

# **HIV Incidence Among Sentinel Surveillance Groups in Cambodia 1999-2002**

Part of a dissertation submitted by Vonthanak Saphonn in  
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## Outline of the presentation

1. Rationales
2. Objectives and specific aims
3. Literature reviews
4. Methodology
5. Results
6. Discussion
7. Implications and Recommendations
8. Conclusion

## SIGNIFICANT MILESTONE

- **1991**: First HIV infection detected
- **1993**: First AIDS Patient reported
- **1995**: First round of HSS (8 rounds)
- **1996**: First round of SSS (2 rounds)
- **1997**: First round of BSS (6 rounds)

## HSS Trends 1995-2002

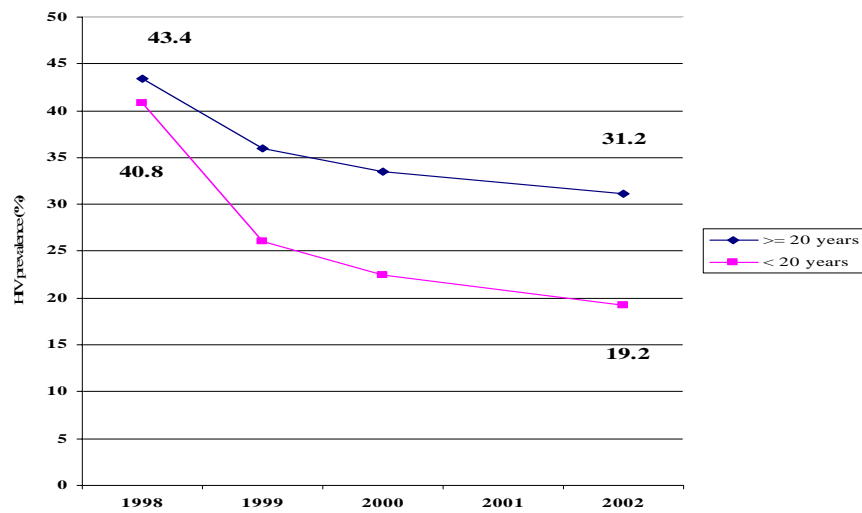
What are the trends of HIV prevalence over time?

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## Provinces and Population in HSS

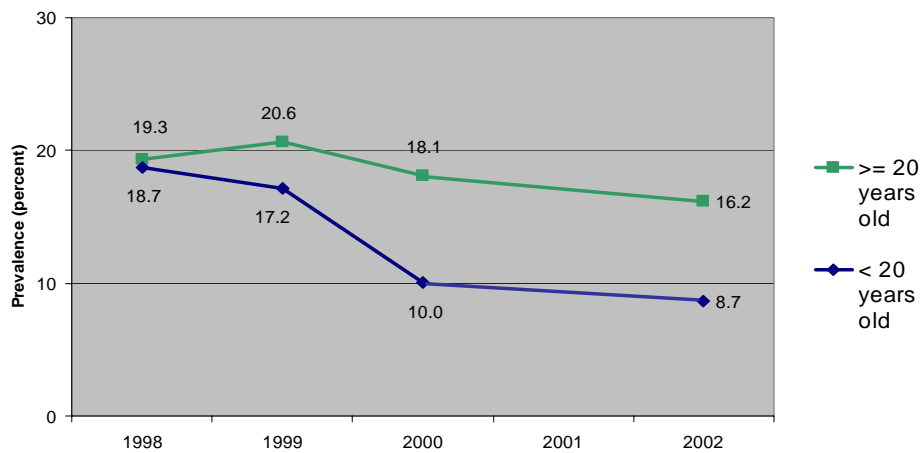
|                  | HSS I<br>1995 | HSS II<br>1996 | HSS III<br>1997 | HSS IV<br>1998 | HSS V<br>1999 | HSS VI<br>2000 | HSS VII<br>2002 |
|------------------|---------------|----------------|-----------------|----------------|---------------|----------------|-----------------|
| <b>Provinces</b> | <b>9</b>      | <b>18</b>      | <b>22</b>       | <b>19</b>      | <b>20</b>     | <b>21</b>      | <b>20</b>       |
| <b>CSWs</b>      | X             | X              | X               | X              | X             | X              | X               |
| <b>IDSWs</b>     | X             |                |                 | X              | X             | X              | X               |
| <b>POLICE</b>    | X             | X              | X               | X              | X             | X              | X               |
| <b>ANC</b>       | X             | X              | X               |                | X             | X              | X               |

## HIV prevalence among direct sex workers by age category



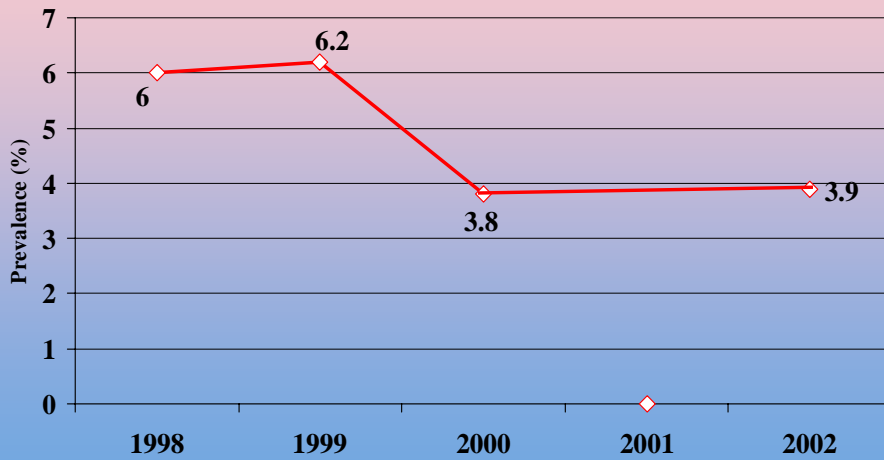
Source: HSS 2002 dissemination workshop. National Center for HIV/AIDS, Dermatology and STDs

## HIV prevalence by age category, indirect sex workers, HSS 1998-2002



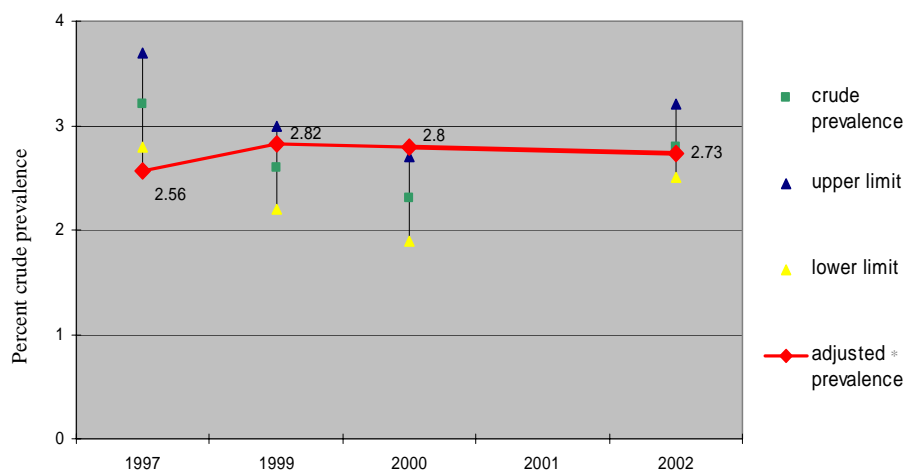
Source: HSS 2002 dissemination workshop. National Center for HIV/AIDS, Dermatology and STDs

## The Trend of HIV Seroprevalence among Urban Police



Source: HSS 2002 dissemination workshop. National Center for HIV/AIDS, Dermatology and STDs

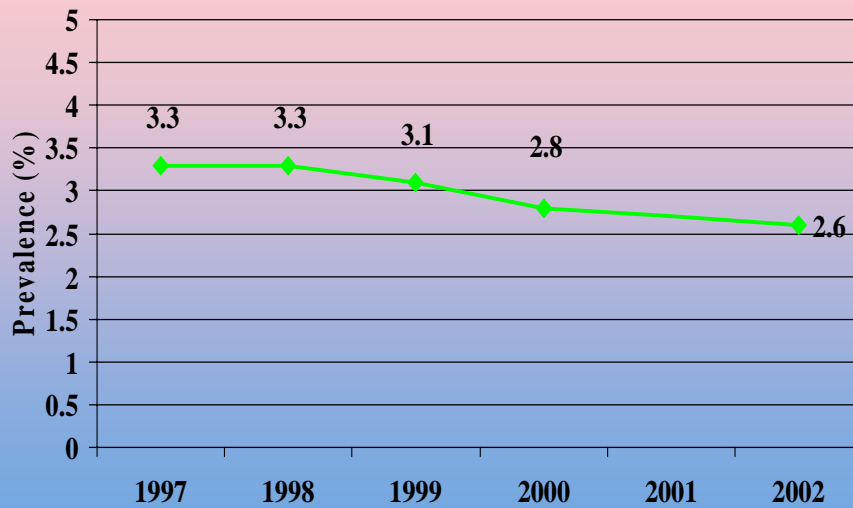
## Crude and Adjusted ANC Prevalence by Year, HSS 1997-2002



\*Adjusted prevalence calculated by smoothing provincial level prevalence and aggregating into national estimate

Source: HSS 2002 dissemination workshop. National Center for HIV/AIDS, Dermatology and STDs

## National HIV Prevalence among adult aged 15-49, Cambodia



Source: HSS 2002 dissemination workshop. National Center for HIV/AIDS, Dermatology and STDs

## Why this study?

- Twelve years after the first HIV infection was reported in Cambodia, UNAIDS recognized that Cambodia's epidemic appears to be stabilizing. HIV prevalence among pregnant women in major urban areas declined slightly from 3.2% in 1996 to 2.8% in 2002. Prevalence among sex workers declined from 42% in 1998 to 29% in 2002.
- Question about the relationship of the decline in prevalence to the incidence and the mortality has been raised.
- All specimens collected for HIV sentinel surveillance from 1999 to 2002 were kept refrigerated.
- New testing strategy to detect HIV recent infection has been available

## Objective

- To explain the dynamic of the HIV epidemic in different sentinel groups in Cambodia, in terms of incidence measure

## Specific aims

- To estimate the prevalence of “recent infection” among different sentinel groups in HIV sentinel surveillance using the newly developed IgG BED-CEIA technique.
- To approximate the incidence of HIV infection among different target groups from the prevalence of persons with recent HIV infection

## Methods used to estimate the incidence of HIV infection

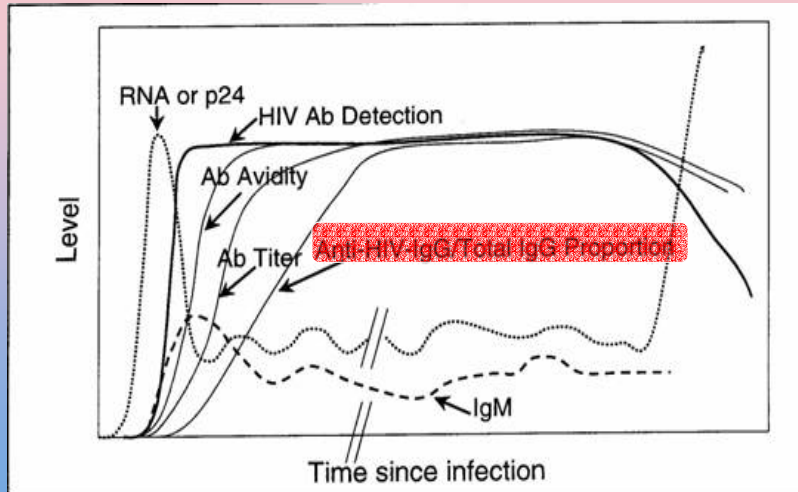
- Direct method
  - using open or dynamic cohort
  - using closed or fixed cohort method
- Indirect methods
  - using seroprevalence data to estimate HIV incidence
  - using back-calculation, which uses reported AIDS cases to reconstruct historical infection rates or
  - using the birth cohort method, which uses the slopes of trend lines from repeated samples of birth cohorts.

## How to Use Seroprevalence Data to Estimate HIV Incidence

- p24 antigenemia individuals who have not seroconverted: HIV p24 antigen test or combination of HIV p24 antigen test with reverse transcriptase-polymerase chain reaction (RT-PCR) – test the antibody-negative samples
- sensitive/less sensitive serologic testing strategies – test the antibody-positive samples



A schematic depicting changes in various parameters that define early and late HIV infection



## Methods



## Data sources

- This study used available specimens collected for the 1999, 2000 and 2002 HIV sentinel surveillance in Cambodia as a data source.
- Four sentinel groups were selected for this study:
  - pregnant women attending antenatal clinic (ANC),
  - police personnel (police),
  - brothel-based commercial sex workers (CSWs)
  - indirect commercial sex workers (IDSWs).

## Sample size and sampling design

The sample size and sampling design were developed by the National Center for HIV/AIDS, STD and Dermatology.

### Sample size

- ANC: 300 (provincial capital) and 300 (remaining districts)
- Police and IDSWs: 300 (where the most recent estimate of prevalence was 5% or less) and 100-150 (where the prevalence was greater than 5%)
- CSWs: 100-150

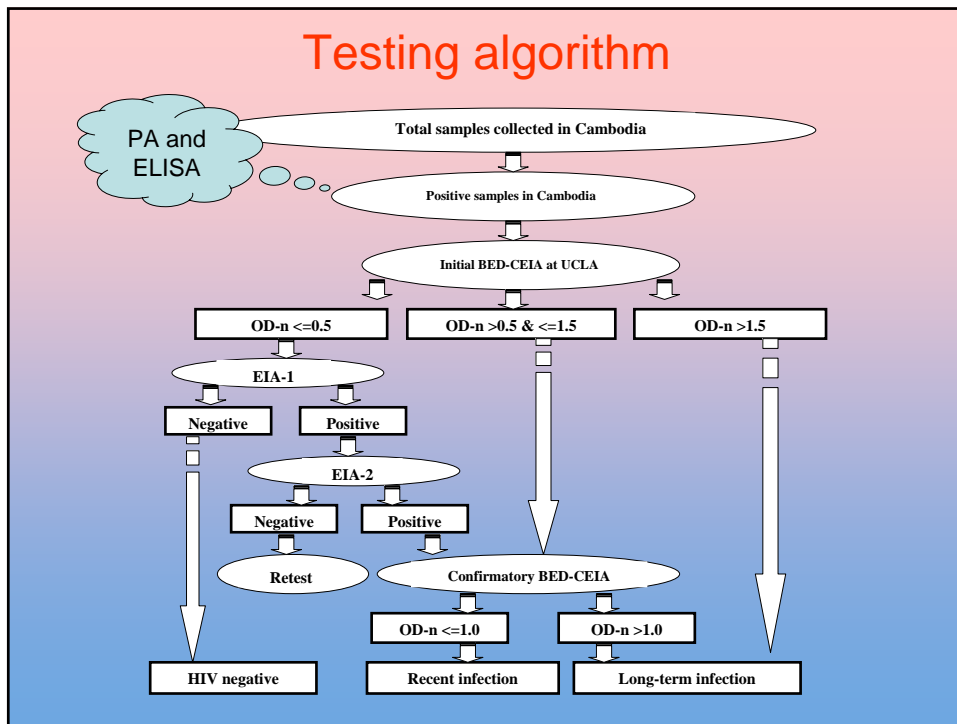
### Sampling strategy:

- ANC: consecutive sampling
- CSWs and IDSWs: cluster sampling design or take all
- Police: cluster sampling

## Specimens collection

- 5ml of blood were drawn into a blood tube from each subject
- 2 ml of sera was transferred to a cryotube for storage and testing.
- All the specimens were accumulated, processed, and stored at  $-20^{\circ}\text{C}$  at NCHADS.
- All HIV-positive specimens identified in Cambodia were transferred to UCLA for BED-CEIA testing

## Testing algorithm



## Estimation of HIV incidence from prevalence of recent HIV infection

$$P = I \times D$$

Prevalent cases = Incident cases x Duration in disease state

## Results

### Regions in Cambodia

- **Western region** borders with Thailand, composed of 8 provinces: Banteay Meanchey, Battambang, Koh Kong, Pailin, Pursat, Preash Vihear, Odor Meanchey and Sihanoukville.
- **Eastern region** borders with Vietnam, composed of 10 provinces: Kampong Cham, Kampot, Kep, Krotie, Preyveng, Ratanakiri, Modulkiri, Steung Treng, Svay Rieng and Takeo.
- **Central region** composed of 6 provinces: Kampong Chhang, Kampong Speu, Kampong Thom, Kandal, Phnom Penh and Siem Reap

## Percentage of refusal rate (minimum-maximum) among different sentinel groups

|        | 1999           | 2000          | 2002          |
|--------|----------------|---------------|---------------|
| ANC    | 6.70(0-23.45)  | NA            | 1.9 (0-18.5)  |
| CSW    | 21.50(0-46.99) | 4.9 (0-18.0)  | 4.8 (0-16.2)  |
| IDSW   | 35.70(0-58.00) | 11.9 (0-32.3) | 11.6 (0-37.7) |
| Police | 24.30(0-54.20) | 8.6 (0-58.0)  | 14.6 (0-57.8) |

## False positive specimen

| Year           | Group | Specimen transferred to UCLA | HIV + after two different ELISA at UCLA | False positive |
|----------------|-------|------------------------------|---|----------------|
| 1999           | ANC   | 119                          | 94                                      | 21.01%         |
|                | CSW   | 730                          | 678                                     | 7.12%          |
|                | IDSW  | 228                          | 193                                     | 15.35%         |
|                | POL   | 189                          | 148                                     | 21.69%         |
| 2000           | ANC   | 140                          | 106                                     | 24.29%         |
|                | CSW   | 649                          | 622                                     | 4.16%          |
|                | IDSW  | 276                          | 245                                     | 11.23%         |
|                | POL   | 143                          | 128                                     | 10.49%         |
| 2002           | ANC   | 239                          | 178                                     | 25.52%         |
|                | CSW   | 588                          | 524                                     | 10.88%         |
|                | IDSW  | 168                          | 148                                     | 11.90%         |
|                | POL   | 130                          | 107                                     | 17.69%         |
| <b>Overall</b> |       | 3599                         | 3171                                    | 11.89%         |

## Demographic characteristics of ANC

| Characteristics  | 1999      |       | 2000      |       | 2002      |       |
|------------------|-----------|-------|-----------|-------|-----------|-------|
|                  | Frequency | %     | Frequency | %     | Frequency | %     |
| <b>Age</b>       |           |       |           |       |           |       |
| 14-19 years      | 531       | 10.42 | 559       | 9.35  | 1,618     | 18.53 |
| 20-29 years      | 2,854     | 55.99 | 3,294     | 55.12 | 4,494     | 51.45 |
| 30-39 years      | 1,490     | 29.23 | 1,779     | 29.77 | 2,272     | 26.01 |
| 40-49 years      | 222       | 4.36  | 344       | 5.76  | 350       | 4.01  |
| <b>Schooling</b> |           |       |           |       |           |       |
| <=4 years        | 1,842     | 36.14 | 2,179     | 36.77 | 3,687     | 42.2  |
| 5-8 years        | 2,057     | 40.36 | 2,734     | 46.14 | 3,660     | 41.9  |
| 9-12 years       | 733       | 14.38 | 978       | 16.5  | 1,347     | 15.42 |
| >12 years        | 465       | 9.12  | 35        | 0.59  | 42        | 0.48  |
| Married          | 5,097     | 100   | 5,976     | 100   | 8,720     | 99.82 |
| Urban            | 3,238     | 63.53 | 3,546     | 59.34 | 4,928     | 56.41 |

## Demographic characteristics of CSW

| Characteristics  | 1999      |       | 2000      |       | 2002      |       |
|------------------|-----------|-------|-----------|-------|-----------|-------|
|                  | Frequency | %     | Frequency | %     | Frequency | %     |
| <b>Age</b>       |           |       |           |       |           |       |
| 14-19 years      | 607       | 27.9  | 430       | 21.11 | 406       | 19.72 |
| 20-29 years      | 1,411     | 64.84 | 1,450     | 71.18 | 1,505     | 73.09 |
| 30-39 years      | 145       | 6.66  | 153       | 7.51  | 145       | 7.04  |
| 40-49 years      | 11        | 0.51  | 4         | 0.2   | 3         | 0.15  |
| <b>Schooling</b> |           |       |           |       |           |       |
| <=4 years        | 1,712     | 78.68 | 1,512     | 74.68 | 1,545     | 75.4  |
| 5-8 years        | 422       | 19.39 | 472       | 23.16 | 457       | 22.2  |
| 9-12 years       | 39        | 1.79  | 44        | 2.16  | 57        | 2.77  |
| >12 years        | 3         | 0.14  | 0         | 0     | 0         | 0     |
| Married          | 447       | 20.54 | 658       | 32.29 | 556       | 27    |
| Urban            | -         | -     | -         | -     | -         | -     |

## Demographic characteristics of IDSW

| Characteristics  | 1999      |       | 2000      |       | 2002      |       |
|------------------|-----------|-------|-----------|-------|-----------|-------|
|                  | Frequency | %     | Frequency | %     | Frequency | %     |
| <b>Age</b>       |           |       |           |       |           |       |
| 14-19 years      | 394       | 27.46 | 418       | 24.62 | 235       | 19.36 |
| 20-29 years      | 973       | 67.8  | 1,177     | 69.32 | 890       | 73.31 |
| 30-39 years      | 67        | 4.67  | 100       | 5.89  | 85        | 7     |
| 40-49 years      | 1         | 0.07  | 3         | 0.18  | 4         | 0.33  |
| <b>Schooling</b> |           |       |           |       |           |       |
| <=4 years        | 541       | 37.7  | 725       | 42.76 | 664       | 54.7  |
| 5-8 years        | 662       | 46.13 | 809       | 47.64 | 477       | 39.29 |
| 9-12 years       | 132       | 9.2   | 163       | 9.6   | 70        | 5.77  |
| >12 years        | 100       | 6.97  | 0         | 0     | 3         | 0.25  |
| Married          | 321       | 22.37 | 602       | 35.45 | 502       | 41.35 |
| Urban            | -         | -     | -         | -     | -         | -     |

## Demographic characteristics of Police

| Characteristics  | 1999      |       | 2000      |       | 2002      |       |
|------------------|-----------|-------|-----------|-------|-----------|-------|
|                  | Frequency | %     | Frequency | %     | Frequency | %     |
| <b>Age</b>       |           |       |           |       |           |       |
| 14-19 years      | 25        | 0.65  | 22        | 0.53  | 20        | 0.48  |
| 20-29 years      | 912       | 23.74 | 738       | 17.85 | 575       | 13.87 |
| 30-39 years      | 1,969     | 51.26 | 2,252     | 54.46 | 2,210     | 52.32 |
| 40-49 years      | 809       | 21.06 | 935       | 22.61 | 1,096     | 26.44 |
| >=50 years       | 126       | 3.28  | 188       | 4.55  | 244       | 5.89  |
| <b>Schooling</b> |           |       |           |       |           |       |
| <=4 years        | 350       | 9.11  | 436       | 10.54 | 531       | 12.8  |
| 5-8 years        | 1,987     | 51.73 | 2,456     | 59.4  | 2,278     | 54.9  |
| 9-12 years       | 1,135     | 29.55 | 1,233     | 29.82 | 1,332     | 32.1  |
| >12 years        | 369       | 9.61  | 10        | 0.24  | 8         | 0.19  |
| Married          | 3,291     | 85.58 | 3,704     | 89.58 | 3,835     | 92.43 |
| Urban            | -         | -     | -         | -     | -         | -     |



### HIV incidence trends in different sentinel surveillance groups, 1999-2002

|               | 1999   | 2000   | 2002   | OR**        | 95% CI           | P-value       |
|---------------|--------|--------|--------|-------------|------------------|---------------|
| <b>ANC</b>    | 0.72%* | 1.11%* | 0.59%* | 0.96        | 0.79-1.17        | 0.69          |
| <b>CSW</b>    | 13.90% | 9.02%  | 6.45%  | <b>0.79</b> | <b>0.69-0.90</b> | <b>0.0003</b> |
| <b>IDSW</b>   | 5.08%  | 5.08%  | 2.87%  | <b>0.82</b> | <b>0.66-1.03</b> | <b>0.09</b>   |
| <b>Police</b> | 1.74%* | 1.30%* | 0.26%* | <b>0.64</b> | <b>0.48-0.84</b> | <b>0.001</b>  |

\* Incidence adjusted for the provincial population size

\*\* odds ratio adjusted for age, marital status, location, school and province

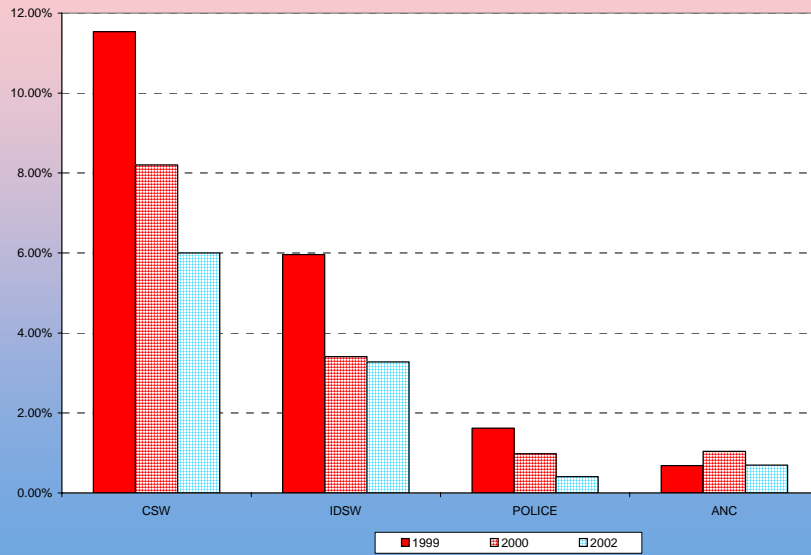
### HIV incidence trends in pregnant women attending ANC by location, 1999-2002

|              | 1999   | 2000   | 2002   | OR** | 95% CI    | P-value |
|--------------|--------|--------|--------|------|-----------|---------|
| <b>Urban</b> | 1.00%* | 0.74%* | 0.24%* | 0.82 | 0.64-1.05 | 0.13    |
| <b>Rural</b> | 0.11%* | 0.23%* | 0.42%* | 1.27 | 0.89-1.77 | 0.17    |

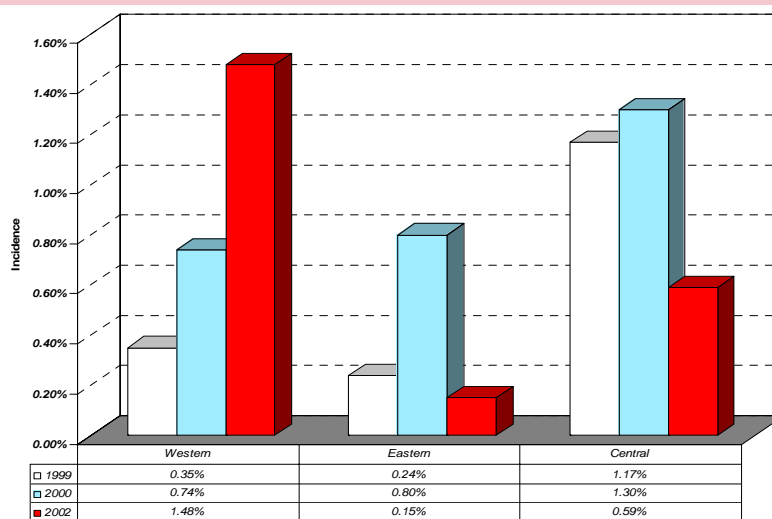
\* Incidence adjusted for the provincial population size

\*\* odds ratio adjusted for age, marital status, school and province

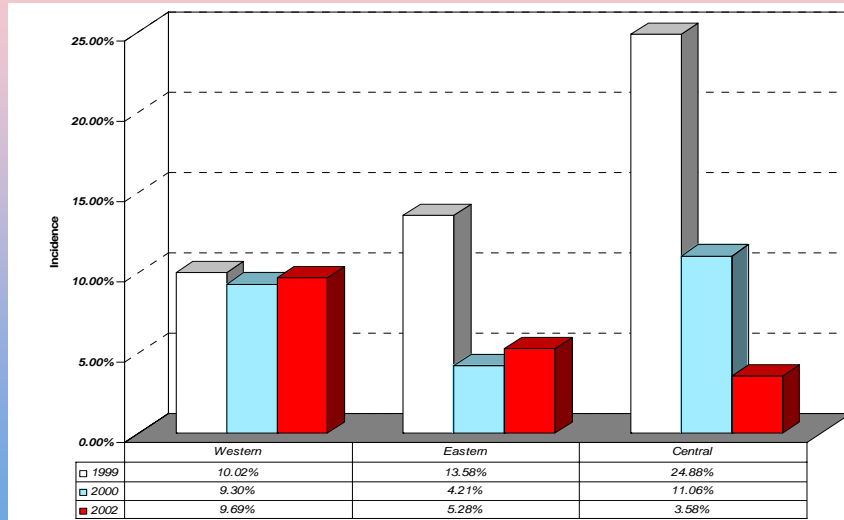
## Incidence trends among different sentinel groups in Cambodia



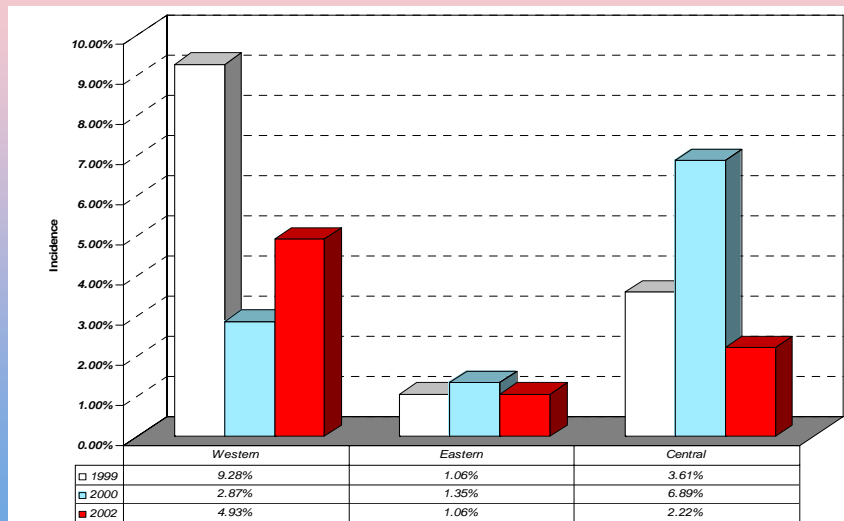
## Trend of HIV incidence among ANC in different regions in Cambodia



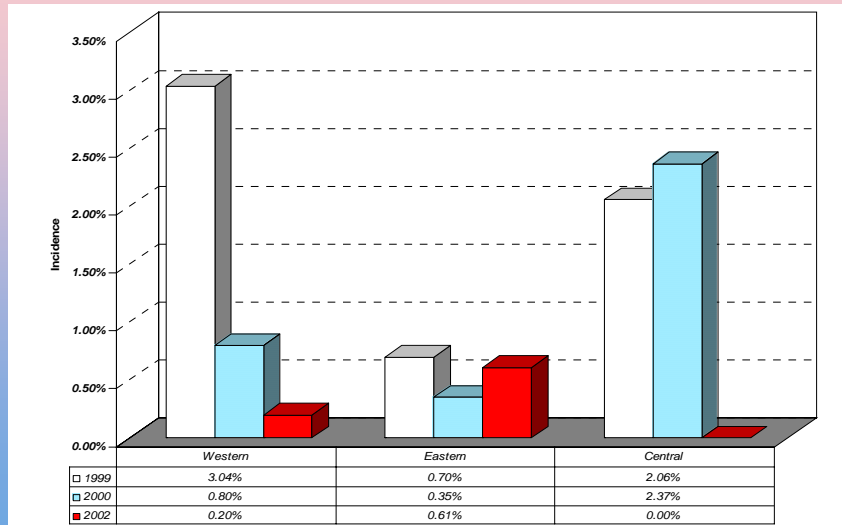
## Trend of HIV incidence among CSW in different regions in Cambodia



## Trend of HIV incidence among IDSW in different regions in Cambodia



## Trend of HIV incidence among Police in different regions in Cambodia



## Discussion

## Summary of the findings

- To our knowledge, this is the first application of the BED-CEIA to estimate HIV incidence in HIV sentinel surveillance data in the world in general and in Cambodia in particular.
- Our results suggest that there has been a decline in incidence from 1999 to 2002 in three sentinel groups: CSWs, IDSWs and police personnel. Pregnant women attending ANC was the only group for which the overall trend did not show any decline.

## Consistency

- The decline in incidence among CSWs, IDSWs and Police personnel may reflect the effectiveness of the intervention program
- It is not unexpected that the intervention program has had little or no impact on the transmission from those who are already infected to their usual sexual partners and wives since testing and counseling is not widely available in this country and condom use is low with wives and girlfriends

## BED-CEIA testing most appropriate for Cambodia

- Needs to be performed only on those specimens that are HIV antibody positive by conventional testing
- Performed at a 1:100 dilution of specimen which is much simpler than other less-sensitive EIA assays which requires 1:20,000 dilution
- Excellent performance characteristics in detecting recent infections among individuals infected with subtypes B,D or E

## BED-CEIA testing

- Four percent of the persons at the end stage of the AIDS may have low levels of HIV antibody and be falsely classified by BED/CEIA as recent infection ---not likely to occur
- Misclassification may also occur because some person who receive antiretroviral treatment that includes a protease inhibitor early in the course of their infection may have a decline in antibody and may be falsely identified as recent infection by BED-CEIA ---unlikely
- Misclassification can also be due to the optical density cutoff levels may have biased our estimate of incidence - --non-differential

## Human resources and logistics

- Wide coverage of the surveillance program in Cambodia coupled with some rotation in personnel supervisors at the national levels make the task of keeping the standard operating procedure comparable over years a real challenge

## Sampling

- The sample of pregnant women from HIV sentinel surveillance may not be generalizable to the pregnant population in the country.
- Since the younger women were oversampled in 2002, the HIV incidence in 2002 might be higher than what if this population were sample as the one in 1999 or 2000. Because, younger infected women are more likely to be recently infected than older women. Similar discussion point can be raised for CSW and IDSW.

## Refusal to participation

- The refusal rate was highest in 1999 and the characteristics and sexual behaviors of those who refused to participate in the study were not known.
- If those who refused to participate in the study had higher risk behavior than those who participated, the results would have been changed. This would ultimately affect the analyses of HIV incidence trends as well

## False positive vs False negative

- We found that among those specimens brought to UCLA, some were false positives and some did not have sufficient quantity for further testing with BED-CEIA.
- It is then important to know what the false negative rate is among those negative specimens.



## Assumptions

- No false negative among the negative specimen. If this is not true, one can predict incidence estimated in each year to be an underestimate. However, the trend of HIV incidence over time will be unpredictable
- Since the duration of the infection detected by BED-CEIA was only 168 days, the theoretical condition of “stationary population with no net migration” as described here is likely to hold true ----- need further study to validate this duration

## Assumptions

- The absolute estimate of incidence depends on the accuracy of T. Continued validation of BED-CEIA in cross-sectional specimens with known HIV-1 incidence will be important to assess findings of this study. However, in trend analysis, the error introduced by any inaccuracy of T would be systematic, and the trend over time are likely to be valid
- The rate of false positive and recent infection was similar between those positive specimens that were tested at UCLA and those positive specimens that were missing”. A sensitivity analysis were done assuming three different scenario showed the trends were basically the same

## Statistical considerations

- Cluster sampling design---SRS analysis---smaller variance
- Sample size was calculated based on the expected prevalence which is higher than expected incidence---low power

## Implications and recommendations

(1)

- Cambodia is having a slow down transmission among small size high risk population but is now facing a fairly constant transmission among general population
- The epidemic will continue to spread in the general population if no effective measures are implemented to reduce the transmission in general population.
- Further Studies should also focus on strategies to protect wives and girlfriends in Cambodia and more intervention programs need to be designed for this population
- The high HIV incidence rate in CSWs and IDSWs in Cambodia makes this population well suited for studies of HIV-1 prevention including vaccine trials.

## Implications and recommendations

(2)

- Development of a standard operating procedure (SOP) specifically for the HIV surveillance program is needed.
- Quality control and assurance of testing should be set up as part of the current surveillance program.
- Integrating the testing strategies that could reduce the refusal and differentiate recent HIV infection from long term infection (e.g. BED-CEIA) into surveillance program.

## Conclusion

- HIV epidemic in Cambodia seems to be stabilizing. HIV incidence rate among three sentinel groups (CSWs, IDSWs and Police) are declining over the study period. However, the epidemic persists in pregnant women group. The observed decline in HIV prevalence among high risk groups was contributed by the decline of incidence.