

## **Rakai Health Sciences Program (formerly Rakai Project)**

### **1. Physical Geography**

Rakai District is one of the 56 administrative districts of Uganda and lies between longitudes 31°E and 32°E, and latitudes 0°S and 1°S. The district is located in the south-west of the country bordering the Republic of Tanzania in the south. The district has a total area of 4,973 Sq. Kms, with 3,889 sq. kms being land with a total population of 467,215.

The Rakai Health Sciences program, was initiated as Rakai Project in 1988 to study the magnitude and dynamics of the HIV disease. It represents a collaboration between the Uganda Virus Research Inst. of Uganda's Ministry of Health, researchers at Makerere University, Kampala, Columbia University, New York and Johns Hopkins University, Baltimore.

### **2. Procedures**

The project conducts extensive community epidemiologic and behavioral studies to document the HIV/STD epidemics and risk factors, implements HIV/STD preventive services and undertakes large community randomized intervention trials for HIV prevention, STD control and prevention of adverse outcomes of pregnancy.

The Rakai Community Cohort Study (RCCS) conducted by the Rakai Health Sciences Program in Rakai District, provides a unique resource for hypothesis generating and hypothesis testing research on HIV and other infections (including TB, malaria, STDs, HPV) and on maternal and child health (including prevention of mother-to-child HIV transmission and screening for cervical neoplasia). Using the RCCS as the basis for all activities, the Rakai Program has conducted major randomized HIV prevention trials, innovative operations research on prevention strategies; and has made fundamental contributions to knowledge of HIV transmission dynamics, viral molecular epidemiology (in preparation for HIV and HPV vaccine trials), novel findings regarding interactions between HIV and other co-infections (e.g., HSV-2, HHV-8, HCV, malaria, STDs and BV), and on the impact of HIV on fertility, family stability, marital violence and many other behavioral and demographic factors.

The RCCS is a population laboratory that provides prospective epidemiologic and behavioral data linked to biological samples. Multiple research studies are embedded within the cohort, making specific research projects feasible and highly cost effective. Also, the RCCS data and sample archives form a unique repository which facilitates research at low cost and with minimum time delays, allowing Rakai to rapidly address important policy questions (for example, the role of contaminated injections in HIV transmission). Through dissemination of research findings and dialogue with Ugandan health authorities at the District and Ministry of Health levels, as well as international agencies, the Rakai Program has enhanced translation of research into policy. The central role of the cohort in ongoing research is illustrated in the attached figure.

Using trained field teams for data collection, forms are brought in to the data department comprising of five graduate data supervisors and 19 data entry clerks. Using Foxpro applications all known data management practices including double data entry, scheduled inconsistency checks and edits, backup and routine archives are ensured.

### **Strategic research plan**

The Rakai **Program** has a strategic plan for hypothesis testing/generating and policy directed research for maximum utilization of the RCCS as follows:

***Hypothesis testing***

1. Randomized trials of male circumcision for HIV/STD prevention in men (HIV- men NIH-sponsored) and HIV+ men and in women and the community (Gates sponsored). (Both ongoing)
2. Randomized trial of male circumcision for HPV and cervical cancer prevention (Ongoing, embedded in 1)
3. Randomized trial of intensive malaria suppression during pregnancy for the prevention of mother to child HIV transmission. (Planned)
4. Future phase three trials of HIV vaccines
5. Future phase three trials of HPV vaccines.

***Hypothesis generating research***

1. Interactions between HIV and other endemic infections (HSV-2, HPV, malaria, TB, helminths) ongoing and planned
2. Molecular epidemiology of HIV, HPV and other infections in preparation for randomized trials
3. Microbiology of respiratory infections in HIV+ persons to determine appropriate prophylaxis and therapy
4. The role of sexual coercion, domestic violence and alcohol in HIV risk (ongoing observational studies)
5. Time trends in risk behaviors and condom use to assess potential behavioral disinhibition (ongoing)
6. Assessment of the utilization and effectiveness of VCT (ongoing)
7. The effects of maternal HIV status on child morbidity, growth, disability, mortality and social welfare (R01 being submitted Jan 1, 2004)

***Policy directed research:***

Operations research on:

1. Provision of antiretroviral therapy and OI prophylaxis/treatment in rural communities, including studies of cheap and feasible clinical and laboratory methods for screening and monitoring of therapy (planned)
2. Prevention of mother-to-child HIV transmission. (Study on proof of concept and effectiveness of maternal self-medication with nevirapine and maternal provision of infant syrup has been completed within the RCCS. Prevention of breast milk transmission and evaluation of PMTCT-Plus are being planned within RCCS. Expansion of nevirapine self-medication to communities outside the RCCS in process with the District Health Office.)
3. Utility of HPV assays from self-collected vaginal swabs for cervical cancer screening, and utility of colposcopy versus visual inspection with acetic acid in rural communities (ongoing observational studies, operation research planned)
4. Innovative approaches to family planning for prevention of unwanted pregnancy and reduced risk of MTCT (ongoing).
5. Mitigation of behavioral disinhibition and prevention of domestic violence, sexual coercion and mitigation of alcohol abuse for HIV prevention

***Direct study outputs include:***

1. Efficacy of circumcision for HIV, STD and HPV prevention in men and women

2. Effectiveness of innovative approaches for the prevention of MTCT, adult HIV, cervical neoplasia and unwanted pregnancy
3. Effectiveness of ARVs and OI prophylaxis/treatment, and impact on HIV transmission in populations
4. Molecular epidemiology and immunology of HIV and HPV for planning of vaccine trials

### **Clinical facilities**

We operate a mobile clinic that addresses general ailments presented during surveys. We also operate a static clinic at the field station that mostly addresses STDs and refers serious ailments to the district hospital.

### **Laboratory**

We have field based laboratory that performs routine tests for HIV and other STDs. In Entebbe the laboratory is being equipped for HIV basic sciences research.

### **IRB**

We have an Institutional Review Board (UVRI IRB) with an assurance number.

### **Some Publications**

#### **Rakai Publications:**

1. Wawer MJ, RH Gray, NK Sewankambo, D Serwadda, N Kiwanuka, TC Quinn. The probability of HIV acquisition per coital act among HIV-negative partners in monogamous, HIV-discordant couples; Rakai, Uganda. Submitted.
2. Wawer MJ, RH Gray, D Serwadda, X Li, N Kiwanuka, G Kigozi, MP Meehan, F Wabwire-Mangen, M Kiddugavu, T Lutalo, F Nalugoda, NK Sewankambo. HIV transmission per coital act by stage of index partner infection in discordant couples, Rakai Uganda. Submitted, *Lancet*.
3. Wabwire-Mangen F, G Kigozi, F Makumbi, MJ Wawer, NK Sewankambo, D Serwadda, LH Moulton, T Lutalo, MZ Chen, C Li, KL O'Brien, The Rakai Team, and RH Gray. Estimation of anthropometry and gestational age during the first two weeks of life: Rakai, Uganda. Accepted, *International J Obs Gyn*.
4. Bishai D, et al. Does biological relatedness predict survival? Accepted, *Demographic Research*.
5. Orroth KK, EL Kororomp, RG White, J Changalucha, SJ de Vlas, RH Gray, P Huges, A Kamali, A Ojwiya, D Serwadda, MJ Wawer, RJ Hayes, H Grosskurth. Comparison of STD prevalences in the Mwanza, Rakai and Masaka trial populations: the role of selection bias and diagnostic errors. *Sex Trans Infect* 2003, 79(2): 98-105.
6. Koenig MA, T Lutalo, F Zhao, F Nalugoda, F Wabwire-Mangen, N Kiwanuka, J Wagman, D Serwadda, M Wawer, R Gray. Domestic violence in rural Uganda: evidence from a community-based study. *Bull World Health Organ*, 2003: 81: 53-60.
7. Kelly RJ, RH Gray, NK Sewankambo, D Serwadda, F Wabwire-Mangen, T Lutalo, MJ Wawer. Age differences in sexual partners and risk of HIV-1 infection in rural Uganda. *J Acquir Immune Defic Syndr*. 2003, 32: 445-51.

8. Kiddugavu M, F Makumbi, MJ Wawer, D Serwadda, NK Sewankambo, F Wabwire-Mangen, T Lutalo, M Meehan, X Li, RH Gray. Hormonal contraceptive use and HIV-1 infection in a population-based cohort in Rakai, Uganda. *AIDS* 2003, 17: 233-40.
9. Korenromp, EL, R Bakker, SJ de Vlas, RH Gray, MJ Wawer, D Serwadda, NK Sewankambo, JD Habbema. HIV dynamics and behavioral change as determinants of the impact of sexually transmitted disease treatment on HIV transmission in the context of the Rakai trial. *AIDS* 2002, 16: 2209-18.
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11. Gray RH, MJ Wawer, N Kiwanuka, D Serwadda, NK Sewankambo, F Wabwire-Mangen. Male circumcision and HIV acquisition and transmission: Rakai, Uganda. *AIDS* 2002; 16: 809-10.
12. Korenromp EL, R Bakker, R Gray, MJ Wawer, D Serwadda, JD Habbema. The effect of HIV, behavioral change and STD syndromic management on STD epidemiology in sub-Saharan Africa: Simulation for Uganda. *Sex Trans Infect*. 2002, SI: i55-63.
13. Brahmabhatt H, D Bishai, F Wabwire-Mangen, G Kigozi, M Wawer, The Rakai Project Group and RH Gray. Polygyny, maternal HIV status and child survival: Rakai, Uganda. *Soc Sci and Med*, 2002, 55: 585-92.
14. Korenromp EL, NK Sudaryo, SJ de Vlas, RH Gray, NK Sewankambo, D Serwadda, MJ Wawer, JD Habbema. What proportion of episodes of gonorrhoea and chlamydia become symptomatic? *Int J STD AIDS* 2002; 13: 91-101.
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21. Wawer MJ, SM Eng, D Serwadda, MK Sewankambo, N Kiwanuka, C Li, RH Gray. Prevalence of Kaposi sarcoma-associated Herpesvirus compared with selected sexually transmitted diseases in adolescents and young adults in rural Rakai District, Uganda. *Sex Trans Dis*, 2001; 28: 77-81.

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