ECDC work on estimating HIV prevalence in EU/EEA/EFTA countries

Ard van Sighem

14 September 2011

HIV Monitoring

People living with HIV 2009

Total: 33.3 million [31.4 million – 35.3 million]
2.6 million new infections in 2009

source: UNAIDS

HIV Monitoring

HIV in Europe

- ±1 million people living with HIV/AIDS in Europe.
- Infection with HIV does not always produce symptoms that lead to diagnosis around the time of infection.
- As a result, many people with HIV are not aware of their infection.
- Accurate estimates of the number of people with HIV for all countries in the region are necessary for a full response to the HIV epidemic.

HIV Monitoring

Estimating number of HIV infections

- Relatively easy for *generalised* epidemics:
  - HIV prevalence is high (>5%) in the general population.
- More difficult for *concentrated* epidemics:
  - HIV prevalence is high in certain risk populations.
  - Need data on all subpopulations, often difficult to reach.

HIV Monitoring

Estimating number of HIV infections

2 main approaches for estimating the number of HIV infections:

- **based on prevalence surveys**
- **based on reported number of HIV diagnoses**
  - **reconstruction of HIV incidence curve**
  - **using the relationship between AIDS and CD4**

HIV Monitoring

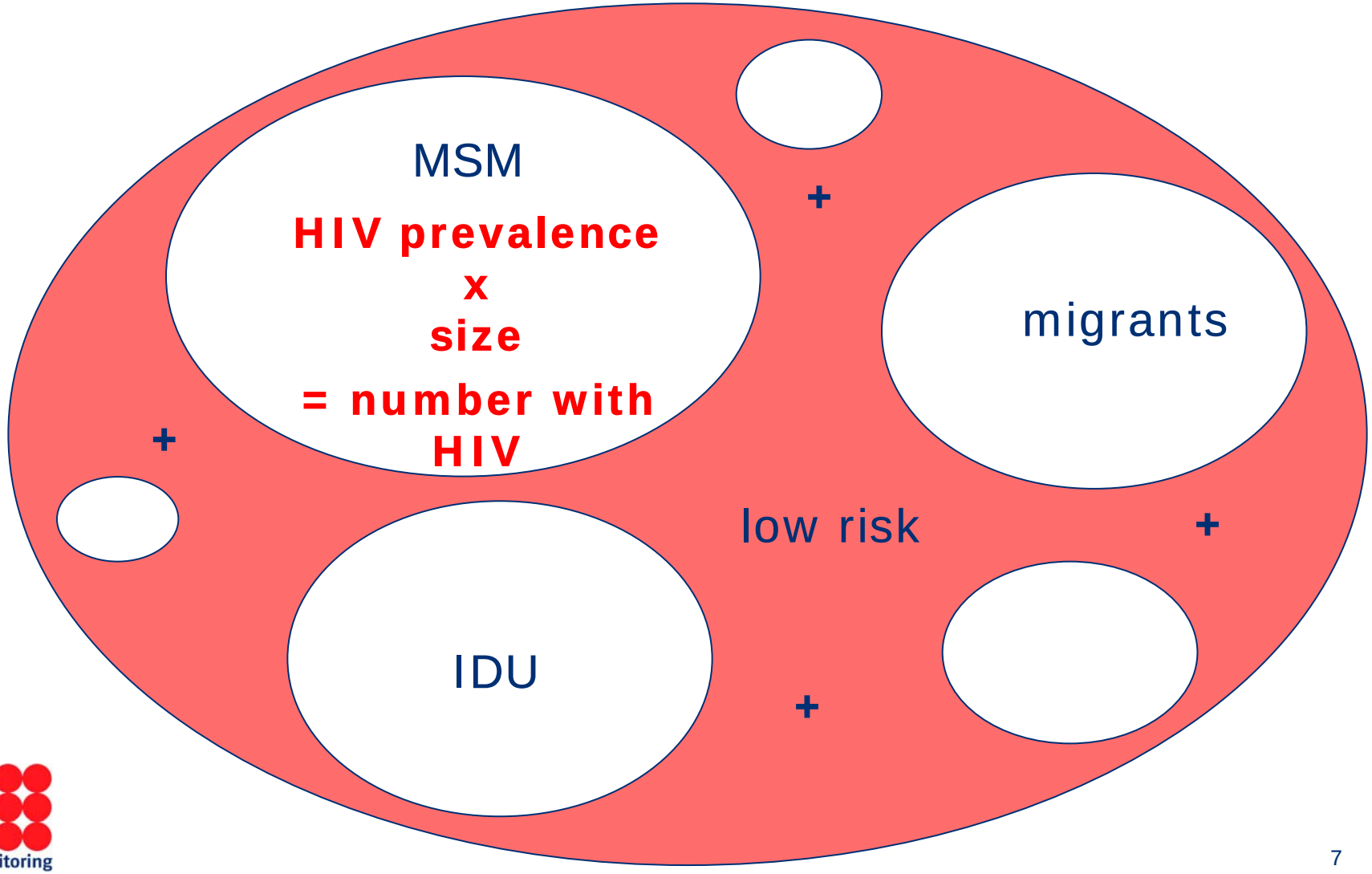
Number of HIV infections

2 main approaches for estimating the number of HIV infections:

- **based on prevalence surveys**
- **based on reported number of HIV diagnoses**
  - **reconstruction of HIV incidence curve**
  - **using the relationship between AIDS and CD4**

HIV Monitoring

Mutually exclusive risk groups



Available software

- **Workbook**
  - **Spreadsheet in XL**
- **Estimation and Projection Package (EPP) & Spectrum**
  - **Transmission model**
  - **Calculates trends in incidence & prevalence**
- **Multi-Parameter Evidence Synthesis**
  - **Formal statistical triangulation**

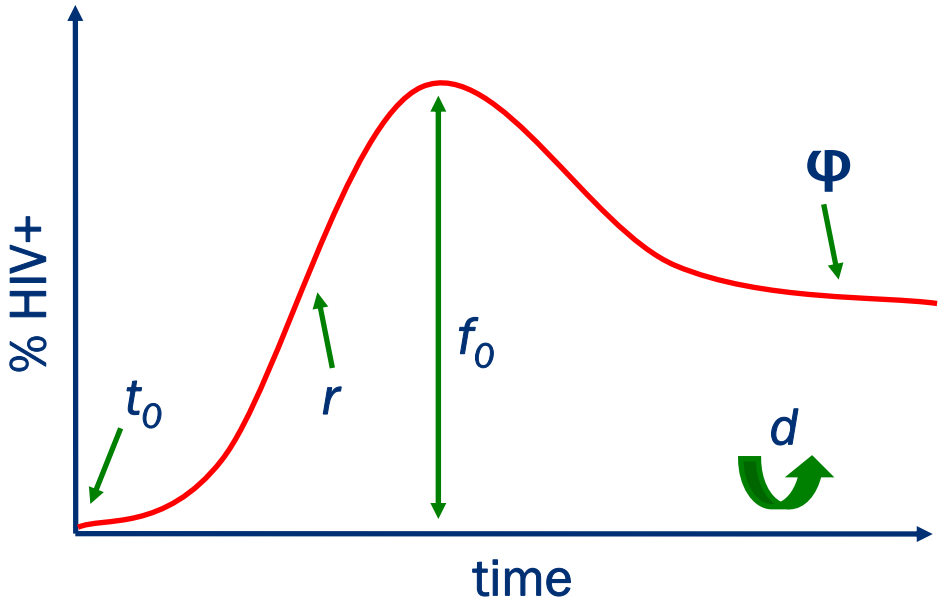
HIV Monitoring

Workbook method

- Spreadsheet developed by UNAIDS to estimate HIV prevalence.
- Requires lower and upper bounds on estimated group sizes and HIV prevalence.
- HIV-infected population estimated by taking the product of the midpoints.
- User-friendly and easy to use.

EPP-Spectrum method

- **Estimation and Projection Package (EPP) & Spectrum is a tool for estimating HIV prevalence and making short-term projections.**
- **Fits a transmission model with 5 parameters:**



r	rate of growth of the epidemic
f_0	fraction at risk of infection at start of the epidemic
t_0	start year
φ	behavioural response to the epidemic
d	average time spent in a risk group

EPP-Spectrum

- 3 prevalence estimates per risk group.
- Level fits: all surveillance sites in a region follow a similar pattern of changing prevalence but at different levels.
- Effect of antiretroviral treatment on prevalence is taken into account.
- Epidemic curves for subpopulations are combined to form a national estimate of HIV prevalence.
- Spectrum uses (EPP) incidence curves to generate numbers of programmatic concern such as death and children with HIV.

HIV Monitoring

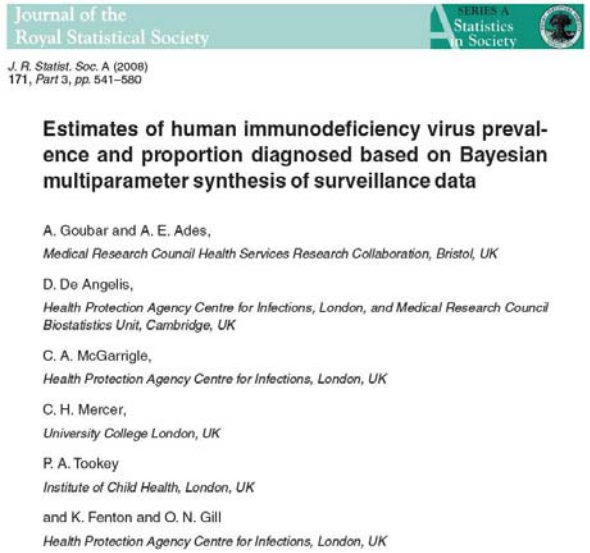
Issues Workbook and EPP-Spectrum

- Often multiple sources of data informing on the size or prevalence of the same risk group.
- Data may be contradictory.
- Often no or sparse information for some of the risk groups.
- Not clear what to do with case report data, which are collected by many countries.
- No full uncertainty analysis for concentrated epidemics.

HIV Monitoring

Multi-Parameter Evidence Synthesis

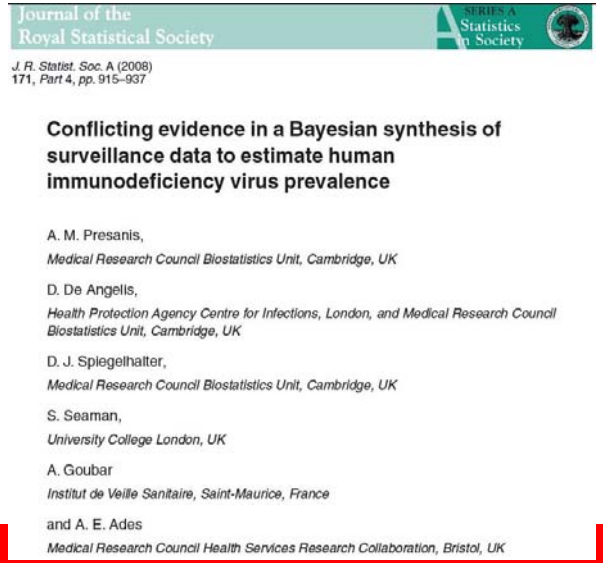
- Developed by the Health Protection Agency in the UK
- Bayesian modelling framework
- Uses all available data in a coherent way
- Can use data on diagnosed infections
- Multiple data sources can inform on the same parameter
- Estimates “true” prevalence and diagnosed proportions with credibility intervals
- Applied to HIV epidemic in England and Wales and, recently, in the Netherlands



Journal of the Royal Statistical Society
SERIES A Statistics in Society
J. R. Statist. Soc. A (2008)
171, Part 3, pp. 541–580

Estimates of human immunodeficiency virus prevalence and proportion diagnosed based on Bayesian multiparameter synthesis of surveillance data

A. Goubar and A. E. Ades,
Medical Research Council Health Services Research Collaboration, Bristol, UK
D. De Angelis,
Health Protection Agency Centre for Infections, London, and Medical Research Council Biostatistics Unit, Cambridge, UK
C. A. McGarrigle,
Health Protection Agency Centre for Infections, London, UK
C. H. Mercer,
University College London, UK
P. A. Tookey
Institute of Child Health, London, UK
and K. Fenton and O. N. Gill
Health Protection Agency Centre for Infections, London, UK



Journal of the Royal Statistical Society
SERIES A Statistics in Society
J. R. Statist. Soc. A (2008)
171, Part 4, pp. 915–937

Conflicting evidence in a Bayesian synthesis of surveillance data to estimate human immunodeficiency virus prevalence

A. M. Presanis,
Medical Research Council Biostatistics Unit, Cambridge, UK
D. De Angelis,
Health Protection Agency Centre for Infections, London, and Medical Research Council Biostatistics Unit, Cambridge, UK
D. J. Spiegelhalter,
Medical Research Council Biostatistics Unit, Cambridge, UK
S. Seaman,
University College London, UK
A. Goubar
Institut de Veille Sanitaire, Saint-Maurice, France
and A. E. Ades
Medical Research Council Health Services Research Collaboration, Bristol, UK

HIV Monitoring

MPES

- Total population divided into mutually exclusive risk groups *g* in different regions *r* with population N_r.

- For each group, 3 basic parameters are estimated:
  - $\rho_{r,g}$ relative size of the risk group
  - $\pi_{r,g}$ prevalence of HIV in the group
  - $\delta_{r,g}$ proportion diagnosed amongst those infected

- Data informing on a combination of these parameters can be used, e.g.:
  - $\pi_{r,g}\,\delta_{r,g}$ HIV prevalence diagnosed
  - $N_r\,\pi_{r,g}\,\delta_{r,g}\,\rho_{r,g}$ diagnosed infections

HIV Monitoring

MPES - limitations

- No simple user interface.
- Uses non-standard software that has to be adapted to each estimation problem depending on available data.
- Statistical and epidemiological knowledge is needed.
- Lots of data are necessary as there are many parameters that have to be estimated.
- Assumptions have to be made on parameters that are not constrained by available data.
- Biases and contradictions have to be understood.

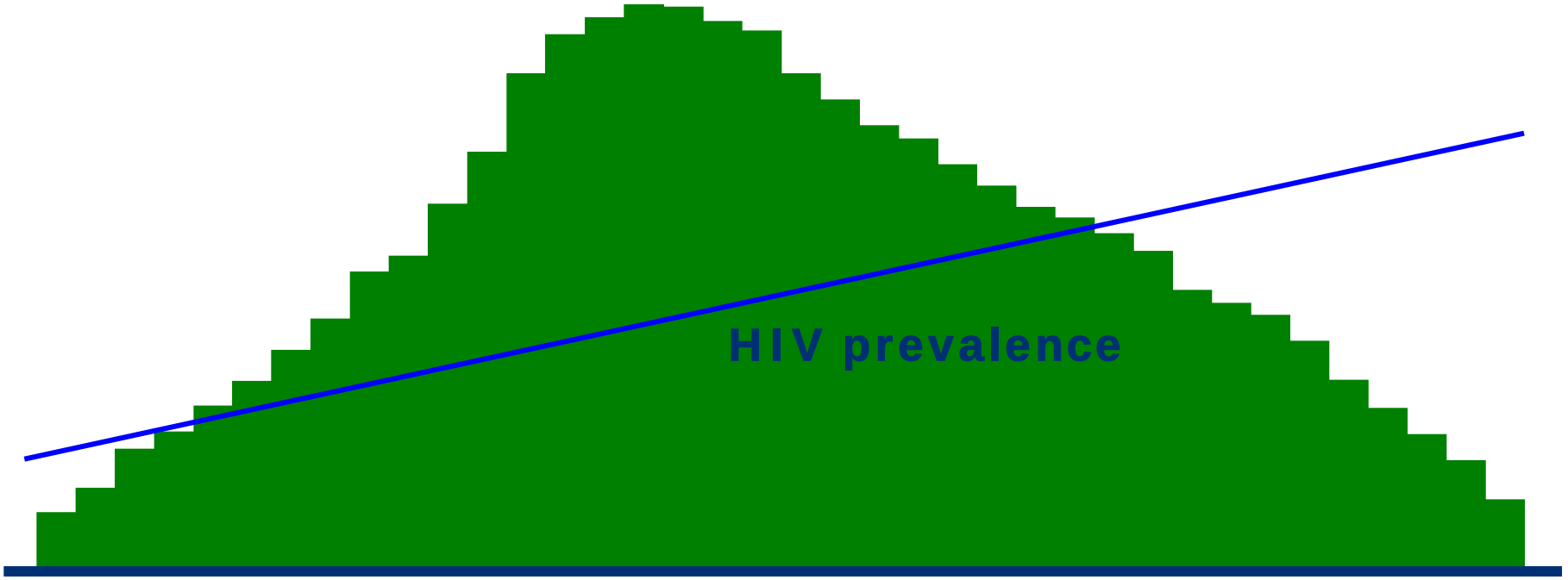
HIV Monitoring

Other issues

- **Matching populations sampled in the prevalence surveys with the populations for which size is estimated.**
- Measuring prevalence.
- Uncertainty in risk group sizes.
- Available data should be from the same time period.
- Which risk groups to divide the population into?

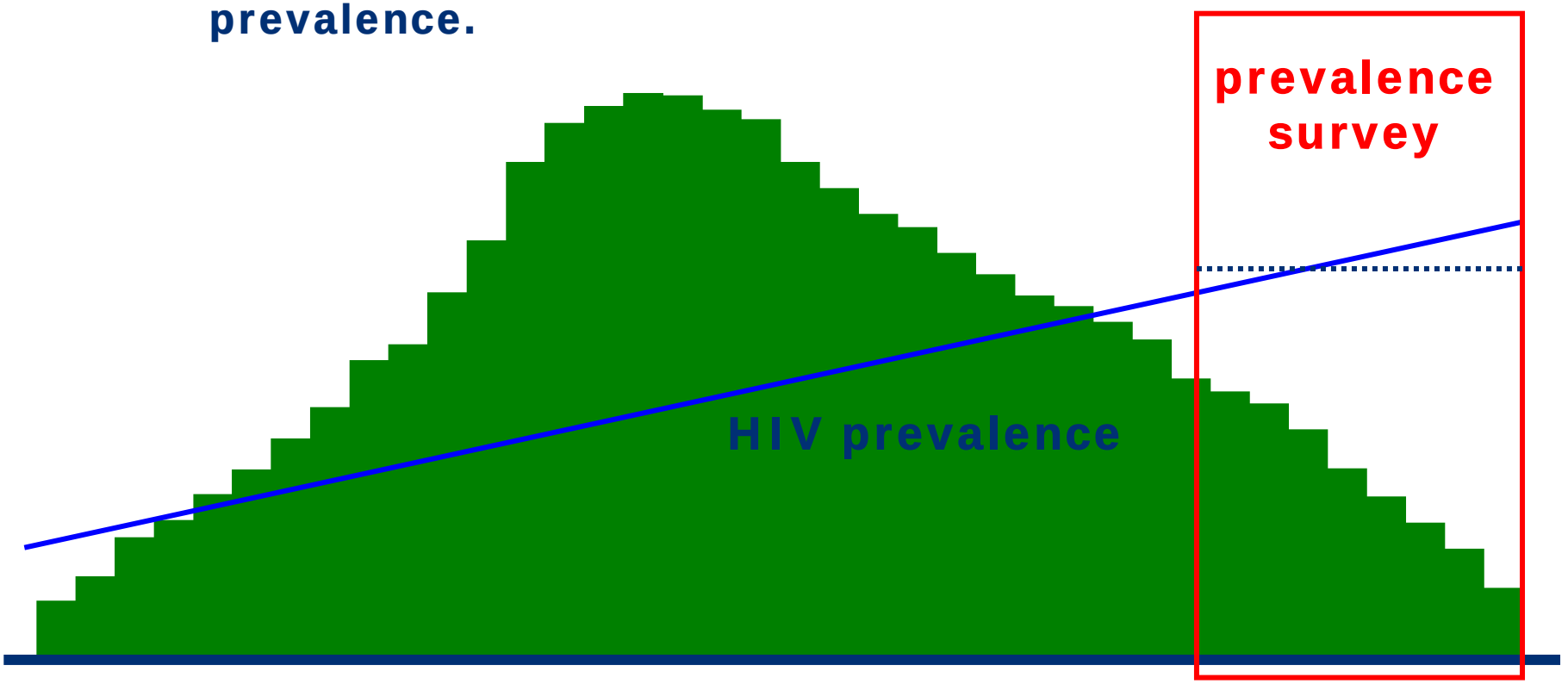
Matching - example

- A prevalence survey should be based on a representative sample of the risk group of which the size is estimated.



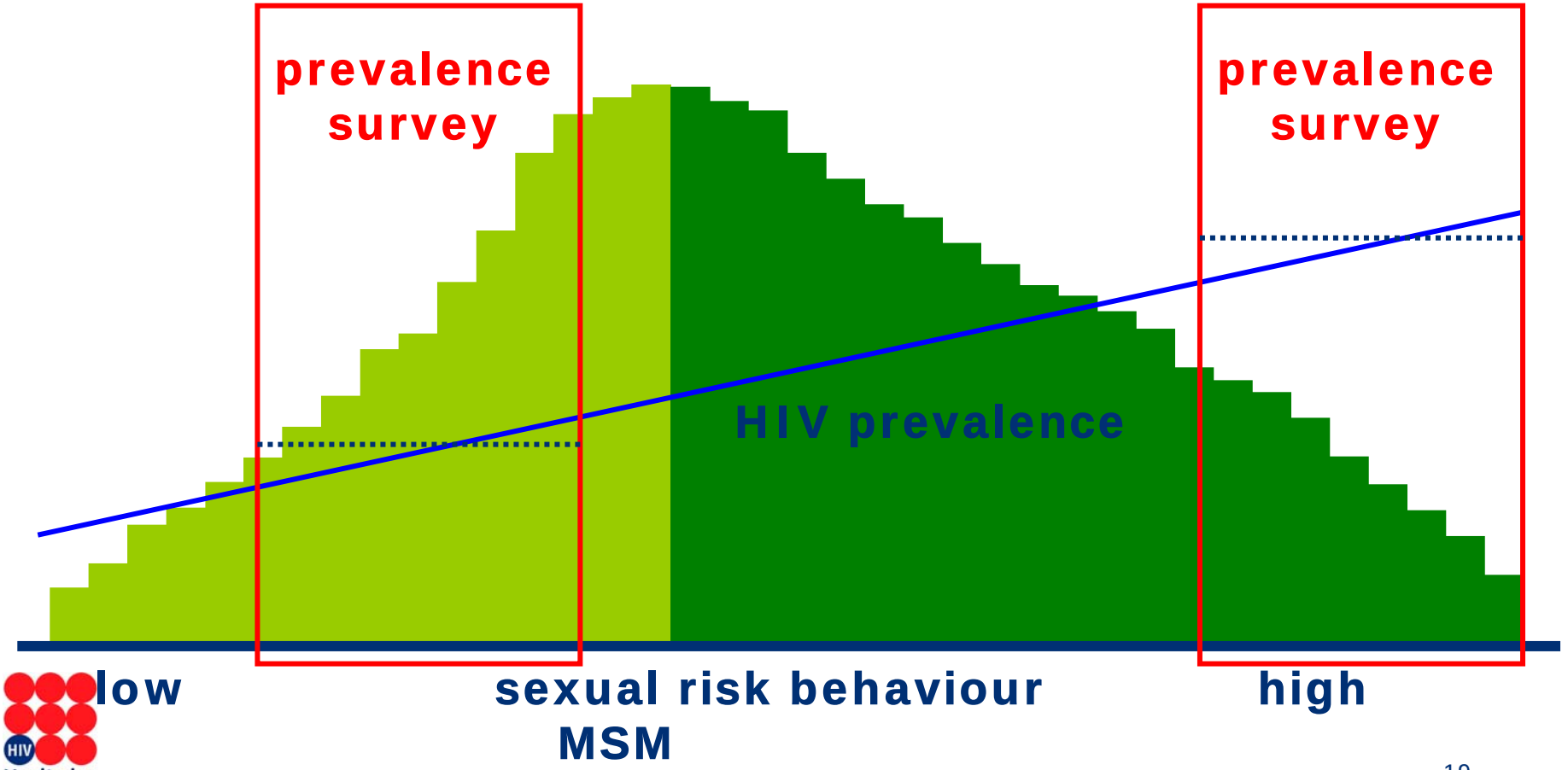
Matching - example

- Applying the prevalence found in the survey to all MSM will result in overestimation of the HIV prevalence.



Matching - example

- A solution is splitting MSM in two groups of high and low risk, each with a prevalence survey



Other issues

- Matching populations sampled in the prevalence surveys with the populations for which size is estimated.
- **Measuring prevalence.**
- Uncertainty in risk group sizes.
- Available data should be from the same time period.
- Which risk groups to divide the population into?

Prevalence

- STI clinics
  - informed consent versus opt-out
  - visitors are already a selection
- Respondent driven sampling
  - target members recruit for you
  - needs population with a social network
- Time location sampling
  - sampling people at locations where they may be found
  - suitable for hard-to-reach populations, e.g. street children
- How to determine prevalence in low-risk groups?
  - blood donors
  - screening of pregnant women

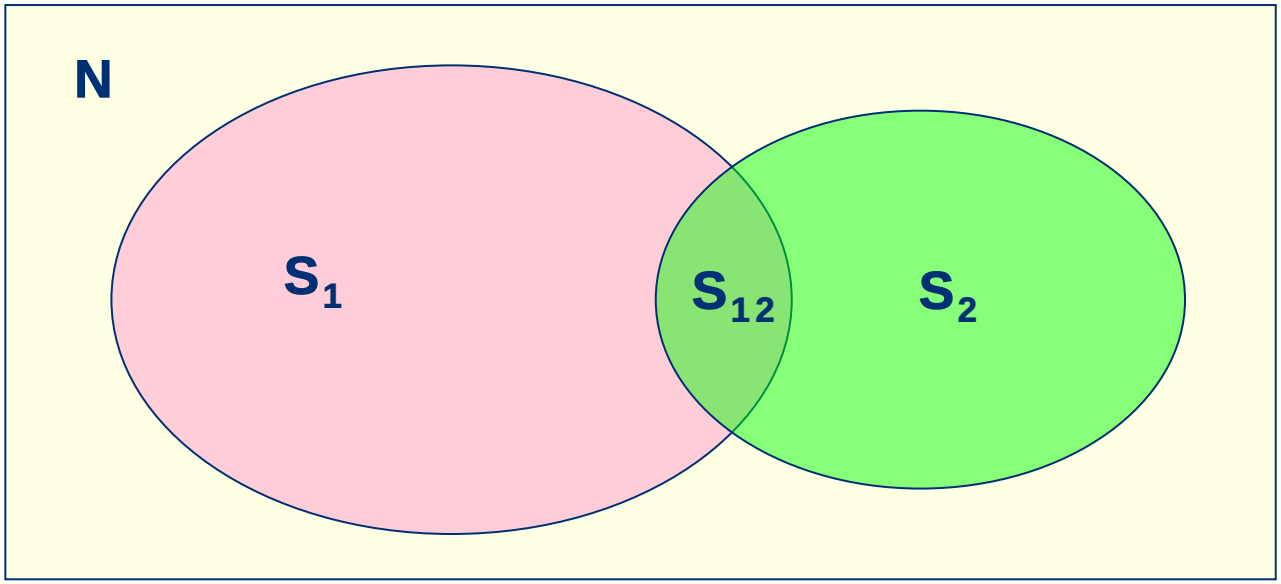
HIV Monitoring

Other issues

- Matching populations sampled in the prevalence surveys with the populations for which size is estimated.
- Measuring prevalence.
- **Uncertainty in risk group sizes.**
- Available data should be from the same time period.
- Which risk groups to divide the population into?

Risk group sizes

- Capture-recapture methods
  - overlap of 2 or more *independent* samples in same population
- Multiplier method
  - overlap of 2 or more *independent* datasets



$S_{12} / S_2 = S_1 / N$

Risk group sizes

Other methods

- household surveys
- network scale-up method, using data on people's network of acquaintances
- for MSM only, proportion of men aged 45 years and over who have never been married

Potential biases

- not always clear what is meant by IDU or MSM
- triangulation: use different methods
- Bayesian methods are currently being developed

HIV Monitoring

Other issues

- Matching populations sampled in the prevalence surveys with the populations for which size is estimated.
- Measuring prevalence.
- Uncertainty in risk group sizes.
- **Available data should be from the same time period.**
- Which risk groups to divide the population into?

Other issues

- Matching populations sampled in the prevalence surveys with the populations for which size is estimated.
- Measuring prevalence.
- Uncertainty in risk group sizes.
- Available data should be from the same time period.
- **Which risk groups to divide the population into?**

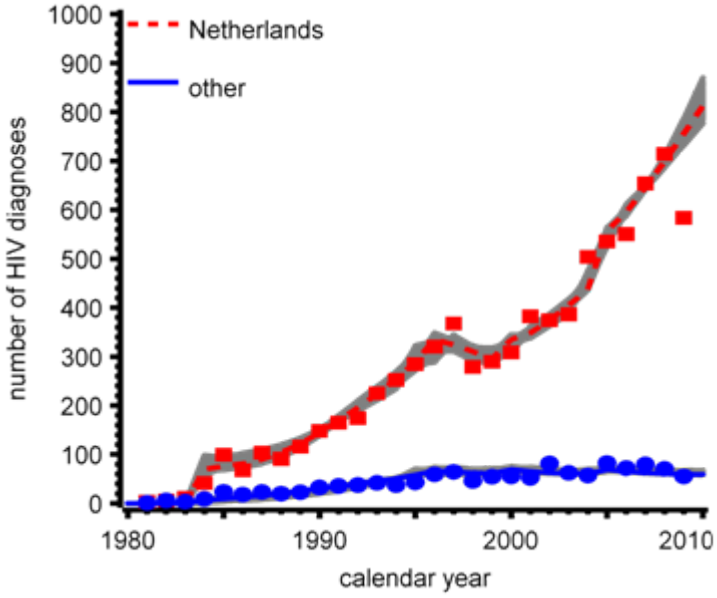
Number of HIV infections

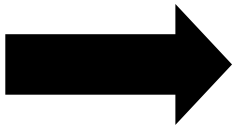
2 main approaches for estimating the number of HIV infections:

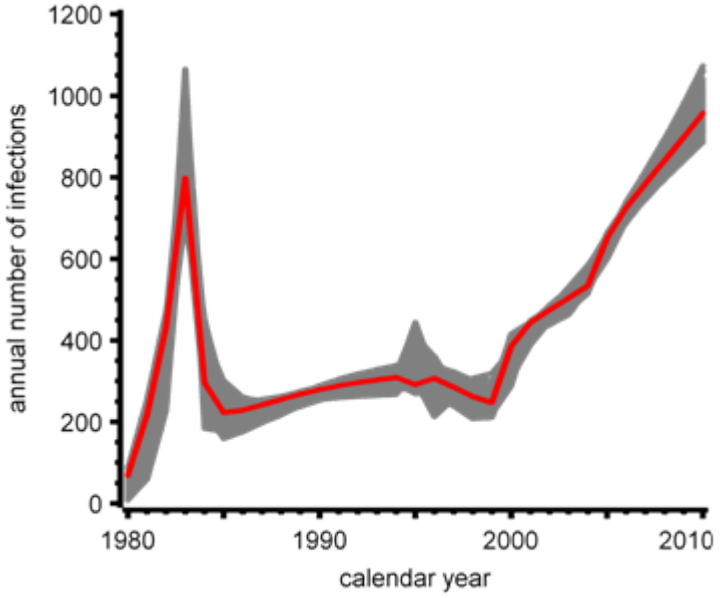
- **based on prevalence surveys**
- **based on reported number of HIV diagnoses**
  - **reconstruction of HIV incidence curve**
  - **using the relationship between AIDS and CD4**

HIV Monitoring

Back-calculation



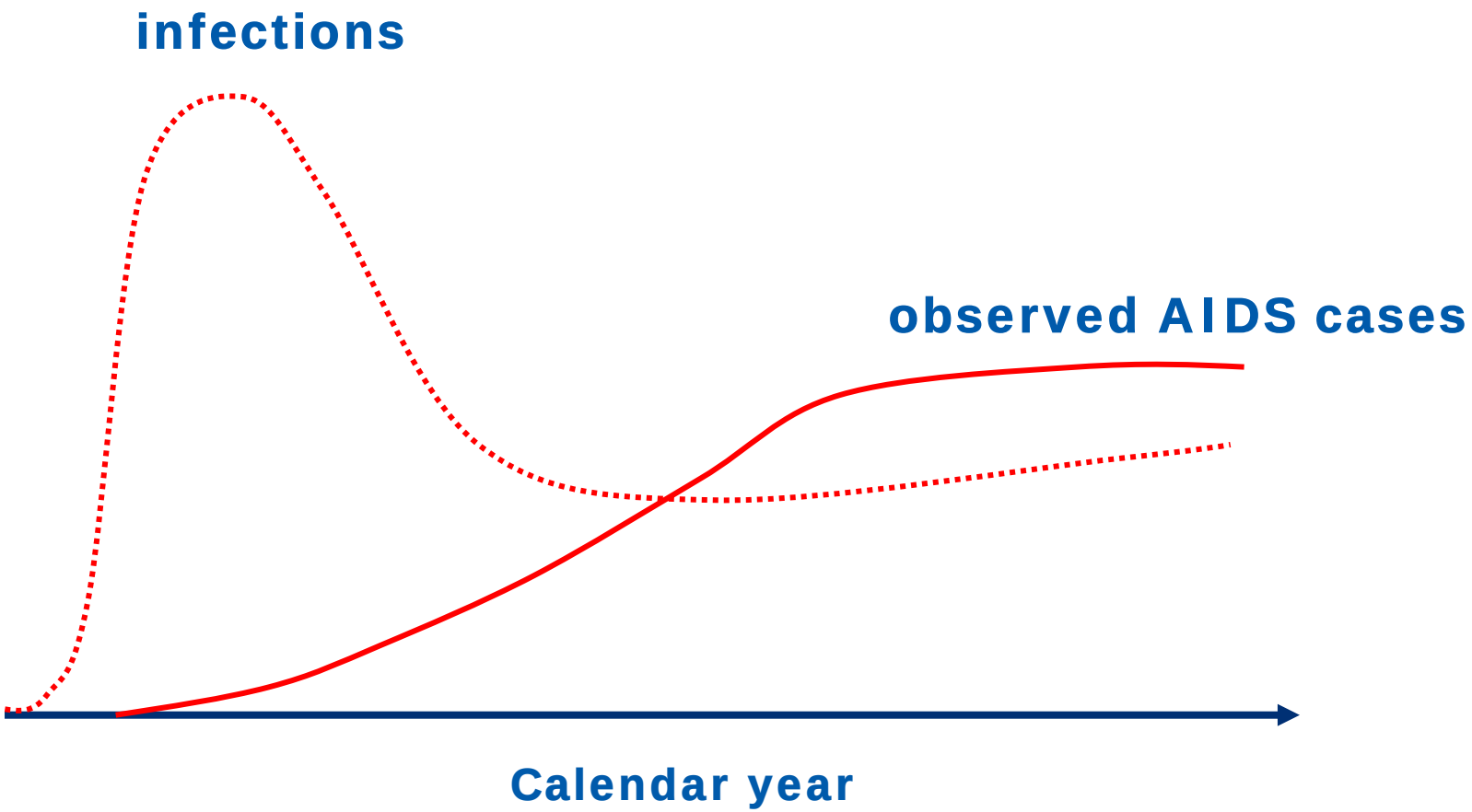




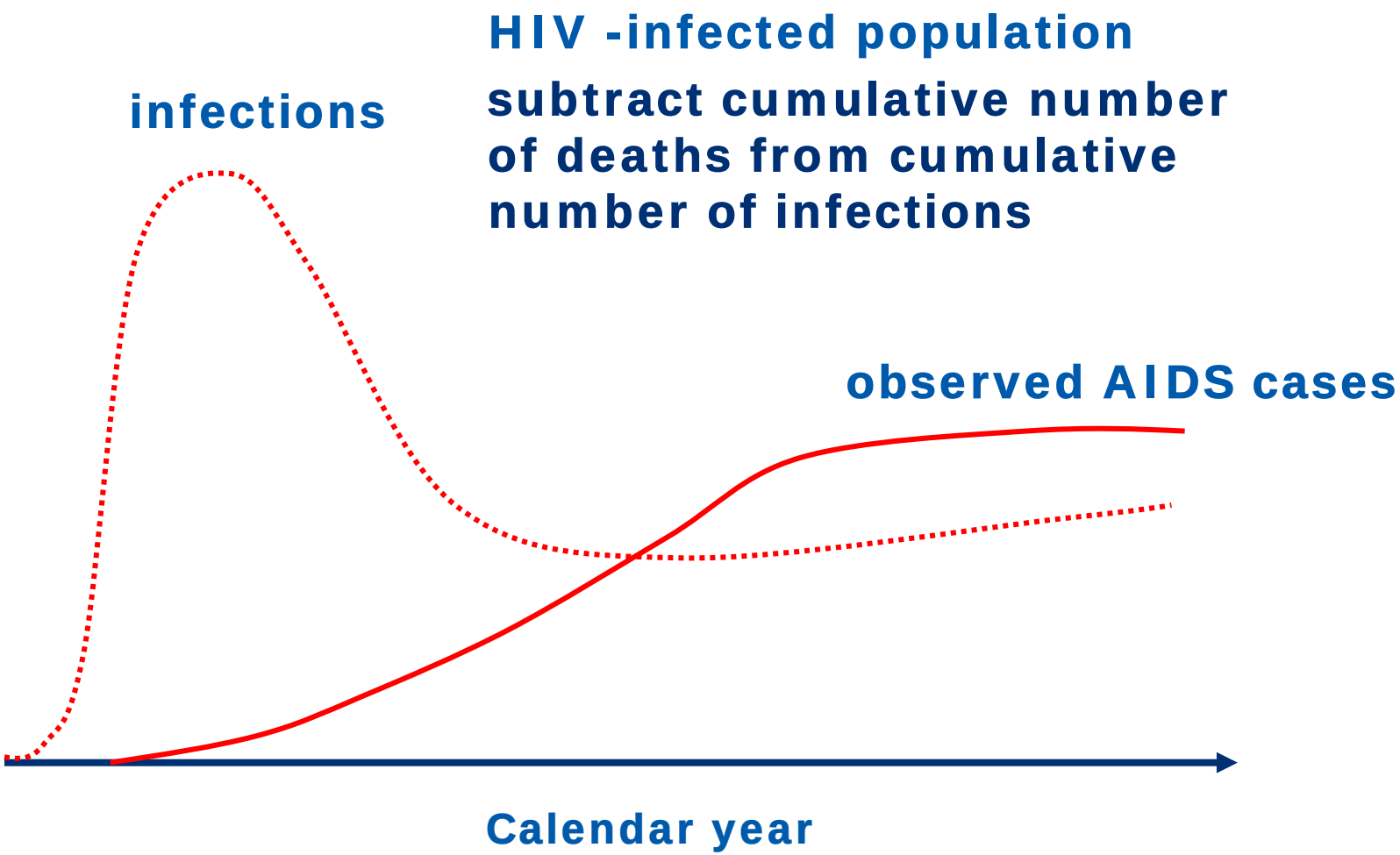
diagnoses **infections**

Original back-calculation

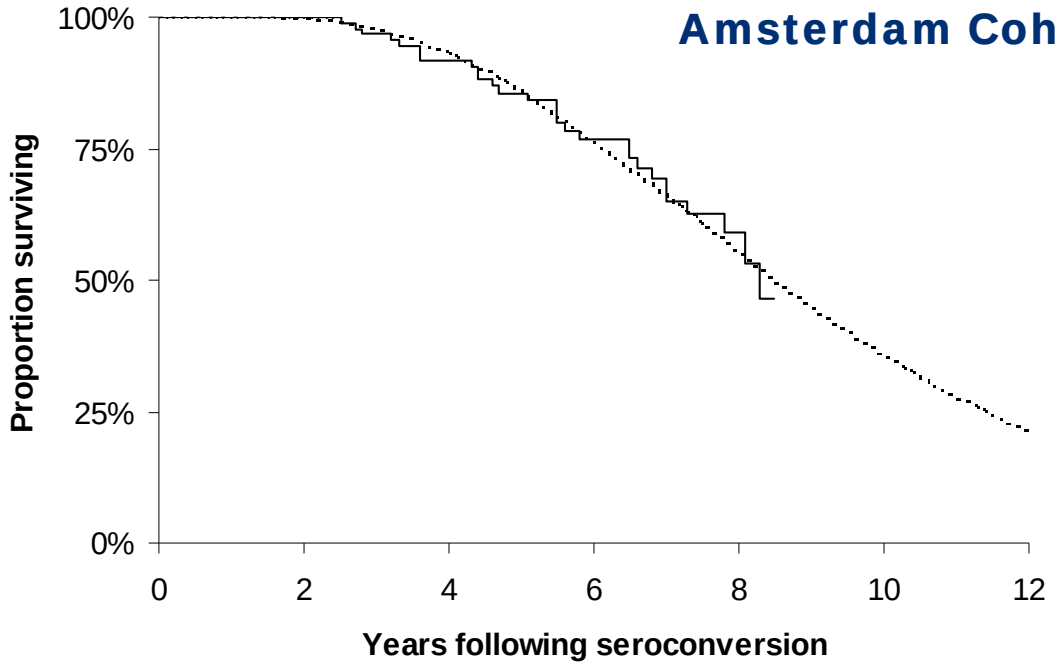
HIV ⟶ AIDS



Original back-calculation



Curve linking infection and AIDS / death



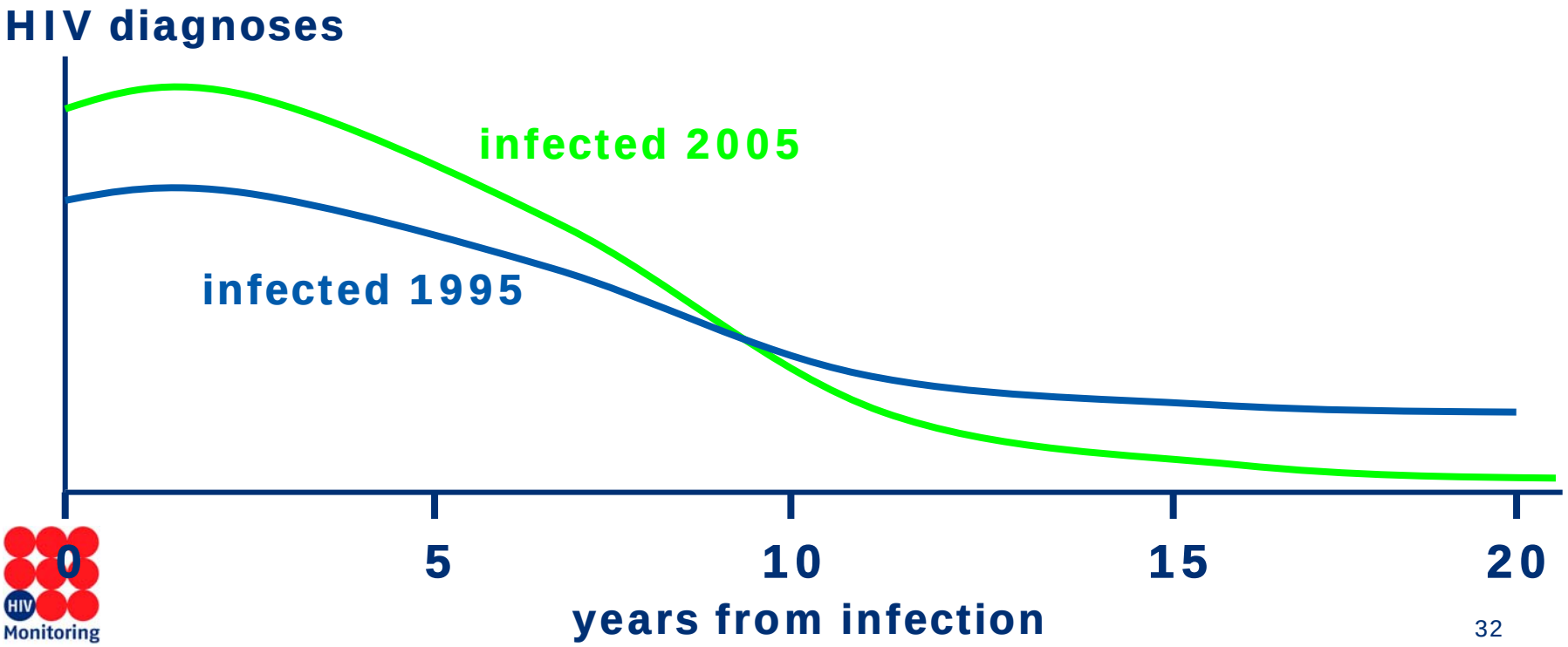
- **Effective treatment changed the duration between infection and AIDS in a way that is hard to quantify.**
- **Use time between infection and diagnosis.**

HIV Monitoring

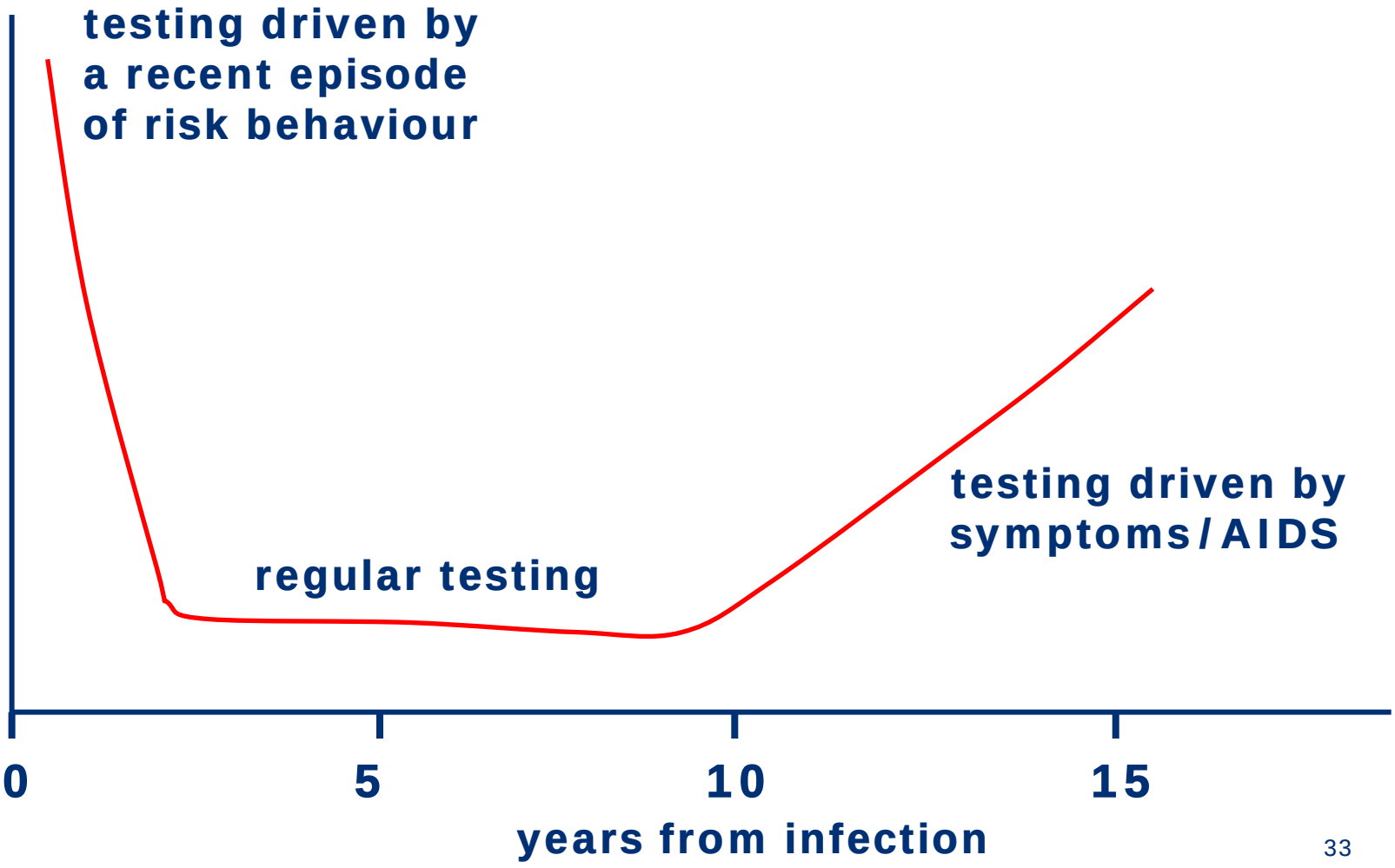
Curve linking infection and diagnosis

Complications

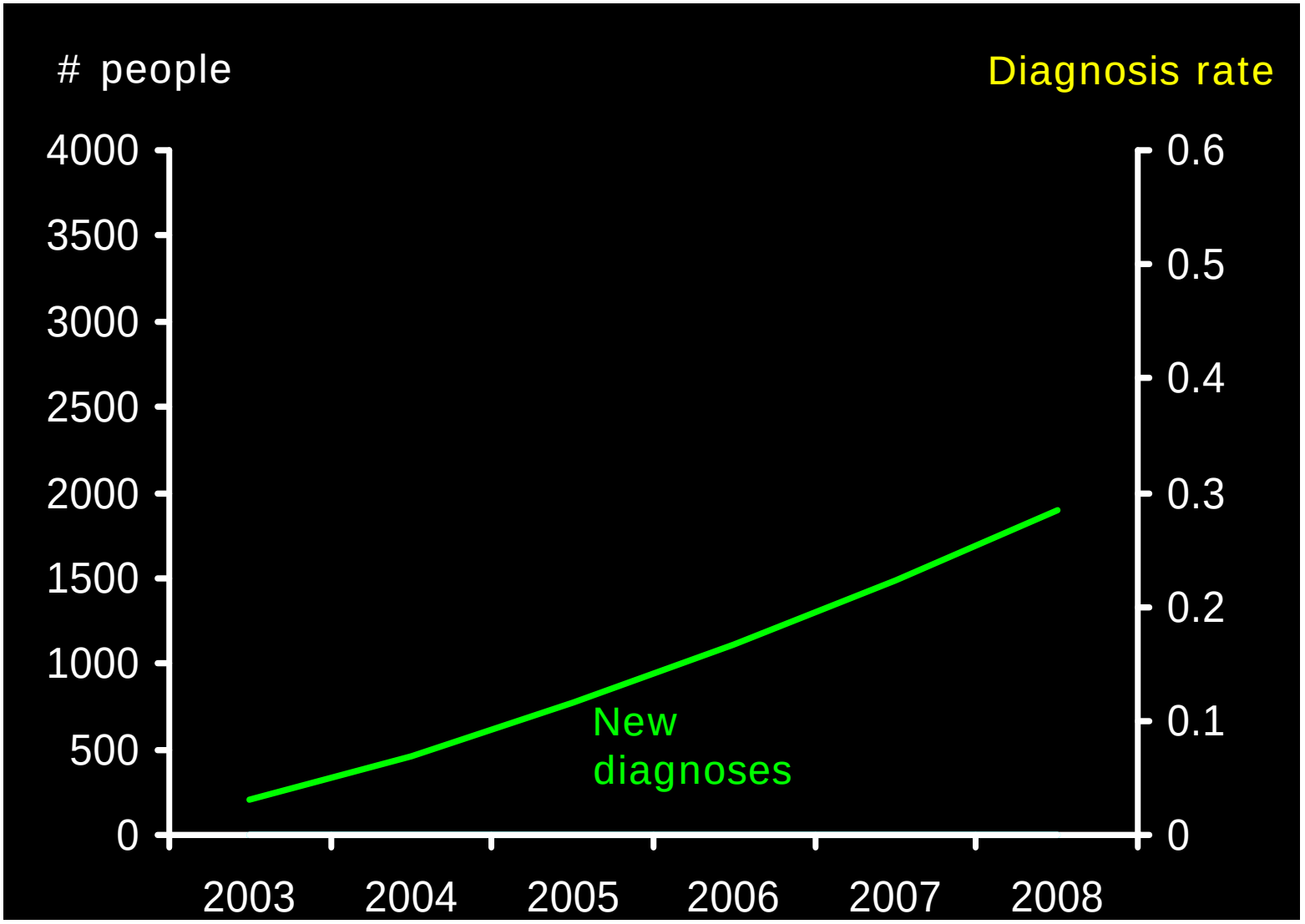
- curve is unknown
- curve changes over time (more testing in recent years)



Hazard of diagnosis

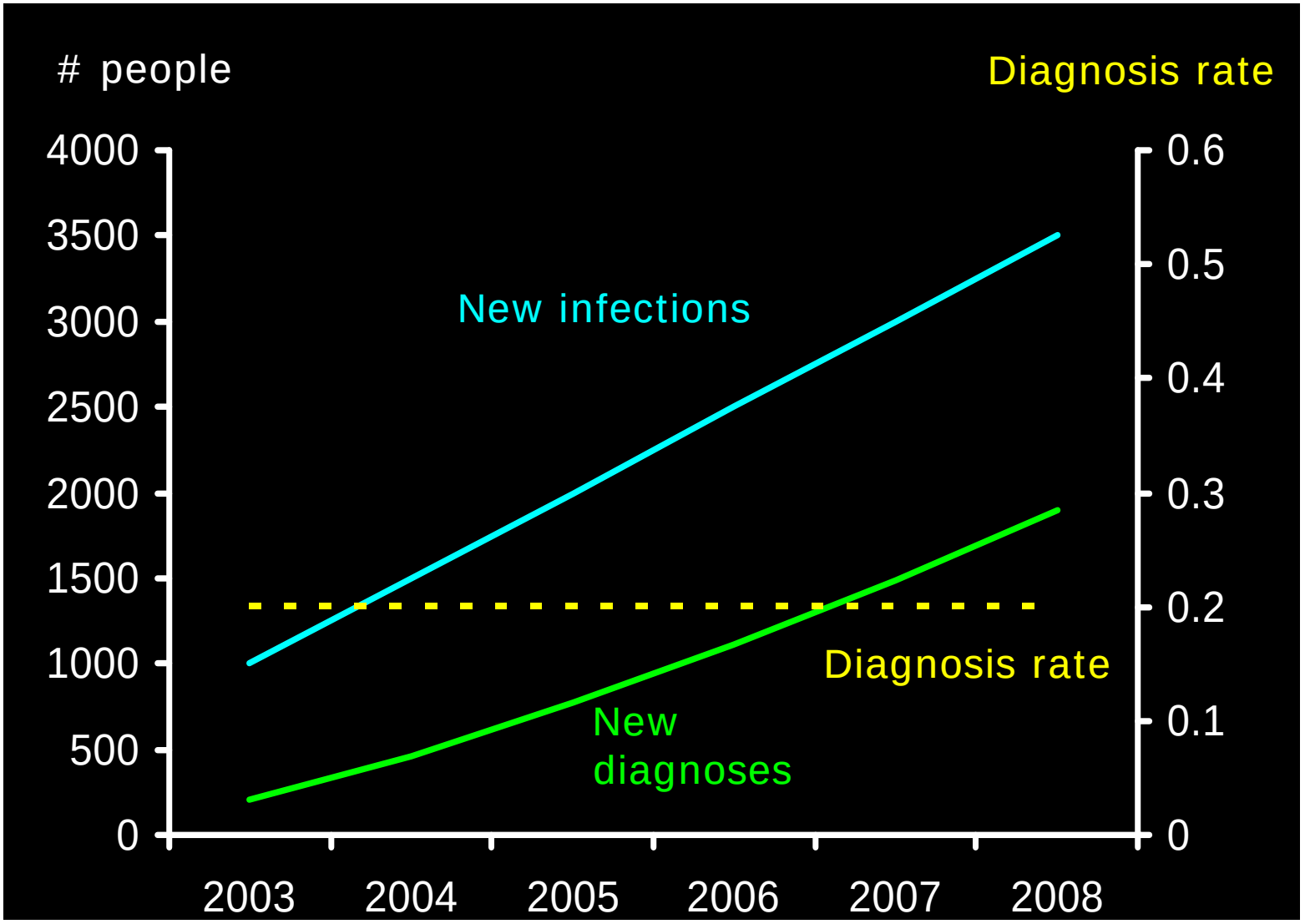


New infections and diagnosis rate



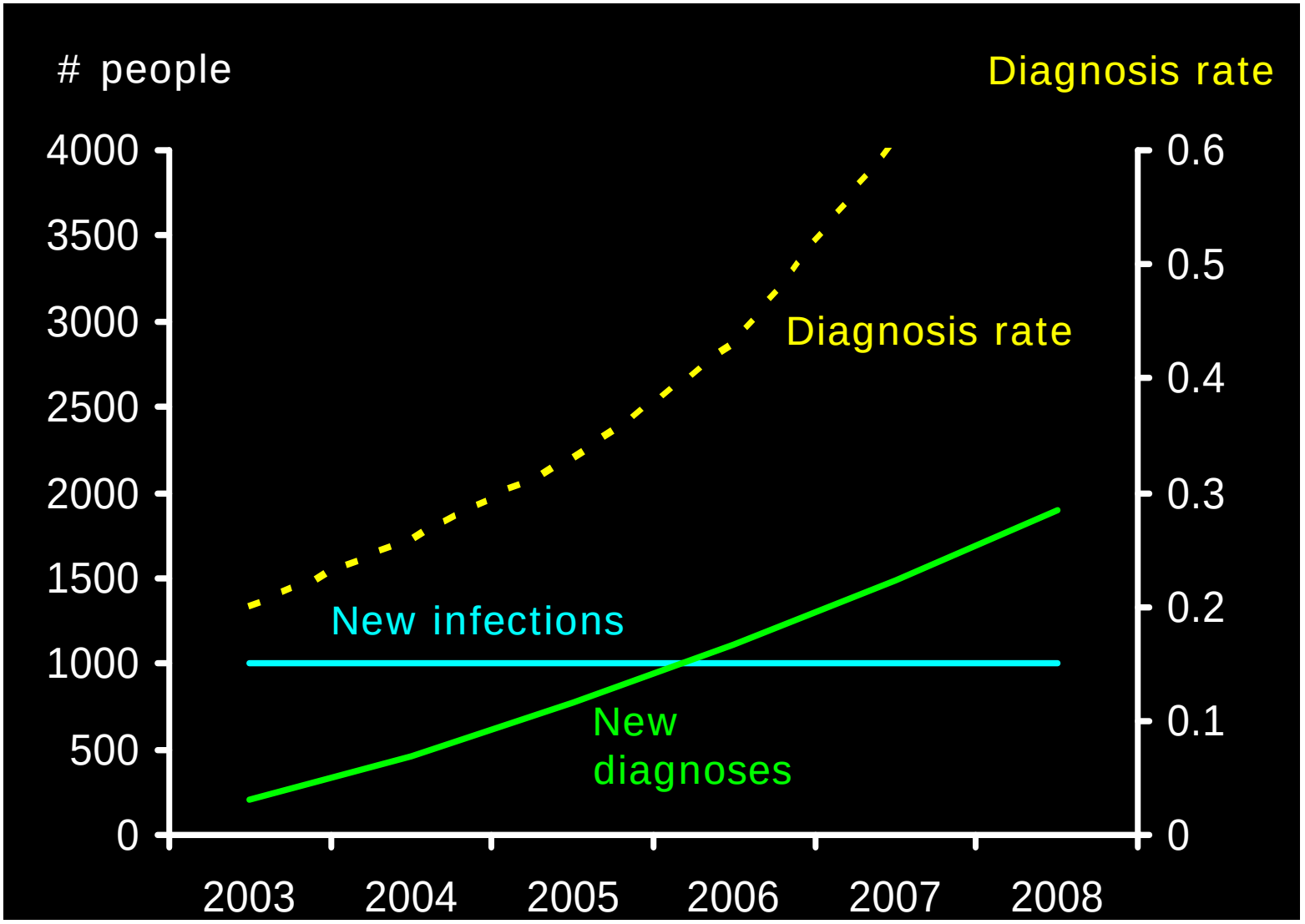
HIV Monitoring

New infections and diagnosis rate



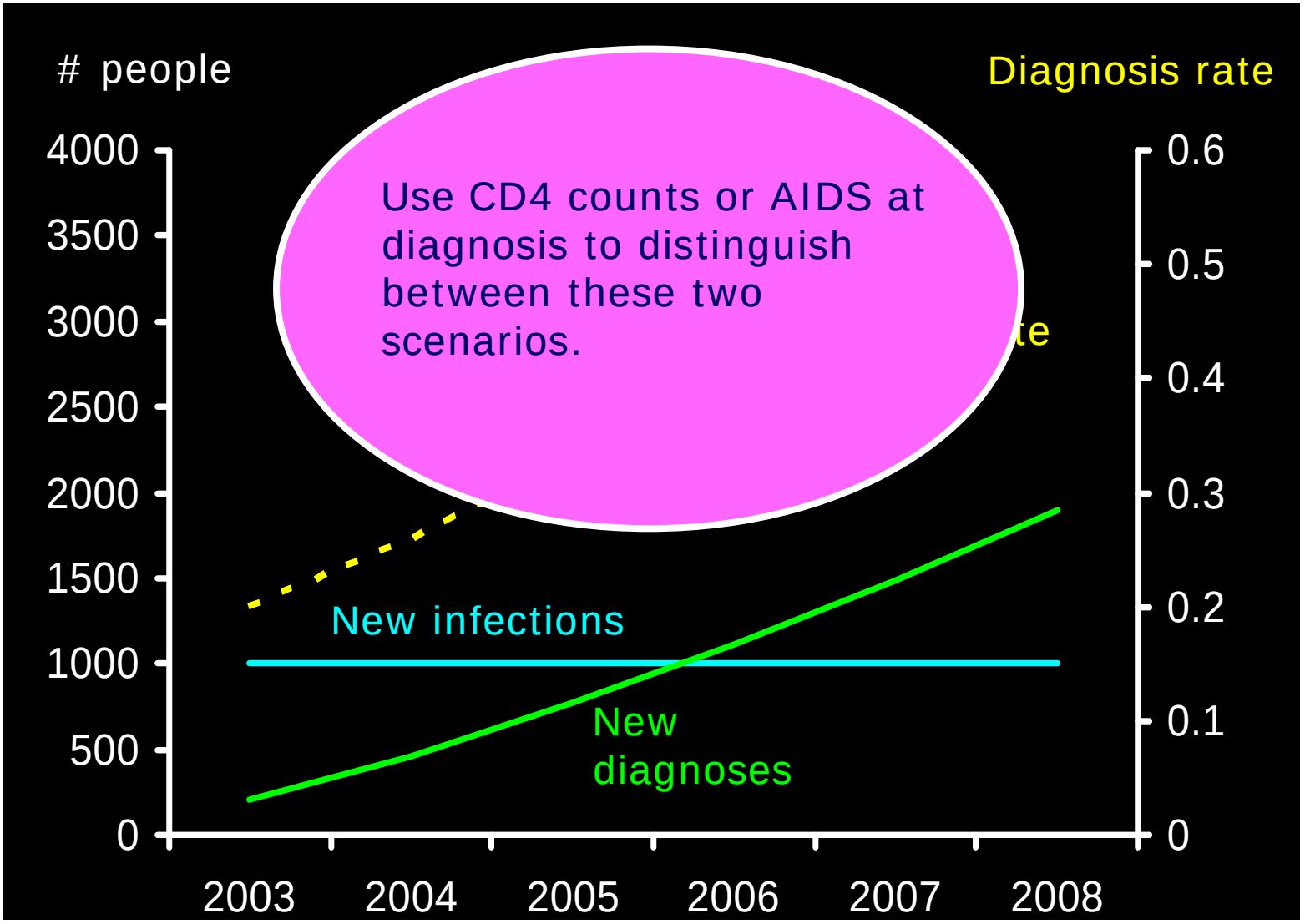
HIV Monitoring

New infections and diagnosis rate



HIV Monitoring

New infections and diagnosis rate



HIV Monitoring

Several methods exist

Bayesian back-calculation using a multi-state model with application to HIV

Michael J. Sweeting[1,*,†], Daniela De Angelis[1,2,‡] and Odd O. Aalen

STATISTICS IN MEDICINE
Statist. Med. 2005; **24**:3991–4007

A resurgent HIV-1 epidemic among men who have sex with men in the era of potent antiretroviral therapy

Daniela Bezemer[a], Frank de Wolf[a,b], Maarten C. Boerlijst[c], Ard van Sighem[a], T. Deirdre Hollingsworth[b], Maria Prins[d,e], Ronald B. Geskus[d,f], Luuk Gras[a], Roel A. Coutinho[g,h] and Christophe Fraser[b]

AIDS 2008, **22**:1071–1077

Estimation of HIV Incidence in the United States

H. Irene Hall, PhD
Ruiguang Song, PhD
Philip Rhodes, PhD
Joseph Prejean, PhD
Qian An, MS

Context Incidence of human immunodeficiency virus (HIV) in the United States has not been directly measured. New assays that differentiate recent vs long-standing HIV infections allow improved estimation of HIV incidence.

Objective To estimate HIV incidence in the United States.

Design, Setting, and Patients Remnant diagnostic serum specimens from pa-

JAMA. 2008;300(5):520-529

Ndawinz JDA, Costagliola D, Supervie V. Recent Increase in the Incidence of HIV Infection in France. 17th Conference on Retroviruses and Opportunistic Infections. San Francisco, USA. 16th-19th February 2010.

A multistate approach for estimating the incidence of human immunodeficiency virus by using HIV and AIDS French surveillance data

Cécile Sommen[1,2,*,†], Ahmadou Alioum[1,2] and Daniel Commenges[1,2]

[1]*INSERM U897, Epidemiology and Biostatistics Research Center, Bordeaux, F-33076, France*
[2]*University of Bordeaux 2, Bordeaux, F-33076, France*

STATISTICS IN MEDICINE
Statist. Med. 2009; **28**:1554–1568

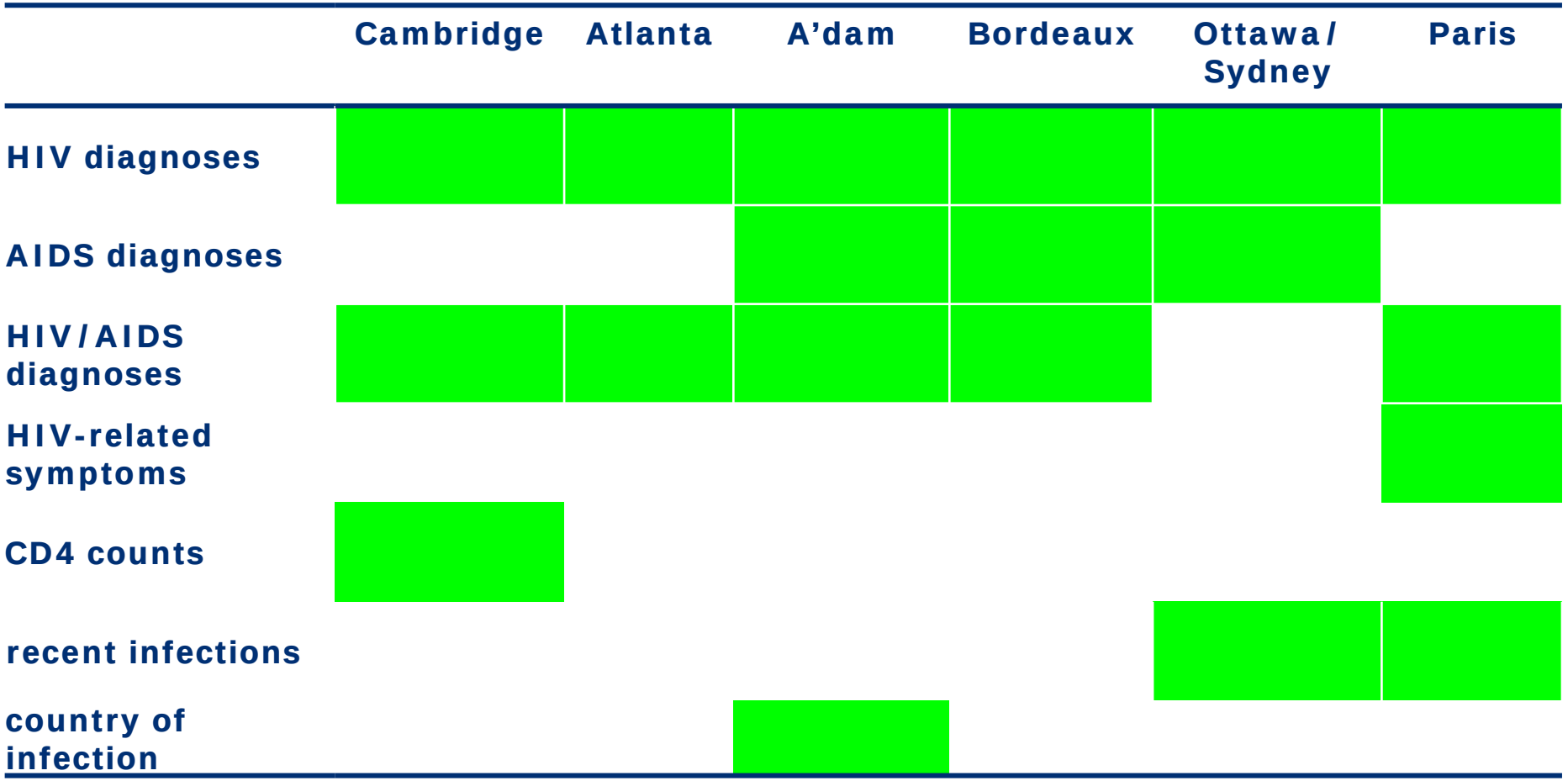
HIV Monitoring

Increasing HIV transmission through male homosexual and heterosexual contact in Australia: results from an extended back-projection approach

H Wand,[1] P Yan,[2] D Wilson,[1] A McDonald,[1] M Middleton,[1] J Kaldor[1] and M Law[1]
[1]*National Centre in HIV Epidemiology and Clinical Research, Sydney, Australia and* [2]*Center for Infectious Disease Prevention and Control Population and Public Health Branch, Ottawa, Canada*

HIV Medicine (2010)

Data needed for back-projection



Complications

- Delayed reporting to national surveillance system.
- Underreporting.
- Double counting.
- Incomplete information.
- Implicit assumption that everyone will be diagnosed eventually.
- Mortality before HIV diagnosis.
- Linkage between databases.
- Are data representative?

HIV Monitoring

Number of HIV infections

2 main approaches for estimating the number of HIV infections:

- **based on prevalence surveys**
- **based on reported number of HIV diagnoses**
  - **reconstruction of HIV incidence curve**
  - **using the relationship between AIDS and CD4**

HIV Monitoring

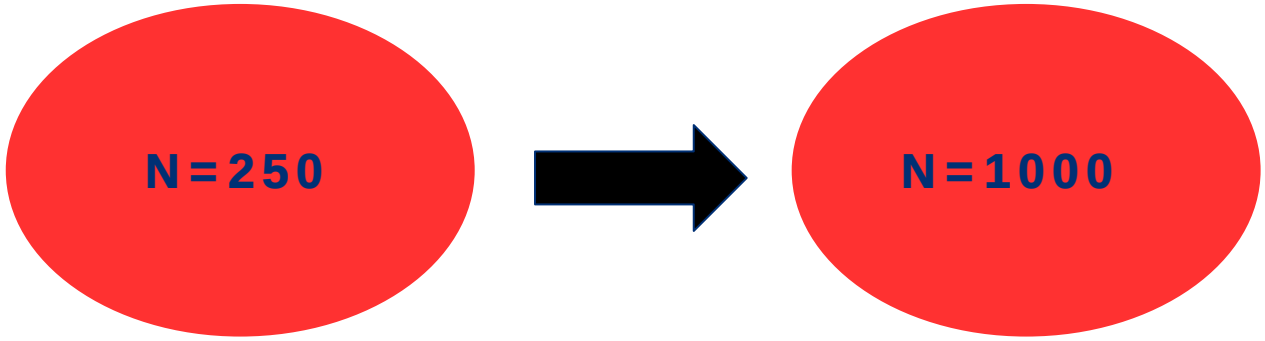
Relationship CD4 count and AIDS

Suppose that

- **25% of individuals with CD4 <200 develop AIDS within 1 year**
- **AIDS is diagnosed immediately**

diagnosed HIV/AIDS with CD4 <200

total with CD4 <200



Two approaches

1 Use this approach for all CD4 strata and sum up.

2 Use CD4 count distribution in asymptomatic patients.

Lodwick et al PE 18.1/5. European AIDS Clinical Society (EACS) meeting, Cologne, October 2009.

Complications

- **Low event rate at high CD4 counts so the uncertainty in the estimate will be large.**
- **Under-diagnosis.**
- **Underreporting.**

HIV Monitoring

Summary and conclusions

- Three main approaches to determine the size of the HIV-infected population in a country :
  - based on prevalence surveys
  - based on case report data
  - based on relation between CD4 count and AIDS

- All approaches have their limitations.

- For most countries with concentrated epidemics, methods based on case reports or the CD4-AIDS relation are most likely the best way to estimate the size of the HIV epidemic.

HIV Monitoring

Road map

- Develop method to reconstruct HIV incidence curve using:
  - HIV diagnoses
  - HIV/AIDS diagnoses
  - AIDS diagnoses (before 1996)
  - CD4 counts at diagnosis

- Apply method to countries with different epidemics:
  - Denmark MSM, small scale
  - Germany MSM, large scale
  - Bulgaria IDU
  - Estonia IDU

- In parallel, test methods based on CD4-AIDS relation.

HIV Monitoring

Acknowledgements

Imperial College, London, UK
Christophe Fraser, Geoff Garnett

University College, London, UK
Andrew Phillips, Rebecca Lodwick

University of Bern, Bern, CH
Olivia Keiser, Matthias Egger

Stichting HIV Monitoring, Amsterdam, NL
Frank de Wolf

ECDC, Stockholm, SE
Tommi Asikainen, Mika Salminen, Marita van de Laar, Tobias Bergroth

HIV Monitoring