

**Framework in Global Health**  
**Global Health Scholars Program**

**February 2009 Fellowship Recipient**

**Proposal Title:**

**“Behavioral and Biological Correlates of HIV and STI Acquisition Among Women in South Africa”**

## **Brown Interdisciplinary Framework in Global Health: Global Health Scholarship**

### **Title: Behavioral and biological correlates of HIV and STI acquisition among women in South Africa**

#### **I. RESEARCH TRAINING SYNOPSIS**

##### ***A. Proposed dates of study:***

proposes to undertake research at the Perinatal HIV Research Unit (PRHU), Chris Hani Baragwanath Hospital (Soweto, Johannesburg, South Africa) between June 7, 2009 (immediately after completing his Year 1 and 2 PhD competency exams) and August 10, 2009. In order to optimize his research time while on-site, is already undertaking formative research and data analysis with Dr Lurie and his South African collaborators this upcoming academic semester.

##### ***B. Description of location and foreign institution:***

PHRU, established in 1996, is one of the largest HIV clinical care centers on the African continent (website: <http://www.phru.co.za/>). Located on site at Hani Baragwanath Hospital, PHRU is a research unit of the University of Witwatersrand. The research conducted at PHRU spans HIV clinical care, treatment, prevention, and other social science disciplines. Several Brown students have conducted research at the PHRU under the mentorship of Dr Lurie, and planned research at the PHRU will be conducted within the context of strengthening the HIV clinical and prevention research collaborations between the PHRU and Brown University.

##### ***C. Description of mentors:***

At Brown, has been mentored by Dr Mark Lurie and Dr Kenneth Mayer since embarking on his MD/PhD training program three years ago. Dr Lurie has provided regular advising and mentoring support for continued research examining HIV prevention and natural history in South India, and increasingly both he and have undertaken multiple projects examining HIV treatment outcomes and migration from African settings. Dr Lurie also serves as one of research advisors for his PhD dissertation in epidemiology. In South Africa, will be mentored by Dr Lurie's collaborators, Dr Neil Martinson and Dr Guy De Bruyn. Both Drs Martinson and Dr De Bruyn have expressed their commitment to mentoring and working closely with before, during, and after his research rotation in South Africa. has been in regular electronic and telephonic correspondence with both Dr Martinson and Dr De Bruyn planning his summer research as well as undertaking some preliminary analyses over the next few months in order to optimize his onsite research rotation.

##### ***D. Research and academic background of applicant:***

has extensive fieldwork experience working with clinical, biological, and social datasets from resource-limited settings. Over the last three years of his MD and PhD training, has completed six research rotations at YRGCARE, a tertiary care HIV/AIDS center in South India under the mentorship of Dr Mayer. This collaboration has led to close to thirty published scientific papers on HIV primary/secondary prevention and natural history (See appendix for list). The current proposed research in South Africa will extend and complement his research in India and will also be an integral module of his PhD dissertation. recently completed a study of correlates of HIV transmission among discordant South Indian heterosexual

couples (Int J of AIDS/STDS, in press), and the proposed study in South Africa examining further correlates of HIV acquisition will build on his global research under the joint mentorship of Drs Mayer and Lurie.

***E. Institutional Review Board (IRB) Approval:***

has currently completed certification in human subjects research of the Brown University IRB. Since his research at the PHRU will involve secondary data analyses of data already collected for pre-existing studies which will be de-identified (without personal patient information), separate IRB approval is not required at this time.

## **II. STUDY BACKGROUND**

***A. Conceptual basis:***

Of the estimated 40 million individuals living with HIV globally, it is estimated that 65% reside in sub-Saharan Africa, with heterosexual transmission as the primary mode of transmission[1]. Studies from the developed world have documented that a sizeable number of HIV-infected individuals continue to engage in unprotected sexual intercourse with HIV-serodiscordant partners[2, 3]. Unprotected intercourse may be more common among HIV-infected individuals in steady or regular relationships than in casual or non-regular sexual encounters[4]. Additionally, high plasma HIV ribonucleic acid (RNA) levels and sexually transmitted infections (STIs) may put the HIV-uninfected partner at continued risk of infection [5-11].

The increasing feminization of the HIV epidemic in resource-limited settings calls for the need of examining correlates of HIV transmission among women to further identify women-mediated HIV/STI prevention options. In sub-Saharan Africa, women have twice the risk of HIV infection compared to their male counterparts [12]. Current research suggests that there are multiple biological and behavioral risk factors for HIV transmission among women in serodiscordant relationships. Uninfected spouses are particularly at high risk for acquiring HIV due to high viral load, low condom use, and frequent STIs. In traditional societies, the use of preventive measures by HIV-uninfected partners may be further hampered by social stigma, reproductive issues, and gender inequality[13].

***B. Significance:***

The heterosexual transmission of HIV involves the complex interaction of both biological and behavioral factors. Improving our understanding of the behavioral and biological correlates of HIV transmission in women will assist in the development of culturally tailored counseling and care models for HIV-discordant couples[14], especially in the increasingly generalized and feminized epidemics of the developing world.

***C. Study aims:***

The present study aims to examine the biological and behavioral correlates of STI and HIV transmission among a sample of South African women:

1. Describe the incidence and correlates of acquisition of sexually transmitted infections
2. Examine the association between sexual risk taking behaviors and sexually transmitted infections and acquisition of HIV

## **III. STUDY METHODS AND DATA COLLECTION**

***A. Setting and participants:***

## IV. STUDY ANALYSIS AND PLAN FOR DISSEMINATION

### A. Study analysis

and his mentors will first examine the behavioral and biological correlates associated with the acquisition of STIs, with subset analysis utilizing PAP smear data to examine Human Papillomavirus (HPV) and ELISA for HSV-2. The next steps will be to longitudinally identify associations between sexual behaviors, demographic characteristics, and biologicals and the acquisition of STIs and HIV. and his mentors may also decide to employ a nested case-control study design to examine correlates of HIV transmission after further analysis of the data. It is anticipated that due to utilizing ACASI based data collection, bias will have been reduced due to the sensitivity associated with self-report of sexual behaviors.

Among the 1008 participants enrolled at PHRU accounting for a total of 1391 women-years of follow-up, a total of 47 seroconversions were documented. The overall incidence of HIV infection was 3.4 per 100 woman-years. Condom use increased at last sex reported, suggesting an increase in overall condom uptake. The primary aim of this study found no protective benefit in the provision of diaphragm and lubricant gel in addition to the provision of male condoms in the acquisition of HIV[15]. The secondary aim of this study found that the diaphragm and condoms compared to condoms alone did not significantly decrease the risk of acquisition of *C Trachomatis* or *N gonorrhoea*[16].

Current prevention technologies for HIV undergoing clinical trials, such as microbicides containing ART, pre-exposure prophylaxis, or vaccines, may not prevent STI infections. However, STI prevention remains crucial because these infections can increase the risk for HIV acquisition. The present study will add to our understanding of the behavioral and biological correlates of acquiring both STIs and HIV, and assist in the development of further women-centered STI/HIV prevention interventions.

### B. Study dissemination and future directions

Under the research mentorship of Dr Mayer, Dr Lurie, and Dr Cu-Uvin, is currently planning the themes of his PhD dissertation. The proposed research in South Africa with Dr Lurie will serve as one of his dissertation modules. The secondary prevention work completed among HIV-infected individuals receiving clinical care at YRGCARE, Chennai, India with Dr Mayer and his work examining HSV-2 in the genital tract of HIV-infected women with Dr Cu-Uvin will serve as the other themes.

As the present study is being conducted within the context of a wider research collaboration over the next few years, along with Dr Lurie, Dr. Martinson and Dr. De Bruyn also plan to conduct additional studies of the natural history of HIV in the era of highly active antiretroviral therapy. Some of the studies include: correlates and predictors of plasma viral load suppression, rate and presentation of opportunistic infections, impact of smoking on HIV immunological and virological disease progression, and spectrum of symptoms and signs of pre-malignant lesions among HIV infected patients receiving clinical care. These secondary clinical studies will provide with multiple opportunities for data analysis and opportunities for publication with the Brown and PHRU study teams within the context of his MD/PhD training program. It is anticipated that will return to continue research at the PHRU longitudinally as part of his MD/PhD training and that this formative summer experience will be the beginning of an ongoing scientific collaboration.

## V. BUDGET

Itemization	\$
Economy airfare (Roundtrip: Boston to Johannesburg)-cheapest obtainable flight	1,700
Living costs (housing)	1000
Food costs	300
Miscellaneous costs (transportation, copies, etc)	150
<b>TOTAL</b>	<b>\$3150</b>

### References

- [1] UNAIDS. UNAIDS/WHO AIDS epidemic update. 2007 [cited May 9, 2008]; Available from: <http://www.unaids.org/epidemic-update/>
- [2] van der Straten A, Gómez CA, Saul J, Quan J, Padian N. Sexual risk behaviors among heterosexual HIV serodiscordant couples in the era of post-exposure prevention and viral suppressive therapy. *AIDS*. 2000;14(4):F47-F54.
- [3] Hugonnet S, Moshia F, Todd J, Mugeye K, Klokke A, Ndeki L, Ross D, Grosskurth H, Hayes R. Incidence of HIV infection in stable sexual partnerships: a retrospective cohort study of 1802 couples in Mwanza Region, Tanzania. *Journal of Acquired Immune Deficiency Syndrome*. 2002;30(1):73-80.
- [4] Kalichman S, Rompa D, Luke W, Austin J. HIV transmission risk behaviours among HIV-positive persons in serodiscordant relationships. *International Journal of STD & AIDS*. 2002;13(10):677-82.
- [5] Serwadda D, Gray RH, Sewankambo NK, Wabwire-Mangen F, Chen MZ, Quinn TC, Lutalo T, Kiwanuka N, Kigozi G, Nalugoda F, Meehan MP, Ashley Morrow R, Wawer MJ. Human immunodeficiency virus acquisition associated with genital ulcer disease and herpes simplex virus type 2 infection: a nested case-control study in Rakai, Uganda. *Journal of Infectious Disease*. 2003;188(10):1492-7.
- [6] Quinn TC, M.J. Wawer, N. Sewankambo, D. Serwadda, C. Li, F. Wabwire-Mangen, M.O. Meehan, T. Lutalo, R.H. Gray. Viral load and heterosexual transmission of human immunodeficiency virus type 1. Rakai Project Study Group. *New England Journal of Medicine*. 2000;342:921-9.
- [7] Wawer M, Gray RH, Sewankambo NK, Serwadda D, Li X, Laeyendecker O, Kiwanuka N, Kigozi G, Kiddugavu M, Lutalo T, Nalugoda F, Wabwire-Mangen F, Meehan MP, Quinn TC. Rates of HIV-1 transmission per coital act, by stage of HIV-1 infection, in Rakai, Uganda. *Journal of Infectious Disease*. 2005;191(9):1403-9.
- [8] Malamba S, Mermin JH, Bunnell R, Mubangizi J, Kalule J, Marum E, Hu DJ, Wangalwa S, Smith D, Downing R. Couples at risk: HIV-1 concordance and discordance among sexual partners receiving voluntary counseling and testing in Uganda. *Journal of Acquired Immune Deficiency Syndrome*. 2005;39(5):576-80.
- [9] Gray R, Wawer MJ, Brookmeyer R, Sewankambo NK, Serwadda D, Wabwire-Mangen F, Lutalo T, Li X, vanCott T, Quinn TC; Rakai Project Team. Probability of HIV-1 transmission per coital act in monogamous, heterosexual, HIV-1-discordant couples in Rakai, Uganda. *Lancet*. 2001;357(9263):1149-53.
- [10] Freeman E, Glynn JR; Study Group on Heterogeneity of HIV epidemics in African Cities. Factors affecting HIV concordance in married couples in four African cities. *AIDS*. 2004;18(12):1715-21.
- [11] Fideli U, Allen SA, Musonda R, Trask S, Hahn BH, Weiss H, Mulenga J, Kasolo F, Vermund SH, Aldrovandi GM. Virologic and immunologic determinants of heterosexual transmission of human immunodeficiency virus type 1 in Africa. *AIDS Research and Human Retroviruses*. 2001;17(10):901-10.
- [12] WHO. HIV/AIDS epidemiological surveillance report for the WHO African Region: 2005 Update. WHO 2005.
- [13] Parker R, Aggleton P. HIV and AIDS-related stigma and discrimination: a conceptual framework and implications for action. *Social Science and Medicine*. 2003;57(1):13-24.
- [14] Lingappa J, Lambdin B, Bukusi EA, Ngure K, Kavuma L, Inambao M, Kanweka W, Allen S, Kiarie JN, Makhema J, Were E, Manongi R, Coetzee D, de Bruyn G, Delany-Moretlwe S, Magaret A, Mugo N, Mujugira A, Ndase P, Celum C; Partners in Prevention HSV-2/HIV Transmission Study Group. Regional differences in prevalence of HIV-1 discordance in Africa and enrollment of HIV-1 discordant couples into an HIV-1 prevention trial. *PLoS ONE*. 2008;3(1):e1411.
- [15] Padian N, van der Straten A, Ramjee G, Chipato T, de Bruyn G, Blanchard K, Shiboski S, Montgomery ET, Fancher H, Cheng H, Rosenblum M, van der Laan M, Jewell N, McIntyre J; MIRA Team. Diaphragm and lubricant gel for prevention of HIV acquisition in southern African women: a randomised controlled trial. *The Lancet*. 2007;370(9583):251-61.
- [16] Ramjee G, van der Straten A, Chipato T, de Bruyn G, Blanchard K, Shiboski S, Cheng H, Montgomery E, Padian N; MIRA team. The diaphragm and lubricant gel for prevention of cervical sexually transmitted infections: results of a randomized controlled trial. *PLoS ONE*. 2008;3(10):e3488.