Patterns of HIV and syphilis infection in Northern Thailand 1998–2001

Chris Beyrer MD MPH*, **Surinda Kawichai** MA PhD*, **Joseph A Hyder** MS-IV MHS†, **Sompoth Borwornsin** MPH‡, **Namtip Srirak** PhD§, **Chawalit Natpratan** MD MPH**, **David D Celentano** ScD* and **Chirasak Khamboonruang** MD PhD§

*Johns Hopkins Bloomberg School of Public Health, Baltimore, MD; †School of Medicine, University of California San Diego, San Diego, CA, USA; ‡Ministry of Public Health, Communicable Diseases Control Region 10, Chiang Mai; §Research Institute for Health Sciences, Chiang Mai University, Chiang Mai, Thailand; **Family Health International HIV/AIDS Program, Phnom Penh, Cambodia

Summary: Northern Thailand has been the epicentre of a largely heterosexually transmitted HIV epidemic that has recently involved married women. In preparation for HIV-prevention trials, we investigated patterns of HIV and syphilis risk through annually measured HIV and syphilis prevalence among northern Thai, peri-urban, community-dwelling men ($n = 2564$) and women ($n = 3907$) aged 18–35 years between 1998 and 2001. Crude HIV and syphilis prevalence were 3.3% and 2.7% for men and 2.3% and 2.1% for women, respectively. In logistic regression models of HIV and syphilis, compared with married men/women, widowers and widows were at increased risk (odds ratio; 95% confidence interval) of syphilis (7.86; 1.56–39.6 and 3.3; 1.14–9.61, respectively) and HIV (12.68; 3.23–49.8 and 41.3; 24.3–70.3, respectively). The oldest women were at lower risk of HIV (0.43; 0.22–0.85). For men and women, those with syphilis were approximately three times more likely to have HIV. These unique population data illustrate evolving sex parity of HIV burden in northern Thailand.

Keywords: HIV/AIDS, syphilis, Thailand, widow

INTRODUCTION

Northern Thailand has been the epicentre of the Thai HIV/AIDS epidemic that began in 1988. The rapid growth of the Thai epidemic in the early 1990s was due, in part, to high rates of male patronage at commercial sex establishments[1,2] and high prevalence of sexually transmitted diseases (STDs), including syphilis,[3] among female commercial sex workers (CSWs)[3] and their male clients.[4] Throughout the early 1990s, HIV prevalence in northern Thai provinces was several times higher than in other regions, as shown by sentinel surveillance among military conscripts and female CSWs.

Begun in the early 1990s, Thailand's '100% Condom Campaign' focused on increasing condom use in commercial sex and this resulted in decreased incidence of STDs in the Thai military and dramatic decreases in HIV prevalence over time in serial cohorts of the new military recruits[5] as well as decreases in HIV prevalence among CSWs.[6]

By the mid-1990s, surveillance data from antenatal clinics (ANCs) revealed a risk shift towards married women as HIV prevalence among ANC attendees peaked at more than 6.4% in northern Thailand around 1994 and at 10% among first-time mothers.[7] This shift in risk signalled the beginnings of a generalized HIV epidemic in Thailand as HIV spread from historically 'high-risk groups' of injection drug users, CSWs, and their clients to the general population. Since 1997, however, few reports have described HIV or other STD prevalence levels in the general northern Thai population. Such information is critical to evaluate the latest changes in the Thai epidemic and to design relevant prevention strategies.

In this report, we present data from serial measures of HIV and syphilis prevalence among peri-urban, northern Thai men and women aged 18–35 years who enrolled in a prospective study of HIV incidence between 1998 and 2001. Serial prevalence data were examined to reveal more recent demographic patterns of HIV and syphilis.

Correspondence to: Dr Chris Beyrer, Johns Hopkins Bloomberg School of Public Health, Suite EH52, 615 N Wolfe St, Baltimore, MD 21205, USA
Email: cbeyrer@jhsph.edu

METHODS

This study was reviewed and approved by the Institutional Review Boards of The Johns Hopkins University Bloomberg School of Public Health, Baltimore, MD, USA, and the Medical Ethics Committee of Chiang Mai University, Chiang Mai, Thailand.

Participants were recruited as part of an investigation to assess the feasibility of peri-urban community-based cohorts for large-scale HIV vaccine prevention trials. Study

participants were recruited from among in the general adult population living in peri-urban communities in northern Thailand through a multi-pronged 'snowball' recruitment network described previously.[8] All enrolled participants were 18–35 years of age, Thai nationals, resided in the target communities around Chiang Mai, intended to remain in the community for at least six months, and were willing to give informed consent to participate. Participants in the 1998 study were aged 18–35 years.

The data reported here are the baseline results from four, prospective studies conducted annually between 1998 and 2001. Each study consisted of two phases, a baseline and a six-month follow-up. The follow-up data will be reported separately.

At baseline, potential participants were seen at community study sites. Trained counsellors provided group pre-test counselling and explanation of the study objectives and process. Participant right to decline to enroll or continue was emphasized to assure there was no coercion to participation. After the participants had signed the consent form, they were issued a study ID card with a unique study identification number. The participants then had blood drawn for testing for HIV antibodies, and one-on-one gender-matched interviews using a structured questionnaire. The interview included sociodemographic data and a history of syphilis and HIV counselling and testing history. Participants were scheduled to receive their individual HIV test results and confidential individual post-test counselling 2–3 weeks later at a community health clinic or hospital. For all participants, the counsellors re-assessed the client's risk behaviour and discussed a personalized risk-reduction plan, when appropriate. Participants were referred for treatment or clinical evaluation, as appropriate, at this visit. The participants received 200 baht (about $5 US at the time) for their time and travel costs.

All participants had HIV-1 enzyme-linked immunosorbent assay (ELISA) testing on specimens collected at baseline. All HIV-1 ELISA reactive sera from the baseline visit were confirmed by Western blot. Syphilis status was first investigated among all participants with the rapid plasma reagin (RPR) test. Reactive RPR samples were further tested with the *Treponema pallidum* haemagglutination (THPA) test. Positive results for both tests were necessary to be considered active.

Individual data were entered twice in separate files and then validated using EpiInfo version 6.04 (US Centers for Disease Control and Prevention, Atlanta, GA, USA). Percent distributions, χ^2tests, odds ratios (OR) and 95% confidence intervals (CI) were utilized for data analysis. *P* values were not adjusted for multiple comparisons. Annual HIV and syphilis prevalence were compared for men and women separately. Initial data were investigated by year of enrolment, and similarity across years allowed for collapsing of data to investigate demographic attributes. Multiple logistic regression models were used to identify independent-risk attributes, or adjusted OR, for prevalent HIV and syphilis infection. Data analyses were performed using SAS version 9.1 (SAS Institute, Cary, NC, USA).

RESULTS

Characteristics of the study participants by year of enrolment are shown in Table 1. Between 1998 and 2001,

Table 1 **Characteristics of study participants by sex and year of study**

	Men					Women				
	1998	**1999**	**2000**	**2001**	***P* value**	**1998**	**1999**	**2000**	**2001**	***P* value**
n	351	964	813	436		509	1370	1384	644	
Age (SE)	28.4	28.0	27.9	27.4	0.0128	29.6	29.0	28.6	28.1	0.001
Age percent					0.0164					0.001
18–24	25.6	28.0	25.5	31.0		17.1	19.5	22.2	23.5	
25–30	31.0	31.1	40.5	37.6		30.5	33.4	35.8	39.8	
30–35	42.5	40.9	34.1	31.4		52.5	47.2	42.0	36.8	
Marital history (%)					0.841					0.537
Never married	35.6	36.3	34.0	31.9		9.6	12.9	10.6	14.0	
Still married	58.7	58.2	60.9	64.0		84.1	80.4	79.6	75.6	
Separated/divorced	4.3	4.9	4.4	3.7		2.6	4.4	6.7	7.3	
Widow/er	1.1	0.4	0.5	0		2.6	1.8	2.5	2.5	
Missing (*n*)	1	2	2	2		(6)	(8)	(9)	(4)	
Education					0.001					0.001
⩽Primary	25.4	16.8	12.4	13.3		31.4	27.0	16.1	14.6	
Middle School	35.9	35.5	39.6	39.7		42.6	41.2	50.7	47.4	
High School	27.9	33.5	36.5	32.8		17.9	21.7	24.9	26.1	
Post-Secondary	10.8	14.2	11.4	14.0		11.1	10.1	8.3	11.8	
Missing (*n*)	0	0	0	1		(0)	(0)	(0)	(1)	
Prevalent HIV										
% (*n*)	4.8 (17)	4.4 (42)	1.7 (14)	2.5 (11)	0.004*	3.0 (15)	2.0 (27)	2.3 (32)	2.6 (17)	0.593
Prevalent syphilis										
% (*n*)	4.6 (16)	2.3 (22)	2.5 (21)	2.3 (10)	0.134	2.2 (11)	2.0 (27)	2.0 (28)	2.5 (16)	0.891

*P for trend=0.003

a total of 2564 men and 3907 women, all ethnic Thai and aged between 18 and 35 years in age at the time of enrolment, participated in the study. Although each year of the study enrolled progressively younger participants, mean ages (SD) varied little across years for both men (27.9 [4.7] years) and women (28.8 [4.5] years).

The younger demographic profile over time is confirmed by the increasing fraction of women who have never been married. No significant differences in marital status by cohort year were observed for either men or women. Over the study period, significantly greater fractions of both male and female participants had more than minimal levels of education. Across years of the study, greater rates of syphilis testing, but not HIV testing, were observed over time for both men (P for trend = 0.0046) and women (P for trend = 0.001). Between 1998 and 2001, prevalence of HIV among male study participants declined from 4.8% in 1998 to 2.5% in 2001 (P for trend = 0.003). Syphilis prevalence among men also declined between 1998 (4.6%) and 2001 (2.3%), but did not differ significantly over the time of the study (P for trend = 0.15).

Characteristics of HIV prevalence in the study population are displayed in Table 2. Among men, 84 of 2564 (3.3%) were HIV seropositive compared with 91 of 3907 (2.3%) among women ($P = 0.02$). HIV prevalence did not vary significantly across age categories among men ($P = 0.34$) or women ($P = 0.07$). Although greater HIV prevalence occurred with increasing age among men, the trend was not significant (P for trend = 0.14).

Marital status was significantly associated with HIV prevalence among men ($P = 0.002$) and women ($P = 0.001$). HIV prevalence was significantly greater among never married (4.3%) and widowed (25.0%) men than among currently married (2.5%) and divorced (3.5%) men. Among women, those currently separated and divorced had significantly higher HIV prevalence (4.2%) than those currently married (1.5%). No unmarried women in the sample population had HIV. Education was significantly associated with HIV prevalence for men ($P = 0.003$) but not for women ($P = 0.29$). Previous HIV test, reported by 25.2% of men and 29.6% of women, was significantly associated with having HIV, among women (crude OR = 1.90; 95% CI 1.28–2.89) but not men (crude OR = 1.05; 95%CI 0.64–1.72).

Characteristics of syphilis prevalence in the study population are displayed in Table 3. Among men, 69 of 2564 (2.7%) had syphilis compared with 82 of 3907 (2.1%) among women. The prevalence between groups did not differ significantly ($P = 0.12$).

Age was significantly associated with syphilis among both men ($P = 0.001$) and women ($P = 0.005$), with greater syphilis prevalence among older age groups in both men and women.

Marital status was associated with syphilis prevalence among both men ($P = 0.045$) and women ($P = 0.002$) with the lowest rates among the unmarried and highest rates observed among widows and widowers. Widows in this study were not significantly older than the newly married women (mean ages 29.4 and 29.3 years, respectively; $P = 0.73$). Greater levels of education were significantly associated with lower syphilis prevalence among men ($P = 0.001$) but did not reach significance for this association among women ($P = 0.091$).

Previous syphilis test, but not previous HIV test, was significantly associated with syphilis status among men (crude OR = 2.7, $P = 0.001$).

Table 4 presents the results from four multiple logistic regression models. Sex-specific, disease-specific models examined attributes of prevalent HIV and prevalent syphilis for each sex separately.

Among men, age was significantly associated with syphilis ($P = 0.001$). The oldest age group (31–35 years) had the greatest risk (OR = 5.99; 95% CI 2.20–5.82) relative to the youngest age group (18–24 years). Age was not significantly associated with HIV among men ($P = 0.710$).

Table 2 **HIV prevalence of the study population by sex and demographic characteristics**

	Men				Women			
		HIV-positive				HIV-positive		
	No.	*n*	%	OR	No.	*n*	%	OR
	2564	84	3.3		3907	91	2.3	*P*=0.022
Age (years)				*P*=0.339				*P*=0.067
18–24	702	18	2.6	1	812	20	2.5	1
25–30	905	29	3.2	1.26	1364	41	3.0	1.23
31–35	957	37	3.9	1.53	1731	30	1.7	0.70
Marital history				*P*=0.002				0.001
Never	890	38	4.3	1.72	461	0	0	—
Currently	1541	39	2.5	1	3118	47	1.5	1
Separated	114	4	3.5	1.40	213	9	4.2	2.88
Widowed	12	3	25.0	12.8	88	34	38.6	41.1
Missing	7	(0)	(0)	—	27	1	3.7	—
Education				*P*=0.008				*P*=0.315
⩽Primary	410	25	6.1	2.88	847	20	2.4	1.12
Middle School	963	36	3.7	1.72	1788	48	2.7	1.28
High School	861	19	2.2	1	901	19	2.1	1
Post-Secondary	329	4	1.2	0.55	370	4	1.1	0.51
Missing	1	0				1	0	

Table 3 **Syphilis prevalence of the population by sex and demographics characteristics**

	Men				Women				
		Syphilis positive				Syphilis positive			
	No.	*n*	%	OR	No.	*n*	%	OR	
	2564	69	2.7		3907	82	2.1	*P*=0.123	
Age (years)				*P*=0.001				*P*=0.005	
18–24	702	5	0.7	1	812	4	0.5	1	
25–30	905	17	1.9	2.70	1364	32	2.4	4.85	
31–35	957	47	4.9	7.20	1731	46	2.7	5.51	
Marital history				*P*=0.045				*P*=0.002	
Never	890	21	2.4	0.88	461	3	0.7	0.32	
Currently	1541	41	2.7	1	3118	63	2.0	1	
Separated	114	5	4.4	1.68	213	10	4.7	2.39	
Widowed	12	2	16.7	7.32	88	5	5.7	2.92	
Missing	7	0	0.0	—	27	1	3.7	—	
Education				*P*=0.001				*P*=0.091	
⩽Primary	410	21	5.1	6.59	847	28	3.3	2.34	
Middle School	963	38	4.0	5.01	1788	41	2.3	1.60	
High School	861	7	0.8	1	901	13	1.4	1	
Post-Secondary	329	3	0.9	1.12	370	0	0.0	NA	NA

Table 4 **Results of four, sex-specific multiple logistic regression models of current infection**

	Men				Women			
	HIV		Syphilis		HIV		Syphilis	
Variable	**OR**	**95% CI**	**OR**	**95% CI**	**OR**	**95% CI**	**OR**	**95% CI**
Age (years)		*P*=0.71		*P*=0.001	*P*=0.039		*P*=0.063	
18–24	1	—	1	—	1	—	1	—
25–30	1.26	0.67–2.37	2.25	0.80–6.36	0.77	0.42–1.39	3.5	1.23–10.2
31–35	1.31	0.67–2.58	5.99	2.20–5.82	0.43	0.22–0.85	3.3	1.14–9.61
Marital history		*P*=0.001		*P*=0.021		*P*=0.001		*P*=0.007
Never	2.26	1.39–3.69	1.65	0.94–2.90	NA	NA	0.69	0.21–2.24
Currently	1	—	1	—	1	—	1	—
Separated	1.56	0.54–4.48	2.21	0.84–5.82	2.84	1.37–5.90	2.72	1.37–5.42
Widow(er)	12.68	3.23–49.8	7.86	1.56–39.6	41.3	24.3–70.3	2.70	1.05–6.95
Education		*P*=0.002		*P*=0.002		*P*=0.758		*P*=0.359
⩽Primary	2.95	1.51–5.75	3.73	1.53–9.11				
Middle School	1.73	0.98–3.08	4.32	1.90–9.79				
Secondary	1	—	1	—	1			
Post-Secondary	0.51	0.17–1.53	1.32	0.34–5.21				

Among women, however, those 25-30 years and 31-34 years old were at significantly greater risk of syphilis compared with the younger women (OR = 3.5; 95% CI 1.23–10.2 and OR = 3.3; 95% CI 1.14–9.61, respectively). Compared with the youngest women, the oldest women had significantly less risk of HIV (OR = 0.43; 95% CI 0.22-0.85).

Married men were at the lowest risk for both HIV ($P = 0.001$) and syphilis ($P = 0.021$). Relative to married men, widowers were significantly more likely to have HIV (OR = 12.68; 95% CI 3.23-49.8) and syphilis (OR = 7.86; 95% CI 1.56-39.6).

Compared with married women, widows were at exceptionally high risk for HIV (OR = 41.3; 95%CI 24.3-70.3) and were at significantly elevated risk of prevalent syphilis (OR = 2.70; 95% CI 1.05-6.95), similar to that of separated women (OR = 2.72; 95%CI 1.37-5.42). Both syphilis and HIV were uncommon among unmarried women, including older unmarried women (analyses not shown).

Among men, education level was significantly associated with HIV ($P = 0.002$) and syphilis ($P = 0.002$), with the more educated at lower risk of disease. Patterns of decreased risk associated with educational level were observed among women, but these patterns were not significant for either HIV ($P = 0.758$) or syphilis ($P = 0.359$) (data not shown). Current HIV infection was associated with current syphilis infection among both men (crude OR 4.84; 95% CI 2.32–10.12) and women (crude OR 4.16; 1.86–9.29).

DISCUSSION

This study reports on patterns of HIV and syphilis prevalence between 1998 and 2001, among a large number of community-dwelling, peri-urban, northern Thai men

and women aged 18–35 years, populations for whom estimates of these diseases are sparse. The patterns of disease documented provide unique information on the evolution of the Thai HIV epidemic, with the benefit of syphilis, a bacterial, curable, and regularly screened-for STD, as a referent. Key findings include the following: (1) HIV prevalence was not associated with age among men but was significantly associated with younger age among women, (2) the risk for HIV was very high among widowers and widows relative to their married counterparts. Despite a compelling anecdotal literature on HIV vulnerabilities associated with spousal death,[9] this study quantitatively documents the greater HIV burden among this group.This study demonstrated a significant association between HIV and younger age among women, a pattern previously documented among ANC attendees.[10] Women in this study aged 18–24 years had an HIV prevalence (2.5%) nearly equal to that of men in the same age group (2.6%).

In contrast to HIV patterns, risk of prevalent syphilis was significantly greater among older men and older women. This finding in a population under 35 years old warrants further investigation, particularly given the possibility of regular re-infection by a male spouse.

Most striking, however, are the distribution of HIV and syphilis by marital status; among the 88 widows in the study, HIV prevalence was comparable with prevalence among female CSWs in Bangkok at the peak of the Thai epidemic. Widow status is most likely attributable to partner death from HIV/AIDS, and HIV status is the result of infection during marriage rather than during widowhood. This is confirmed by HIV prevalence nearly eight times that of syphilis among widows. The comparatively lower risk of prevalent syphilis among widows also suggests that HIV may have been acquired during marriage rather than after. Studies of sexual behaviour among northern Thai women confirm this possibility.[11]

Conclusions from this study are constrained given non-random recruitment methods and the measure of prevalent rather than incident disease. Further, participants enrolled did so anticipating follow-up in six months. Despite this, all baseline participants are included in analysis and rates of HIV are on par with regional estimates indicating external validity. HIV and syphilis were prevalence measures and reflect lifetime prior risk for HIV and more recent prior risk for syphilis.

This study provides evidence of a generalized HIV epidemic among younger men and women in northern Thailand and substantial HIV burden among men and women who have lost a spouse. Separated/divorced men and women as well as widows and widowers would stand to benefit especially from voluntary HIV counselling and HIV testing, and STD screening and services.

REFERENCES

1 Celentano DD, Nelson KE, Suprasert S, *et al.* Dynamics of risk behavior for HIV infection among young Thai men. *J Acquir Immune Defic Syndr Hum Retrovir* 1995;**10**:477–83

2 Celentano DD, Nelson KE, Suprasert S, *et al.* Behavioral and socio-demographic risks for frequent visits to commercial sex workers among northern Thai men. *AIDS* 1993;**7**:1647–52

3 Ungchusak K, Rehle T, Thammapornpilap P, Spiegelman D, Brinkmann U, Siraprapasiri T. Determinants of HIV infection among female commercial sex workers in northeastern Thailand: results from a longitudinal study. *J Acquir Immune Defic Syndr Hum Retrovir* 1996;**12**:500–7

4 Celentano DD, Nelson KE, Suprasert S, *et al.* Risk factors for HIV-1 seroconversion among young men in northern Thailand. *JAMA* 1996;**275**:122–7

5 Nelson KE, Eiumtrakul S, Celentano D, *et al.* The association of herpes simplex virus type 2 (HSV-2), *Haemophilus ducreyi*, and syphilis with HIV infection in young men in northern Thailand. *J Acquir Immune Defic Syndr Hum Retrovir* 1997;**16**:293–300

6 Celentano DD, Bond KC, Lyles CM, *et al.* Preventive intervention to reduce sexually transmitted infections: a field trial in the Royal Thai Army. *Arch Intern Med* 2000;**160**:535–40

7 Bunnell RE, Yanpaisarn S, Kilmarx PH, *et al.* HIV-1 seroprevalence among childbearing women in northern Thailand: monitoring a rapidly evolving epidemic. *AIDS* 1999;**13**:509–15

8 Kawichai S, Beyrer C, Khamboonruang C, *et al.* IV incidence and risk behaviours after voluntary HIV counselling and testing (VCT) among adults aged 19–35 years living in peri-urban communities around Chiang Mai city in northern Thailand, 1999. *AIDS Care* 2004;**16**:21–35

9 Ojikutu BO, Stone VE. Women, inequality, and the burden of HIV. *N Engl J Med* 2005;**352**:649–52

10 Xu F, Kilmarx PH, Supawitkul S, *et al.* HIV-1 seroprevalence, risk factors, and preventive behaviors among women in northern Thailand. *J Acquir Immune Defic Syndr* 2000;**25**:353–9

11 Kilmarx PH, Supawitkul S, Wankrairoj M. Explosive spread and effective control of HIV in northeast Thailand: the epidemic in Chiang Rai province, 1988–99. *AIDS* 2000;**14**:2731–40

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