Distribution Agreement

In presenting this thesis or dissertation as a partial fulfillment of the requirements for an advanced degree from Emory University, I hereby grant to Emory University and its agents the non-exclusive license to archive, make accessible, and display my thesis or dissertation in whole or in part in all forms of media, now or hereafter known, including display on the world wide web. I understand that I may select some access restrictions as part of the online submission of this thesis or dissertation. I retain all ownership rights to the copyright of the thesis or dissertation. I also retain the right to use in future works (such as articles or books) all or part of this thesis or dissertation.

Signature:

_____ _____

Caitlin Lam Date

Subtypes and risk behaviors among incident HIV cases in the Bangkok Men Who Have Sex with Men Cohort Study, 2006–2012

By

Caitlin Lam
MPH

Global Epidemiology

Patrick Sullivan, Committee Chair

Marcel E. Curlin, Chair Member

Timothy H. Holtz, Chair Member

Subtypes and risk behaviors among incident HIV cases in the Bangkok Men Who Have Sex with Men Cohort Study, 2006–2012

Caitlin Lam

MPH Candidate, 2013

ABSTRACT

Background

Recently, HIV transmission rates in Thailand have declined partly due to HIV policies established by the Thai Ministry of Public Health (MoPH). Nevertheless, within the men who have sex with men (MSM) community, the incidence and prevalence are alarmingly high. These high infection rates can partly be attributed to the greater prevalence of high-risk behaviors in this community. Thus, it is critical that we improve our knowledge of the epidemiology within this high-risk group and their behaviors, in order to effectively respond to the disproportionate disease burden in this population. We sought to describe the association between HIV strains and risk behaviors among urban Thai MSM seroincident HIV cases enrolled in the Bangkok MSM Cohort Study (BMCS).

Methods

The BMCS is an open longitudinal cohort study, with a maximum of 60 months of follow-up at 4-monthly intervals. Study variables included HIV subtype, HIV risk behaviors and sexually transmitted infection laboratory variables. The outcome variable was a dichotomoized measure of HIV strain, either circulating recombinant form (CRF) 01_AE or non-CRF01_AE. HIV strain was determined at time of seroconversion. Bivariate and multivariate analyses were conducted separately for each strain (non-CRF01_AE used an inclusion criteria of p-value ≤0.25 due to the small sample size) using Cox proportional hazard to assess the association between behavioral risk factors, laboratory variables, and incident HIV infection by subtype.

Results

A total of 188 seroconverters were included in this analysis: 154 were CRF01_AE strain and 34 were non-CRF01_AE strain, enrolled from April 2006 till May 2012. In the final model, use of drugs to enhance sexual pleasure (adjusted hazard ratio [AHR] 0.45, 95% CI: 0.28-0.73), intermittent condom use (AHR 1.82, 95% CI: 1.32-2.51), receptive only or both anal sex positions (AHR 1.92, 95% CI: 1.34-2.76), and HSV-1 (AHR 1.52, 95% CI: 1.09-2.11) and *T. pallidum* positivity (AHR 0.35, 95% CI: 0.20-0.62) were significantly associated with CRF01_AE seroconversion. Younger age, 18-21 year olds (AHR 3.65, 95% CI: 1.06-23.53) and 22-29 year olds (AHR 3.03, 95% CI: 1.04-8.82), use of club drugs (AHR 2.22, 95% CI: 0.89-5.52), group sex (AHR 2.32, 95% CI: 1.08-5.00) and HBV surface antigen positivity were significantly associated with non-CRF01_AE seroconversion.

Conclusion

There were some differences in the risk behaviors associated with incident CRF01_AE and non-CRF01_AE HIV subtype infection. Continued focus on this high-risk group, especially for young MSM, where most of incident cases are originating from, will be necessary in order to decrease HIV prevalence and transmission rates in future years.

Subtypes and risk behaviors among incident HIV cases in the Bangkok Men Who Have Sex with Men Cohort Study, 2006–2012

Caitlin Lam

MPH Candidate, 2013

Rollins School of Public Health | Emory University

Global Epidemiology

April 25th, 2013

Acknowledgements

I would like to thank the researchers and staff at the Thai Ministry of Public Health (MoPH), and the Silom Clinic, especially Dr. Timothy Holtz, Dr. Marcel Curlin, and Dr. Phillip Mock, for giving me the opportunity to research the HIV epidemic in Thailand, and for all of their support and mentorship from the conception, analysis, execution and writing of my thesis. I would also like to thank Dr. Patrick Sullivan for his mentorship and guidance throughout my thesis project. Lastly, I would like to thank the participants in the Bangkok MSM Cohort Study, without whom, this research would not be possible. Their participation in this study is instrumental to understanding the HIV epidemic, and their contribution to understanding the high-risk behaviors in this community will help prevent the spread of HIV/AIDS in Thailand.

Table of Contents

LITERATURE REVIEW

Thailand has the third highest adult HIV prevalence in Asia and the Pacific region (1); however, the country has attained exceptional success in decreasing transmission rates because of early and aggressive HIV prevention efforts. As early as 1991, HIV incidence in Thailand decreased dramatically (2). This accomplishment has made Thailand one the first countries to have achieved the sixth Millennium Development Goal, to reverse the spread of HIV/AIDS by 2015 (2).

Strong commitments from public health organizations, non-governmental organizations (NGOs) (3), the community, and government ministries facilitated a broad and effective early response to the epidemic. Interventions, such as the Royal Thai Government's policy of "100% condom use in commercial sex program" in 1991 (4, 5) played a pivotal role in the early decline in HIV transmission rates (6). This policy resulted in an increased awareness and knowledge of HIV transmission, in addition to a decrease in HIV prevalence and incidence.

Despite these achievements, recent evidence has shown that the epidemic is changing (1). The virus is spreading quite alarmingly among certain high-risk groups. Overall, young people in Thailand are becoming increasingly vulnerable to HIV infection. Additionally, as the epidemic matures, there will continue to be an increasing number of young adults who are living with HIV/AIDS and are reaching the stage in their infection when care and treatment are urgently required (2).

In recent years, HIV transmission rates in Thailand have declined as a result of HIV policies and prevention efforts established by the Thai Ministry of Public Health (MoPH) and NGOs (6). In particular, The Thailand National HIV/AIDS Plan targets marginalized and high-risk populations that currently drive the epidemic (7). However, within the men who have sex with men (MSM)

community, both the incidence and prevalence are alarmingly high (8). The Thai government currently estimates the MSM population to be around 550,571, or approximately 3 percent of the adult male population (9). In 2009, the prevalence in the MSM community was approximately 24.7% in 2009, while the prevalence was 1.3% within the general population (1). In Bangkok, surveillance data has shown an increase in HIV prevalence within MSM in the past decade. In 2003, 17.3% of MSM were infected with HIV, and these numbers rose to 28.3% in 2005 (10, 11).

The higher HIV infection rates among MSM can be attributed at least in part to the greater prevalence of high-risk behaviors in this community, including unprotected anal intercourse (UAI), especially receptive versus insertive UAI (12, 13, 14, 15), inconsistent condom use (16, 17), multiple sexual partners (18), group sex (19), recreational drug use (20), and binge drinking (21, 22). Cáceres (23) estimated the prevalence of same sex sexual activity among males in Southeast Asia to be around 6-12%, and approximately 50% of this MSM population engaged in high-risk behaviors. Recent evidence (4) suggests that a significant proportion of MSM engage in these risky behaviors placing them at an elevated risk of acquiring or transmitting HIV.

Currently Asia has the second highest HIV prevalence in the world (24). Countries in this region, including Hong Kong, Singapore and Japan, have experienced a significant increase in the rate of new infections between 2002 and 2008 (24). HIV incidence in MSM, especially young MSM, is remarkably high (15, 25, 26). This suggests that this young, high risk group experiences a greater risk of acquiring HIV infection. Reported rates are as high as 9/100 person-years in certain MSM under the age of 22 (15, 26). An understanding of the epidemiology of HIV transmission can be achieved through studying viral molecular epidemiology. These studies can help characterize transmission networks (27, 28) viral

transmission pathways between certain risk groups, and ultimately contribute to a better understanding of the changing trends in the evolution of the HIV epidemic.

Globally, HIV subtypes display different distribution patterns. Hemelaar (29) estimates that 50% of infections worldwide are subtype C, which also accounts for 56% of the infections in Africa. In Europe and Latin American HIV infections are dominated by subtype B, 74% and 88%, respectively, while the HIV subtypes present in Thailand reflect similar patterns to those seen in other Asian countries, such as China. Additionally, similar subtype distribution patterns are becoming more common within MSM in China (30, 31).

Historical HIV patterns within Thailand are also important to note, especially with regard to the subtype distribution among high-risk groups. The HIV epidemic in Thailand started around the late 1980's among intravenous drug users (IVDU) (32, 33). HIV subtype B and the circulating recombinant form (CRF) CRF01_AE were predominant during this time, and occurred independently as largely separate epidemics within risk groups: subtype B was the predominant subtype observed among IVDU whereas CRF01_AE was the most common strain among those exposed to HIV during heterosexual sex (33, 34). As the epidemic unfolded, CRF01_AE gradually became increasingly prevalent among the IVDU community (35). Currently, CRF01_AE is the dominant strain across all high-risk HIV groups, and the inter-mixing of these two common HIV-1 subtypes, through coinfection, has led to new CRF01_AE/B recombinant forms developing in Thailand (35, 36, 37, 38). Arroyo (37) estimated that within MSM, CRF01_AE accounted for 74.7% of HIV infections, and 81.1% of HIV infections among the general Thai population.

In light of these alarmingly high HIV infection rates, it is critical that we maximize the efficacy of our HIV prevention and control programs. This will in turn require that we improve our

understanding of HIV within Thailand. In response to documented HIV prevalence of 17% among MSM in Bangkok in 2003 (4), the Thailand Ministry of Public Health (MoPH) and U.S. Centers for Disease Control and Prevention (CDC) Collaboration (TUC) and its local partners established the Silom Community Clinic (SCC) in the Bangkok Christian Hospital in 2005, to serve as a dedicated HIV testing and STI testing and treatment clinic for MSM. Its broad aim is to be a model for the integration of HIV services and prevention research in MSM. Efforts to improve prevention and diagnosis of HIV infection among the MSM community in Thailand were initiated in 2006 by TUC, which established the Bangkok MSM Cohort Study (BMCS) at SCC. The BMCS conducts research on the epidemiology and prevention of HIV and (STI), and offers services, such as free, anonymous and confidential HIV voluntary counseling and testing (VCT) and STI services, and support and funding is provided by TUC. The research and findings from this cohort study have improved the understanding of the HIV epidemic in Thailand and have contributed to efforts to develop more effective behavioral interventions and methods to address the young MSM community, and helped bridge these interventions with care and treatment services to address the needs of this high-risk group.

The HIV prevalence and incidence rates in MSM in Thailand remain alarmingly high (15) in spite of progress made within the general population by health organizations, NGOs, and the government to prevent the spread of this disease. These high transmission rates highlight the urgent need for optimizing HIV prevention and control programs. Current efforts are hampered by an incomplete understanding of individual and social risk factors and behaviors leading to HIV transmission in MSM. Consequently, there is a critical need to improve our knowledge by conducting epidemiology research focusing on this high-risk group and their behaviors in order to effectively respond to the disproportionate disease burden in this community. Additionally, an

understanding of individuals' behavioral risk factors, as well as societal and environmental factors that contribute to the epidemic within this high-risk community can be useful in developing more effective and specific prevention and control programs targeting this high-risk group. With this in mind, we sought to describe the association between HIV strains and risk behaviors among urban Thai MSM seroincident HIV cases enrolled in the Bangkok MSM Cohort Study (BMCS). The findings from this study could serve as an important resource for HIV researchers, public health officials and HIV vaccine developers.

METHODS

Design

The BMCS is an open longitudinal cohort study, conducted at the SCC, with a maximum of 60 months of follow-up at 4-monthly intervals. The primary focus of the study is to assess the prevalence and incidence of HIV-1, distribution of subtypes among new infections, and behavioral risk factors associated with HIV infection in Thai MSM in Bangkok. During the process of recruitment, men are invited to the clinic where they are presented with information about the study and the option of voluntary participation. Volunteers willing to participate are then asked to provide written documentation of consent. All MSM are screened for HIV-1, and complete a survey administered by audio computer assisted self-interview (ACASI) at the time of study enrollment to assess behavioral factors. After the baseline visit, participants are expected to return for follow-up visits every four months. At each follow-up visit, participants complete a follow-up ACASI survey in order to track behavior changes. Additionally, individuals are screened for HIV, and receive pre- and post-test counseling. Participants who test HIV-positive are referred for treatment services. All participants schedule an appointment for a follow-up visit in 4 months, and the participant's phone number and email are checked to ensure that they are current. Individuals are reminded of this scheduled visit via a short message service (SMS) and by email two weeks before the appointment. At each visit, the participant receives 500 Thai Baht (approximately $US 16.60) to provide compensation for lost time at work and transportation expenses. The Thailand Ministry of Public health Ethical Review Committee for Human Subjects and a U.S. CDC Institutional Review Board Office of the Associate Director for the Science of the US CDC reviewed and approved the BMCS protocol.

Population and analytic sample

Participants are recruited by advertisement at MSM venues and popular Thai MSM Internet sites, during HIV voluntary counseling and testing (VCT) services provided at the study clinic, and by word of mouth. Additionally, potential participants are recruited through regular outreach activities conducted by local MSM community-based organizations, and are referred to the study site. Inclusion criteria for eligibility in the BMCS are Thai national, male at birth, at least 18 years of age, resident of Bangkok, reporting oral, or insertive or receptive anal sex with another man in the preceding six months of inclusion, committed for a minimum of 36 and a maximum of 60 months of follow-up at 4 month intervals, and willing and able to provide written informed consent.

Study variables

The study variables included HIV subtype, HIV risk behaviors and STI laboratory variables (Table 1).

Outcome variable

The outcome variable we assessed in this study was a dichotomized measure of HIV strain, either CRF01_AE or non-CRF01_AE. The latter category included both subtype B and CRF01_BE strain. HIV strain was determined at the time of seroconversion, as described below. Prevalent HIV infection cases were not included in the analysis.

Laboratory Analyses

The variable "HIV status at time of visit" was defined as the result of the HIV test on the day of the current visit. Participants were tested for HIV infection at each visit using OraQuick® HIV-1/2 Rapid Test (OraSure Technologies Inc., Oregon USA). If individuals tested positive with OraQuick®, three other different HIV rapid tests (Determine™ HIV 1&2, Abbott, Japan; Doublecheck™ II HIV 1&2 Organics Ltd., Israel; and Cappilus™ HIV-1/HIV-2, Trinity Biotech, USA) were performed on blood samples. If all three tests were positive, HIV infection was confirmed.

HIV-1 Genotyping by MHA

HIV-1 RNA was extracted from 200 µL of plasma using the QIAamp Viral RNA Mini Kit (Qiagen, USA). HIV-1 negative samples and water, and previously characterized HIV-1 positive samples were used as negative and positive controls, respectively. HIV-1 genotyping was performed by multi-region hybridization (MHAbce), optimized for the detection of HIV-1 subtype B, subtype C and CRF01_AE (39), using an ABI HT 7900 real-time PCR machine (Applied Biosystems, USA). Identification of circulating HIV-1 subtypes by MHA was performed according to established criteria (37) 1) a genotype was assigned when probe hybridization occurred in at least four of eight genomic regions; 2) a single subtype (B, C, or CRF01_AE) was assigned when all hybridizing probes were of the same subtype; 3) recombinant forms (BE, BC, CE, or BCE) were assigned when two or more different subtype probes hybridized in different regions of the genome; 4) infection with multiple subtypes was tentatively assigned when probes of two or more different subtypes hybridized in the same genome region; 5) "non-typeable" was assigned when there was probe reactivity in fewer than

four genomic regions; and 6) “non-amplifiable” was assigned when no evidence of PCR amplicon determined by SyberGreen, a fluorescent dye staining double-stranded DNA.

All apparent cases of dual infections were confirmed by cloning of PCR-amplified nucleic acids, followed by repeating MHA of individual clones. Briefly, PCR amplicons corresponding to the regions showing dual probe reactivity in MHA were ligated into TOPO vector (TOPO TA cloning, Invitrogen, USA) carrying plasmid encoding antibiotic resistance, and then transformed into competent cells. Transformants carrying ligated plasmids were selected on LB plates containing 50 μg/mL Kanamycin and β galactose. Subsequently, 16-32 ligated clones were used for repeated genotyping by MHAbce and for sequencing.

Genotyping by targeted genomic sequencing

All samples classified as “apparent dual infections” and seroincident samples classified as “recombinant” and “non-typeable” by MHA were further characterized by targeted genomic sequencing. For apparent dual infections, 2-12 transformed clones reactive by MHA were used for sequencing. For samples designated as “recombinant”, amplicons from all gene regions showing possible recombination by MHA were used for bulk sequencing. For samples designated as “non-typeable” by MHA (i.e., fewer than 4 gene regions with interpretable results), amplified DNA from all gene regions without MHA results were used for bulk sequencing. All sequencing was performed with Big Dye terminators on an ABI 3130 Capillary sequencer (Applied Biosystems, USA) as previously described (39, 40). Target gene sequences from the HIV-1 *p17, gag, rt, int, nef, gp41, pg120, tat* were aligned with selected reference strains from the Los Alamos HIV-1 database corresponding to HIV subtypes A, B, C, D, F, G, H, J, K, and circulating recombinant forms CRF01_AE, CRF15_01B, CRF33_01B, and CRF34_01B.

Alignments were made using ClustalW and manually edited using Genetic Data Environment (GDE 2.4, Rockville, USA) or MacClade 4.08a. Neighbor-joining phylogenetic trees were reconstructed in PHYLIP 3.68 and Geneious Pro5.5.6. Sequences clustering with a reference strain with a bootstrap value ≥70% were considered to be of the same subtype as the reference subtype (41). Visual inspection of the analyzed trees was used to verify apparent HIV-1 recombinant strains.

Other variables of interest

Time-constant variables, measured at baseline, and time-varying variables, measured at each visit, were collected using ACASI. These variables include socio-demographic and behavioral characteristics of the participants and laboratory variables (Table 1).

Behavioral Variables

The variable "binge drinking" was defined as "yes" for individuals who reported alcohol intoxication more than one time per week in the past four months. "Asian partner" was defined as Asian, but not Thai nationality. The variable "club drugs" included cannabis, ecstasy (MDMA), amphetamine, methamphetamine, ketamine, cocaine, and gammahydroxybutyrate.

For the variable "anal sex position with male", individuals were characterized as either "insertive" or "never receptive". Insertive anal position is considered to be less risky than receptive (42), and thus was used as the reference category for this variable (12, 13, 14, 15).

Laboratory Variables

Laboratory variables were tested at baseline and annually thereafter. Infection status with *N. gonohrrea*, rectal *C. trachomatis* was determined by performing ELISA on rectal swabs.

Hepatitis A virus (HAV), hepatitis B virus (HBV), hepatitis C virus (HCV), Anti-herpes simplex virus type 1 and 2 (HSV-1 and -2) infection status was determined by ELISA. *T. pallidum* antibody was confirmed by immunochromatography.

Statistical analysis

All analyses were performed using SAS (Version 9.2, SAS Institute, NC, USA) and OpenEpi.

Descriptive Analyses

Mean and proportion were used to describe the socio-demographic characteristics and sexual behaviors at baseline and follow-up visits. Crude HIV incidence was calculated as follows: number of newly HIV positive cases / number of person-years of follow-up. Associations between socio-demographic characteristics and sexual behaviors and HIV strain were assessed using the Pearson's chi-square test. Variables associated with the outcome with a p-value ≤ 0.05 were considered to be significant.

Bivariate and multivariate analysis

To identify behavioral risk factors and socio-demographic characteristics associated with HIV strain, variables and relevant interactions with a p-value ≤ 0.05 for CRF01_AE strain in bivariate logistic regression analysis were entered into a backward stepwise multivariate logistic regression. Due to the small analytic sample of non-CRF01_AE seroconverters, variables and relevant interactions with a p-value of ≤ 0.25 in the bivariate analysis were included in a backward stepwise multivariate logistic regression model. Cox proportional hazard analysis using a competing risk model was used to evaluate bivariate and multivariate behavioral risk

factors and laboratory variables for incident HIV infection by subtype to identify independent risk factors for incident HIV infection.

RESULTS

Descriptive Analyses

The analytic sample (N=1740) included participants enrolled from April 2006 till May 2012. We included a total of 188 seroconverters in this analysis: 154 were CRF01_AE strain and 34 were non-CRF01_AE strain.

As shown in Table 2, the mean age of CRF01_AE seroconverters was 28 years (age range: 18-52 years), 41.6% had university education, and 68.2% lived away from the family. During the 4 months prior to seroconversion, 7.1% reported binge drinking, 13.0% used drugs, 11.0% used 'club' drugs, 12.3% used drugs to enhance sexual pleasure, 9.1% inhaled nitrates and 12.3% used erectile dysfunction drugs. During the same time period, six or more sexual partners was reported by 33.1% of CRF01_AE seroconverters, intermittent condom use by 54.5%, anal sex position (receptive only or both) by 74.0%, having an Asian partner by 9.1%, having a foreign partner by 8.4%, having been coerced into sex by 20.1%. In the 4 months prior to seroconversion, having paid money for sex was reported by 9.1% of CRF01_AE seroconverters, received money for sex by 13.0%, and engaged in group sex by 24.0%.

The mean age of non-CRF01_AE seroconverters was 27 years (age range: 19-37 years), 50.0% had university education, and 61.8% lived away from the family (Table 2). During the 4 months prior to seroconversion, 8.8% reported binge drinking, 20.6% used drugs, 17.6% used 'club' drugs, 20.6% used drugs to enhance sexual pleasure, 17.6% inhaled nitrates and 11.8% used erectile dysfunction drugs. During the same time period, six or more sexual partners was reported by 35.3% of non-CRF01_AE seroconverters, intermittent condom use by 50.0%, anal sex position (receptive only or both) by 29.4%, having an Asian partner by 11.8%, having a foreign partner by 20.6%, having been coerced into sex by 20.6%. 8.8% paid money for sex,

2.9% received money for sex, and 29.4% engaged in group sex in the 4 months prior to seroconversion.

Prevalence of sexually transmitted infections

Rectal *N. gonorrhoea* and *C. trachomatis* was detected in 13.6% and 20.1% of CRF01_AE seroconverters, respectively. Laboratory evidence of past HAV infection, HBV surface antibody, HBV core antibody, HCV, HSV-1, and HSV-2 infection was detected in 26.0%, 4.5%, 58.8%, 44.4%, 1.3%, 64.3%, and 21.4% of CRF01_AE seroconverters, respectively. 8.4% tested positive for a history of *T. pallidum*.

Rectal *N. gonorrhoea* and *C. trachomatis* was detected in 14.7% and 20.6% of non-CRF01_AE seroconverters. Past HAV infection, HBV surface antibody and HBV core antibody, HSV-1, HSV-2, and *T. pallidum* infection was detected in 11.8%, 9.1%, 76.2%, and 30.0%, 55.9%, 17.6%, and 2.9% of non-CRF01_AE seroconverters, respectively.

Bivariate analysis

The overall HIV incidence in CRF01_AE seroconverters (Table 3) was 4.25 per 100 PY; among 18-21 and 22-29 year olds, and those 30 and older, the incidence was 6.50, 4.41 and 2.90 per 100 PY, respectively. Younger age, use of drugs, club drugs, inhaled nitrates, drugs to enhance sexual pleasure, erectile dysfunction drugs, having multiple sex partners, anal sex position (receptive only or both), receiving money for sex, engaging in group sex, HBV surface antibody, HSV-1, HSV-2 and *T. pallidum* antibodies were associated with incident CRF01_AE seroconversion.

The overall HIV incidence in non-CRF01_AE seroconverters (Table 4) was 4.24 per 100 PY. Among 18-21 year olds, the HIV incidence was 1.45, among 22-29 year olds it was 1.28, and among those 30 and older, it was 0.40 per 100 PY. Younger age, use of drugs, club drugs, inhaled nitrates, drugs to increase sexual pleasure, greater than 6 sexual partners, anal sex position (receptive only or both), engaging in group sex, positive laboratory test for HAV antibody and HBV surface antigen were independently associated with non-CRF01_AE seroconversion.

Multivariate analysis

In the final model (Table 3), use of drugs to enhance sexual pleasure (adjusted hazard ratio [AHR] 0.45, 95% CI: 0.28-0.73), intermittent condom use (AHR 1.82, 95% CI: 1.32-2.51), receptive only or both anal sex positions (AHR 1.92, 95% CI: 1.34-2.76), and HSV-1 (AHR 1.52, 95% CI: 1.09-2.11) and *T. pallidum* positivity (AHR 0.35, 95% CI: 0.20-0.62) were significantly associated with CRF01_AE seroconversion.

Younger age, 18-21 year olds (AHR 3.65, 95% CI: 1.06-23.53) and 22-29 year olds (AHR 3.03, 95% CI: 1.04-8.82), use of club drugs (AHR 2.22, 95% CI: 0.89-5.52), group sex (AHR 2.32, 95% CI: 1.08-5.00) and HBV surface antigen positivity were significantly associated with non-CRF01_AE seroconversion (Table 4).

DISCUSSION

Our study highlights the patterns of high-risk behaviors in Thai MSM seroconverters enrolled in the Bangkok MSM Cohort Study (BMCS). Binge drinking, intermittent condom use, anal sex position (receptive only or both), and positive HSV-1 antibody were found to be significantly associated with CRF01_AE seroconversion. Use of drugs to enhance sexual pleasure and positive *T. pallidum* antibody had a significant inverse association with CRF01_AE seroconversion. Non-CRF01_AE seroconverters had different high-risk behaviors associated with seroconversion. Younger age (<30 years old), use of club drugs, group sex and positive HBV surface antigen were significantly associated with non-CRF01_AE seroconversion. These results confirm the role that younger age, use of club drugs, binge drinking, intermittent condom use, anal sex position, group sex, and STIs play in the acquisition of HIV infection.

Our results are consistent with the literature on HIV-risk behaviors in MSM. Younger age has been recognized as an important risk factor for HIV seroconversion in previous studies (43), possibly due to lack of experience in anal sex and how to engage in safe sex, as well as a higher background prevalence of acute HIV infection.

Illicit drug use has also been associated with HIV infection in the literature (44). The use of recreational drugs should be a focus for public health education and prevention efforts as this could be a potential way to decrease HIV infection rates. Using these drugs may impair decision-making regarding safe sex practices, such as intermittent condom use, misjudgment of HIV infection risk, and engaging in sex with multiple partners at a time. Prevention and education about drug use should therefore be included in HIV prevention programs for MSM.

Our analysis also confirms known behaviors such as unprotected anal intercourse and receptive

anal intercourse as high-risk factors for HIV infection in MSM (30), especially for CRF01_AE seroconverters.

Coinfection of HIV and *T. pallidum* are often presented at the same time in infected individual, and it has been recognized that syphillis aids in the transmission and acquisition of HIV (45). In the US population, these coinfections are present in approximately 25% of primary and secondary cases of syphilis (45). It is interesting that in our study, *T. pallidum* infection had an inverse association with CRF01_AE seroconversion. This may be partly due to the fact that laboratory STI testing was conducted only once a year, unlike HIV testing which was done at every follow-up visit (three times per year). Depending on when an individual was diagnosed with HIV, he could already have been infected with *T. pallidum* before the annual visit to check for STIs was conducted.

Strengths and Limitations

This study included several limitations that should be addressed. Firstly, the men in this study were not a random sample of MSM in Bangkok. As a result, risk behaviors and HIV incidence may be different in the MSM community at large. A second limitation was the small number of seroincident cases (n=188) across the time period in this study, which decreased the power of the study and made it more difficult to observe differences between the two strains. Additionally, there was a disproportionate number of non-CRF01_AE compared to CRF01_AE seroconverters, which led to difficulties in finding differences in behavior patterns for non-CRF01_AE because of the small sample size. Consequently, there were more risk factors associated with CRF01_AE seroconversion as compared to non-CRF01_AE.

Our study had several strengths as well, including the long study period of six years, as well as the ability to evaluate STI infection, risk factors for HIV incidence and subtypes simultaneously in one design.

Future Directions

Directions for future study in this area include investigating whether the sexual behaviors associated with CRF01_AE are also consistent with the MSM population in Northern Thailand. Additionally, studying local epidemics where multiple subtypes co-circulate, and determining whether HIV subtype may be a virologic marker distinguishing diverse groups at risk of HIV infection will help improve the understanding of the transmission of HIV among high-risk populations. Given the historical link between non-CRF01_AE and drug use, it might be interesting to examine the possibility that older non-CRF01_AE IVDU men, engaging in insertive anal sex position, are introducing HIV infection into a population of younger HIV-receptive MSM. With additional research, this could be one important behavioral route worth targeting with specific prevention measures.

High rates of HIV transmission within the MSM community remain a public health concern for Thailand. The government has acknowledged that improvements can be made in this subgroup. The 2008 10th National Economic and Social Development Plan addressed the need for more provision and easy-access to condoms, lubricants, and education targeting MSM (6). Continued focus on this high-risk group, especially for young MSM where most of incident cases are originating from (46, 4), will be necessary in order to decrease HIV prevalence and transmission rates in future years.

REFERENCES

1) Office of the National Economic and Social Development Board. *Thailand Millennium Development Goals Report 2009*. Bangkok, Thailand; 2009.

2) United Nations Development Programme (Thailand). *Thailand's HIV Response: Progress and Challenges*. Bangkok, Thailand: United Nations Development Programme; 2004.

3) Denduang N, Charusomboon W. Role of NGOs in Prevention and Control of HIV/AIDS. Bangkok, Thailand: Mahidol University; 1993.

4) van Griensven F, Wimonsate W, Tanpradech S, et al. Trends in HIV prevalence, estimated HIV incidence and risk behavior among men who have sex with men in Bangkok, Thailand, 2003-2007. *J Acquir Immune Defic Syndr*. 2010;**53**:234-9.

5) Valdiserri RO, Ogden LL, McCray E. Accomplishments in HIV prevention science: implications for stemming the epidemic. *Nature Med* 2003;**9**:881-6.

6) Park LS, Siraprapasiri T, Peerapatanapokin W, et al. HIV transmission rates in Thailand: Evidence of HIV prevention and transmission decline. *J Acquir Immune Defic Syndr* 2010;**54**: 430-6.

7) Chitwarakorn A, Tantisak B. National plan for the prevention and alleviation of AIDS in Thailand 2002-2006. *Int Conf AIDS* 2002;Jul 7-12:14.

8) Solares D. Country Snapshots: Thailand HIV and men who have sex with men. UNDP, December 2012.

9) Peerapatanapokin, W. Estimated sizes of men who have sex with men (MSM), Power Point Presentation at Size Estimation Stake-Holder Seminar, 2012. Nonthaburi.

10) Mastro T, Limpakaarnjanart K. Condom use in Thailand: How much is it slowing the HIV/AIDS epidemic?. *AIDS* 1995;**9**: 523-25.

11) van Griensven F, Thanprasertsuk S, Jommaroeng R, et al. Evidence of a previously undocumented epidemic of HIV infection among men who have sex with men in Bangkok, Thailand. *AIDS* 2005;**19**:521-6.

12) van Griensven F, Tielman RA, Goudsmit J, et al. Risk factors and prevalence of HIV antibodies in homosexual men in the Netherlands. *Am. J. Epidemiol* 1987;**125**:1048-57.

13) Tindall B, Swanson C, Donovan B, Cooper DA. Sexual practices and condom usage in a cohort of homosexual men in relation to human immunodeficiency virus status. *Med. J. Aust.* 1989;**151**:318-22.

14) Piaseczna MA, Craib KJ, Li K, et al. Longitudinal patterns of sexual behavior and condom use in a cohort of HIV-negative gay and bisexual men in Vancouver, British Columbia, Canada, 1995-2000. *J. Acquir. Immune Defic. Syndr*. 2001;**28**:187-93.

15) van Griensven F, Thienkura W, McNicholl J, et al. Evidence of an explosive epidemic of HIV infection in a cohort of men who have sex with men in Bangkok, Thailand. *AIDS*, 2012; **26** (epub).

16) van Griensven F, van Winjgaarden JWDL, Baral S, Grulich A. The global epidemic of HIV infection among men who have sex with men. *Curr Opin HIV AIDS*, 2006;**4**:300-7.

17) Mansergh G, Naorat S, Jommaroeng R, et al. Inconsistent condom use with steady and casual partners and associated factors among sexually-active men who have sex with men in Bangkok, Thailand. *AIDS Behav*, 2006; DOI 10.1007/s10461-006-9108-4.

18) Valleroy, LA, MacKellar DA, Karon JM, et al. HIV prevalence and associated risks in young men who have sex with men. *JAMA* 2000;**284**:198-204.

19) Danta M, Brown, D, Bhagani S, et al. Recent epidemic of acute hepatitis C virus in HIV-positive men who have sex with men linked to high-risk sexual behaviours. *AIDS*. 2007;**21**:983-91.

20) Colfax G, Vittinghoff E, Husnik MJ, et al. Substance use and sexual risk: a participant- and episode-level analysis among a cohort of men who have sex with men. *Am J Epidemiol* 2004;**159**:1002-1012.

21) Woolf SE, Maisto SA. Alcohol use and risk of HIV infection among men who have sex with men. *AIDS Behav*. 2009;**13**:757-82.

22) George WH, Stoner SA. Understanding acute alcohol effects on sexual behavior. *Annu Rev Sex Res*, 2000;**11**:92-124.

23) Cáceres C, Konda K, Pecheny M, et al. Estimating the number of men who have sex with men in low and middle income countries. *Sex Transm Infect* 2006;**82** Suppl 3:iii3-9.

24) van Griensven F, de Lind van Wijngaarden JW. A review of the epidemiology of HIV infection and prevention responses among MSM in Asia. *AIDS* 2010;**24 Suppl 3**:S30-40.

25) Beyrer C, Artenstein A, Kunawararak P, et al. The Molecular Epidemiology of HIV-1 Among Male Sex Workers in Northern Thailand. *J Acquir Immune Defic Syndr and Hum Retroviruses* 1997;**15**:304-307.

26) Ananworanich J, Phanuphak N, de Souza M, Paris R, Arroyo M, Trichavaroj R, *et al.* Incidence and characterization of acute HIV-1 infection in a high-risk Thai population. *J Acquir Immune Defic Syndr* 2008,**49**:151-155.

27) Kouyos RD, von Wyl V, Yerly S, Boni J, Taffe P, Shah C*, et al.* Molecular epidemiology reveals long-term changes in HIV type 1 subtype B transmission in Switzerland. *J Infect Dis* 2010;**201**:1488-1497.

28) Hughes GJ, Fearnhill E, Dunn D, Lycett SJ, Rambaut A, Leigh Brown AJ. Molecular phylodynamics of the heterosexual HIV epidemic in the United Kingdom. *PLoS Pathog* 2009,**5**:e1000590.

29) Hemelaar J, Gouws E, Ghys P, Osmanov S. Global and regional distribution of HIV-1 genetic subtypes and recombinants in 2004. *AIDS*. 2006;**20**: W13-W23.

30) Beyrer C, Baral SD, van Griensven F, et al. Global epidemiology of HIV infection in men who have sex with men. *The Lancet* 2012;**380**:367-377.

31) Wang W, Jiang S, Yang K, et al. Identification of subtype B, multiple circulating recombinant forms and unique recombinants of HIV type I in an MSM cohort in China. *AIDS Res and Hum Retroviruses*. 2008;**24**:1245-54.

32) Xiridou M, van Griensven F, Tappero JW. The spread of HIV-1 subtypes B and CRF01_AE among injecting drug users in Bangkok, Thailand. *J Acquir Immune Defic Syndr*. 2007;**45**:468-75.

33) Tovanabutra S, Beyrer C, Sakkhachornphop S, et al.: The changing molecular epidemiology of HIV type 1 among northern Thai drug users, 1999 to 2002. *AIDS Res and Hum Retroviruses*. 2004;**20**:465–475.

34) Tovanabutra S, Polonis V, De Souza M, et al. First CRF01_AE/B recombinant of HIV-1 is found in Thailand. *AIDS*. 2001;**15**:1063-5.

35) Ramos A, Hu DJ, Vanichseni S, et al. New HIV type 1 CRF01_AE/B recombinants displaying unique distribution of breakpoints from incident infections among injecting drug users in Thailand. *AIDS Res and Hum Retroviruses*. 2003; 19(8): 667-74.

36) Praparattanapan J, Pathom-aree W, Kotarathitihum W, et al. Current molecular epidemiology recombination of HIV type 1 subtypes in Northern Thailand. *AIDS Res and Hum Retroviruses*. 2011; 27(11): 1201-6.

37) Arroyo MA, Phanuphak N, Krasaesub S, et al. HIV type 1 molecular epidemiology among high-risk clients attending the Thai Red Cross Anonymous Clinic in Bangkok, Thailand. *AIDS Res and Hum Retroviruses* 2010;**26**:5-12.

38) McCutchan FE, Hegerich PA, Bennan TP, et al. Genetic variants of HIV-1in Thailand. *Aids Res Hum Retroviruses*, 1992;**8**:1887-1895.

39) Kijak GH, Tovanabutra S, Sanders-Buell E, Watanaveeradej V, de Souza MS, Nelson KE, *et al.* Distinguishing molecular forms of HIV-1 in Asia with a high-throughput, fluorescent genotyping assay, MHAbce v.2. *Virology* 2007;**358**:178-191.

40) Carr JK, Torimiro JN, Wolfe ND, Eitel MN, Kim B, Sanders-Buell E, *et al.* The AG recombinant IbNG and novel strains of group M HIV-1 are common in Cameroon. *Virology* 2001,**286**:168-181.

41) Hillis DM, Allard MW, Miyamoto MM. Analysis of DNA sequence data: phylogenetic inference. *Methods Enzymol* 1993;**224**:456-487.

42) Vittinghoff E, Douglas J, Judson F, et al. Per-contact risk of human immunodeficiency virus transmission between male sexual partners. *American Journal of Epidemiology*1999;**150**:306-311.

43) Buchbinder SP, Vittinghoff E, Heagarty PJ, et al. Sexual risk, nitrite inhalant use, and lack of circumcision associated with HIV seroconversion in men who have sex with men in the United States. *J Acquir Immune Defic Syndr* 2005;**39**:82–89.

44) Nelson KE, Celentano DD, Eiumtrakol S, et al. Changes in sexual behavior and a decline in HIV infection among young men in Thailand. *N Engl J Med*. 1996; 335:297-303.

45) Chesson HW, Heffelfinger JD, Voigt RF, Collins D. Estimates of primary and secondary syphilis rates in persons with HIV in the United States, 2002. *Sex Transm Dis* 2005;**32**:265-269.

46) Prejean J, Song R, Hernandez A, et al. Estimated HIV incidence in the United States, 2006-2009. *PLoS One,* 2011;6:e17502.

Tables

Table 1. Time-varying and time-constant variables assessed in this study.

Time-varying variables		Time-constant variables
Behavior risk factors	**Laboratory variables**	
HIV status at time of visit	Rectal *N. gonorrhea**	Age at time of seroconversion
Engaged in binge drinking*	Rectal *C. trachomatis**	Education level at baseline
Used drugs*	HAV antibody*	Living situation at baseline
Used club drugs*	HBV surface antigen*	
Used erectile dysfunction drugs*	HBV core antibody*	
Inhaled nitrates (poppers)*	HCV antibody*	
Number of sexual partners*	HSV-1 antibody*	
Condom used with male partners*	HSV-2 antibody*	
Anal sex position with male partners*	*Treponema pallidum* antibody*	
Asian partner (not Thai)*		
Foreign partner*		
Coerced into sex*		
Paid for sex*		
Received money for sex*		
Group sex*		

*Time frame is past four months prior to the visit

Table 2. Demographic and behavioral risk factors for HIV prevalence in a cohort of MSM in Bangkok, Thailand, 2006-2012.

Characteristic	CRF01_AE n (%)	Non-CRF01_AE n (%)
Age group		
18-21	35 (22.7)	7 (20.6)
22-29	86 (55.8)	23 (67.6)
≥30	33 (21.4)	4 (11.8)
Education		
Primary	3 (1.9)	17 (50.0)*
Secondary/vocational	87 (56.5)	
University or higher	64 (41.6)	17 50.0
Current living situation		
Alone, roommate	105 (68.2)	16 (47.1)
With partner	11 (7.1)	5 (14.7)
With family	20 (13.0)	13 (38.2)
Binge drinking[1]		
Yes	11 (7.1)	3 (8.8)
No	143 (92.9)	31 (91.2)
Used drugs		
Yes	17 (11.0)	7 (20.6)
No	137 (89.0)	27 (79.4)
Nitrate inhalation[2]		
Yes	14 (9.1)	6 (17.6)
No	140 (90.9)	28 (82.4)
Drug use to increase sexual pleasure		
Yes	19 (12.3)	7 (20.6)
No	135 (87.7)	27 (79.4)
Erectile dysfunction drug use		
Yes	19 (12.3)	4 (11.8)
No	135 (87.7)	30 (88.2)
Number of sexual partners		
0	1 (0.6)	
1-5	102 (66.2)	22 (64.7)
≥6	51 (33.1)	12 (35.3)
Condom used with male partner		
Always	69 (44.8)	17 (50.0)
Not always	84 (54.5)	17 (50.0)
No anal sex partner	1 (0.6)	
Anal sex position with male partner		
Receptive only or both	114 (74.0)	10 (29.4)
Insertive	40 (26.0)	24 (70.6)
Asian partner		
Yes	14 (9.1)	4 (11.8)
No	140 (90.9)	30 (88.2)
Foreign partner		
Yes	13 (8.4)	7 (20.6)
No	141 (91.6)	27 (79.4)
Coerced into sex		

Yes	31 (20.1)	7 (20.6)
No	123 (79.9)	27 (79.4)
Paid for sex		
Yes	14 (9.1)	3 (8.8)
No	140 (90.9)	31 (91.2)
Received money for sex		
Yes	20 (13.0)	1 (2.9)
No	134 (87.0)	33 (97.1)
Group sex		
Yes	37 (24.0)	10 (29.4)
No	117 (76.0)	24 (70.6)
Rectal *N. gonorrhea*		
Yes	21 (13.6)	5 (14.7)
No	133 (86.3)	29 (85.3)
Rectal *C. trachomatis*		
Yes	31 (20.1)	7 (20.6)
No	123 (79.9)	27 (79.4)
HAV antibody		
Yes	40 (26.0)	4 (11.8)
No	114 (74.0)	30 (88.2)
HBV surface antigen		
Yes	7 (4.6)	3 (9.1)
No	136 (88.9)	30 (90.9)
HBV surface antibody		
Yes	60 (58.8)	16 (76.2)
No	42 (41.2)	5 (23.8)
HBV core antibody		
Yes	60 (44.4)	9 (30.0)
No	75 (55.6)	21 (70)
HCV antibody		
Yes	2 (1.3)	0 (0)
No	152 (98.7)	34 (100)
HSV-1 antibody		
Yes	99 (64.3)	19 (55.9)
No	55 (35.7)	15 (44.1)
HSV-2-antibody		
Yes	33 (21.4)	6 (17.6)
No	121 (21.4)	28 (82.4)
***T. pallidum* antibody**		
Yes	13 (8.4)	1 (2.9)
No	141 (91.6)	33 (97.1)

[1]Alcohol intoxication 2-3 times a week or more

[2]Club drugs include: annabis, 3,4-methylenedioxy-N-methylamphetamine (MDMA or ecstasy), amphetamine, methamphetamine, ketamine, cocaine, and gamma hydroxy butyrate (GHB)

* Primary and secondary/vocational education were merged together due to the small sample size

Table 3. Demographic, behavioral, and laboratory characteristics for HIV-incidence in a cohort of men who have sex with men CRF01_AE seroconverters in Bangkok, Thailand, 2006-2012.

			Bivariate analysis		Multivariate analysis	
Characteristic	HIV Incident cases/PY	Crude incidence (95% CI)	HR (95%CI)	P-value	HR (95%CI)	P-value
Total	154/3623	4.25 (3.61-4.96)				
Age group						
Mean (±SD)	28 (6.0)					
18-21	35/536	6.50 (4.60-8.94)	2.23 (1.38-3.58)	<0.01		
22-29	86/1949	4.41 (3.55-5.42)	1.53 (1.02-2.28)	0.04		
≥30	33/1138	2.90 (2.03-4.02)	1			
Education						
Primary	3/49	6.08 (1.55-16.55)	1.79 (0.565.71)	0.32		
Secondary/vocational	87/1692	5.14 (4.14-6.31)	1.51 (1.10-2.09)	0.01		
University or higher	64/1886	3.39 (2.64-4.31)	1			
Current living situation						
Alone, roommate	83/1563	5.31 (4.26-6.55)	1.67 (1.18-2.38)	<0.01		
With partner	22/521	4.22 (2.71-6.28)	1.33 (0.81-2.20)	0.26		
With family	49/1543	3.18 (2.38-4.16)	1			
Binge drinking[1]						
Yes	11/280	3.92 (2.0-6.82)	1.10 (0.59-2.03)	0.769		
No	143/3347	4.27 (3.61-5.02)	1			

Used drugs						
Yes	20/308	6.50 (4.08-9.86)	1.61 (1.01-2.58)	0.04		
No	134/3319	4.04 (3.40-4.77)	1			
Nitrate inhalation[2]						
Yes	14/147	9.50 (5.41-15.56)	2.40 (1.39-4.17)	<0.01		
No	140/3480	4.02 (3.40-4.73)	1			
Drug use to increase sexual pleasure						
Yes	19/186	10.19 (6.32-15.62)	0.38 (0.23-0.61)	<0.0001	0.45 (0.28-0.73)	<0.01
No	135/3441	3.92 (3.30-4.63)	1			
Erectile dysfunction drug use						
Yes	19/273	6.97 (4.32-10.68)	1.73 (1.07-2.80)	0.03		
No	135/3354	4.03 (3.39-4.75)	1			
Number of sexual partners, past 4 months						
0	1/259	0.39 (.019-1.90)	1			
1-5	102/2433	4.19 (3.44-5.07)	10.62 (1.48-76.11)	0.02		
≥6	51/935	5.46 (4.10-7.12)	13.65 (1.89-98.85)	0.01		
Condom used with male partner						
Always	69/2003	3.45 (2.70-4.33)	0.10 (0.01-0.75)	<0.01	0.12 (0.02-0.83)	<0.001
Not always	84/1332	6.31 (5.06-7.77)	1.85 (1.35-2.55)	<0.001	1.82 (1.32-2.51)	0.03
No anal sex partner	1/292	0.34 (0.017-1.69)	1			
Anal sex position with male partner						
Receptive only or both	114/2140	5.33 (4.42-	1.98 (1.38-	<0.01	1.92 (1.34-2.76)	<0.001

		6.38)	2.83)	
Insertive		2.69		
	40/1487	(1.95-3.63)	1	
Asian partner				
Yes		4.33	1.00	
	14/323	(2.47-7.10)	(0.58-1.75)	0.98
No		4.24		
	140/3304	(3.58-4.98)	1	
Foreign partner				
Yes		4.36	1.10	
	13/298	(2.42-7.26)	(0.57-1.79)	0.96
No		4.24		
	141/3329	(3.58-4.98)	1	
Coerced into sex				
Yes		5.31	1.33	
	31/584	(3.67-7.45)	(0.90-1.97)	0.16
No		4.05		
	123/3041	(3.38-4.81)	1	
Paid for sex				
Yes		3.54	1.22	
	14/395	(2.02-5.80)	(0.70-2.11)	0.48
No		4.33		
	140/3232	(3.66-5.10)	1	
Received money for sex				
Yes		6.61	1.61	
	20/299	(4.15-10.02)	(1.00-2.59)	0.04
No		4.03		
	134/3328	(3.39-4.76)	1	
Group sex				
Yes		6.98	1.85	
	37/530	(4.99-9.53)	(1.28-2.68)	<0.01
No		3.78		
	117/3097	(3.14-4.51)	1	
Rectal *N. gonorrhea*				
Yes		4.61	1.11	
	21/455	(2.93-6.93)	(0.70-1.76)	0.65
No	133/3167	4.20	1	

		(3.53-4.96)				
Rectal *C. trachomatis*						
Yes	31/532	5.83 (4.03-8.17)	1.48 (1.00-2.19)	0.05		
No	123/3091	3.98 (3.32-4.73)	1			
HAV antibody						
Yes	40/948	4.22 (3.06-5.69)	0.99 (0.69-1.42)	0.1		
No	114/2677	4.23 (3.53-5.10)	1			
HBV surface antigen						
Yes	7/92	7.64 (3.34-15.11)	1.78 (0.83-3.81)	0.14		
No	136/3337	4.08 (3.43-4.81)	1			
HBV surface antibody						
Yes	60/1911	3.14 (2.42-4.01)	0.54 (0.36-0.81)	<0.01		
No	42/708	5.94 (4.33-7.95)	1			
HBV core antibody						
Yes	60/1197	5.01 (3.86-6.41)	1.24 (0.88-1.73)	0.22		
No	75/1847	4.06 (3.22-5.06)	1			
HCV antibody						
Yes	2/24	8.48 (1.42-28.02)	0.49 (0.12-1.99)	0.32		
No	152/3602	4.22 (3.59-4.93)	1			
HSV-1 antibody						
Yes	99/1926	5.14 (4.20-6.23)	1.59 (1.15-2.22)	<0.01	1.52 (1.09-2.11)	0.01
No	55/1699	3.24 (2.46-4.18)	1			

HSV-2-antibody						
Yes	33/563	5.87 (4.10-8.14)	1.47 (1.00-2.17)	0.04		
No	121/3063	3.95 (3.29-4.70)	1			
***T. pallidum* antibody**						
Yes	13/97	13.43 (7.47-22.38)	0.30 (0.17-0.52)	<0.001	0.35 (0.20-0.62)	<0.001
No	141/3530	3.99 (3.38-4.70)	1			

[1]Alcohol intoxication 2-3 times a week or more

[2]Club drugs include: annabis, 3,4-methylenedioxy-N-methylamphetamine (MDMA or ecstasy), amphetamine, methamphetamine, ketamine, cocaine, and gamma hydroxy butyrate (GHB)

Table 4. Demographic, behavioral, and laboratory characteristics of non-CRF01_AE seroconverters in Bangkok, Thailand, 2006-2012.

			Bivariate analysis		Multivariate analysis	
Characteristic	HIV Incident cases/PY	Crude incidence (95% CI)	HR (95%CI)	P-value	HR (95%CI)	P-value
Total	34/3627	4.24 (3.6-4.9)				
Age group						
Mean (±SD)	7/484	1.45 (0.63-2.86)	3.75 (1.10-12.82)	0.04		
18-21	23/1799	1.28 (0.83-1.89)	3.38 (1.17-9.77)	0.02	3.65 (1.06-23.53)	0.04
22-29	4/1006	0.40 (0.13-0.96)	1		3.03 (1.04-8.82)	0.04
≥30	27 (4.1)				1	
Education						
Primary/Secondary/ vocational	17/1741	0.98 (0.59-1.53)	1.09 (0.55-2.13)	0.81		
University or higher	17/1886	0.90 (0.54-1.41)	1			
Current living situation						
Alone, roommate	16/1563	1.02 (0.61-1.63)	1.23 (0.59-2.57)	0.57		
With partner	5/521	0.96 (0.35-2.13)	1.15 (0.41-3.23)	0.79		
With family	13/1543	0.84 (0.47-1.40)	1			
Binge drinking[1]						
Yes	3/280	1.07 (0.27-2.91)	1.18 (0.36-3.88)	0.78		
No	31/3347	0.93 (0.64-1.30)	1			
Used drugs						
Yes	7/308	2.28 (1.00-4.50)	2.77 (1.20-6.37)	0.02		

No	27/3319	0.81 (0.55-1.17)	1			
Club drugs						
Yes	6/246	2.44 (0.99-5.08)	2.89 (1.19-6.98)	0.02	2.22 (0.89-5.52)	0.09
No	28/3381	0.83 (0.56-1.18)	1			
Nitrate inhalation[2]						
Yes	6/246	2.44 (0.99-5.08)	2.89 (1.19-6.98)	0.02		
No	28/3381	0.83 (0.56-1.18)	1			
Drug use to increase sexual pleasure						
Yes	7/186	3.76 (1.64-7.43)	4.66 (2.02-10.74)	0.0003		
No	27/3441	0.78 (0.53-1.13)	1			
Erectile dysfunction drug use						
Yes	4/273	1.47 (0.47-3.54)	1.59 (0.56-4.51)	0.39		
No	30/3354	8.94 (6.45-12.61)	1			
Number of sexual partners, past 4 months						
0						
1-5	22/2433	0.90 (0.58-1.35)	1			
≥6	12/935	1.28 (0.70-2.18)	1.60 (0.79-3.23)	0.19		
Condom used with male partner						
Always	17/1980	0.86 (0.52-1.35)	1			
Not always	17/1309	1.30 (0.78-2.03)	1.53 (0.78-2.99)	0.81		
No anal sex partner						
Anal sex position with male partner						
Receptive only or both	10/1487	0.67 (0.34-1.20)	1.67 (0.80-3.49)	0.17		

Insertive	24/2140	1.12 (0.74-1.64)	1			
Asian partner						
Yes	4/323	1.24 (0.39-2.99)	1.38 (0.49-3.62)			
No	30/3304	0.91 (0.62-1.28)	1			
Foreign partner						
Yes	7/514	1.36 (0.60-2.70)	1.55 (0.54-4.39)	0.41		
No	27/3113	0.87 (0.58-1.24)	1			
Coerced into sex						
Yes	7/584	1.2 (0.52-2.37)	1.36 (0.59-3.12)	0.47		
No	27/3041	0.89 (0.60-1.27)	1			
Paid for sex						
Yes	3/395	0.76 (0.19-2.07)	1.26 (0.39-4.13)	0.7		
No	31/3232	0.96 (0.66-1.35)	1			
Received money for sex						
Yes	1/299	0.33 (0.02-1.63)	0.35 (0.05-2.52)	0.29		
No	33/3328	0.99 (0.69-1.38)	1			
Group sex						
Yes	10/530	1.89 (0.96-3.36)	2.43 (1.16-5.08)	0.02	2.32 (1.08-5.00)	0.03
No	24/3097	0.77 (0.51-1.14)	1			
Rectal *N. gonorrhea*						
Yes	5/455	1.10 (0.40-2.43)	1.22 (0.47-3.15)	0.68		
No	29/3167	0.92	1			

		(0.62-1.30)				
Rectal *C. trachomatis*						
Yes	7/532	1.32 (0.58-2.60)	1.53 (0.67-3.52)	0.31		
No	27/3091	0.87 (0.59-1.25)	1			
HAV antibody						
Yes	4/948	0.42 (0.13-1.02)	0.38 (0.13-1.07)	0.07		
No	30/2677	1.12 (0.77-1.58)	1			
HBV surface antigen						
Yes	3/92	3.27 (0.83-8.91)	3.69 (1.12-12.13)	0.03	3.18 (0.97-10.48)	0.06
No	30/3337	0.90 (0.62-1.27)	1			
HBV surface antibody						
Yes	16/1911	0.84 (0.50-1.33)	1.19 (0.44-3.28)	0.73		
No	5/704	0.71 (0.26-1.57)	1			
HBV core antibody						
Yes	9/1197	0.75 (0.37-1.38)	0.66 (0.30-1.45)	0.3		
No	21/1847	1.14 (0.72-1.71)	1			
HCV antibody						
Yes	0/24					
No	34/3602					
HSV-1 antibody						
Yes	19/1926	0.99 (0.61-1.51)	1.11 (0.57-2.19)	0.76		
No	15/1699	0.88 (0.51-1.42)	1			
HSV-2-antibody						
Yes	6/563	1.06 (0.43-2.22)	1.16 (0.48-2.80)	0.74		

No	28/3063	0.91 (0.62-1.30)	1	
***T. pallidum* antibody**				
Yes	1/97	1.03 (0.05-5.09)	1.13 (0.16-8.30)	0.9
No	33/3530	0.93 (0.65-1.30)	1	

[1]Alcohol intoxication 2-3 times a week or more

[2]Club drugs include: annabis, 3,4-methylenedioxy-N-methylamphetamine (MDMA or ecstasy), amphetamine, methamphetamine, ketamine, cocaine, and gamma hydroxy butyrate (GHB)