rift and North Nyaanza Provinces. We have screened 21,610 individuals with our cough questionnaire, collected sputum on 19,630 TB suspects and diagnosed 1367 individuals with Smear positive TB since October 1, 2013. For AIm 2, we have access to 8 Xpert machines. We have designed HUBs around 6 of these. We have screened 806 smear negative TB Suspects and confirmed 125 as having TB since January 2014. The benefits of Xpert screening in this case are two fold: earlier confirmed diagnosis in smear negative patients as well as allowing patients who are smear negative and Xpert negative to move on for evaluation for other causes of their symptoms. In the pediatric aim, we have instituted the program at 14 sites. To date we have screened 431 children and diagnosed 89 with active TB and linked them into care. Of the remainder, 342 are receiving IPT . In the District hospital arm, we have initiated the program at 14 District Hospitals since April 2014. Data is pending on cases identified. At MTRH the program has screened 1881 patients with questionnaires, collected sputa on 422 suspects who had a positive questionnaire and found 47 smear positive pulmonary cases since October 1, 2013. Key challenges remain that field supervision is difficult to verify and perform reliably. Supply chain management is critical; we supply supplies when the national program runs out.This includes INH for pediatric IPT which is stocked out at the national level. At the request of the National TB Program we have initiated both ICF with Cough monitors as well as Xpert testing in Turkana; the distance remains a challenge for supply chain management and supervision.
Future Plans	We hope to evaluate the district hospital program as well as to monitor outcomes for the pediatric aim (for both TB disease as well as IPT). We also hope to establish all Xpert HUBs so that the labs can be turned over to the National TB Program in 2015.
Publication(s)	Abstract - accepted for The Union World Congress on Lung Health in Barcelona, Spain November 2014. Title: When TB Reach eliminates cost, other barriers to screening child household TB contacts are revealed in Eldoret, Kenya First Author: Daria Szkwarko

Study Title	**Innovative public-private partnership to target subsidized antimalarials in the retail sector**
Principal Investigator(s)	Wendy O'Meara, Duke University Dr. Diana Menya, Moi University
Co-Investigator(s)	Laktabai, Jeremiah Mohanan, Manoj Turner, Elizabeth
Working Group(s)	Adult (Primary) Public Health/Primary Care (Secondary)
Description	In most of the malaria-endemic world, fevers are often treated with medicine purchased over the counter in pharmacies, drug shops and general stores. Antimalarials of varying quality and efficacy are widely available in a range of regulated and unregulated outlets. Effective artemisinin combination therapies (ACTs) recommended by the World Health Organization are considerably more expensive than counterfeit drugs or older antimalarials to which high levels of resistance exist. As a result, fewer than 15% of fevers treated for malaria receive appropriate, effective therapy. This project therefore seeks to implement and evaluate an innovative public-private partnership designed to improve targeting of ACTs to individuals with confirmed malaria infection. The partnership will leverage an existing network of trained community health workers and a vibrant retail medicine sector that has been shown to be an efficient conduit for subsidized antimalarials. Unlike other approaches that attempt to improve targeting of ACTs by offering subsidized RDTs, our approach allows the subsidy itself to be targeted through linking the subsidy to a positive malaria test using a coupon system. The proposed work addresses a time-sensitive problem with significant policy implications, both nationally and internationally. In Aim 1, we will determine the effect of varying levels of subsidy on patients' decision to purchase ACTs, and determine the level of subsidy required to maximize targeting of ACTs to clients with confirmed malaria infection. This approach will allow us to quickly generate information that will 1) assist the Division of Malaria Control to set subsidy levels nationwide and 2) guide Aim 2 to set subsidy levels for ACTs to maximize the community-level impact of expanding availability of malaria diagnosis on appropriate treatment. In Aim 2, we will scale up and evaluate an innovative public-private partnership between government-trained community health workers (CHWs) and retail outlets designed to target the subsidized antimalarials to those people with confirmed malaria infection. CHWs will be trained to perform malaria rapid diagnostic tests (RDTs) at the household level and give a coupon to those individuals who have a positive malaria test. The coupon will entitle the holder to a discount on a subsidized, quality-assured ACT purchased in the retail sector. The subsidy is provided by the coupon rather than directly to the wholesaler/retailer. This strategy allows not just the ACT, but the subsidy to be targeted to those individuals with confirmed infection.
Site(s)	Other
Project Period	2/15/2014 – 1/31/2018
Funding Status	Funded – NIH
Direct Award (USD)	Not Reported
Update	The project received an IREC and Duke IRB approval in June 2014.It was then started by

	sensitization meetings with shop owners in the study area, meeting the district health management team of Bungoma East sub county and training of enumerators, community health volunteers, and community health extension workers. The study team also met with community leaders including sub-chief of Ndivisi division and village elders to make them aware of this study in their community. Piloting has already began.
Future Plans	We hope to launch the study within this period and also target to have recruited 500 participants in aim 1.
Publication(s)	

Study Title	**Vincristine Optimization in Kenyan Children with Cancer**
Principal Investigator(s)	Jodi Skiles, Indiana University - Purdue University in Indianapolis (IUPUI) Festus Njuguna, Moi University
Co-Investigator(s)	G Olbara, MBBS S Langat J Musimbi T Vik, MD S Mostert, MD,PhD GJL Kaspers,MD,PhD N Busakhala F Asirwa P Loehrer J Renbarger, MD1
Working Group(s)	Oncology (Primary) Pediatrics (Secondary)
Description	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.
Site(s)	Moi's Bridge Health Centre
Project Period	2/3/2014 – 1/31/2018
Funding Status	Funded – NIH - National Cancer Institute (NCI), NIH - Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD)
Direct Award (USD)	$103,254
Update	This study commenced in February 2014 and 8 subjects have been enrolled to date and we are currently recruiting subjects for Phase I, Dose level 2. Recruitment has been slower than anticipated due to issues with access to chemotherapeutic agents, however that issue is now resolved and recruitment is starting to pick back up. Additionally, it took longer than anticipated to get the NCI/Leidos Biomedical contract with IU (and subcontract with Moi) in place, which delayed the hiring of a dedicated study nurse. All contract issues have now been resolved and the study nurse has been hired.
Future Plans	Ideally, we would like to complete recruitment for Phase I of this study within the next 6

	months. At that time, we will conduct an interim analysis in preparation for Phase II of this study, although funds have not yet been secured to conduct Phase II of this study. To this end, the other objective over the next 6 months is to secure funding for Phase II.
Publication(s)	

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

The following comprehensive progress report provides updates for all of the East Africa International Epidemiologic Database to Evaluate AIDS (IeDEA) sites and projects including AMPATH. It was submitted to the NIH in May 2014 and activities from August 2013 – July 2014.

East Africa International Epidemiologic Database to Evaluate AIDS (IeDEA)

Year 8 Science Report

August 1, 2013- July 31, 2014

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Grant Number: 5U01AI069911-08
May 23, 2014

A. Specific Aims:

No change in specific aims from the last report.

B. 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) and five U.S. universities (UC Berkeley is the fifth and only has access to de-identified data). The Kisesa clinic, under the direction of the Tanzanian National Medical Research Institute (NMRI), officially joined the consortium this year and submitted their first dataset. The composition of the consortium is outlined in Table 1.

Table 1: Status of Regulatory Approvals

Country	Site	Formal Name of IRB/IREC	Original Approval	Continuing Review Approval	Expiration
Kenya	AMPATH	Moi University College of Health Sciences (MU/CHS) & Moi Teaching and Referral Hospital (MTRH) Institutional Research and Ethics Committee (IREC)	20 Jun 2006	28 Oct 2013	27 Oct 2014
	FACES	Kenya Medical Research Institute/National Ethics Review Committee (ERC)	11 Nov 2008	10 Dec 2013	9 Dec 2014
Tanzania	ORCI	The United Republic of Tanzania National Institute for Medical Research Coordinating Committee	25 May 2007	02 Oct 2013 Report of 17 Sep 2013	11 Sep 2014
	Tumbi Regional Hospital		25 May 2007		
	Morogoro Regional Hospital		25 May 2007		
	Kisesa		11 Sept 2012		
Uganda	Mbarara University ISS Clinic	Mbarara University of Science & Technology Institutional Review Committee (MUST-IRC)	Local : 20 Jun 2006 UNCST: 20 Jul2006	07 Jun 2103 2 Jul 2012	28 Jun 2014 16 Jul 2016
	Masaka Regional Hospital		Local : 20 Jun 2006 UNCST: 20 Jul 2006	07 Jun 2103 2 Jul 2012	28 Jun 2014 16 Jul 2016
	IDI	Makerere University School Medicine Research & Ethics Committee (MUSOMREC)	Local : 3 Sep 2008 UNCST: 3 Feb 2009	16 Sep 2013 2 Jul 2012	2 Sep 2014 16 Jul 2016
	Rakai	Uganda Virus Research Institute Science & Ethics Committee (UVRI-SEC)	Local : 9 Nov 2010 UNCST: 8 Apr 2011	22 Nov 2013 29 Jul 2011	9 Nov 2014 16 Jul 2016
US	Indiana University	Indiana University Institutional Review Board	24 May 2006	09 Dec 2013	08 Dec 2014
	University of California at San Francisco (UCSF)	University of California at San Francisco Committee on Human Research	20 June 2006	11 Mar 2013	7 Apr 2015
	Columbia University	Columbia University Medical Center Institutional Review Board	8 July 2006	Exempt	N/A
	New York University	New York University Committee on Activities Involving Human Subjects	Moved from Yale	Exempt	NA

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 activities of the consortium continue to be divided between three cores (Scientific Development, Data, and Statistics/Methodology). Each core has a U.S.-based and an East-African-based co-chair. The Core Chairs meet at regular intervals to

discuss interactions between the cores and to prioritize projects. The Scientific Core is composed of senior investigators within the consortium and meets on alternate months from the Executive Committee. It is charged with prioritizing projects from a scientific perspective, and mentoring junior researchers within the consortium. The Data Core is composed of the regional data managers and meets 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 and Glidden along with Drs. Maya Petersen, Ann Mwangi and Ms. Agnes Kiragga, (a doctoral student candidate). 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 for the main proposal are outlined in Table 1.

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 Rakai, Kisesa and IDI. All sites have functional EMRS and have not had significant issues over the last year. During this grant year, the Masaka data team retrospectively entered all available records for 94% of the 3041 patients for whom there was a data entry backlog. The records for the remaining 186 patients have not been entered due to missing charts though every effort is being to trace those charts. It is suspected that many of these records/charts were relocated in 2005-2006, when Masaka regional ART program decided to extend ART provision to the lower level health facilities in the region.

Table 2: Patient Enrollment as of 28 March 2014

Country	Program /Site	Adults Enrolled		Adults Receiving ART		Children Enrolled		Children HIV Infected		Children Receiving ART	
		No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)
Kenya	AMPATH	121,009	57.7	84,103	69.5	35,470	85.6	21,564	60.8	16,603	77.0
	FACES	9,591	4.6	5,708	59.5	2,782	6.7	1,352	48.6	984	72.8
Uganda	Masaka	5,887	2.8	3,048	51.8	664	1.6	596	89.8	343	57.6
	Mbarara (UCSF)	21,996	10.5	11,374	51.7	74	0.2	74	100.0	27	36.5
	IDI	25,199	12.0	11,130	44.2	7	0.0	7	100.0	0	0.0
	Rakai	6,538	3.1	3,087	47.2	516	1.2	516	100.0	216	41.9
Tanzania	Morogoro	8,055	3.8	4,922	61.1	889	2.1	752	84.6	521	69.3
	ORCI	1,411	0.7	1,244	88.2	44	0.1	44	100.0	33	75.0
	Tumbi	8,093	3.9	3,890	48.1	880	2.1	795	90.3	461	58.0
	Kisesa	1,928	0.9	1,094	56.7	120	0.3	120	100.0	79	65.8
TOTAL		209,707	83.5	129,599	61.8	41,446	16.5	25,820	62.3	19,267	74.6

Regional Data Center: During the past year the Regional Data Center has received data from Kisesa and updated data from the FACES sites. The current composition of the regional database is outlined in Table 2. A data audit was conducted at Kisesa in February 2014 and site visits were completed at the remaining three Tanzanian sites in July 2013 with follow-up visits conducted at ORCI and Tumbi in February 2014. The Regional Data Center continues to receive and process data requests from the consortium investigators and has generated analysis data sets for 11 concept proposals and has updated existing analysis data sets for 6 other proposals in the past year. 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).

Education and Training: In the past year, a Ph.D. candidate, **Dr. Agnes Kiragga,** mentored by Dr. Yiannoutsos, successfully defended her doctoral thesis at Makerere University in Kampala, Uganda. Ms.

Kiragga will receive a doctoral degree in Epidemiology from the University. She continues to be employed as a statistical analyst at the Infectious Diseases Institute (IDI) in Kampala Uganda. She has produced two papers (see next section) and is working on a third one from her thesis in an ongoing collaboration a with Professor Yiannoutsos and Dr. Judith Lok, Associate Professor at the Department of Biostatistics at Harvard University School of Public Health. A Biostatistics intern, **Mr. Philani Mpofu**, originally from Zimbabwe, was partially supported by IeDEA funds over the past year. Mr. Mpofu has completed one analysis, and is working on a new project, related to the causal effect of ART on TB incidence in East Africa (also see below). Mr. Mpofu has applied and was successfully admitted to the doctoral program in Biostatistics at the Indiana University Fairbanks School of Public Health in Indianapolis. He will be mentored by Dr. Yiannoutsos 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 as well as a course in STATA statistical programming in Mwanza. Mr. Nondi is employed at the National AIDS Control Programme in Dar es Salaam and is the principal statistician for NACP in Tanzania. In his role as the coordinator of the CTC national AIDS database in that country, 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, was submitted in April and 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.

Dr. Kara Wools-Kaloustian and Professor Yiannoutsos are participating in a doctoral research of **Ms. Samiha Sarwat, Ph.D**. candidate within the Department of Biostatistics at the Indiana University Fairbanks School of Public Health. The research is sponsored by the Clinical and Translational Sciences Institute (Indiana CTSI). As part of her research, Ms. Sarwat is developing methodology to address patterns in weight evolution among patients starting ART (see below; Concept15). Dr. Nash and Dr. Yiannoutsos are mentoring **Mr. Eduardo**, a PhD student at Columbia University who is using EA-IeDEA data to complete for his thesis (Concept 14). Dr. Wools-Kaloustian and Dr. Yiannoutsos are co-mentors with Dr. Braithwaite for **Dr. Kessler**'s K-08 application entitled "Optimizing retention in care among HIV infected alcohol misusers in East Africa". This proposal will utilize data from the East African IeDEA cohort to refine models that assess the impact of various retention strategies directed toward alcohol misusers.

Dr. A. Semeere is completing a University of California Global Health Institute (UCGHI) GloCal Health Fellowship, a career development fellowship sponsored by the National Institutes of Health (NIH) Fogarty International Center (FIC). www.glocalfellows.org. Under the auspices of this fellowship he has continued his IeDEA-affiliated research in Kaposi's Sarcoma (KS) with the mentorship of Dr. Jeff Martin. Dr. Semeere is using advanced statistical methods to assess the causal effect of antiretroviral therapy on the incidence of KS in East Africa (Concept 37). Dr. Wools-Kaloustian is mentoring **Dr. Salma Abbas**, an internal medicine resident, in the development of a manuscript summarizing the findings of the IeDEA site survey with regard to Pediatric Cancer (Concept 50). **Dr. Suzanne Goodrich** took a faculty position this year at IUSM and under Dr. Wools-Kaloustian's mentorship has developed and is overseeing the NIDA supplement that is looking at the impact of alcohol use on retention in care. 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 Consortium has continued to produce significant contributions to statistical methodology, most of it in the area of adjusting various estimates of patient outcomes for incomplete outcome ascertainment due to lost to the program. Specifically, we have worked in the following areas of statistical and epidemiologic methodology:

Mortality estimates:

A paper was recently published by our collaborators Ming-Wen An and Constantine Frangakis, along with Professor Yiannoutsos, in Statistics in Medicine entitled "Choosing profile double-sampling designs for survival estimation with application to President's Emergency Plan for AIDS Relief evaluation" (Publications 1). This paper expands previous work where estimates of mortality are adjusted for loss to program, using information obtained on the vital status of patients who are lost to program and are subsequently located by patient

outreach.[1] This work adds covariates (predictors) to the model, thus significantly expanding its flexibility and applicability and opens up the possibility of substantially improving the efficiency of the sampling design. It assists in determining which lost patients should be included in the outreach effort resulting in the reduction of the number of patients that need to be outreached and located. Dr. Frangakis from Johns Hopkins, along with Donald Rubin from Harvard University, Dr. Ming-Wen An from Vassar College and Professor Yiannoutsos, have successfully applied for an R01 grant to expand these designs and further increase the efficiency of dropout sampling.

A major methodological paper has been accepted at the Scandinavian Journal of Statistics jointly with Dr. Menggang Yu of the University of Wisconsin entitled "Marginal and conditional distribution estimation from double-sampled semi-competing risks data" (Publications 2). This paper involves methodology to include outreach data on a subset of subjects when performing analyses in the context of semi-competing risks (analyses of the time to two events, one of which precludes observation of the other – the terminal event – and the other which does not) when the ascertainment of the terminal event is incomplete (i.e., missing on some of the subjects). The technique is illustrated by an example with loss to program and death being the two events (death being the terminal event of interest which is incompletely ascertained). It models explicitly the association between the two events (as, for example, patients who drop out are at elevated risk strata for mortality) and extends complex mathematical theory in the context where only a (random) sub-sample of those who are lost to the program have vital status ascertained.

Agnes Kiragga published a study of mortality adjustment methods from data available at the Infectious Diseases Institute (IDI) entitled "Comparison of methods for correction of mortality estimates for loss to follow-up after ART initiation: A case of the Infectious Disease Institute, Uganda" (Publications 3). The paper used data from the IDI Research Cohort, in which vital status is completely ascertained, with data from the routine clinical cohort along with data available from IDI's outreach activity. The study compared the sampling-based approach to mortality adjustment, using outreach data, along with the nomogram approach proposed by Egger and others.[2] The conclusion of the study was that the estimates provided by both adjustment methods worked equally well but underestimated early mortality in the routine clinical cohort (or at least failed to reach the levels of mortality in the research cohort). This study contradicts a recently published similar study in Malawi which found significant underestimation of mortality by the nomogram in a cohort in rural Malawi.[3] The two studies underscore the contextual variation of the association between mortality and loss to program and the fact that no one-size-fits-all approach can be applied to the problem.

<u>Informative censoring and longitudinal measures:</u>

Agnes Kiragga and Dr. Yiannoutsos continue to collaborate with Dr. Lok to address longitudinal CD4 count estimation in the presence of incompletely ascertained mortality (Concept 55). The paper resulting from this collaboration is under review at the Journal of the International AIDS Society and is entitled "CD4 trajectory adjusting for dropout among HIV-positive patients receiving combination antiretroviral therapy in an East African HIV care center" (Drafts 1). This analysis shows that, because patients with lower CD4 counts are those most likely to be lost to program or die, estimates of CD4 count which are based only on those patients who continue to engage in care at their original site, significantly overestimate the true values. If mortality is taken into consideration as a further downward adjusting factor, the overestimation can be dramatic.

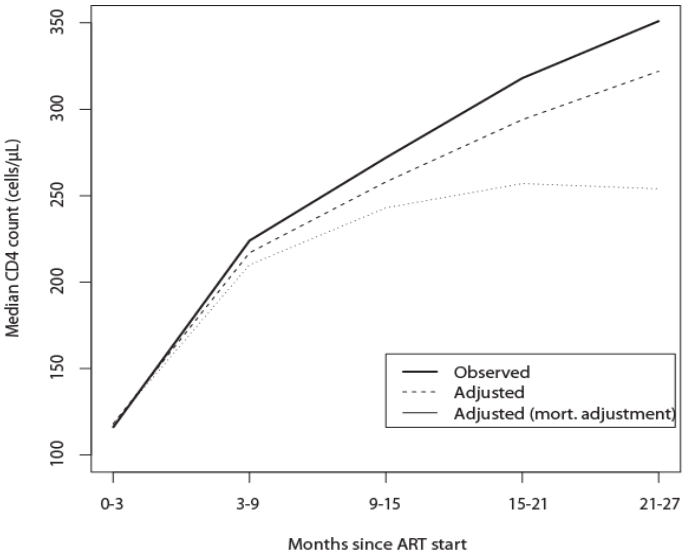


Figure 1:
Observed (solid line) and adjusted (dashed lines).

Figure 1 shows the magnitude of the adjustment. A follow-up paper, outlining the theoretical underpinnings of the estimation, is in process. A significant implication of this estimation procedure is that fewer patients than previously estimated are reconstituted immunologically (see Figure 2). While it appears that about 50% of patients starting ART have CD4 above 350 cells/μL by two years after ART initiation, the revised estimate is about 35% when dropout and mortality are taken into consideration (Figure 2).

A follow-up of the study led by Dr. Kiragga extends the statistical methodology to address the situation where patients remaining on therapy are not representative of those who are lost (a fact demonstrated by numerous studies in our setting). Previously, this issue could only be addressed through sensitivity analyses while making unverifiable conjectures on the increased

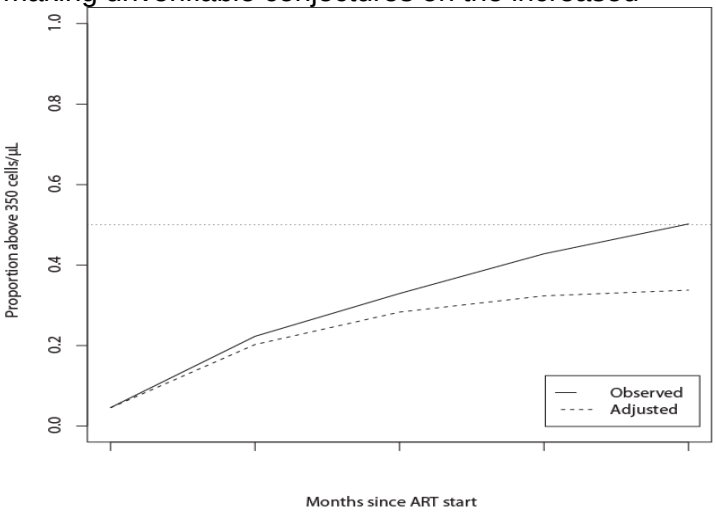


Figure 2:
Proportion of patients reaching 350 cells/μL after start of ART.

risk of death and levels of treatment access after disengagement from care at the current program. We have developed extensive statistical theory which can take into consideration
information on vital status and treatment access (i.e., whether a patient who is lost to program is accessing care elsewhere) to provide estimates for the CD4 trajectories of all patients who started ART (as opposed to the current practice which involves only those patients who are engaged in care at their original clinic). A major statistical article entitled “Inverse probability of censoring weights under missing not at random with application to CD4 outcomes in HIV-positive patients in Kenya” (Drafts 2) is under review at the Journal of the American Statistical Association, the flagship journal of the American Statistical Association.

New User Approach:

We continue to assess the causal effect of ART on the incidence of KS. As noted in last year's report, previous research in other areas has shown that incorporating both new treatment (ART) users and prevalent users in an analysis of incidence may result in significant biases in the estimation of the causal effect of therapy on the incidence of a disease. This is particularly true when the disease risk decreases as the duration of therapy increases (as is the case with prolonged ART use). Dr. Semeere, with the assistance of Drs. Glidden and Professor Vittinghoff, continue to implement a "new user" design to assess the impact of ART on KS incidence.[4,5] A similar project is being initiated at IU by Mr. Mpofu to assess the impact of ART use on incidence of TB in East Africa.

Contributions to the Global IeDEA Consortium: Dr. Rachel Vreeman was elected as chairperson of the Pediatric Working Group in March, 2014 and Dr. Jeff Martin continues to serve as the co-Chair of the Cancer Working Group.

B2. Scientific Productivity:

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 analysis data sets for this project have been completed and statistical analysis has been initiated by Dr. George Bakoyannis, a Post-Doctoral Fellow supervised by Professor Yiannoutsos. It is anticipated that the analysis will be completed by mid-summer and a manuscript will be circulated by autumn, 2014.

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

As noted in last year's report 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. A data request has been developed for this project, reviewed, and approved by the data management and analysis teams. The analysis to assess the incidence of adverse drug reactions (ADR) per person-months of TB drug exposure will be initiated within the next few months with the goal of completing the analysis and submitting a manuscript in early 2015.

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. ADRs/symptoms reported from January 2012 – December 2012 were compared to the number of ADRs/symptoms reported from January 2013 to July 2013. The team's hypothesis is that the use of a symptom screening tool will capture more ADRs/symptoms than what is captured by clinicians during a routine clinical encounter.

Preliminary results: Through the Eldoret and Chulaimbo Oncology Clinic sites, 133 patients with Kaposi's Sarcoma were evaluated. Of the 133 patients, 77 patients received chemotherapy in 2012, serving as the comparison group. In the 2012 group, 150 (0.38/per patient visit) ADRs/symptoms were reported in the patient files. In the 2013 group (n=39), preliminary results suggest that 269 (1.38/per patient visit) ADRs/symptoms were reported by the symptom screening form. These data suggest that patients are more likely to report ADRs/symptoms if specific questions are asked that probe for potential ADRs. These data are being cleaned and processed. We anticipate that the analysis will be completed by the end of May 2014 and that a manuscript will be ready for submission by December 2014.

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 objective of this project evolved to evaluate the feasibility and effectiveness of five approaches to targeted spontaneous reporting (TSR) for documenting treatment-threatening serious adverse drug reactions (SADR) to antiretroviral medications in a large clinical program within a resource-constrained clinical setting. All five arms have been closed to enrollment and all data collection has been completed. Associate clinical data have been requested for analysis. Below is a description of the different arms and their preliminary data analysis:

TSR1. *Completion of the "Kenya National Suspected Adverse Drug Reaction" form for patients with a change or discontinuation in their ART.* From October 1st, 2012 to December 31st, 2013 there have been 262 cases of treatment-limiting SADRs documented on the Poison's and Pharmacy Board (PPB) SADR forms and reported to the national pharmacovigilance center. For further details of comparisons between source documents and reporting to PPB see TSR5.

Table 3: SADR and Drug	
Suspected Drug	SADR cases No. (%)
Stavudine	207 (79.0)
Zidovudine	29 (11.1)
Nevirapine	12 (4.6)
Tenofovir	6 (2.3)
Efavirenz	7 (2.7)
Abacavir	1 (0.4)
Total	262

TSR2. *Clinical encounter forms that have been enhanced to collect a limited amount of Suspected Adverse Drug Reaction data.* In February 2014 a data request was submitted to the AMPATH Data Analysis Team (ADAT) to extract the data collected in the AMPATH Medical Record System (AMRS) related to this approach. A data quality assessment of 28 randomly sampled patient charts carried out in January 2014 showed significant differences in the number of symptoms reported during patient interviews (see below) and the data obtained from the AMRS (data collected using the enhanced encounter form). The chart review identified 81 medication-related symptoms captured during the patient interviews as compared to none captured by the clinicians using the enhanced encounter forms.

TSR3. *Patient in-depth interviews conducted by HIV-infected peers and (TSR4) Patient in-depth interviews conducted by pharmacy personnel.* A total of **844** participants out of the planned 1000 were enrolled into the study. The following interview categories were filled: Adult 1st line initiation (250), Adult 2nd line initiation (50), Adults stable (200), PMTCT (38) and Child stable (200). The child 1st line initiation (38/150) and the 2nd line initiation (6/50) groups did not reach full enrollment. Non- disclosure of HIV status to children and adolescents coming to clinic unaccompanied made recruitment of children challenging.

Table 4: Reason for ART Change		
Cause of ART regimen	**No.**	**(%)**
SADR	458	(61.3)
Treatment failure	96	(12.9)

Drug-drug interactions (mostly Rifampicin)	52 (7.0)
Pregnancy	7 (0.9)
Undocumented	50 (6.7)
Phasing out	84 (11.2)
Total	**747**

TSR5. *Routinely captured pharmacy data*. From the pharmacy data we documented **747** changes in ART regimen over the study period. Table 4 provides a summary of the reasons given for the regimen changes. Of the 458 SADR cases identified through pharmacy data, 262 were reported to the national pharmacovigilance center while the remaining 196 (42.8%) were not reported due to inadequate documentation on the pharmacy prescription form and/or clinical encounter forms.
This study resulted in an invited presentation at the technical review meeting of country experiences in ARV toxicity surveillance *Sharing Preliminary Results and Lessons learnt, Identifying Solutions. Geneva, Switzerland, 2013. The presentation was entitled "*Pharmacovigilance in a resource limited setting: Approaches to Targeted Spontaneous Reporting for Suspected Adverse Drug Reactions to Antiretroviral Treatment" and presented by Ms. M Maina. Analysis is on-going for this project and should be completed by 2015 (Abstracts 1).

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. The data sets for this project were completed in July 2013 and updated on March 24, 2014. The analysis is ongoing and nearing completion. The results of the preliminary analysis were included in an abstract entitled "**Time to First-Line ART Failure and Switch to Second-Line ART in the IeDEA Pediatric Cohort"** submitted to the 6th International Workshop on HIV Pediatrics, Melbourne, Australia. July 18-19, 2014 (abstract below). We plan to complete this analysis by September 2014 and have a draft paper for circulation by the end of 2014.

Background: There are limited data on durability of first-line antiretroviral treatment (ART) in children in resource-constrained settings. The objectives of this study were to determine the time from first-line ART initiation to treatment failure and to assess the time from failure to initiation of second-line ART in children.

Materials & Methods: This study was collaboration between five regional Pediatric Cohorts within The International Epidemiologic Databases to Evaluate AIDS (IeDEA) Consortium. Each IeDEA region harmonizes patient-level data collected during routine clinical care at affiliated HIV-care and treatment sites. Children initiating their first ART regimen between age 2 and 14 years were eligible. The outcomes of interest were: 1) ART failure defined by clinical (new or recurrent WHO 3/4 event or increase in WHO stage), immune (CD4 count <200 or CD4% <10% for children 2-5 years; CD4 count <100 cells/µl for children ≥5 years), and viral (VL ≥5,000 copies/µl) parameters at ≥24 weeks of ART; 2) Change to second-line ART defined as a class change in the backbone (e.g. change from an NNRTI to a PI) plus a change in ≥1 NRTI; 3) death and loss to follow-up (LTFU; ≥6 months without a clinic visit). Cumulative incidence was computed for first-line failure and second-line initiation respectively, with death or LTFU treated as a competing event. A cause-specific proportional hazards model was used to identify factors associated with each outcome.

Results: Outcomes of 21,977 children from Asia-Pacific (8.6%), Central (0.2%), East (32.3%), Southern (52.8%) and West (6%) Africa were analyzed. The median age at ART initiation was 6.8 (IQR 4.4-9.7) years and 49.4% were female. Median CD4% for children ≤ 5 years was 15% (IQR 8.0-24.4) and CD4 count for children > 5 years was 240 cells/µl (IQR 91-429). Most children initiated NNRTI-based ART (98.3%); 1.4% initiated PI and 0.3% triple NRTI-based ART. Failure was identified in 6,091 children and 4,257 died or were LTFU. At 1 year after ART initiation 12.7% (95%CI: 12.3-13.2) were dead/LTFU and 14.9% (95%CI: 14.4-15.4) had failed; by 5 years, the rates were 25.4% (95%CI: 24.7-26.2) and 39.1% (95%CI: 38.3- 40.0), respectively. Factors associated with higher failure rates were male sex, older age at ART initiation and region while starting

non-NNRTI based ART was associated with lower rates. Factors associated with increased rates of death/LTFU were younger age at ART initiation, starting triple-NRTI ART, and region while starting PI-based ART was associated with lower rates. At 1 year after failure, 1.8% (95%CI: 1.5-2.2) were dead/LTFU and 9.5% (95%CI: 8.7-10.3) had changed to second line; by 5 years the rates were 4.7% (95%CI: 3.9-5.7) and 35.6% (95%CI: 33.5- 37.8), respectively. Factors associated with higher rates of change to second line were male sex, older age, starting non-NNRTI based ART, and region.

Conclusions: High rates of death/LTFU and first-line failure were identified in children 5 years after ART initiation. Of children meeting criteria for failure, only a third was changed to second-line ART by 5 years. Despite low rates of change to second line, death/LTFU rates were low.

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

Following the development, validation and debugging of a simulation model of the HIV epidemic in East Africa that captures important heterogeneity on HIV transmission (in particular, individuals who are highly sexually active are more likely to partner with other highly sexually active individuals than would be expected based on the number of partnering opportunities alone, and age-asymmetry may also exist in partnerships) we have begun a series of portfolio analyses. These initial analyses have involved instantiating a group of evidence-based HIV prevention interventions within the simulation model, evaluating the effects in terms of infections averted and costs of implementation of each of these interventions independently, and evaluating the impact and cost of all relevant multi-component combinations of these HIV prevention approaches. This first set of analyses has focused on the outcomes of HIV infections averted and costs per infection averted. We have expanding our initial analysis to include the additional outcomes of quality adjusted life years and cost-per-QALY gained.

Dr. Braithwaite and his team are currently working on finalizing their first set of analyses that will evaluate a broad portfolio of HIV related treatment and prevention strategies and compare the cost-effectiveness of each independently and as constituents of combination based portfolios. These analyses have been drafted into manuscript form which they plan on submitting for peer review in the upcoming quarter. Future plans include model enhancements focusing on emerging high-risk groups in this setting, most notably men who have sex with men and substance abusers (including injection drug users and alcohol misusers). In line with these enhancements future portfolio analyses can be broadened to include measures focused on risk mitigation targeted at these particular populations and evaluate comparisons to previously determined portfolios found to be particularly efficient and or of high value.

Other projects that fall within Specific Aim 1:

There are a number of other projects that fall under the umbrella of Specific Aim 1 (see Appendix 1- Concept Tracking Document).

Concept 9: “A comparison of the immunologic efficacy of antiretroviral therapy in resource-replete versus resource-limited settings”

This is a multi-regional analysis led by Dr. Geng and Dr. Martin. A paper entitled, “CD4+ T cell Recovery during Suppression of HIV Replication: a Global Comparison of the Immunologic Efficacy of Antiretroviral Therapy” resulting from this project is currently under review at International Journal of Epidemiology (Drafts 3; abstract below).

Background: Even among HIV-infected patients who fully suppress plasma HIV RNA replication on antiretroviral therapy, genetic (e.g., CCL3L1 copy number), viral (e.g., tropism) and environmental (e.g.,

chronic exposure to microbial antigens) factors influence CD4 recovery. These factors differ markedly around the world and therefore the expected CD4 recovery during HIV RNA suppression may differ globally.

Methods and Findings: We evaluated HIV-infected adults from North America, West Africa, East Africa, Southern Africa and Asia who achieved at least one HIV RNA level < 500/µl in the first year of therapy and observed CD4 changes during HIV RNA suppression. We used a piecewise linear regression to estimate the influence of region of residence on CD4 recovery, adjusting for socio-demographic and clinical characteristics. We observed 28,217 patients from 105 cohorts over 37,825 person-years. After adjustment, patients from East Africa showed diminished CD4 recovery as compared to other regions. Three years after ART initiation, the mean CD4 count for a prototypical patient with a pre-therapy CD4 count of 150/µl was 529/µl (95% CI: 517-541) in North America, 494/µl (95% CI: 429-559) in West Africa, 515/µl (95% CI: 508-522) in Southern Africa and 503/µl (95% CI: 478-528) in Asia, and 437/µl (95% CI: 425-449) in East Africa.

Conclusions: CD4 recovery during HIV RNA suppression is diminished in East Africa as compared other regions of the world and observed differences are large enough to adversely influence clinical outcomes. Epidemiologic analyses on a global scale can identify macroscopic effects unobservable at the clinic, nation or individual regional level.

Concept 13: "Models of patient outreach and their associated rates of loss to follow-up in the East African IeDEA consortium" are led by Dr. Braitstein. The data sets are completed and a preliminary analysis has been conducted. A draft manuscript is in preparation and finalization is pending completion of the analysis. The key findings are outlined in Table 5.

Table 5: Program Factors Associated with Loss to Follow-up

Characteristic	Adjusted Hazard Ratio Risk of LTFU (95% CI)	P-Value
Telephone only or no dedicated staff	3.36 (1.72, 6.57)	0.001
Dedicated staff	Reference	
Public means/bicycle/on foot	3.12 (1.41, 6.88)	0.009
All available means (including private vehicle)	Reference	
Searching after 30 days of a missed visit	2.32 (1.26, 4.24)	0.011
Searching within 30 days of a missed visit	Reference	

Concept 14: "Factors associated with CD4 count and ART initiation and their relationship to survival" is led by PhD student Eduard Eduardo under the direction of Dr. Nash. The goal of the project is to assess whether, and to what extent, implementation of approaches to active screening (e.g. Provider Initiated Counseling and Testing) at the programmatic level translate into higher patient CD4 cell counts at ART initiation and improved patient survival. Furthermore, the project aimed to assess whether a detected association between active screening and patient survival was mediated by patient CD4 cell count. Sites were classified as active or non-active screening based on whether 1) they conducted active screening at the site and 2) their primary source of patients were referred from entry points known to historically conduct active screening. The data set for this project was finalized in May 30 2012. Three analyses have been 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. Manuscripts summarizing these analyses are currently in development and will be completed prior to the end of the next funding year. The key

finding for Analysis 1-Mean patient CD4 cell count at ART initiation does not differ materially between sites with and without active screening; Analysis 2- Sites with active screening entry points have higher patient CD4 cell count at ART initiation than sites without active screening entry points; Analysis 3 - Patients in sites with active screening entry points have a rate of death that is 18% lower than patients in sites without active screening entry points (results narrowly miss statistical significance – 95% CI 0.64-1.06). The relationship between active screening entry point and survival is mediated by patient CD4 cell count at ART initiation as hypothesized.

Concept 15: "Weight evolution in patients on effective ART: a comparison among different regions and different regimens" is a multi-regional analysis led by Dr. Colebunders and the previous leadership of the Central African IeDEA region. Since the beginning of the current funding cycle the leadership of this project has been transferred to the West African region. The analyses for this project were recently completed under the leadership of West-Africa IeDEA and a manuscript, titled "Determinants of weight evolution among HIV-positive patients initiating antiretroviral treatment in low resource settings, the IeDEA collaboration" (Drafts 4) has been circulated and will be submitted for publication. A sub-analysis of the same data, undertaken by the East Africa IeDEA Consortium, is addressing the narrower question of the durability of weight gain among patients starting stavudine (d4T) based first-line regimens versus regimens not containing d4T (non-d4T-based regimens). This analysis is part of the dissertation work of a doctoral candidate in the Department of Biostatistics, Ms. Sarwat. It is using a new method called Significance of Zero Crossings of the Derivative (SiZer), which focuses on the time point where the first derivative of the weight changes over time crosses from above the horizontal (zero) axis. When this happens, weight gain has effectively stopped (as positive derivative signifies weight gain, while a negative derivative denotes weight loss; a zero derivative signifies no weight change). Coupled with smoothing techniques, the preliminary results suggest that d4T-based regimens are associated with faster earlier weight gain which however has a much shorter duration compared to non-d4T-based regimens among patients starting ART. In East Africa (Figure 3) the estimated duration of weight gain was 54.8 weeks versus 80.1 weeks for d4T-based and non-d4T-based regimens respectively.

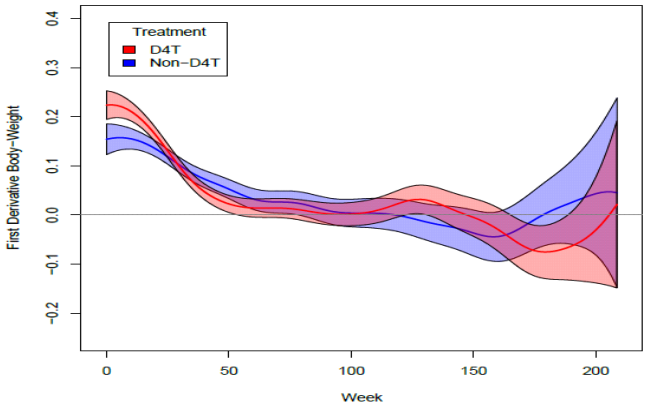


Figure 3. Plot of the first derivative of weight among patients who start ART on d4T-based and a non-d4T-based regimens in East Africa (with 95% confidence interval).

These results were consistent across all five regions participating in this project. A number of limitations of this approach, including change of ART regimen (either substitutions of first-line regimens or changes to second-line regimens) as well as the fact that these data are based on patients who engage in care (similar to the traditional approach at CD4 count estimation which we have shown to be biased) need to be addressed in the near future. In addition, issues such as administration of a specific type of therapy, timing of ART initiation among sicker patients (confounding by indication), who may experience different rates of weight gain (time-varying confounding) have not been widely addressed in the context of non-linear longitudinal measurements such as weight gain. Nevertheless, the results suggest that d4T-based regimens, in addition to the well-documented problems with respect to neuropathic pain, may also be associated with shorter durability of weight gain among ART-naïve patients. A poster presentation was recently submitted to the national meeting of the Clinical and Translational Sciences Institutes (Abstracts 2).

Concept 19: "Estimates and correlates of pediatric ART adherence" This concept is led by Dr. Vreeman. The analysis was completed last month. The team identified good overall adherence levels among children within

the East African IeDEA pediatric cohort. However, rates of adherence vary by clinical site/program. The Tanzanian sites, which used pill counts to measure adherence, had the highest reported levels of adherence. Longer time on ART was associated with slightly higher adherence, and older age was associated with slightly lower adherence. Average rates of reported adherence increased over the follow-up period. In other words the longer a program provided care to children, the higher the reported adherence rates. There was some suggestion that adherence was higher within the programs that saw a higher volume of children however this factor did not reach statistical significance.

There was a delay in the manuscript submission planned for this funding year as the team chose to conduct additional analyses prior to completing the manuscript. The plan for the next funding year is to circulate a revised manuscript by the end of May 2014 with a submission to JAIDS planned for June 2014.

Concept 20: "Adolescent Care in East Africa" is led by Dr. Gisore, a Pediatrician at AMPATH. The core dataset for this analysis was completed at the end of February, 2014 however there are additional variables (adherence and orphan status) that are in the process of being added to the dataset. The analysis for this project has been initiated and is ongoing with planned completion by the end of June.

Concept 25: "Sub-optimal CD4 reconstitution among patients on antiretroviral therapy in the developed and developing countries; Frequency and patterns, determinants and clinical significance" is led by Dr. Easterbrook and supported by Ms. Kiragga. The data analysis for this project is complete and a draft manuscript entitled "AIDS-related illnesses among sub-optimal immune responders to first-line HAART within the IeDEA-East Africa cohorts" is being reviewed by co-authors (Drafts 5; abstract below). The team plans to submit this paper for publication by June 2014.

Background: With more Africans on long-term antiretroviral therapy (cART), there is need to consider 'normalization' of immune responses; after overcoming the initial threats of early post-cART morbidity due to AIDS-related illnesses. We described patterns of suboptimal immune response (SO-IR) and associated AIDS-related illnesses during cART at seven sites in East Africa.

Methods: SO-IR was determined by i) CD4 threshold criteria (CD4 count <200 cells/µl at 6, 12 and 24 months), i) magnitude criteria (CD4 increase <50 cells at 6 months, <100 cells at 12 months and <200 cells at 24 months and iii) Non-normalization (failure to attain a CD4 count ≥500 cells/µl). SO-IR criterion ii) was used to analyze frequency of AIDS-related events since SO-IR using criterion i) was a subset of SO-IR using criteria ii). Kaplan Meier survival analysis techniques were used to assess the cumulative probability of 'normalization' competing-risks adjusted cumulative incident rates were calculated.

Results: Overall 80,843 adults initiated NNRTI-based first-line cART. Using criteria i) of the patients in-care with a CD4 count, 10355/29,050 (36%), 6376/22,347(29%) and 2803/14,058 (20%) had an absolute CD4 counts <200 cells at 6, 12 and 24 months, respectively. Using criteria ii) of patients in-care with CD4 counts, 5228/23029 (23%), 5816/17260 (34%) and 5183/10232 (51%) had SO-IR at 6, 12 and 24 months, respectively. AIDS-related illnesses were higher among SO-IR [996/5228 (18%)] versus optimal immune responders (OP-IR) with 14% at 6 months (p<0.0001); comparable at 12 months 851/5816 (15%) among SO-IR versus 1336 (12%) among OP-IR (p=0.637) and; higher among SO-IR 612/5183 (12%) versus OP-IR 9% at 24 months (p=0.0001). Using criteria iii) 'Non-normalization' was at 51% after 8 years of first-line cART. Male gender, older age, and severe disease with CD4<100 cells, predicted 'non-normalization'; HR: 0.68 (95%CI: 0.66 – 0.70), HR: 0.94 (95%CI: 0.93 – 0.95) and HR: 0.52 (95%CI: 0.51 - 0.54), respectively.

Conclusion: Sub-optimal immune response was associated with a high incidence of AIDS-related illnesses. Half of cART-treated adults 'normalized' their CD4 counts after 5 years after starting cART. Further knowledge of mechanisms sub-optimal immune recovery, including genetic predictors, is required to inform targeted therapeutic interventions to optimize short and long-term immune recovery**.**

Concept 27: "Predicators and factors associated with treatment failure among HIV-infected children on ARVs" is led by Dr. Marete a Pediatrician at AMPATH. The data sets are finalized for this project and a preliminary analysis has been completed. The results of the preliminary analysis were reviewed in February 2014 by the

concept team and an updated analysis has been undertaken based on the comments provided. It is anticipated that the updated analysis will be completed in May 2014 and will be forwarded to Dr. Marete who will be responsible for drafting the manuscript.

Concept 31: "Modification of the effect of deferred regimen modification following loss of viral suppression on first-line therapy by CD cell count and HIV RNA level" is led by Dr. Petersen. The manuscript is entitled "Delayed Switch of Antiretroviral Therapy Following Confirmed Virologic Failure is Associated with Elevated Mortality among HIV-infected Adults in Africa" has been accepted at AIDS (Publications 4; abstract below).

Objective: Routine monitoring of plasma HIV RNA among HIV-infected patients on antiretroviral therapy (ART) is unavailable in many resource-limited settings. Alternative monitoring approaches correlate poorly with virologic failure and can substantially delay switch to second-line therapy. We evaluated the impact of failure to switch on mortality among patients with virologic failure in Africa.

Methods: We examined patients with confirmed virologic failure on first-line NNRTI based regimens from four cohorts with routine HIV RNA monitoring in Uganda and South Africa. Marginal structural models aimed to estimate the effect of delayed switch on mortality in a hypothetical trial in which switch time was randomly assigned. Inverse probability weights adjusted for measured confounders including time updated CD4 and HIV RNA.

Results: Of 823 patients with confirmed virologic failure, 358 patients had their ART switched; the cumulative incidence of switch 180 days after failure was 30% (IQR 63-198 days). Adjusted mortality was higher for subjects who remained on first-line therapy than for those who had switched (OR:2.2, 95%CI:1.1-4.4). The majority of patients (61%) had not failed immunologically (as defined by WHO criteria) by time of virologic failure. Among those without immunologic failure, the relative harm of failure to switch was similar (OR:2.0; 95%CI: 0.8-5.4) to that of the entire cohort, although no longer significant.

Conclusions: Among HIV-infected patients with confirmed virologic failure on first-line ART, remaining on first-line therapy led to a substantial increase in mortality relative to switching. Our results suggest that access and prompt response to routine RNA monitoring could decrease mortality.

Concept 32: "Revising mortality estimates and predictors of mortality among HIV-infected children in western Kenya" is led by Dr. Braitstein. As has previously been shown, the true mortality rate among 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 we published our findings from having traced a random sample of 98 HIV-infected and exposed children. We are now aiming to use these data to revise pediatric mortality estimates. A draft of the analysis data sets has been created and is currently under review at the Regional Data Center. We estimate that the data sets will be ready for analysis by the end of May, 2014.

Concept 33: "What is the Capacity for the Conduct of Adverse Event/Toxicity Monitoring in Resource-Constrained Settings?" this is a multi-regional analysis being led by Dr. Braitstein, East African IeDEA. This project was found to be more complex than initially anticipated. Dr. Braitstein has involved international experts at the World Health Organization and Upsala Monitoring Center, as well as local expertise in Eldoret, Kenya (funded by WHO to study the methodology of Targeted Spontaneous Reporting (TSR) as a mechanism for pharmacovigilance in a resource-constrained setting) in addressing this concept. Using a combination of the literature (published and grey) and in consultation with policy experts and clinical implementers, we are working to identify some of the core capacity required to conduct at least minimal pharmacovigilance. Since October 2013 Dr. Braitstein has had a post-doctoral epidemiologist assisting her with achieving the goals of this project. The updated goals and timelines for this project are to: 1. Develop consensus on the core required components of a facility/program to conduct pharmacovigilance (Sept 2014), 2.Compare the identified components with current capacity (documented by the IeDEA site assessment) (Dec 2014) 3. Submit an abstract to an international conference (Feb 2015) 4. Submit a manuscript (July 2015).

Concept 34: "Development of low-tech and context-appropriate tools for monitoring ART in children in resource poor-settings: weight and CD4 velocity reference standards" is a multiregional concept led by Dr.

Yotebieng from Central African IeDEA. The analysis for this concept is complete and a final draft manuscript is currently circulating to the co-authors and awaiting final regional approval. Dr. Yotebieng plans to submit this to Lancet by the end of May 2014 (Drafts 6).

Concept 38: "Natural history of HIV-infection in children presenting before 1-year of age in East Africa: An IeDEA Collaboration" led by Dr. Ciaranello resulted in a publication this year (Publications 5).

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" is led by Dr. Goodrich. This concept resulted in a poster that was presented at IWHOD, Sitges Spain, March 2014 (Abstracts 3). In addition, an abstract from this project was accepted for a poster at IAS, Melbourne Australia, in July 2014 (abstract below).

Background: Access to viral load (VL) testing is limited in resource-constrained settings leading to reliance on immunologic and clinical criteria to identify antiretroviral (ART) failure.

Methods: Patients ≥18 years initiating first-line ART from January 2005-June 2012 with >6 months follow-up at database closure and cared for at EA-IeDEA consortium sites were evaluated. Sites used ≥1 of the following definitions of ART failure: 1) clinical (new or recurrent WHO 3 or 4 event); 2) immunologic (CD4 count< pre-ART; ≥50% CD4 decrease from peak; persistent CD4<100); or 3) virologic (VL>10,000 copies/mL). Cumulative incidence rates (CIR)

Table 6: CIR for first-line ART failure

Failure Type	N(%)	1 yr	3 yr	5 yr	7 yr
Clinical	10,333 (11.5%)	0.053	0.117	0.144	0.161
Immunologic	11,065 (12.3%)	0.044	0.117	0.161	0.193
Virologic	1,341 (1.5%)	0.002	0.014	0.021	0.026
Death or LTFU	31,170 (34.8%)	0.239	0.343	0.396	0.450

Table 7: CIR of change to second-line ART

Failure Type (N)	Change to second-line N(%)	Death/LFTU N(%)	Change to second-line ART				Death/LTFU			
			1 yr	3 yr	5 yr	7 yr	1 yr	3 yr	5 yr	7 yr
Any (22,739)	2,913 (12.8%)	5,714 (25.1%)	0.096	0.151	0.181	0.190	0.158	0.291	0.396	0.495
Clinical (12,526)	1,275 (10.2%)	3,491 (27.9%)	0.064	0.112	0.143	0.152	0.163	0.298	0.413	0.515
Immunologic (13,203)	2,028 (15.4%)	3,102 (23.5%)	0.105	0.184	0.224	0.237	0.140	0.271	0.373	0.464
Virologic (3,336)	2,080 (62.4%)	399 (12.0%)	0.435	0.684	0.782	0.806	0.071	0.129	0.157	0.161

for first-line failure were calculated using competing risks models with three definitions of failure. CIR of time from failure to second-line initiation was calculated for those with first-line failure under each criterion. Death and lost-to-follow-up (LTFU) were treated as competing events.

Results: 89,610 patients (69% female; median age 36.7(IQR 30.8-43.9) years; CD4 count 128 (IQR 54-202) cells/μL) from 101 sites were analyzed. 22,739 patients failed by ≥1 criterion. Virologic failure accounted for the fewest failures due to poor accessibility to testing at most sites. Virologic failure did result in the highest rates of ART change and the fewest deaths/LTFU (Tables 6 and 7).

Conclusions: Numerous patients met criteria for first-line ART failure but rates of change to second-line therapy were low. We speculate clinicians are aware of the inaccuracy of clinical and immunological criteria in predicting ART failure and are thus reluctant to change to second-line regimens when only one alternative ART regimen is available.

Concept 45: "Clinical characteristics and outcomes of adolescents attending HIV clinics in IeDEA East Africa" is led by Dr. Nuwagaba-Biribonwoha, Columbia University, ICAP, and supported by Dr. Kiragga at IDI. The data set was completed in October 2013 and the analysis is ongoing. The preliminary findings show that the **CD4 counts at enrollment into care and at ART initiation are higher for adolescents than adults. In addition, a lower proportion of adolescents have WHO stage III and IV than adults at enrollment and ART initiation.** It is anticipated that the statistical analysis will be completed during the summer 2014 and a manuscript will be forthcoming by October of 2014.

Concept 53: "Switching of ART to second- and third-line regimens: global view" is a multi-regional concept led by Dr. Egger of the Southern African Region. The East African data was transferred on May 21, 2013 and this project has resulted in an IWHOD oral presentation entitled "Rates and Predictors of Switching to Second-Line ART in Sub-Saharan Africa" (Abstracts 4).

Concept 54: "Treatment outcomes on first-line, second-line and third-line ART: global view" is a multi-regional concept led by Dr. Egger of the Southern African Region. The East African data was transferred on May 21, 2013

Concept 55: "CD4 trajectory adjusting for dropout among HIV-positive patients receiving combination antiretroviral therapy in an East African HIV care center" is led by Ms. Kiragga and Dr. Yiannoutsos. This concept resulted in a manuscript that has been submitted to JIAS, the team has received reviewer comments and is currently in the process of revising and re-submitting this manuscript (Draft 1; abstract below).

Objective: Estimates of CD4 response to antiretroviral therapy (ART) obtained by averaging data from patients in care, overestimate population CD4 response and treatment program effectiveness because they do not consider data from patients who are deceased or not in care. We use mathematical methods to assess and adjust for this bias based on patient characteristics.

Design: We examined data from 25,261 HIV-infected patients from the East Africa IeDEA Consortium.

Methods: We used inverse probability of censoring weighting (IPCW) to represent patients not in care by patients in care with similar characteristics. We address two questions: What would the median CD4 be "had everyone starting ART remained on observation?" and "were everyone starting ART maintained on treatment?"

Results: Routine CD4 count estimates were higher than adjusted estimates even under the best-case scenario of maintaining all patients on treatment. Two years after starting ART, differences between estimates diverged from 30 cells/μL, assuming similar mortality and treatment access among dropouts as patients in care, to over 100 cell/μL assuming 20% lower survival and 50% lower treatment access among dropouts. When considering only patients in care, the proportion of patients with CD4 above 350 cells/μL was 50% adjusted to below 30% when accounting for patients not in care. One-year mortality diverged 6%-14% from the naïve estimates depending on assumptions about access to care among lost patients.

Conclusions: Ignoring mortality and loss to care results in over-estimation of ART response for patients starting treatment and exaggerates the efficacy of treatment programs administering it.

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" is led by Dr. Easterbrook. Analysis datasets for this project were finalized in October 2013 and the statistical analysis is underway. We expect that the statistical analysis will be completed by June 2014 and a manuscript will be circulated by the end of the summer 2014.

Concept 58: "Adherence to Antiretroviral Therapy (ART) for HIV-infected Children and Adolescents Followed in Global IeDEA Sites" is a multi-regional analysis led by Dr. Vreeman. The primary objectives of the proposed analyses are to describe pediatric ART adherence and associated factors among children and adolescents followed in IeDEA. With these analyses, we will achieve the following **specific aims**: (1) Describe pediatric ART adherence and measurement methods among HIV-infected children in the global IeDEA cohort; (2) Determine site-level and individual-level factors associated with ART adherence; and (3) Assess evidence of

the impact of non-adherence on clinical outcomes such as treatment failure and mortality, and programmatic factors such as loss-to-follow up. This project will use an adherence-focused pediatric site survey and analysis of existing pediatric patient-level data. The REDCap data management system for the supplemental survey has been completed. We are waiting for the sites to identify the personnel who will be completing the survey. The SOP for patient-level data transfer has also been finalized and the Regional Data Center is ready to receive data from other regions. All regions are expected to submit data by July 1, 2014. East African data set preparation is scheduled to begin in May 2014. We anticipate that data analysis will be completed by early 2015 with manuscript submission by the end of the next grant year.

Concept 60: "Effect of nucleos(t)ide reverse transcriptase inhibitor sequencing on second-line antiretroviral therapy outcomes in sub-Saharan Africa" is a multiregional concept led by Southern Africa. Data for this analysis was submitted in May 2013.

Concept 62: "2014 Update of concept-Immunodeficiency at the start of ART: a global view" this multi-regional analysis is led by Southern Africa. East Africa submitted data in February 2014.

Concept 63: "Disparities in the overall and cause-specific mortality between HIV-positive women from Europe, North America and sub-Saharan Africa" is a multi-regional analysis led by Dr. del Amo. This concept is currently being reviewed by East African for consideration of participation.

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" is **Concept 52** and led by Drs. Geng and Martin at UCSF. All data collection is complete and data analysis and manuscript preparation are underway. An abstract entitled "Comparative effectiveness of HIV care and treatment programs in East Africa" was presented at CROI, Boston USA, March 2014 (Abstract 5; abstract below) and the first manuscript titled "Implementing a Sampling-Based Strategy to Ascertain Outcomes of HIV-infected Patients Lost to Follow-up from Care and Treatment Programs in East Africa" was submitted in March 2014 (Drafts 7). A second manuscript titled, "Mortality among HIV-infected Persons on Antiretroviral Treatment and the in East Africa: Assessing the Comparative Effectiveness of HIV Programs using a Sampling Based Approach" is in preparation.

Background: Survival after initiation of antiretroviral treatment (ART) among HIV-infected patients in Africa is a critical measure of the effectiveness of the public health response. Regional differences in mortality, after adjustment for biological factors (e.g., pre-therapy CD4 value), would suggest that variability in the behavior of health care systems and patient populations play an important role in effectiveness. In routine program settings, however, high loss to follow-up (i.e., unknown outcomes) is common and many deaths are not ascertained. As a result, effectiveness and comparative effectiveness of programs is unknown.

Methods: We evaluated HIV-infected adults on ART in five HIV care programs in Kenya, Uganda and Tanzania. Socio-demographic and clinical data were recorded during routine care on standardized forms issued by respective Ministries of Health. To manage the effects of loss to follow-up, we intensively traced a random sample of patients without unknown outcomes (defined as at least 90 days late for last visit) in the community. Outcomes in this sample of traced patients were incorporated into survival analysis using probability weights to revise estimates of mortality in the entire clinic population.

Results: Over two years, we followed 33,947 adults on ART: 15,613 from Kenya program 1; 4,844 from Kenya 2; 2,615 from Uganda 1; 7,532 from Uganda 2 and 3,343 from Tanzania 1. The median age was 35 years (IQR: 29-42), 66% were women, median pre-therapy CD4 count was 155/µl (IQR: 70-237). Overall 5,801 (25%) were lost to follow-up and of these, 980 (17%) were randomly selected for tracing in the community. Vital status was ascertained in 89% of the 980 traced patients. Using only deaths known to programs before tracing, the two-year cumulative incidence of mortality was 2.4% (95% CI: 2.3%-2.6%). Incorporated outcomes among the lost lead to a two year cumulative mortality estimate of 7.5% (95% CI: 6.9%-8.1%). After adjustment for age, sex, pregnancy, whether patient was new to clinic at observation

start, pre-therapy CD4 value, and tuberculosis at ART initiation, the clinical care program of the patient remained associated with mortality. Using Kenya program 1 as reference group, the adjusted hazard ratio for death in Kenya 2 was 1.04 (95% CI: 0.78-1.38), in Uganda 1 was 1.36 (95% CI: 1.0-1.84), in Uganda 2 was 0.56 (0.38-0.79) and in Tanzania 1 was 1.91 (95% CI: 1.46-2.52).

Conclusions: After accounting for measured biological drivers of mortality, program-to-program differences in survival of HIV-infected patients on ART remain substantial. Even within the standardized and simplified public health approach to HIV treatment, therefore, effectiveness in real-world settings appears to vary. Understanding health care systems behavior (e.g., quality, patient-centeredness) and well as patient behavior (e.g., engagement, adherence) is needed to optimize the effectiveness of HIV treatment in Africa.

Supplement from NIAD: "HIV-1 genotypic diversity and drug resistance in western Kenya at times of political crisis" led by Dr. Kantor resulted in a publication by M. Mann in JAIDS (Publications 6).

Supplement from NIDA: "Prevalence and Impact of Alcohol Use in Patients Enrolling in HIV Care: An East African International Epidemiologic Databases to Evaluate AIDS (IeDEA-EA) Project" is led by Dr. Wools-Kaloustian and Dr. Goodrich. The aims of this project are to determine: 1) the prevalence of hazardous alcohol consumption in patients newly enrolling in care and compare their baseline characteristics to non-drinkers; 2) compare clinician and research assistant collected AUDIT screening data at AMPATH; and 3) assess the impact of hazardous drinking on patient outcomes including time to ART initiation, medication adherence, retention in care and death. AMPATH and Mbarara have completed enrollment with 277 and 264 patients enrolled, respectively. Enrollment at FACES in ongoing and as of the end of April the program had enrolled 64 patients. The plan is to complete enrollment by the end of June 2014 and complete follow-up by end of December 2014. Data cleaning and analysis is slated to begin in early 2015.

Supplement from NIAID: "Linkages from Testing to Care in the USAID-AMPATH Partnership" is led by Dr. Braitstein. This project is designed to address questions related to the uptake and engagement of care both by persons previously known to be HIV-positive but who haven't engaged with care, as well as for persons newly testing HIV-positive in a large home-based HIV counseling and testing (HBCT) program in western Kenya. Specifically, this supplement will support the electronic merging of data from HBCT with clinical HIV data of persons who have enrolled into HIV care through AMPATH programs. The aims of this supplement are to: 1) Determine the time from testing to initial linkage to care; 2) Estimate the rate and determinants of initial linkage to care following HIV testing in HBCT through ART initiation; 3) Examine the determinants of failure to link to care.

Measures of linkage included: self-reported enrollment in HIV care, registration within AMPATH, and having had an initial encounter with an HIV care provider verified by AMRS. Engagement in care outcomes included: CD4 testing and an initial plus an additional follow up visit with an HIV care provider. Sensitivity, specificity, positive and negative predictive values were calculated for each linkage measure compared to each engagement outcome. Logistic regression analysis was used to examine associations between demographics (i.e., sex, age, monthly income and marital status) and sensitivity/specificity of each linkage measure. The characteristics of the 3,788 who tested HIV-positive between December 2009 and February 2011, were 63% female, mean age 33 years, 56% married, and 43% with monthly income $\leq$1000 KES (12 USD). Eighty-seven percent registered with AMPATH, 58% self-reported enrollment in care, and 58% had an initial encounter with a clinician. The linkage measure that maximized both sensitivity and specificity for both engagement outcomes was having an initial encounter. Those under 30 years (OR = 0.29, 95% CI: 0.22, 0.37) and with income of $\leq$1000 KES (OR = 0.58, 95% CI: 0.44, 0.76) were less likely to accurately self-report enrollment. Registration was less likely to correctly identify males (OR = 0.56, 95% CI: 0.48, 0.66) who engaged in care. Self-reported enrollment and registration are biased measures of linkage to HIV care, particularly for younger males with lower incomes. Research and programmatic efforts focused on linkage to HIV care should use a verified clinical encounter as the outcome of interest to accurately predict further engagement in HIV care.

Dr. Braitstein and her team are currently in the process of merging in the HIV re-testing data for the catchment. The data to be merged are those which have been collected by the PHCT Counsellors as at 16th January, 2014 in the Port Victoria catchment area. The total number of records under review is 13,854. The data were compared against the baseline data collected by the HCT Data Collection Process conducted in the year 2011. The data have been under review by four data assistants during the period February - March, 2014. A preliminary breakdown of the analysis is as shown in Table 8. The major challenges encountered in the data review process have been poor documentation of dates of birth and names. The merging exercise depends heavily on these two variables. This has been relayed to the PHCT data team and necessary steps will be taken to ensure that the date of birth and all three names are recorded correctly in the future. This project has resulted in two abstracts both by Dr. Genberg one accepted to IAPAC 2014 and the other to IWHOD 2014 (Abstracts 6).

Table 8: Matching Between HCT and Re-Testing In PHCT

PHCT PORT vs. HCT PORT	FREQUENCY	%
True match	4,679	33.77
Gray area	596	4.31
Non match	8,579	61.92
	13,854	**100.00**

Collaborations with international organizations within specific aim 1:

Professor Yiannoutsos has continued his collaboration with the United Nations Joint Program in HIV/AIDS (UNAIDS). Most recently, an analysis of mortality has been completed using data from the Collaboration of Observational *HIV* Epidemiological Research in Europe (COHERE). A report was sent to this group. In addition, Dr. Peter Ghys, Director of Strategic Information and Evaluation at UNAIDS, has requested that a multi-regional project be carried out under the leadership of Professor Yiannoutsos and the East Africa IeDEA Consortium, to produce temporal trends of the number of patients on ART within each country by the end of each year by age group and by demographic factors with a specific focus on older populations. A multi-regional concept proposal is under preparation and is expected to be submitted to the worldwide IeDEA network executive committee in early summer 2014.

Dr. Wools-Kaloustian has been working with the Collaborative Initiative for Paediatric HIV Education and Research (CIPHER) on the development of two concepts: “Duration of first-line antiretroviral regimens in children: a global perspective” (Concept 59) on which she service as the scientific Co-Chair and “Global epidemiology of adolescents with perinatal HIV-infection” (Concept 61).

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

Project 2.1: Automating the linkages between mother and infant records. This project is led by Dr. Wools-Kaloustian.

As of April 2014, reporting utilities have been developed to map exported OpenMRS concepts from AMPATH and FACES to the INC Research data exchange standard that was finalized in December 2013. The first pregnancy cohort was transferred in March, this included February data from FACES. The data have been reviewed and we are addressing queries and updating the processes for data transfer. The project will start sending AMPATH data in May 2014, and reports for both sites will continue at an interval of once per month thereafter. Dr. Wools-Kaloustian is working with Dr. Edith Apondi a Pediatrician at AMPATH (Moi University) to develop a concept proposal utilizing these data. We anticipate that the finalized proposal will be circulated by the end of July.

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

The Pediatric/PMTCT breakout session at the East African IeDEA Investigators meeting in Kampala Uganda in February 2013, initiated the development of a concept sheet designed to look at the outcomes of Option A versus B/B+ with regards to maternal outcomes such as retention rate, time to antiretroviral initiation, maternal outcomes and infant outcomes (transmission rates, birth weight, and gestation age at delivery). After looking at

the available data within East African IeDEA it was determined that this analysis could not move forward without pulling data from sources outside of IeDEA. The exploration of other data sources has delayed movement of this project. We plan to readdress this concept in the next month or two and determine the group's interest in continuing to move this forward.

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. An extensive review of the eligible cohort within East Africa revealed insufficient numbers in the group exposed to single- or dual-drug pMTCT as such the concept proposal has been modified accordingly and the analysis data set is expected to be completed by June 15, 2014.

Other projects that fall within Specific Aim 2:

Concept 8: "Incidence and determinate of pregnancy in women enrolled in care and treatment programs in East Africa" is led by Dr. Elul. The analyses for this concept have been completed. Numerous analyses have been undertaken over the past year to ensure that the preliminary results, which showed a tendency toward lower incidence rates for pregnancy among women on ART, were correct. This was of particular concern given that a major publication by the MTCT-Plus group documented the opposite trend (i.e., that ART was associated with a *higher* incidence of pregnancy). In addition, CD4 count is a time-updated confounder, that is, it is both a cause for the initiation of and effect of ART (along with other factors such as weight and WHO stage). These factors are also related to the likelihood of an incident pregnancy. To adjust for all of these factors and ensure that the somewhat surprising initial results were not an artifact, an analysis based on marginal structural models was performed. All analyses suggest that the effect of ART on pregnancy is nuanced and is weaker than previously reported. This suggests that previous articles which reported strong increases in the rate of pregnancy while on ART, may have not adequately considered the issues of confounding and/or both patient and site-level characteristics, which have a strong association with the likelihood of future pregnancies (particularly, prevalent pregnancies, which probably account for a large number of factors which predispose a woman to get pregnant). The manuscript for this concept is currently being written by Dr. Elul and it is anticipated that this manuscript will be submitted for publication by August 2014.

Concept 46: "PEPFAR: Programmatic and Clinical HIV Treatment Outcomes in Pregnancy" is led by Dr. Holmes and was initiated as a collaboration with OGAC. The analyses for this project are complete and a draft manuscript is circulating to the co-authors, the working abstract is outlined below (Drafts 8; abstract below). We anticipate that this manuscript will be completed and ready for submission by the end of June 2014.

Importance: New World Health Organization (WHO) guidelines will result in a sharp rise in the numbers of HIV-infected pregnant women eligible for antiretroviral therapy (ART). However, there is limited knowledge about pregnant women currently on ART in sub-Saharan Africa.

Objective: To determine whether pregnant women represent an increasing proportion of those starting ART in large HIV programs and to compare their clinical characteristics and outcomes with others starting ART.

Design: A retrospective cohort study from 2004 to 2011.

Setting: Large HIV care and treatment programs in Kenya and Uganda, supported in part by the U.S. President's Emergency Plan for AIDS Relief (PEPFAR)

Participants: 90,324 HIV-infected adults consecutively initiating ART

Intervention: Combination ART for the treatment of HIV infection

Main Outcomes: Trends in the proportion and baseline characteristics of pregnant women and others starting ART over time. Attrition (non-retention or death) among pregnant women, non-pregnant women and

men, and between women who became pregnant while stable on ART versus those starting ART while pregnant.

Results: The cohort included 90,324 HIV-infected adults (67.6% women) starting ART during the study period. The proportion pregnant at ART initiation rose from 7.5% in 2004 to 13.2% in 2011. Pregnant women were healthier at ART initiation (79.8% WHO stage I/II vs. 44.9% and 35.8% for non-pregnant women and men; median CD4 cell count 357/mm^3 (IQR 215-526) vs 141/mm^3 (IQR 62, 221) and 115/mm^3 (IQR 43-198, respectively). Pregnant women starting ART had higher rates of attrition during the 12 weeks after ART initiation, compared to men and non-pregnant women; after 12 weeks the attrition rates for these women declined below that of other groups.

Conclusions and Relevance: Pregnant women are healthier than men and non-pregnant women starting ART and comprise an increasing proportion of those initiating ART in African HIV programs. Women starting ART while pregnant are at elevated risk of attrition especially in the first 3 months after initiation. These results should be considered as treatment retention programs and monitoring strategies are tailored for pregnant women starting ART.

Year 6 Administrative Supplement: "Understanding low uptake of PMTCT services by HIV-infected women in rural Tanzania" is led by Ms. Gourlay under the direction of Dr. Zaba and Dr. Urassa. The quantitative portion of this study links ANC records with VCT, clinic and sero-servalence records in order to assess the PMTCT cascade. The following questions are being addressed 1) Do HIV infected (compared to uninfected) pregnant women avoid or seek out ANC services in the only clinic in the area that provides HIV testing 2) How do self-reports of ANC use and past VCT compare with clinic reports? 3) Are women who first discover they are infected during provider-initiated testing at ANC more or less likely to take-up PMTCT and ART services than women who originally find out they are infected at a VCT session? 4) What is the influence of the partner's HIV status and partner's knowledge of his HIV status on ANC/VCT service uptake? The qualitative portion of this project is designed to identify motives and barriers to uptake of PMTCT services.

The qualitative investigation has resulted in one publication in *BMC Med Res Methodol.* by Ms. Gourlay, one manuscript submitted to *Social Science and Medicine, and three poster presentations* (Drafts 9, Abstracts 7-9)

With regard to the quantitative investigation (double) data entry and cleaning of routine clinic data was completed in December 2013. This was later than originally proposed due to limited data manager capacity at the National Institute of Medical Research, time taken to make repeated field trips to locate missing data, and complexity of the project including the need to develop many different data entry screens for each register series. Linkage of the clinic data to the community surveillance data and a draft statistical analysis was conducted in January-February 2014 (based on linkage methods that were being developed during 2013), and an abstract submitted to the AIDS 2014 conference Melbourne Australia, July 2014. Preliminary logistic regression analysis prepared for the abstract indicates that 43% of 928 HIV-positive female residents aged 15-49 accessed HIV care at the ANC or ART clinic. Residence in more urbanized areas and earlier voluntary counselling and HIV testing, were associated with greater access to HIV care, while separated or widowed women were less likely to access HIV care. Further analyses will investigate uptake of other PMTCT outcomes at a community level, including ARV drugs. More complex factors associated with PMTCT service access, such as knowledge of ART and partner characteristics will also be investigated. It is anticipated that the complete the statistical analysis and manuscript development will be completed by September 2014.

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

Project 3.1: Evaluate the use and determinants of IPT for HIV-infected patients in East Africa screened negative for active TB.

(Roughly corresponds to the original proposal project 3.3: Evaluate the uptake and impact of screening for and initiation of IPT in HIV care and treatment sites in East Africa)

Project 3.2: Characterize the rate and determinants of ART initiation for HIV-infected, ART naïve patients with newly diagnosed active TB

(Roughly corresponds to the original proposal project 3.1: Characterize the timing of ART initiation and assess the impact of ART delay in TB co-infection).

Project 3.3: Evaluate the effect of IPT use and time to ART initiation on survival using a sampling based approach to estimate mortality in setting where loss to follow-up is high

(Replaces the original proposal project 3.2: Assess penetration of automated molecular diagnostic testing in HIV care and treatment programs in East African and the impact of their adoption on identification of active TB and mortality).

All of the projects outlined under Specific Aim 3 continue to require optimization and validation of the TB data available within the HIV care and treatment program databases. Because of the complexity in addressing these issues, the focus on optimization of this data has been at two sites within the consortium (AMPATH and Mbarara). The AMPATH system is complex and includes co-management of TB patients at some sites while other sites refer co-infected patients to the TB clinic for management. Though many of the previously-identified challenges to ascertainment of accurate TB data at AMPATH have been addressed, additional issues have continued to require intervention during this year in order to optimize TB data collection and validation. The team has focused on improving data at each of the following time points: 1) Time from symptom screen to sputum order 2) Sputum order to collection 3) Collection to receipt in laboratory 4) Receipt of sputum in laboratory to testing 5) Testing to result reporting and 6) Result reporting to clinical action.

The AMPATH TB group is working to ensure that data improvement and documentation is occurring at all steps in this process in a way that is readily accessible for analysis. The following issues were addressed at each time point: 1) Incomplete documentation of TB screening data in patient visit notes; 2) Sputum collection cups were given to patients with no spot-sputum collection or record of data to assure patients return with their samples; 3) Lab request forms did not include all necessary information (i.e. AMPATH number and module number); 4) Incomplete records of time of sputum collection and transport to lab. 5) Incomplete recording of sputum testing dates; 6) Incomplete recording of clinician receipt of test results.

In response to the above issues the program re-educated staff on documenting TB screening data at the initial patient visit and all subsequent follow-up visits. Patient's initial visit to the TB clinic now includes collection of a spot-sputum. Cough monitors' logs added documentation of the patient's AMPATH number, module number, telephone contact number as well as the dates of sputum collection, lab delivery and return results. Lab request forms now include the patient's AMPATH number and module number as needed for data entry into the Laboratory Information Management System (LIMS). The laboratory also logs the date of specimen receipt and processing. Laboratory personnel enter patient identification information and lab results into LIMS which is currently being programmed to send data directly to the AMPATH Medical Record System (AMRS).

The next step at AMPATH will be to assess each step of the cascade in order to identify points of patient/specimen drop out and determine the median time for each interval in the cascade. The AMPATH TB team goals for the upcoming year are: 1) Complete programming for transfer of data from LIMS to AMRS; 2) Assure recognition in LIMS of all co-infected patient identification numbers; 3) Utilize data collected through the multi-regional TB project led by Dr. Petit to provide QA/QC for the data collected within the AMRS.

During Year-7 the TB Team at Mbarara set-up data collection mechanisms to capture the TB diagnostic process. At this point they have collected over a year of data on the HIV/TB diagnostic process. They have

sought to characterize the fraction of diagnostic and clinical steps taken in the HIV TB diagnostic process that are actually completed and to summarize completion across the entire cascade of diagnostic activities required for one patient. This has required setting up triplicate order forms and establishing logs at each of the diagnostic stations (clinic, laboratory, specimen collection room, etc.). They have entered and conducted quality checks on these data. Capture and storage of these data has necessitated the development of the clinical data system to collect this information, and has required additional database development. The Mbarara TB team has carried out preliminary exploratory analyses that suggest that the overall completion rate of the diagnostic process is not optimal and that the level of completion of each step varies (Figures 4 and 5).

Figure 4: Mbarara

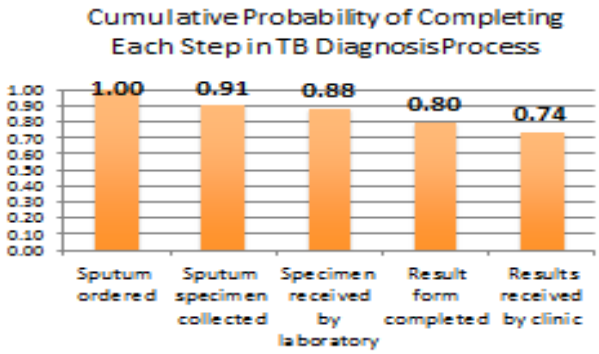
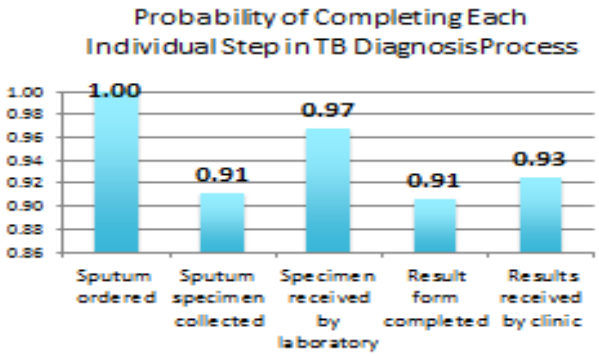


Figure 5: Mbarara



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" was initially led by Dr. Tsiouris at Columbia University and has transitioned to Ms. Suzue Saito working under the direction of Dr. Elul. Analysis data sets for this project were generated in November, 2013 and the analysis has been completed. A manuscript is currently being drafting with plans for circulation to co-authors in June 2014. The key finding of this analysis is the decreasing trend in TB incidence rates in all of the cohorts studied that coincides temporally with anti-retroviral therapy (ART) ramp-up in these countries. A causal association between ART scale-up and TB incidence will be the objective of a follow-up paper.

(Fenner) Multi-regional Project: "Tuberculosis in HIV treatment programmes in low-income countries within the global IeDEA network: A survey on integration of services, diagnostic, screening, preventive and treatment practices." This multiregional project was led by Dr. Fenner from the Southern African Region. Eight East African sites participated in this project. This year the findings from this study led to the publication of one paper (Publications 7) and four meeting abstracts (Abstracts 10-13).

***(*Sterling, Petit) 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. Petit and Sterling from CCASAnet. Four programs within East Africa are taking part in this project including: AMPATH, Kenya; Masaka

Hospital, Uganda; Kisesa Clinic, Mwanza, Tanzania; and Tumbi Regional Hospital, Kibaha, Tanzania. The East African Group developed the protocol document that was circulated as a template for other regions/sites that required regulatory approval prior to project initiation. The East African sites have reviewed the records for and entered data on 344 TB patients (AMPATH 61, Kisesa 25, Masaka 155, and Tumbi 103) into the REDCAP database for this project. This year the East African sites plan to complete chart review and data entry on an additional 1,356 patients.

Multi-regional Project: "Impact of HIV infection on the population genomics of drug-resistant Mycobacterium tuberculosis: insights from macro-evolutionary analyses" is led by the Southern African Region. One East African site (AMPATH) participated in the pilot phase and is currently participating in the project phase of this study.

DMID Malaria Supplement: "Rakai Health Facility-Based Malaria Surveillance Study" was completed and publication this year (Publications 8).

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

This analysis is being led by Dr. Martin and his team at UCSF. The final analysis data sets have been completed. The cohort includes 159,036 patients (67% women), with a median age of 36 years (interquartile range (IQR): 30 to 43) and median CD4 count of 226 cells/mm^3 (IQR: 90 to 415) at clinic enrollment. Median follow-up was 5.4 years (IQR: 3.6 to 6.9) during which 1326 incident KS diagnoses were made (32% biopsy-proven), reflecting an overall incidence of 260 per 100,000 person-years (p-y). In the unadjusted analysis, patients not on ART had higher KS incidence than those on ART (347 vs 227/100,000 p-y). In the nested new user cohort analysis, which properly accommodates for time-dependent confounding/mediation, patients on ART had an 80% (95% CI: 70% to 90%; p<0.001) reduction in incident KS compared to those not on ART. CD4+ T cell count significantly modified the effect of ART; patients with the lowest CD4 counts (<100 cells/mm^3) had the greatest effect of ART (p<0.01) on KS incidence. The analysis to date used a complete case analysis and adjusted for most recently observed CD4 count (amongst other variables) as the main confounder. The team is in the process of deriving time-of-nested new user cohort enrollment CD4 count as a better indication of patient's clinical appearance to more completely capture what the clinician observed when deciding whether or not to prescribe ART. The team is also multiply imputing a variety of missing values (e.g., hemoglobin, WHO status) to move away from the complete case analysis. If the team's current estimate holds after further analysis, they will conclude that in East Africa, an area of high prevalence of both HIV and HHV-8, use of ART results in a substantial reduction in KS incidence. The ART effect would be similar if not greater than in resource-rich areas with lower HHV-8 prevalence. Despite this beneficial ART effect, however, KS incidence among persons with optimal CD4 count restoration remains considerably higher than pre-HIV era levels. Further investigation is needed to explain this residual elevated risk.

Progress has been delayed for three main reasons. First, confounding by indication is the main threat to validity in this analysis, and thus the team sought to remove confounding to the extent that they could with the available measurements. This required complex derivation of new variables such as estimated CD4 count on the day of each nested new user cohort enrollment, which required the creation of a linear mixed effects regression model to singly impute values for each patient. It also required the request from the main IeDEA database for variables which the team had not originally foreseen as being useful when the analysis first was conceived (e.g., hemoglobin). Second, as expected, there are substantial missing data amongst the covariates (e.g., hemoglobin or WHO stage) and this required the performance of multiple imputations to avoid

the bias inherent in a complete case analysis. Third, after accounting for the multiple copies of the dataset which ensues from multiple imputation, the multiple (30) non-randomized trials which are created in the nested new user analysis approach, and the discretized (by level of month) nature of the follow-up which is used in pooled logistic regression, the dataset has become extremely large and time-consuming to run estimation commands. The team has remedied this by identifying a university-based multiprocessor version of Stata which can accommodate very large datasets. All of these problems are compounded by the analysis being led by a junior African investigator who is just gaining experience with these techniques. In any case, the team is aware of only one other analysis of this nature in sub-Saharan Africa that uses modern approaches for adjustment to accommodate for time-dependent confounding/mediation. The team believes that this approach offers the best chance for a valid inference for the research question.

Two meeting abstracts have resulted from this project during the past year (Abstracts 14-15). The team anticipates that a manuscript from this project will be submitted for publication by the end of funding year 8 or the beginning of funding year 9.

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. The objectives for this project are to 1) Describe the relationship between CD4 count, WHO stage, ART history and grade of dysplasia 2) Compare recurrence rates between LEEP and cryotherapy at 6, 12 and 18 moths and generate screening interval guidelines for visual inspection with acetic acid (VIA) in HIV-infected women. This project is focused in two EA IeDEA programs (AMPATH and FACES). At the time of the renewal both programs had cervical cancer screening programs (CCSP) affiliated with their HIV-care and treatment programs however at AMPATH the CCSP program did not maintain electronic records and the FACES program maintained an electronic database in ACCESS that could not be linked to the HIV-care and treatment database. As such, in order to address the objectives of this project we have had to merge the cervical cancer screening databases with the HIV-program databases at both FACES and AMPATH. Progress to date on this process is as follows:

At AMPATH the retrospective entry of Cervical Cancer Screening Program (CCSP) logs into Excel is ongoing but nearly complete. Prospective data will continue to be entered into Excel while the beta testing and roll out of point of care data collection using tablet computers is introduced at all CCSP sites. These data are currently being reviewed and the Excel spreadsheets will be converted to HL7 messages for import into AMRS. Additionally, new patient identifiers and protocols are being developed to allow integration of non-HIV positive patients into OpenMRS to capture the entire CCSP cohort. At FACES we are in the process of using HL7 messages to merge CCSP data (ODK data format) with FACES HIV data (OpenMRS format), and integrating the non HIV-positive patients.

At AMPATH we plan to migrate the retrospective CCSP data into AMRS in June 2014, and have processes in place to capture all prospective data from CCSP while tablets continue to be tested and Excel entry is incrementally phased out. We anticipate introduction of direct data entry by early in June 2014. At FACES, mapping of variable is underway so that the ODK database can be incorporated into OPENMRS. For both AMPATH and FACES we plan on to capture data on both HIV and non HIV patients in the same OpenMRS installations by the end of June 2014.

The Reproductive Health Working Group at the East African IeDEA PI meeting in Kampala initiated discussions about the development of a concept sheet that will address objective 1. The group is now meeting via conference call on a monthly basis and is further discussing the development of the concept sheet for this project. If the concept sheet has not been fully developed by the East African PI meeting in October we will set aside time at the meeting to finalize the concept sheet for this project.

Other projects that fall within Specific Aim 4:

NCI Funded: "Systematic identification of biopsy-confirmed KS in the large population base of East Africa" continues to be led by Dr. Martin and the UCSF team. IeDEA continues to support the KS biopsy programs at Mbarara, AMPATH and IDI. This currently includes support for biopsy supplies, data collection, and North American Pathology review of biopsy slides. Data collected through these programs provided the preliminary data for the UCSF team to apply in the past year for three NIH grants related to KS in East Africa. Data from this program were presented at the ICMAOI meeting this year (Abstract 16) The first was a successful application for a supplement to D43 CA153717, and the two others were responses to RFA-CA-13-015 (Cancer Detection, Diagnostic and Treatment Technologies for Global Health (UH2/UH3)), and RFA-CA-13-010 (Sub-Saharan African Collaborative HIV and Cancer Consortia (U54)).

NCI Supplement: "*Survival among HIV-infected individuals with Kaposi's Sarcoma in Sub-Saharan Africa in the era of potent antiretroviral therapy".* This multi-regional supplement is led by Dr. Martin and the UCSF team. Survival after diagnosis is one of the most fundamental parameters in cancer epidemiology. In resource-rich settings, ambient clinical databases and municipal data (e.g., death registries) combine to make survival estimation in real-world populations relatively straightforward. In resource-poor settings, it is less clear how well we can determine cancer-specific survival with ambient data. The aims of this study are 1) Determine survival after KS diagnosis in Africa in the ART era. 2) Determine the excess mortality associated with KS compared to other HIV patients both stage 3 and 4 (indicator diseases TB and Cryptococcus) and patients with stage 1 or 2 disease 3) Evaluate pace and determinants of ART-initiation after a diagnosis of HIV-associated KS in sub-Saharan Africa.

This supplement is being undertaken in the four IeDEA Regions in sub-Saharan Africa:
At AMPATH, Kenya, a total of 470 patients were identified as lost to follow-up from the perspective of examination of the electronic medical record database since 2010 amongst those with Kaposi's sarcoma (KS) and the two comparator groups. Of these, 404 were confirmed to be lost to follow-up after manual examination of the medical chart. Of these 404, 322 (80%) have been sought for in the community and had their vital status updated. Of the remaining, 14 (3.5%) were sought but the search revealed no new information and 68 (17%) are still being sought.

At the ISS Clinic, Mbarara, Uganda Since 2010 amongst those with Kaposi's sarcoma (KS) and the two comparator groups, selected for review, 276 were confirmed to be lost follow-up after manual examination of the medical chart. Of these 276, 160 (58%) have been sought after in the community and had their vital status updated. Of the remaining, 22 (8.0%) have been sought but the search revealed no new information and 94 (34%) are still being sought.

The team is working with the leadership of West, Central and Southern Africa IeDEA to move this project forward in those regions however there have been significant barriers which have included issues with prioritization of resources, absent data on KS, and data accuracy.

As part of this project the team has attempted to estimate survival after the diagnosis of Kaposi's sarcoma (KS) in sub-Saharan Africa in the era of antiretroviral therapy (ART) by using ambient data from clinics participating in the East, West, and Central Africa IeDEA Consortia. In East Africa, the clinics included the ISS Clinic in Mbarara, Uganda and AMPATH in Kenya. Patients were followed from KS diagnosis until death, loss to follow-up, or database closure. Attempts at survival estimation were made using the Kaplan-Meier technique. To calculate incidence of loss to follow-up (defined as unknown vital status within the 3 months prior to database closure), we employed the cumulative incidence approach with death as a competing event. Among the 939 adults with KS we identified, 41% were women and the median age was 35 years (IQR: 30-41) and median CD4+T cell count 154/mm3 (IQR: 51-300) at time of diagnosis. There were 677 cases from 26 clinics in the AMPATH network in Kenya, 172 from the ISS Clinic, 23 from Nigeria, and 67 from 3 clinics in Cameroon.

Nominally, 22% of patients were estimated to be dead by 2 years (range 17%-28% across sites) but this estimate was clouded by 51% cumulative lost to follow-up by 2 years (range across sites 40% to 76%). With no functional regional or national death registry, the vital status among the lost is unknown. We concluded that with half of all patients with KS lost to follow-up by the end of two years, we could not accurately estimate survival. Until we either generally strengthen data systems or implement cancer-specific enhancements to derive more accurate estimates (e.g., tracking of the lost in the community, as is now ongoing in this supplement, insights from cancer epidemiology will be severely limited in sub-Saharan Africa.

Data from this supplement contributed to 3 meeting abstracts this year (Abstracts 17-19). We anticipate that a manuscript describing the magnitude of lost to follow-up amongst patients with KS will be completed by mid-May 2014. Tracking of the remaining patients in East Africa who are lost to follow-up will be completed by June 2014. The analysis describing mortality after a diagnosis of KS in East Africa, after accounting for the lost to follow-up, and comparing it to the two relevant patient groups will be completed by July 2014.

Collaboration with IARC: "Risk of Cancer in Persons Infected with HIV in Western Kenya" Due to the geographic overlap of the Moi Teaching and Referral Hospital Cancer Registry overlap with the AMPATH catchment linking the data from the AMPATH Medical Records System (AMRS) and the MTRH Cancer Registry appeared feasible. We facilitated the work of an Informatics Fellow Judy Wawira with IARC to link the AMPATH and MTRH CANREG databases. Unfortunately this project was more challenging than initially anticipated due to problems with backlogs in data entry into the CANREG and issues with matching identifiers between the two databases. Dr. Wawira attempted to validate matching between the CANREG and the AMRS by using the KS registry that we a maintaining for IeDEA. She identified 200 matches between CANREG and the AMRS which was significantly fewer than the 600 KS patients that should have been documented within both systems. In linking the KS database to the CANREG system, she obtained 525 matches (4 % of all cancers in the CANREG linked to the KS registry data), while significantly improving the matching, 100% matching even between the limited KS registry data and the CANREG was not achieved.

Dr. Wawira believes that some of this discrepancy results from a backlog of forms (nearly 1,000) that have not yet been entered into the CANREG system. The Oncology Program is providing resources to catch-up on the backlog of data entry however to date the program continues struggle with the record backlog. She also experienced problems related to inaccurate data elements within both registries. For example, in CANREG, there are only 84 patients out of 15,671 with a valid date of birth. All the rest are recorded as 99/99/yyyy which greatly lowers matching potential. Dr. Wawira believes that additional training centered around data collection and data entry for the CANREG is need in order to improve the data quality in the CANREG, which is necessary prior to any further attempts to merge the two data systems.

Concept 57: "African Network for Cervical Cancer Screening and Treatment" 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. The survey assessing cervical cancer screening practices within sub-Saharan African sites within ACTG, AMC, CFARs, and IeDEA was completed in November 2013 and the data from this survey were presented at the CFAR Meeting in Cape Town, South Africa in December 2013. Fifty-three sites responded to the questionnaire of which 50% were IeDEA affiliated sites, 96% had access to cervical cancer screening programs, and 77% had screening available on-site. The number of clinics providing each type of screening by country is outlined in figure 6. Of the clinics that provide screening, 18 clinics capture this data within an electronic medical record and thus have the potential to contribute retrospective data to a multi-regional analysis related to cervical cancer and HIV. This collaboration and these data provided the basis for a successful application to the CDC-Foundation's RFA "Rapid Baseline Situational Assessments in Improving Data for Decision-making in Global Cervical Cancer Programs" led by Dr. Were and Dr. Wools-Kaloustian.

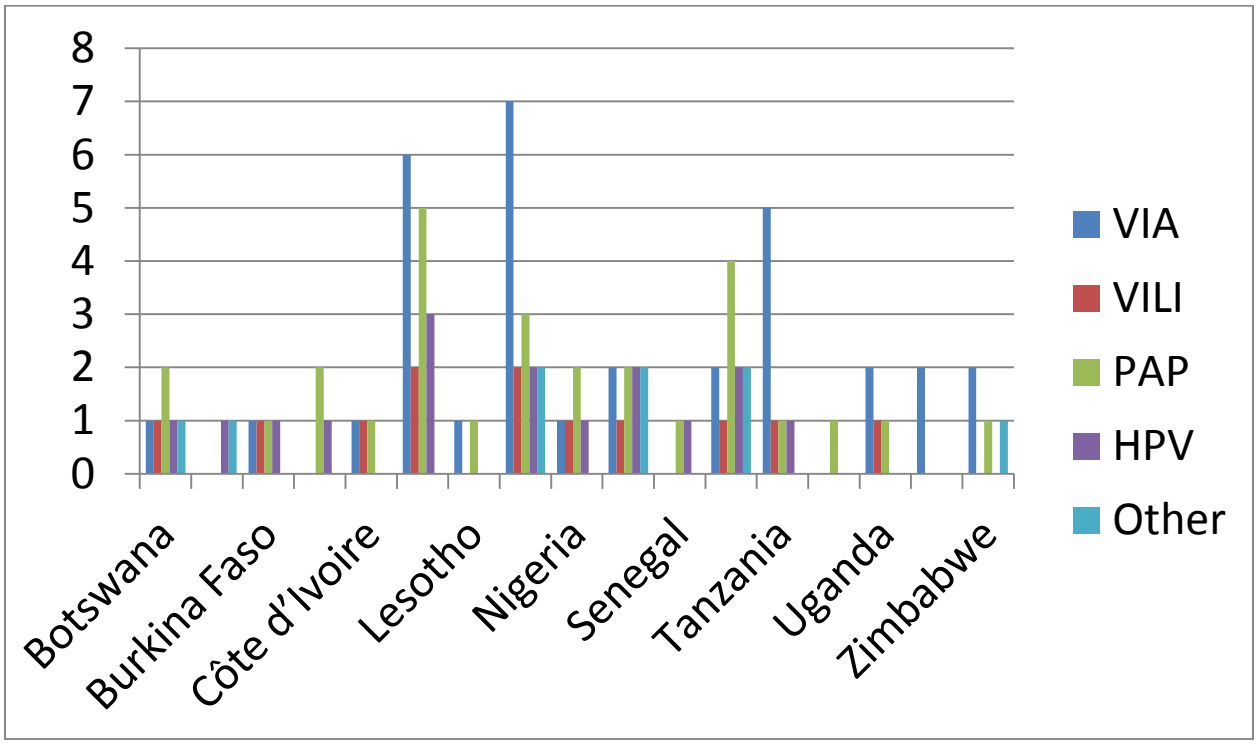


Figure 6: Diagnostic Methods Used at Sites by Country

C. Significance:

The overall significance of this work remains the same as that outlined in the initial grant application. Significance is also outlined specifically for each new project in the narrative above.

D. Plans

The plans for each project are outlined within the project narrative.

Figures & Tables

Figure 1: AMPATH Research & Training Awards (1998 – 2014)

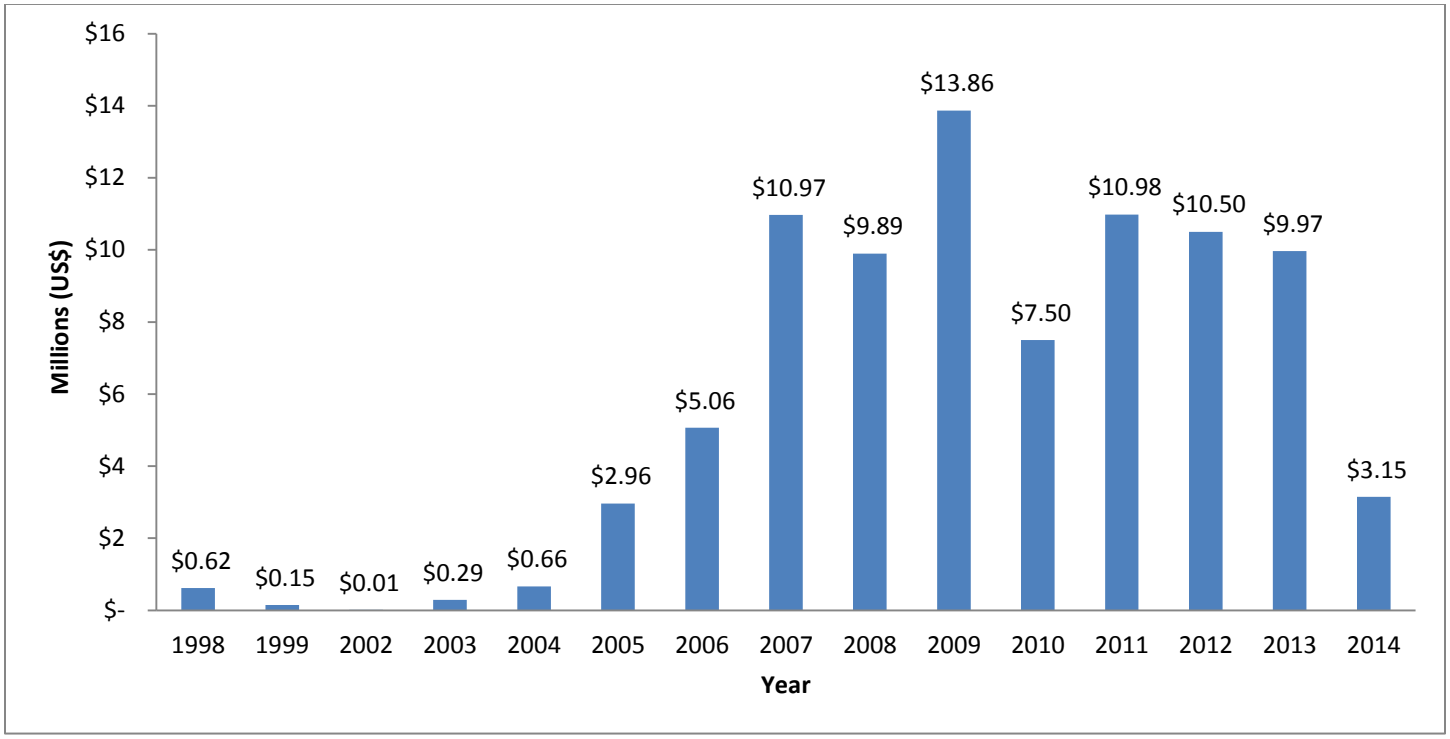


Figure 2: Sponsors of AMPATH Research (January - June 2014) (Total Directs = US$ 3.15 million)

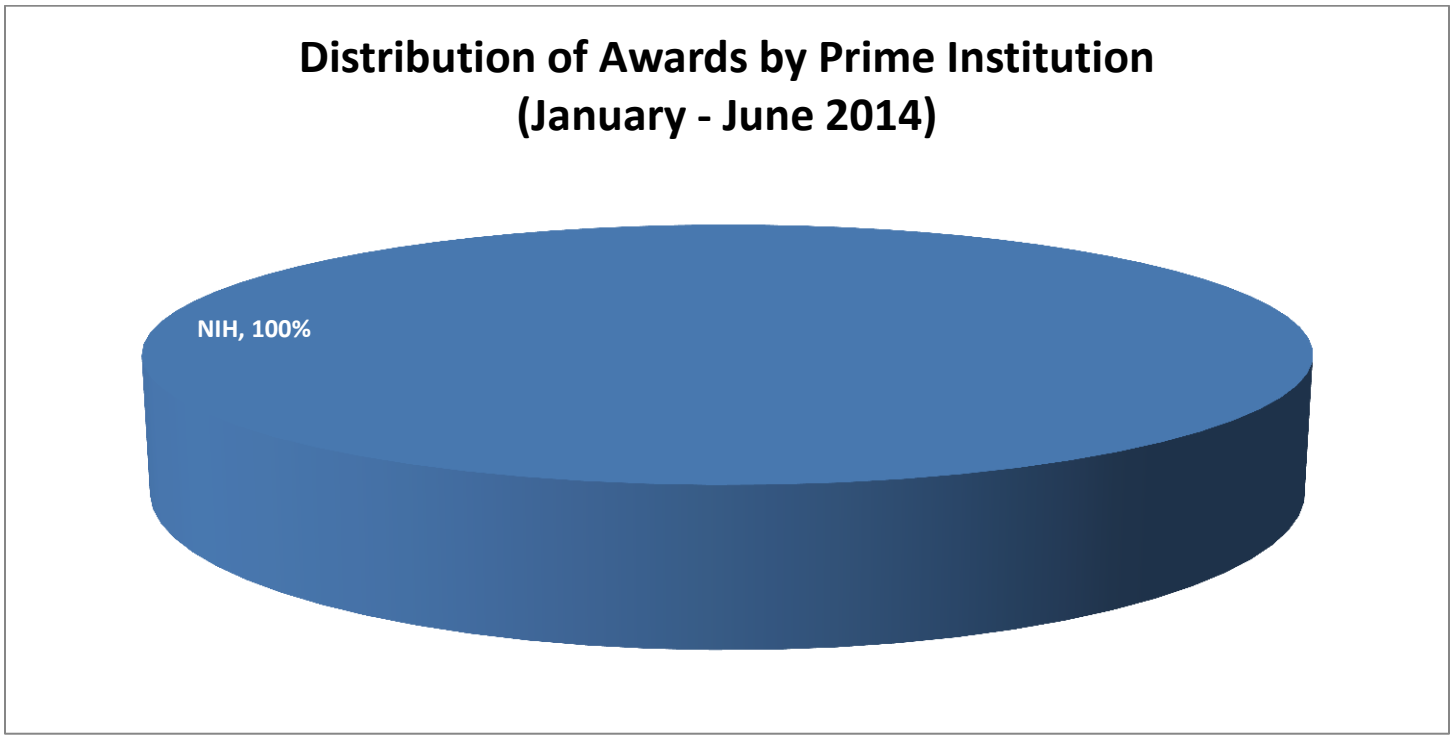


Figure 3: AMPATH Research Sponsors (1998-2014) (Total Directs = US$86.6 million)

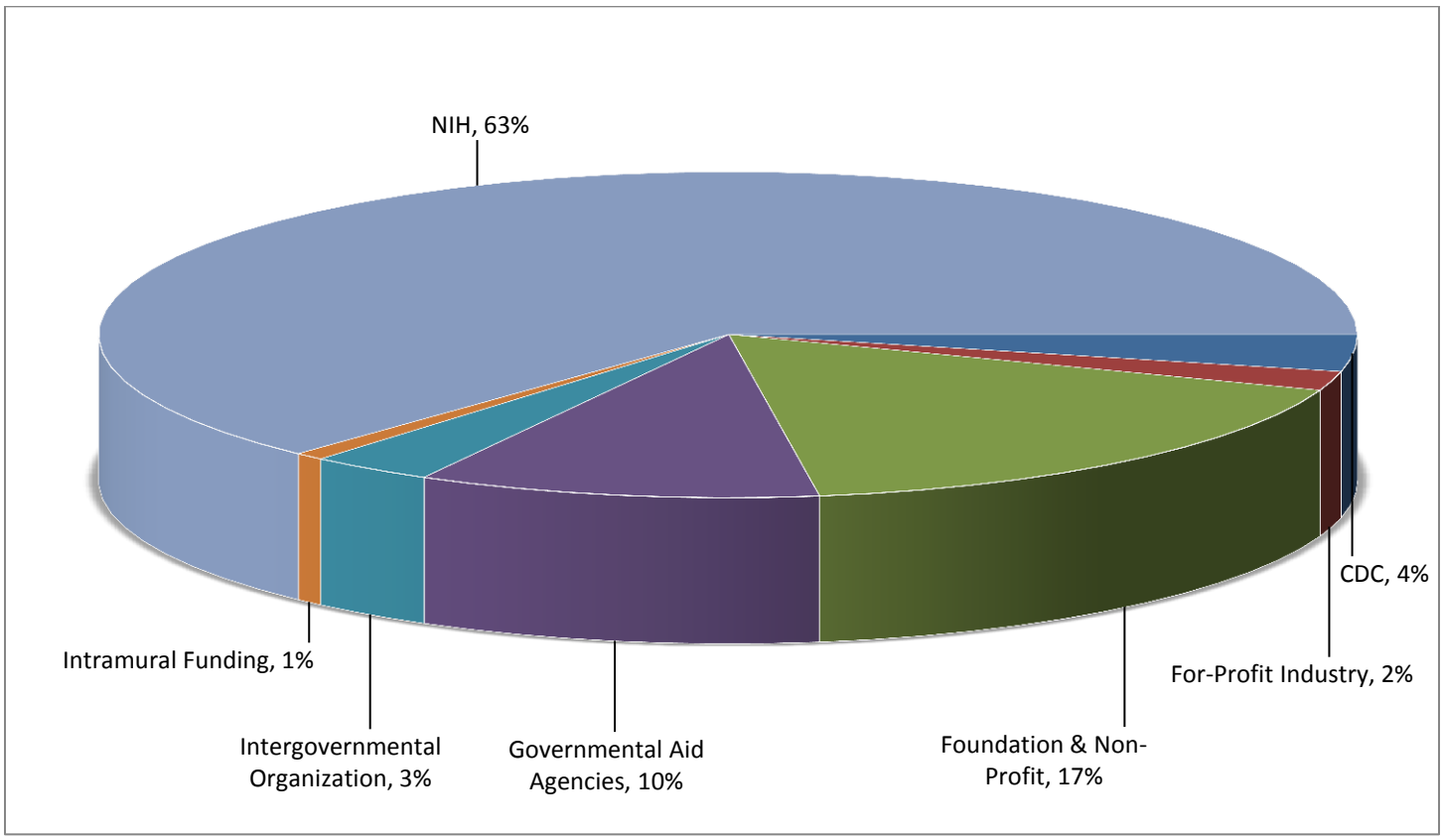


Figure 4: AMPATH Publications by year published (1989-2014) (Total Publications = 314)

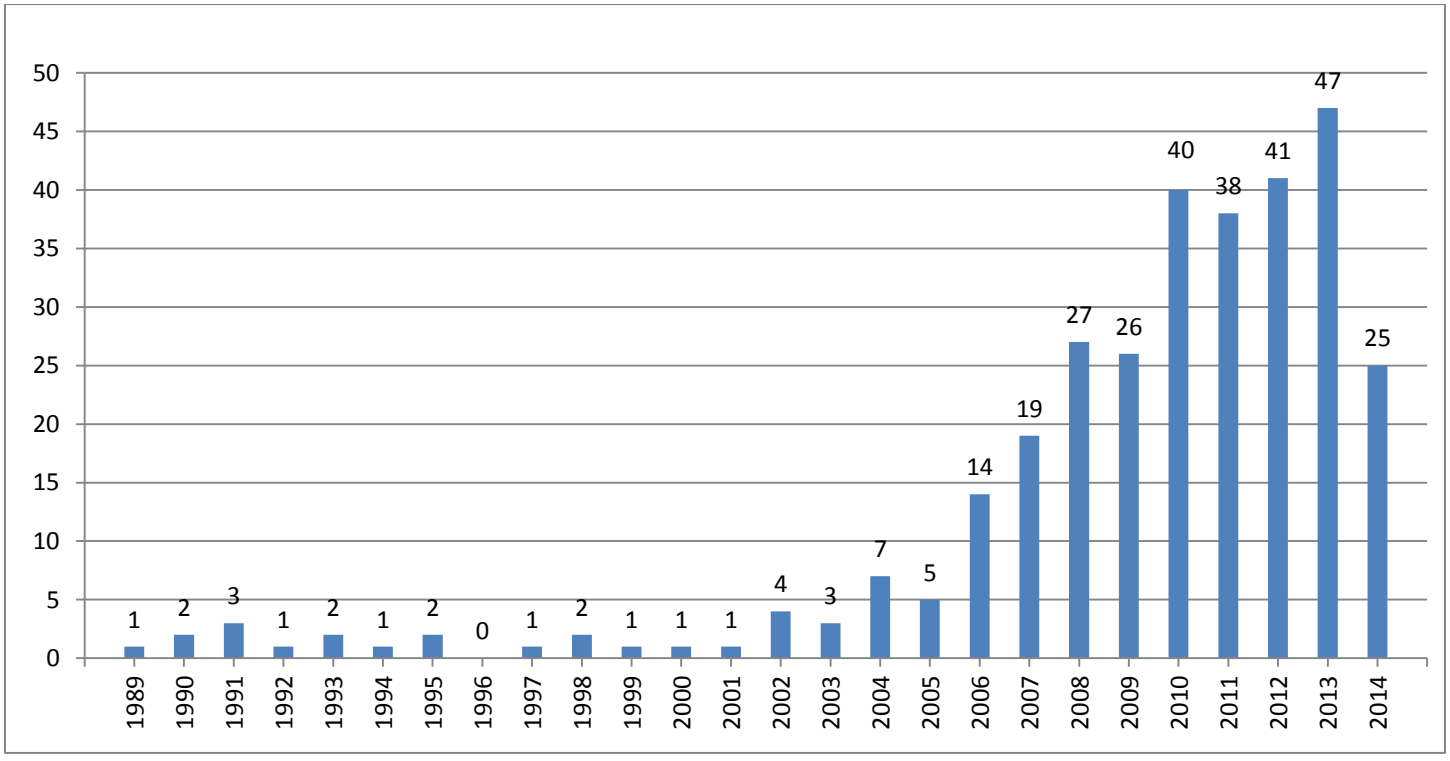
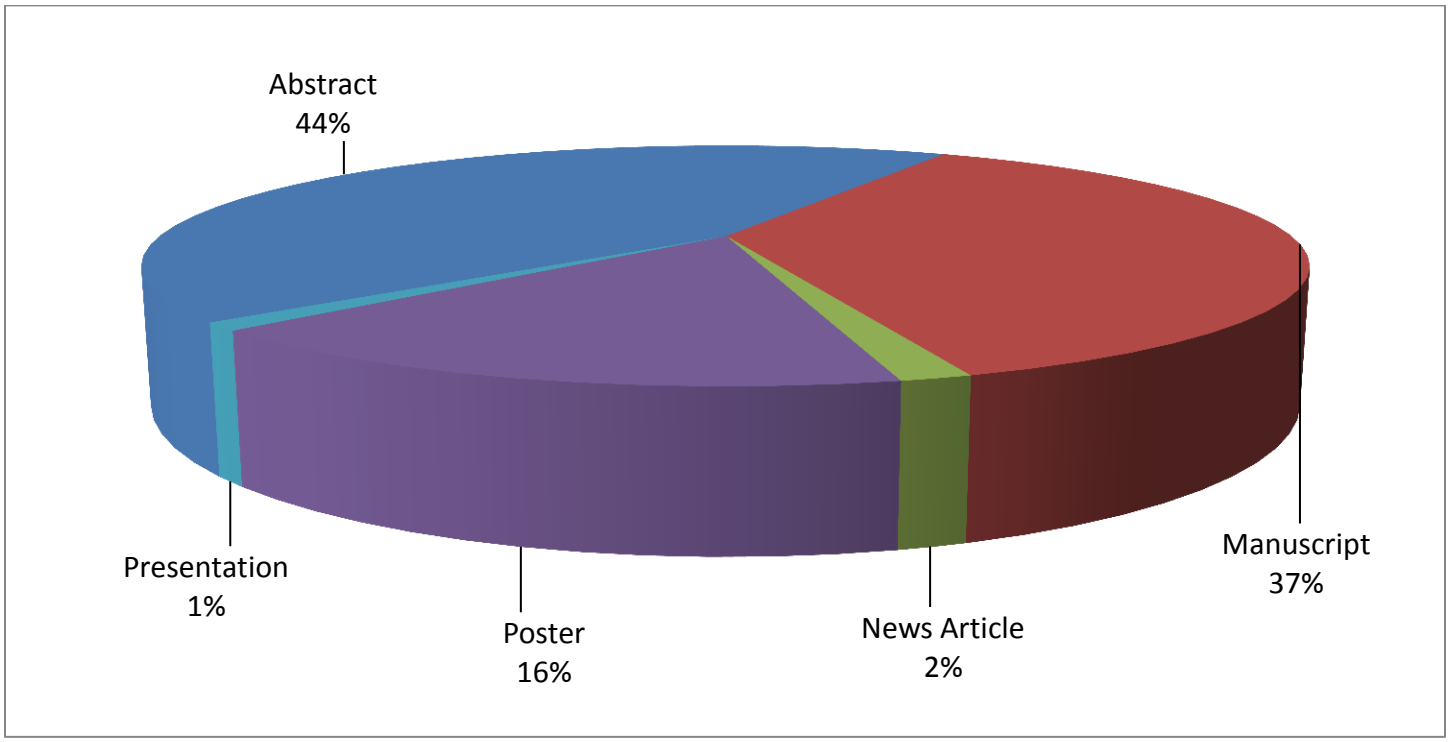


Figure 5: Types of Publications Reviewed by the AMPATH Publications Committee in 2014 (Total Reviewed = 79)



AMPATH Research Bibliography

The following bibliography includes AMPATH research publications that were published between January and June 2014. 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.

1. Atwoli, L., D. Ayuku, J. Hogan, J. Koech, R.C. Vreeman, S. Ayaya, and P. Braitstein, *Impact of domestic care environment on trauma and posttraumatic stress disorder among orphans in western Kenya.* PLoS ONE [Electronic Resource], 2014. **9**(3): p. e89937.
2. Atwoli, L., M.K. Nock, D.R. Williams, and D.J. Stein, *Association between parental psychopathology and suicidal behavior among adult offspring: results from the cross-sectional South African Stress and Health survey.* BMC psychiatry, 2014. **14**: p. 65.
3. Bloomfield, G., J. Hogan, A. Keter, T. Holland, E. Sang, S. Kimaiyo, and E. Velazquez, *Blood pressure level impacts risk of death among HIV seropositive adults in Kenya: a retrospective analysis of electronic health records.* BMC infectious diseases, 2014. **14**(1): p. 284.
4. Bloomfield, G.S., P. Khazanie, A. Morris, C. Rabadán-Diehl, L.A. Benjamin, D. Murdoch, V.S. Radcliff, E.J. Velazquez, and C. Hicks, *HIV and Noncommunicable Cardiovascular and Pulmonary Diseases in Low- and Middle-Income Countries in the ART Era: What We Know and Best Directions for Future Research.* JAIDS Journal of Acquired Immune Deficiency Syndromes, 2014. **67**: p. S40-S53 10.1097/QAI.0000000000000257.
5. Bloomfield, G.S., R. Vedanthan, L. Vasudevan, A. Kithei, M. Were, and E.J. Velazquez, *Mobile health for non-communicable diseases in Sub-Saharan Africa: a systematic review of the literature and strategic framework for research.* Globalization and health, 2014. **10**: p. 49.
6. Ciaranello, A., Z. Lu, S. Ayaya, E. Losina, B. Musick, R. Vreeman, K.A. Freedberg, E.J. Abrams, L. Dillabaugh, K. Doherty, J. Ssali, C.T. Yiannoutsos, and K. Wools-Kaloustian, *Incidence of World Health Organization Stage 3 and 4 Events, Tuberculosis and Mortality in Untreated, HIV-infected Children Enrolling in Care Before 1 Year of Age: An IeDEA (International Epidemiologic Databases To Evaluate AIDS) East Africa Regional Analysis.* The Pediatric infectious disease journal, 2014. **33**(6): p. 623-9.
7. Embleton, L., D. Ayuku, A. Kamanda, L. Atwoli, S. Ayaya, R. Vreeman, W. Nyandiko, P. Gisore, J. Koech, and P. Braitstein, *Models of care for orphaned and separated children and upholding children's rights: cross-sectional evidence from western Kenya.* BMC international health and human rights, 2014. **14**: p. 9.
8. Inui, T., R. Frankel, and S. Kimaiyo, *Leadership and Management in Two Different Cultures: "It's not what you say..."*, in *Wisdom Leadership in Academic Health Science Centers Leading a Positive Change*, M. Plews-Ogan and G. Beyt, Editors. 2014, Radcliffe Publishing Ltd: London, New York. p. 3-6.
9. Kipkore, W., B. Wanjohi, H. Rono, and G. Kigen, *A study of the medicinal plants used by the Marakwet Community in Kenya.* Journal of ethnobiology and ethnomedicine, 2014. **10**: p. 24.
10. Knopf, A., K. Agot, J. Sidle, V. Naanyu, and M. Morris, *"This is the medicine:" A Kenyan community responds to a sexual concurrency reduction intervention.* Social science & medicine, 2014. **108**(0): p. 175-184.
11. Lagat, D.K., A.K. DeLong, G.A. Wellenius, E.J. Carter, G.S. Bloomfield, E.J. Velazquez, J. Hogan, S. Kimaiyo, and C.B. Sherman, *Factors Associated With Isolated Right Heart Failure in Women: A Pilot Study From Western Kenya.* Global Heart, 2014. **9**(2): p. 249-254.
12. Meslin, E.M., D. Ayuku, and E. Were, *"Because It Was Hard …": Some Lessons Developing a Joint IRB Between Moi University (Kenya) and Indiana University (USA).* The American Journal of Bioethics, 2014. **14**(5): p. 17-19.

13. Mostert, S., F. Njuguna, S.C. Langat, A.J. Slot, J. Skiles, M.N. Sitaresmi, P.M. van de Ven, J. Musimbi, R.C. Vreeman, and G.J. Kaspers, *Two overlooked contributors to abandonment of childhood cancer treatment in Kenya: parents' social network and experiences with hospital retention policies.* Psycho-oncology, 2014. **23**(6): p. 700-7.
14. Nichols, J., L. Embleton, A. Mwangi, G. Morantz, R. Vreeman, S. Ayaya, D. Ayuku, and P. Braitstein, *Physical and sexual abuse in orphaned compared to non-orphaned children in sub-Saharan Africa: a systematic review and meta-analysis.* Child Abuse & Neglect, 2014. **38**(2): p. 304-16.
15. Njuguna, F., S. Mostert, A. Slot, S. Langat, J. Skiles, M.N. Sitaresmi, P.M. van de Ven, J. Musimbi, H. Muliro, R.C. Vreeman, and G.J. Kaspers, *Abandonment of childhood cancer treatment in Western Kenya.* Archives of disease in childhood, 2014.
16. Nyandiko, W., R. Vreeman, A. Mwangi, S. Ayaya, P. Kiptoon, B. Musick, P. Braitstein, J.M. Abuya, J. Koech, and J. Hogan, *Survival and Loss to Follow Up Among HIV and Tuberculosis Co-Infected Children Below 3 Years of Age Initiating Anti-Tuberculosis Treatment in Western Kenya.* International Journal of Advanced Research, 2014. **2**(8): p. 249-262.
17. Paton, N.I., C. Kityo, A. Hoppe, A. Reid, A. Kambugu, A. Lugemwa, J.J. van Oosterhout, M. Kiconco, A. Siika, R. Mwebaze, M. Abwola, G. Abongomera, A. Mweemba, H. Alima, D. Atwongyeire, R. Nyirenda, J. Boles, J. Thompson, D. Tumukunde, E. Chidziva, I. Mambule, J.R. Arribas, P.J. Easterbrook, J. Hakim, A.S. Walker, and P. Mugyenyi, *Assessment of Second-Line Antiretroviral Regimens for HIV Therapy in Africa.* The New England journal of medicine, 2014. **371**(3): p. 234-47.
18. Sorber, R., S. Winston, J. Koech, D. Ayuku, L. Hu, J. Hogan, and P. Braitstein, *Social and economic characteristics of street youth by gender and level of street involvement in eldoret, kenya.* PLoS ONE [Electronic Resource], 2014. **9**(5): p. e97587.
19. Stone, G.S., T. Tarus, M. Shikanga, B. Biwott, T. Ngetich, T. Andale, B. Cheriro, and W. Aruasa, *The association between insurance status and in-hospital mortality on the public medical wards of a Kenyan referral hospital.* Global health action, 2014. **7**.
20. Vedanthan, R., J.H. Kamano, C.R. Horowitz, D. Ascheim, E.J. Velazquez, S. Kimaiyo, and V. Fuster, *Nurse management of hypertension in rural Western kenya: implementation research to optimize delivery.* Annals of global health, 2014. **80**(1): p. 5-12.
21. Vedanthan, R., J.H. Kamano, V. Naanyu, A.K. Delong, M.C. Were, E.A. Finkelstein, D. Menya, C.O. Akwanalo, G.S. Bloomfield, C.A. Binanay, E.J. Velazquez, J.W. Hogan, C.R. Horowitz, T.S. Inui, S. Kimaiyo, and V. Fuster, *Optimizing linkage and retention to hypertension care in rural Kenya (LARK hypertension study): study protocol for a randomized controlled trial.* Trials, 2014. **15**(1): p. 143.
22. Vreeman, R., W. Nyandiko, E. Liechty, N. Busakhala, I. Bartelink, R. Savic, M. Scanlon, S. Ayaya, and T. Blaschke, *Impact of Adherence and Anthropometric Characteristics on Nevirapine Pharmacokinetics and Exposure among HIV-Infected Kenyan Children.* Journal of acquired immune deficiency syndromes, 2014.
23. Vreeman, R.C., M.L. Scanlon, A. Mwangi, M. Turissini, S.O. Ayaya, C. Tenge, and W.M. Nyandiko, *A Cross-Sectional Study of Disclosure of HIV Status to Children and Adolescents in Western Kenya.* PLoS ONE [Electronic Resource], 2014. **9**(1): p. e86616.
24. Wachira, J., S. Middlestadt, M. Reece, C.-Y.J. Peng, and P. Braitstein, *Physician communication behaviors from the perspective of adult HIV patients in Kenya.* International Journal for Quality in Health Care, 2014.
25. Were, E.O., R. Heffron, N.R. Mugo, C. Celum, A. Mujugira, E.A. Bukusi, J.M. Baeten, and f.t.P.P.S. Team, *Pre-exposure prophylaxis does not affect the fertility of HIV-1-uninfected men.* AIDS, 2014. **28**(13): p. 1977-1982 10.1097/QAD.0000000000000313.

Index

E

F

G

H

I

J

K

L

M

N

O

P

R

S

T

U

V

W

Y

Z