

Summary of FACES-Affiliated Studies in Kenya

Lost to Follow-up from Care in HIV Positive Adolescents in Kisumu, Kenya

Adolescents represent 60% of all new HIV infections in sub-Saharan Africa. However, a significant proportion of HIV+ adolescents become lost to follow-up (LTFU), placing them at increased risk for HIV-related morbidity and mortality. Research has suggested that the school environment, specifically school-based stigma, discrimination, and disclosure, may play an important role in uptake and retention in HIV care by adolescents. Our multi-disciplinary collaborative group, based at KEMRI and at UCSF, will employ qualitative methods to explore: (1) the multi-level determinants why adolescents become LTFU in Kisumu, Kenya and (2) the role the secondary school environment plays among HIV+ adolescents who are LTFU. We will conduct: (1) focus groups with HIV+ adolescent peer educators who work with LTFU adolescents and are in care, (2) semi-structured interviews with HIV+ adolescents who are LTFU, and (3) semi-structured interviews with student-nominated teachers and administrators from local secondary schools. The purpose of these interviews and focus groups will be to better understand the barriers adolescents have in accessing HIV care and how the school environment may affect adolescents' ability to positively or negatively access and remain in care. Information regarding the multi-level determinants of LTFU among adolescents and specifically of the school-based environment will inform the development of interventions to improve the retention of East African adolescent in healthcare. This study is funded through the Reproductive Infectious Disease fellowship at UCSF.

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ART treatment effects on HIV-associated neurocognitive impairment

Combination ART is the most effective treatment for HIV-associated neurocognitive disorder (HAND) to date and some studies have suggested that ART with higher penetration into the central nervous system (CNS) leads to improved neurologic outcomes. However, these studies have important limitations and thus there is insufficient evidence to recommend ART with high CNS penetration effectiveness (CPE) for the treatment of HAND. The objective of this application is to determine whether it is important to treat HIV-infected individuals with neurocognitive disorders with ART with high CPE. Because of limited ART choices in Kenya, we will be able to directly compare the effects of specific ART regimens thus avoiding the limitations of prior studies. The central hypothesis is that, among individuals with HAND, ART with high CPE leads to improved neurologic outcomes as compared to ART with low CPE. We will enroll a prospective observational cohort of 200 HIV-infected ART-naïve adults with HIV-associated cognitive impairment. This study is funded by a K01 through the Fogarty International Center of the National Institutes of Health.

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Practice Effects on Neuropsychological Tests

One important confounder of observational and clinical trials assessing effects of treatments on HIV-associated neurocognitive disorders is the practice effect, or improvement on tests due to practice alone. We will recruit 100 individuals, previously studied, and repeat neuropsychological testing. This study is funded by a K01 through the Fogarty International Center of the National Institutes of Health.

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Treatment of Early Cryptococcal Infection

In sub-Saharan Africa and southeast Asia, invasive cryptococcal disease is the second most common life-threatening HIV-associated opportunistic infection after tuberculosis and is responsible for up to 20% of deaths. Since invasive cryptococcal disease primarily affects HIV-infected individuals with advanced immunosuppression, one potential strategy to detect early cryptococcal infection in resource-limited settings is to screen asymptomatic individuals with advanced HIV-related immunosuppression for serum cryptococcal antigen (CrAg) as they enter outpatient HIV care and treatment programs. Preliminary

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evidence suggests that fluconazole monotherapy is not an effective treatment in a heterogeneous population of individuals with early cryptococcal infection. This phase IIb clinical trial is designed to provide a screening evaluation for the hypothesis that combination therapy with fluconazole and flucytosine improves survival as compared to fluconazole alone for the treatment of early cryptococcal infection in HIV-infected individuals with advanced immunosuppression. This study is funded through an R21 through the National Institute of Neurological Disorders and Stroke and Fogarty International Center through the National Institutes of Health.

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Improving Uptake of Early Infant Diagnosis of HIV for PMTCT: A Randomized Trial of a Text Messaging Intervention

There is little information on evidence-based interventions that specifically target improved attendance of postpartum clinic visits and subsequent infant HIV testing in the context of prevention of mother-to-child transmission of HIV (PMTCT) programs. This study is examining, in a randomized controlled trial, the effect of text messages sent to women enrolled in PMTCT programs on improving adherence to postpartum clinic visits and uptake of early infant diagnosis by DNA polymerase chain reaction (PCR). Findings from this study will provide randomized trial evidence to inform HIV prevention program planners and implementers. This study will also provide further information on the feasibility of using mobile phone-based technology for public health interventions in resource-limited settings. It is funded by the National Institutes of Health through the Fogarty International Clinical Research Fellowship Program at Vanderbilt University.

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Acceptability, Feasibility and Efficacy of Vaginal Insemination for Conception in HIV Discordant Couples Desiring Pregnancy in Kenya

This study will evaluate the acceptability, feasibility and efficacy of vaginal insemination with semen for conception among HIV discordant relationships (female positive ♀+, male negative ♂-) in Kenya. Couples desiring pregnancy will receive targeted reproductive counseling for six months. Consistent condom use will be emphasized and couples will be taught assisted vaginal insemination for conception. It is hoped that the findings of this study will provide evidence to support the routine use of vaginal insemination as a safe method of conception in (♀+/♂-) HIV discordant couples desiring children. This study is of significant public health importance because the use of vaginal insemination for conception in ♀+/♂- HIV discordant couples is expected to reduce the likelihood of riskier sexual practices for childbearing and decrease the incidence of HIV in sub-Saharan Africa. This study is funded by a RAP pilot award from the UCSF-GIVI Center for AIDS Research.

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Pilot agricultural intervention for food security and HIV health outcomes in Kenya

Food insecurity contributes to increased HIV transmission risk and higher HIV-related morbidity and mortality. This pilot study will test the hypothesis that a multi-sectoral agricultural intervention will prevent HAART treatment failure, reduce co-morbidities, and decrease secondary HIV transmission risk. One hundred and twenty HIV-infected farmers on HAART in Western Kenya (60 at an intervention clinic and 60 at a control clinic) will be enrolled and followed for 1 year. This intervention will include: a) human-powered water pumps and other required farm commodities, b) microfinance loans (~\$75) to purchase the pump and agricultural implements, and c) education in sustainable farming practices. The impacts of the intervention on mediating factors (food security and economic indicators) will be examined, and pathways for how improvements in these mediating factors impact health outcomes will be explored. The ultimate goal of this work is to contribute to sustainable solutions to tackle the

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intersecting challenges of food insecurity, poverty, and HIV/AIDS in sub-Saharan Africa. This study is funded by a National Institutes of Health/National Institute of Mental Health R34 grant.

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Identifying Opportunities for HIV Prevention among Female Migrants in Kenya

This study aims to assess the degree to which women's participation in migration in Southern and East Africa contributes to HIV/AIDS in the regions. It also seeks to characterize features of the contexts of African women's migration experiences- and the behavioral and mental health consequences of migration- that place female migrants at particularly high risk of HIV infection and transmission. This study is comprised of two distinct phases: a secondary data analysis using population-based survey and HIV serological data from Southern and East Africa, and an in-depth qualitative study in Kenya. The ultimate goal of this research is to reduce HIV transmission risks via a multi-level HIV prevention intervention with female migrants in western Kenya. This study is funded by an National Institutes of Health K01 mentored research scientist development award.

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Integration of HIV Care and Treatment into Maternal and Child Health

This study is being carried out to determine the most effective way to reach and provide pregnant women with accessible, comprehensive, and high quality HIV care and treatment. It is taking place in Migori District, Kenya with implications for other sites in Kenya and sub-Saharan Africa. This study utilizes a prospective cluster randomized design. Twelve clinics similar in size, population, and services in Migori District, Kenya that provide antenatal care have been randomly assigned to either receive "integrated antenatal care, Prevention of Mother-to Child Transmission & HIV services" (intervention arm) or "non-integrated services" (control arm). This study is funded by the U.S. Centers for Disease Control and Prevention (CDC) as a Public Health Evaluation.

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Integration of Family Planning Services into HIV Care and Treatment

This study is being conducted to determine how to best meet the family planning needs of HIV-infected women in Kenya. It is a cluster-randomized trial comparing the effects of integrating family planning services into HIV care and treatment programs in Nyanza Province, Kenya, with the standard referral for family planning services outside of HIV care and treatment programs. The study is specifically looking at contraceptive uptake, contraceptive continuation, and unintended pregnancy rates. This study is funded by the Tides and Gates Foundations.

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HIV/AIDS Stigma and Use of Services by Pregnant Women

This study is examining the effects of different types of HIV/AIDS stigma on use of maternity services and HIV services by pregnant women in Kenya. This is a prospective study among pregnant women using antenatal care clinics in Migori and Rongo Districts of Nyanza Province. It involves structured interviews using PDAs and collection of data from medical records, as well as qualitative in-depth interviews. This study is funded by the U.S. National Institute of Mental Health.

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Cervical Cancer Screening and Treatment in HIV-infected Women in Kenya

Cervical cancer and HIV are intersecting epidemics that both disproportionately affect low-income women. The impact of the socioeconomic disparity and biologic synergy of these two diseases is seen dramatically in Kenya, where cervical cancer is the most common cancer killer. Two potentially low-cost

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and effective cervical cancer screening methods are currently being tested: visual inspection with acetic acid (VIA) and protein biomarkers expressed in the presence of cervical dysplasia. Additionally, the potential impact of the presence, diagnosis and treatment of HPV-related dysplasia on HIV genital shedding (a major risk factor for HIV transmission) is being studied. This research is funded by the National Institutes of Health through the UCSF-GIVI Center for AIDS Research and UCSF Clinical and Translational Science Institute.

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Effect of HAART on Surgically Treated HGCIN in HIV-infected Women

This study is being carried out to assess the effect of Highly Active Antiretroviral Therapy (HAART) on the recurrence of surgically treated High-Grade Cervical Intraepithelial Neoplasia (HGCIN) in HIV-infected women in Kenya. This is a prospective cohort study of HIV-infected women receiving care in the city of Kisumu. Women with HGCIN are being followed for two years after their initial surgical excision to determine the effect of HAART on the recurrence of HGCIN after surgical excision. This study is funded through UCSF discretionary funds, including private donations.

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Application of weighted time-series to address bias in evaluation of clinic- and community-level research

The study is using a simulation to develop, test, and apply new analytic methods (weighted time-series) for evaluation the effectiveness of community- and clinic-level interventions. It will then compare results using weighted time-series and conventional methods within the context of a clinic-level intervention, namely at FACES-supported clinics in Kenya. The results of this study will be used to seek funding to test the broader application of these methods in both community- and clinic-level interventions. Application of these methods has the potential to improve evaluation of many community-level interventions, particularly in settings where it is difficult to obtain individual-level information or to follow individuals in the community over time (e.g. rural or other hard to reach populations). The study is funded through UCSF Center for AIDS Prevention Studies (CAPS) Innovative Grants.

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Prevention of Tuberculosis in HIV-Infected Children

This study is being carried out in Kenya to evaluate the effectiveness of Isoniazid Preventive Therapy (IPT) in HIV-infected children to reduce TB incidence, morbidity and mortality. The hypothesis is that IPT will effectively reduce TB and overall morbidity and mortality in the study population. If this should occur, the Kenya National Leprosy and Tuberculosis Program can consider national guidelines for IPT in children. This study is funded through UCSF discretionary funds, including private donations.

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International Epidemiologic Databases to Evaluate AIDS (IeDEA)

IeDEA is striving to build regional population-based HIV knowledge and information. IeDEA is pooling data from collaborating provider and research networks in East Africa to cost-effectively generate large data sets to address high priority research questions. Data collection, merging, storage, and sharing across sites in the East African Region, is focusing on:

- cost-effectiveness of HIV care, treatment, and prevention strategies;
- appropriate guidelines for initiation of first-line therapy for treatment of HIV/AIDS;
- genetic variability of HIV;
- issues related to first-line therapy failure;
- adherence to HIV treatment;

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- contextual issues and resource limitations of HIV care delivery in resource-limited settings;
- impact of tuberculosis infection on HIV/AIDS care and treatment in developing world;
- prevention of mother-to-child transmission of HIV

This study is supported by NIH through Indiana University.

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Engagement in Care among HIV-Infected Patients in Resource-Limited Settings

This study assesses the magnitude of and reasons for failure to engage in care among HIV-infected patients in the East Africa International Epidemiologic Databases to Evaluate AIDS (IeDEA) Consortium. This study aims to optimize the validity of a sampling-based approach to estimating failure to retain in care and failure to initiate ART in diverse settings. This study will also use the sampling-based approach to estimate the fraction of ART-eligible patients who fail to initiate, and the fraction of patients on ART who fail to be retained in care in 11 diverse clinics in the East Africa IeDEA consortium. This study is funded by a supplement from IeDEA as well as funds from the UCSF Center for AIDS Research (CFAR).

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Fertility Desires and Family Planning among HIV-Infected Couples

This study is exploring decision-making and relationship power around fertility and family planning among HIV-affected couples and community leaders in Nyanza Province, Kenya. This is a qualitative, hypothesis-generating research project which involves in-depth, open-ended interviews with couples who present to HIV clinics for care, couples from high prevalence HIV communities, and individual community leaders. The study is funded by the Hellman Foundation and by the Center for AIDS Research at UCSF.

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Formative Research for Intervention of HIV/AIDS Service Providers on Gender-Based Violence

Preliminary data from pregnant women in rural Kenya indicate that fear of violence from a male partner is an important reason why some women refuse HIV testing, and that pregnant women who test HIV-positive or refuse testing may be more likely to be victims of violence. In response to these findings, an intervention on gender-based violence (GBV) for health workers who provide HIV-related services to pregnant women in this setting is being developed. In order to first gain in-depth contextual understanding of GBV, focus groups and in-depth interviews were conducted with pregnant women, men, and a variety of service providers (health, law enforcement, education, women's groups, and village leadership) in rural Nyanza Province, Kenya. The knowledge gained through this formative research was used to develop a GBV intervention for health workers, taking advantage of existing Kenyan GBV training programs. Subsequently, a preliminary pilot of the adapted intervention was carried out to assess feasibility and acceptability. The results of this pilot study will form the basis for future research on a larger scale to examine the impact of addressing GBV on prevention of HIV/AIDS. This pilot study was funded by the UCSF-GIVI Center for AIDS Research. Funding is currently being sought to scale up and test this intervention.

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FACES Study Partner for Patients in Need of HIV Care and Treatment Referral and Services

(PrEP) Parallel Comparison of Tenofovir and Emtricitabine/tenofovir Pre-Exposure Prophylaxis to Prevent HIV-1 Acquisition within HIV-1 Discordant Couples

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This study addresses the need for novel strategies to prevent HIV-transmission within discordant couples. UCSF-KEMRI is one of nine sites in this multi-site trial that is funded by the Gates Foundation and coordinated by the University of Washington. UCSF-KEMRI maintains one site in Kisumu, Kenya. This study is a double-blind, placebo-controlled, phase III clinical trial to assess the safety and efficacy of taking once-daily pre-exposure prophylaxis (PrEP) for the prevention of HIV infection, using the antiretroviral medication tenofovir (TDF), either alone or in combination with emtricitabine (FTC/TDF). This study hypothesizes that PrEP will decrease HIV-1 acquisition among HIV-uninfected individuals within HIV discordant couples, if found to be safe and efficacious.

This study enrolled 4,758 HIV discordant couples across the nine sites in Kenya and Uganda. Enrollment started in July 2008 and ended in November 2010; some study participants remain in follow up. The HIV-1 infected partners were randomly assigned to one of three study arms: 1) TDF, 2) FTC/TDF, or 3) placebo. All study participants received a comprehensive package of HIV prevention services, which included intensive safer sex counseling (both individually and as a couple), HIV testing, free condoms, testing and treatment for sexually transmitted infections, and monitoring and care for HIV infection.

By 31 May 2011, a total of 78 HIV infections occurred in the study: 18 among those assigned TDF, 13 among those assigned FTC/TDF, and 47 among those assigned placebo. Thus, those who received TDF had an average of 62% fewer HIV infections (95% CI 34 to 78, $p=0.0003$) and those who received FTC/TDF had 73% fewer HIV infections (95% CI 49 to 85, $p<0.0001$) than those who received placebo. PrEP, both TDF and FTC/TDF, reduced HIV risk in women and men. PrEP was also found to be safe: the rate of serious medical events was similar for those assigned to TDF, FTC/TDF, and placebo. Due to these exciting findings study participants originally in the placebo arm will now be re-enrolled and able to receive one of the two intervention arms. The study will continue; it is important to determine if safety or HIV prevention effects are sufficiently different for TDF versus FTC/TDF to warrant one or the other being widely implemented for HIV prevention.

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