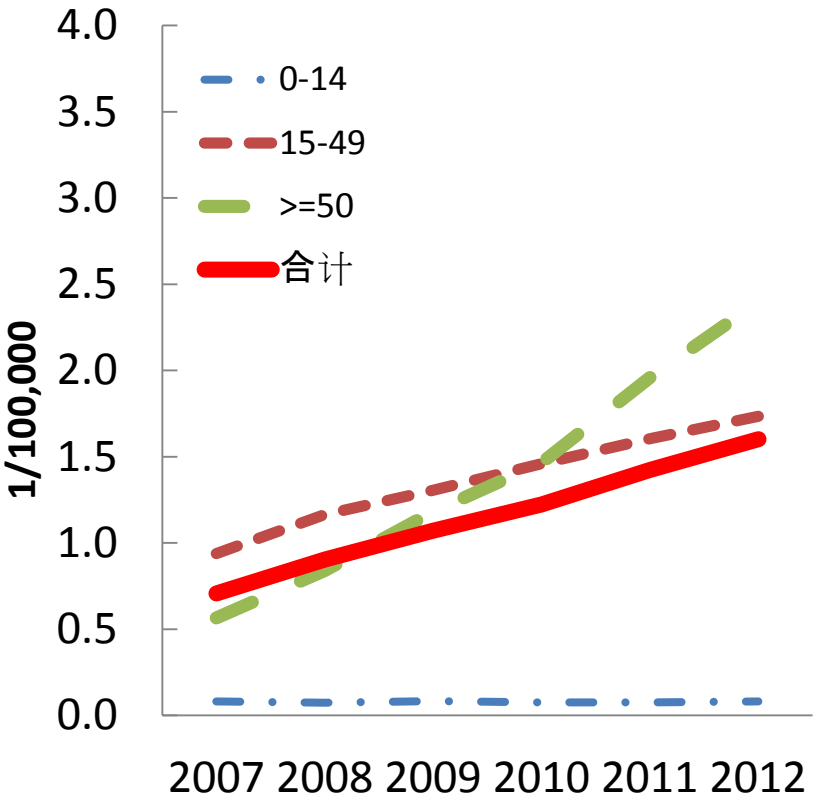
# TRACKING THE HIV/AIDS EPIDEMIC: ISSUES, CHALLENGES and FUTURE DIRECTIONS

November 2015

CHIPTS

# CHINA
# Mortality trends

HIV/AIDS mortality increase



# CHANGING STATISTICS

WORLDWIDE: **UNAIDS**

HIV PREVALENCE - ⬇ 6 million

HIV INCIDENCE ⬇ 42%

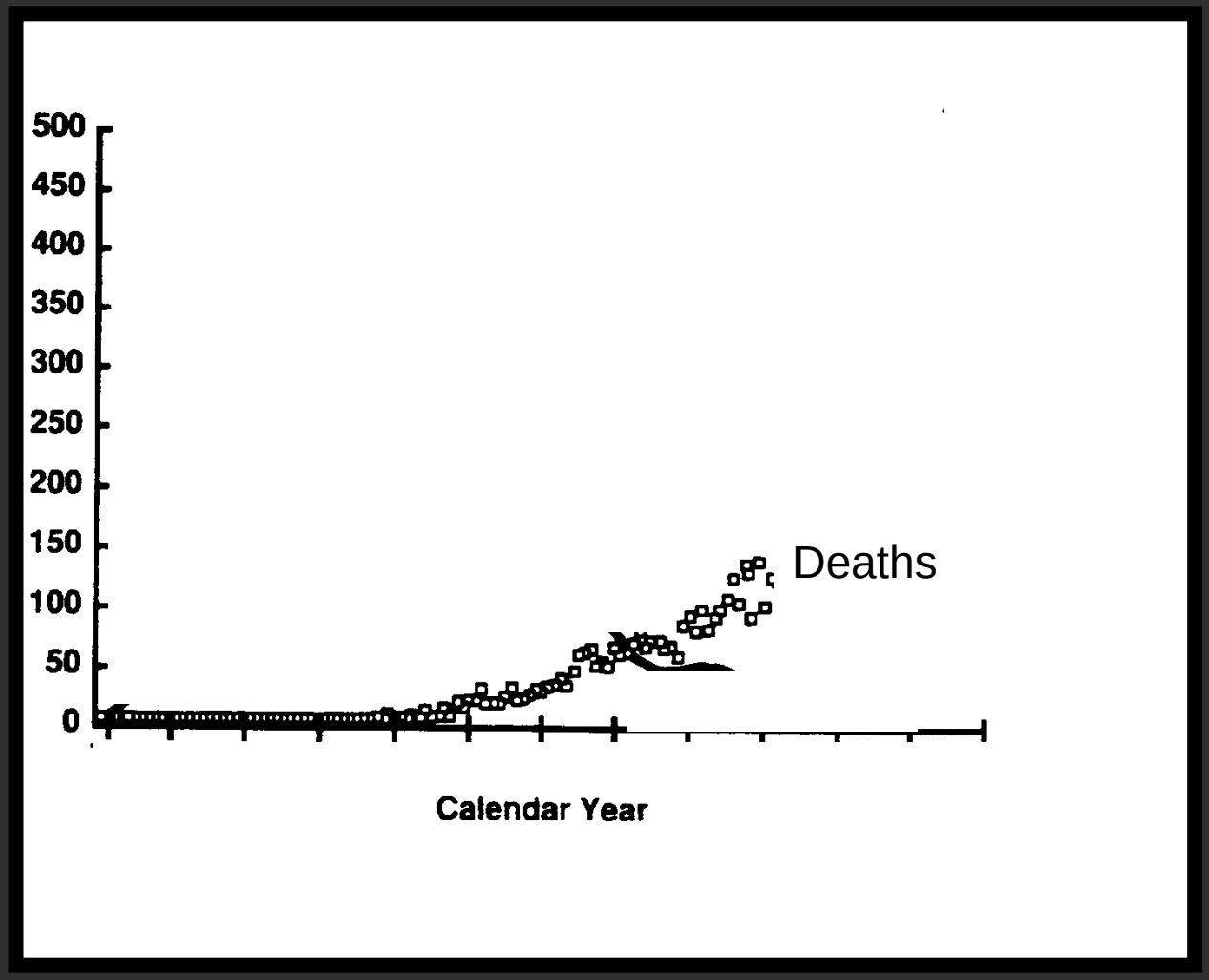
- INTERPETATION OF TRENDS
- MEASUREMENT ISSUES
- SOME FUTURE DIRECTIONS

# VOCABULARY: 3 INDICATORS

- HIV PREVALENCE
- HIV INCIDENCE
- HIV/AIDS MORTALITY RATE
  - -deaths among persons with HIV/AIDS
  - -(usually) regardless of cause of death

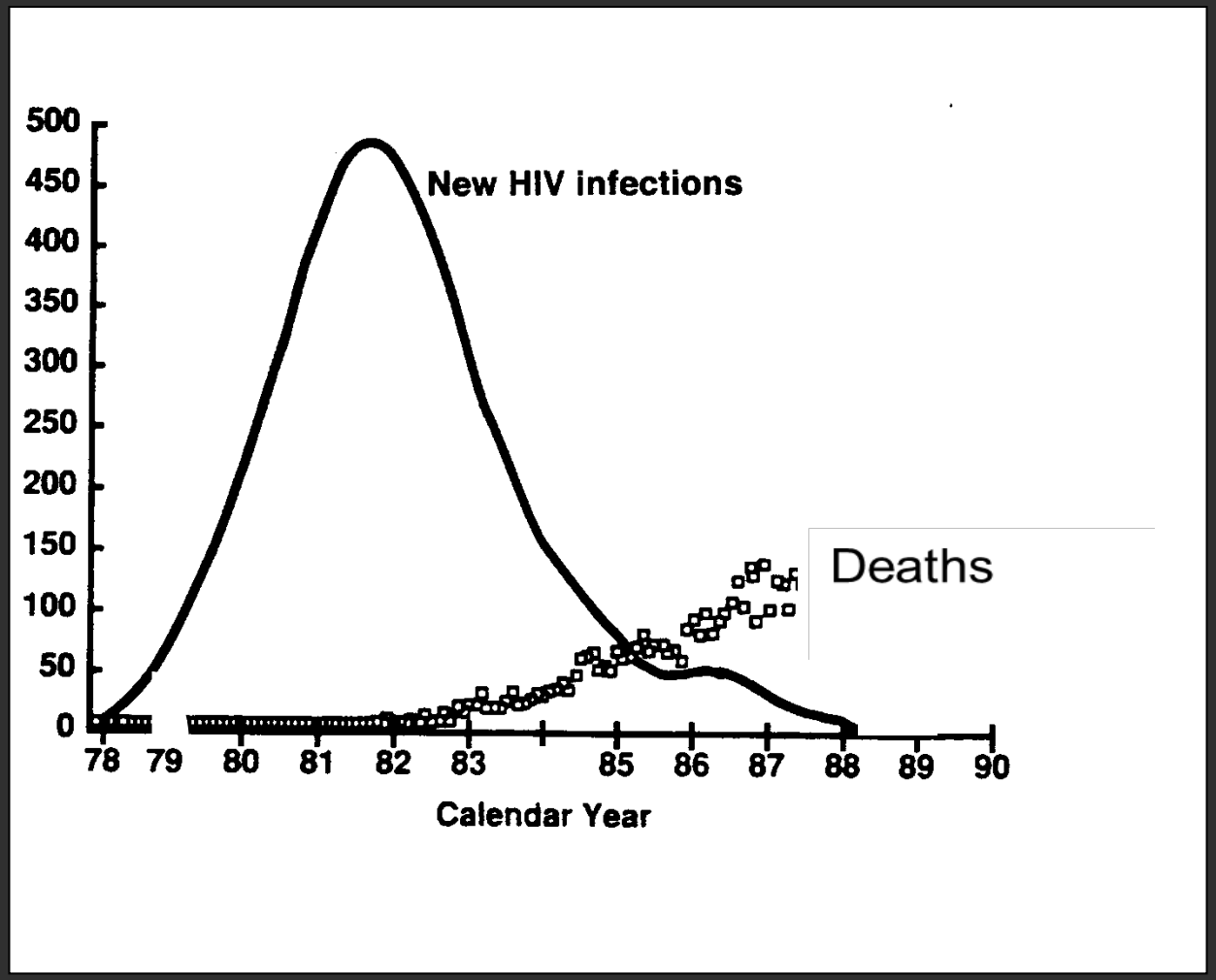
# INTERPETATION of TRENDS

# MORTALITY
# (assume complete reporting of deaths)




BAD NEWS OR GOOD NEWS?

# INCIDENCE VS. MORTALITY




BAD NEWS OR GOOD NEWS?

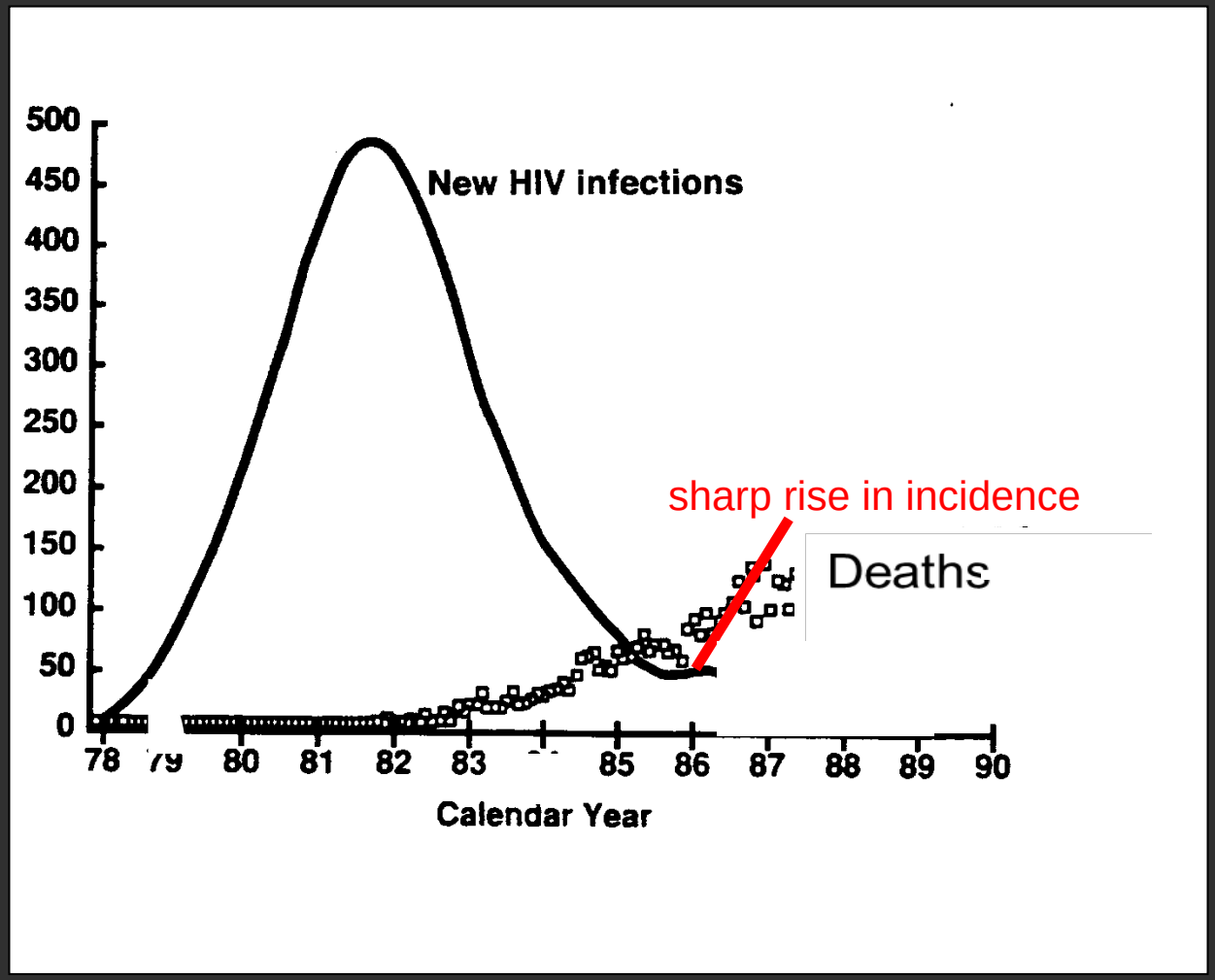
# INTERPRETING TRENDS

**HIV mortality ↑ as current HIV incidence ↓ because…**

**… persons infected years ago are dying**

**… mortality trends do NOT reflect recent incidence trends**

# HIV INCIDENCE VS. MORTALITY



**FURTHERMORE**

**…mortality can still ↑**
**even though ART (TX) is preventing some deaths**

# VOCABULARY

- HIV MORTALITY RATE

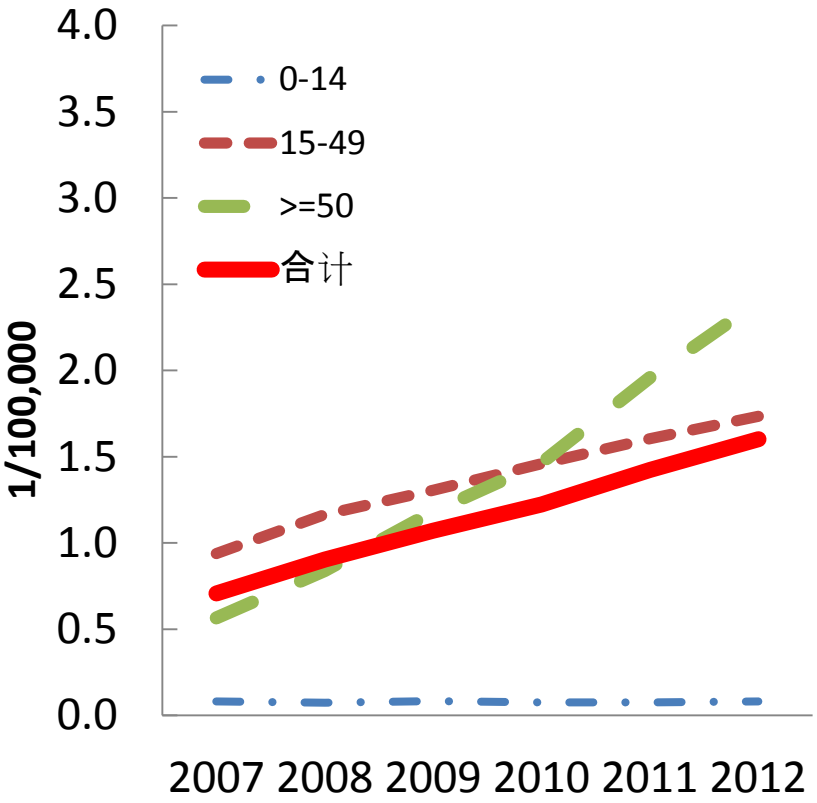
$$\frac{total\ HIV\ deaths\ during\ year\ in\ population}{Population\ size}$$

- CASE FATALITY RATE

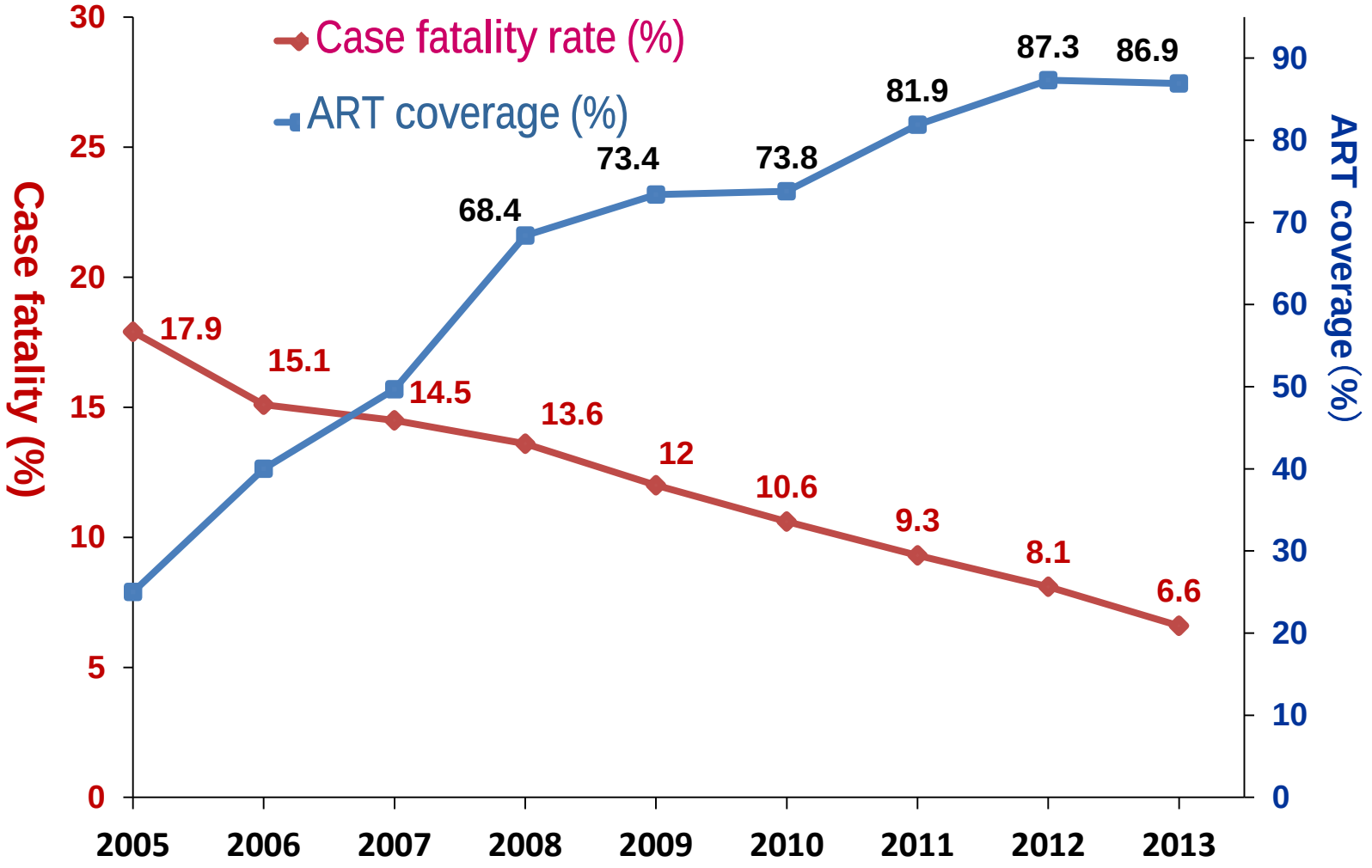
$$\frac{deaths\ durng\ year\ from\ among\ HIV\ cases}{alive\ HIV\ cases}$$

# CHINA
# Mortality trends

HIV/AIDS mortality increase



# ART coverage improved and case-fatality declined



# CASE FATALITY VS. MORTALITY RATES:

## (complete reporting of deaths)

**CAN TRENDS MOVE IN OPPOSITE DIRECTIONS?**

YES!

- Case fatality ↓ because of better survival (tx, access)
- Mortality rates ↑ because of high incidence in the past even though there have been recent improvements in survival of cases

# CASE FATALITY VS. MORTALITY RATES: complete reporting of deaths

## NOTE

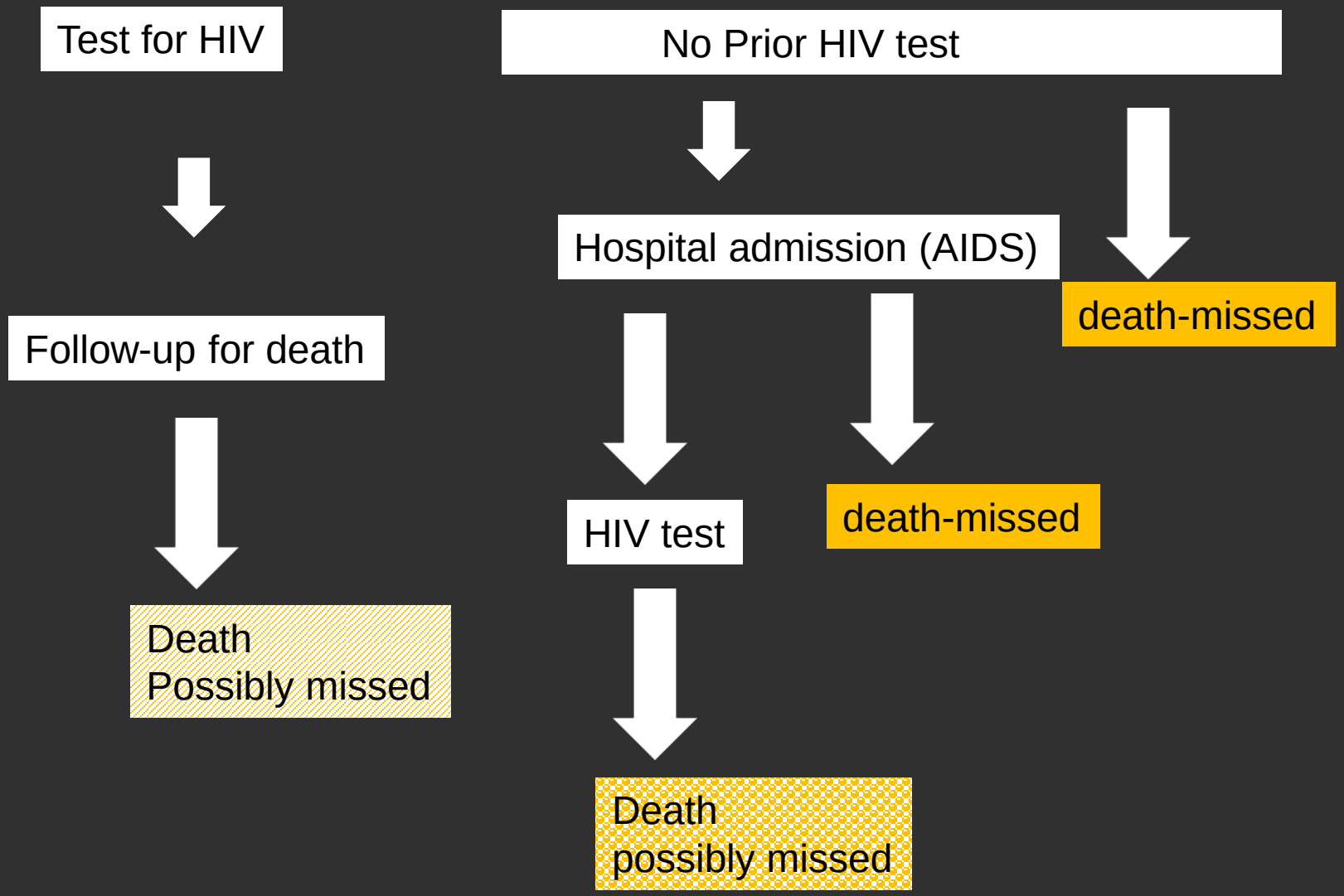
P(HIV DEATH) = P(HIV CASE*) x P(HIV DEATH |HIV CASE*)

Mortality rate = Prevalence rate x Case fatality rate

↓ or ↑ ↑ ↓

*Case here refers to advanced HIV disease to control for changing case mix

# Further Complication in China: Measurement only deaths with prior HIV test counted



# MORTALITY

## ONLY DEATHS WITH PRIOR HIV TEST REPORTED

If counting of deaths requires prior HIV tests,

…then increases in testing can cause increases in the reported mortality rate

… even though the true mortality rate is constant or even decreasing.

# HIV PREVALENCE TRENDS

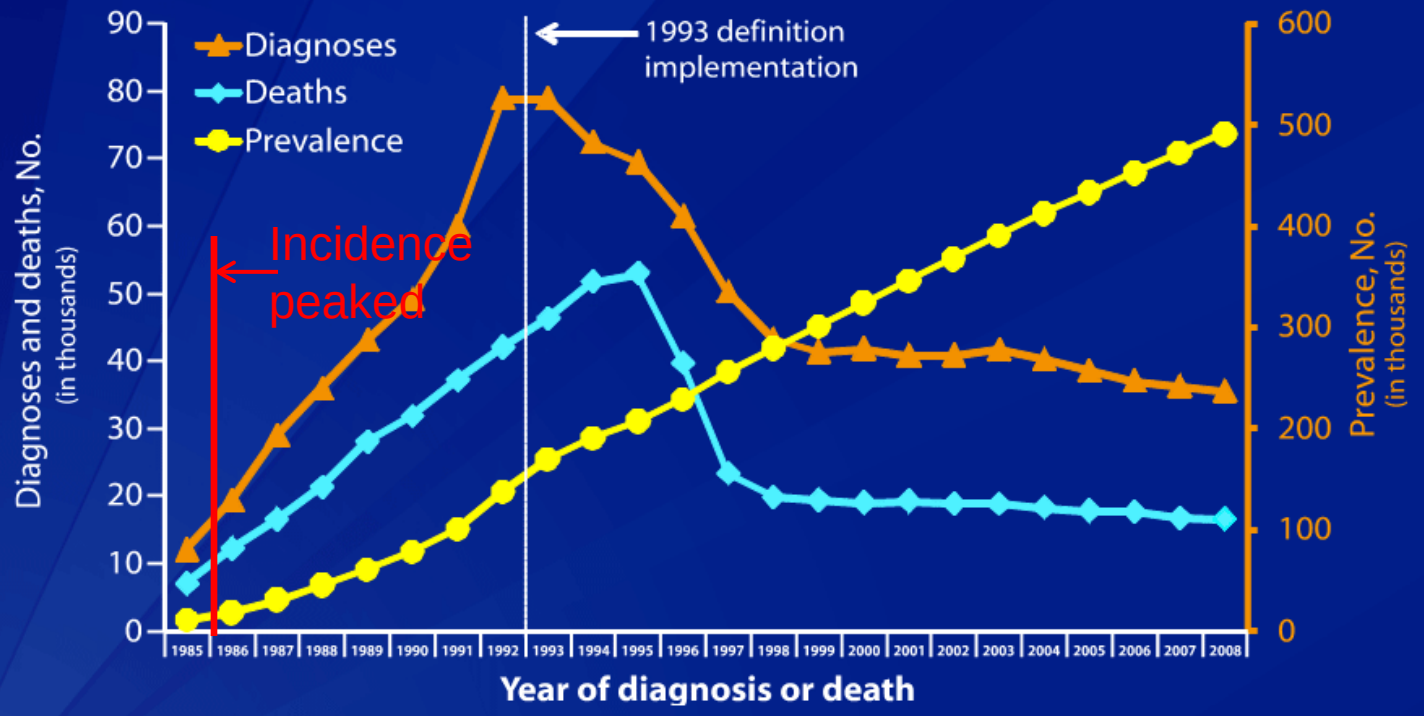
# HIV PREVALENCE TRENDS


- Prevalence may ↓ or ↑depending on whether HIV deaths > or < than new infections
- Prevalence can be constant even though incidence and deaths are rising
- Prevalence may ↑ (↓ )because survival ↑ (↓)
- Prevalence may ↑ (↓) because incidence ↑ (↓)

# SOME TREND SCENARIOS

| Incidence | mortality | prevalence | possible explanation |
|---|---|---|---|
| ↓ | ↑ | ↓ | waning epidemic |
| ↑ | ↑ | ↓ | very recent incidence increase |
| ↑ | ↑ | = | new infections= deaths |
| ↓ | ↓ | ↑ | good news; tx and prevention improvements |

# AIDS Diagnoses, Deaths, and Persons Living with AIDS, 1985–2008—United States and Dependent Areas




*Note*. All displayed data have been statistically adjusted to account for reporting delays, but not for incomplete reporting. Death may be due to any cause.

CDC

# INTERPETATION of TRENDS

- Trends in incidence, prevalence and mortality rates can be difficult to interpret
- They may go in opposite directions
- All indicators need to be considered
- Challenges in measuring indicators makes interpretation even more difficult

# MEASUREMENT ISSUES

***“INDIA SLASHES ESTIMATE OF HIV INFECTED PEOPLE”***

*Science*, 2007

***WORLD HIV PREVALENCE DOWN 6 MILLION***

UNAIDS, 2008

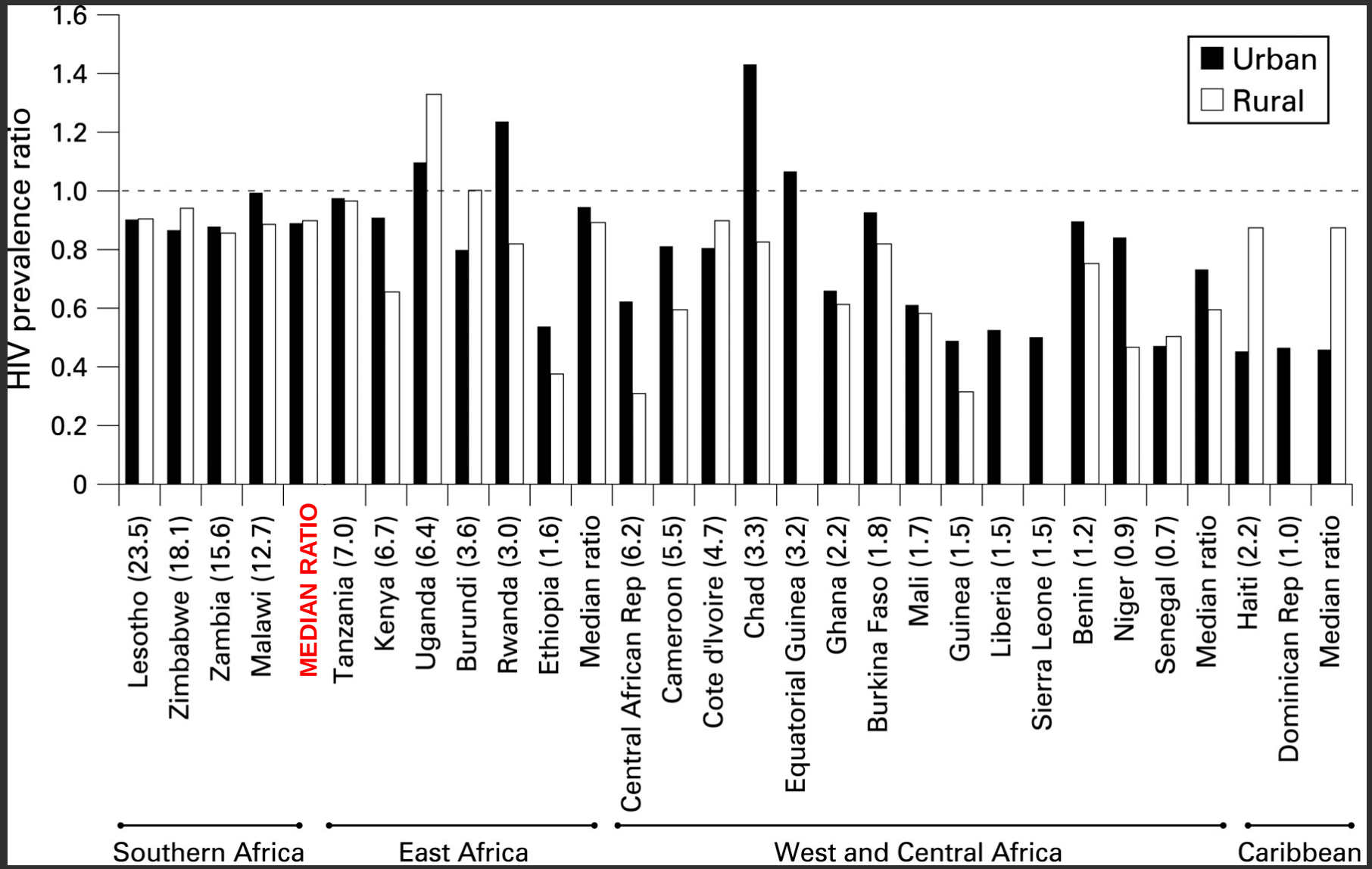
# NATL SURVEYS OF HIV PREVALENCE

household, probability-based

## Demographic & Health Surveys

| ***Central/West Africa*** | ***East Africa*** | ***Southern Africa*** | ***Asia*** | ***Caribbean*** |
|---|---|---|---|---|
| Benin | Ethiopia | Lesotho | Cambodia | Dominican Republic |
| Burkina Faso | Kenya | Malawi | India | Haiti |
| Cameroon | Rwanda | Swaziland | | |
| Cote d'Ivoire | Tanzania | Zambia | | |
| DR Congo | Uganda | Zimbabwe | | |
| Ghana | | | | |
| Guinea | | | | |
| Liberia | | | | |
| Mali | | | | |
| Niger | | | | |
| Senegal | | | | |

# HIV PREV RATIO = NATL SURVEYS / ANC




Gouws (2008)

# SAMPLING

- REPRESENTATIVENESS
- KEY POPULATIIONS
- MARGINALIZED POPULATIONS
- MSM, SW, PWID

# HIV INCIDENCE

# HIV INCIDENCE: APPROACHES

- → •CHANGES IN HIV PREVALENCE
- •COHORT STUDY
- •CROSS-SECTIONAL BIOMARKER APPROACH

# CHANGES IN PREVALENCE

2 serial cross-sectional HIV prevalence surveys

*Δ prevalence* = *new infections* - *deaths + net migration*

## ISSUES

Sensitive to assumptions about deaths
Prohibitively large sample sizes

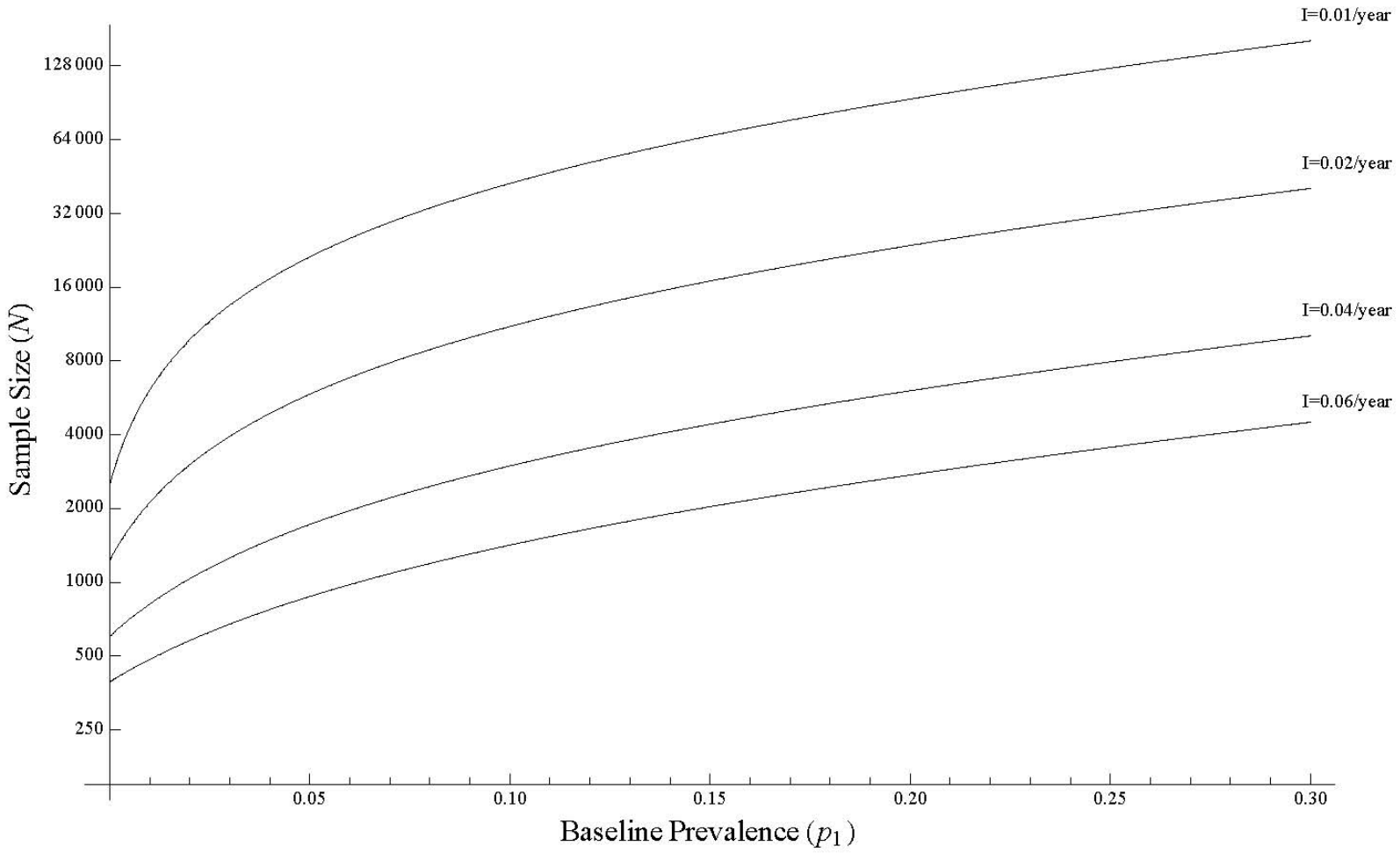

$$\hat{I} = \frac{\left(\hat{p}_2 - \hat{p}_1 R\right)}{\hat{q}_1 \delta}$$

*R*=relative survival

(no migration)

Brookmeyer and Konikoff, 2011

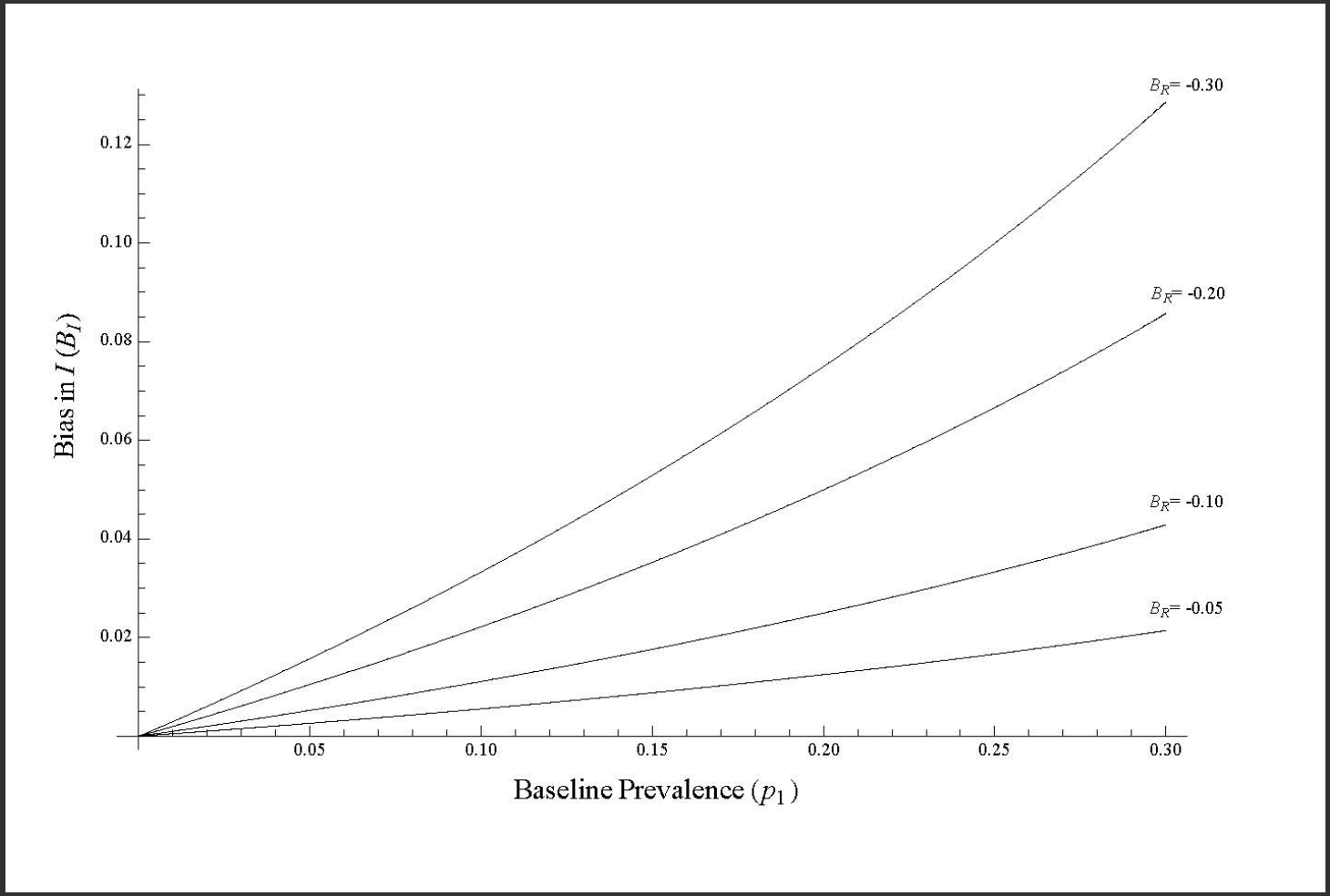
# SAMPLE SIZES WITH CV= 0.20 OF HIV INCIDENCE RATE, *R*=0.80




()

Brookmeyer and Konikoff, 2011

# SENSITIVITY TO MORTALITY ASSUMPTIONS




Brookmeyer and Konikoff, 2011

# Incidence Sensitive to Mortality Assumption

| HIV survival Assumption | Incidence Estimate |
| --- | --- |
| ↑ | ↓ |
| ↓ | ↑ |

**UNAIDS**

Median survival changed from 9 to 11 years, incidence changed from 4.1 to 2.5 million

# COHORT STUDY

$$\textit{HIV INCIDENCE RATE} = \frac{\textit{incident infections}}{\textit{person time}}$$

## ISSUES

- Representative?
- Assembling & following a cohort is difficult
- Counseling may reduce HIV risk
- Incidence is changing over time
- Selection bias: who returns for follow-up?

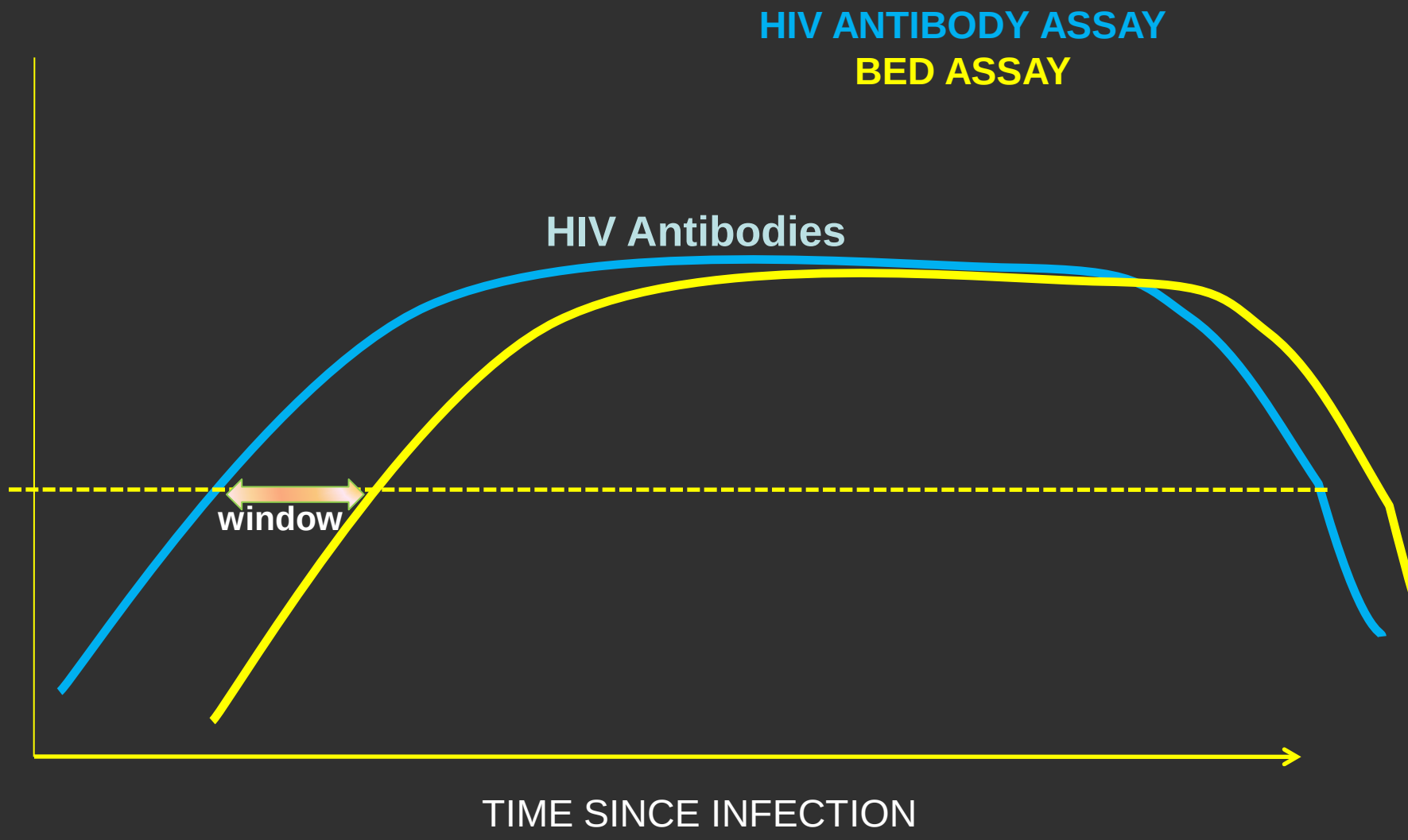
# HIV INCIDENCE: APPROACHES

- CHANGES IN HIV PREVALENCE
- COHORT STUDY
- → CROSS-SECTIONAL BIOMARKER APPROACH

# BIOMARKER APPROACH

- A SINGLE CROSS-SECTIONAL SAMPLE
- COLLECT BIOMARKERS OF RECENT INFECTION
- SNAPSHOT APPROACH

# BIOMARKERS


HIV ANTIBODY ASSAY
BED ASSAY
HIV Antibodies
window
TIME SINCE INFECTION

# BIOMARKER APPROACH

CROSS-SECTIONAL SAMPLE

PREVALENCE = INCIDENCE X $\mu$

$$\hat{I} = \frac{X}{N\mu}$$

X = # in window

N = # HIV neg.

$\mu$ = *mean* duration infected person is + on blue and -- on yellow

*mean "window period"*

NO FOLLOW-UP !

NEED $\mu$

# WHERE DOES $\mu$ COME FROM ?

EXTERNAL DATA SET:

KNOWN DURATION OF INFECTION (INTERVAL CENSORED)
POSSIBLY SERIAL SAMPLES

$\mu$ = mean duration infected person is classified as "recent"
+ ON BLUE AND -- ON YELLOW
mean "window period"

EXAMPLE: HIV + and BED ASSAY -

$\hat{\mu}$ = 187 DAYS reference: Hargrove et al. (2008)

# REPOSITORY OF SAMPLES
# (U.S. CLADE B)

HIVNET 001
MACS
ALIVE
JHU CLINIC

NIH / NIAID R01
Susan Eshleman JHU
Oliver Laeyendecker NIAID/JHU
R Brookmeyer UCLA

# HIV INCIDENCE APPROACHES

BIOMARKERS OF RECENT INFECTION

BED-CEIA
Biorad Avidity Assay
LAG Avidity Assay
Viral Load
CD4

# COST/LOGISTICS

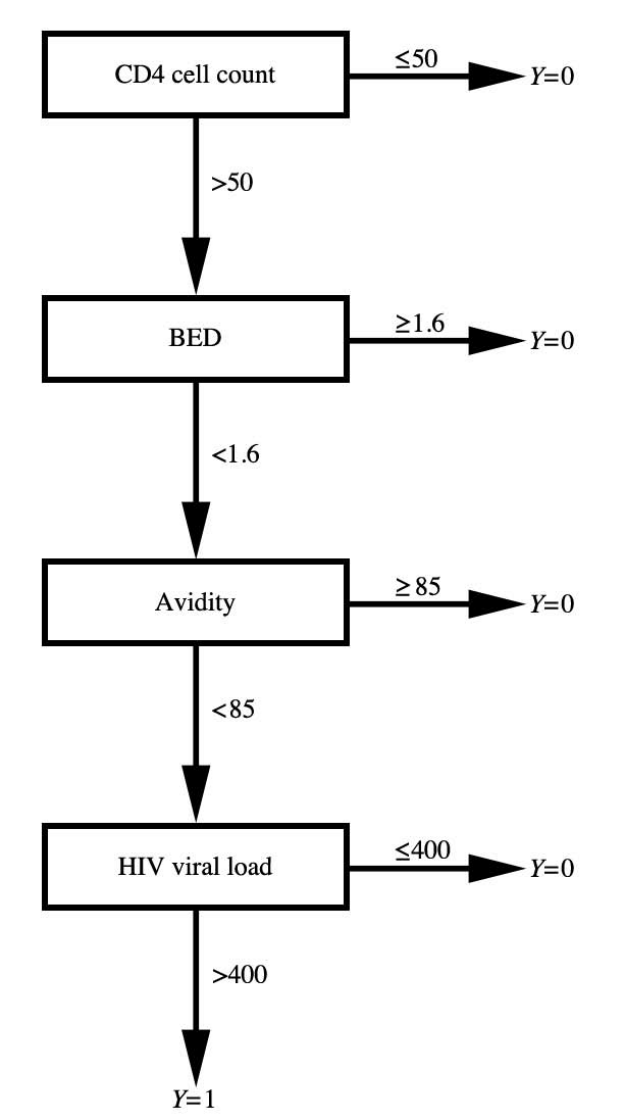
## COST

| | |
|---|---|
| viral load | $$$$$$$$$$ |
| CD4 count | $$$$$ |
| Avidity | $$ |
| BED | $ |

## LOGISTICS

CD4 on whole blood;  performed  in real time

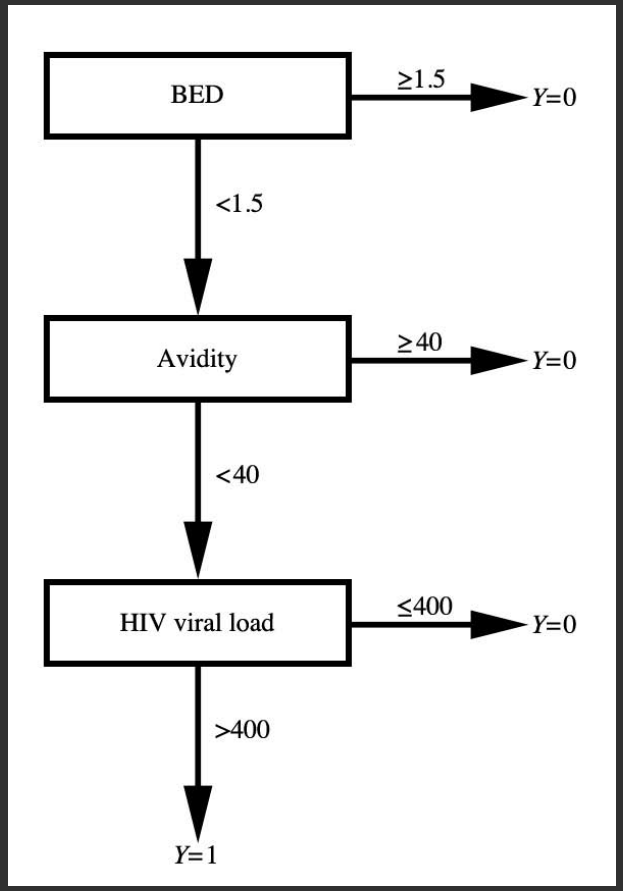
## 4 BIOMARKERS




$\hat{\mu} = 159$ days 95% CI (134,186)

$\hat{\psi} = 184$ days 95% CI (148,225)

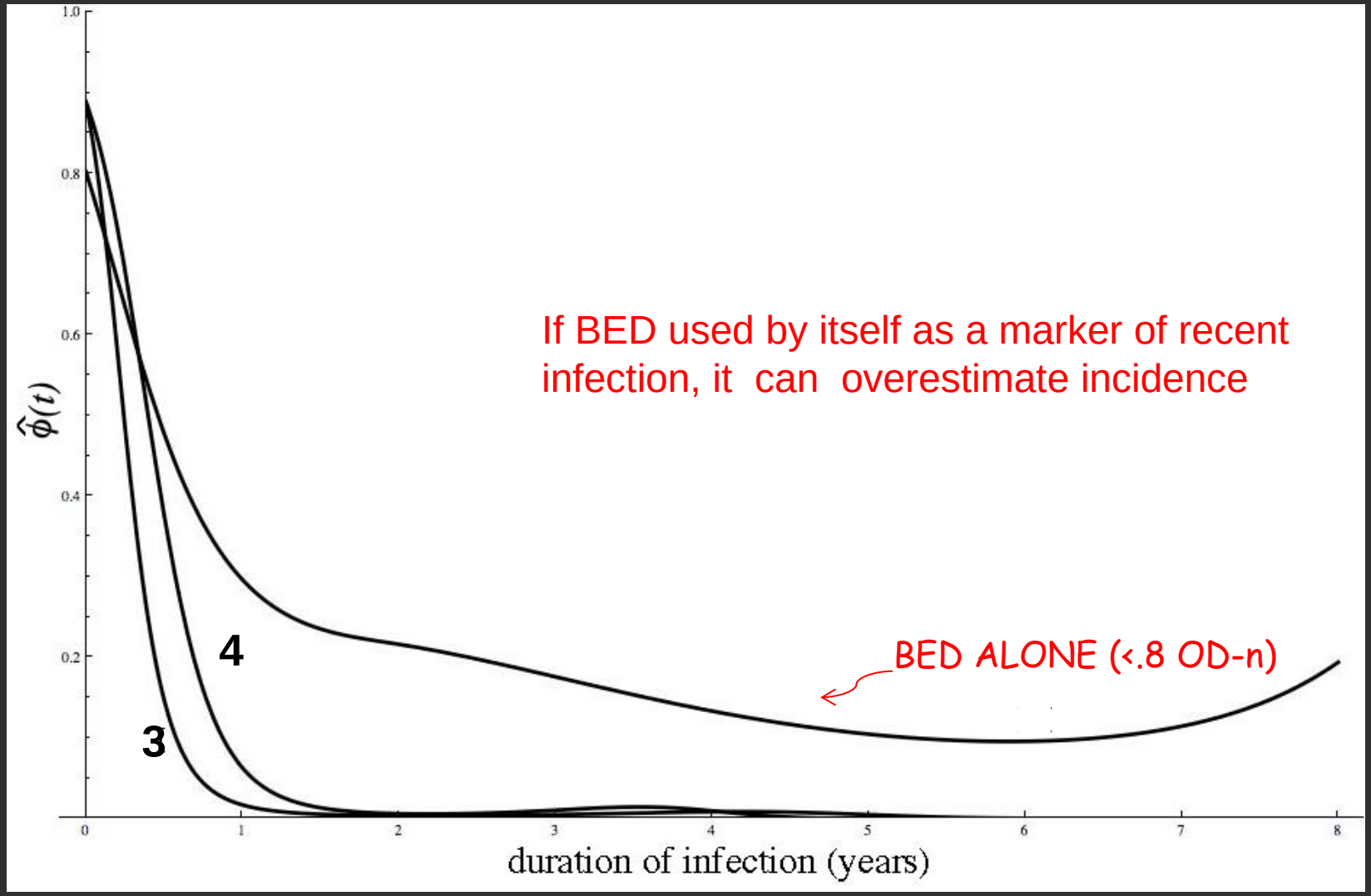
## 3 BIOMARKERS




$\hat{\mu} = 101$ days 95% CI (79,119)

$\hat{\psi} = 194$ days 95% CI (109,289)

# Proportion identifed as recent infection



# COSTS

| | Relative Cost* |
|---|---|
| **4 BIOMARKERS** | **0.44** |
| **3 BIOMARKERS** | **0.13** |

* Relative to testing *all* samples with all 4 biomarkers

# COSTS

| | Relative Cost* |
|---|---|
| **4 BIOMARKERS** | **0.44** |
| **3 BIOMARKERS** | **0.13** |
| **2 BIOMARKERS (LAG & Avidity)** | **0.11** |

* Relative to testing *all* samples with all 4 biomarkers

# COSTS

| | Relative Cost* | Adjusted rel. cost** |
|---|---|---|
| **4 BIOMARKERS** | **0.44** | **1.0** |
| **3 BIOMARKERS** | **0.13** | **0.47** |
| **2 BIOMARKERS (LAG & Avidity)** | **0.11** | **0.33** |

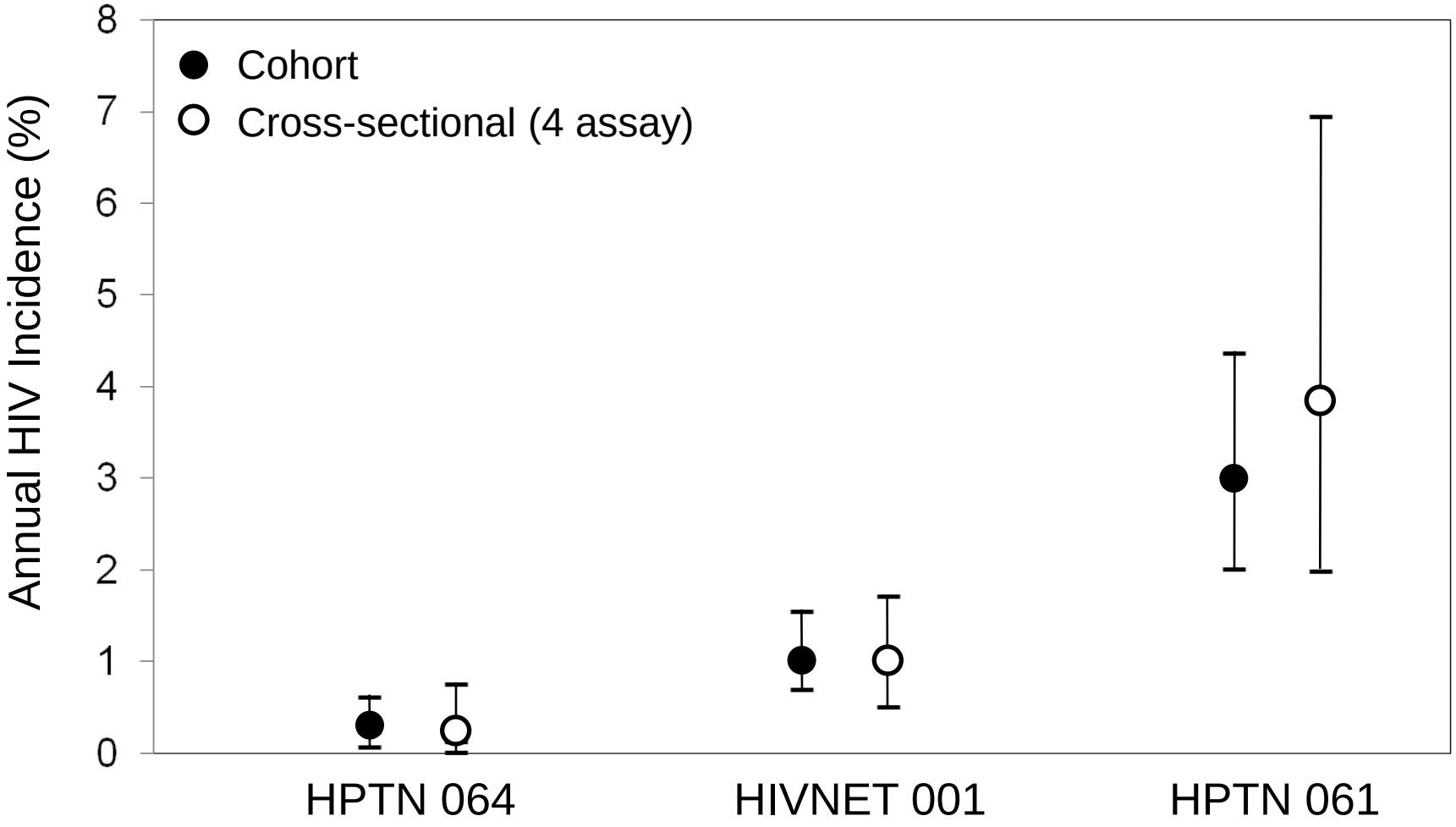
* Relative to testing *all* samples with all 4 biomarkers

** Relative to the 4 biomarker algorithm adjusting for sample sizes to account for differences in μ

# COHORT VS. CROSS-SECTIONAL

## HIV PREVENTION TRIALS NETWORK

- **HIV VACCINE PREPAREDNESS STUDY (HIVNET 001)**
  - U.S. MSM, IDU, high risk women (late 1990's)
  - Celum, Buchbinder, Donnell et al (2001)
- **WOMEN'S SEROINCIDENCE STUDY (HPTN 064)**
  - U.S. high risk women (2009-2012)
  - Eshleman , Hughes, Laeyendecker et al 2013
- **BROTHERS STUDY (HPTN 061)**
  - U.S. Black MSM (2009-2012)
  - Laeyendecker, Wang, Hughes et al 2013


Annual HIV Incidence (%)
8
7
6
5
4
3
2
1
0
Cohort
Cross-sectional (4 assay)
HPTN 064
HIVNET 001
HPTN 061

# CURRENT & FUTURE DIRECTIONS

- RATE RATIO

$$\frac{\hat{I}_2}{\hat{I}_1} = \frac{\frac{X_2}{N_2\mu}}{\frac{X_1}{N_1\mu}} = \frac{X_2 N_1}{X_1 N_2}$$

# CURRENT & FUTURE DIRECTIONS

- RATE RATIO

$$\frac{\hat{I}_2}{\hat{I}_1} = \frac{\frac{X_2}{N_2\mu}}{\frac{X_1}{N_1\mu}} = \frac{X_2 N_1}{X_1 N_2}$$

- Statistical Methods
  (Bayes/continuous; with J. Konikoff, R. Weiss)

- Other subtypes? Countries?

- Representativeness?

- Implementation science

# SUMMARY

- Indicator trends can be difficult to interpret.
- Multiple indicators  to understand and track trends
- Measurement issues
- New biomarker methods for serial cross-sectional studies  promising direction for assessing trends