

The intent of the HIV sentinel surveillance program in Thailand, as in other countries, is to provide early warning of pending epidemics so that public health officials can intensify prevention and control activities to protect their communities. While the intention is clear, questions remain as to how sentinel groups should be selected and if they predict future HIV occurrence. Every six months, serum is collected in Thailand from a sample of six sentinel groups in all provinces of Thailand for determining the prevalence of HIV infection. Among the sentinel groups, the HIV epidemic is rapidly increasing in female sex-workers, males at STD clinics, and females at antenatal clinics, increasing less rapidly among blood donors, and remaining high among IV drug addicts. Two sentinel groups were found to be useful for predicting the future spread of the epidemic to women attending clinics: lower-class female sex-workers and males attending STD clinics. *Asia Pac J Public Health* 1995;8(1):20-6.

Keywords: AIDS, developing countries, HIV, surveillance.

HIV Sentinel Surveillance in Thailand — An Example for Developing Countries

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Introduction

Due to the long incubation period of human immunodeficiency virus (HIV) infection, the causative agent of acquired immune deficiency syndrome (AIDS), the disease may reach epidemic levels before AIDS cases and deaths become evident to public health officials. Thus it is more important for epidemiologists to monitor HIV infections, not just AIDS cases or deaths. Rather than sample surveys of the entire population, the World Health Organization (WHO) recommends sampling sentinel groups for routine surveillance of HIV infection.¹ Surveillance systems, by definition, are both monitoring and control programs.² That is, with respect to HIV, they monitor the occurrence of HIV infection in the population with the specific intention of stimulating control activities. Without action aimed at control, a surveillance program would only be an expensive monitoring process of limited use to the society. Sentinel surveillance requires the same action orientation as other surveillance activities but focuses on selected sentinel groups who will alert the community of the impending spread of the HIV epidemic to the other segments of society.

The major objective of an HIV sentinel surveillance program is to

monitor high-risk groups in order to target intensified HIV intervention programs and to provide early warning that the epidemic will soon reach the low-risk general population. The latter use assumes that high-risk groups are effective sentinels of future HIV infection in the general community. If this is true, local public health officials would have additional time to organize control activities to safeguard the general public. Since these control activities may be costly and divert resources from other important activities, the warnings coming from the HIV sentinel groups must have predictive validity. We describe here the HIV sentinel surveillance program in Thailand, and demonstrate how data on various high- and low-risk groups can be used to warn communities of the approaching epidemic.

Methods

Sentinel Groups

Every six months, the sentinel surveillance program in Thailand reports the prevalence of HIV in a sample of six sentinel groups selected from individual sentinel sites (provinces) throughout the country. The time interval was determined based on cost and logistic constraints. Initially, in June, 1989, the Ministry of Public Health tested

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risk groups in 14 of the country's 73 provinces, then expanded the program six months later to 31 provinces, and again expanded it six months later to include all 73 provinces. The Thai system features six groups classified for this article by risk in 1989: [high risk] 1) intravenous drug users (IVDU), 2) lower-class female sex-workers who work in organized brothels; [middle risk] 3) women who sell sex in massage parlors, bars and similar venues, 4) males attending sexually-transmitted disease clinics; [low risk] 5) blood donors, and 6) pregnant women attending antenatal clinics.

Approximately 100–200 people in each of the six risk groups were selected by Thai health workers in each sentinel site (see Appendix for details of sampling strategy). All blood samples were analyzed for HIV using the ELISA test. If found to be repeatedly positive, the HIV status was confirmed with the Western blot (WB) or Immunofluorescent assay (IFA) test (WHO Testing Strategy III),³ except among intravenous drug users and lower-class female sex-workers (both over 10 percent prevalence) for whom confirmation of a positive ELISA test was done with a second ELISA from a different manufacturer rather than with the more expensive WB or IFA tests (WHO Testing Strategy II).³

Net Predictive Value

To test the ability of the Thai surveillance system to predict the future course of the epidemic, we analyzed the association between increased HIV prevalence among high-risk groups at each sentinel site and the subsequent appearance 12 months later of HIV infection in a group that represents the general population - women attending antenatal clinics. We reasoned that public health administrators are more willing to respond to HIV prevalence being above a set cutpoint, especially when faced with many competing resource requirements, rather than the uncertainty of a continuous range of HIV prevalence values. We felt that if the surveillance system provided early warning in specific sentinel sites, it

might also prove to be equally useful in other parts of Thailand as well as in other countries with a similar demographic and social profile.

We defined our outcome, the "presence" of HIV, as a prevalence of one percent or greater among women attending antenatal clinic attenders. Using information from the various sentinel sites, we determined the predictive value of HIV presence one year later associated with various high-risk groups. We evaluated several prevalence cutpoints in the high-risk groups, and termed the difference between the 12-month predictive value above and below the cutpoint as the "net predictive value" (NPV).

Statistical Analysis

The trends over time are presented for the Thailand sentinel surveillance data from June, 1989 to June, 1994. The mean values for all sentinel sites combined were used to show temporal trends for eleven time points, collected at six-monthly intervals. Means for time points 1, 2 and 3–11 represents 14, 31 and 73 provinces, respectively, as the system was expanded after the first year to all 73 provinces of the nation.

For the net predictive value, we used summary data from the various sentinel sites for the first five collection points, gathered at six-monthly intervals from June, 1989 to June, 1991 (see Figure 1). We use the HIV prevalence observed among specific high- and medium-risk groups at baseline in each sentinel site to predict the subsequent appearance 12 months later of HIV infection in one of the low-risk populations - pregnant women attending antenatal clinics in the same sentinel site. Site-specific data on the high- and middle-risk groups were analyzed in linked pairs with ANC women at the same sentinel site two time points later (12 months). There were three possible linked sets of sentinel sites; June 1989 to June 1990, December 1989 to December 1990, and June 1990 to June 1991, with most analyses comprised of 100 or more linked sentinel site pairs. Two cutpoints have been arbitrarily selected to illustrate the method: sentinel site HIV prevalence

of 5 percent among middle-risk groups, and HIV prevalence of 20 percent among high-risk groups. All analyses were done with *Quattro Pro*, a spreadsheet program. Graphs were created using *Harvard Graphics* software.

Results

HIV/AIDS in Thailand

The first case of AIDS was diagnosed in Thailand in September, 1984. Thereafter, an increasing number of HIV infections and AIDS cases continued to appear in this nation of 55 million people. By October 1994, 13,246 AIDS cases had been reported to WHO.⁴ A few years earlier, when the number of reported AIDS cases was only 179,⁵ research investigators in Thailand had estimated from sentinel surveillance data that there were 200,000 to 400,000 HIV-infected persons,⁶ suggesting the magnitude of the AIDS epidemic to come.

The prevalence of HIV infection from June, 1989 to June, 1994 was high and has remained high among intravenous drug users and low but gradually rising among blood donors (Figure 1). The percentage of infected individuals has rapidly risen, however, in lower-class sex-workers, males at STD clinics, higher-class sex-workers, and females attending antenatal clinics, although the range of prevalence estimates varies considerably among these four groups.

Predictive Value of High-risk Groups

Do various sentinel groups provide early warning of the spread of the HIV epidemic to the general population? To answer this question in quantitative terms, we derived the net predictive value (see Methods). An example of the net predictive value is shown in Table 1 for a cutpoint of 5 percent among males coming to STD clinics. Using data from the first five sentinel surveys (i.e. June, 1989 to June, 1991), we were able to assemble 108 sentinel pairs (male STD-ANC women) 12 months apart. The baseline group in each pair was males coming to the STD clinics at the sentinel site. The second group in each pair was pregnant women attending ANC

Figure 1. HIV prevalence at sentinel sites among high, middle, and low risk groups, Thailand, Six month intervals, June 1989 to June 1994.

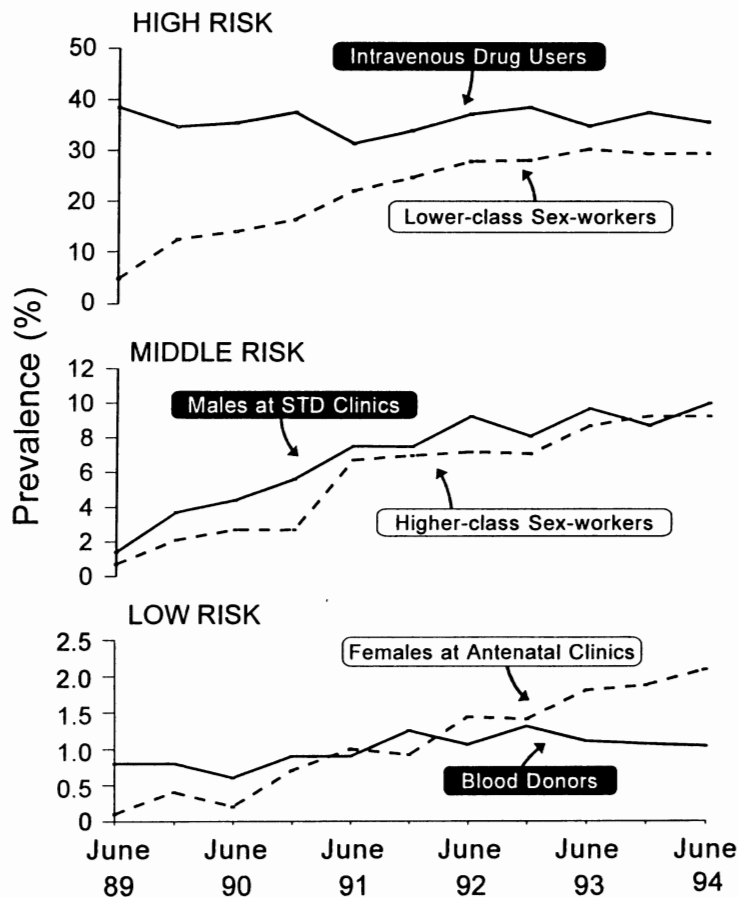


Table 1. Early warning of HIV at sites by sentinel group: males at STD clinics

Baseline HIV prevalence among males at STD clinics (the sentinel sites)	HIV infection among pregnant women at sentinel site 12 months later		
	Yes	No	
≥ 5%	21	5	26
< 5%	21	61	82
	42	66	108
Sites with values at or above cutpoint (≥ 5%)	0.81	(21/26)	
Sites with values below cutpoint (< 5%)	0.26	(21/82)	
Net predictive value	0.55		

clinics at the same sentinel site 12 months later. As presented in Table 1, at baseline the prevalence of HIV infection among males attending STD clinics was 5 percent or greater at 26 sentinel sites (the *at or above cutpoint*

sites) and less than 5 percent at 82 sentinel sites (the *below cutpoint* sites). Twelve months later, HIV infection had spread to ANC women at 21 of the 26 *at or above cutpoint* sentinel sites (81 percent), but only 21 of

the 82 *below cutpoint* sentinel sites (26 percent). The net predictive value — the predictive level of the *at or above cutpoint* sentinel sites (i.e. ≥ 5% at baseline) minus the predictive level of the *below cutpoint* sites (i.e. baseline values < 5%) — was 55 percent. That is, being at a sentinel site (or province) above the specified cutpoint is associated with a 55 percent net increase in risk that the epidemic will appear 12 months later among women attending ANC clinics in the province. The larger the net predictive value, the better is the cutpoint as a warning sign for the future spread of the epidemic.

This analysis was repeated for four high- and middle-risk sentinel groups using various cutpoints at baseline, ranging from an HIV prevalence of 1 to 30 percent among high-risk groups and 1 to 10 percent among middle-risk groups. For each analysis, the outcome or predicted variable was the spread of HIV to pregnant women attending antenatal clinics 12 months later at the same sentinel site. Using the arbitrary but reasonable cutpoints of 20 percent for high-risk groups and 5 percent for low-risk groups, Table 2 shows the net predictive value for four risk groups and two different cutpoints at baseline. The net predictive value was lowest for IV drug addicts, even with a high prevalence cutpoint of 20 percent. Higher net predictive values resulted from using the prevalence cutpoint of 20 percent for lower-class sex-workers and the cutpoint of 5 percent for males at STD clinics. Higher-class sex-workers had a net predictive value at the 5 percent cutpoint which was intermediate between that of drug addicts and the two sexual transmission groups.

Figures 2 and 3 present the net predictive value for a range of cutpoints among two high-risk groups (Figure 2) and two middle-risk groups (Figure 3), with dark vertical lines showing the arbitrary but reasonable cutoff values featured in Table 2. The greater the difference between the lines for those sites at or above the cutpoint and those below the cutpoint, the greater the net predictive value for that cutpoint. The net predictive value at 12 months is least at any cutpoint for intravenous drug

Figure 2. Net predictive value (NPV) for future spread of HIV infection to women attending antenatal clinics at sentinel sites associated with baseline HIV prevalence cutpoints among high-risk groups.

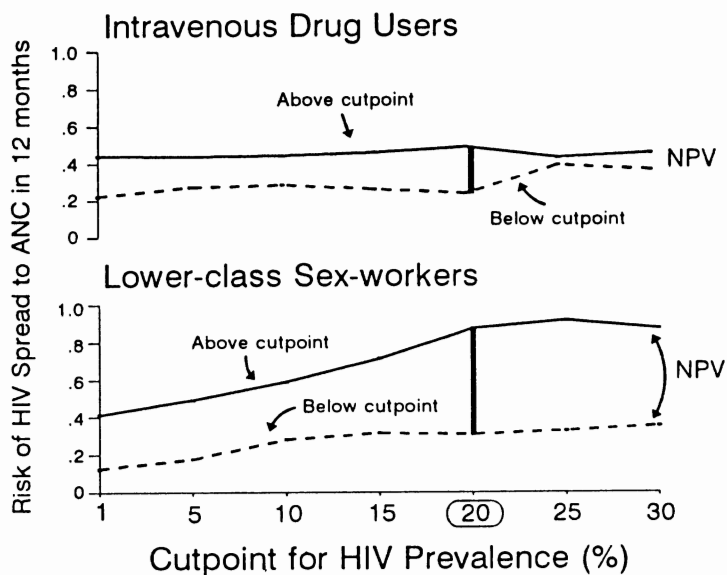
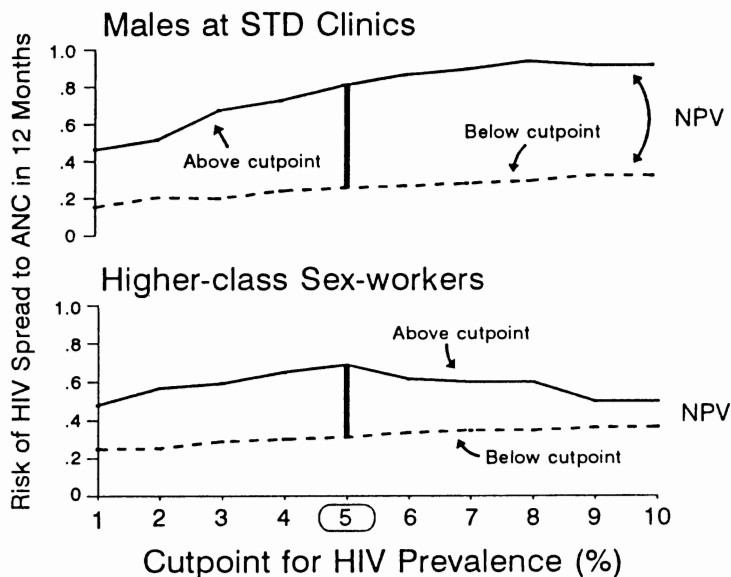


Figure 3. Net predictive value (NPV) for future spread of HIV infection to women attending antenatal clinics at sentinel sites associated with baseline HIV prevalence cutpoints among middle-risk groups.



users. Hence, in Thailand, the prevalence of HIV and IV drug addicts is not very predictive of spread one year later to the sexually-active general population, as represented by pregnant women attending antenatal clinics. The two groups with the highest net predictive values, but at different baseline prevalence cutpoints, are males at STD clinics and lower-class sex-workers, who are visited pri-

marily by Thai rather than foreign males.

Discussion

HIV in Thailand

Based on these and other data, epidemiologists in Thailand hypothesized that infection first occurred among homosexuals, then spread and reached epidemic proportions among

intravenous drug users. Following the drug users, successive waves of HIV spread to commercial sex-workers, then to their male clients, as noted by a rising rate of infection among men attending STD clinics, and finally to sexually-active women and men in the general population.⁶ Recent data on different HIV-1 virus subtypes in Thailand, however, bring into question this chain of transmission. Ou and colleagues have reported finding subtype A primarily in Thai residents infected through sexual transmission and subtype B in injecting drug users, suggesting that patterns of blood-borne and sexual transmission are parallel but independent.⁷ This finding is compatible with the observed lower net predictive value of intravenous drug users as a sentinel group for the spread of HIV infection to pregnant women attending antenatal clinics, although the consistently high levels in IVDUs from the beginning of the sentinel surveillance program could also explain the lack of predictive value of this group.

Independent of the sentinel surveillance program, the enormity of the epidemic has been documented in male military recruits, with prevalence estimates in the northern regions of 12–15 percent.^{8,9} Mastro and colleagues observed that the infectivity of the virus in Thailand may be 30–50 times what had previously been estimated, helping to explain the high rates of transmission.¹⁰

Sentinel Groups

To be effective, a sentinel surveillance system must include those high-risk groups most likely to be infected with HIV. When the epidemic is at the early stages, there is no reason to survey the general public or to include low-risk groups in the surveillance system. Testing of groups in which little disease or infection is occurring is expensive and provides no information on the emerging nature of the epidemic. Instead, the first groups to be included in a sentinel surveillance should be those persons in whom the epidemic is expected to start. Criteria for selecting specific sentinel groups include findings of informal surveys, characteristics of AIDS cases in either

Table 2. Early warning of HIV at sites by high- and middle-risk sentinel groups and selected cutpoints

Risk group at baseline	Cutpoint (%)	Probability of HIV spread to women at ANC 12 months later		Net predictive value [†]
		At or above cutpoint at baseline	Below cutpoint at baseline	
Intravenous drug users	20	0.49	0.24	0.25
Lower-class sex-workers	20	0.88	0.31	0.57
Males at STD clinics	5	0.81	0.26	0.55
Higher-class sex-workers	5	0.69	0.31	0.38

[†]Proportion of sentinel sites with future HIV if risk group prevalence at baseline is at or above cutpoint *minus* proportion of sentinel sites with future HIV if risk group prevalence at baseline is below cutpoint.

the country or similar countries, past experiences in similar countries or areas, and groups with a high frequency of blood exposure or sexual contact with individuals likely to be infected.

In countries which strongly discriminate socially and often legally against members of high-risk groups — especially homosexual and bisexual men and intravenous drug users — it may be difficult to identify and monitor those most likely to be infected. Public health officials may be tempted to include groups that are easy to find rather than groups most likely to be infected. Doing so, however, will only lull them and the public into thinking that HIV is not occurring in their nation while the epidemic rages ever upward without their knowledge. If the surveillance program is to provide early warning, every effort must be made to convince those most likely to be infected by HIV to be tested as sentinel groups. To reach those most likely to be infected, we believe that surveillance testing must be anonymous with no identifying information to link HIV infection to a given individual. Not only must these sentinel individuals be allowed to provide specimens anonymously, they must also be convinced that the surveillance system really is anonymous.

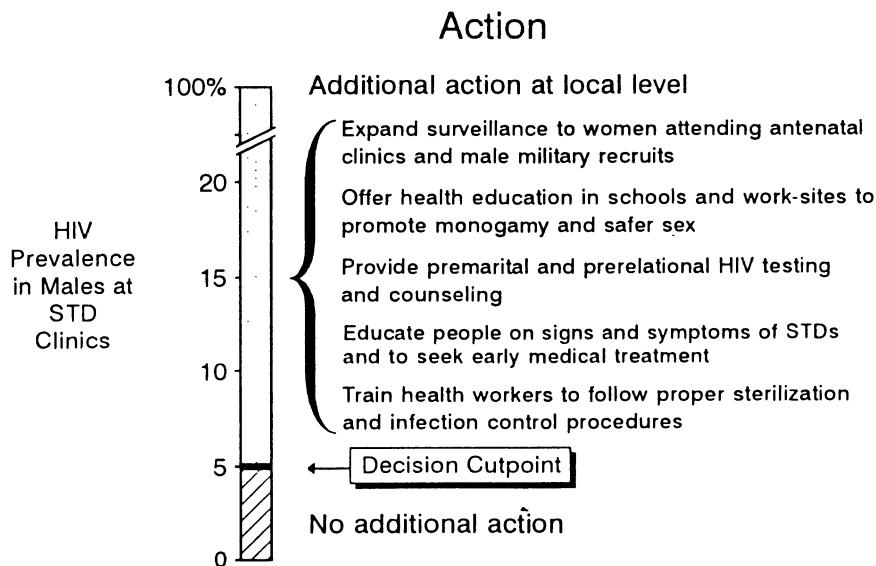
Decision Cutpoints

To use sentinel surveillance for predicting the future of the epidemic at the local level, public health officials need to establish decision cutpoints for HIV prevalence among the high-risk groups under observation. We

make the assumption that budgetary resources are not available to provide intensive intervention support for all areas of the country and subgroups of the population. Thus administrators are forced to use a triage system to define regions of highest need, and to limit high-cost programmatic action in provinces where HIV prevalence is below a specified cutpoint. An example for the HIV prevalence cutpoint of 5 percent in males at STD clinics is shown in Figure 4. Once the prevalence of HIV has reached 5 percent, a series of actions are started at the local level to help control the epidemic. The specific actions are shown only as an example. The link between action and both costs and effects is illustrated in Figure 5 in a fourfold table

with cells A to D. If HIV infection is truly above the predictive cutpoint among all males with STD infections (the high-risk group of interest in the population) and the actions are taken (cell A), the region or community would face the increased cost of the control programs but the people would also benefit from the resultant decline within the coming decade in the number of AIDS cases and deaths. If the HIV prevalence among STD-infected males in the population is truly below the predictive cutpoint (cell D), the government would not launch a costly control program and there would be no change in the number of AIDS cases and deaths. These two scenarios assume that a sentinel surveillance system is in place that

Figure 4. Decision cutpoint for additional action at local level aimed at controlling HIV infection in the population.



provides accurate data on the HIV status of the selected risk group in the population. If the sample of males selected at STD clinics is biased or unstable due to an insufficient sample size, the decision process will be subject to two types of errors. First, if health officials in error ignore the HIV epidemic when it is truly above the cutpoint (cell C), there will be no action and no additional immediate cost for HIV control to the region or community, but there will be an increased number of AIDS cases and deaths. Of course these cases and deaths will ultimately cost the society much more in terms of health care and lost productivity, but the cost would not be apparent for some years to come. Second, if the health officials in error commit resources to control programs when the level of infection is truly below the cutpoint (cell B), scarce resources will be inappropriately spent on HIV infection control when, in reality, there are few HIV infections and AIDS cases. Hence, to effectively guide decision makers, the surveillance program must avoid the two policy errors shown in cells B and C in Figure 5.

To provide complete information, the sentinel groups should ultimately be established throughout the country. In Thailand, testing involves small groups of 100–200 persons sam-

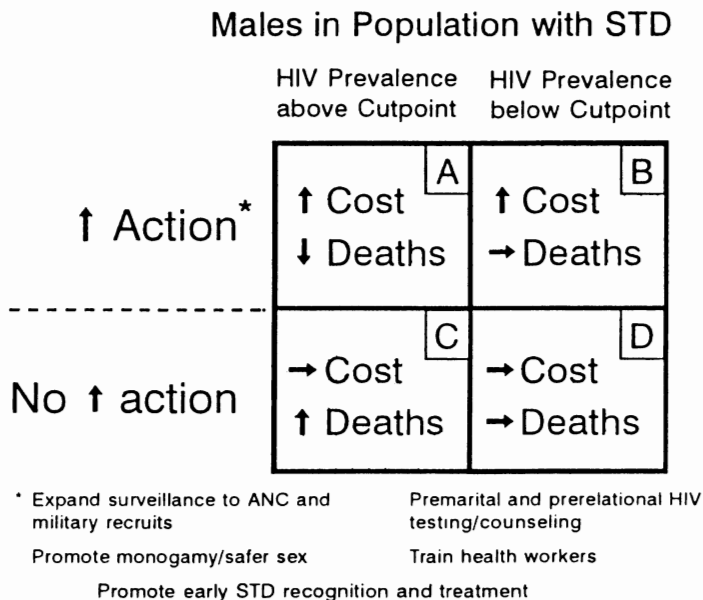
pled every six months using similar methods in all 73 provinces of the country, requiring 7,300 to 14,000 ELISA tests every six months. Such large-scale testing may be too much for many developing countries, especially if HIV/AIDS is still not recognized as an important local problem. To save money, we recommend starting slowly with a few key high-risk groups in a limited number of locations. While HIV antibody tests are usually done on serum, recent studies show that saliva is equivalent to serum,^{11–13} and is more convenient to use among certain sentinel groups such as intravenous drug users.¹⁴ The first sentinel sites should be those regions where informal surveys have shown that HIV infection is prevalent, where AIDS cases have been identified, or in which there has likely been exposure to infected individuals (e.g. tourists, drug users and sex-workers). Instead of six sentinel groups, we recommend starting with two or three groups that have been identified as the highest risk based on other evidence. Additional groups and locations can be added as it becomes evident that HIV infection is spreading through the society. We feel that determining the size and scope of the surveillance system is inherently a political process, requiring the support of taxpayers and government of-

ficials. A smaller, focused sentinel surveillance program that identifies risk groups and publicizes the findings will do much to raise the level of political support for an expanded program to combat and eventually control the HIV epidemic.

Conclusions

The Thailand sentinel surveillance program measures HIV prevalence in a “consistent manner repeated over time and place”, following the WHO definition.¹⁵ With clearly-defined decision cutpoints and a commitment to programmatic action, a similar HIV sentinel surveillance program could do much in other developing countries to lessen the impact of this terrible disease. We have demonstrated that sentinel surveillance of high-risk groups in Thailand provides predictive information of the spread of HIV to a low-risk group, typical of the general population. We believe that this analytic strategy can be used to predict the spread of the epidemic to other areas of Thailand where substantial infection in the general population has not yet occurred, and to guide administrators when making difficult funding decisions. Furthermore, we believe that this approach has relevance to other countries, particularly those in South-east Asia such as Myanmar, Laos, Cambodia and Vietnam, which have a similar mix of risk groups.

Figure 5. Costs and effects of action of control HIV infection.



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APPENDIX

Sampling of Sentinel Groups in Thailand

Intravenous drug users. At the beginning of June or December, all persons coming to the provincial hospital for methadone treatment are asked to be tested. Participation is voluntary and confidential. The clinic visitors are selected consecutively by existing staff until 100-200 have been sampled.

Lower-class female sex-workers. Sampling is a two-stage process. First, a random sample is drawn from a list of all identified brothels in the sentinel sites of each province. The list also includes the number of prostitutes reported to be working in each brothel. At the second stage, a team of local health workers visits the selected brothels and obtains a blood sample from all women working on the day of

sampling. The team proceeds to the next brothel on the sampling list and continues collection until blood samples from 100-200 women have been obtained. As with intravenous blood donors, testing is voluntary and confidential.

Higher-class female sex-workers. Sampling also involves two stages. At the first stage, a random sample is selected of institutions such as bars or massage parlors employing female sex-workers. At the second stage, all women working at the selected institutions on a given day are asked to participate. Collection is voluntary and confidential, and proceeds until 100-200 women have been sampled.

Males at STD Clinics. As part of the diagnostic process, men who come to STD clinics are required to give a blood sample for VDRL (syphilis) testing. The same blood is tested for HIV status, but with no identifying

information to match patient and blood. Hence the testing is unlinked and anonymous. Collection continues in a consecutive manner until 100-200 have been sampled.

Pregnant Women at ANC Clinics. Pregnant women who attend antenatal clinics are routinely tested for syphilis with the VDRL test. The blood is also tested for HIV status, but is unlinked and anonymous. Sampling is consecutive and continuous until 100-200 women have been included.

Blood Donors. All blood donated to local blood banks is tested for HIV infection as part of a mandatory screening program. Data on HIV infection from all blood samples collected in the sentinel area during June and December are submitted to the Ministry of Public Health for inclusion in the sentinel surveillance program.