Disease Progression and Survival with Human Immunodeficiency Virus Type 1 Subtype E Infection among Female Sex Workers in Thailand

Peter H. Kilmarx,1,5 Khanchit Limpakarnjanarat,1 Jaranit Kaewkungwal,1,2 Renu Srismith,1
Supachai Saiisorn,4 Wat Uthaivoravit,1 Nancy L. Young,1,5 and Timothy D. Mastro1,5

This study describes rates and correlates of disease progression and survival among 194 female sex workers in northern Thailand who were infected with human immunodeficiency virus type 1 (HIV-1; 96% with subtype E). The median rate of CD4 T lymphocyte decline (3.9 cells/µL/month), median time from infection to <200 CD4 T lymphocytes/µL (6.9 years), and time to 25% mortality (6.0 years) were similar to those found in studies performed in Western countries before highly active antiretroviral therapy was available to populations infected with HIV-1 subtype B. Mortality rates among women with >100,000 HIV-1 RNA copies/mL were 15.4 times higher (95% confidence interval, 5.2–45.2) than among women with <10,000 copies. Initial CD4 T lymphocyte counts and serum virus load were independently strong predictors of survival. These results can help in assessing the effects of the epidemic in Thailand and in determining the prognoses for individual patients.

Rates of disease progression and survival in individuals with human immunodeficiency virus (HIV) type 1 infection must be known in order to determine patient prognosis and to assess the demographic, economic, and social effects of the epidemic. Most information about disease progression comes from developed countries [1–14] or from Africa [15, 16]. HIV infection was not widespread in Asia until the late 1980s, so, although >6.7 million persons in South and Southeast Asia are living with HIV [17], there are few studies on HIV disease progression from the region [18–20]. Population-specific rates are important because geographic areas may differ as a result of factors such as the availability of treatment and the presence of other infectious diseases, such as tuberculosis [15, 18–20] or penicilliosis [21]. In addition, although most of the limited data do not indicate subtype differences in pathogenesis, infecting HIV-1 viral subtype may also be a factor [16, 22–25].

The quantity of virus in the peripheral circulation has emerged as one of the most important predictors of disease progression [7, 12]. However, the studies in which this determination was made were performed in Western countries with HIV-1 subtype B, and data on virus levels and pathogenesis from other geographic areas or for other HIV-1 subtypes are very limited.

We report on HIV-1 disease progression and survival rates among women in the Chiang Rai Health Club; these women are part of an ongoing cohort study of female sex workers (FSWs) in upper northern Thailand. Typical of heterosexually transmitted HIV infection in Thailand, subtype E predominates in this population. Northern Thailand was one of the areas first and most severely affected by the AIDS epidemic in Asia [26], and FSWs, along with injection-drug users, were one of the first groups to exhibit high infection rates [26].

Materials and Methods

The Chiang Rai Health Club study has been described elsewhere [27, 28]. In order to be eligible, women needed to be ≥16 years old, have Thai national identification cards, and report current employment as an FSW in the Chiang Rai province. They were approached by the study staff in the Chiang Rai provincial sexually transmitted diseases (STD) clinic, in other district medical clinics in the province, and at their workplaces. Enrollment took place from 1991 through 1994, and prevention counseling and condoms were provided at each study visit. Epidemiologic data were double-entered and validated. Epi Info, version 6.04 (Centers for Disease Control and Prevention, Atlanta); Statistical Analysis Software
Table 1. Risk factors for rapid rate of decline in CD4 T lymphocyte counts (higher than median, 3.9 cells/μL/month) among 107 human immunodeficiency virus (HIV)-infected female sex workers in northern Thailand.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No. of patients</th>
<th>Rapid decline, %</th>
<th>Relative risk (95% CI)</th>
</tr>
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<tbody>
<tr>
<td>Age at infection, years</td>
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<tr>
<td>&lt;19</td>
<td>50</td>
<td>54.0</td>
<td>1.18 (0.81–1.73)</td>
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<td>≥20</td>
<td>57</td>
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<td>Education, years</td>
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<td>&lt;6</td>
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</tr>
<tr>
<td>≥6</td>
<td>64</td>
<td>57.8</td>
<td>1.55 (1.00–2.42)</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Brothel</td>
<td>85</td>
<td>52.9</td>
<td>1.46 (0.81–2.62)</td>
</tr>
<tr>
<td>Nonbrothel</td>
<td>22</td>
<td>36.4</td>
<td>Referent</td>
</tr>
<tr>
<td>Oral contraceptive use</td>
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<tr>
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<td>76</td>
<td>51.3</td>
<td>1.14 (0.73–1.77)</td>
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<td>Depot medroxyprogesterone use</td>
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<td>1.23 (0.84–1.80)</td>
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<td>62</td>
<td>45.2</td>
<td>Referent</td>
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<td>Infection status</td>
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<tr>
<td>Seroconverted</td>
<td>22</td>
<td>36.4</td>
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</tr>
<tr>
<td>Seroconvertive at enrollment</td>
<td>85</td>
<td>52.9</td>
<td>1.46 (0.81–2.62)</td>
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<tr>
<td>Virus load, HIV-1 RNA copies/mL</td>
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<td></td>
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<td>&lt;10,000</td>
<td>26</td>
<td>26.9</td>
<td>Referent</td>
</tr>
<tr>
<td>10,000–100,000</td>
<td>67</td>
<td>52.2</td>
<td>1.94 (0.99–3.80)</td>
</tr>
<tr>
<td>&gt;100,000</td>
<td>14</td>
<td>78.6</td>
<td>2.92 (1.46–5.82)</td>
</tr>
<tr>
<td>First CD4 count, cells/μL</td>
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<tr>
<td>&gt;500</td>
<td>26</td>
<td>50.0</td>
<td>1.01 (0.65–1.58)</td>
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<tr>
<td>≤500</td>
<td>81</td>
<td>49.4</td>
<td>Referent</td>
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<tr>
<td>Vital status</td>
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<td>Alive</td>
<td>72</td>
<td>33.3</td>
<td>Referent</td>
</tr>
<tr>
<td>Dead</td>
<td>35</td>
<td>82.9</td>
<td>2.49 (1.73–3.56)</td>
</tr>
<tr>
<td>Total</td>
<td>107</td>
<td>49.5</td>
<td></td>
</tr>
</tbody>
</table>

NOTE. CI, confidence interval.

(SAS), version 6.12 (SAS Institute, Cary, NC); and Stata, version 6.0 (Stata, College Station, TX) were used for data analysis.

Data collection. Study participants were evaluated at the provincial STD clinic at baseline and at 3-month follow-up visits. Use of contraceptives and antiretroviral agents or antimicrobials for opportunistic infection prophylaxis was ascertained at each study visit. HIV-infected women were referred to the only isoniazid (INH) tuberculosis prevention program in the province, and information on INH use was obtained from that clinic. This report includes data that was obtained through October 1998.

Laboratory testing. At enrollment and at follow-up visits, serum specimens were collected and screened for HIV antibodies (until participants were seropositive) using EIA (HIV-1/HIV-2 EIA; Genetic Systems, Redmond, WA) and, if positive, using Western blot (WB; NovaPath HIV-1 Immunoblot; BioRad Diagnostics Group, Hercules, CA). HIV-1 envelope (env) subtype was determined for seropositive specimens with subtype E and B′ (Thai B) V-3 loop peptide EIA (PEIA); nucleic acid sequencing of the C2-V3 env region was performed on PEIA-negative specimens [29]. Serum specimens were stored at −70°C. In 1998 they were tested for serum HIV-1 RNA virus levels (Amplipcr HIV-1 Monitor Test, version 1.5; Roche Molecular Systems, Branchburg, NJ). In this test, a new primer pair enhances the ability to amplify non–B subtypes, allowing for improved HIV-1 RNA detection and quantitation of the subtype E specimens found in Thailand [30]. An enrollment specimen was used for women who were seropositive at enrollment. Because RNA levels stabilize about 6 months after infection [6], for the women who seroconverted, we used the first specimen collected 180 days after the first positive EIA and WB specimen. If no specimen was available after 180 days, we used the latest available specimen. CD4 T lymphocyte count was determined every 3 months for the HIV-seropositive participants. A complete blood count quantitative buffy-coat analysis (QBC; Centrifugal Hematology System; Becton Dickinson, Franklin Lakes, NJ) of an EDTA blood specimen was performed at the Chiang Rai field station. Another EDTA specimen collected at the same time was sent on the day of collection via overnight express (in a ice temperature-controlled cooler) for lymphocyte immunophenotyping by flow cytometry (FACScan; Becton Dickinson Immunolfow-cytometry Systems, San Jose, CA), which was performed the following day at the HIV/AIDS Collaboration Laboratory in Nonthaburi (a suburb of Bangkok, Thailand).

Ascertaining vital status. Vital status was determined by several redundant mechanisms. Study staff learned of patient deaths from coworkers and family members of the participants. They also reviewed records at the provincial public hospital and mortality report forms from the provincial public health office. In Thailand, deaths are noted in Ministry of Interior district housing registration records and are reported to the national office. From December 1997 through March 1998, study staff reviewed the housing registration records of all participants registered in Chiang Rai province. In December 1998, the Ministry of Interior database was queried with regard to all 500 women by using the women’s unique 13-digit national identification number. A copy of the mortality report form was requested for all reported cases of death, and cause and date of death were abstracted from this report.

Time of infection. For women who seroconverted, infection was assumed to have occurred at the midpoint between the last negative and first positive EIA and WB test results. For women who were seropositive at enrollment, we made several assumptions, based on the unique dynamics of the Thai epidemic, about the timing of infection. HIV infection was introduced in Thailand shortly before this study began, and it spread very rapidly. The seroprevalence among brothel-based sex workers in Chiang Rai increased from 0% in 1987, to 0.5% in 1988, to 46% in 1989, and then to 60% in 1990 [26]. In addition, infection rates were much higher among FSWs (32% at enrollment in this cohort), compared with women of reproductive age in general (3%–6% among pregnant women in Chiang Rai during 1991–1994) [31]. Therefore, infection was assumed to have occurred after a woman began commercial sex work. Finally, in this cohort [27, 28] and in other studies of Thai FSWs [22], HIV infection was more likely to occur shortly after the beginning of commercial sex work, so we assumed that infection occurred relatively close to that time. Women who began sex work during or before 1987 were assumed to have been infected in 1989, and those who began during 1988 were assumed to have been infected in 1990. For women who began sex work during or after 1989, we assumed that they were infected 1 year after they began sex work. A woman who began sex work at her current age or 1 year earlier was assumed to have been infected 6 months before enrollment. We also did a sensitivity analysis of the effect of our assumptions on rates of disease progression and survival by using early and late extreme assumptions about the time of infection among women who were HIV seropositive at enrollment.
157 female sex workers in northern Thailand. A, were used to analyze time from infection to first CD4 count progression. Survival analysis and Cox proportional hazard models were used to analyze time to first CD4 count progression, and vital status). Infection status (seropositive at enrollment vs. reported use of oral contraceptives or depot medroxyprogesterone after HIV infection; infection status (seropositive at enrollment vs. later seroconversion); and initial CD4 T lymphocyte count, virus load, and vital status at the end of follow-up. Relative risks and 95% confidence intervals were calculated.

Outcome 1: CD4 T lymphocyte decline. The rate of CD4 T lymphocyte decline was determined by fitting regression slopes of CD4 counts for each woman for whom there was 30 months between first and last CD4 measurements after HIV infection. Women with faster rates of CD4 decline (faster than the median rate) were compared with women with slower rates of decline using the following covariates: age when infected; educational attainment and type of sex work (brothel or nonbrothel) as reported at study enrollment; reported use of oral contraceptives or depot medroxyprogesterone after HIV infection; infection status (seropositive at enrollment vs. later seroconversion); and initial CD4 T lymphocyte count, virus load, and vital status at the end of follow-up. Relative risks and 95% confidence intervals were calculated.

Outcome 2: time to first CD4 T lymphocyte count <200 cells/μL. Lymphocyte subpopulations of healthy Thai females are similar to those of whites [33]. A CD4 count <200 cells/μL was added to the CDC AIDS case definition in 1993 [34] and, like other populations [4, 35], most Thai patients have <200 CD4 cells/μL when AIDS develops [19, 20, 36]. In Thailand, opportunistic infections are often diagnosed without laboratory confirmation, and women’s medical records were often not available if the women had been treated at a nonstudy facility. Therefore, a CD4 count <200 cells/μL was used as the primary indicator of disease progression. Survival analysis and Cox proportional hazard models were used to analyze time from infection to first CD4 count <200 cells/μL. For women who were seropositive at enrollment, observations were left-censored at the time of enrollment. Observations were right-censored at the time of the last CD4 count for women whose counts remained >200 cells/μL. We analyzed associations with the same factors that were used for the rate of decline of the CD4 count, as listed in Outcome 1 (except for initial CD4 count and vital status). Infection status (seropositive at enrollment vs. later seroconversion) was controlled in the Cox proportional hazard models. All covariates in longitudinal analyses were treated as time-independent variables. To account for possible confounding between initial health status and hormonal contraceptive use and to account for possible ascertainment bias for this outcome and for survival, we also used Cox proportional hazard models to analyze the effects of use of oral contraceptives or depot medroxyprogesterone on time to first CD4 count <200 cells/μL with initial CD4 count (<200, 200–500, or >500 cells/μL) and number of visits (≥7 or <7 visits [median]) controlled.

Outcome 3: survival. Survival analysis and Cox proportional hazard models were used to analyze survival from time of infection. For women who were seropositive at enrollment, observations were left-censored at the time of enrollment. Because there is a delay of ≈2 months before deaths are recorded in the Ministry of Interior database, observations were right-censored at October 1998, 2 months before the search of the database. We analyzed associations with the same factors used in the analysis of time to first CD4 count <200 cells/μL, and we controlled infection status in the Cox proportional hazard models. Survival analysis and Cox proportional hazard models were also used to analyze time from first CD4 count to death—by subgroup of initial CD4 count and by virus load.

Results

Enrollment and HIV infection. Of the 500 women enrolled during 1991–1994, 160 (32%) were HIV-seropositive. For these women, the presumed date of infection (based on the assumptions described in Materials and Methods) was a mean of 20.6 months (median, 12; range, 6.0–60.0) before enrollment. Through October 1998, 34 women seroconverted. The median seroconversion time interval (time from last negative to first positive HIV test result) was 3.5 months. Of these 194 cases of HIV infection, 190 (97.9%) were subtype E and 4 (2.1%) were subtype B’ (Thai B) by PEIA or nucleic acid sequencing (performed for 5 cases that were nonreactive to PEIA). The mean age of HIV infection was 20.9 years (median, 19).

Follow-up and antimicrobial use. For the 306 seronegative women, the mean follow-up time was 23.4 months. Women who were seropositive at enrollment had a median of 5 study visits at which use of contraceptives or antimicrobials was ascertained, and women who seroconverted had a median of 8 such visits after seroconversion. No antiretroviral use was reported by the study participants through the end of 1997. In
1998, 3 women used antiretrovirals. Most women did not receive prophylaxis for opportunistic infections. Six HIV-infected women received cotrimoxazole for the prevention of opportunistic infections, and 34 HIV-infected women used INH for at least 6 months for the prevention of tuberculosis.

**Virus load measurement.** HIV-1 RNA was detected in all 157 human immunodeficiency virus (HIV)-infected female sex workers in northern Thailand.

**CD4 T lymphocyte initial counts.** A CD4 count was performed at least once for 157 (80.9%) of the 194 HIV-infected women. For 125 women who were HIV-seropositive at enrollment, the specimen for the first count was collected a median of 7.2 months after the first positive HIV test result, and the mean value was 42,929 RNA copies/mL (median, 29,222; range, 404–1,534,830). For the 160 women who were HIV-seropositive at enrollment, the mean value was 67,839 RNA copies/mL (median, 45,785; range, 404–1,534,830). For the 157 HIV-infected women for whom >1 CD4 count was performed, the median time from infection to first CD4 count was 6.4 years (censor date) was 59.6 months, and 62 women (36%) had done so by 6.9 years (figure 1). In the sensitivity analysis, times to 50% progression were 6.4 and 7.4 years at the 2 extremes of assumptions. Disease progression was strongly correlated with virus load (figure 1, table 2). Progression was not significantly associated with any other factors. Adjusted risk ratios (ARRs) for use of oral contraceptives (ARR, 1.3; 95% CI, 0.7–2.3) or depot medroxyprogesterone (ARR, 0.7; 95% CI, 0.7–2.3) were not statistically significant associations (P < .05) with other factors. Adjusted risk ratios (ARRs) for use of oral contraceptives (ARR, 1.3; 95% CI, 0.7–2.3) or depot medroxyprogesterone (ARR, 0.7; 95% CI, 0.7–2.3) were not statistically significant associations (P < .05) with other factors.
95% CI, 0.3–1.2) were slightly higher when the initial CD4 count and the number of follow-up visits were controlled. Results were similar when the 37 women who reported neither type of hormonal contraceptive were used as the referent group.

**Mortality.** Through October 1998, 68 study participants died. Fifty-nine deaths (86.8%) were reported by family members or coworkers or were ascertained by review of hospital or provincial public health office records; 3 deaths (4.4%) were discovered from review of housing registration records for the 401 women whose housing registration addresses were in Chiang Rai; and 6 deaths (8.8%) were discovered from the search of the Ministry of Interior national database. The district housing registration records were relatively complete: for 43 (97.7%) of the 44 women whose deaths had been reported and for whom the district housing registration records were reviewed, the deaths were also reflected in the housing registration record. The Ministry of Interior records were also relatively complete: of the 59 previously reported deaths, 57 (96.6%) were also recorded in the Ministry database.

Of the 68 women who died, 59 (86.8%) were HIV seropositive at enrollment, 7 (10.3%) had seroconverted, and 2 (2.9%) were HIV seronegative 5 and 8 months before death. The median age at death of the 66 HIV-infected women was 26 years (range, 18–50). For 30 of these 66 women, a CD4 lymphocyte count had been performed within 12 months of death. The median value was 23 cells/µL (range, 0–223), which suggests that these deaths were very likely due to HIV infection and immunosuppression. Mortality report forms listing ≤3 causes of death were obtained for 66 women; 64 of these women were HIV infected. Among the HIV-infected women, the most common reported causes of death (combined primary, secondary, or tertiary causes) were AIDS (23 cases), tuberculosis (9 cases), respiratory failure (8 cases), pneumonitis (6 cases), heart failure (5 cases), and cryptococcal meningitis (5 cases). No deaths were reported to be due to injury or other causes that were clearly not related to immune suppression. The reported causes of death of the 2 HIV-seronegative women were postpartum amniotic embolism and gunshot wound.

**Survival.** For the 194 HIV-infected women, the median follow-up time from infection to censoring or death was 81.2 months. By 5 years after infection, the survival rate was 85.9%; by 7 years, it was 68.7%; 25% mortality occurred after 6.0 years (figure 2). For the 34 women who seroconverted, the median time from infection to death or censoring was 58.4 months. Three years after seroconversion, the survival rate was 93.3%; after 5 years, it was 77.8%; 25% mortality occurred at 5.8 years. In the sensitivity analysis, times to 25% mortality were 5.6 and 6.7 years at the 2 extremes of assumptions. Survival was significantly associated with virus load (figure 2) but not with other factors (table 3). ARR for use of oral contraceptives (ARR, 1.1; 95% CI, 0.6–2.0) or depot medroxyprogesterone (ARR, 1.0; 95% CI, 0.5–1.9) were slightly higher when the initial CD4 count and the number of follow-up visits were controlled. Results were similar when the 38 women who reported neither type of hormonal contraceptive were used as the referent group.

For the 157 HIV-infected women for whom ≥1 CD4 count was performed, the median time from first CD4 count to death or censoring was 56.8 months. Survival from time of first CD4 count was strongly related to first CD4 count and virus load (figure 3, table 4). Multivariable analysis showed that both initial CD4 lymphocyte count and virus load were independently associated with survival (table 4).

**Discussion**

In this group of FSWs in northern Thailand, in whom HIV-1 subtype E infection predominated, 50% of the women progressed to a CD4 lymphocyte count <200 cells/µL by 6.9 years after infection, and 25% mortality occurred after 6.0 years. As in studies of subtype B infection [7, 12], serum viral HIV-1 RNA level was a strong predictor of disease progression, and baseline CD4 lymphocyte count and virus load were independent, strong predictors of survival. This is the first prospective study of disease progression and survival in Asia or of subtype E with a large number of HIV-infected persons for many of whom the time of seroconversion was well documented or for whom virus level measurements were available.

Overall, disease progression in this study was similar to, or
somewhat more rapid than, that noted in other studies that were performed before highly active antiretroviral therapy was available. Most of those studies were performed in Western populations infected with HIV-1 subtype B. In our study, the median rate of decline in CD4 count was 3.9 cells/µL/month. This rate is similar to rates in other studies, which typically range from 2 to 8 cells/µL/month [1–6, 25]. The median time from infection to <200 CD4 T lymphocytes/µL was 6.9 years. In other studies, the median time from infection to AIDS (by the 1987 CDC definition) ranged from 8 to 12 years [4, 5, 8, 9, 11, 14, 37]; typically, another 12–18 months elapsed from CD4 counts <200 cells/µL to a 1987 CDC-defined AIDS diagnosis [34]. In our study, 25% mortality occurred after 6.0 years. In other studies, 25% mortality occurred 6–10 years after infection. [5, 8–11, 14]. The median virus load (an important predictor of progression) in our participants was similar to those levels found in other studies [6,13, 38].

Comparisons of disease progression rates between studies must account for numerous factors. Older age has been associated with faster rates of disease progression in most studies [3, 4, 8–11, 14], and the young average age at infection of our participants (in comparison with average ages in other studies) is probably the most important factor that should have tended to make progression rates in our study slower relative to those seen in other studies. The young women in our study progressed more rapidly than did their similarly aged cohorts in other studies. In one study, 5 years after seroconversion and among those aged 15–34 years at infection, 7% had progressed to AIDS, and 6% had died [14]. In our study, the median age at infection was 19 years; after 5 years, 19% of patients had <200 CD4 cells/µL, and 14% had died.

On the other hand, several factors may have tended to make progression rates in our study faster than those seen in other studies. One such factor may have been prevalent infectious diseases such as tuberculosis, which may accelerate HIV-1 disease progression [39] and which was a relatively common cause of death in this cohort, in comparison with Western studies. Only a small number of participants used potentially life-prolonging antiretrovirals or preventive therapies such as INH [39] and cotrimoxazole [9, 40]. People in Thailand, a lower-middle-income country with limited resources, have less access to aggressive, life-prolonging treatment than do people in Western countries. Also, in contrast to our study population, most participants in Western studies were men and had acquired infection through sex with other men or through injection-drug use. Sex and transmission route are not thought to affect rates of disease progression [2, 4, 8, 10, 20], but higher rates of disease progression among FSWs have been observed in Kenya [15] and in the Philippines [18], possibly because of the generally lower socioeconomic conditions noted in these countries and because of the effect of exposure to multiple HIV-1 genotypes and other STDs. Furthermore, conservatively censoring women at their last CD4 count may have led to overestimation of the rates of disease progression [41]. Finally, population differences

### Table 3. Survival from time of infection of 194 human immunodeficiency virus (HIV)-infected female sex workers in northern Thailand.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No. of patients</th>
<th>No. of patients who died, %</th>
<th>7-Year survival, % (95% CI)</th>
<th>Rate ratio (95% CI)</th>
</tr>
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<tbody>
<tr>
<td><strong>Age at infection, years</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;19</td>
<td>105</td>
<td>31 (29.5)</td>
<td>72.3 (62.1–80.1)</td>
<td>Referent</td>
</tr>
<tr>
<td>≥20</td>
<td>89</td>
<td>35 (39.3)</td>
<td>63.3 (50.5–73.6)</td>
<td>1.50 (0.92–2.45)</td>
</tr>
<tr>
<td><strong>Education, years</strong></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>&lt;6</td>
<td>73</td>
<td>25 (34.2)</td>
<td>70.1 (56.8–80.0)</td>
<td>Referent</td>
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<td>≥6</td>
<td>121</td>
<td>41 (33.9)</td>
<td>67.5 (57.5–75.6)</td>
<td>1.19 (0.72–1.96)</td>
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<td><strong>Sex work</strong></td>
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<tr>
<td>Brothel</td>
<td>159</td>
<td>54 (34.0)</td>
<td>69.6 (61.1–76.6)</td>
<td>1.34 (0.71–2.52)</td>
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<td>Nonbroth</td>
<td>35</td>
<td>12 (34.3)</td>
<td>62.9 (41.6–78.2)</td>
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<td><strong>Oral contraceptive use</strong></td>
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<tr>
<td>Yes</td>
<td>112</td>
<td>36 (32.1)</td>
<td>69.6 (59.2–77.9)</td>
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<td>No</td>
<td>82</td>
<td>30 (36.6)</td>
<td>67.1 (54.7–76.8)</td>
<td>Referent</td>
</tr>
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<td><strong>Depot medroxyprogesterone use</strong></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>55</td>
<td>18 (32.7)</td>
<td>70.9 (55.7–81.7)</td>
<td>0.78 (0.45–1.37)</td>
</tr>
<tr>
<td>No</td>
<td>139</td>
<td>48 (34.5)</td>
<td>67.8 (58.4–75.5)</td>
<td>Referent</td>
</tr>
<tr>
<td><strong>Infection status</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Seroconverted</td>
<td>34</td>
<td>7 (20.6)</td>
<td>Referent</td>
<td>1.42 (0.63–3.22)</td>
</tr>
<tr>
<td>Seropositive at enrollment</td>
<td>160</td>
<td>59 (36.9)</td>
<td>69.6 (61.4–76.4)</td>
<td>Referent</td>
</tr>
<tr>
<td><strong>Virus load, HIV-1 RNA copies/mL</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;100,000</td>
<td>34</td>
<td>24 (70.6)</td>
<td>34.5 (18.8–50.9)</td>
<td>15.40 (5.25–45.2)</td>
</tr>
<tr>
<td>10,000–100,000</td>
<td>113</td>
<td>38 (33.6)</td>
<td>70.3 (60.1–78.4)</td>
<td>4.63 (1.64–13.1)</td>
</tr>
<tr>
<td>&lt;10,000</td>
<td>47</td>
<td>4 (8.5)</td>
<td>92.5 (78.4–97.5)</td>
<td>Referent</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>194</td>
<td>66 (34.0)</td>
<td>68.7 (61.0–75.2)</td>
<td></td>
</tr>
</tbody>
</table>

NOTE. CI, confidence interval.

a Survival analysis.

b Cox proportional hazard model.

c Insufficient follow-up time in this more recently infected group; 5-year survival is 77.8% (95% CI, 56.8–89.5).
[33] and laboratory differences [37] may lead to differences in CD4 counts and may bias results in either direction.

Considering the multiplicity of study- and population-specific factors that may affect disease progression, caution must be used in generalizing the results of this study to other populations in Asia or to those with HIV-1 subtype E infection; caution must also be used in comparing the rates of disease progression with subtype E in this study with the rates for other subtypes in other studies. However, our results suggest that disease progression with HIV-1 subtype E in Asia was not markedly different from that observed in most other studies, which dealt predominantly with subtype B.

The use of medication to prevent opportunistic infections by these FSWs was uncommon, and, in pilot programs, the FSWs’ adherence to INH [42] and cotrimoxazole (authors’ unpublished data) has been poor. HIV-infected patients in northern Thailand generally do not receive longitudinal primary care between episodes of acute illness. The cost of highly effective antiretroviral therapy remains out of the reach of most people living with HIV in Thailand, and adherence to these regimens is especially difficult. Efforts are now needed to provide the available, inexpensive, potentially life-prolonging treatments[9, 39, 40] to prevent opportunistic infections and thus to improve the clinical care infrastructure while more affordable, simpler antiretroviral therapies are developed.

Our finding that the use of hormonal contraceptives did not accelerate disease progression is reassuring. Steroid hormones stimulate HIV replication in in vitro and in vivo models [43], and disease may progress more rapidly during pregnancy, when the levels of endogenous sex steroids are high [44, 45]. Conversely, the use of hormone-replacement therapy has been associated with a reduced mortality rate [46], and, although disease progression rates are generally similar for men and women [2, 8, 13, 20], virus load levels are lower in women than in men [13, 38]. Results from observational studies must be interpreted cautiously because of the potential for confounding between health status and use of hormonal contraceptives. Indeed, as expected, the slight protective effects of hormonal contraception with regard to disease progression and mortality in our analyses were negated when we controlled the stage of disease.

### Table 4. Mortality from time of first CD4 T lymphocyte count of 157 human immunodeficiency virus (HIV)-infected female sex workers in northern Thailand (125 women were HIV seropositive at study enrollment and 32 seroconverted during study).

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No. of patients</th>
<th>No. of patients who died, %</th>
<th>5-Year survival, % (95% CI)</th>
<th>Rate ratio (95% CI)</th>
<th>Adjusted rate ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial CD4 lymphocyte, cells/μL</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;200</td>
<td>15</td>
<td>14 (93.3)</td>
<td>0</td>
<td>20.9 (9.00–48.7)</td>
<td>15.5 (6.46–37.4)</td>
</tr>
<tr>
<td>200–500</td>
<td>88</td>
<td>34 (38.6)</td>
<td>63.4 (51.8–72.9)</td>
<td>2.46 (1.21–5.01)</td>
<td>1.42 (0.67–3.00)</td>
</tr>
<tr>
<td>&gt;500</td>
<td>54</td>
<td>10 (18.5)</td>
<td>84.7 (70.4–92.4)</td>
<td>Referent</td>
<td>Referent</td>
</tr>
<tr>
<td>Virus load, HIV-1 RNA copies/mL</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;100,000</td>
<td>30</td>
<td>23 (76.7)</td>
<td>26.7 (12.6–43.0)</td>
<td>13.9 (4.78–40.6)</td>
<td>12.5 (4.09–38.2)</td>
</tr>
<tr>
<td>10,000–100,000</td>
<td>89</td>
<td>31 (34.8)</td>
<td>65.0 (53.1–74.5)</td>
<td>3.87 (1.36–11.0)</td>
<td>3.42 (1.19–9.81)</td>
</tr>
<tr>
<td>&lt;10,000</td>
<td>38</td>
<td>4 (10.5)</td>
<td>96.7 (78.6–99.5)</td>
<td>Referent</td>
<td>Referent</td>
</tr>
<tr>
<td>Total</td>
<td>157</td>
<td>58 (36.9)</td>
<td>64.6 (56.0–71.9)</td>
<td>Referent</td>
<td>Referent</td>
</tr>
</tbody>
</table>

**NOTE.** CI, confidence interval.

* Survival analysis.

* Cox proportional hazard model.

* Cox proportional hazard model adjusted for initial CD4 lymphocyte count and virus load.
Most HIV-infected women in this study were seropositive at enrollment, so the precise time of infection was unknown. However, in contrast to the situation in most other areas of the world, due to the explosive onset of the epidemic and other unique characteristics of the HIV epidemic among FSWs in northern Thailand (described in Materials and Methods), we were able to assign a presumed date of infection. Sensitivity analysis over a range of tenable assumptions of the time of infection did not substantially influence the rates of disease progression and survival. However, women whose infection progressed rapidly were likely to have been underrepresented among those who were seropositive at enrollment, because they would have already been debilitated or would have died by the time of study enrollment [47]. Indeed, as expected, the rates of progression and survival were slightly higher among women who seroconverted than among women who were seropositive at enrollment [47]. These differences were not statistically significant (P < .05), but the reported progression rates among women who seroconverted may provide a more accurate, if less-precise, result. Additional prospective studies in other populations are needed to confirm these initial results on HIV-1 subtype E in Asia.

By 1998, the prevalence of infection in the adult population in Thailand as a whole was estimated at 2.3%, or 800,000 persons [17]. Our data may be used to refine predictions and assessments of the HIV/AIDS epidemic, which is profoundly affecting northern Thailand [48]. FSWs were among the first groups in Thailand to be infected [26], but fewer than one-half of the HIV-infected women in this cohort have died, suggesting that the greatest effects of the epidemic in northern Thailand are yet to come.

Acknowledgments

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