MU-UCSF-LSHTM YOUNG INVESTIGATOR RESEARCH SYMPOSIUM

Tororo, Uganda

THURSDAY, SEPTEMBER 29, 2011

Dear Colleagues,

Welcome to the second annual MU-UCSF-LSHTM Young Investigator Research Conference. The purpose of this conference is to provide a forum for young investigators to present and discuss ongoing research in our collaboration. As a part of our broader East Africa collaboration, it is also a forum for us to host and share our research with our colleagues in the FACES Program in Kenya.

Our research collaboration focuses on epidemiology, biology, and treatment of malaria, HIV and TB. To date, the scientists of the MU-UCSF Research Collaboration have led 17 clinical trials of infectious diseases involving over 7,500 participants. The scientific leadership of the collaboration currently consists of Ugandan and US Principal Investigators with expertise in HIV, malaria and TB; extensive experience in clinical and translational research, and a track record of developing and overseeing rigorously conducted trials in Uganda. The MU-UCSF Research Collaboration conducts clinical trials and laboratory research in Kampala, Tororo, and Mbarara and has surveillance programs and cohort studies throughout Uganda at government health facilities. The collaboration has also sought advice and worked with the Ugandan Ministry of Health and a variety of Ugandan country partners to ensure research programs are harmonized with local priorities. The MU-UCSF Research Collaboration has had investigator participation in over 150 publications since its inception in 1998, many which were first-author papers by trainees. In addition, the MU-UCSF Research Collaboration has trained 31 Ugandan researchers in degree accredited programs at UCSF, MU, UC Berkeley and the London School of Hygiene and Tropical Medicine.

Our research collaboration is committed to capacity building of young investigators. This year we have established two new research awards, the New Investigator Award and the Distinguished Scholar Award, which will be presented at this conference. The New Investigator Abstract Award acknowledges excellence in research designed and conducted by young scientists. The Distinguished Scholar Abstract Award recognizes the top ranking abstract of the meeting.

We look forward to a successful and stimulating conference.

Moses R. Kamya, MD, Ph.D
Professor and Chair
Dept. of Medicine
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Diane Havlir, MD
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MU-UCSF-LSHTM YOUNG INVESTIGATOR RESEARCH SYMPOSIUM THURSDAY, SEPTEMBER 29th 2011

WELCOME AND INTRODUCTION **09:00 – 09:15hrs**
Moses R. Kamya, MD, Ph.D.

SESSION 1: HIV AND TUBERCULOSIS **09:15 – 11:00hrs**
CHAIRS: Jane Achan, MD, Ph.D, Diane Havlir, MD

09:15hrs 1. Implementation of a Rapid, Multi-disease Community Health Campaign offering Diagnostic, Preventive, Treatment and Referral services in rural Uganda. ***Gabriel Chamie,*** *Dalsone Kwarisiima, Tamara Clark, Vivek Jain, Jane Kabami, Elvin Geng, Moses Kamya, Diane Havlir, Edwin Charlebois*

09:30hrs 2. Self-Disclosure of HIV Test Results: Results from a Randomized Controlled Trial of Home-Based versus TB Clinic-Based HIV Voluntary Counseling and Testing for Family and Household Members of TB Evaluation Patients in Uganda. ***Wandera B,*** *Talemwa N, Babirye E, Nabwegyako J, Okwera A,Plenty A, Mugerwa R, Charlebois*

09:45hrs 3. HIV-infected African girls have lower plasma HIV RNA levels and higher CD4 percentages compared to boys. ***Theodore D. Ruel****, Brian C. Zanoni , Isaac Ssewanyana, Huyen Cao, Diane V. Havlir, Moses Kamya, Jane Achan, Edwin D. Charlebois, Margaret E. Feeney*

10:00hrs *4.* Impact of automated nucleic acid amplification testing on tuberculosis management and outcomes in Uganda. ***Winceslaus Katagira****, Adithya Cattamanchi, William Worodria, Saskia den Boon, Nelson Kalema, Sylvia Kaswabuli, Cecily Miller, Alfred Andama, Heidi Albert, Pamela Nabeta, Christen Grey, Irene Ayakaka, Laurence Huang, J. Lucian Davis*

10:15hrs *5.* Gender disparities in TB suspect evaluation and treatment in rural Uganda. ***Priscilla Haguma****, Cecily Rose Miller, J. Lucian Davis, Achilles Katamba, Asadu Sserwanga, Stella Kakeeto, Fred Kizito, Adithya Cattamanchi*

10:30hrs 6. Mother to child transmission prior to revised Kenyan PMTCT guidelines: A retrospective review of PMTCT implementation in rural Kenya. *Lisa Dillabaugh, Khady Diouf, Valerie Ndege,* ***Patrick Oyaro****, Elizabeth Bukusi, Craig Cohen*

10:45hrs ***7.*** Social exchange theory explains sexual concurrency among women married to fishermen along Lake Victoria, Kenya. ***Zachary Kwena****, Chris Shisanya, Isaac Mwanzo, Solomon Majiwa, Lilian Achiro, Elizabeth Bukusi*

11:00 – 11:15hrs
BREAK FOR TEA

SESSION 2: MALARIA SURVEILLANCE AND PATHOGENESIS **11:15 – 13:00hrs**
CHAIRS: Philip Rosenthal, MD, Adoke Yeka, MD

11:15hrs 1. Malaria-related morbidity and mortality among hospitalized children in regions of varying malaria transmission intensity in Uganda. ***Arthur Mpimbaza,*** *Anne Gasasira, Asadu Sserwanga, Sussann Nasr, Scott Filler, Moses Kamya, Sarah Staedke, Grant Dorsey*

11:30hrs 2. A programmatic evaluation of sulfadoxine-pyrimethamine for the prevention of placental malaria in Uganda. ***Arinaitwe E****, Ades V, Walakira A, Ninsiima B, Muggaga O, Kamya M, Nasr S, Filler S, Dorsey G*

11:45hrs 3. District-based household survey data and associated biomarkers in indoor residual spraying (IRS) and non-IRS districts in Northern Uganda. ***Adoke Yeka****, Ruth Kigozi, Laura Steinhardt, Susie Nasr, Denis Rubahika, Asadu Sserwanga, Moses Kiggundu, Humphrey Wanzira, Geoff Lavoy, Scott Filler, Grant*

Dorsey, Moses Kamya

12:00hrs ***4.*** Impact of indoor residual spraying on morbidity trends in Apac district. *Anne Gasasira,* ***Ruth Kigozi****, Sanjiv M. Baxi, Asadu Sserwanga, Stella Kakeeto, Sussann Nasr, Moses R. Kamya, Scott Filler, Grant Dorsey*

12:15hrs ***5.*** The T cell response to Pre-erythrocytic and Erythrocytic Stage Malaria Antigens. ***Felistas Nankya,*** *Prasanna Jagannathan, Marco Morelli, Ijeoma Eccles-James, Katherine Bowen, Muhindo Mary K, Emmanuel Osilo, Patrick Tumwebaze, Samuel Wamala, Charles Ebusu, Jessica Briggs, Jane Achan, Grant Dorsey, Margaret Feeney*

12:30hrs 6. Ex vivo drug sensitivity of malaria parasites under selective pressure. ***Patrick Tumwebaze****, Oswald Byaruhanga, Amethyst Gillis, Hannah Yemane, Roland A. Cooper, Samuel L. Nsobya, Philip J. Rosenthal*

13:00 – 14:00hrs
BREAK FOR LUNCH

SESSION 3: NUTRITION **14:00 – 15:15hrs**
CHAIRS: Emmanuel Arinaitwe, MD, Deb Cohan, MD

14:00hrs 1. Maternal nutritional status predicts adverse obstetric & fetal outcomes among HIV-infected rural Ugandan women receiving combination ART. ***Julia Mwesigwa****, Sera Young, Katherine Murray, Paul Natureeba, Beth Osterbauer, Jane Achan, Emmanuel Arinaitwe, Tamara Clark, Veronica Ades, Edwin Charlebois, Theodore Ruel, Moses Kamya, Diane Havlir, Deborah Cohan*

14:15hrs 2. HIV-infected Ugandan children suffer high rates of malnutrition and minimal recovery following the initiation of antiretroviral therapy. *Achan J,* ***Ikilezi G****, Kakuru A, Young S, Havlir D, Kamya M, Charlebois E, Ruel T*

14:30hrs 3. Cross-sectional study of risk factors for malnutrition, anemia, and parasitemia among HIV-exposed and –unexposed infants enrolled in the PROMOTE- chemoprevention trial. ***Osterbauer B,*** *Kapisi J, Bigira V, Kamya M, Dorsey G*

14:45hrs ***4.*** The association between malnutrition and the incidence of malaria among young HIV-infected and HIV-uninfected Ugandan children: a prospective cohort study. ***Emma Osilo****, Victor Bigira, Mary Muhindo, Abel Kakuru, Humphrey Wanzira, Moses Kamya, Grant Dorsey, Emmanuel Arinaitwe*

15:00hrs ***5.*** Nutritional Behaviors, Perceived Needs and Acceptability of Micronutrient and Macronutrient Supplementary Foods Among Pregnant and Lactating HIV-Infected Women: Preliminary Findings from the Formative Nutrition Study. ***Flavia Luwedde****, Barnabas Natamba, Grace Akello, Wilfred Olwortho, Julia Mwesigwa, Beth Osterbauer, Albert Plenty, Deborah Cohan, Diane Havlir, Jane Achan, Sera Young*

15:15 – 15:30hrs
BREAK FOR TEA

SESSION 4: MALARIA TREATMENT & CARE DELIVERY **15:30 – 17:00hrs**
CHAIRS: Grant Dorsey, MD, Ph.D, Moses Kamya, MD, Ph.D

15:30hrs 1. The ACT PRIME Study: Evaluating the impact of enhanced health facility-based care for malaria and febrile illnesses in children in Tororo, Uganda: Preliminary Findings. ***Catherine Maiteki-Sebuguzi,*** *Florence Nankya, Samuel Gonahasa, Fred Mudangha, Deborah DiLiberto, Sarah Staedke*

15:45hrs 2. ACT PROCESS Study: Evaluating the process, context, and impact of the PRIME Study: preliminary results. ***Susan Nayiga****, Clare Chandler, Lilian Taaka, Christine Nabirye, Deborah DiLiberto, Sarah Staedke*

16:00hrs 3. Association between trimethoprim-sulfamethoxazole and plasmodium falciparum gametocytemia in a cohort of Ugandan children. ***Abel Kakuru****, Prasanna Jagannathan, Humphrey Wanzira, Emmanuel Arinaitwe, Victor Bigira, Jaco Homsy, Moses Kamya, Jordan Tappero, Mary Muhindo K, Emmanuel Osilo, Anne Gasasira, Grant Dorsey*

16:15hrs ***4.*** Incidence of malaria following discontinuation of trimethoprim-sulfamethoxazole prophylaxis given for different durations among HIV-exposed children. ***Muhindo Mary K****, Victor Bigira, Abel Kakuru,*

Emmanuel Arinaitwe, Humphrey Wanzira, Jaco Homsy, Taylor Sandison, Prasanna Jagannathan, Jessica Briggs, Moses Kamya, Jordan W. Tappero, Grant Dorsey

16:30hrs ***5.*** Artemether-lumefantrine versus dihydroartemisinin-piperaquine for the treatment of uncomplicated malaria: longitudinal outcomes in a cohort of young Ugandan children. ***Humphrey Wanzira****, Taylor G. Sandison, Abel Kakuru, Victor Bigira, Emmanuel Arinaitwe, Jaco Homsy, Jordan Tappero, Moses R. Kamya, Grant Dorsey*

16:45hrs 6. Malaria chemoprevention in a high transmission setting: A randomized controlled trial of monthly dihydroartemisinin-piperaquine versus monthly sulfadoxine-pyrimethamine versus daily trimethoprim-sulfamethoxazole versus no therapy. ***Victor Bigira****, James Kapisi, Stephen Kinara, Florence Mwangwa, Beth Osterbauer, Abel Kakuru, Gloria Ikilezi, Julia Mwesigwa, Jane Achan, Moses Kamya, Grant Dorsey*

17:00hrs ***7.*** Significant reduction in risk of malaria among HIV-infected children receiving PI-based ART compared to NNRTI-based ART: a randomized open label trial. ***Jane Achan Jane****, Theodore Ruel, Abel Kakuru, Gloria Ikilezi, Tamara Clark, Edwin Charlebois, Philip Rosenthal, Grant Dorsey, Diane Havlir, Moses Kamya*

PRESENTATION OF AWARDS **17:00 – 17:30hrs**
Grant Dorsey, MD, Ph.D and Diane Havlir, MD

MU-UCSF New Investigator Award 2011
MU-UCSF Distinguished Scholar Award 2011

ABSTRACTS PRESENTED AT THIS CONFERENCE

SESSION 1: HIV and TUBERCULOSIS:

1 Implementation of a Rapid, Multi-disease Community Health Campaign offering Diagnostic, Preventive, Treatment and Referral services in rural Uganda

Gabriel Chamie, Dalsone Kwarisiima, Tamara Clark, Vivek Jain, Jane Kabami, Elvin Geng, Moses Kamya, Diane Havlir, Edwin Charlebois

Background: Large-scale community public health campaigns in resource-limited settings often focus on single diseases or interventions (e.g. HIV testing, bed net distribution). To catalyze progress towards achieving the Millennium Development Goals, novel strategies to provide multi-disease diagnostic, preventive and referral services at a community-level are needed.
Methods: We performed a multi-disease health campaign in rural Kakyerere Parish, Mbarara District, Uganda over five days in May, 2011, following one month of mobilization activities by village leaders. Services included on-site testing, counseling and linkage-to-care for HIV, diabetes, and hypertension; malaria rapid testing in febrile participants with on-site treatment, tuberculosis (TB) symptom screening, and prevention services (pre- and post-test counseling, deworming and vitamin A for young children, and male condoms for adults). HIV-infected participants were provided point-of-care CD4 cell count testing, trimethoprim-sulfamethoxazole, referral to HIV-specific care (with expedited antiretroviral therapy (ART) if CD4<100) and near-point-of-care rapid, PCR-based TB screening and HIV viral load measurement.
Results: 2,323 adults (≥18 years) and 2,020 children participated in the campaign: 74% and 64% of estimated adult and child parish residents, respectively. HIV prevalence was 8.1% in 15-49 year-old adults, and 0.6% in children. 119 (66%) of 180 HIV-infected adults reported being unaware of their HIV status prior to the campaign, and the median CD4 count among adults not on ART was 416 cells/μL (IQR:283-568). 7 of 8 adults with CD4<100 initiated ART within one week of the campaign's completion. No TB cases were identified among the 124 HIV-infected adults screened by PCR-based sputum testing, though 3 of 180 HIV-infected adults reported taking TB therapy at the time of the campaign (for an estimated TB prevalence of 1,667 per 100,000 population). Hypertension and diabetes were common (adult prevalence: 28% and 3.5% respectively), with 66% and 23% of hypertensive and diabetic participants reporting they were newly diagnosed at the campaign. Median time through the campaign was 95 minutes per participant.
Conclusions: Rapid, high throughput campaigns that provide multi-disease diagnostic, treatment, prevention and referral services facilitated by point-of-care technologies are feasible and can effectively reach a large proportion of the population in a rural African setting. Health campaigns focused on communicable diseases can serve as a platform for non-communicable disease diagnosis and referral to care.

2 Self-Disclosure of HIV Test Results: Results from a Randomized Controlled Trial of Home-Based versus TB Clinic-Based HIV Voluntary Counseling and Testing for Family and Household Members of TB Evaluation Patients in Uganda.

Wandera B, Talemwa N, Babirye E, Nabwegyako J, Okwera A,Plenty A, Mugerwa R, Charlebois E

Background: TB evaluation patients and their families are a high priority group for HIV testing; however testing rates in this population remains low. Disclosure of HIV test results may motivate sexual partners to seek HIV testing, and adoption of positive behaviour change to reduce acquisition or transmission of HIV. We showed that Home-based HIV VCT is superior to TB clinic-based VCT for successful HIV testing of family and household members of TB evaluation patients. We now evaluate self-disclosure of HIV test results to spouse and sexual partners of TB evaluation subjects.
Methods: TB evaluation patients presenting to the National Tuberculosis and Leprosy Control Program Clinic in Kampala, Uganda were tested for HIV, thereafter randomized within HIV strata to either home-based or TB clinic-based HIV VCT for Household(HH) members. TB-clinic randomized testers were reimbursed for travel costs to the clinic. Subjects were followed

every 3 months to assess disclosure, linkage to care and document consequences of household HIV testing. The proportion of married subjects who reported disclosing their HIV test results was calculated and we evaluated key factors associated with HIV status disclosure.
Results: Overall, 493 subjects TB evaluation subjects were randomized to have their HH members undergo either home-based or TB clinic-based HIV VCT. Of these 468(95%) were aged at least 15 years and retained for subsequent analyses, with median (IQR) age of 29(22-39.5) years, and 221(47.2%) were married. A total of 193/221(87.3%) subjects disclosed their HIV results to their spouses/sexual partner, of whom 159 (82.3%) were married. Of the 28 subjects who did not disclose their HIV test results, 18(64.3%) had tested HIV positive. Nine subjects reported relationship breakups after HIV testing, of which 6 had disclosed the HIV status as compared to 3 who had not disclosed. Compared to TB evaluation subjects who tested HIV positive, those who tested HIV negative were more likely to disclose their results (Odds ratio, OR= 3.71, 95% CI; 1.62-8.51) , while Venue of HH member testing (Clinic Vs Home OR=1.01, 95% CI; 0.46-2.23), being married Vs Single/separated OR= 2.21, 95% CI; 0.92-5.31), male gender(OR=0.78, 95% CI; 030-1.81), and reporting relationship breakup (OR= 3.74, 95% CI; 0.88-15.9) were not associated with disclosure of HIV test results to their partners.
Conclusions: HIV Sero-status disclosure rates to spouses are high and not associated with relationship break- ups, among TB evaluation patients, irrespective of place of HIV testing for their family and household members. HIV positive index subjects are less likely to disclose results compared to HIV negative subjects. Scaling up family based VCT should be fast tracked especially among individual at high risk for HIV.

3 HIV-infected African girls have lower plasma HIV RNA levels and higher CD4 percentages compared to boys

Theodore D. Ruel, Brian C. Zanoni , Isaac Ssewanyana, Huyen Cao, Diane V. Havlir, Moses Kamya, Jane Achan, Edwin D. Charlebois, Margaret E. Feeney

Background: HIV-infected women have lower HIV RNA levels and higher CD4 counts than men. This observation has been attributed to the immunomodulatory effects of sex steroid hormones such as estrogen and progesterone. Limited data exist regarding potential sex differences in HIV RNA and CD4 parameters among pre-pubertal children with untreated HIV infection.
Methods: We examined the relationship of sex to HIV RNA and CD4 parameters among 670 perinatally HIV-infected, ART-naïve African children <18 years (median age 4.8 years) using multivariate linear regression. In a subset of 188 children, we utilized longitudinal data to compare changes in HIV RNA levels and CD4 percentage over time. Levels of CD4 and CD8 T cell activation (CD38+HLA-DR+) were also compared between boys and girls.
Results: Female children had lower HIV RNA levels (p=0.0004) and higher CD4 percentages (p<0.0001) compared to male children. Multivariate linear regression demonstrated an independent association of sex with both HIV RNA level and CD4 percentage after controlling for other covariates. Multilevel mixed-effects linear regression analysis of longitudinal HIV RNA and CD4 data showed that sex differences persisted across all observed ages. Levels of T cell activation did not differ between the sexes.
Conclusions: Significant sex differences in HIV RNA levels and CD4 parameters are present in HIV-infected children long before the onset of puberty. These data suggest that intrinsic genetic differences between males and females, unrelated to sex steroid hormone levels, influence HIV RNA and CD4 parameters in HIV-infected individuals.

4 Impact of automated nucleic acid amplification testing on tuberculosis management and outcomes in Uganda

Winceslaus Katagira, Adithya Cattamanchi, William Worodria, Saskia den Boon, Nelson Kalema, Sylvia Kaswabuli, Cecily Miller, Alfred Andama, Heidi Albert, Pamela Nabeta, Christen Grey, Irene Ayakaka, Laurence Huang, J. Lucian Davis

Background: Automated nucleic acid amplification testing (NAAT) using the Xpert MTB/RIF assay has been reported to improve the accuracy and speed of tuberculosis (TB) diagnosis. However, the clinical impact of automated NAAT on patient outcomes has not been evaluated. We therefore sought to determine the diagnostic accuracy and clinical impact of Xpert MTB/RIF for TB diagnosis among TB suspects at high risk of early mortality in a high HIV/TB prevalence setting.
Methods: We prospectively enrolled consecutive patients with cough ≥ 2 weeks duration presenting to Mulago Hospital in Kampala, Uganda in two phases: a baseline phase in which automated NAAT results were not reported to clinicians and an implementation phase in which automated NAAT results were provided to clinicians. We determined the diagnostic accuracy of automated NAAT in reference to mycobacterial culture and compared patient outcomes between and within the two study phases.
Results: Of 477 patients included in the analysis, 287 were enrolled during the baseline phase and 190 during the implementation phase. Automated NAAT had high sensitivity (79%, 95% CI 73-84%) and specificity (96%, 95% CI 92-98%), reduced the median time-to-TB diagnosis (0 vs. 1 day, p<0.001), and increased the proportion of TB patients diagnosed rapidly (80% vs. 63%, p=0.003). However, following implementation of automated NAAT, the proportion of TB patients treated prior to hospital discharge did not increase significantly (78% vs. 85%, p=0.15) and two-month mortality among all patients did not decrease significantly (21% vs. 17%, p=0.33). In contrast, TB patients diagnosed rapidly by smear microscopy (baseline and implementation phases) or automated NAAT (implementation phase only) had decreased two-month mortality compared to TB patients diagnosed by culture (13% vs. 27%, p=0.01).
Conclusions: Automated NAAT facilitates more accurate and earlier TB diagnosis. Although rapid diagnosis decreased mortality among TB patients, additional interventions are needed to improve outcomes among severely ill, hospitalized TB suspects in high HIV/TB burden settings.

5 Gender disparities in TB suspect evaluation and treatment in rural Uganda

Priscilla Haguma, Cecily Rose Miller, J. Lucian Davis, Achilles Katamba, Asadu Sserwanga, Stella Kakeeto, Fred Kizito, Adithya Cattamanchi

Background: Tuberculosis (TB) case notification rates in women universally lag behind those in men. TB represents the third leading cause of death among women ages 15-44, yet women account for just 35% of the total 9.4 million TB cases reported worldwide [1, 2].Although several studies have documented social and economic barriers faced by women in accessing care, there is sparse data on gender disparities in TB evaluation.
Methods: We utilized a comprehensive monitoring and evaluation system to measure the quality of TB suspect evaluation at six geographically dispersed primary health centers in rural Uganda between January 2009 and December 2010, using indicators derived from the International Standards of Tuberculosis Care (ISTC). We compared the proportions of male and female TB suspects receiving recommended care practices at each step of TB evaluation using chi-

squared tests. We then developed multivariate logistic models of the effect of gender on the odds of completing each step, adjusting for site and time of clinical encounter using generalized estimating equations with robust standard errors in order to account for higher expected correlation among patient encounters occurring at the same health center compared to those occurring at different health centers [12]. We performed all analyses using STATA 11.0 (Stata Corporation, College Station, Texas).
Results: There were 161,550 patient encounters during the study period, involving 112,470 (70%) women. Of 3,341 TB suspects (i.e., patients with cough ≥2 weeks), 1,881 (56%) were women. Female TB suspects were less likely to be referred for sputum smear examination (46% vs. 62%, difference 16%, 95% Confidence Interval (CI) 12-19%, p<0.001) and to complete sputum smear examination if referred (74% vs. 78%, difference 4%, 95% CI 0.4-8%, p=0.03). While there were no significant differences in the proportions of smear-positive women and men starting TB treatment (72% vs. 73%, difference 3%, 95% CI -13 to +14%, p=0.92), overall, women were significantly less likely to receive a standard-of-care TB evaluation (33% vs. 45%, difference 12%, 95% CI 9%-16%). After adjusting for clinic site and encounter date, female TB suspects remained less likely to be referred for sputum examination (Odds Ratio (OR) 0.57, 95% CI 0.49-0.67, p<.001), and the odds of being fully evaluated for TB were significantly lower for women (OR 0.70, 95% CI 0.57-0.88).
Conclusions: These data provide strong evidence of gender disparities in TB suspect evaluation in primary health facilities in rural regions of sub-Saharan Africa. Strategies to ensure that women receive appropriate TB testing are critical for ensuring equitable and universal access to TB care, and provide a valuable opportunity for increasing case detection.

6 Mother to child transmission prior to revised Kenyan PMTCT guidelines: A retrospective review of PMTCT implementation in rural Kenya

Lisa Dillabaugh, Khady Diouf, Valerie Ndege, **Patrick Oyaro**, Elizabeth Bukusi, Craig Cohen

Background: Prevention of mother to child transmission services are widely decentralized in Kenya. However, there have been few efforts to document vertical transmission rates under operational circumstances. This project sought to document the mother-to-child HIV transmission (MTCT) rates within select sites prior to implementation of the revised Kenyan PMTCT guidelines.
Methods: We conducted a retrospective chart review of all HIV positive pregnant women and their HIV-exposed infants (HEI) enrolled from antenatal or maternal child health clinics from August 2008-May 2009 at three FACES-supported PMTCT sites: Lumumba Health Centre, Oyani Dispensary and Migori District Hospital. Data were abstracted from ANC registers, laboratory records, and patient files to determine key outcomes and predictor variables.
Results: A total of 362 HIV positive pregnant women and their infants were identified during the time period. Data on infant testing was available for 329 (91%) of infants. Mean maternal CD4 count was 439 (SD 258) for those with CD4 data available. Of these, 111 (33.7%) were eligible for HAART based on CD4 count of ≤350 cells/mm^3 collected during their pregnancy. Overall, 162 women were on HAART of whom 66 (20%) were started prior to pregnancy. Mean gestational age at birth was 38.5 weeks (SD 2.7), mean age at enrollment to HEI care was 10.1 weeks (SD13.1) and mean age of infant HIV PCR testing was 12.7 weeks (SD 11.8). 115 (35%) of HEI had a six week PCR test. Overall, 44 infants were confirmed HIV-infected giving a crude MTCT rate of 13.3%. MTCT was 7.3% in infants of mothers who received complete ART prophylaxis, 17.2% in those who received partial ART prophylaxis, and 31.1% in those who did not receive any ART prophylaxis. As compared to those infants who received no prophylaxis risk of transmission was reduced OR 0.26 (0.12-0.54) significantly if any prophylaxis was given. The overall infant mortality rate was 7%, with 10 of the 23 deaths among confirmed HIV-infected infants.
Conclusion: These results demonstrate the operational MTCT rates under the old Kenyan guidelines. Overall, MTCT was reduced by 74% in those who received any kind of PMTCT prophylaxis. MTCT was quite low in those who received complete prophylaxis. This shows that PMTCT can work when operationalized in real-world settings. We plan to compare these outcomes with MTCT rates following implementation of expanded PMTCT guidelines including early prenatal prophylaxis for mothers and extended nevirapine prophylaxis for infants.

7 Social exchange theory explains sexual concurrency among women married to fishermen along Lake Victoria, Kenya

Zachary Kwena, Chris Shisanya, Isaac Mwanzo, Solomon Majiwa, Lilian Achiro, Elizabeth Bukusi

Background: Sexual concurrency has been associated with elevated risk of STI/HIV infections. Married couples in Kenya as elsewhere in Sub-Saharan Africa have been observed to engage in sexual concurrency leading to STI and HIV infections. The circumstances under which married women get involved in sexual concurrency are not clear. In this paper, we employ social exchange theory to explain married women's involvement in sexual concurrency.
Methods: This is part of a mixed method cross-sectional study to establish risk factors for sexual concurrency among fishermen and their spouses along Lake Victoria in Kisumu County, Kenya. We conducted 12 focus group discussions (FGDs) with fishermen and their spouses from 6 of the 33 beaches in Kisumu County. All but 2 FGDs had 10 participants each segregated based on gender. Fishermen, who were our index participants, were approached and asked their willingness to participate in the study with their spouses. Those who were interested were asked to discuss it with their spouses and inform the study staff about their decision at the earliest opportunity for scheduling. On the scheduled days, participants were introduced to the study and consented as couples and thereafter separated for discussion by gender-matched moderators that happened concurrently. The resultant audiofiles were transcribed verbatim and translated into English for coding and analysis in NVivo 9.
Results: Social exchange theory argues that dyadic relationships operate in quasi-economical manner producing rewards and/or costs to partners within the dyad. The individual feelings about a relationship are governed by: (a) the balance between what is put into the relationship and what is obtained out of it, (b) the kind of relationship individuals deserve and, (c) the chances of having a better relationship elsewhere in their social network. Women married to fishermen invest time, money, self-disclosure, children and other resources in their relationships. However, when they feel that they are, comparatively, not getting what they deserve in their current relationships, they make a case for alternatives. Women married to fishermen feel that don't get expected rewards such as sexual satisfaction in terms of sex-on-desire, emotional attachment, commitment to the relationship, and attractiveness that they deserve in their current relationships. They attribute this to the fact that their husbands (1) migrate and spend a long time away from home (2) engage in extra-marital relationships with other women at their expense, (3) consume alcohol and illicit drugs that render them useless at the time of need and, (4) engage in exhaustive work at the lake to the extent that they are unable to provide for their spouses' emotional needs. This happens to the women yet their social networks are rich in rewards that their spouses are unable to provide.

Even though they, from time to time, source for these rewards from other relationships they establish within their social networks, the high levels of investment in their primary relationships require that they continue to keep them. This effectively results in sexual concurrency and formation of sexual networks that enhance the spread of STIs and HIV infections within network members. Otherwise, women tend to end relationships where they feel that they can bear with the loss of their investment.
Conclusion: The act of balancing the desire for unforthcoming rewards from primary sexual relationships and the level of investment in such relationships propel women married to fishermen to engage in sexual concurrency. Women are unable to end non-performing relationships because of their 'massive' level of investment in such relationships.

SESSION 2: MALARIA SURVEILLANCE and PATHOGENESIS:

1 Malaria-related morbidity and mortality among hospitalized children in regions of varying malaria transmission intensity in Uganda

Arthur Mpimbaza, Anne Gasasira, Asadu Sserwanga, Sussann Nasr, Scott Filler, Moses Kamya, Sarah Staedke, Grant Dorsey

Background: Malaria is a significant public health problem in Uganda and the Ministry of Health has scaled up control interventions. However, measuring impact of interventions is a challenge due to lack of quality malaria morbidity and mortality data. In April 2010 – June 2011, the Uganda Malaria Surveillance Project with support of the President's Malaria Initiative began health facility-based surveillance with a goal of providing high quality inpatient malaria morbidity and mortality data.
Methods: Six public hospitals, in areas with varying malaria endemicity were selected: Tororo and Apac (high transmission), Jinja and Mubende (medium transmission) and Kambuga and Kabale (low transmission). At each site, a standardized case record form is used to collect individual patient level data, and a malaria diagnostic test is done at admission for all children.
Results: As of July 2011, a total of 19,464 children were hospitalized, 89% of whom were below five years of age. The proportion of hospitalized children under five with malaria parasitemia was highest in Tororo (66%) and Apac (63%) followed by Mubende (52%) and Jinja (49%) and lowest in Kambuga (27%) and Kabale (10%). The proportion of children who died with a positive malaria test was relatively low at all sites (2.1% in Apac, 2% in Mubende, 1.3% in Jinja, 0.9% in Tororo and 0% in Kambuga and Kabale), but the case-fatality rate for children with lab-confirmed malaria varied (3.2 % in Apac, 3.7 % in Mubende, 2.6 % in Jinja, 1.3 % in Tororo and 0% in Kambuga and Kabale). However, when analysis was restricted to children who fulfilled WHO criteria for severe malaria, the case-fatality rate increased slightly (3.9 % in Apac, 4.1 % in Mubende, 2.7 % in Jinja, 2.1 % in Tororo and 0% in Kambuga and Kabale). Prescription of antimalarials for children with negative test results was high in Jinja (71%), Kambuga (67%), Mubende (61%) and Kabale (47%) and was less of a problem in Apac (31%) and Tororo (19%). Among children who were prescribed an antimalarial, the unadjusted risk of dying with a negative test result (2.7%) was higher than among those with positive test results (1.7%; RR 1.58, 95% 1.25-1.99; $p<0.001$).
Conclusion: In high and medium transmission settings in Uganda, the proportion of hospitalized children under-five with malaria parasitemia is high, but the risk of dying with malaria parasitemia is surprisingly low. Over diagnosis and treatment of malaria potentially resulting in neglect of alternative diagnosis could lead to avoidable morbidity and mortality. In addition, excessive prescription of antimalarials despite negative test results burdens health services and is a matter of concern, particularly when policy is shifting to use of IV artesunate as first line treatment for severe malaria. Trends in malaria morbidity and mortality and antimalarial treatment practices across all six sites will be presented.

2 A programmatic evaluation of sulfadoxine-pyrimethamine for the prevention of placental malaria in Uganda.

Arinaitwe E, Ades V, Walakira A, Ninsiima B, Muggaga O, Kamya M, Nasr S, Filler S, Dorsey G

Background: Despite widespread administration of sulfadoxine-pyrimethamine intermittent preventive treatment in pregnancy (SP IPTp), placental malaria continues to have adverse effects on obstetrical and neonatal outcomes such as growth restriction, preterm birth, spontaneous abortion, stillbirth, and neonatal death. SP IPTp may be less effective in areas of high resistance.
Methods: HIV-uninfected pregnant women were enrolled at delivery and completed a questionnaire about SP and other medication use, bed net use and other antenatal care events. Specimens collected include placental biopsy, placental blood, cord blood, maternal peripheral blood. Blood smear, filter paper for PCR and rapid diagnostic test (RDT) were collected on placental and cord blood specimens. Blood smear was performed on maternal blood. Infant birth weight was measured.
Results: 565 women were enrolled. Of these, 183 (32.4%) were primigravida, 115 (20.3%) were secundigravida and 267 (47.26%) had a gravidity of three or more. Thirty two (5.7%) women did not take any sulfadoxine-pyrimethamine (SP) during pregnancy, 202 (35.8%) took one dose, and 331 (58.6%) took at least two SP doses. Mean birth weight was 3082 grams with 56 (9.9%) infants with low birth weight (< 2500 grams). There was a trend towards decreasing LBW with an increase in the number of SP doses taken with 5 (15.6%) infants among women who did not take any SP, 25 (12.4%) infants in mothers who took one SP dose, and 26 (7.9%) infants in those who took at least two SP doses. Additionally, mean birthweight in primigravidae who did not take any SP was extremely low, with a mean of 2157g for this group, and 50% of the infants being LBW. On testing for malaria, 105 (19%) placenta blood smears, 108 (19%) maternal peripheral blood smears, and 132 (23%) placental blood RDTs were positive. Among the women who did not take any SP, 9 (28.1%) had a positive placental blood smear, and 42 (20.8%) and 54 (16.3%) women among those who took one dose and two or more doses of SP respectively had a positive placental blood smear. On stratifying for gravidity, the effect of SP on placenta malaria was more pronounced in mothers gravida 3 or more with 12 (29%) women in those who took no SP, 7 (7.6%) in those who took one SP dose and 15 (9.5%) in those who took at least two SP doses.
Conclusions: In this area of high malaria transmission, the effect of SP on prevention of placental malaria is more pronounced in multigravidae as compared to primigravidae; however the protective effect of SP in multigravidae does not appear to be dose-dependent, as there was no benefit of two doses over one dose. Taking SP was associated with a lower risk of LBW. Additionally, primigravidae who did not take SP seem to be at extremely high risk for LBW, and while their placental blood smears were positive more frequently than women of other gravidities, the difference was not as marked as LBW. Therefore, placental blood smear may not reflect the severity of placental disease and/or clinical sequelae of malaria.

3 District-based household survey data and associated biomarkers in indoor residual spraying (IRS) and non-IRS districts in Northern Uganda

Adoke Yeka, Ruth Kigozi, Laura Steinhardt, Susie Nasr, Denis Rubahika, Asadu Sserwanga, Moses Kiggundu, Humphrey Wanzira, Geoff Lavoy, Scott Filler, Grant Dorsey, Moses Kamya

Background: In highly malaria-endemic Northern Uganda, selected districts have been sprayed since 2007 with DDT and pyrethroids, before documented resistance prompted shifts to carbamates in 2010. The objectives of the study were to measure the impact of IRS on malaria transmission intensity (as measured by parasitemia and anaemia) in northern Uganda.
Methods: A household survey was used to compare one non-sprayed district (Lira) with two IRS districts (Apac, sprayed once with carbamates in 2010 after one round each of DDT (2008) and pyrethroids (early 2010) and Pader, which received two rounds of carbamate spraying in 2010, following four rounds of pyrethroids (2007–2009)). The survey was based on district-wide representative samples of households using a two-stage cluster sampling procedure within each district. The primary sampling units were the enumeration areas (EAs) of the 2002 National Housing and Population Census. A total of 30 EAs were randomly selected in each of the three districts using probability proportionate to size (PPS) sampling. Within each sampled EA, all households were listed and 20 households were randomly sampled from the listing for inclusion in the survey (n=600 households per district). The surveys consisted of three components: (1) a household survey consisting of a questionnaire administered to heads of households, (2) women's survey consisting of a questionnaire administered to all women of child-bearing age (15-49 years), and (3) clinical surveys consisting of biomarker testing (anaemia, blood smear and Rapid Diagnostic Test for malaria) of all children under five years of age. District-level prevalence estimates from a total of 1,773 children less than five years of age were calculated from the two-stage, cluster sample survey, using sampling weights and accounting for clustering.
Results: Parasitemia levels were significantly lower in both IRS districts compared to the non-sprayed district. In Apac, 37.2% of children had positive malaria blood smears, compared to 50.1% of children in non-sprayed Lira district, $p<0.01$. Parasitemia prevalence was lowest in Pader (16.9%, $p<0.001$ compared to both Apac and Lira), which had been sprayed twice with carbamates in 2010. Anemia (hemoglobin<11g/dL) was less common in Apac (38.4%) and Pader (36.9%), compared to Lira (53.0%), $p<0.001$. Bednet use by children was significantly higher in the IRS districts (69.6% in Apac and 64.6% in Pader) than in Lira (49.5%), but there were no significant differences between the districts in terms of food security or distance to the nearest health facility.
Conclusion These results indicate lower malaria burdens, according to biomarkers, in IRS districts compared to non-sprayed districts in Northern Uganda

4 Impact of indoor residual spraying on morbidity trends in Apac district

Anne Gasasira, **Ruth Kigozi**, Sanjiv M. Baxi, Asadu Sserwanga, Stella Kakeeto, Sussann Nasr, Moses R. Kamya, Scott Filler, Grant Dorsey

Background: Malaria control efforts in Uganda include case management with artemisinin combination therapy (ACT), widespread coverage with long lasting insecticide nets and intermittent preventive therapy in pregnancy. To expand its control activities, the National Malaria Control programe has included indoor residential spraying (IRS) as one of the key control strategies in high endemic areas. To this effect, five rounds of IRS have been implemented in Apac district since March 2008 using dichlorodiphenyltrichloroethane (DDT), Alpha cypermenthrin and carbamates with over 90% household coverage. Round one of IRS was implemented in March to May 2008 using DDT. Round two was implemented in March 2010 (two years after round 1) using Alpha cypermenthrine. Round 3 and round 4 were implemented in August to September 2010 and January 2011 (four months apart) respectively using carbamates. This study assessed the changes in slide positivity rate in Apac district following these IRS rounds.
Methods: Through the sentinel site surveillance system under the Uganda Malaria Surveillance Project, individual level malaria morbidity data was collected at Aduku health centre IV in Apac district. Data collected included but not limited to number of patients with suspected malaria sent to the lab and number of patients with a positive blood smear. Associations between 6 month periods (with the exception of only 4 months between the 2nd and 3rd rounds) related to IRS and relative changes in the slide positivity rate (SPR) were estimated using Poisson regression after controlling for age and seasonality.
Results: Over the 52 month observation period a total of 83,829 patients were seen, 41,294 (49%) had suspected malaria, and 77% of those with suspected malaria underwent microscopy. The SPR was 52% during the 18 months prior to completion of the 1st round of IRS. The 6 months following completion of the 1st round was associated with a 7% relative reduction in the SPR ($p=0.22$) compared to the 6 months before completion of the 1st round. The 4 months following completion of the 2nd round was associated with a 12% relative reduction in the SPR ($p=0.01$) compared to the 6 months before completion of the 2nd round. The 6 months following completion of the 3rd round was associated with a 27% relative reduction in the SPR ($p<0.001$) compared to the 4 months before completion of the 3rd round.
Conclusion: In this area of very high transmission intensity, the 2nd and 3rd rounds of IRS were associated with a significant decrease in the SPR. These results suggest that at least two rounds of IRS administered consecutively are needed to create significant reduction in slide positivity rates in a high transmission setting.

5 The T cell response to Pre-erythrocytic and Erythrocytic Stage Malaria Antigens

Felistas Nankya, Prasanna Jagannathan, Marco Morelli, Ijeoma Eccles-James, Katherine Bowen, Muhindo Mary K, Emmanuel Osilo, Patrick Tumwebaze, Samuel Wamala, Charles Ebusu, Jessica Briggs, Jane Achan, Grant Dorsey, Margaret Feeney

Background: Understanding of naturally acquired immunity to malaria remains limited. Elucidation of correlates of protective immunity is needed to inform vaccine design. Several lines of evidence suggest that malaria-specific T cells, particularly those targeting antigens expressed during pre-erythrocytic infection, may confer protection from subsequent episodes of malaria. The primary goal of this study was to measure T cell responses using ex vivo elispot to a wide panel of pre-erythrocytic and erythrocytic antigens in children living in a highly endemic area. Secondary aims were to identify factors that predict the breadth of responses to pre-erythrocytic and erythrocytic antigens, and whether responses were associated with the risk of future malaria.
Methods: *Sample Collection:* Samples were obtained from an ongoing cohort study (TCC) of HIV unexposed and exposed, uninfected children being conducted in Tororo. Using convenience sampling, 5 ml of blood was collected and processed from 37 TCC study participants. *Antigens:* Pools of overlapping peptides (18mers overlapping by 11 amino acids) spanning 7 pre-erythrocytic (CSP, TRAP, LSA, SIAP1, SIAP2, CelTos, P52) and 3 erythrocytic-stage antigens (AMA1, MSP1, HGXPRT) were used for stimulation. *Ex Vivo IFNγ Elispot:* Fresh PBMC were isolated and plated at $2x10^5$ cells/well in 96-well plates that were pre-coated with 2 µg/ml anti-IFNγ monoclonal antibody. Cells were stimulated by the addition of

pooled peptides(10 μg/ml/peptide), PHA (pos control) or media alone. Plates were incubated overnight at 37°C and developed using standard methods. Individual IFNγ-secreting cells were visualized as purple spots, and counted manually and by a plate reader. Results were calculated as the number of spot-forming cells (SFC) per million input cells after subtraction of the background response (mean SFC/10^6 cells of 3 negative control wells). A response was considered positive if it was >3x the average negative control wells and >10 SFCs/10^6 PBMC. *Statistical Analysis:* The proportion of subjects recognizing antigens between groups was compared using Fisher's exact test. Multivariate logistic regression was used to correlate Elispot responses with prior malaria incidence, age, and exposure to TMP/SMX. Kaplan-Meier survival curves were used to correlate responses with time to next malaria episode.
Results: The median age in months of children tested was 39.8 (IQR 37.5-42.8), with 24% HIV unexposed and 76% HIV exposed. Elispot responses were detected in 21/37 children (15/37 pre-erythrocytic, 18/37 erythrocytic antigens), with a median magnitude of 17 SFC/10^6 PBMC. MSP1 was the most frequently recognized antigen, with 41% children responding to this pool. Elispot responses were not associated with age or TS exposure, but children with a prior incidence of malaria >2.5ppy were significantly more likely to have a response to erythrocytic antigens compared with children with an incidence<2.5 ppy (OR 12.96, 95% CI 1.34-125.3, p=0.027). Elispot responses were not associated with time to next malaria episode.
Conclusions: T cell responses to pre-erythrocytic and erythrocytic antigens can be detected using ex vivo elispot, albeit at low frequencies. Responses to erythrocytic antigens correlate with prior exposure, but do not appear to correlate with time to next malaria episode.

6 Ex vivo drug sensitivity of malaria parasites under selective pressure

Patrick Tumwebaze, Oswald Byaruhanga, Amethyst Gillis, Hannah Yemane, Roland A. Cooper, Samuel L. Nsobya, Philip J. Rosenthal

Background: Artemisinin-based combination therapies (ACTs) are standard for the treatment of uncomplicated malaria in Africa. Antifolates and antiretroviral protease inhibitors have been shown to prevent malaria. Widespread use of these drugs may select for parasites with decreased sensitivity, jeopardizing strategies for the treatment and prevention of malaria. Measurement of the ex vivo sensitivity of freshly isolated malaria parasites offers insight into drug resistance patterns. Culturing parasites with selective concentrations of malaria drugs may identify novel mechanisms of drug resistance.
Methods: Blood samples are being collected from febrile children enrolled in the PROMOTE-1 and PROMOTE-3 projects, consisting of HIV-infected children randomized to protease inhibitor or NNRTI-based antiretroviral therapy (Project 1) or children randomized to one of four treatment arms for the prevention of malaria (Project 3). In select samples collected since May, 2010, parasites from children with malaria were placed into culture following standard methods. Drug sensitivities were assessed by incubating cultured parasites for 72 h in pre-dosed 96-well culture plates with a range of concentrations of drugs of interest and then assessing parasite growth spectrophotometrically with a histidine-rich protein-2 (HRP2) ELISA. Optical density values were fitted to normal curves based on serial dilutions of HRP-2 standards, and IC_{50}s were calculated based on a nonlinear regression model. In separate experiments, freshly isolated parasites were incubated with a range of concentrations of drugs of interest for up to 28 days, parasitemias were assessed intermittently by HRP2 ELISA, and parasite DNA was stored for subsequent molecular analysis.
Results: Ex vivo sensitivities were assessed to: (1) commonly used treatment components (chloroquine (CQ), monodesethylamodiaquine (AQ), quinine (QN), lumefantrine (LU), piperaquine (PQ), and dihydroartemisinin (DHA)); (2) antifolates (pyrimethamine , trimethoprim, sulfadoxine, and sulfamethoxazole); and (3) HIV protease inhibitors (lopinavir, ritonavir, atazanavir). Results varied widely for CQ, AQ, and QN; parasites were universally highly sensitive to LU and DHA; and results varied for PQ, with sensitivities decreasing over time. Results also varied widely for the studied antifolates. For HIV protease inhibitors, parasites consistently had IC_{50}s for lopinavir below levels of the drug achievable in the plasma with standard dosing of lopinavir-ritonavir. In preliminary analysis, IC_{50}s did not clearly correlate with prior treatment or preventive therapy. Parasites were also selected for growth in selective concentrations (1/4-4 X IC_{50}) of lumefantrine, piperaquine, and DHA. Concentrations of 1-4 X the IC_{50} frequently led to diminished, but persistent growth, suggesting that drug resistant parasites may have been selected. Molecular analysis of parasite DNA is now underway.
Conclusions: Parasites with a range of sensitivities to many drugs currently used for the treatment or prevention of malaria and other infections were identified in ex vivo studies. Considering sensitivities to ACT components, parasites were uniformly highly sensitive to DHA and LU, but sensitivities to PQ varied. In preliminary analyses drug sensitivity did not clearly correlate with prior therapy. Parasites were also selected for growth under selective in vitro drug pressure. It will be of interest to study associations between in vitro drug sensitivities, parasite genetic features, and the clinical outcomes of children, and also to characterize parasites selected by in vitro drug pressure.

SESSION 3: NUTRITION:

1 Maternal nutritional status predicts adverse obstetric & fetal outcomes among HIV-infected rural Ugandan women receiving combination ART

Julia Mwesigwa, Sera Young, Katherine Murray, Paul Natureeba, Beth Osterbauer, Jane Achan, Emmanuel Arinaitwe, Tamara Clark, Veronica Ades, Edwin Charlebois, Theodore Ruel, Moses Kamya, Diane Havlir, Deborah Cohan

Background: Maternal nutritional status is an important predictor of obstetric and fetal outcomes, yet little is known about the nutritional status of HIV-infected pregnant women treated with combination antiretroviral therapy (cART). We therefore examined the relationship between maternal body mass index (BMI), gestational weight gain (GWG), and hemoglobin concentration (Hb) among women initiating cART in rural Uganda.
Methods: This was a prospective cohort study of 158 HIV-infected, ART-naïve pregnant women from an ongoing clinical study in Tororo, Uganda. Participants were enrolled between 12 and 28 weeks gestation and treated with a protease inhibitor or non-nucleoside reverse transcriptase inhibitor-based combination regimen. Baseline data were collected on demographics, socio-economic status, HIV and obstetric history. Maternal nutritional status was assessed using BMI, maternal weight change during pregnancy, baseline Hb, and mean Hb during pregnancy. Maternal weight was measured to the nearest 500g at scheduled clinic visits. Maternal height was measured to the nearest 0.1 cm. Laboratory evaluations included Hb, HIV RNA PCR, and CD4/CD8 lymphocyte subsets. At birth, infant weight, length and head circumference were measured to the nearest 10grams and 0.1 cm respectively. Infant outcomes included low birth weight (LBW), small for gestational age (SGA), stunting, wasting, underweight, preterm delivery, head-sparing growth restriction, and

fetal death. Outcomes were evaluated using Wilcoxon signed-rank tests and logistic regression models.
Results: Of the 231 women who had been enrolled between December 2009 and May 24, 2011, 158 had delivered a singleton gestation and their data were analyzed. Median age was 29 years, median gestational age was 22 weeks, and baseline BMI was 21.9. Ninety percentof participants were diagnosed with WHO Stage 1 HIV disease, and 45% of participants were diagnosed with anemia prior to the initiation of cART. Mean GWG was 0.17kg/week, 14.6% of women experienced weight loss during pregnancy, and 44.9% were anemic. Adverse fetal outcomes included LBW (19.6%), preterm delivery (17.7%), fetal death (3.9%), stunting (21.1%), small-for-gestational age (15.1%), and head-sparing growth restriction (26%). No infants were HIV-infected. Gaining < 0.1kg/week was associated with LBW, preterm delivery, head-sparing growth restriction, and a composite adverse obstetric/fetal outcome. Maternal weight at 7 months gestation predicted LBW. Each additional day of trimethoprim-sulfamethoxazole use during pregnancy decreased the odds of preterm delivery by 3%, while for each g/dL higher mean Hb, the odds of small-for-gestational age decreased by 52%.
Conclusions*:* Women on cART had grossly inadequate GWG. Infants whose mothers gained <0.1kg/week were at increased risk for LBW, preterm delivery, and head sparing growth restriction. cART by itself may not be sufficient for decreasing the burden of adverse obstetric/fetal outcomes among HIV-infected women. Future studies are needed to characterize the scope and causes of nutritional deficiencies among this population and to design interventions that improve the health of HIV-infected mothers and development of their HIV-unexposed, uninfected offspring.

2 HIV-infected Ugandan children suffer high rates of malnutrition and minimal recovery following the initiation of antiretroviral therapy

Achan J, **Ikilezi G**, Kakuru A, Young S, Havlir D, Kamya M, Charlebois E, Ruel T.

Background: HIV-infected children in Africa suffer high rates of wasting and stunting, but there are limited longitudinal data about what factors lead to improvements in growth. We sought to chacterize the extent of growth recovery that followed the intiation of ART in a cohort of rural Ugandan HIV-infected children.
Methods: Subjects were HIV-infected children from an ongoing clinical study in Tororo, Uganda that were either ART-suppressed (HIV RNA < 400 copies/ml) on first line therapy or ART-naive and initiating ART per WHO guidelines. Weight-for-age (WAZ), height-for-age (HAZ), and weight-for-height (WHZ) Z-scores were calculated monthly; CD4 count and percentage, HIV RNA and hemoglobin levels were obtained every 12 weeks. A measure of socioeconomic status (SES) was generated using principal components analysis of household assets. Associations between WAZ, HAZ or WHZ and enrollment age, CD4 count and percentage, hemoglobin, HIV RNA level (log(copies/ml), and SES were analyzed using multivariate logitistic regression. Predictors of individual growth rates (Z-score change per month) were evaluated using multivariate linear regression modelling. Predictors of growth recovery among children who were underweight (WAZ<-2), stunted (HAZ<-2) and wasted (WHZ<-2) to Z-scores > -2 after 12 months of therapy were characterized using Kaplan-Meier survival plots and Cox proportional hazard modelling.
Results: ART-naive children (n=110) had similar ages (median 3.1 vs 2.9, p=0.2) but lower CD4 percentage (median 16 vs 30, p<0.001) and CD4 count (median 548 vs 1275, p<0.001) compared to ART-suppressed children (n=56, median duration of prior ART 568 days, IQR:197,670). Greater portions of ART-naive children were underweight (38% vs 20%, p=0.02), stunted (63% vs 45%, p=0.03), and wasted (11% vs 2%, p=0.11). Among ART-naive children, older age (odds ratio, OR:0.014 for age >4 yrs vs < 2yrs, p=0.01) and lower WHO stage (1 or 2 vs 3 or 4, OR:0.08, p=0.003) were associated with reduced odds of wasting at enrollment, but only HIV RNA level was associated with significantly altered risk of stunting (OR 2.2 per log(copies/ml), p =0.004). The majority of ART-naive children demonstrated growth recovery after initiating ART as indicated by increasing Z-scores for WAZ (58%), HAZ(69%), and WHZ(51%). However, after 12 months of therapy, recovery among the severly malnourished from below to above a Z-score of -2 was seen in only 4 of 42 underweight, 3 of 69 stunted, 1 of 11 wasted children. In univariate analysis, severely wasted children with baseline CD4% of at least 25 had shorter median time to recovery (p=0.02) compared to children with CD4%< 25.
Conclusions: In this rural cohort of HIV-infected African children, high rates of malnutrition persisted after the intiation of ART. After 12 months, less than 10% of the underweight, stunted, or wasted had recovered to above Z-scores of -2. Notably, WAZ worsened in 42% of children and HAZ worsened in 31% of children. Further study to identify predictors of growth recovery and interventions to complement ART is needed to optimize health outcomes in HIV-infected African children.

3 Cross-sectional study of risk factors for malnutrition, anemia, and parasitemia among HIV-exposed and –unexposed infants enrolled in the PROMOTE- chemoprevention trial.

Osterbauer B, Kapisi J, Bigira V, Kamya M, Dorsey G

Background: Malnutrition, anemia and malaria are common among African infants living in rural areas. Limited data exist comparing the prevalence of these morbidities and their associated risk factors among HIV-exposed (HIV-negative infants born to HIV-infected mothers) and HIV-unexposed (HIV-negative infants born to HIV-infected mothers) infants.
Methods: Infants aged 4-5 months were enrolled using convenience sampling as part of a randomized controlled trial of antimalarial chemopreventive therapy being conducted in Tororo, Uganda, a rural area with high malaria transmission intensity. At enrollment a cross-sectional survey was performed to collect basic demographic, preventative health, anthropomorphic, and laboratory data. Multivariate logistic regression was performed to identify risk factors associated with the following outcomes of interest: 1) parasitemia (defined as a positive blood smear), 2) anemia (defined as a hemoglobin < 8 gm/dL), and 3) stunting (defined as a length-for-age z-score < -2).
Results: Of the 600 participants enrolled, 200 were HIV-exposed and 400 were HIV-unexposed. Compared to HIV-exposed infants, HIV-unexposed infants had younger mothers (mean age 25.5 vs. 30.6 years, p<0.001), were less likely to have slept under and insecticide treated bednet (ITN) the previous night (29% vs. 46%, p<0.001), were less likely to be exclusively breastfeeding (12% vs. 48%, p<0.001), and were less likely to be taking trimethoprim-sulfamethoxazole (TS) prophylaxis (0% vs. 15%, p<0.001). Compared to HIV-exposed infants, HIV-unexposed infants were more likely to have parasitemia (24% vs. 14%, p=0.003) and anemia (14% vs. 8%, p=0.04), but less likely to be stunted (8% vs. 15%, p=0.009). Independent risk factors for parasitemia included an increased risk for infants born to younger mothers (OR=0.95 per 1 year increase, p=0.003) with trends for lower risks of parasitemia among infants sleeping under an ITN (OR=0.65, p=0.07) or taking TS prophylaxis (OR=0.18, p=0.10). The only risk factor for anemia was having parasitemia (OR=6.5, p<0.001). Risk factors for stunting included being HIV-exposed (OR=2.3, p=0.004) and not sleeping under an ITN (OR=1.9, p=0.04).

Conclusion: Significant difference in demographics and health related behaviors were see among HIV-exposed and –unexposed infants. HIV-unexposed children were more likely to have parasitemia, however, these differences could be explained by differences in maternal age and the use of ITNs and TS prophylaxis. HIV-unexposed children were also more likely to be anemic, but this was primarily explained by their higher risk of parasitemia. In contrast, being HIV-exposed was an independent risk factor for stunting along with failure to use an ITN. Additional analyses are planned to include socioeconomic indicators and fever treatment practices.

4 The association between malnutrition and the incidence of malaria among young HIV-infected and HIV-uninfected Ugandan children: a prospective cohort study

Emma Osilo, Victor Bigira, Mary Muhindo, Abel Kakuru, Humphrey Wanzira, Moses Kamya, Grant Dorsey, Emmanuel Arinaitwe

Background: In sub-Saharan Africa, malnutrition and malaria remain major causes of morbidity and mortality in young children. There are conflicting data as to whether malnutrition is associated with an increased or decreased risk of malaria. In addition, data are limited on the potential interaction between HIV infection and the association between malnutrition and the risk of malaria.
Methods: A cohort of 100 HIV-unexposed, 203 HIV-exposed (HIV negative children born to HIV-infected mothers) and 48 HIV-infected children aged 6 weeks to 1 year were recruited from an area of high malaria transmission intensity in rural Uganda and followed until the age of 2.5 years. All children were provided with insecticide-treated bed nets at enrollment and daily trimethoprim-sulfamethoxazole prophylaxis (TS) was prescribed for HIV-exposed breastfeeding and HIV-infected children. Monthly routine assessments, including measurement of height and weight, were conducted at the study clinic. Measure of malnutrion including stunting (low height-for-age) and underweight (low weight-for-age), classified as mild (mean z-scores between -1 and -2 during follow-up) and moderate-severe (mean z-scores < -2 during follow-up) were considered. Malaria was diagnosed when a child presented with fever and a positive blood smear. The incidence of malaria was compared using negative binomial regression controlling for potential confounders with measures of association expressed as an incidence rate ratio (IRR).
Results: The overall incidence of malaria was 3.64 cases per person year. Mild stunting (IRR=1.24, 95% CI 1.06-1.46, p=0.008) and moderate-severe stunting (IRR=1.24, 95% CI 1.03-1.48, p=0.02) were associated with a similarly increased incidence of malaria compared to non-stunted children. Being mildly underweight (IRR=1.09, 95% CI 0.95-1.25, p=0.24) and moderate-severe underweight (IRR=1.12, 95% CI 0.86-1.46, p=0.39) were not associated with a significant difference in the incidence of malaria compared to children who were not underweight. There were no significant interactions between HIV-infected, HIV-exposed children taking TS and the associations between malnutrition and the incidence of malaria.
Conclusions: Stunting, indicative of chronic malnutrition, was associated with an increased incidence of malaria among a cohort of HIV-infected and -uninfected young children living in an area of high malaria transmission intensity.

5 Nutritional Behaviors, Perceived Needs and Acceptability of Micronutrient and Macronutrient Supplementary Foods Among Pregnant and Lactating HIV-Infected Women: Preliminary Findings from the Formative Nutrition Study

Flavia Luwedde, Barnabas Natamba, Grace Akello, Wilfred Olwortho, Julia Mwesigwa, Beth Osterbauer, Albert Plenty, Deborah Cohan, Diane Havlir, Jane Achan, Sera Young

Background: HIV-infected women in rural Uganda have extremely low weight gain in pregnancy, which is associated with poor infant outcomes. It is important to understand maternal knowledge, attitudes and practices related to nutrition in order to design interventions to ameliorate these poor outcomes. Therefore, our objective was to understand nutritional behaviors and perceived nutritional needs during pregnancy, and to assess acceptability of nutrient-dense supplementary foods among HIV-infected women receiving either protease inhibitor (PI) or non-nucleoside reverse transcriptase (NNRTI) based antiretroviral therapy (ART) in Tororo, Uganda.
Methods: A convenience sample of participants in PROMOTE Pregnant Women and Infants (PROMOTE-PIs) were asked to participate in this formative nutrition study during routine study visits in July and August 2011. Pregnant women were oversampled in order to achieve a more balanced number of pregnant and lactating women. In-depth individual interviews covered maternal diet, infant feeding practices, and challenges with food and ART. A subset of participants were asked to rank 6 local nutrient-dense foods and 2 imported foods: PlumpyNut (macronutrient supplement) and Sprinkles (micronutrient supplement). Descriptive statistics were calculated for the interviews with complete data available.
Results: Fifty-six of the 59 women approached consented for participation: 23 were pregnant and 33 were lactating; 31 were receiving a PI-based regimen and 25 were receiving a NNRTI-based regimen. Over 93% of the 45 women with complete data reported poor nutritional intake during pregnancy for a variety of reasons, most often insufficient resources (31.1%) and reduced appetite (21.4%). Approximately half (48.9%) of participants ate earth (geophagy) while pregnant. Nearly half (48.9%) of participants reported poor adherence to multivitamins, due to smell of the pills (8/22, 36.4%) and nausea (10/22, 45.5%). Women reported numerous barriers to ART adherence, including non-disclosure of HIV status to household members (62.2%), perceived ART side effects (37.8%), and limited food availability (17.8%). Of the 13 women who ranked the local nutrient-dense foods, 46% chose soy porridge as most preferable followed by peanut paste (15.4%), dried fish (15.4%), millet flour (15.4%), and sesame paste (7.8%). On a scale of 1-5, with 5 most acceptable, PlumpyNut and Sprinkles both scored a median of 5 (range 1-5). Seventy-eight percent of women stated they would feel compelled to share nutritional supplements with household members if they were the sole recipients.
Conclusions: Pregnant HIV+ women reported poor nutritional intake due to insufficient resources and decreased appetite. A targeted intervention of Sprinkles and Plumpynut may be the most acceptable micronutrient and macronutrient supplements, respectively. A family food ration may be required to reduce sharing and ensure women receive the supplement

SESSION 4: MALARIA TREATMENT and CARE DELIVERY:

1 Significant reduction in risk of malaria among HIV-infected children receiving PI-based ART compared to NNRTI-based ART: a randomized open label trial.

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Background: HIV-infected children living in sub-Saharan Africa continue to suffer high morbidity and mortality from malaria. In areas of high malaria transmission, additional measures to decrease the risk of malaria in these children are therefore warranted. HIV protease inhibitors have shown some activity against *P.falciparum* in vitro. We evaluated the efficacy of PI-bases versus NNRTI-based ART regimens for malaria risk reduction in HIV-infected children.
Methods: We conducted a randomized open label trial in Tororo, Uganda. Participants were HIV- infected children aged 2 months to 5 years eligible for antiretroviral therapy (ART) or currently receiving non-nucleoside reverse transcriptase inhibitor (NNRTI) based ART regimen with virological suppression (HIV RNA<400 copies/ml). Participants were randomized to receive either PI-based (LPV/r) ART or NNRTI-based ART and followed up for 2 years. Episodes of uncomplicated malaria were treated with artemether-lumefantrine. Using intent-to-treat analysis, we compared the incidence-density of malaria between the study arms using Poisson regression. Secondary outcomes included response to antimalarial therapy and incidence of any adverse events
Results: Between September 2009 and July 2011, we enrolled 176 children and randomly assigned 89 to NNRTI-based ART and 87 to PI-based ART. The median age was 3 years, more than 70% were in WHO stage I and the majority were ART naïve (67%). Malaria incidence was significantly higher in the NNRTI arm compared to that in the PI arm176 episodes in 78.2 person years vs. 109 episodes in 82.3 person years (2.25 vs. 1.32 episodes/person year, IRR 0.59, 95% CI 0.36-0.97, p=0.037). Using survival analysis adequate clinical and parasitological response rates after treatment with artemether-lumefantrine were 86.0% (92/107) in the PI arm compared to 57.2% (99/174) in the NNRTI arm, p< 0.0001. The cumulative 28-day risk of treatment failure unadjusted by genotyping was significantly higher in the NNRTI arm compared to the PI arm; 41.1%, 95% CI 34.1 - 48.8 vs. 14.0%, 95% CI 8.7 – 22.2; HR 0.31, 95% CI 0.14 – 0.68 (p= 0.004). Median serum lumefantrine levels were significantly higher in the PI arm compared to the NNRTI arm on follow-up days 3, 7 and 14. In the PI arm, day 7 lumefantrine levels >300ng/ml were associated with a > 85% reduction in the risk of recurrent malaria after 63 days with an apparent dose dependent reduction in risk when compared to the serum levels < 300ng/ml. This effect was not observed in the NNRTI arm. None of the participants were found to have a prolonged QTc interval.
Conclusions: Use of PIs was associated with a significant reduction in the incidence of malaria and the risk of recurrence which may be explained by pharmacokinetic interactions and potential synergy between PIs and lumefantrine. The use of PI-based ART could be considered as one of the strategies for malaria prevention in HIV-infected children.

2 Malaria chemoprevention in a high transmission setting: A randomized controlled trial of monthly dihydroartemisinin-piperaquine versus monthly sulfadoxine-pyrimethamine versus daily trimethoprim-sulfamethoxazole versus no therapy

Victor Bigira, James Kapisi, Stephen Kinara, Florence Mwangwa, Beth Osterbauer, Abel Kakuru, Gloria Ikilezi, Julia Mwesigwa, Jane Achan, Moses Kamya, Grant Dorsey

Background: Malaria is one of Africa's leading causes of morbidity and mortality in young children. One promising new control intervention is the use of antimalarial drugs as chemoprophylaxis or intermittent preventative therapy (IPT). The WHO recently endorsed the use IPT with sulfadoxine-pyrimethamine (SP) at the time of routine immunization in infants (termed IPTi) in areas of high malaria burden and low-moderate SP resistance or the use of combination therapy in older children in areas where malaria transmission is highly seasonal (termed IPTc). However, given the high levels of SP resistance and perennial transmission in Uganda, neither of these recommendations is appropriate and therefore new strategies are needed.
Methods: A cohort of 400 HIV-unexposed and 200 HIV-exposed infants living in Tororo was enrolled at 4-5 months of age. At enrollment all children received insecticide-treated bed nets and HIV-exposed children received trimethoprim-sulfamethoxazole (TS) prophylaxis. HIV-unexposed children were randomized to monthly dihydroartemisinin-piperaquine (DP), monthly SP, daily TS or no therapy at 6 months of age while HIV-exposed children were randomized to one of the same four arms when confirmed to be HIV-uninfected after breastfeeding cessation. The primary endpoint was the incidence of malaria defined as the number of treatments for new episodes of malaria per time at risk. Time at risk begins when study participants are randomized to therapy and ends when study participants reach 24 months of age or early study termination. The incidence of malaria was compared using negative binomial regression with measures of association expressed as the protective efficacy (1- incidence rate ratio). Preliminary results are presented below.
Results: Of the 400 HIV-unexposed children enrolled, 393 were randomized to therapy. The incidence of malaria PPY among those on no therapy (n=98), daily TS (n=99), monthly SP (n=98), and monthly DP (n=98) was 5.18, 3.42, 4.78, and 1.50, respectively. Compared to the no therapy arm, daily TS was associated with a 35% reduction in the incidence of malaria (95% CI 18-49%, p<0.001), SP was associated with non-significant 10% reduction in the incidence of malaria (95% CI -13-28%, p=0.37) and monthly DP was associated with a 71% reduction in the incidence of malaria (95% CI 62-78%), p<0.001). Of the 200 HIV-exposed children enrolled, 100 have been randomized to therapy. The incidence of malaria PPY among those on no therapy (n=25), daily TS (n=25), monthly SP (n=25), and monthly DP (n=25) was 5.55, 1.57, 2.90, and 0.32, respectively. Compared to the no therapy arm, daily TS was associated with a 70% reduction in the incidence of malaria (95% CI 40-85%, p<0.001), SP was associated with non-significant 46% reduction in the incidence of malaria (95% CI -1-71%, p=0.06) and monthly DP was associated with a 94% reduction in the incidence of malaria (95% CI 81-98%), p<0.001).
Conclusions: Chemoprevention with daily TS or monthly DP reduced the incidence of malaria and monthly DP was the most effective regimen among young children living in an area of high transmission intensity. Early evidence also suggests that chemoprevention was more effective in HIV-exposed children compared to HIV-unexposed children.

3 Association between trimethoprim-sulfamethoxazole prophylaxis and *Plasmodium falciparum* gametocytemia in a cohort of Ugandan children

Abel Kakuru, Prasanna Jagannathan, Humphrey Wanzira, Emmanuel Arinaitwe, Victor Bigira, Jaco Homsy, Moses Kamya, Jordan Tappero, Mary Muhindo K, Emmanuel Osilo, Anne Gasasira, Grant Dorsey

Background: The use of sulfadoxine-pyrimethamine has been associated with an increased risk of gametocytes, the transmissible stage of malaria. Daily prophylaxis with another antifolate combination, trimethoprim-sulfamethoxazole (TS), has been shown to reduce the incidence of malaria; however data on the impact of TS on gametocytemia is limited.
Methods: A total of 100 HIV–unexposed, 203 HIV-exposed (born to HIV-infected mothers) and 48 HIV-infected children were enrolled between 1.5-12 months of age and followed until 3 years of age. At enrollment all children were given long lasting insecticide treated nets and HIV-infected and breastfeeding HIV-unexposed children were prescribed TS prophylaxis. HIV-exposed children were randomized to discontinue TS after breastfeeding cessation and excluding HIV, discontinue TS at 2 years of age, or continue TS through 3 years of age. HIV infected children were prescribed TS prophylaxis for the duration of the study. Blood smears were performed when children presented with fever, during standardized 28-day malaria follow-up, and at routine monthly visits. Gametocytes were diagnosed by microscopy and reported as present or absent. We compared the monthly risk of gametocytemia in children prescribed TS and not prescribed TS, stratified by visit type, using generalized estimating equations adjusting for residence, age, and assigned antimalarial treatment group.
Results: There were 4000 complete months of observation with at least one blood smear done where TS was prescribed and 5061 months where TS was not prescribed. The median age in children not prescribed TS was 23 months compared with 15 months for those prescribed TS. Daily TS prophylaxis was associated with a lower monthly risk of malaria (19% vs. 43%, p<0.001). The overall monthly prevalence of gametocytemia in the cohort was 4.7% and gametocytemia was more common in months in which incident malaria occurred. Overall, there was no significant difference in the monthly risk of any gametocytemia (4.4% vs. 4.9%, adjusted RR=1.26, p=0.15). However on stratifying for visit type, TS prophylaxis was associated with a significant higher monthly risk of gametocytemia during months where malaria was diagnosed (7.7% vs. 4.8%, aRR=1.74, p=0.005) and during malaria follow-up (8.0% vs. 5.4%, aRR=1.74, p=0.001). There was a trend towards a higher risk during monthly routine and non-malaria follow-up visits (2.0% vs. 1.7%, aRR=1.55, p=0.09).
Conclusion: In our cohort, daily TS prophylaxis reduced the risk of malaria but increased the risk of gametocytemia when malaria occurred, which could potentially increase malaria transmission. There remains a need to assess the impact of TS prophylaxis on the risk of gametocytemia and malaria transmission in randomized controlled trials.

4 Incidence of malaria following discontinuation of trimethoprim-sulfamethoxazole prophylaxis given for different durations among HIV-exposed children

Muhindo Mary K, Victor Bigira, Abel Kakuru, Emmanuel Arinaitwe, Humphrey Wanzira, Jaco Homsy, Taylor Sandison, Prasanna Jagannathan, Jessica Briggs, Moses Kamya, Jordan W. Tappero, Grant Dorsey

Background: As per WHO guidelines, African children born to HIV-infected mothers (termed "HIV-exposed") are placed on trimethoprim-sulfamethoxazole (TS) prophylaxis until HIV infection can be excluded. There is strong evidence that TS reduces morbidity and mortality in adults and children infected with HIV. However, there are no recommendations for the use of TS prophylaxis among HIV-uninfected children beyond the period of exposure to HIV. We recently showed that TS prophylaxis in HIV-exposed children from cessation of breastfeeding until 2 years of age was associated with a 39% reduction in malaria incidence. However, it is not known what effect TS prophylaxis has on the development of antimalarial immunity and the incidence of malaria after TS is discontinued.
Methods: Data comes from an ongoing cohort study (TCC) being conducted in Tororo. HIV-exposed children aged 6 weeks – 9 months who were breastfeeding were enrolled and given a LLITN and prescribed daily TS prophylaxis. Children were randomized to one of the 3 following groups based on the duration TS was prescribed: Group 1 (n=87) – discontinuation after cessation of breastfeeding and confirmation of HIV-negative status (median 10 months of age); Group 2 (n=46) – discontinuation at 2 years of age; Group 3 (n=45) – discontinuation at 4 years of age. Malaria incidence was measured using a passive surveillance system with malaria defined as a fever and positive thick blood smear with a period of 14 days following each new episode of malaria excluded. Malaria episodes were treated with one of two randomly assigned artemisinin-based combination therapies. Malaria incidence following discontinuation of TS (allowing for a 1 month lag time) was compared among the 3 groups stratified by age categories using a negative binomial regression model controlling for location of residence and assigned antimalarial treatment regimen. Children will be followed until 5 years of age, however, results are preliminary as most children are currently between 3.5-4.5 years of age.
Results: Between the ages of 25-<49 months the incidence of malaria was similar for those who stopped TS at 2 years of age (7.20 episodes PPY) compared to those who stopped after breastfeeding (7.71 episodes PPY) (IRR=0.95, 95% CI 0.75-1.20, p=0.66). Between the ages of 49-<60 months the incidence of malaria was lower for those who stopped TS at 2 years of age (5.71 episodes PPY) and those who stopped at 4 years of age (4.89 episodes PPY) compared to those who stopped after breastfeeding (8.00 episodes PPY) although statistical significance was achieve for only the 2nd comparison (IRR=0.72, 95% CI 0.46-1.12, p=0.15 and IRR=0.57, 95% CI 0.35-0.93, p=0.03, respectively).
Conclusion: A longer duration of TS prophylaxis was associated with a lower incidence of malaria following discontinuation of TS among children over 4 years of age. These findings suggest chemoprophylaxis may enhance the development of antimalarial immunity among children living in an area of high transmission intensity.

5 Artemether-lumefantrine versus dihydroartemisinin-piperaquine for the treatment of uncomplicated malaria: longitudinal outcomes in a cohort of young Ugandan children

Humphrey Wanzira, Taylor G. Sandison, Abel Kakuru, Victor Bigira, Emmanuel Arinaitwe, Jaco Homsy, Jordan Tappero, Moses R. Kamya, Grant Dorsey

Background: There are limited comparative data on the long term effects of ACTs for the treatment of malaria. In a cohort of young Ugandan children living in a highly endemic area, we previously reported that artemether-lumefantrine (AL) and dihydroartemisinin-piperaquine (DP) were both highly efficacious, but DP was associated with better post-treatment prophylactic effect after 28 day follow-up. Here we aimed to compare longitudinal outcomes in this cohort.
Methods: Children were given a long-lasting insecticide treated bednet (LLITN) at enrollment and followed for all their health care needs. 39 children with a median age of 10.5 months (range 4-40) were randomized to AL (n=157) or DP (n=152) at the time of their first episode of uncomplicated malaria. The same treatment was given for all subsequent episodes of uncomplicated malaria and episodes of complicated malaria were treated with quinine. The incidence of malaria, complicated malaria, and hospitalizations with malaria were compared using a negative binomial regression model.

Results: Following randomization, children were followed a median of 31 months and a total of 3,671 treatments for malaria were given. The incidence of malaria following randomization was higher in the AL arm (5.58 episodes PPY) compared to the DP arm (4.78 episodes PPY), resulting in a 15% increase in the incidence of malaria (IRR=1.15, 95% CI 1.10-1.32, p=0.04). Following randomization, only 40 treatments with quinine (1%) were given for complicated malaria with the incidence of complicated malaria high in the AL arm compared to the DP arm (IRR=6.32, 95% CI 2.23-17.93, p=0.001). Similarly, the incidence of hospitalizations was higher in the AL arm compared to the DP arm (IRR 3.48, 95% CI 1.36-8.88, p=0.009). There was one death due to malaria in a children randomized to AL.
Conclusions: In this cohort of young children living in a highly endemic area the incidence of malaria was very high despite the use of LLITNs. Treatment with DP was associated with a modest decrease in the incidence of malaria and large relative decrease in the incidence of complicated malaria and hospitalizations with malaria. DP should be considered for first line therapy in young children living in highly endemic areas.

6 The ACT PRIME Study: Evaluating the impact of enhanced health facility-based care for malaria and febrile illnesses in children in Tororo, Uganda: Preliminary Findings

Catherine Maiteki-Sebuguzi, Florence Nankya, Samuel Gonahasa, Fred Mudangha, Deborah DiLiberto, Sarah Staedke

Background: The current approach to management of malaria and febrile illnesses in Ugandan children is inadequate. Substantial attention and resources have been focused on developing community-based interventions to deliver antimalarial treatment; however, the impact of these interventions compared to health facility-based care is not clear. ACT PRIME is designed to assess whether enhancing health facilities by training health workers and supplementing the supply of malaria drugs and diagnostics improves the health of children and quality of care delivered at lower-level government health facilities, as compared to 'standard care' currently available in Tororo, Uganda.
Methods: Twenty level II and III health centers in 7 sub-counties have been randomly assigned to the health facility intervention (HFI) or to standard care using a cluster-randomized design. The HFI has three components including: (1) training in-charges in health center management, (2) providing training to health workers in fever case management and patient-centered services, and (3) ensuring adequate supplies of artemether-lumefantrine and RDTs. To evaluate the impact of the intervention, a cross-sectional survey (CSS) was conducted at baseline in randomly selected children from each cluster, and will be repeated annually. A cohort of children has been recruited from households randomly selected per cluster at the start of the intervention, and will be closely followed for 2 years. All health facilities in the area will also be assessed; patient exit interviews will be conducted every 6 months in patients from each health facility, health care worker knowledge questionnaires will be administered annually, and health facility surveillance is being conducted monthly.
Results: Field activities began in early Dec 2010, and preliminary results are available. The baseline CSS was conducted from Dec 2010 to June 2011. A total of 8799 children were enrolled (4403 under-fives, 4396 aged 5-15 years). Of those enrolled, half (49%) had slept under an ITN during the previous night, 42% had a hemoglobin < 11.0 g/dL, 64% had a positive blood smear, and 42% were reported to have a fever or history of fever in the prior 48 hours; 81% of these had a positive RDT. Initial recruitment for the cohort study was conducted from Dec 2010 to March 2011, and a total of 840 children from 501 households were enrolled. Since then, an additional 46 children have been recruited from participating households. Of those enrolled, 44% had slept under an ITN during the previous night, 55% had a hemoglobin < 11.0 g/dL, 57% had a positive blood smear, and 46% were reported to have a fever or history of fever in the prior 48 hours; 79% of these had a positive RDT. The intervention was rolled out in May-June 2011, monthly health facility surveillance began in June 2011, and patient exit interviews and health worker knowledge questionnaires began in August 2011.
Conclusions: The ACT PRIME study runs until March 2013. Comparative data collection has just begun, limiting out ability to draw conclusions about the impact of the intervention. Here, we will present early results, specifically of the baseline CSS, cohort study, and monthly surveillance.

7 ACT PROCESS Study: Evaluating the process, context, and impact of the PRIME Study: preliminary results

Susan Nayiga, Clare Chandler, Lilian Taaka, Christine Nabirye, Deborah DiLiberto, Sarah Staedke

Background: The ACT PRIME trial aims to assess the impact on malaria-related health outcomes of a complex health facility intervention (HFI) to improve services provided by 10 public health centers compared with 10 standard care health centers in Tororo Uganda. The ACT PROCESS study is a comprehensive evaluation to further our understanding about the outcomes of the PRIME study. Our objectives are to understand (1) the process of the intervention: how it is implemented by the delivery team, how it is interpreted and operates in practice and what mechanisms of change can be identified, (2) the context of the intervention: what health center, community, district and political factors affect the uptake or interpretation of the intervention and what activities or externalities affect the outcome measures of the study; and (3) the wider impact of the intervention: how it affects other health center services, community perceptions and treatment seeking, private sector services and any unintended consequences within the district.
Methods: We are using a mixed-methods approach to the evaluation. We first developed a logic model to detail intended intervention activities and their mechanisms of effect on health outcomes and wider impacts, as well as contextual factors affecting mechanisms of effect and outcomes. We designed tools to test the logic model's hypotheses of change and to investigate alternative mechanisms of change as enacted in practice. Our data collection methods include self-filled questionnaires with trainers and participants, communication assessments of digital recorded consultations, contextual records at health centers, communities and districts, interviews with health workers, stakeholders and private sector workers and focus groups with community members.
Results: At the 9 workshops where the PRIME training intervention packages in health center management and patient-centered services were delivered, 37 participants and 5 trainers completed a total of 168 and 16 self-filled questionnaires, respectively. Likert scales were used to express opinions on the objectives, content, materials, and implementation of the workshops. The first of a series of 3-monthly context evaluations has taken place, consisting of interviews with the district health officer and other district-level officials, 20 in-charges from health centers, and 14 health assistants and opinion leaders from the community. Data have been collected about health-related activities carried out in the previous 3 months including distribution of bed nets, preventive drugs, educational materials, staffing changes and others. Communication assessments with health workers from both the HFI and standard care arms were conducted, 100 before and 111 after the PRIME training, consisting of coding of audio transcripts of consultations together with patient exit interviews.
Conclusions: The ACT PROCESS study runs until May 2012. Here, we will present analysis of early results, specifically of the communication assessments before and after the training. We will draw conclusions from our early results as far as possible,

particularly implications for our understanding of the mechanisms of change within the intervention as well as contextual factors affecting these and the overall PRIME outcomes.