# Measuring HIV incidence: Where are we?:

# Update on HIV incidence assays

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World Health Organization

# Overview of presentation

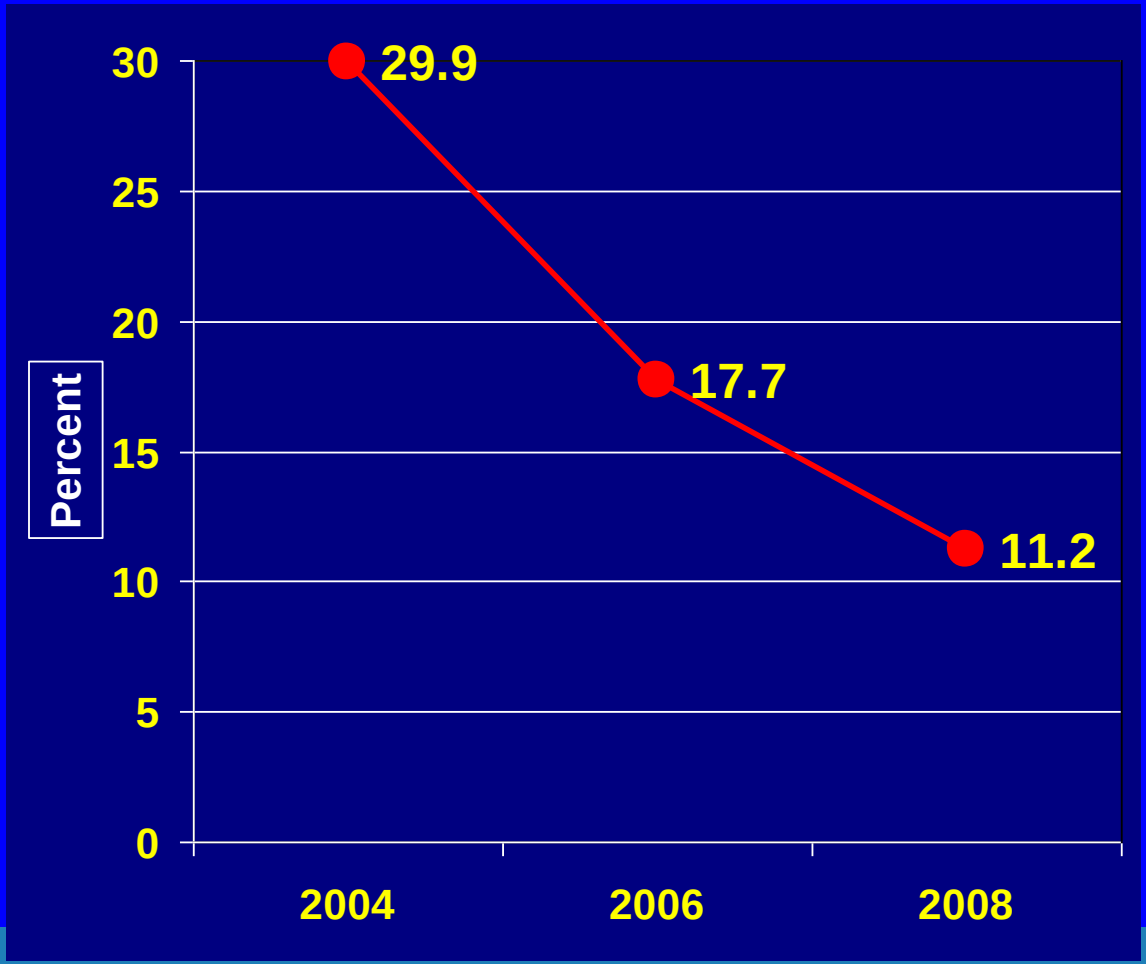
- Methods for estimating HIV incidence
- Issues related to incidence assays
- New incidence assay developments
- Conclusions

# Methods for approximating population incidence trends

- **Method 1: Prevalence trends among young adults (aged 15-24 years)**
  - Used as a proxy for **incidence trends** in the general population as prevalent infections are likely to be recent infection in this group.
  - Selection bias: HIV infections in 15-24 population may not be reflective of new infections in country.
  - In Concentrated epidemics new injectors or young MSM

- **Method 2: Mathematical modeling**
  - Easy to use and inexpensive
  - Requires assumptions about mortality which may not be available.
  - DHS analysis

# HIV among new injectors in Ukraine:




HIV prevalence among recent IDUs (less then 2 years of injection drugs), median. sentinel surveillance 8 cities, Ukraine - ***International HIV/AIDS Alliance, 2009***



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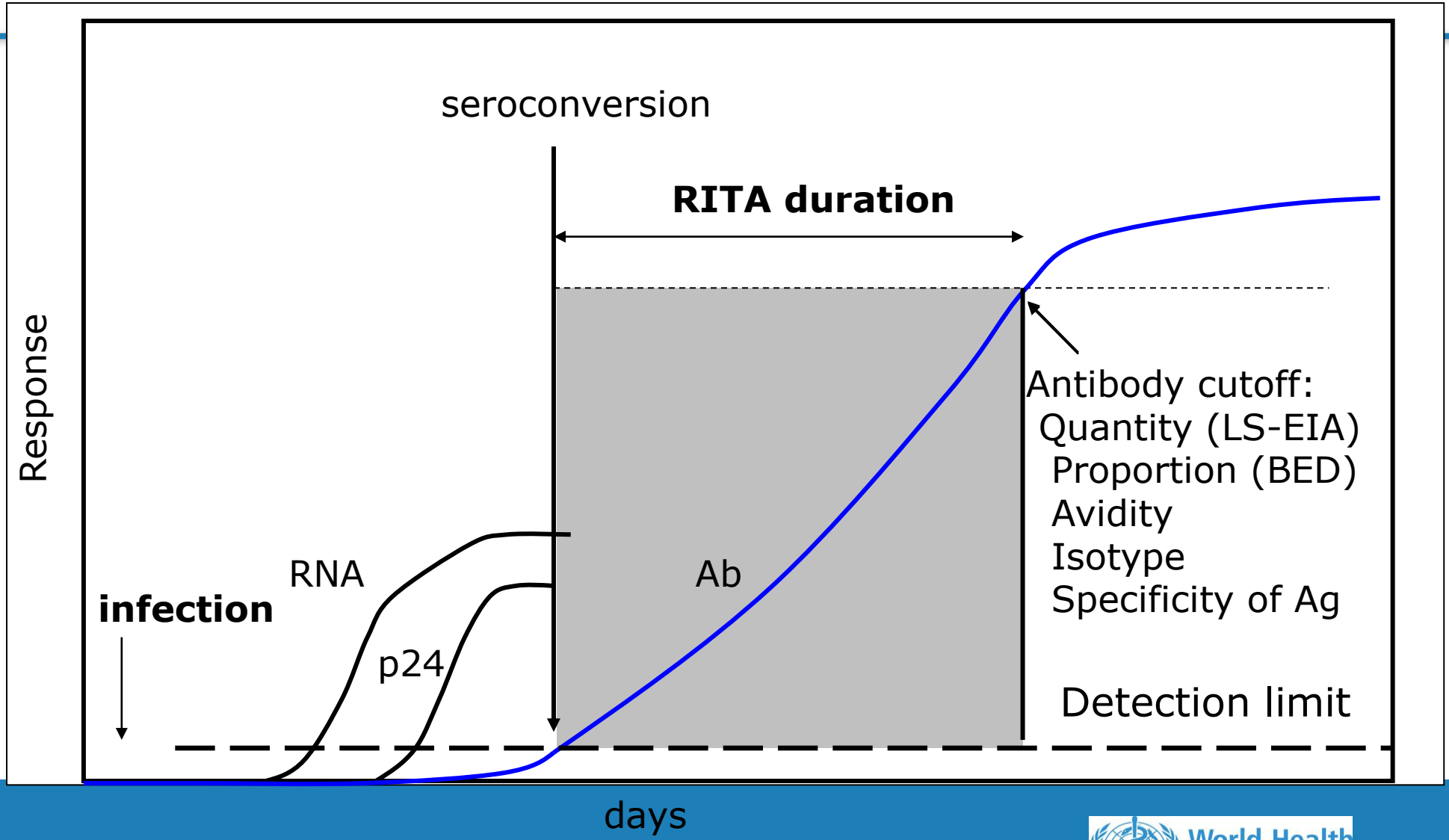
# Methods for approximating population incidence trends

- **Method 3: Laboratory assays**
  - Simple, fast, low cost (applied to HIV+ only).
  - Overestimates incidence due to assay: (non-progressors, AIDS,ART) who misclassify as recent infection on the assay even though they have been infected for many years.

- **Method 4: Prospective cohort studies**
  - “Gold standard” measure of incidence
  - Costly, logically difficult to implement, prone to bias

# HIV incidence assays

# Recent Infection Testing Algorithm (RITA): based in Antibody response



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# FROM DETUNED TO RITA

**1995 1998 2000 2002 2003 2004/5 2006/7 2008 2010 2011**

Detuned SALSA STARHS RITA CEPHIA project launched

P24 for incidence

Janssen Jama-detuned paper

Ad-hoc incidence meetings around AIDS conferences

AxSYM avidity, BED

Vironostika detuned assay

UNAIDS statement

RT-LS
IDE-V3
Anti-p24 IgG3

Vitros, Bio-rad avidity assays

Toronto AIDS meeting -WHO working group formed – funders start to support projects. Laboratory and statistical workshops

Molecular approaches

LAg assay

Critical path determined

Architect avidity



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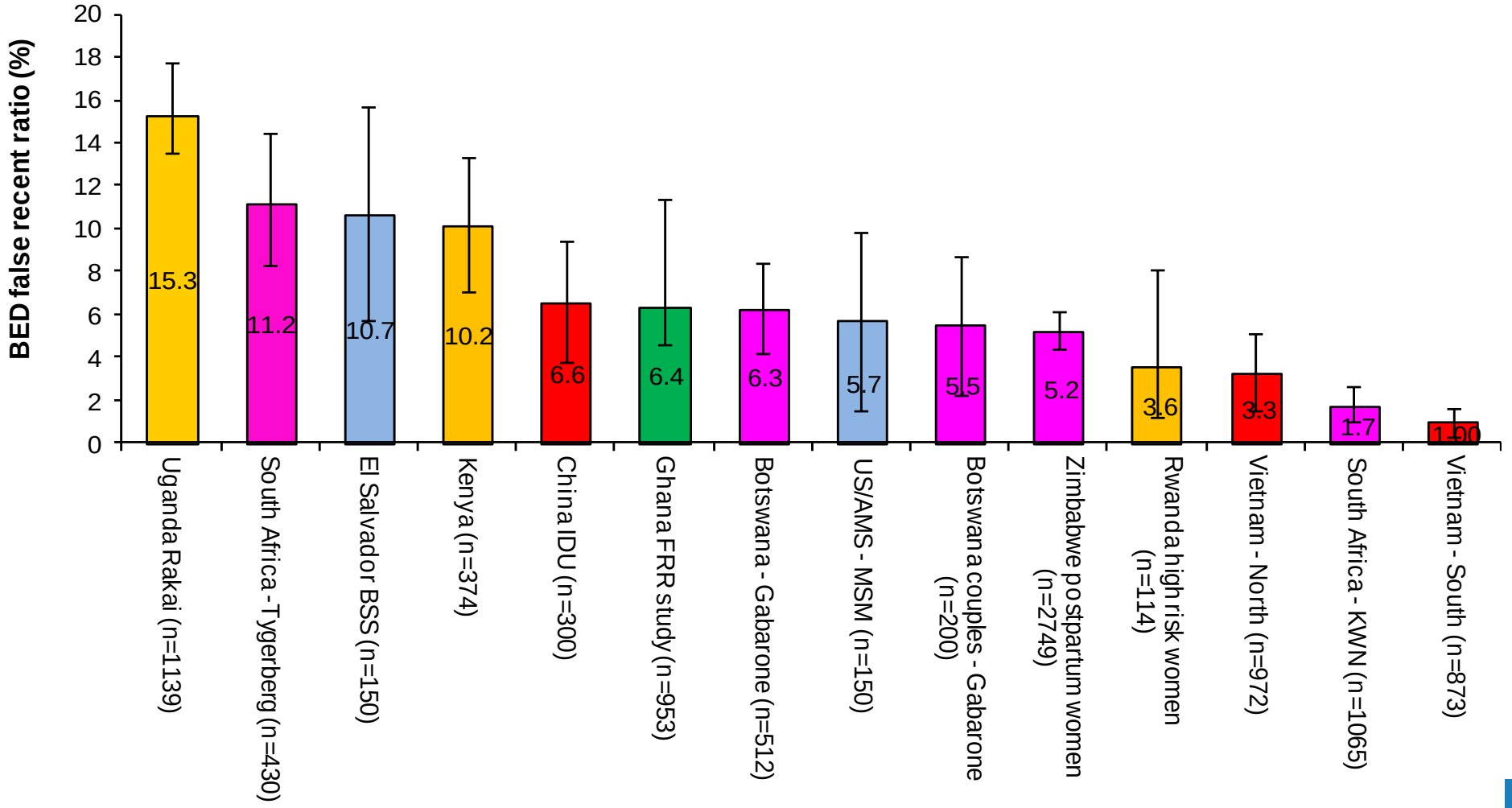
# Challenges to Using Antibody Maturation to Identify Recent Infection

- Variable immune response among individuals
  - Antibody response related to viral level
- Variability by HIV-1 subtypes
- False-recent status
  - Elite controllers (low viral levels)
    - Accumulate in population
  - ART use (low viral levels)
  - Advanced HIV disease (AIDS)

# BED CEIA: False Recent Rates Vary by Setting



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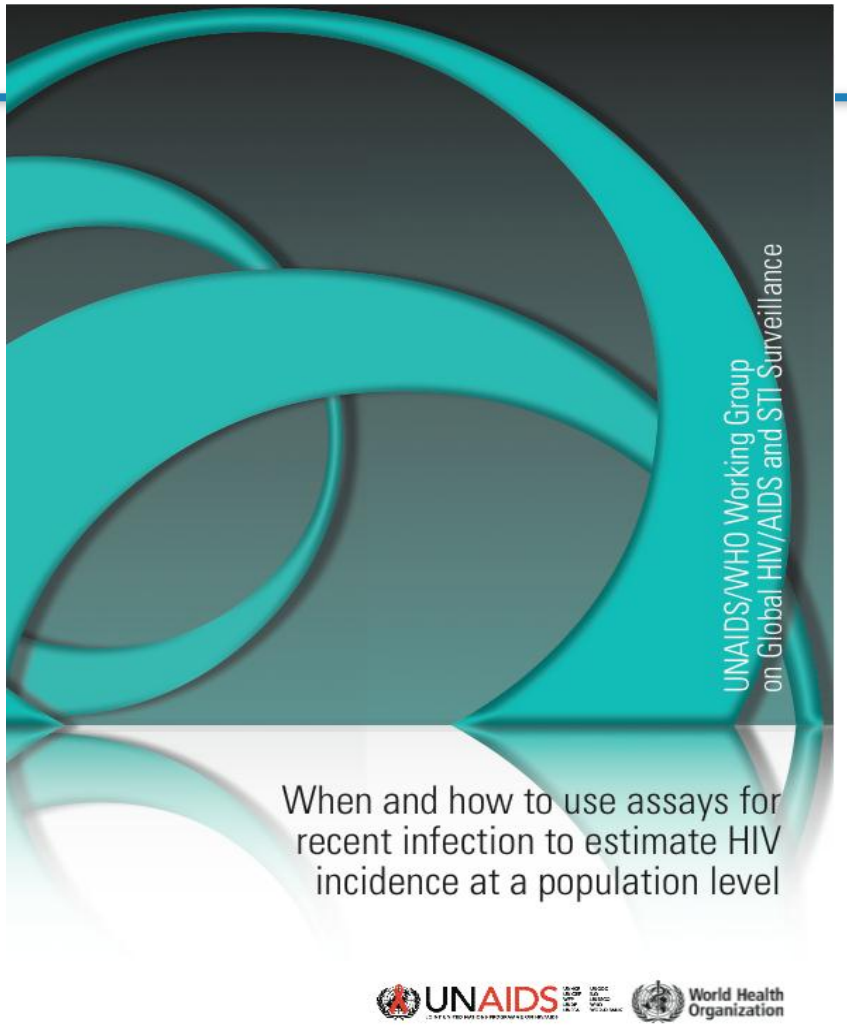
# When and how to use assays for recent infection to estimate HIV incidence at a population level

Provided guidance on use of RITAs, false recent rates, and sample sizes.




www.who.int/diagnostics_laboratory/links/hiv_incidence_assay



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# Overestimation problems and solutions

# SACEMA

- South African Department of Science and Technology/ National Research Foundation Centre for Epidemiological Modeling and Analysis
- Tools
  - Incidence from recent infection biomarkers
  - Incidence from prevalence and mortality

www.incidence-estimation.com

# New incidence calculator tools

| Incidence Calculator | Inputs | Outputs | |
|---|---|---|---|
| Calculates point estimate and confidence intervals for Incidence and Annual Risk of Infection | | | |
| | | | |
| **TRI/Assay Characteristics** | | | |
| Estimated Mean Window Period (days) | 155 | | |
| CoV (Coefficient of Variation) of Mean Window Period Estimate | 10.0% | | |
| Estimated FPR (False Positive Rate = 1 minus specificity) | 3.0% | | |
| CoV of FPR Estimate | 25.0% | | |
| | | | |
| **Sample Counts** | | | |
| HIV negative | 10000 | | |
| HIV positive | 1000 | | |
| TRI positive (i.e. classified recent) | 100 | | |
| Total sample size | 11000 | | |
| | | | |
| **Estimated Incidence** | | | |
| Instantaneous incidence (95% Confidence Interval) | 1.70% | ( 1.04% - 2.36% ) | |
| CoV of incidence | 19.84% | | |
| | | | |
| Annual Risk of Infection (95% Confidence Interval) | 1.69% | ( 1.03% - 2.33% ) | |

Available at: http://www0.sun.ac.za/sacema/collaboration/ABIE/

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# New incidence calculator tools (cont):

## TRI Incidence and Prevalence Calculator

Let:
T = Total # persons tested
N = # persons HIV negative
P = # persons HIV positive
Q = # persons tested with TRI
R = # persons recent on TRI
w = recency period or window period in days
CI w = 95% confidence interval for window period w. Specify lower and upper limits
FRR = long-term false-recent rate for the TRI
CI FRR = 95% confidence interval for FRR. Specify lower and upper limits.

1. The w and CIw should be based on the reported mean w and 95% CI for the TRI provided in the 'Reported Mean w and 95% CI' worksheet
2. The FRR should be based on the sample size given in the 'Minimum sample size for FRR' worksheet
3. The CI FRR should be based on the 95% CI reported in the 'Reported FRR (e) and 95% CI' worksheet
4. Incidence formula described in Welte, A., T. A. McWalter, et al. (2009). "A Simplified Formula for Inferring HIV Incidence from Cross-Sectional Surveys Using a Test for Recent Infection." AIDS Res Hum Retroviruses 25(1): 125-126.

| | INPUT YOUR DATA HERE | | | | | | | | | | PREVALENCE AND INCIDENCE CALCULATIONS | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Population | T | N | P | Q | R | w[1] | CI w | | FRR[2] | CI FRR[3] | | Prevalence | CI Prevalence | | Incidence[4] | CI Incidence | |
| Example | 10000 | 9000 | 1000 | 900 | 100 | 197 | 173 | 229 | 0.0520 | 0.0440 | 0.0610 | 10.00% | 8.45% | 9.58% | 1.28% | 0.76% | 1.80% |

*To be available at www.pepfar.net



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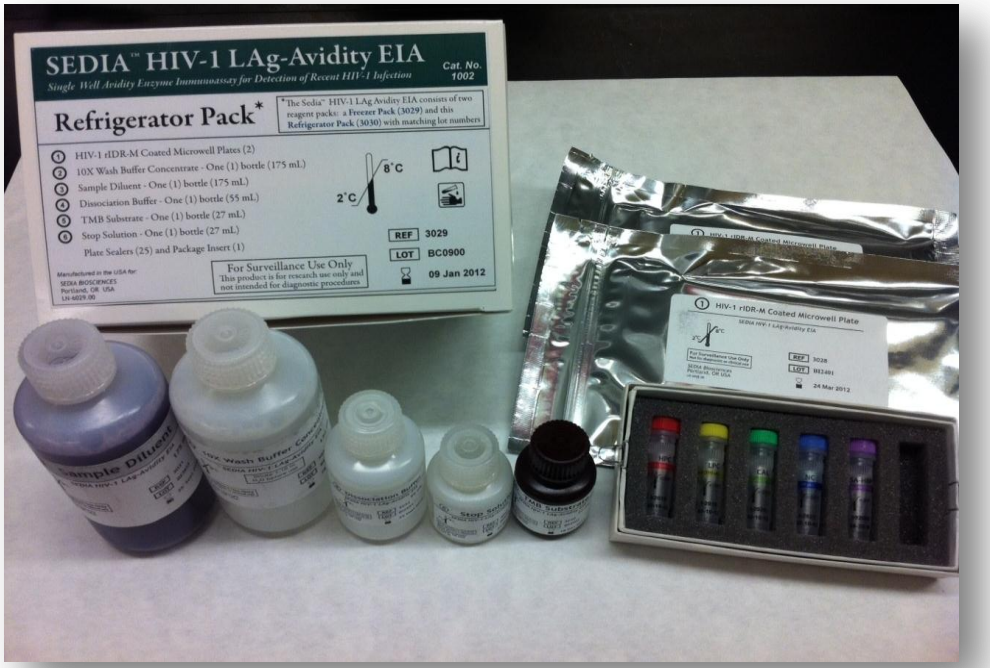
# Current Status of LAg-Avidity Assay

- Available as a commercial kit
- Similar mean recency period in 4 different subtypes
- Low FRR (~1-2%)
- Multiple validation studies with promising results
- **LBPE27 (Track C):** Performance of new LAg-Avidity EIA to measure HIV-1 Incidence in a cross-sectional population:




**Swaziland HIV Incidence Measurement Survey (SHIMS)**



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# Mean recency period (in days) for LAg-Avidity EIA by cohort/subtypes (cutoff 1.0)

| Cohort | No. of Subjects (No. Spec) | HIV-1 Subtypes | Mean Recency Period (95% CI) |
|---|---|---|---|
| Amsterdam & Trinidad | 32 (170) | B | 132 (104-157) |
| Ethiopia | 23 (143) | C | 139 (106-178) |
| Kenya | 34 (80) | A, D | 143 (103-188) |
| **ALL** | **89 (393)** | **A, B, C and D** | **141 (119-160)** |

**Mean window periods are similar among different subtypes and populations**

## Consortium for the Evaluation and Performance of HIV Incidence Assays (CEPHIA)

# Development of specimen repository and evaluation of assays for identification of recent HIV infection and estimation of HIV incidence



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# Country examples of national incidence activities

# Triangulation of methods: Kenya AIDS Indicator survey*

| | (1) EPP/Spectrum incidence | (2) Survey-derived incidence | (3) BED-derived incidence* |
|---|---|---|---|
| Kenya '07 | 0.72 (0.70, 0.74) | 0.7 (0.3, 1.1) | 0.6 (0.1, 1.3) |

***Exclusion of persons on ART and with low CD4 cell count. Corrected using an assumed false recent rate of 15% based on validation data from the 2007 KAIS and samples from neighboring Uganda**



(Andrea Kim IAC 2010 )

# Summary

- New promising approaches to detect recent HIV infections are in development
- Combining two different methods, based on two different principles, significantly improves predictive value and accuracy of incidence estimates
- WHO Working Group sub-committee on guidance for using HIV case surveillance data
- Current requirements for assay-derived estimates
  - Estimate a FRR to calibrate your incidence estimates
  - Measure and exclude ART use in the population
  - Appropriate sample sizes for FRR and incidence survey
  - Triangulate with other sources of incidence

. More in the HIV incidence working group page….

# Acknowledgments


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- Pai Lien Chen
- Alex Welte
- Tom McWalter
- Gary Murphy

# Thank you!



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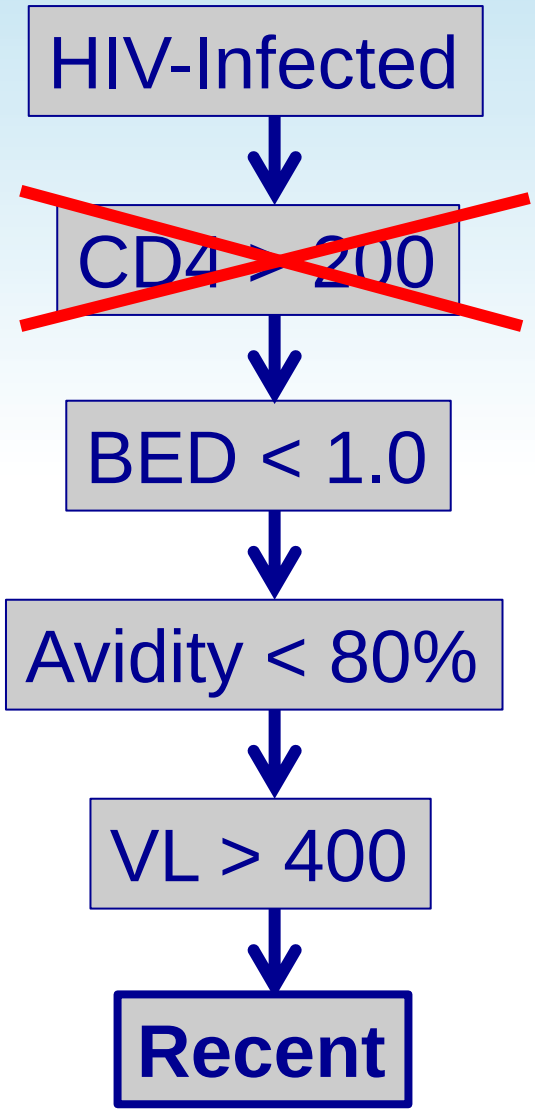
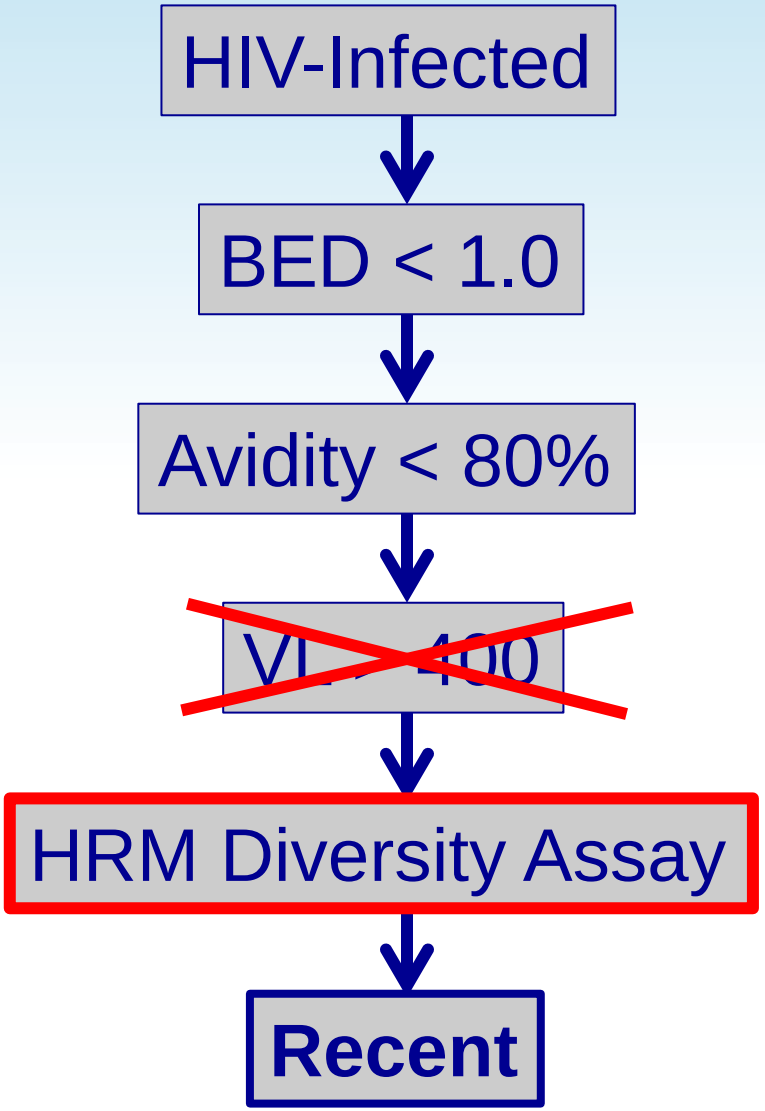
# Extra Slides

## Current MAA




## Next Generation MAA

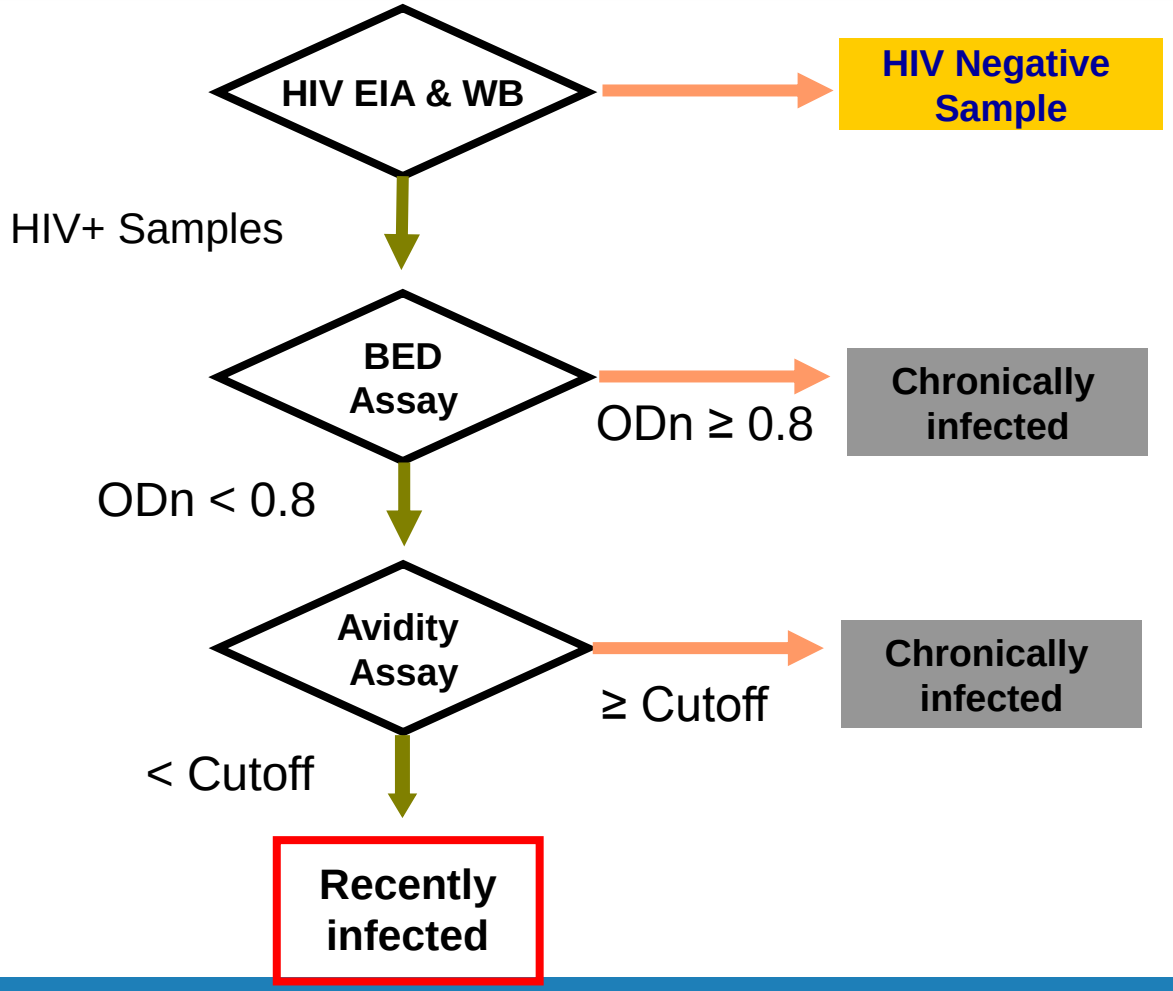


# Comparison of HIV incidence Estimates

| Study | Analysis | Estimated annual incidence (95% CI) | |
|---|---|---|---|
| HIVNET 001/001.1 | Longitudinal 12-18 months | 1.04% | 0.70 – 1.55% |

Eshleman (2012) In Press JID
Laeyendecker (2012) Submitted

# Two-test algorithm for incidence estimation



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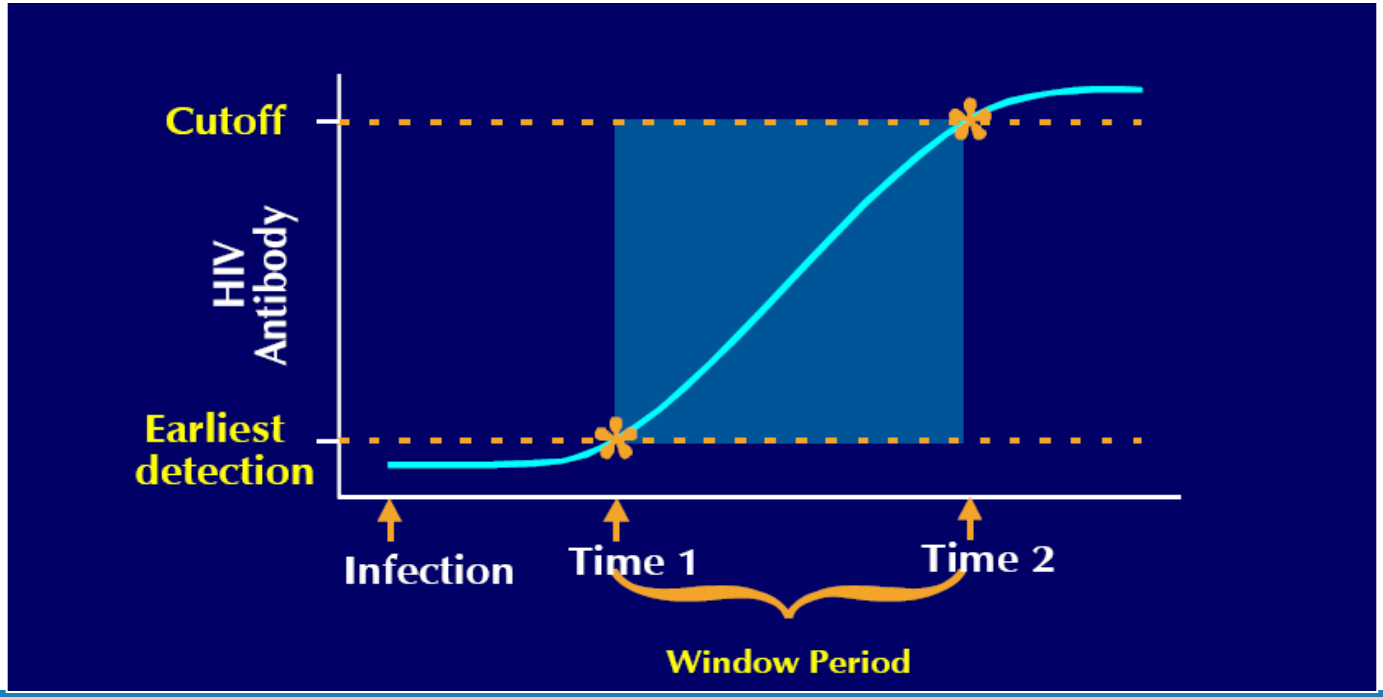
# Estimating a local false-recent rate

- Estimation of a local FRR is essential for all incidence assays with expected FRR > 1%
- In general, the FRR for a population should be reviewed at regular intervals (at least every 5 years), to take into account any change in the population characteristics, which may affect the false recent rate.
- When is the FRR too high for use?
  - The higher the FRR, the higher the uncertainty of the incidence estimate. Efforts should be made to estimate the FRR with an acceptable level of certainty around the estimate (e.g. a coefficient of variance ~30%)

# Mean Recency Period for incidence assay

- Period it takes for newly HIV infected individuals to pass from “recent” HIV infection to “established” HIV infection on an incidence assay
- The mean recency period (MRP) for an assay is incorporated into the incidence formula (denominator) to calculate an annual incidence rate.



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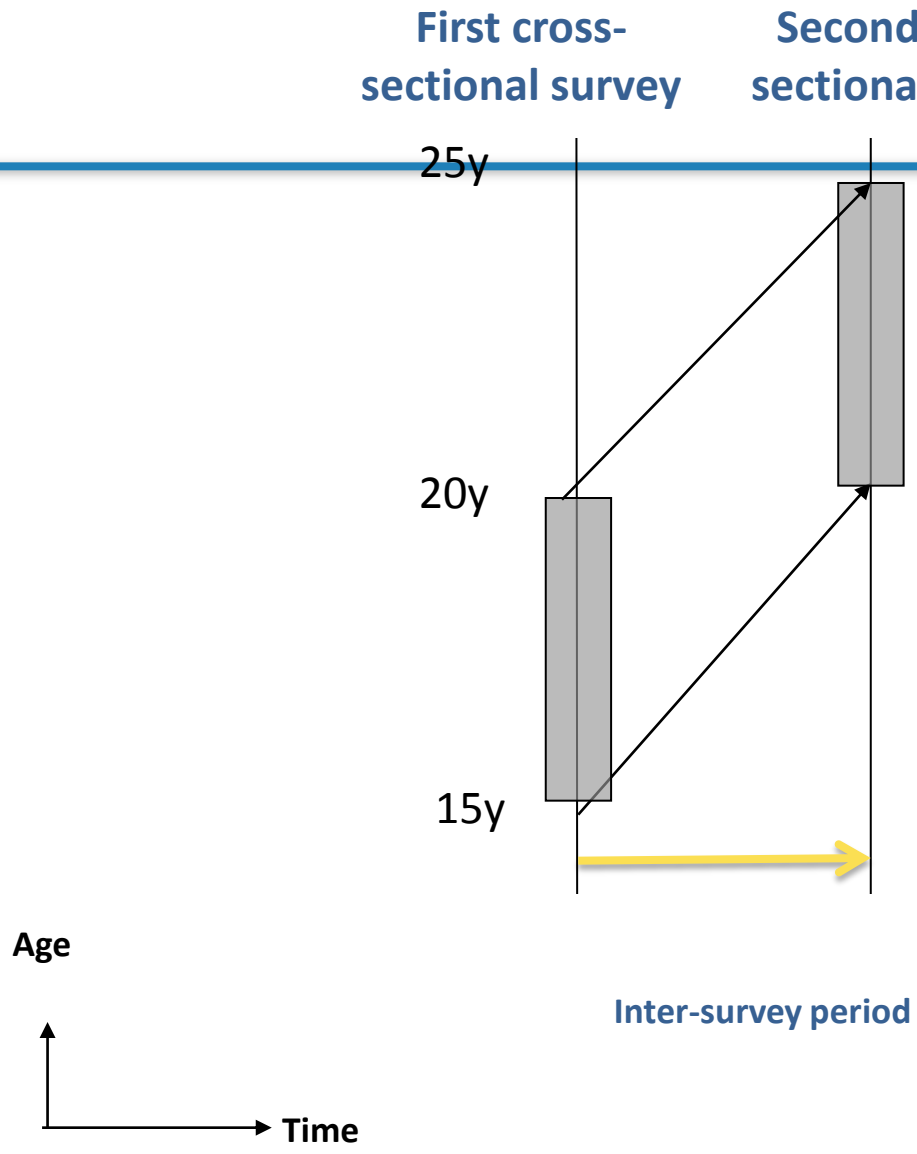
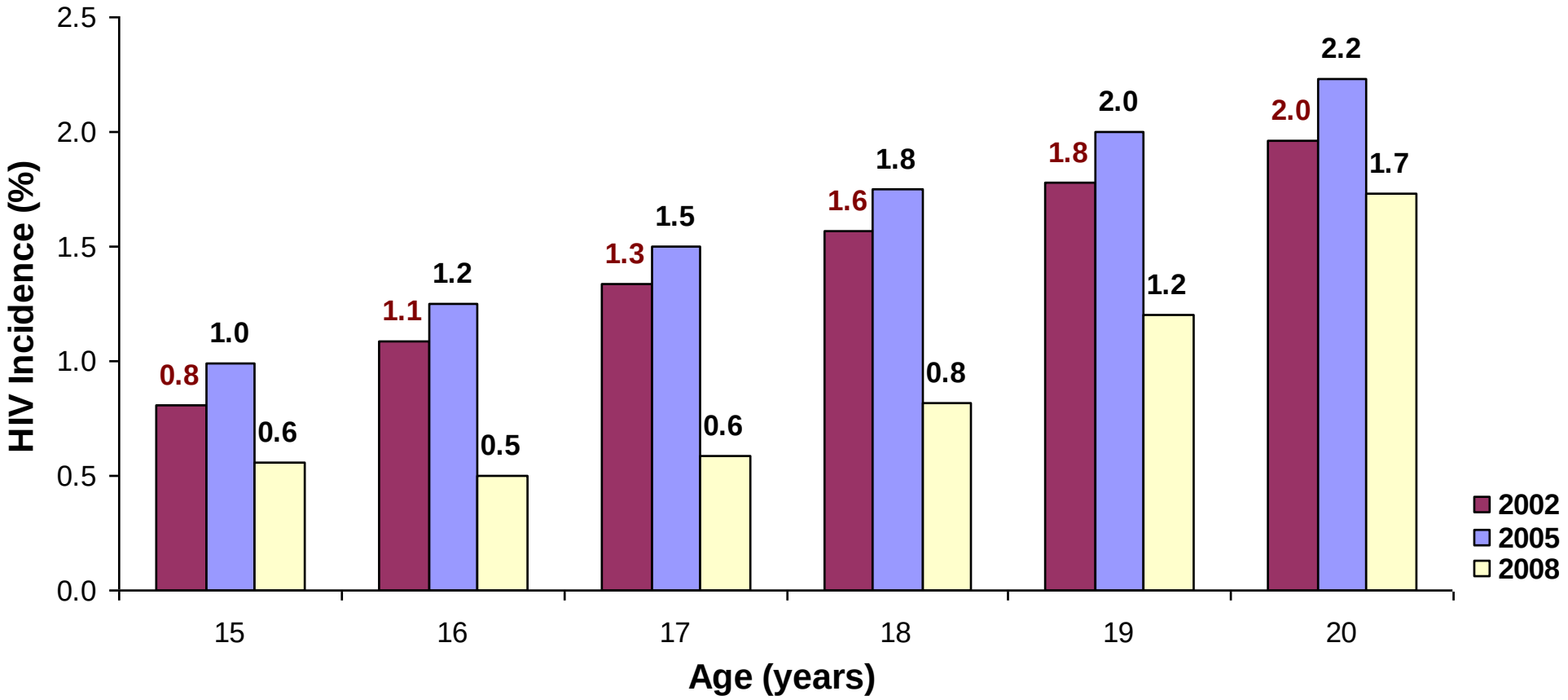



Tim Hallet's method

**Not same individuals followed-up, but the two samples represent the same population.**

# HIV incidence in 15-20 year olds derived from single year age prevalence
# South Africa 2002, 2005, 2008



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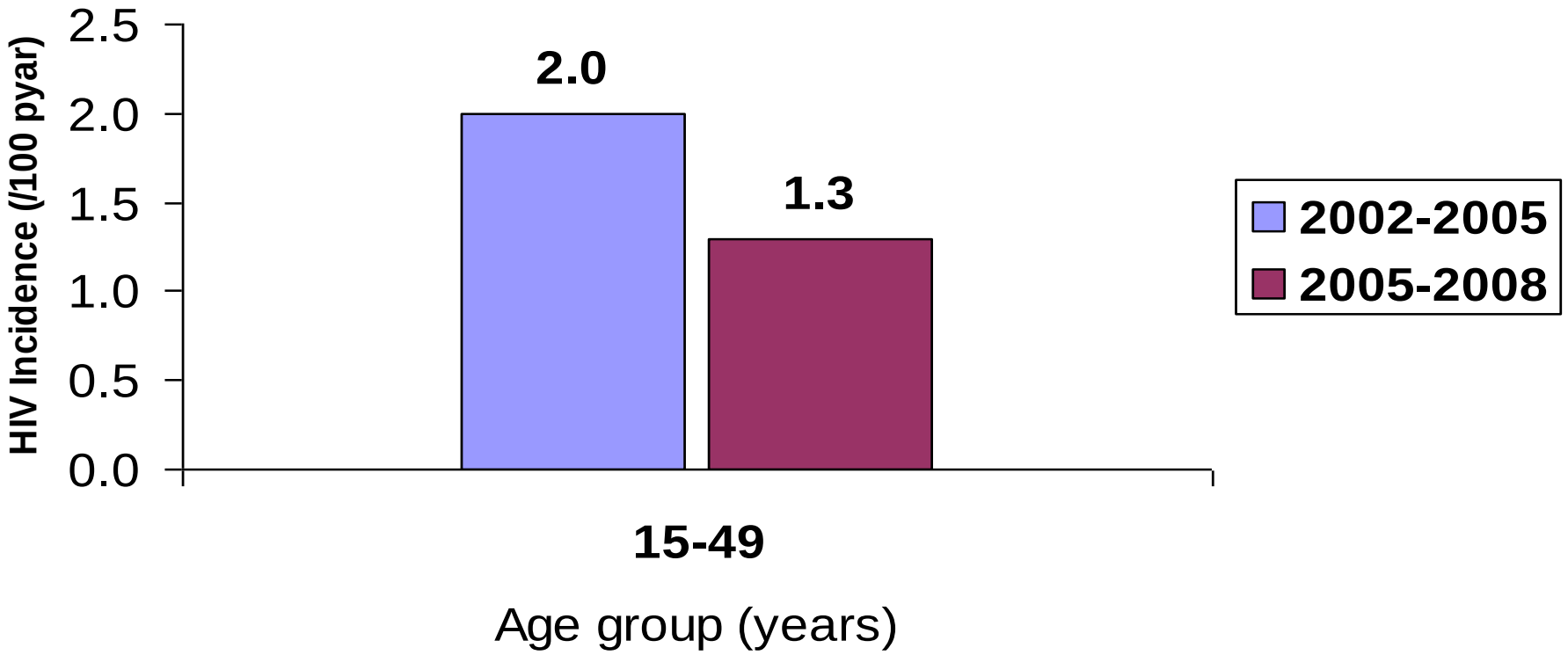
# HIV incidence (/100 pyar), 15-49 age group South Africa 2002-2005 and 2005-2008



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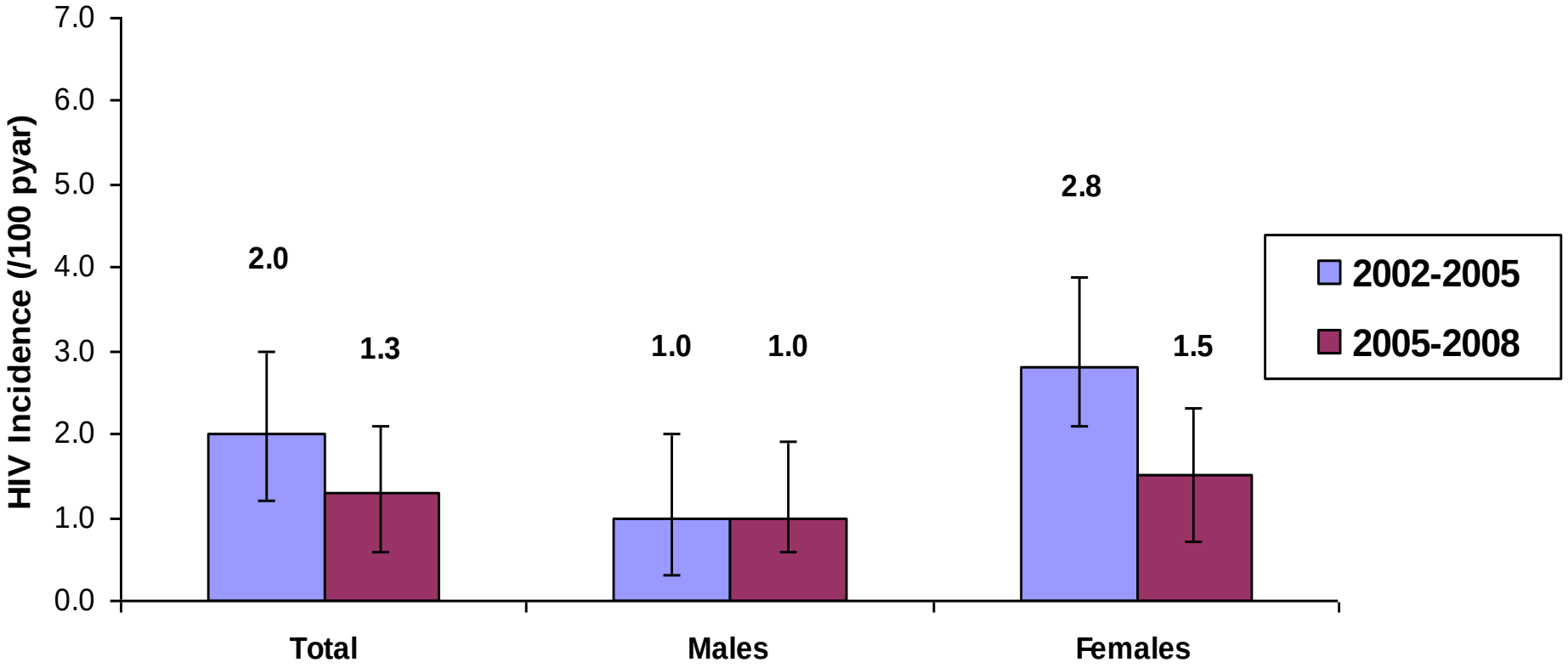




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