Measuring HIV Incidence

Epidemiological methods
Laboratory- based method

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Human Sciences Research Council

HIV Incidence Consultation Meeting
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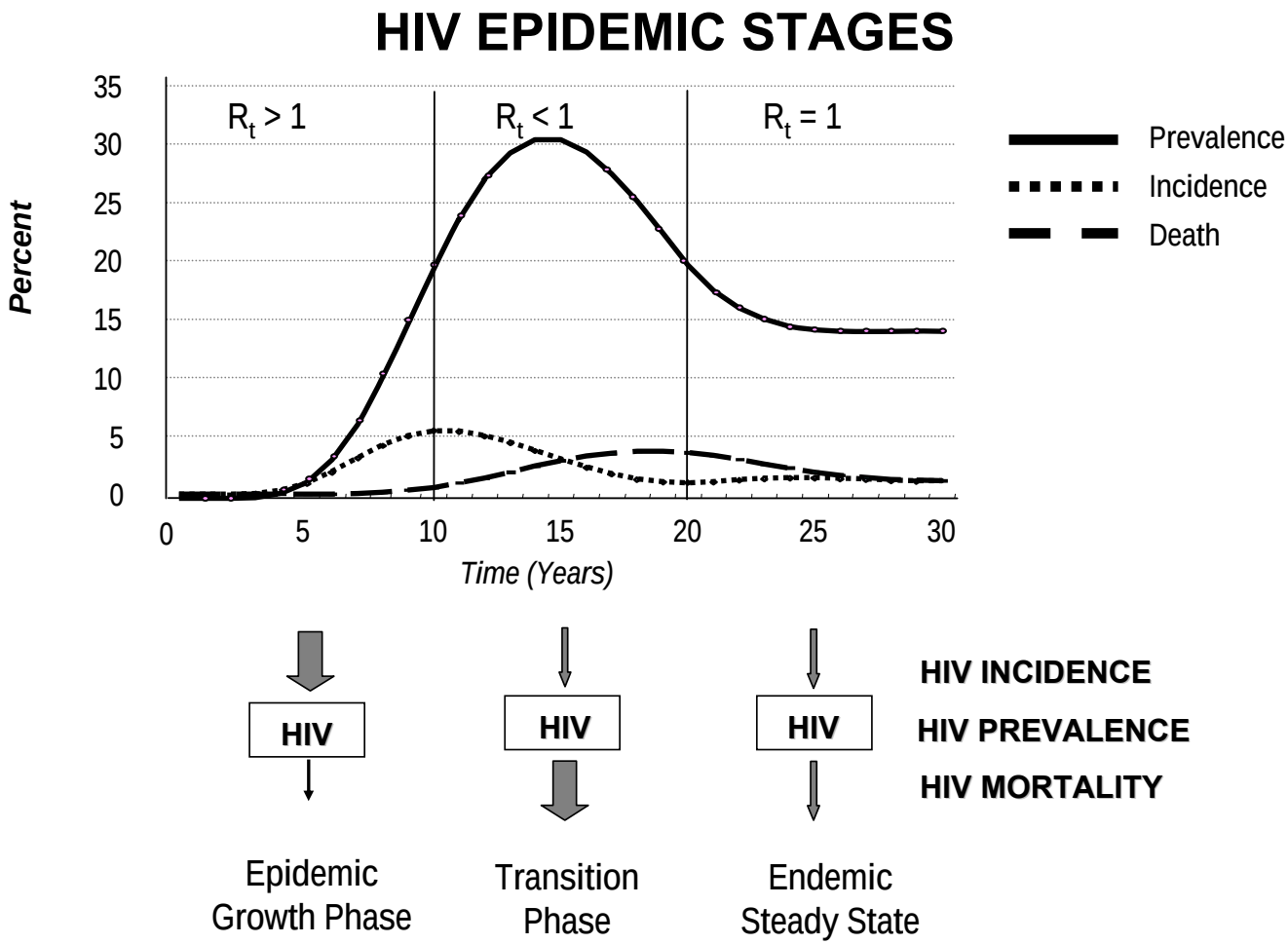
Critical Questions

Are the observed changes in HIV trends:

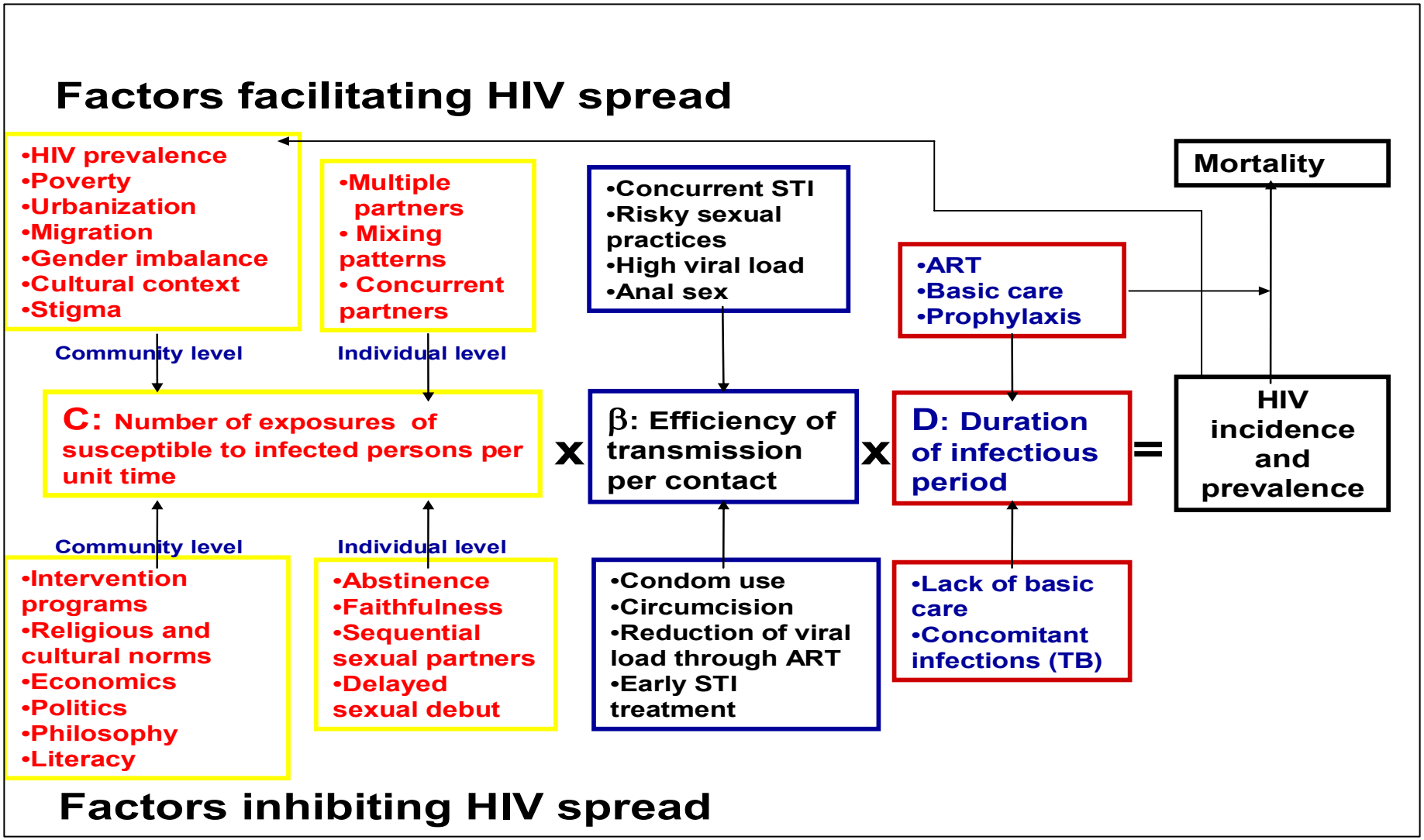
1. **a reflection of the natural history of the epidemic?**
2. **a product of changes in behavior?**
3. **a product of interventions?**

Relationship between incidence, prevalence, and mortality



Source: FHI Evaluation Handbook 2001

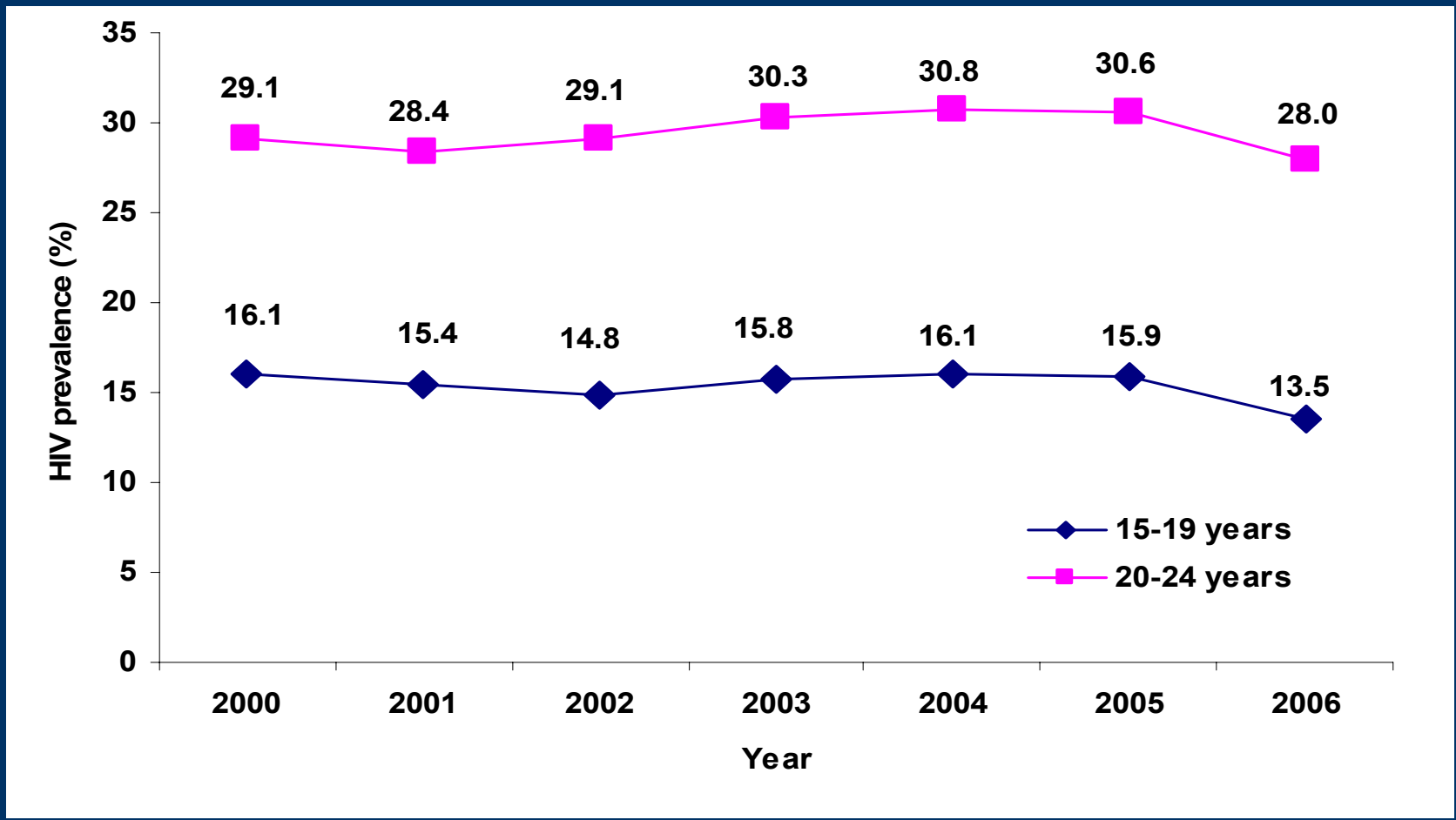
Factors influencing reproductive rate of HIV transmission



Epidemiological methods

- Longitudinal cohort studies
- HIV prevalence in youngest age group
- Mathematical modeling

Antenatal HIV prevalence trends among 15-24 year olds, South Africa, 2000 - 2006



Methods for calculating incidence from age cohort prevalence in 15 to 24 year olds

- Calculate age cohort prevalence estimates
- Smooth prevalence curve for all age cohorts (15-24 years)

4. Calculate difference in prevalence from year to year using smoothed prevalence data
5. Assuming a steady state of HIV transmission from year to year and no AIDS-related mortality

Calculating incidence from single year age cohort prevalence in 15 to 24 year olds

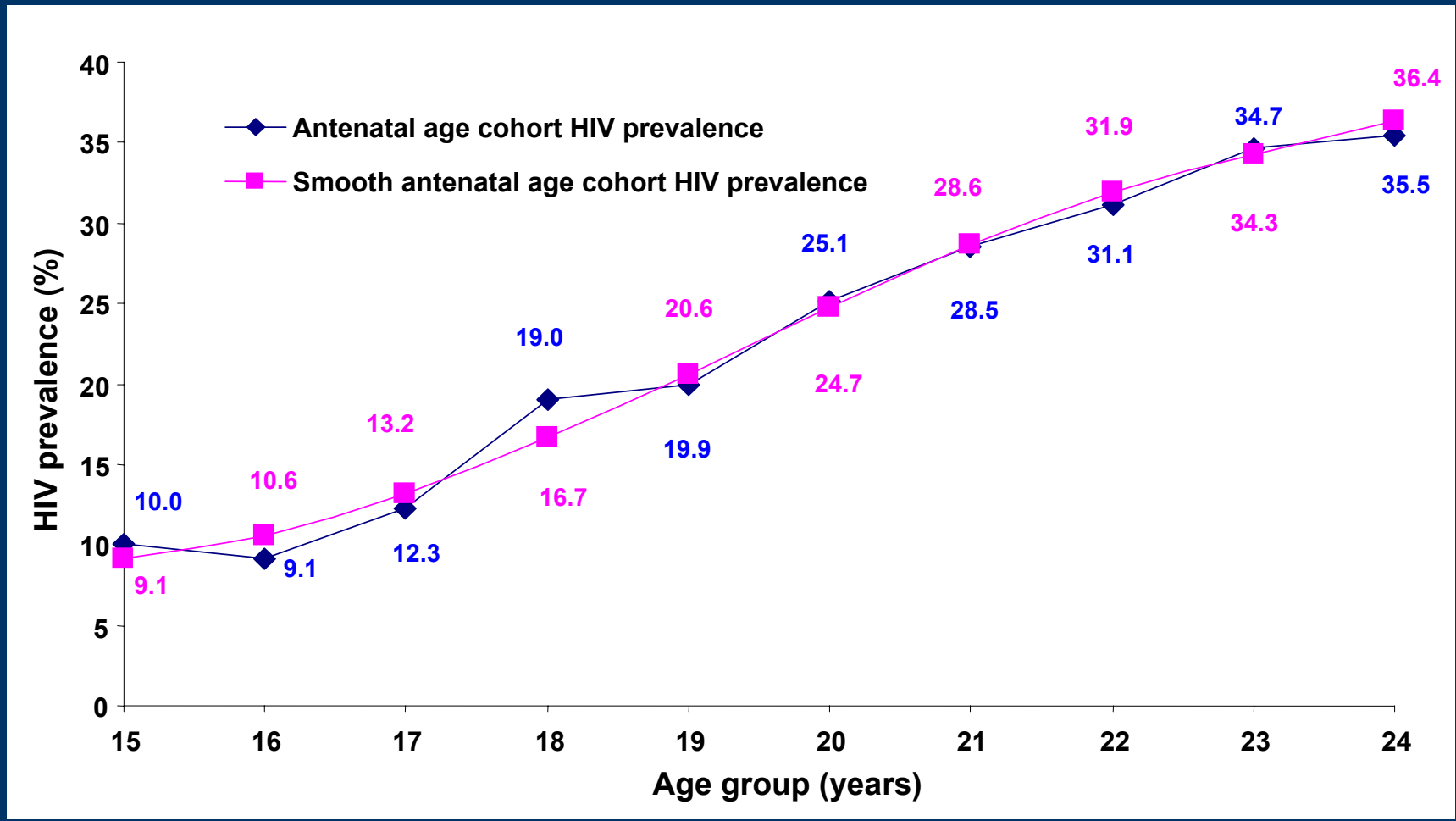
Numerator:

% difference in prevalence from year to year

Denominator:

Population at risk = 1-percentage of smoothed HIV prevalence in the previous year

HIV prevalence estimates by single year of age in 15-24 year old age cohort Antenatal Survey, South Africa 2004



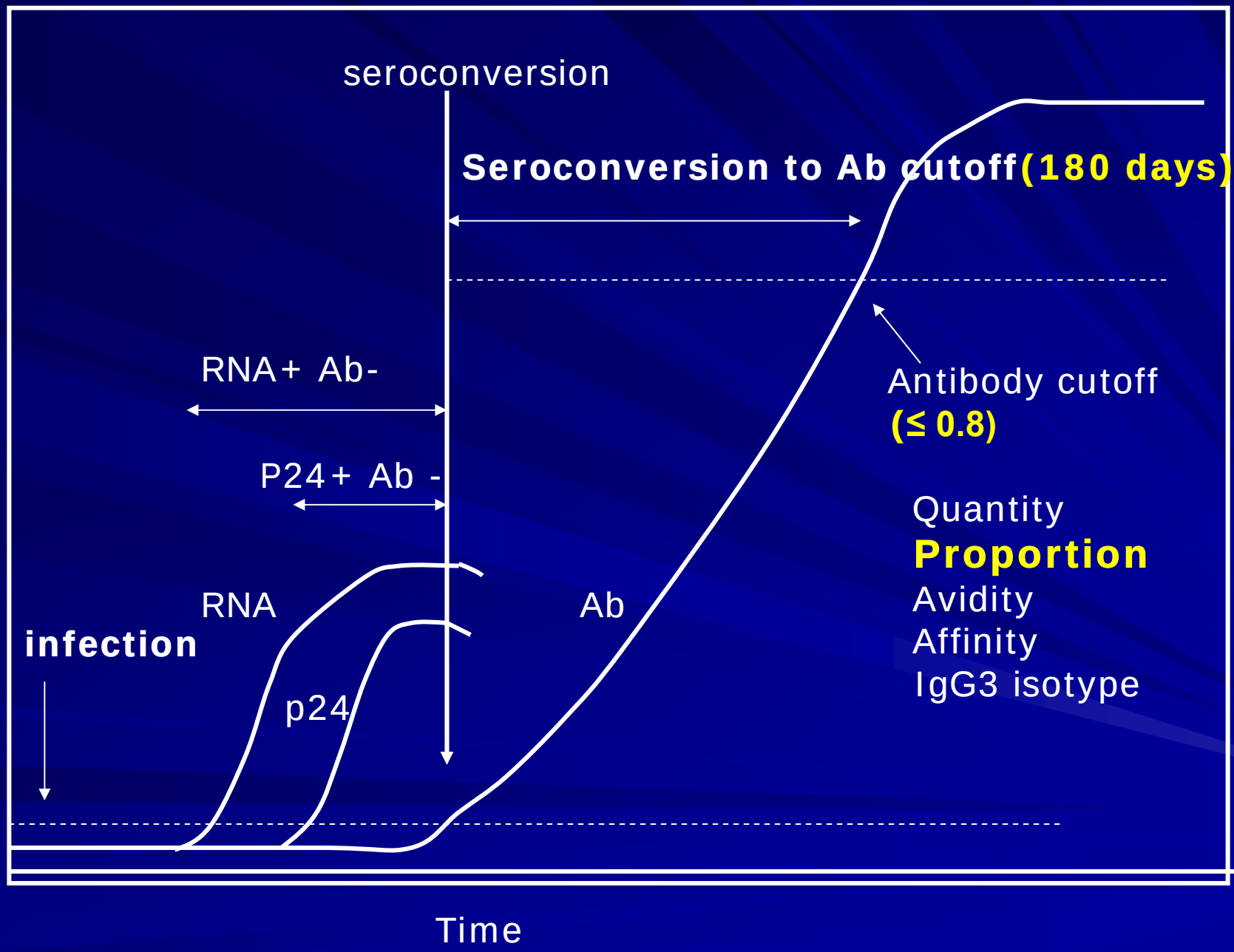
Calculation of age cohort incidence among antenatal attendees, South Africa 2005

Age (years)	Smooth Prevalence (%)	Difference in prevalence (%)	Proportion population at risk	Incidence (%)
15	9.1			
16	10.6	1.438	0.909 (90.9%)	1.6
17	13.2	2.632	0.894 (89.4%)	2.9
18	16.7	3.473	0.868 (86.8%)	4.0
19	20.6	3.961	0.833 (83.3%)	4.8
20	24.7	4.098	0.794 (79.4%)	5.2
21	28.6	3.883	0.753 (75.3%)	5.2
22	31.9	3.315	0.714 (71.4%)	4.6
23	34.3	2.394	0.681 (68.1%)	3.5
24	36.4	2.076	0.657 (65.7%)	3.2

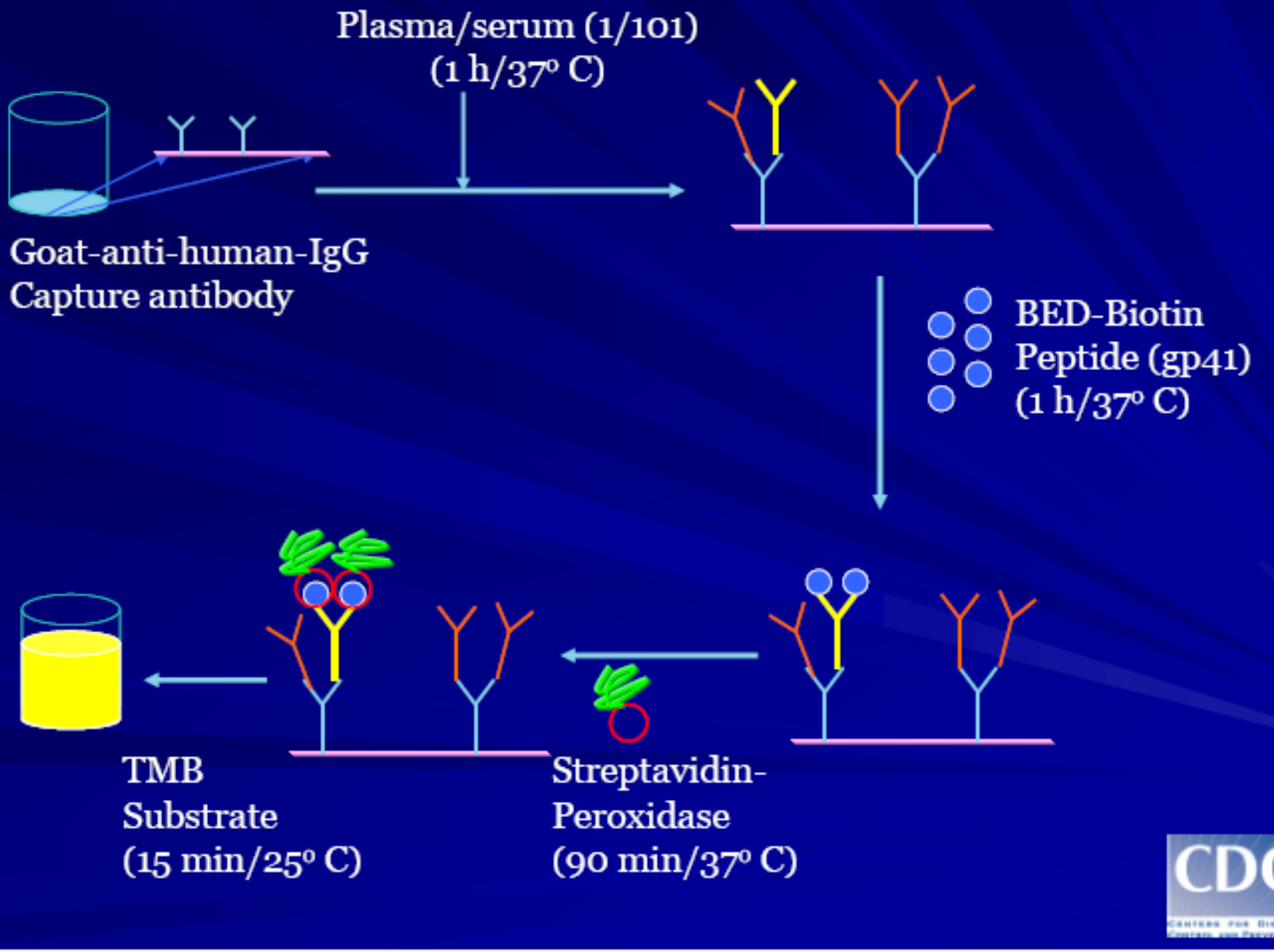
Laboratory- based methods

- direct incidence measure from cross-sectional surveys

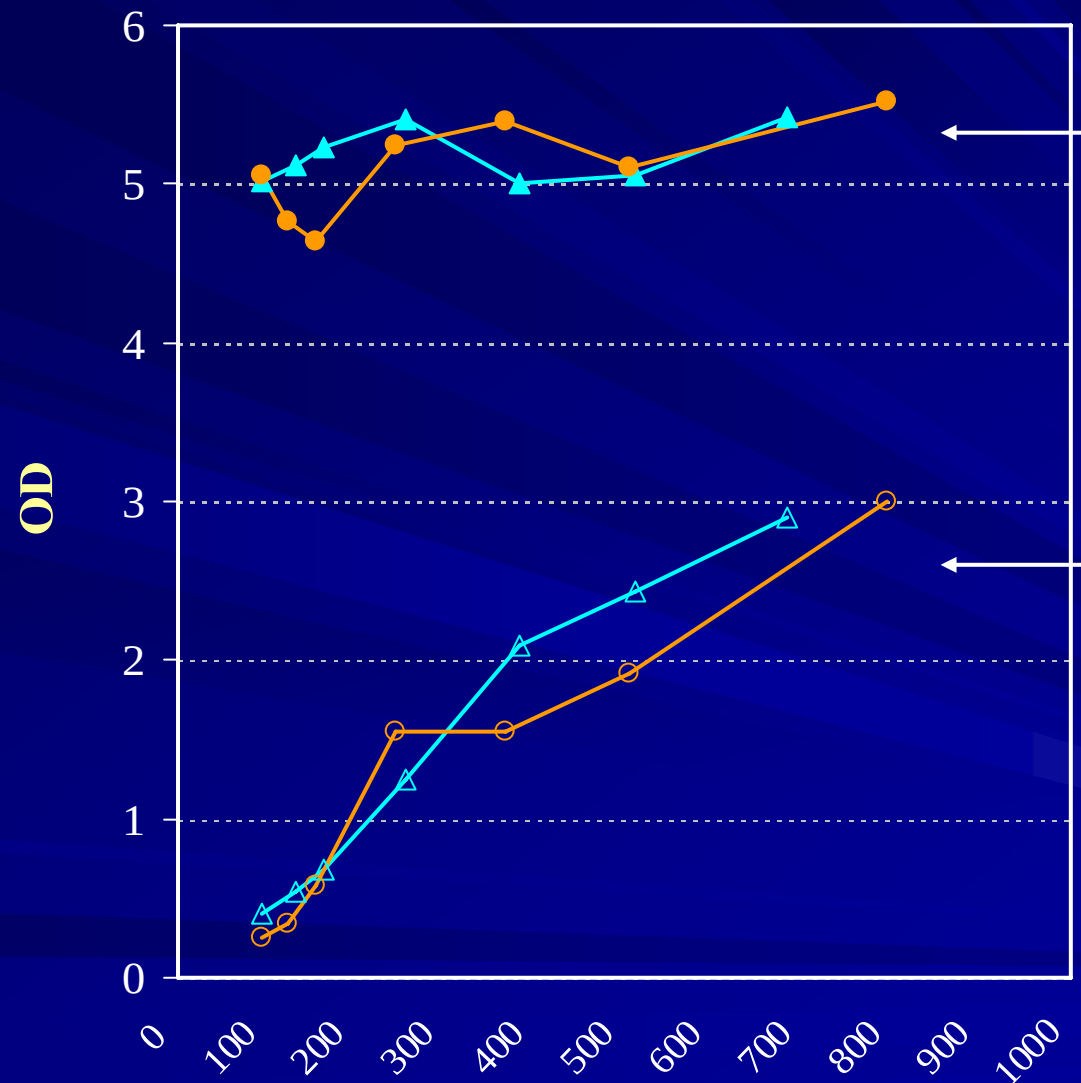
HIV-1 BED incidence EIA (adapted from B. Parekh et al. 2002)



Schematic of the BED-CEIA



Comparison of Conventional EIA (antigen coated plates) and BED-Capture EIA



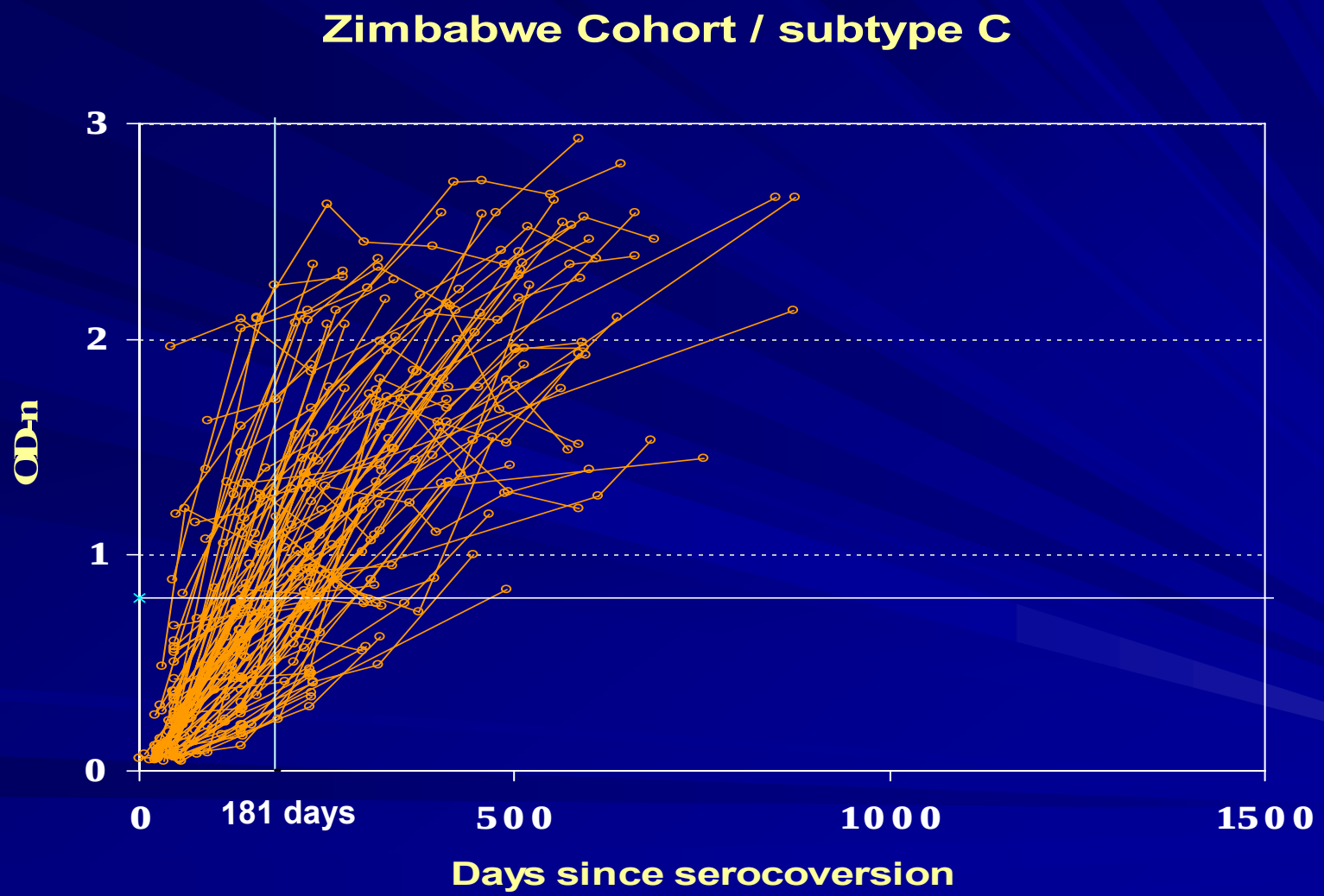
Conventional BED EIA

BED-Capture EIA

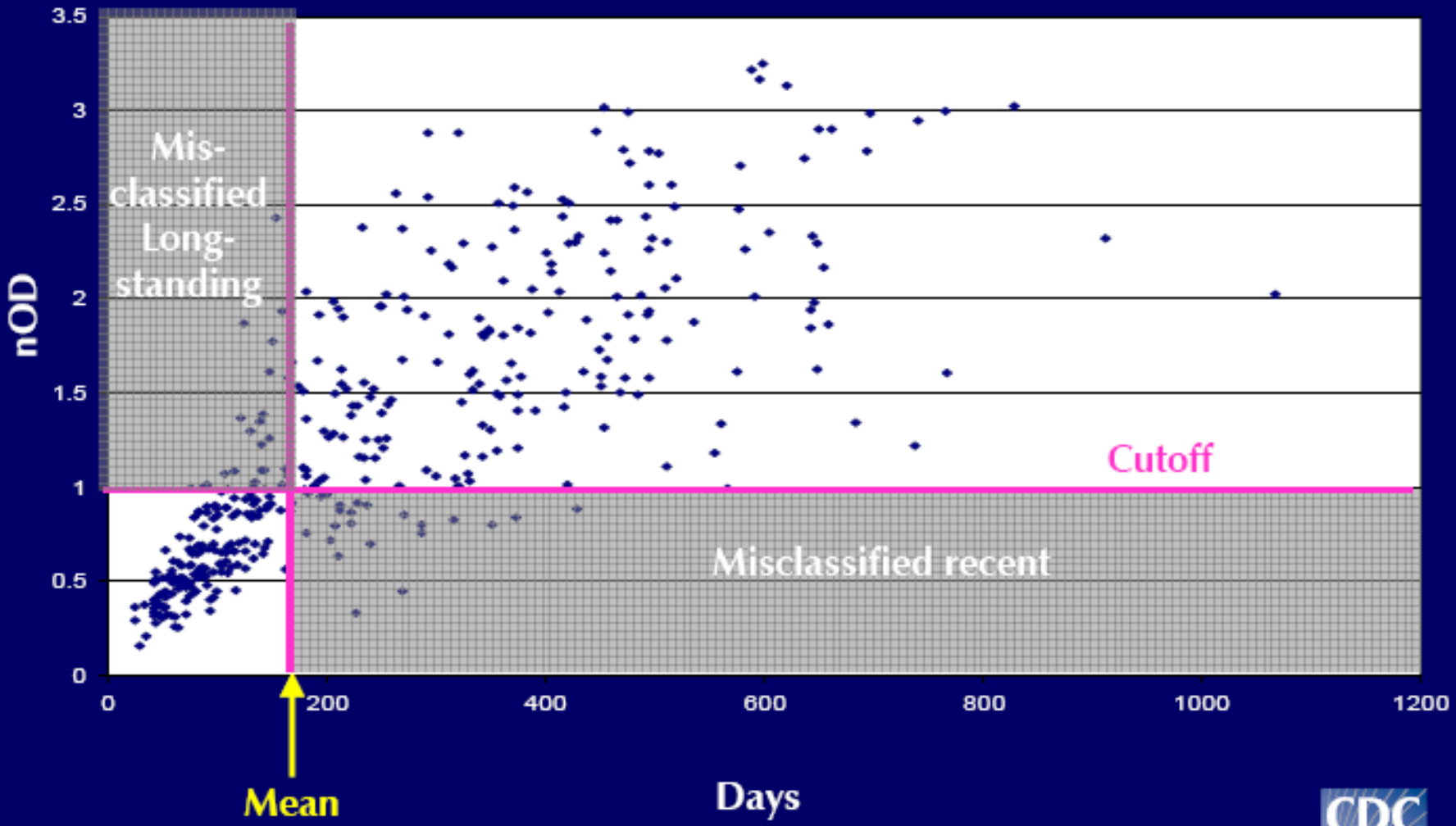
BED window periods at 0.8 cutoff

Subtypes	Country	Window (95% CI)
AD	Kenya	171 (150-199)
B	Amsterdam	127 (113-152)
B	Thailand	143 (118-170)
C	**Zimbabwe**	**181 (165-198)**
C	Ethiopia	167 (154-180)
E	Thailand	115 (106-125)
OVERALL		155 (146-165)

Calibration of window period



Window Period Estimates: Incidence



Validation Studies

- Cohort studies (seronegative at onset; no long term prevalent)
- Cohort studies including accumulated long-term infected
- Eligibility prescreens for enrollment in cohort studies (large number long-term prevalent)
- Cross-sectional surveillance surveys

CDC

BED incidence adjustments

- **UNAIDS 2005: overestimates in cross-sectional studies**

- **BED validation meeting, CDC 2006:**
  - **Sensitivity/Specificity Adjustment (McDougal et al.)**
  - **Specificity Adjustment (Hargrove et al.)**
  - **Validated for HIV-1 subtypes B and C (2 532 specimens from 1 192 individuals)**

Imputed values for adjusted BED HIV incidence calculation

w = window in days (180)
(mean duration of seropositivity in those testing recent)

Sensitivity/Specificity Adjustment (McDougal et al.)

α = sensitivity of BED test for detecting recent ($< w$) infection (0.7682)
β = specificity of the BED test over the period $> w$ to $< 2w$ (0.7231)
γ = specificity of the BED test over the period $> 2\ w$ (0.9443)

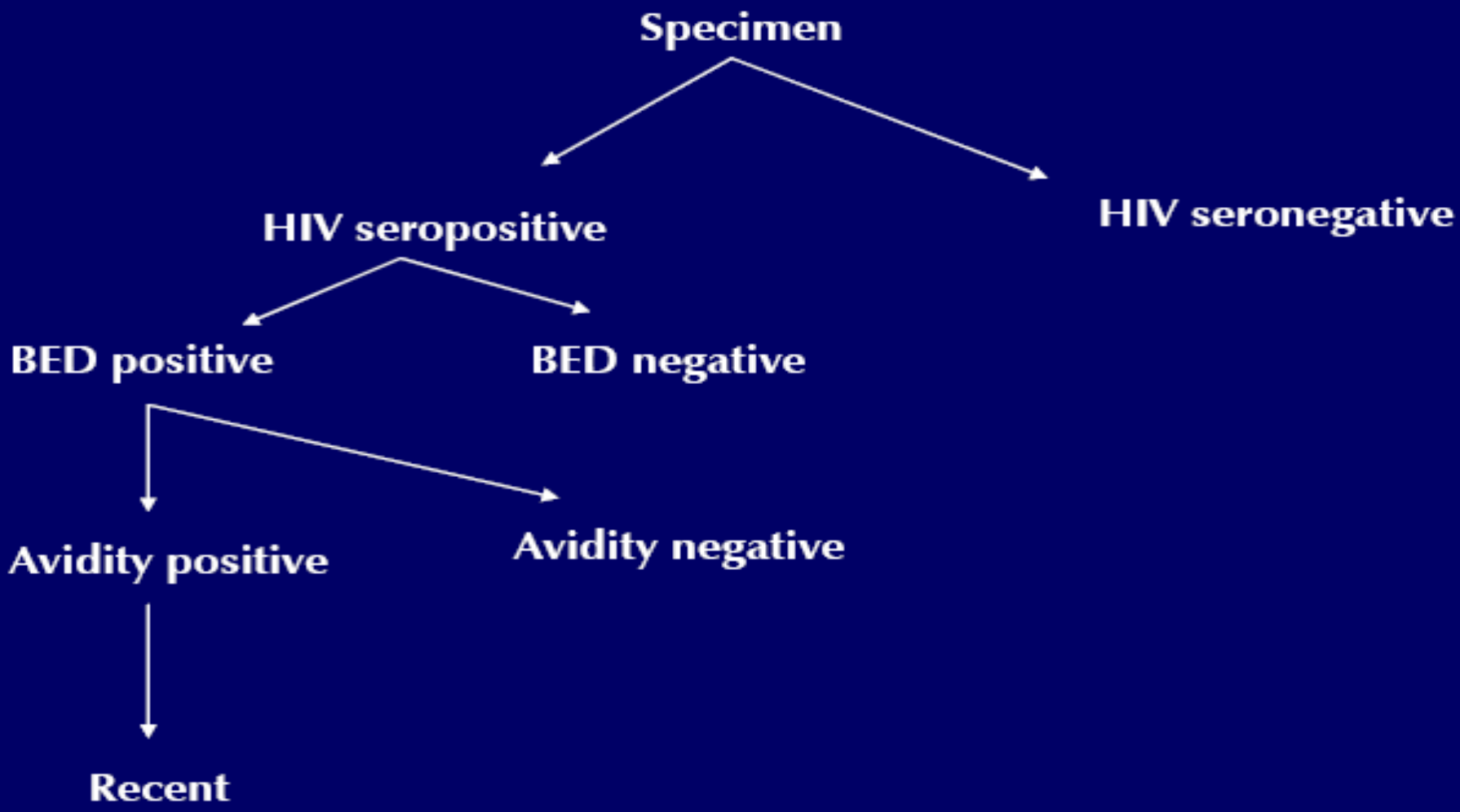
Specificity Adjustment (Hargrove et al):

$$I = \frac{R - \varepsilon P}{(R/2) + N(w/365) - \varepsilon N - \varepsilon(P/2)} \times 100$$

ε = false recent rate in those with long term (> 2 *w*) infection (0.0557)

NOTE: $\varepsilon = (1 - \gamma)$ and $\gamma = (1 - \varepsilon)$

Laboratory-based adjustment: Sequential testing algorithm



BED HIV-1 Incidence Estimates National HIV survey, South Africa 2005

- BED HIV incidence CEIA applied to confirmed HIV-positive specimens
- BED CEIA performed at NICD, Johannesburg
- BED HIV incidence estimates based on weighted analysis

BED HIV incidence calculation

$$I = \frac{F\,(365/w)\,N_{inc}}{N_{neg} + F\,(365/w)\,N_{inc}/2} \times 100$$

$$\text{Adjustment Factor (McDougal)} = \frac{(R/P) + \gamma - 1}{(R/P)\,(\alpha - \beta + 2\gamma - 1)}$$

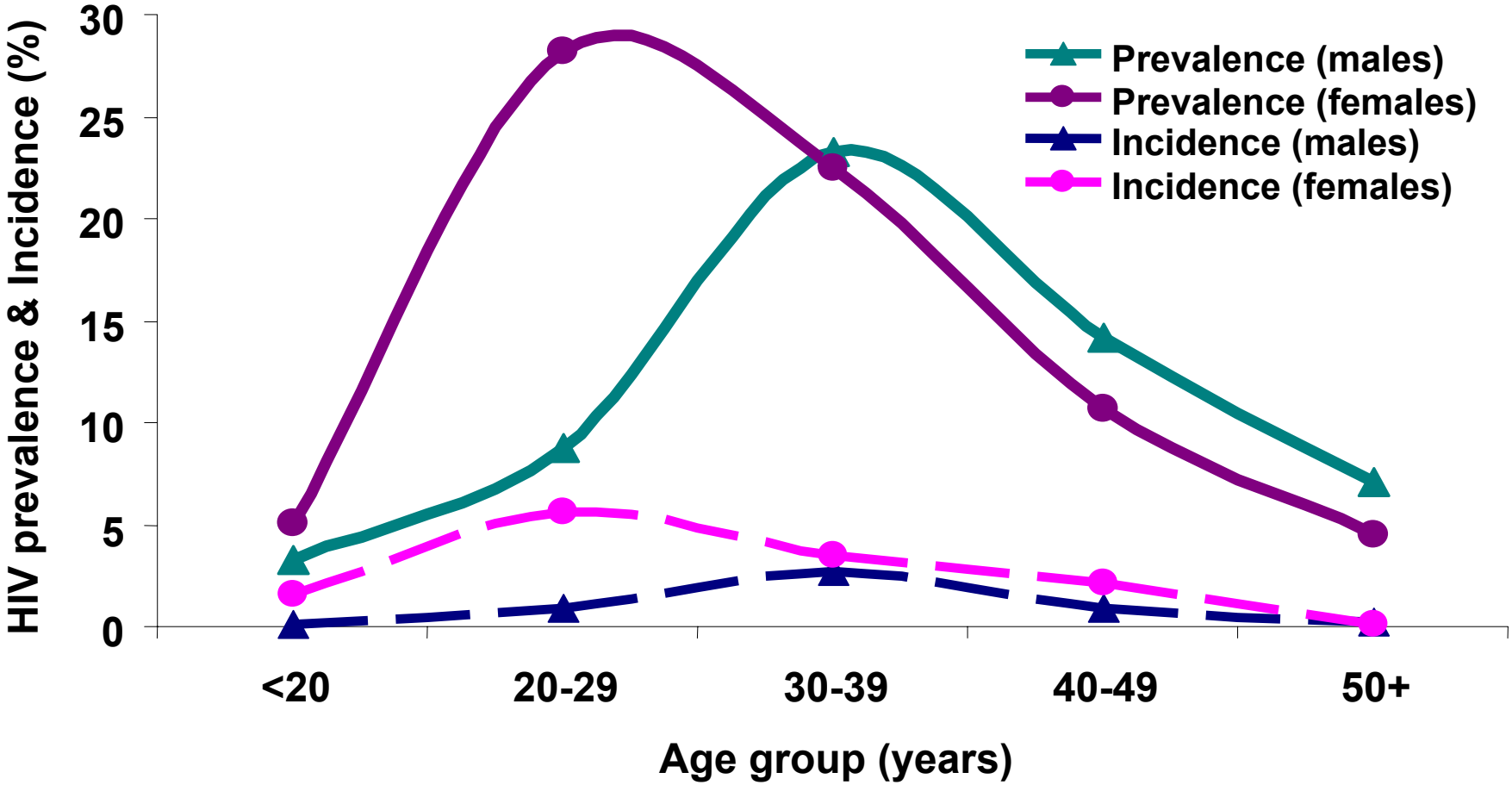
Window period = 180 days

Incidence = number of new infections per year per 100 persons at risk (% / year)

HIV incidence % and number of new infections by age group, South Africa 2005

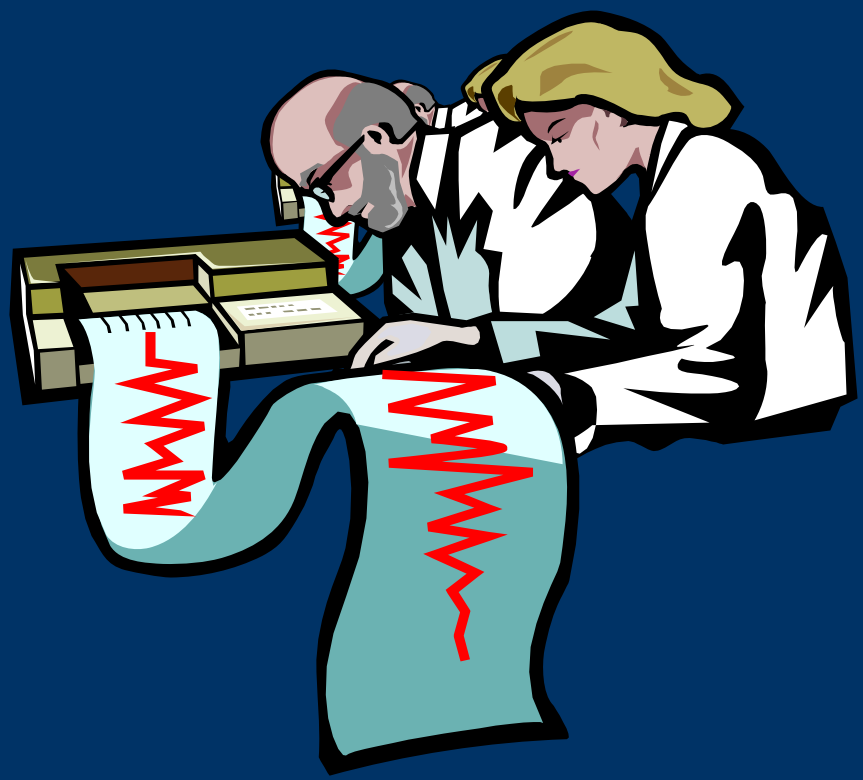
Age group (years)	Weighted sample (n)	HIV incidence % per year [95%CI]	Estimated number of new infections per year (n)
≥ 2	44 513 000	1.4 [1.0 - 1.8]	571 000
2-14	13 253 000	0.5 [0.0 - 1.2]	69 000
15-24	9 616 000	2.2 [1.3 - 3.1]	192 000
15-49	24 572 000	2.4 [1.7 – 3.2]	500 000

HIV prevalence and HIV incidence by age and sex, South Africa 2005

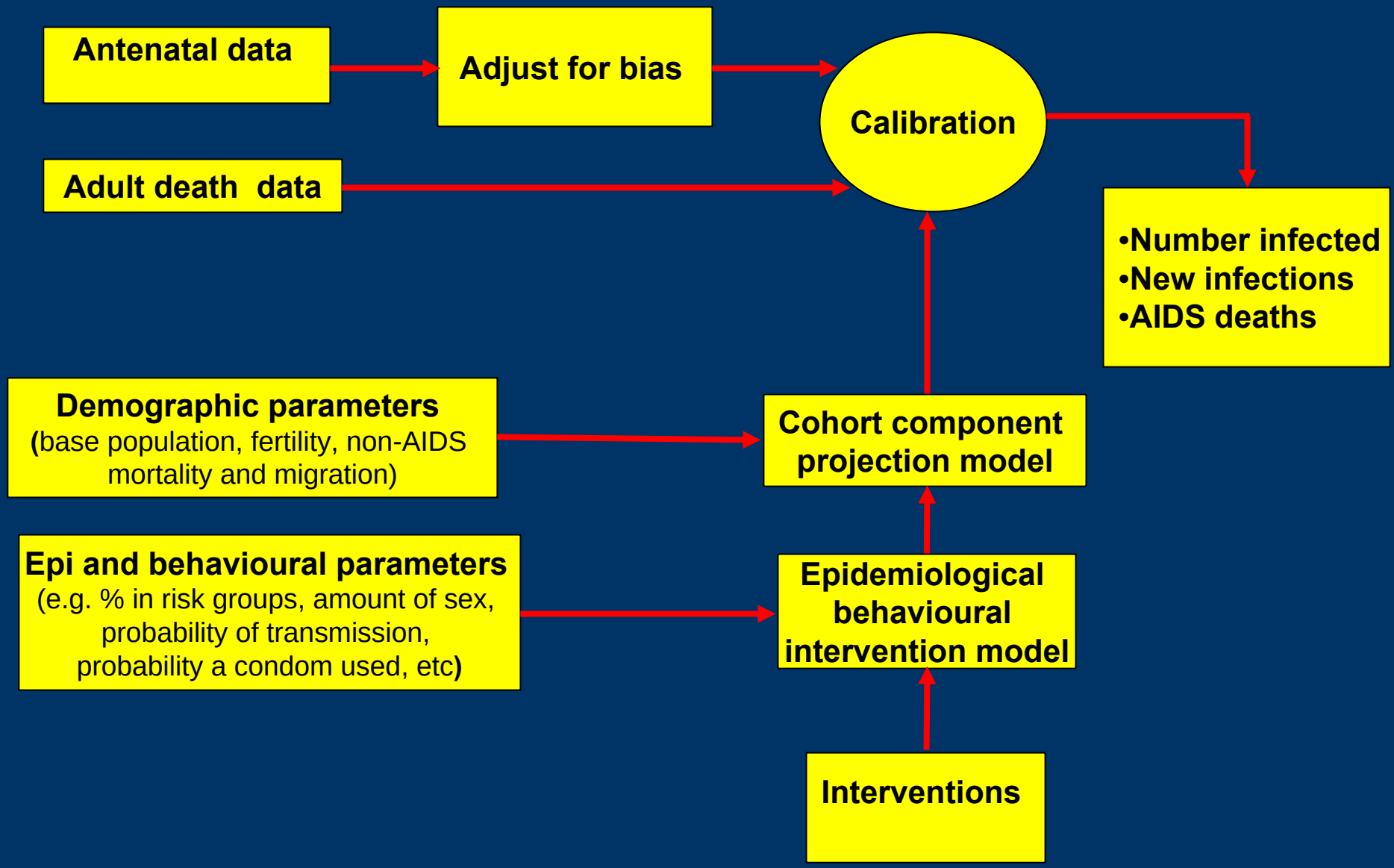


Rehle *et al.* SAMJ 2007; 97: 194-199

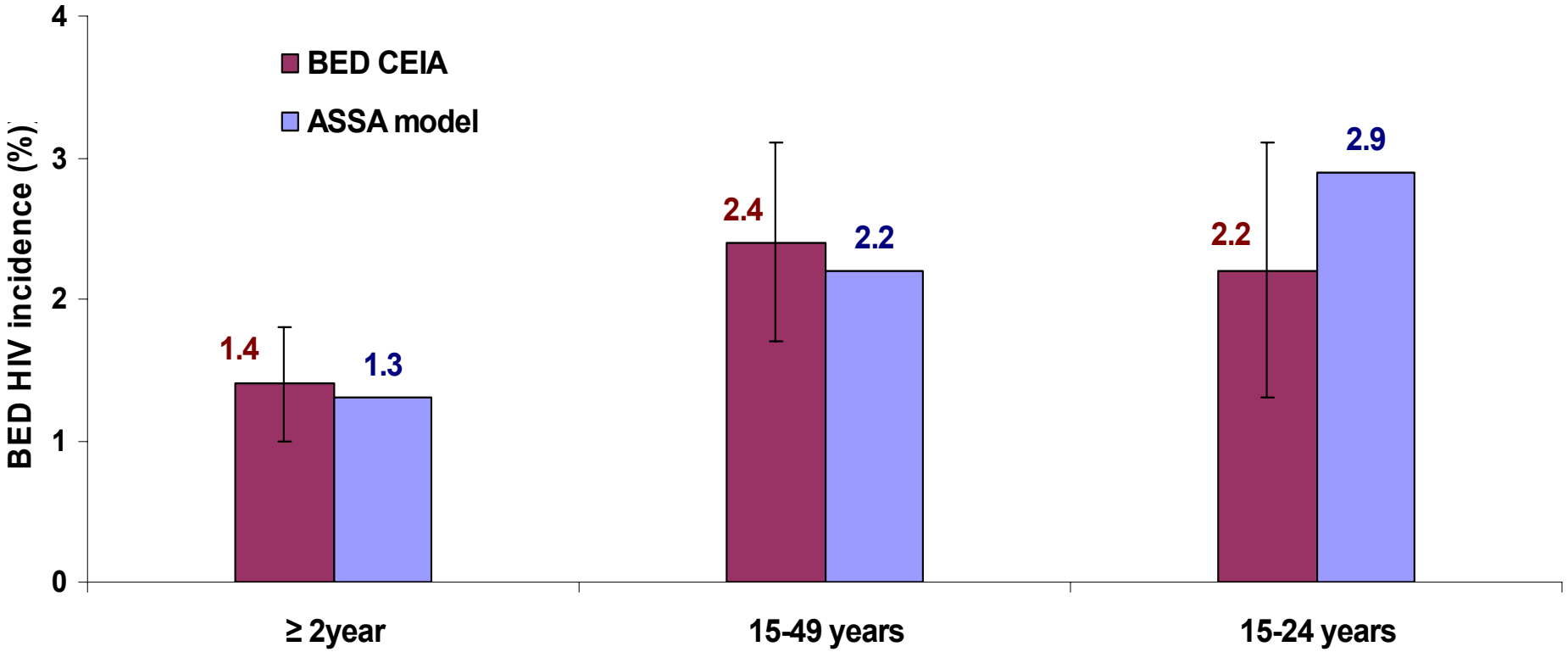
Are the adjusted BED HIV incidence estimates plausible?



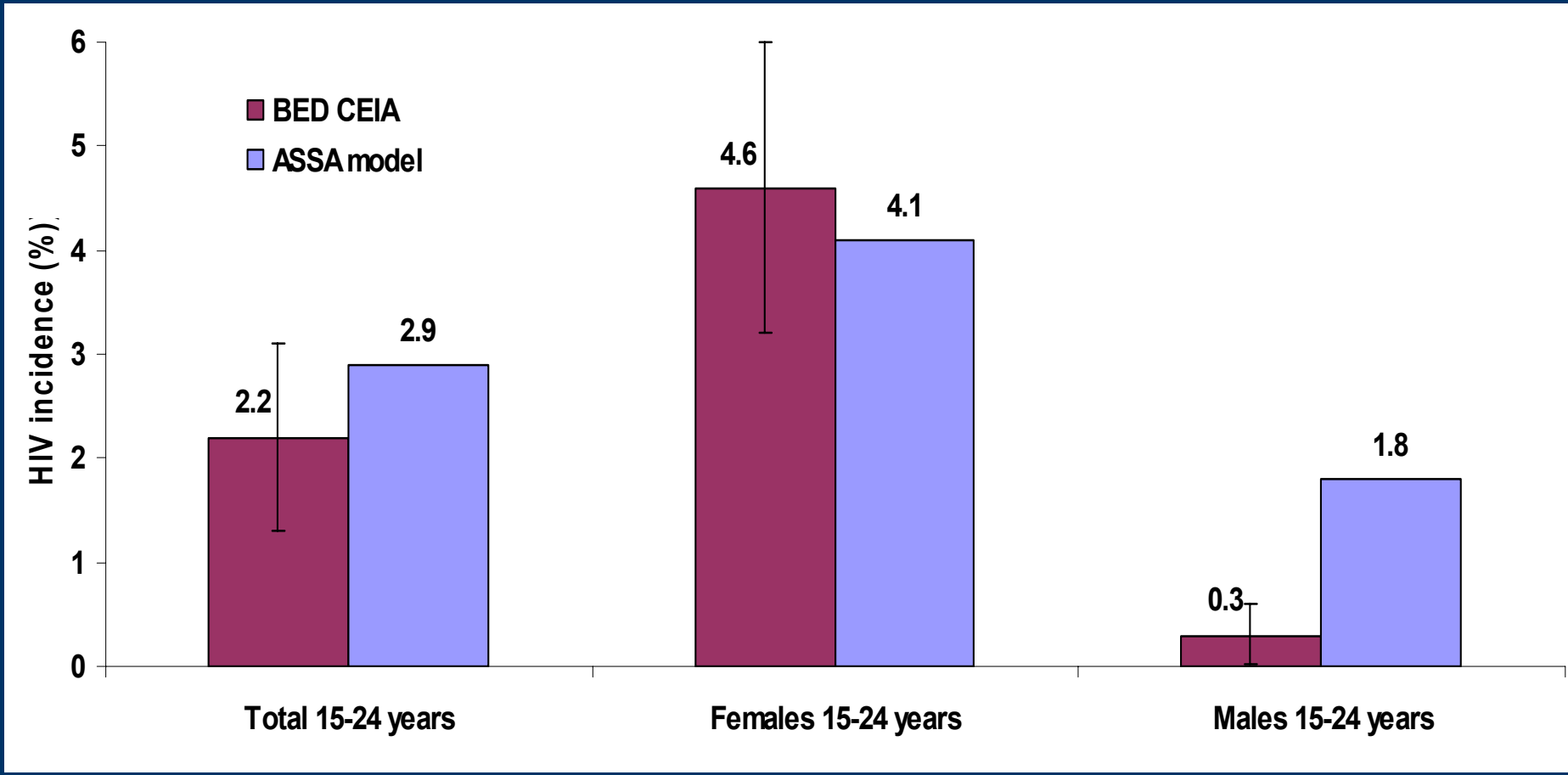
ASSA model


Antenatal data
Adjust for bias
Calibration
Adult death data
•Number infected
•New infections
•AIDS deaths
Demographic parameters
(base population, fertility, non-AIDS mortality and migration)
Cohort component projection model
Epi and behavioural parameters
(e.g. % in risk groups, amount of sex, probability of transmission, probability a condom used, etc)
Epidemiological behavioural intervention model
Interventions

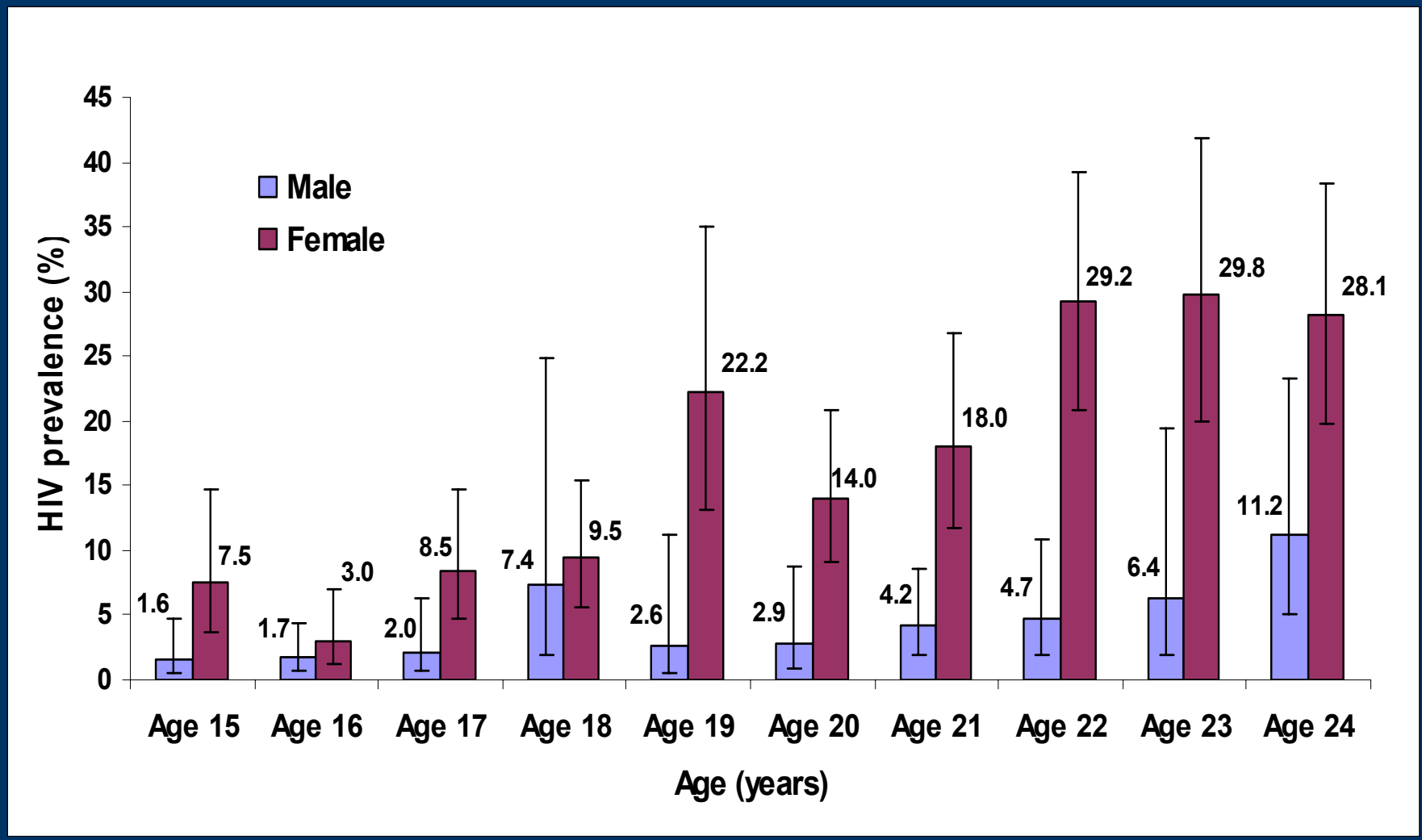
BED HIV incidence vs ASSA model (estimates for 2005)



BED HIV incidence vs ASSA model: male and female youth 15-24 years



HIV prevalence in youth by single year of age HSRC 2005



HIV incidence and behaviour HSRC 2005 (age group 15 – 49 years)

Variable	HIV incidence (% per year)
Marital status	
Single	3.0
Married	1.3
Widowed	5.8
Sexual history	
Sexually active in the past 12 months	2.4
Current pregnancy	5.2
Condom use at last sex (15-24 yrs)	
Yes	2.9
No	6.1

(Rehle et al. S Afr Med J 2007; 97: 194-199)

Conclusion

- **Incidence estimates enable a more timely analysis of the current HIV-transmission dynamics**
- **The adjusted BED HIV incidence estimates provide valid national HIV incidence estimates for South Africa**
- **Prevention campaigns did not have the desired impact, particularly among young women**