

FEASIBILITY OF NORTHERN THAI FACTORY WORKERS AS PARTICIPANTS IN HIV VACCINE TRIALS

Chawalit Natpratan¹, Darawadee Nantakwang¹, Chris Beyrer², Piyada Kunawarak¹, Chadatarn Gunhom³, David D Celentano², Kenrad E Nelson² and Chirasak Khamboonruang³

¹Royal Thai Ministry of Public Health Thailand; ²Johns Hopkins University, Baltimore, MD, USA;

³Chiang Mai University, Chiang Mai, Thailand

Abstract. To determine the feasibility of establishing a cohort of HIV-1 seronegative factory workers for potential HIV vaccine trials, and other HIV preventive interventions, we enrolled and followed 499 male and female industrial workers in Lamphun Province, northern Thailand. A baseline demographic and HIV seroprevalence survey was conducted by a mobile team at worker's housing units in Lamphun Province in 1994. Follow-up HIV and syphilis incidence rates were measured 6 months later. The study was voluntary, anonymous, and included HIV pre- and post-test counseling, HIV and syphilis serology, and a self-administered fact sheet. A total of 106 men and 393 women were recruited. The median age was 22 years, and the mean 23.4 years. Educational levels were moderate; 41.9% had some secondary school and 23.6% had completed secondary school. HIV prevalence was 2.4% overall but differed by sex; among men it was 7/106, 6.6%, among women 5/393, 1.3%, OR = 5.49 (95% CI = 1.52, 20.39). Low educational levels were associated with HIV infection, OR = 7.2 (95% CI = 2.2, 23.4). Syphilis prevalence was 3.8%. Follow-up at 6 months was successful for 420/499 subjects, 84.2%, and varied by sex: 73/106 men, 68.9%, returned while 347/393 women, 88.3%, did so, RR = 1.21 (95% CI = 1.07, 1.37). There were 5 incident HIV-1 infections, a rate of 2.1/100 person years. The HIV seroconversion rate differed by sex, but not significantly; it was 4.1/100 person years for men and 1.5/100 person years for women. This population is largely young, female, and at considerable HIV risk. If follow-up could be improved, factory workers in northern Thailand could be an appropriate population in which to mount HIV preventive efficacy studies, including vaccine trials.

INTRODUCTION

The problem of AIDS in Thailand has been well documented (Weniger *et al*, 1991; Brown *et al*, 1994). Possibly as many as 800,000 people are currently infected with HIV. One model of the future burden of HIV/AIDS in Thailand predicts 3.5 million infected persons by the year 2000, with 320,000 living AIDS cases and 170,000 deaths by midyear 2000 (Viravaida *et al*, 1993), making Thailand one of the most AIDS-prone countries in South-east Asia (Mann *et al*, 1992). The socio-economic impact of HIV and AIDS in Thailand is likely to be extensive, and these losses are projected to be largely due to the effects of HIV and AIDS among the young adult workforce (Viravaida, 1993). Studies of HIV prevalence and incidence among industrial workers are therefore of considerable importance. We report on the first such study among

factory workers in northern Thailand.

While social, behavioral, and public health measures are critical to controlling the HIV epidemic in the densely populated Asian region, an effective prophylactic HIV vaccine would be a powerful tool in the struggle against HIV/AIDS. The Government of Thailand, in collaboration with WHO, published a "National Plan for HIV Vaccine Evaluation" in 1993. The plan calls for the establishment of potential cohorts for vaccine trial evaluations, the collection of baseline epidemiologic data on these populations, and quantification of rates of new HIV infections. While a number of potential HIV vaccine cohorts are currently under development in Thailand, these cohorts have tended to be in special populations somewhat outside the "mainstream" of northern Thai society (Celentano *et al* 1995; Weniger, 1994; Nelson *et al*, 1994a,b) including female commercial sex workers, military conscripts, injecting drug users, and STD clinic attendees. While there are some data on prevalent HIV infections in the general Thai population of sexually active adults, there have been few attempts

Correspondence: Dr Chris Beyrer, Research Institute for Health Sciences, Chiang Mai University, PO Box 80 CMU, Chiang Mai 50200, Thailand.
Tel: 662 53-221966; Fax: 662 53-221849

to establish prospective cohorts drawn from community or workplace based samples which could evaluate incident HIV-1 infection rates in general sexually active population.

Lamphun province is one of the six "upper north" provinces in Thailand, the region with the highest HIV infection rates in the country (Royal Thai MOPH, 1994). The Center for Disease Control Region 10 does semi-annual sentinel surveillance for HIV in select populations throughout these six provinces. In Lamphun the populations surveyed have included female commercial sex workers (CSWs), male STD clinic attenders, antenatal clinic users (ANC), and volunteer blood donors. HIV prevalence rates for these groups (N = 100 or N = 200) are shown in Table 1. A survey done by the Ministry of Public Health in six northern provinces in 1991 found that Lamphun had the highest percentage of outpatient visits for confirmed STDs of any province: 47.5% of all Health Department visits in Lamphun were for confirmed STDs, as opposed to 15.4% for Chiang Mai, and 23.1% for Lampang, Lamphun's two neighboring provinces (Royal Thai MOPH, 1993).

Traditionally an agricultural province, with a population of 406,500 in 1992, of whom about 70% live in rural areas, Lamphun is currently a rapidly industrializing area (Lamphun Provincial Chief Medical Office, 1994). The province is home to the Northern Industrial Estate (Ni Khom Usahakam Park Nua), a manufacturing zone with over 500 factories and mills and a growing population of industrial workers. These factories principally

manufacture electronics, computer components, textiles, processed foods, and animal feeds. In the suburban and rural areas around Lamphun's Northern Industrial Estate a number of workers' hostels and informal worker's housing projects have sprung up to meet the housing demands of this large population of resident workers. Many of the workers live in company housing, but as many as 5,000 live in informal housing around the Estate. These workers tend to be recent secondary or vocational school graduates, with between 6-12 years of education. Approximately 30% are men and 70% are women. The majority are from Lamphun and other northern provinces. A number of brothels, bars and other sites where sexual services are available have also sprung up around this zone, a response to the needs of young male factory workers who are often separated from wives or girlfriends while resident in the area.

MATERIALS AND METHODS

A mobile team of nurses and counseling staff from the Thai Ministry of Public Health STD Clinic in Lamphun conducted all study visits. The study was comprised of 4 visits; a baseline visit, followed by a visit to report HIV test results (approximately 4-6 weeks later), and a follow up visit 6 months after the baseline, with an HIV notification and counseling visit shortly thereafter. At the initial visit, subjects who agreed to participate were given a study number and a numbered study card. No names were used, only unique subject identifiers,

Table 1

Ministry of Public Health HIV Sentinel Surveillance data among female commercial sex workers (CSWs), male STD clinic users, pregnant women (ANC), and blood donors, Lamphun Province, 1992-1995.

Month/year*	%CSWs	%Male STDs	%ANC	%Blood donors
June '92	60.3	36.5	3.5	0.8
Dec '92	54.4	30.6	8.3	2.5
June '93	62.8	24.7	4.6	2.1
Dec '93	61.2	28.0	6.2	1.4
June '94	62.3	20.0	4.6	1.9
Dec '94	58.5	17.1	2.3	1.4
June '95	44.0	19.0	9.9	3.2

* Samples = 100-200 subjects in each risk category per sentinel.

ensuring anonymity. Informed consent was obtained at the enrolment visit. Each subject was given an information sheet explaining the study and a voluntary informed consent to sign. All subjects had pre-test counseling on this first visit. Blood was drawn for HIV and syphilis testing at the time of enrolment, and 6 months later. At both visits subjects filled out a short anonymous questionnaire on demographic data, including age, sex, marital status, length of time at current position, and length of time at current residence. HIV risk factors, reported HIV serostatus, and sexual and reproductive histories were not assessed with this instrument. Subjects were matched across visits by study number and study number card, with age and sex used as validity checks.

Blood samples tested for HIV-1 antibodies using a commercially available (ELISA Behring, Berlin) with confirmation by Western Blot (Organon Teknika, Durham, NC). Syphilis serology was done with VDRL (Cambridge Biomedical, Boston) and THPA (Sero Dia-TP, Fujirebio, Tokyo). Subjects were offered appointments at the MOPH STD clinic in Lamphun city 4-6 weeks after each blood draw for HIV post-test counseling. Subjects found to be HIV-1 seropositive, and or VDRL positive, were given appropriate referrals for clinical care at the MOPH clinic or hospital.

The data were analyzed using odds ratios (OR) and relative risks (RR) and 95% confidence intervals for discrete variables, *t*-tests for continuous variables, and Fisher's exact test.

The study was approved by the ethical committees of the Royal Thai Ministry of Health, Chiang Mai University, the World Health Organization, and the Johns Hopkins University.

RESULTS

A total of 499 subjects were enrolled in the study between July and September, 1994. The sample comprised 106 men, 21.2%, and 393 women, 78.8%. The median age was 22 years, with a mean of 23.4 years, and a range of 15 to 50 years. About 90% were aged 30 years of age or less. The majority of subjects, 69.4%, were never married, 26.8% were currently married, 1.8% divorced, and 1.8% either separated or widowed. Educational levels were moderate; 86/499 subjects, 17.2%, had 6 years of primary school or less, 41.9% had some secondary school, 23.6% had completed secondary school, and 15.4% had either technical school or university level education.

The sample was drawn largely from the northern region of Thailand; 46.7% were from the upper north, 10.4% were from the lower north, 14.0% were from the northeast (Isan), 3.4% were from central Thailand and the rest were from Bangkok or southern Thailand.

A total of 15/499 subjects had reactive HIV ELISAs. Of these, 12 were confirmed with Western Blot, 1 was indeterminate on WB, and 2 were WB negative, for an overall HIV prevalence of 2.4%.

HIV status varied significantly by sex; the prevalence among men was 7/106, 6.6%, and for women it was 5/393, 1.3%; OR = 5.49 (95% CI = 1.52, 20.39) for male sex as a risk factor for HIV infection, *p* = 0.005 by Fisher's exact test (Table 2).

HIV status varied by marital status; 6/347, 1.7%, of never married subjects were HIV infected while 5/134, 3.7% of married subjects were, but the difference failed to attain statistical significance. HIV

Table 2

Demographic risk factors for prevalent HIV infection among factory worker's in northern Thailand, 1994.

Risk factor	Univariate		Multivariate	
	OR	95% CI	OR	95% CI
Male sex	5.5	1.5, 20.4	3.4	0.86, 13.3
Age over 25 years	1.2	0.6, 2.4	1.7	0.78, 3.7
Origin in upper northern region	3.6	0.8, 16.3		
Currently married	1.5	0.8, 2.9		
Education 6 years or less	7.2	2.2, 23.4	6.4	1.5, 26.7
Worktime > 1 year	0.9	0.3, 3.1		

status also varied by geographic place of origin. Comparing subjects from the upper north 9/232, 3.9%, with all others, 3/139, 2.2%, a borderline significance for increased risk was achieved (Yates corrected MHX2, $p = .07$) (Table 2).

An educational level of six years or less was associated with HIV infection; among 86 subjects with this educational level, 7, 8.1%, were HIV infected; among the 408 subjects with more than 6 years of education, 5, 1.2%, were HIV infected, OR = 7.2 (95% CI = 2.2, 23.4). In a multivariate model including age, sex, and educational level, only low education remained independently associated with HIV infection, OR = 6.4 (95% CI = 1.5, 26.7) (Table 2).

Syphilis prevalence, measured by VDRL and TPHA, was relatively low; 4/106 men (3.8%) and 15/393 women (3.8%) had a positive VDRL. Only 6/19 subjects with a positive VDRL were TPHA positive, 3 men and 3 women, and none of the subjects with a positive VDRL was HIV infected in this sample.

To ascertain mobility in this population, subjects were asked how long they had worked at their current job, how long they had been in the Lamphun area, and how long they intended to stay at their job or in the Lamphun area (Table 3). While the median number of months of work was 9.5, 23.3% of subjects had worked 3 months or less, and 36.1% had worked 1 year or longer. Adding the median number of months worked, and the median number of months subjects intend to continue working (24.0 months) gives a crude estimate of 2.5-3 years of work for about half the sample. No association was found between length of work and HIV infection status.

Follow-up was successful for 420/499 subjects, or 84.2%, over 6 months. Retention varied significantly by sex; 73/106 men (68.9%) returned for follow-up compared to 347/393 women (88.3%); RR = 1.21 (95% CI = 1.07, 1.37).

Among the 420 subjects followed there were 13 confirmed HIV infections, and 3 additional subjects with reactive ELISAs who had negative Western Blots. Of confirmed HIV infections, 8 were among prevalent cases, and 5 were incident HIV-1 infections, for an incidence of 5/242 person years, or 2.1/100 person years.

HIV seroconversion rates differed by sex. Among men there were 2 incident infections among 99 baseline seronegatives for an incidence of 2/49 person years, or 4.1/100 person years. Among 388 women uninfected at baseline, there were 3 seroconversions, for an incidence of 3/195 person years, or 1.5/100 person years. This difference was not significant using Fisher's exact test. There was one incident syphilis case, a male subject who also seroconverted to HIV positivity. Among prevalent syphilis cases identified at baseline, all were treated successfully and none had a repeat VDRL titer higher than 1 : 2.

When subjects were asked if they would like to continue in the study, 60.7% were unsure, 30.2% said definitely not, and 9.0% said yes. When asked about interest in long term follow-up (3 years) the responses were similar; 65.2% were unsure, 26.2% said no, and 8.6% said yes. However, 386/420 subjects (91.9%) who were seen twice returned to the Lamphun clinic for their HIV results and post-test counseling.

Table 3

Measures of Mobility among 499 factory workers in Lamphun Province, northern Thailand, 1994-1995.

Mobility measures	Median# months	Mean# months	SD
Have lived at current address	8.0	14.8	2.2
Have worked at current job site	9.5	19.6	3.3
Have been in Lamphun Industrial area	8.0	14.9	1.7
Intend to work at current job site	24.0	30.2	3.6
Intend to stay in Lamphun area	24.0	31.3	3.8

DISCUSSION

The follow up rate we have demonstrated, 84.2% over 6 months, would need to be improved for reliable evaluation of preventive interventions, including HIV vaccine trials (Petricciani *et al*, 1992). It may well be that the strategy used, being anonymous, unlinked, and with visits done at informal housing sites, makes retention difficult because subjects are not in a "medical" setting, which some subjects might prefer (Celentano *et al*, 1995). It is likely that retention could be improved if it were not anonymous, since this would allow regular interactions, as necessary, between volunteers and study personnel. It is also likely that this young population, the majority of whom are not from the Lamphun area, are quite mobile, and may be inherently difficult to follow. Our baseline data suggest that this is the case, as the average duration of expected work in the area was 2.5 to 3 years, and at any given time, a subset would be expected to complete their work time in the factories. It is difficult to understand why women should have had significantly higher follow-up rates than men in this sample. For cohort studies it would be essential to identify subjects just starting their working period, as well as those committed to longer term work.

Low educational level (less than 6 years) was the most significant risk factor for HIV infection in this population, and the only factor independently associated with HIV in a multivariate model. Low educational levels may correlate with lower levels of HIV/AIDS knowledge in both men and women, and suggests that HIV/AIDS education in the workplace may be needed.

The HIV prevalence identified was lower than has been found in other populations in northern Thailand (Nelson *et al*, 1994). The lower than expected HIV prevalence rates in this sample may be due to several factors. First, some factories in the Lamphun Industrial Area may either screen for HIV before employment, or periodically during employment. If employees with HIV infection are terminated from their jobs, as may be the case, this could considerably lower prevalence. Since strict confidentiality was critically important to the success of this study, we did not collect data on place or type of employment; therefore, we cannot assess whether HIV prevalence differed significantly among companies or employment levels. Second,

since potential subjects were informed that HIV testing would be a key part of the study, subjects who either knew or suspected they were HIV positive may have declined participation.

The HIV incidence rate, which can be estimated at about 2%/year overall, is similar to studies of village populations in the northern Thailand (Nelson *et al*, 1994b). The rate in men of approximately 4%/year is somewhat higher than several other populations currently being followed in longitudinal studies, including military conscripts and male STD clinic users (Nelson *et al*, 1994). While the overall HIV incidence rate is somewhat lower than some estimates thought necessary for vaccine trials (3-4%), the incidence in men is similar to those recommended for such trials (Petricciani *et al*, 1992; Paltiel and Kaplan, 1993; Heyward *et al*, 1994).

CONCLUSIONS

The population we identified is largely female, single, relatively young, and of moderate educational level. They are fairly mobile, with an average duration of expected work in the area of 2.5 to 3 years. While prevalent HIV infection levels were fairly low, we have identified an approximately 2% HIV seroconversion rate overall, a rate of 1.5%/year among women, and 4.1%/year among men. If follow up could be improved, this population might be valuable for prospective HIV studies, including vaccine trials. Targeting subjects who plan to remain in the area, moving the study into a more recognizable "medical setting" and offering more concrete health benefits to subjects could improve recruitment, retention, and compliance with a possible cohort in this population.

HIV preventive efforts are clearly called for in this population, and should be targeted at both male and female industrial workers. Despite current prevention efforts, HIV continues to spread through the general young adult population of northern Thailand, and will continue to increase the social and economic costs of AIDS in the future.

ACKNOWLEDGEMENTS

Supported by the Global Programme on AIDS of the World Health Organization, and by the Royal Thai Government.

REFERENCES

- Brown T, Sittitrai W, Vanichseni S, Thisyakorn U. The recent epidemiology of HIV/AIDS in Thailand. *AIDS* 1994; 8 (suppl 2) : S131-9.
- Celentano DD, Beyrer C, Natpratan C, *et al.* Willingness to participate in AIDS vaccine trials among high risk populations in northern Thailand. *AIDS* 1995; 9 : 1079-83.
- Heyward W, Osmanov S, Saba J, *et al.* Preparation for Phase III HIV vaccine efficacy trials: methods for the determination of HIV incidence. *AIDS* 1994, 8 : 1285-91.
- Lamphun Provincial Chief Medical Office, Dr Pradit Vinitchakul, 1994.
- Mann J, Tarantola D, Netter T, eds. *AIDS in the World*. Cambridge: Harvard University Press, 1992; 84-108.
- Nelson KE, Beyrer C, Natpratan C, *et al.* Preparatory studies for possible HIV vaccine trials in Northern Thailand. *AIDS Res Hum Retrovir* 1994a; 10 (suppl 2) : S243-6.
- Nelson KE, Suriyanon V, Taylor E, *et al.* The incidence of HIV-1 infections in village populations of northern Thailand. *AIDS* 1994b, 8 : 951-55.
- Paltiel AD, Kaplan E. The epidemiological and economic consequences of AIDS clinical trials. *AIDS* 1993; 6 : 179-90.
- Petricciani J, Koff W, Ada G. Efficacy trials for HIV/AIDS vaccines. *AIDS Res Hum Retrovir* 1992, 8 : 1527-9.
- Royal Thai Ministry of Public Health, Division of Communicable Disease Control HIV/AIDS Surveillance Data, Bangkok, 1994.
- Royal Thai Ministry of Public Health, Division of Communicable Disease Control HIV/AIDS Surveillance Data, Bangkok, 1993.
- Viravaidya M, Obremsky SA, Myers C. The Economic Impact of AIDS on Thailand, in *The Economic Implications of AIDS in Asia*. New Delhi: UNDP 1993.
- Weniger BG, Limpakarnjanarat K, Ungchusak K, *et al.* The epidemiology of HIV infection and AIDS in Thailand. *AIDS* 1991; 5 (suppl 2) : S71-S85.
- Weniger BG. Experience from HIV incidence cohorts in Thailand: implications for HIV vaccine efficacy trials. *AIDS* 1994; 8 : 1007-10.