Estimating HIV prevalence in sub-Saharan Africa: a brief story of a measure

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1980
emergence of an epidemic

1980

Several gay men in Los Angeles are suffering from immune deficiency.

1981

US physicians decide to call this disease *Acquired Immune Deficiency Syndrome (AIDS).*

1983

First numbers published by WHO:
153 cases diagnosed in 14 different European countries.

October 1985

First WHO workshop on AIDS in Africa in Bangui.
Only 9 countries represented.
(Burundi, Cameroon, Congo, Gabon, Uganda, Tanzania, Rwanda and Zaïre).

March 1986

New WHO workshop in Africa.
41 countries represented.
Only 7 declared AIDS cases.

November 1986

First African data published by WHO.
1069 AIDS cases reported in Africa,
i.e. only 3.1 % of the 34'448 cases in the World.

To be notified, AIDS cases require that:

- infected people are seen by a physician,
- are correctly diagnosed,
- the case is reported to Ministry of Health,
- Ministry of Health transmit numbers to WHO.

AIDS cases are inadequate to describe African epidemics.

In **1992**, only **10** to **30 %** of individuals with AIDS were diagnosed in Africa. This proportion was still estimated by WHO to be **15 %** in **1997**.

late 1980's

HIV testing and sentinel surveillance

1985

With the first HIV tests, new surveys are designed for a new measure: **HIV prevalence**.

1987

The Center for International Research (CIR) of US Census creates the *HIV/AIDS Surveillance Database*. All results published or submitted to a conference are collected in a unique database.

Late 80's

- variety of survey designs
- variety of populations
  (general population, specific sub-groups)
- variety of coverage (local, regional or national)
- variety of sampling methods

Comparisons are difficult,
or even **impossible**.

1988

WHO, within the *Global Programme on AIDS*, decides to formalize principles of a sentinel surveillance.

"The main purpose of sentinel serosurveillance is to detect changes – i.e. to monitor trends and to provide a basis for evaluating preventive strategies and activities. However, it should be pointed out that ***sentinel populations need not to be 'representative'****."*

Slutkin, Chin *et al.* 1988 WHO

Hull 1988 *JAMA* · survey in USA

HIV prevalence of 1.0% among 782 STI patients accepting to be tested

HIV prevalence of 5.4% among the 167 refusals

Jenum 1988 *NIPH Annals* · survey in Norway

4 HIV+ on 36'053 (0.011%) pregnant women accepting to be tested

1 HIV+ on 50 (2.0%) pregnant women refusing to be tested

"Large-scale population serosurveys demand considerable time and resources, and their results may be of limited accuracy because of serious problems arising from selection and participation bias. (…) WHO has therefore recommended the development of sentinel systems for routine public health surveillance of HIV infection."

Chin, 1990, Bulletin of the WHO

WHO differentiates two kinds of test

diagnosis

The objective is to determine with accuracy the status of someone.

public health surveillance

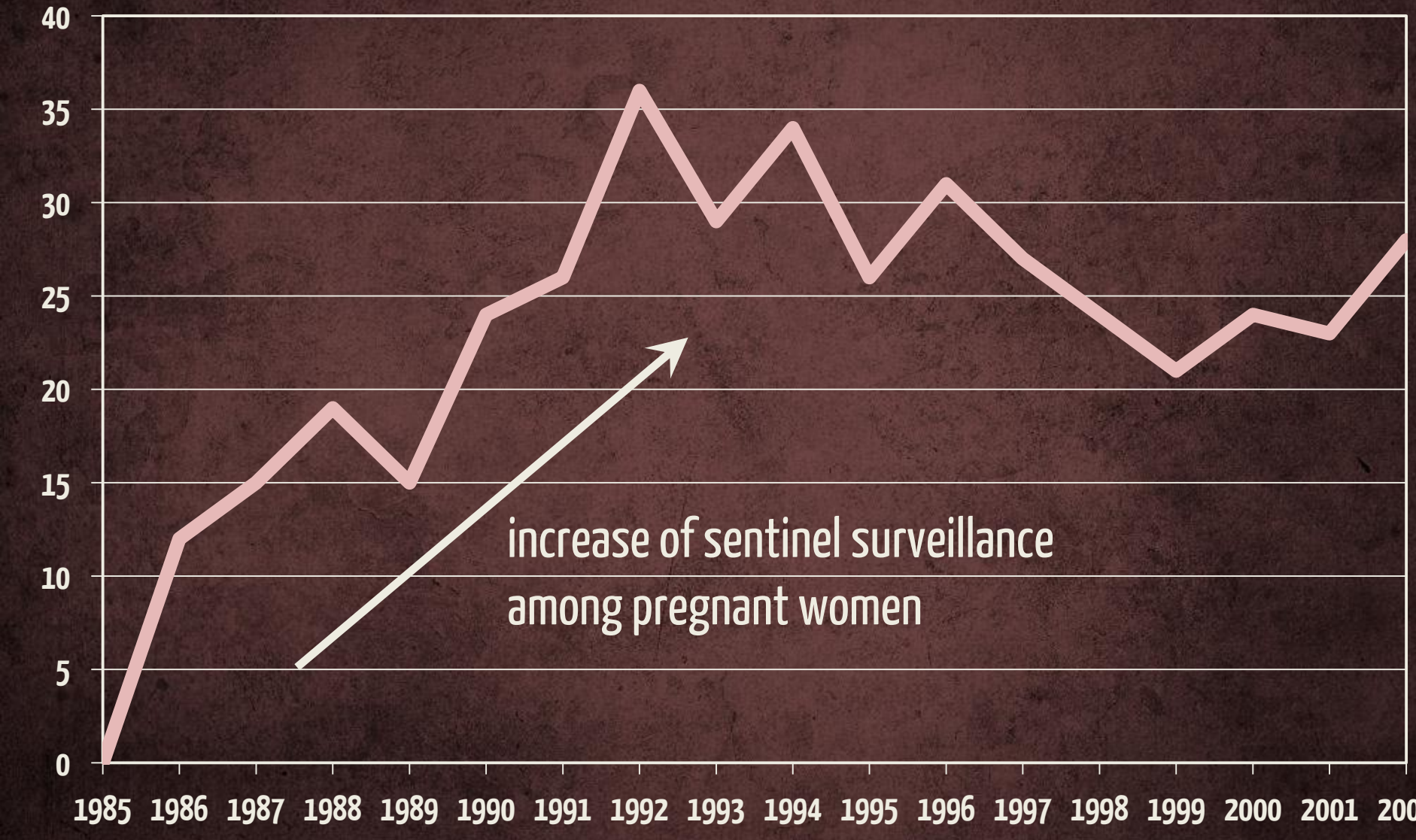
Identity of surveyed participants is not required, nor the exact status
if false positives compensate false negatives.

For surveillance, WHO recommends an approach called
Unlinked Anonymous Testing (UAS):
Testing blood samples obtained for another purpose after
removing all nominative data.

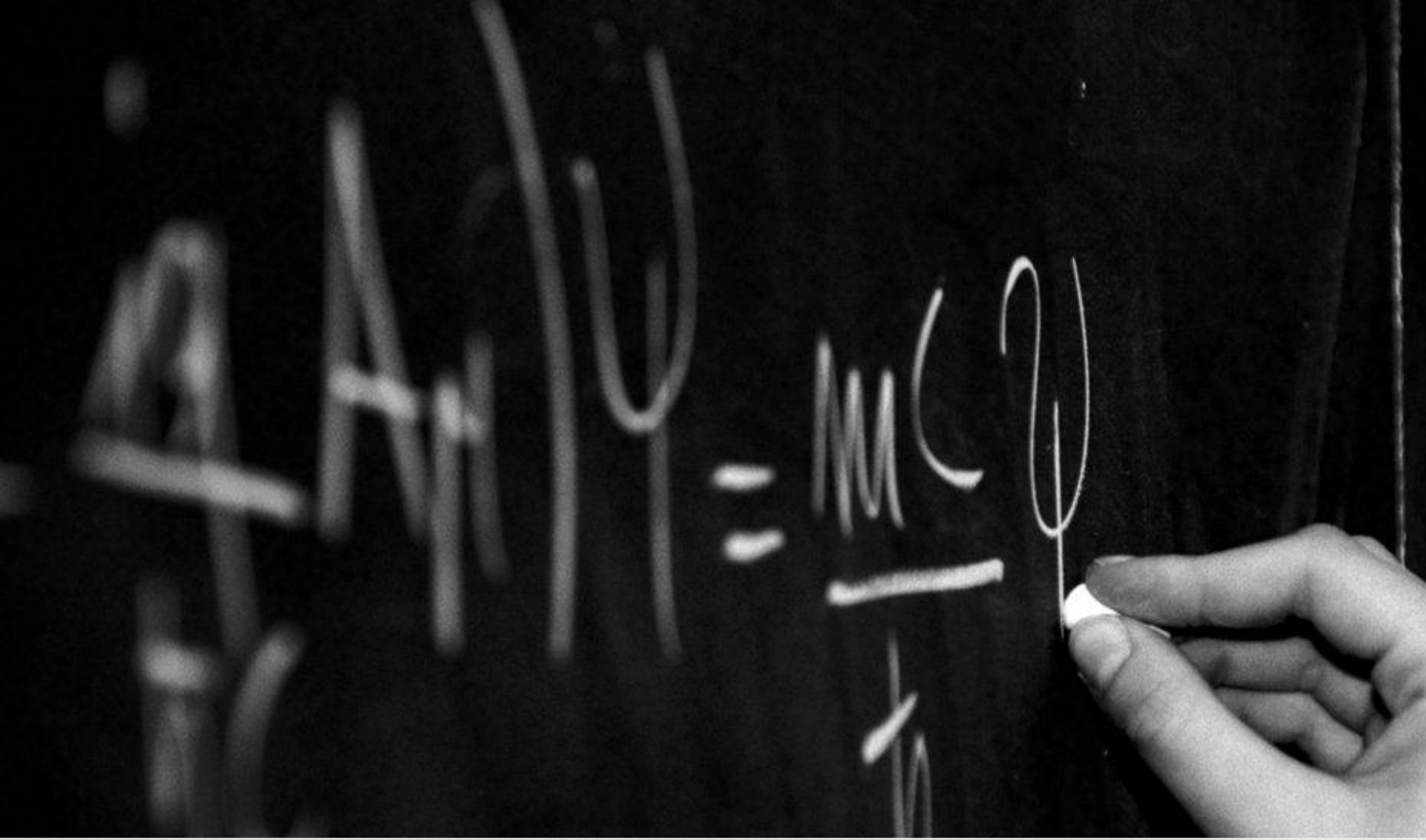
➔ No more refusal bias.

Pregnant women constitute an ideal population because
a blood sample is taken during prenatal visit.

Number of sub-Saharan African countries with a sentinel surveillance survey among pregnant women by year



Source: Garcia-Calleja 2004 *STI*



1990's

modelling epidemics to estimate national HIV prevalence

early 90's

HIV is becoming a pandemic

➔ Evaluation of the global situation
and impacts of the infection is needed.

late 1991

The Global Program on AIDS publish *EpiModel*,
a simple mathematical model using only one measure of prevalence at one date and a starting year of the epidemic to estimate HIV prevalence at 3-4 years.

late 1995

The WHO's *Weekly Epidemiological Report* publishes
the first worldwide estimates of HIV prevalence by country.
For sub-Saharan Africa, they were calculated using EpiModel and data from sentinel surveillance among pregnant women.

➔ Antenatal surveillance designed to measure **trends**, were used to estimate national **levels**.

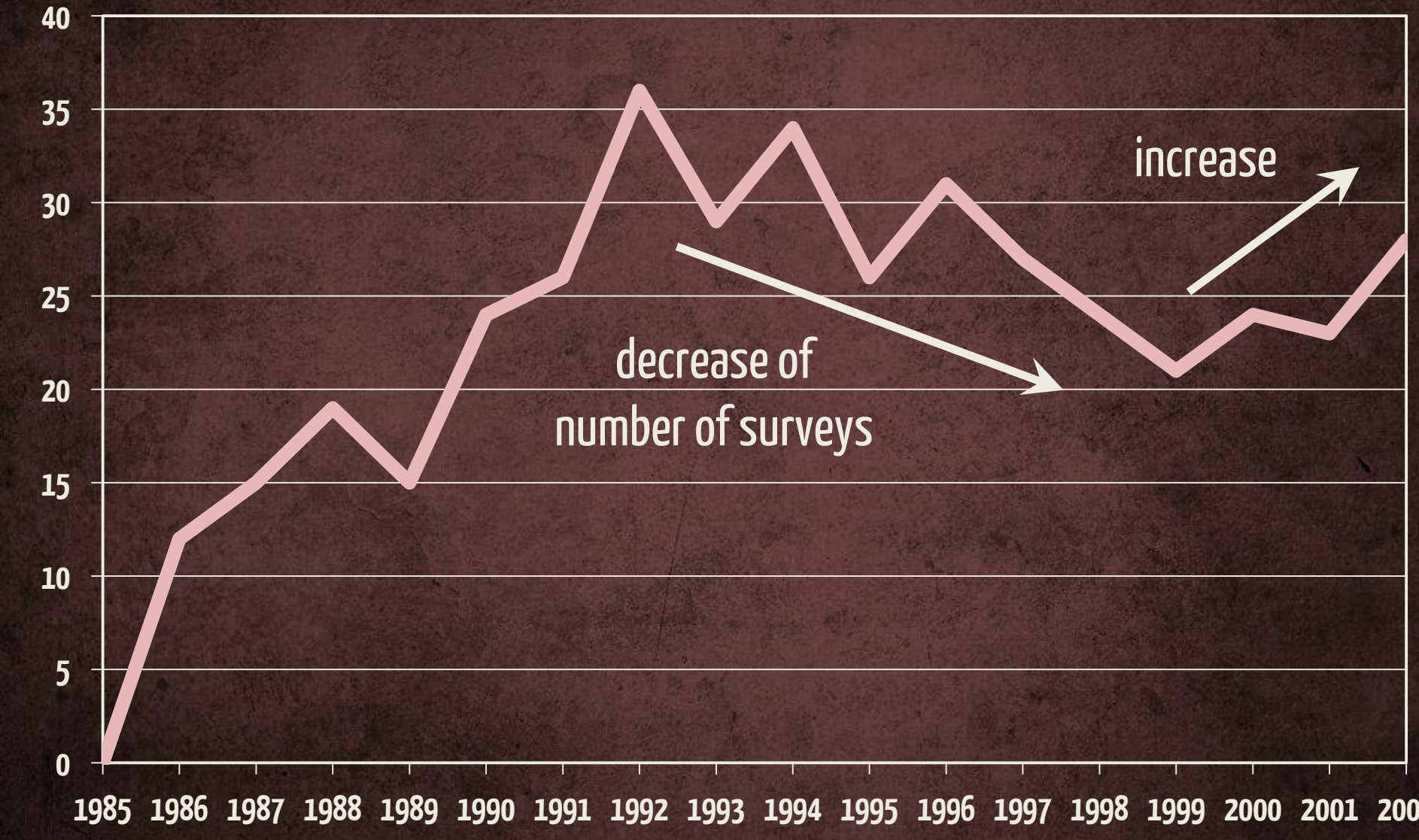
1st December 1995
creation of **UNAIDS**

June 1998 & June 2000
HIV prevalence estimates by country are updated in UNAIDS Global Report, still using EpiModel.

1999
UNAIDS creates an *Epidemiology Reference Group*, renamed *UNAIDS Reference Group on Estimates, Modelling and Projections* in 2002, to elaborate new tools for prevalence estimates.

2000
Quality and quantity of sentinel surveillance surveys is decreasing.
Rural areas are under-represented. Few socio-demographic data.
➔ UNAIDS launches a **second generation surveillance** initiative.

Number of sub-Saharan African countries with a sentinel surveillance survey among pregnant women by year



Source: Garcia-Calleja 2004 *STI*

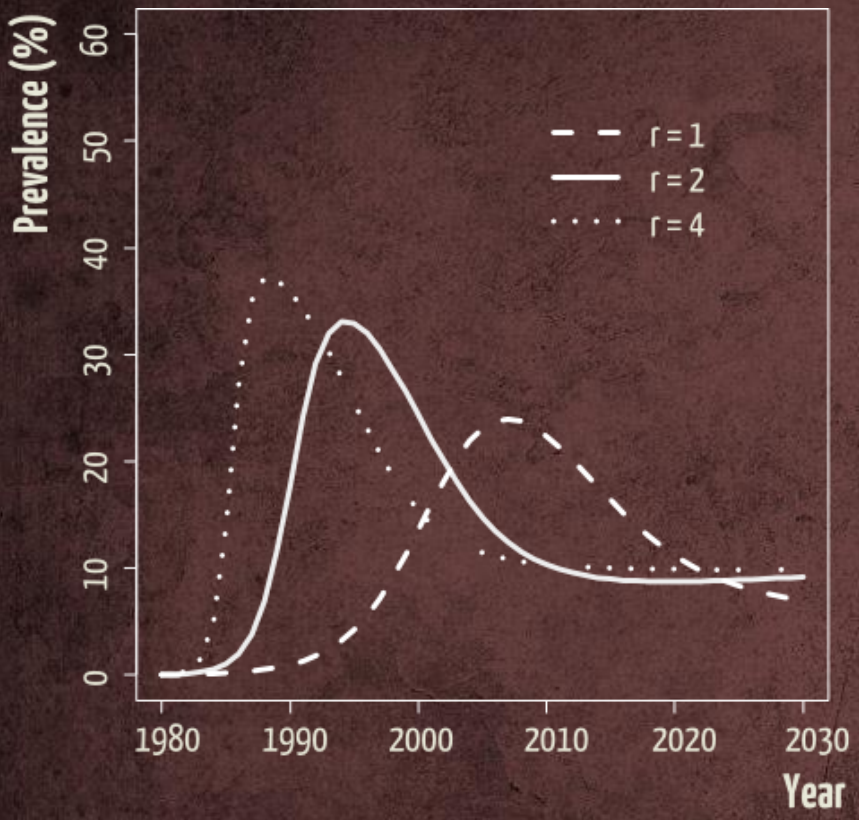
2000-2001

UNAIDS Reference Group proposes a new model: *Epidemic Projection Package* (EPP) published in en 2002, renamed *Estimation and Projection Package* in 2004.

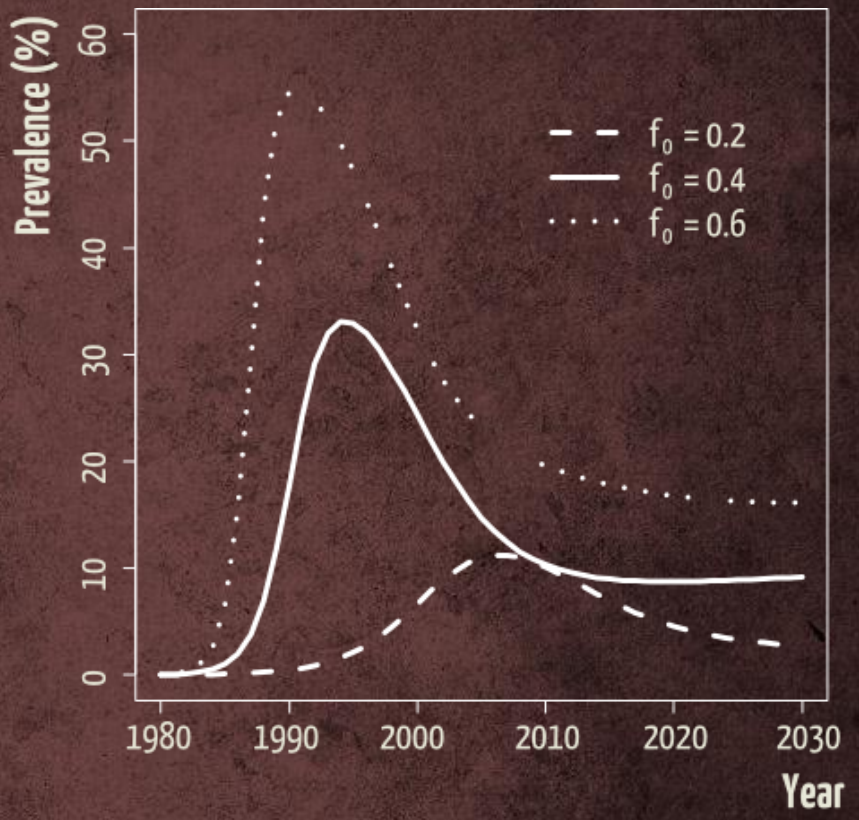
EPP

- Not a mathematical model but an simple epidemiological one, estimating HIV prevalence among 15-49 year olds.
- The population is divided in 3 groups: not at risk, at risk and infected.
- Prevalence curve is determined by 4 parameters and adjusted on available data, i.e. pregnant women in sub-Saharan Africa.
- Usually, prevalence is estimated separately for urban and rural.

Parameters of EPP model (1/2)



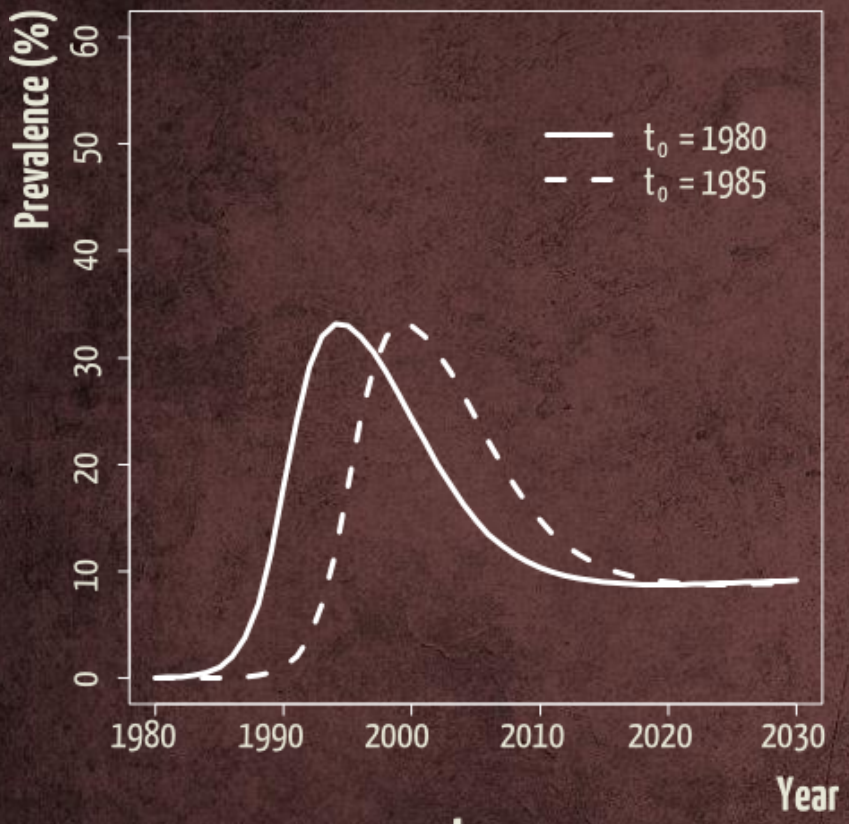
r
(rate of infection)



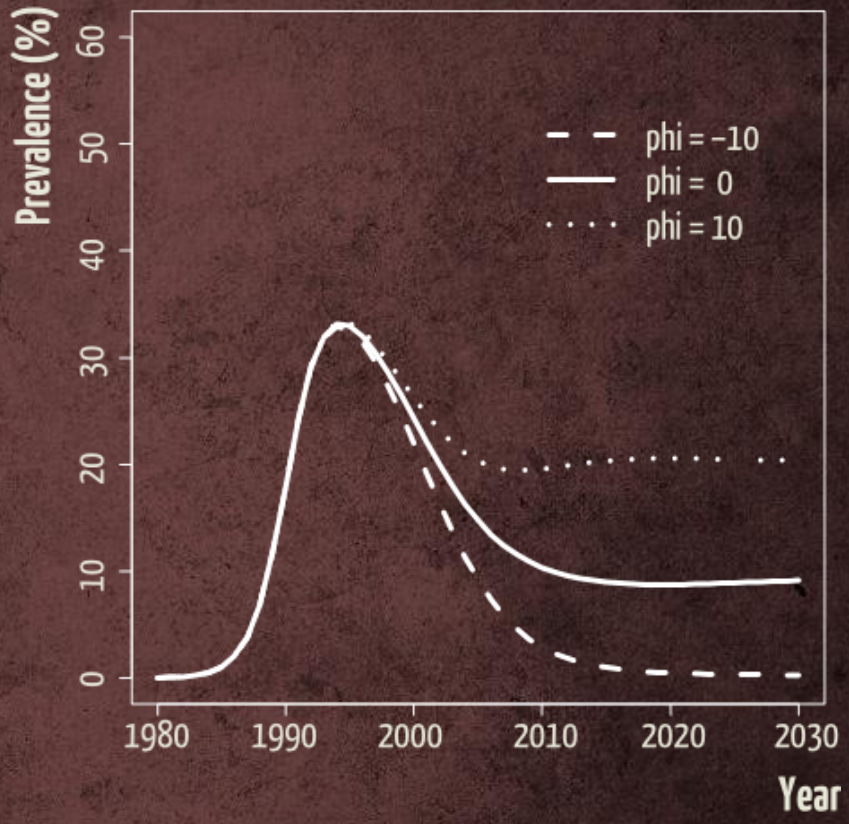
f_0
(fraction of the population in the at-risk category at the start of the epidemic)

Source: from Alkema 2007 *CSSS University of Washington* WP69

Parameters of EPP model (2/2)



to
(start time of the epidemic)



φ
(behavioral response)

Parameters of the model limit the possible shapes of the curve.

June 2002

Estimates of the new UNAIDS Global Report were calculated using EPP.

2004

The new UNAIDS Global Report publishes estimates at two dates (end of 2001 and end of 2003) to indicate trends. A new software, *Spectrum*, was used to estimates impacts (deaths, infected children...) from EPP prevalence results.

2006

New version of EPP, including a procedure called *level fit* to take into account the extension of sentinel surveillance within rural areas (second generation surveillance).

2000's
comeback of national population-based surveys

2001

First Demographic and Health Survey (DHS) with HIV testing in Mali.

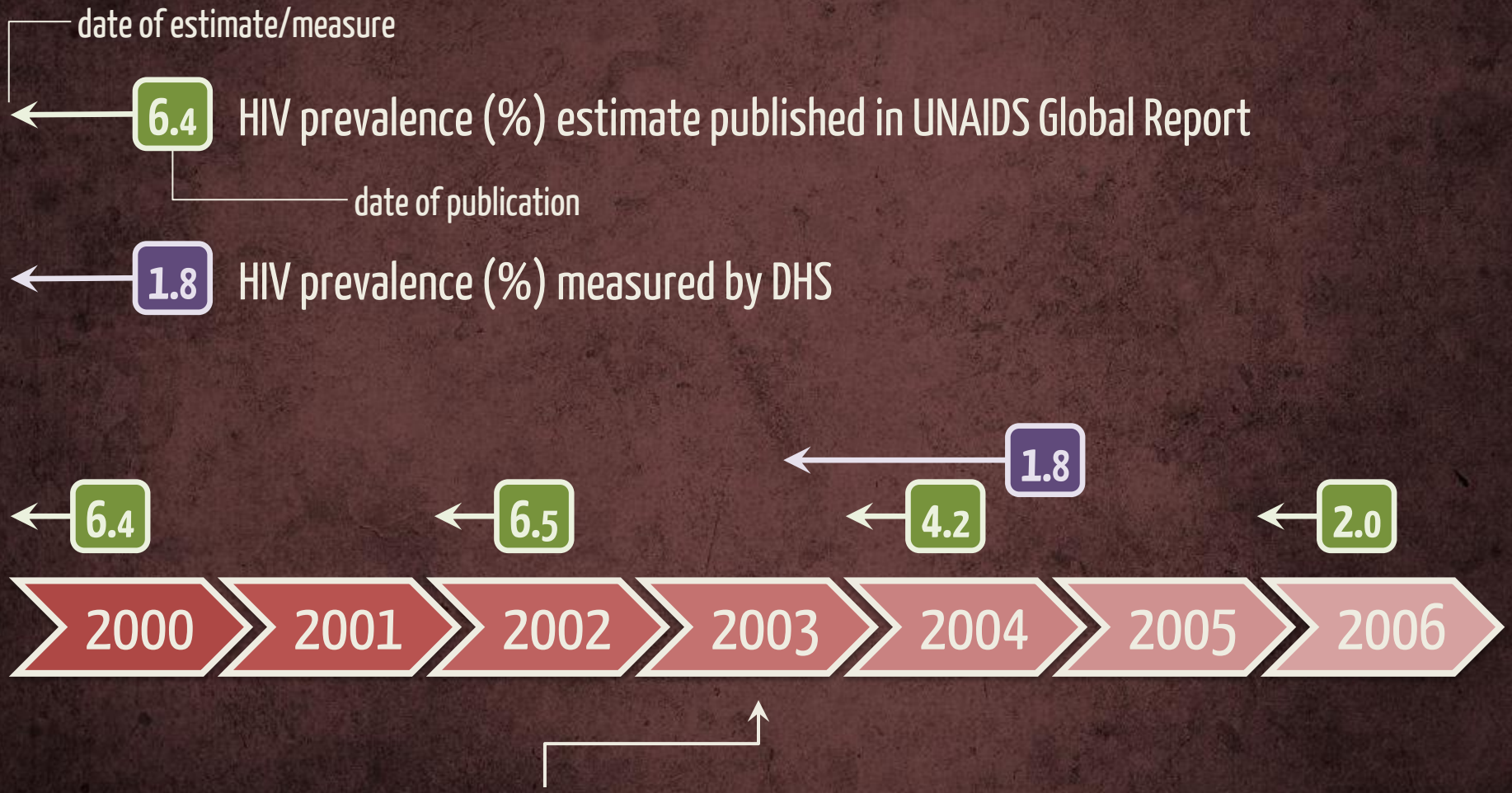
Demographic and Health Surveys (DHS)

International program of national population-based surveys, existing since 1984.
Most developing countries are conducting a DHS every 4-8 years.

during the 2000's

Increasing number of DHS with HIV testing.
For a majority of countries, HIV prevalence measured by DHS were lower than estimates from antenatal clinics data.

Several sources, several figures...
Example of Burkina Faso



Several sources, several figures...

During the 2000's, UNAIDS estimates have changed quite a lot between global reports.

These changes result mainly from a change in estimation methods, not the underlying epidemiology.

➔ HIV prevalence didn't decrease from 6.5% in 2002 to 2.0% in 2006. The epidemic has been overestimated before 2005.

Which source is better?

In DHS, non tested rate (refusals and absence) are not insignificant.

➔ *underestimation*

Prenatal sentinel surveillance is under-represented in rural areas.

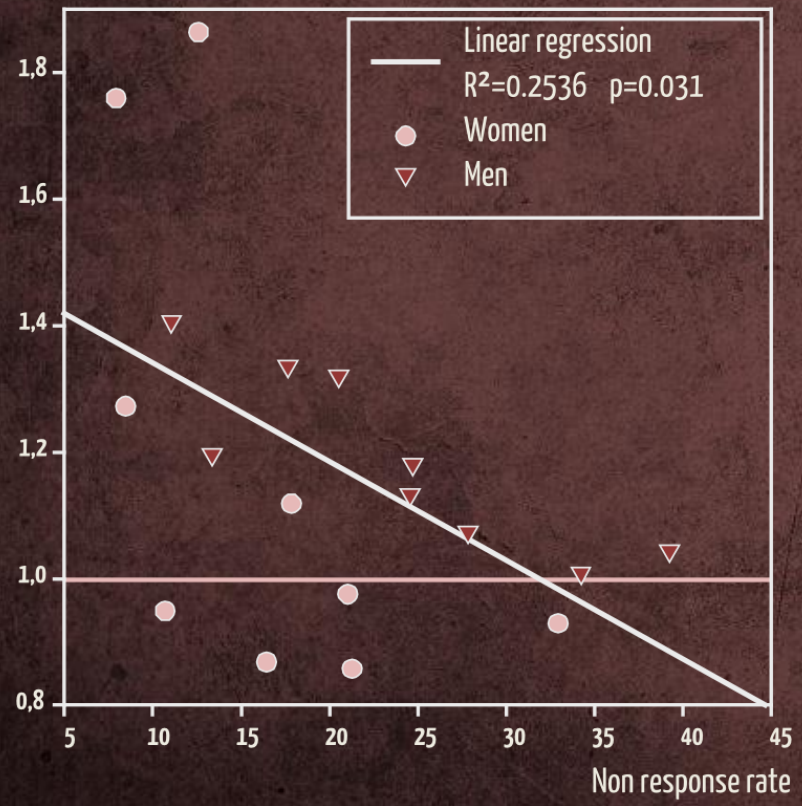
➔ *overestimation*

measuring bias in DHS and prenatal surveillance

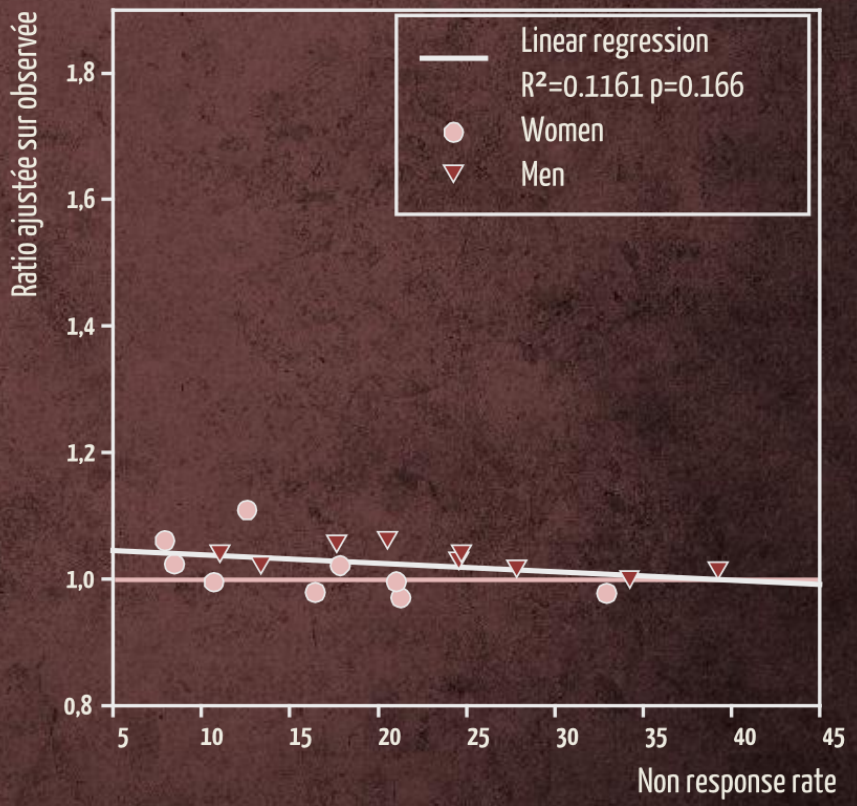
Impact of non response rate in DHS

Analysis on 9 DHS conducted in 2003-2005. Prevalence of non tested people was estimated using logistic regressions on variables from the individual and/or household questionnaires.

Ratio predicted prevalence of non-tested on observed prelavence by non response rate



Ratio adjusted prevalence on observed prelavence by non response rate



If predicted prevalence is significantly higher among refusals, no significant difference among absent individuals.

Source: Larmarange 2007, PhD

Adjusting DHS

Taking into account 5 kinds of bias: serological window; population not living in an ordinary household (including refugees); population changes since the last census; non surveyed households and non tested individuals.

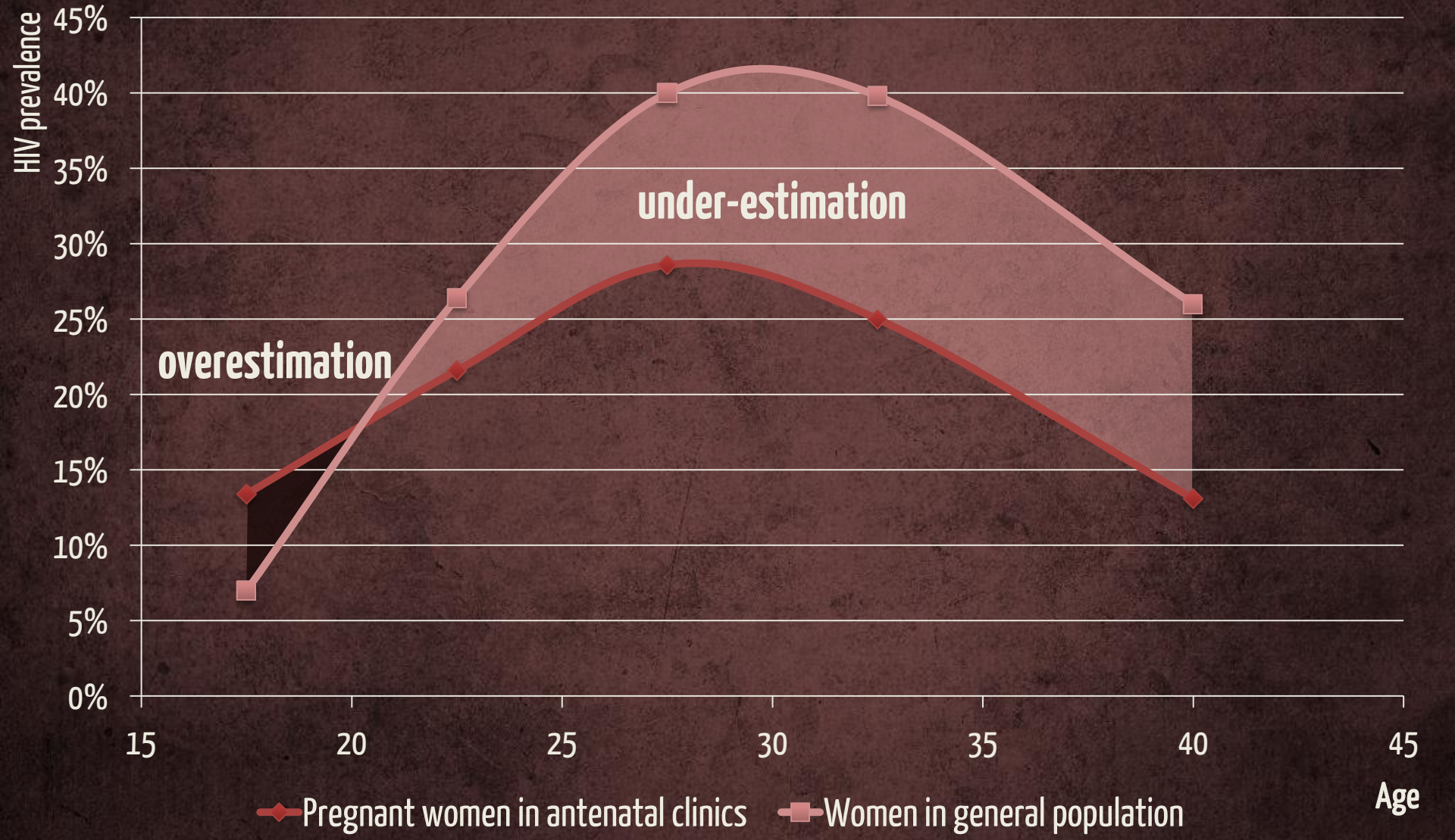
Country Survey	Burkina Faso DHS 2003	Cameroun DHS 2004	Kenya DHS 2003
Observed national prevalence	1.77	5.44	6.88
95% Confidence Interval	1.49-2.11	5.00-5.91	6.27-7.54
75% Confidence Interval	1.59-1.96	5.18-5.71	6.51-7.27
Adjusted prevalence (high scenario)	1.86	5.84	7.16
Adjusted prevalence (low scenario)	1.82	5.43	6.55

Adjusted prevalence are included in 95% confidence interval.

Impact of bias is smaller than uncertainty of the measure.

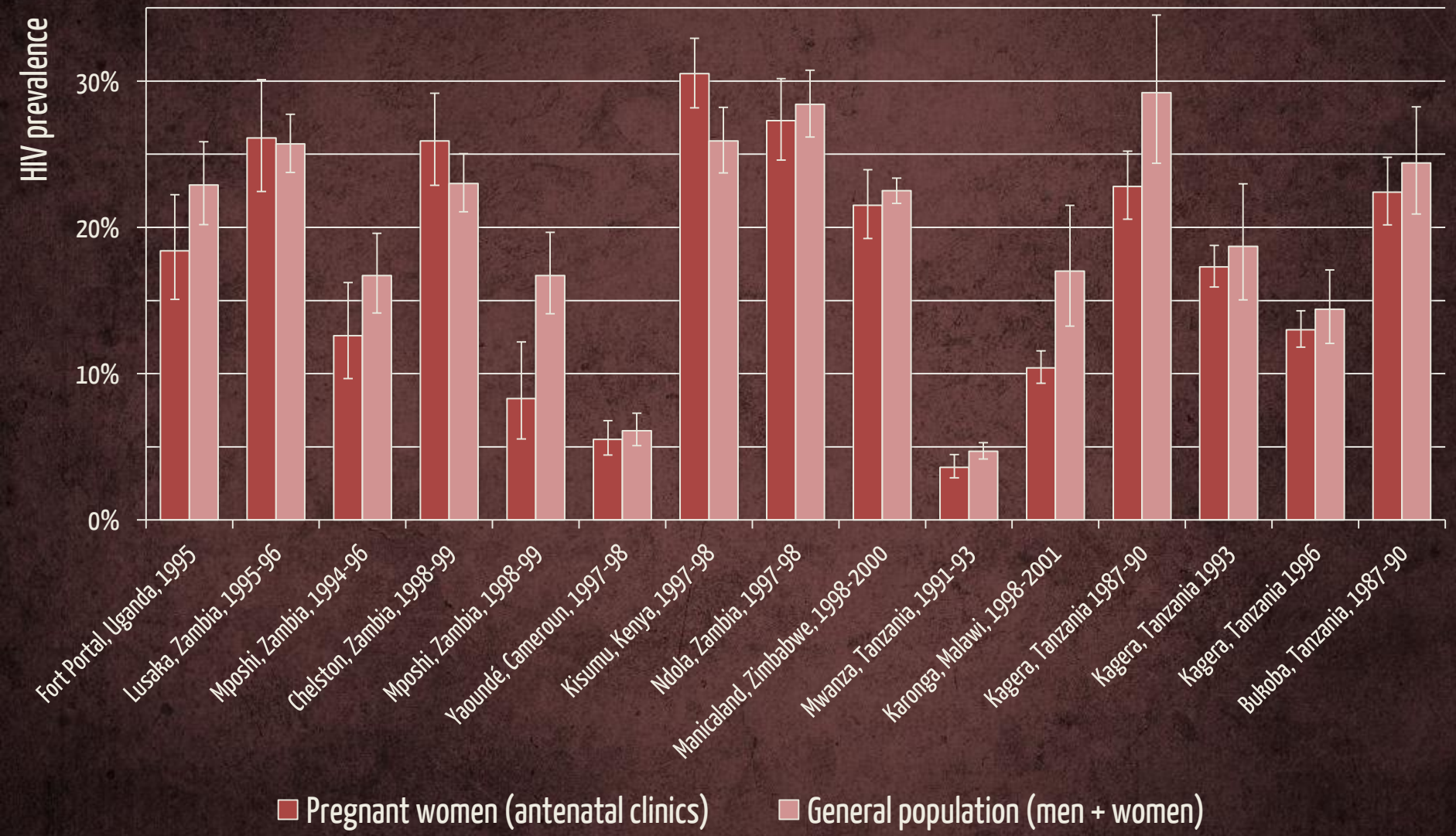
Source: Larmarange 2007, PhD

Local comparison of pregnant women and all women in general population



Source: Gregson 2002 *AIDS*

Local comparison of antenatal clinics and general population (men and women)



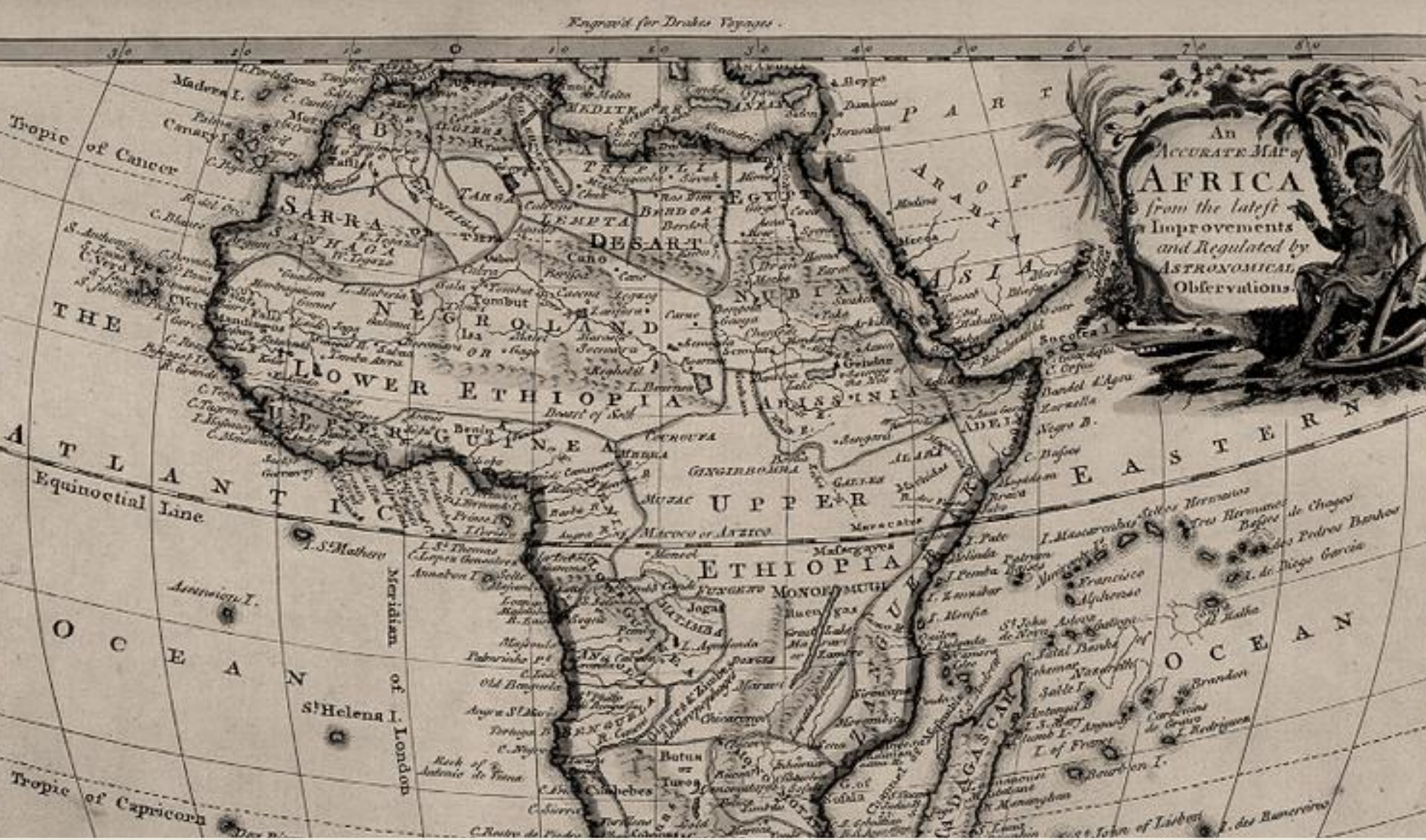
Sources: Larmarange 2007, PhD, from
Kwesigabo 1996, Fylkesnes 1998, Kilian 1999, Kwesigabo 2000, Fylkesnes 2001, Glynn 2001, Changalucha 2002, Gregson 2002b, Crampin 2003.

at local level

Prevalence observed among pregnant women underestimates prevalence of all women in the general population.
Nevertheless, due to male prevalence being usually lower than female, observed prevalence in antenatal clinics is more or less the same than prevalence in adult general population (men and women).

at national level

Antenatal clinics for sentinel surveillance are not randomly selected.
Although they might be an indicator of local levels, there is no guarantee that they will reflect national levels.

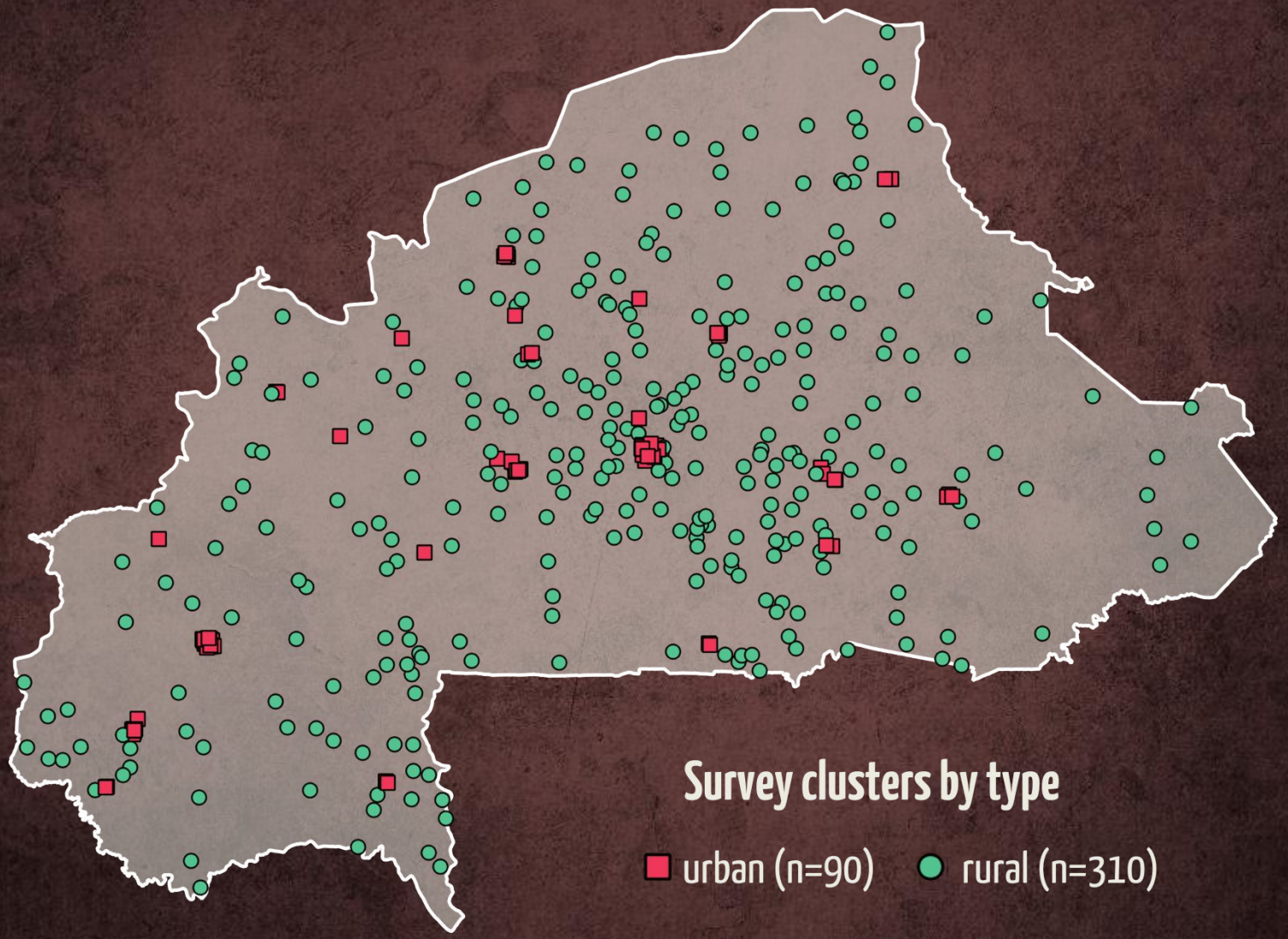


mapping regional trends of HIV prevalence from DHS

DHS sampling design

- DHSs use similar stratified two-stage sample design.
- Firstly, enumerations areas (or clusters) from the last census are selected according their number of households.
- Secondly, in each cluster, eligible households are sampled.
- Most of DHSs provide coordinates of surveyed clusters.
- The scatter plot of clusters reflects variations in population density.

Surveyed clusters in Burkina Faso 2003 DHS



Estimating regional trends of HIV prevalence

The number of tested people by cluster (10 to 40 depending on the DHS) is too small to calculate a prevalence by cluster.

Due to irregularity of spatial cluster distribution, classic smoothing techniques based on fixed bandwidth are not adapted to estimate spatial variations of prevalence.

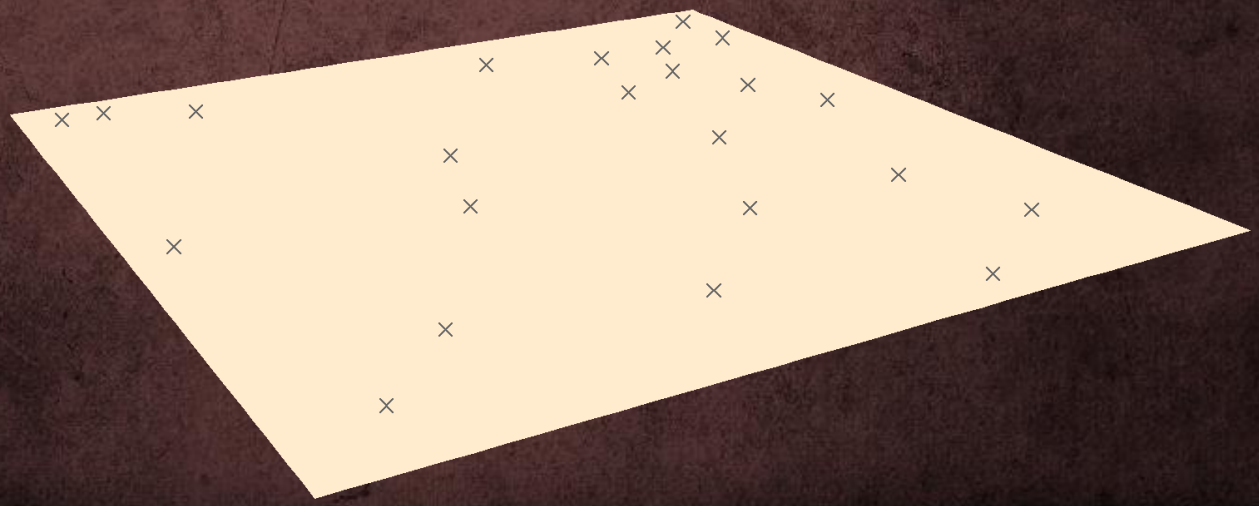
We developed a method using kernel density estimators with adaptive bandwidth size of equal number of observed persons.

We implemented this method in prevR, a bilingual R package available on CRAN:
http://cran.r-project.org/web/packages/prevR/

Larmarange *et al.* (2011) *Cybergeo.* DOI: 10.4000/cybergeo.24606

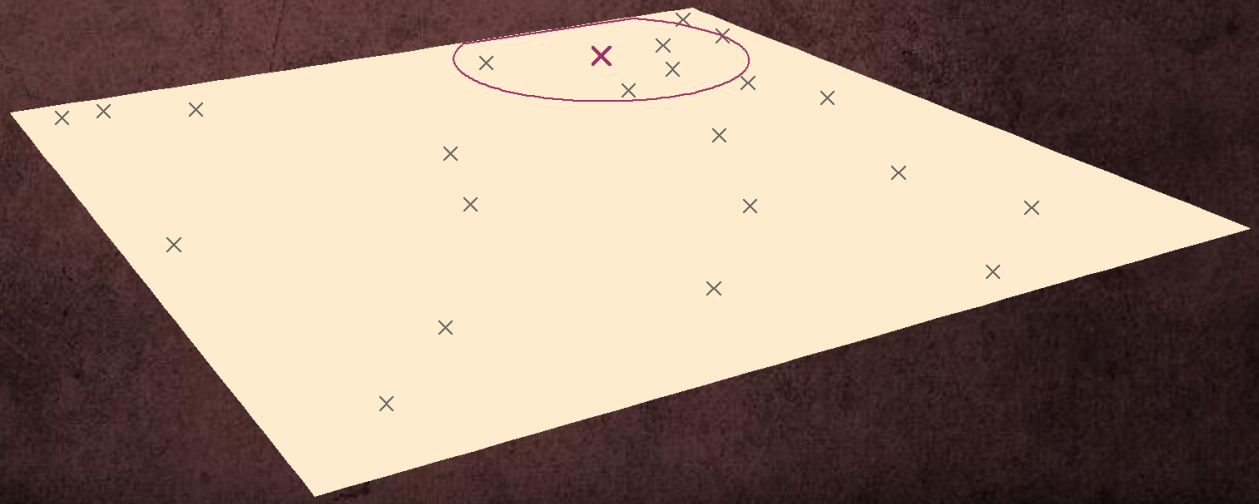
Calculating the surface of observations

» Each dot represents a cluster.



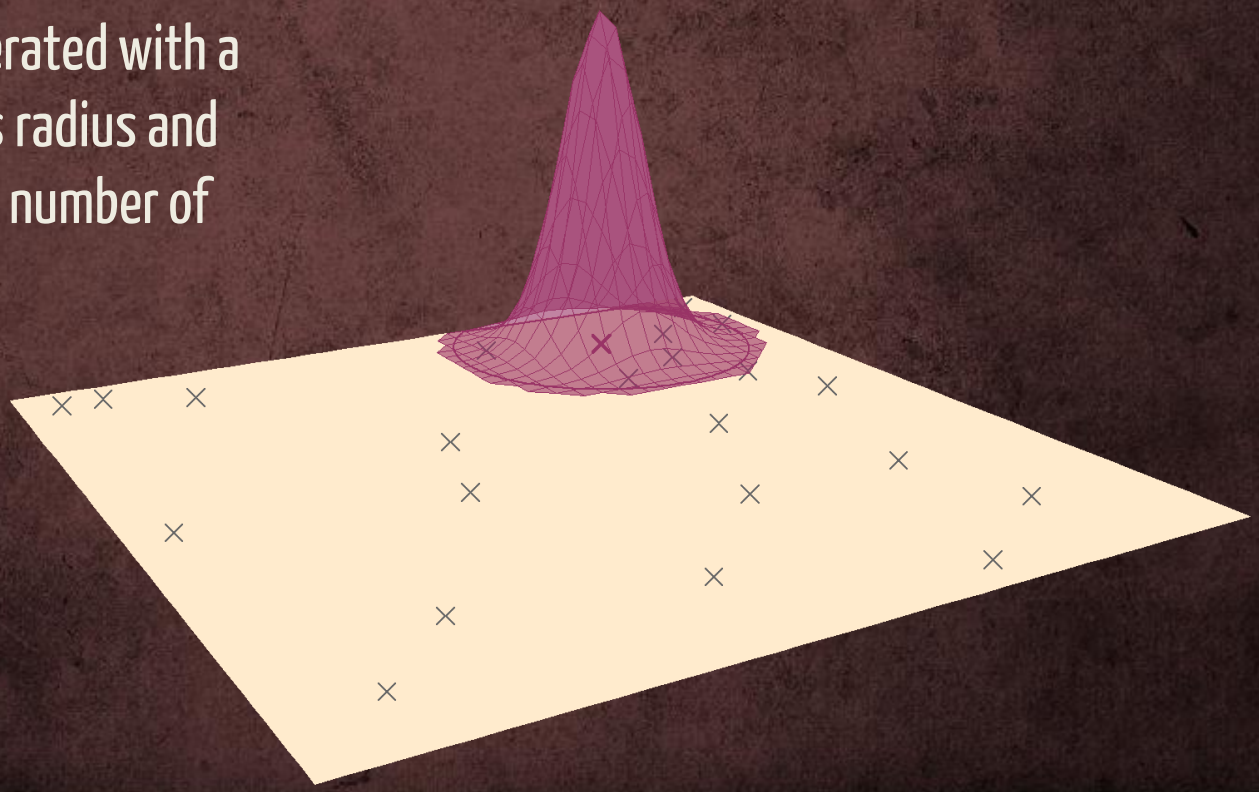
Calculating the surface of observations

- Each dot represents a cluster.
- For each cluster, a circle is drawn such that the number of persons surveyed within is at least equal to a fixed minimum N.



Calculating the surface of observations

- Each dot represents a cluster.
- For each cluster, a circle is drawn such that the number of persons surveyed within is at least equal to a fixed minimum N.
- An intensity surface is generated with a bandwidth depending on its radius and a height proportional to the number of observations.



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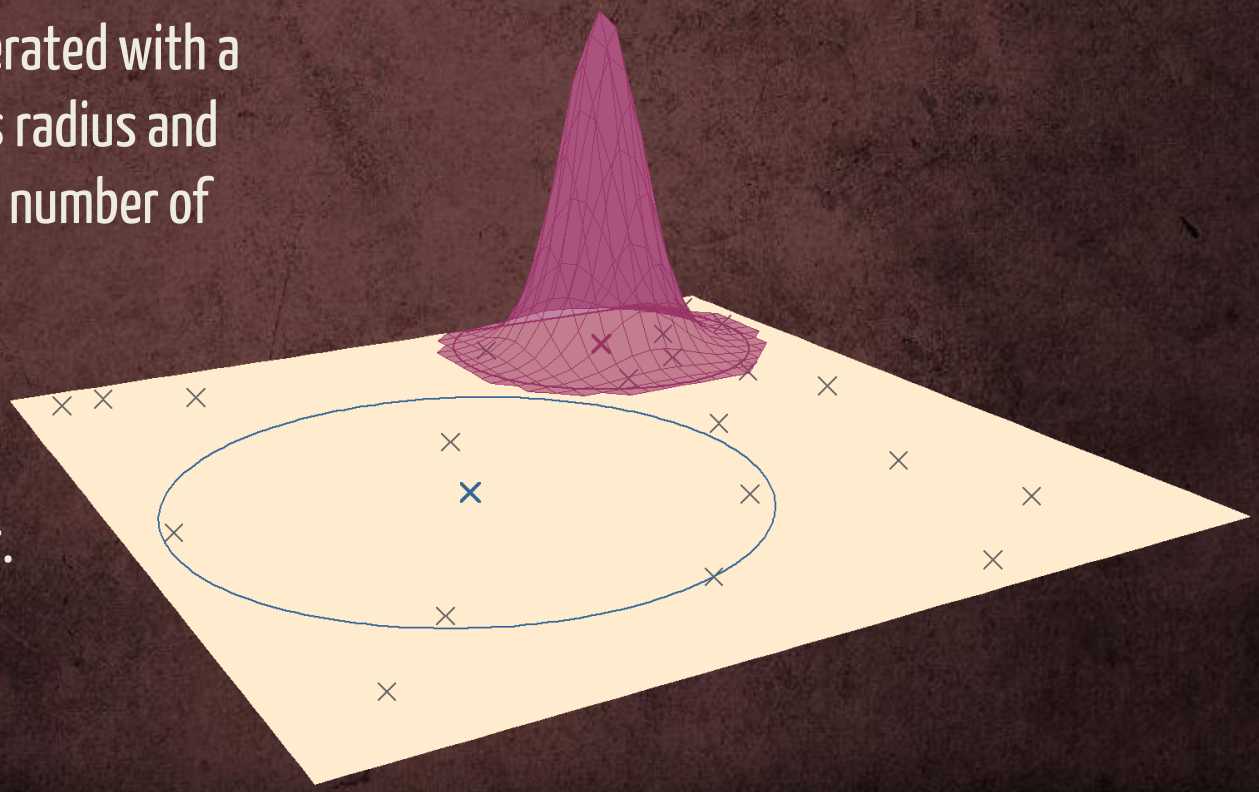
- Where the clusters are widely dispersed, the circle is therefore larger.



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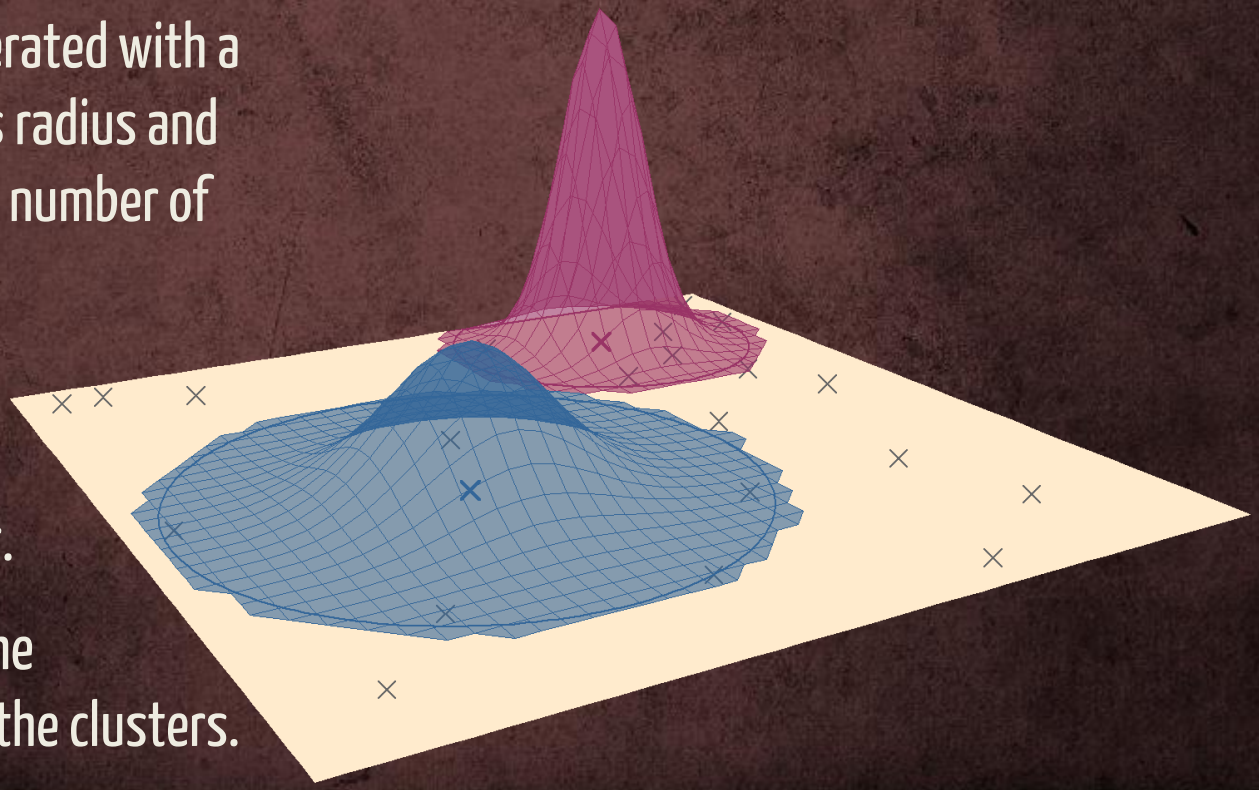
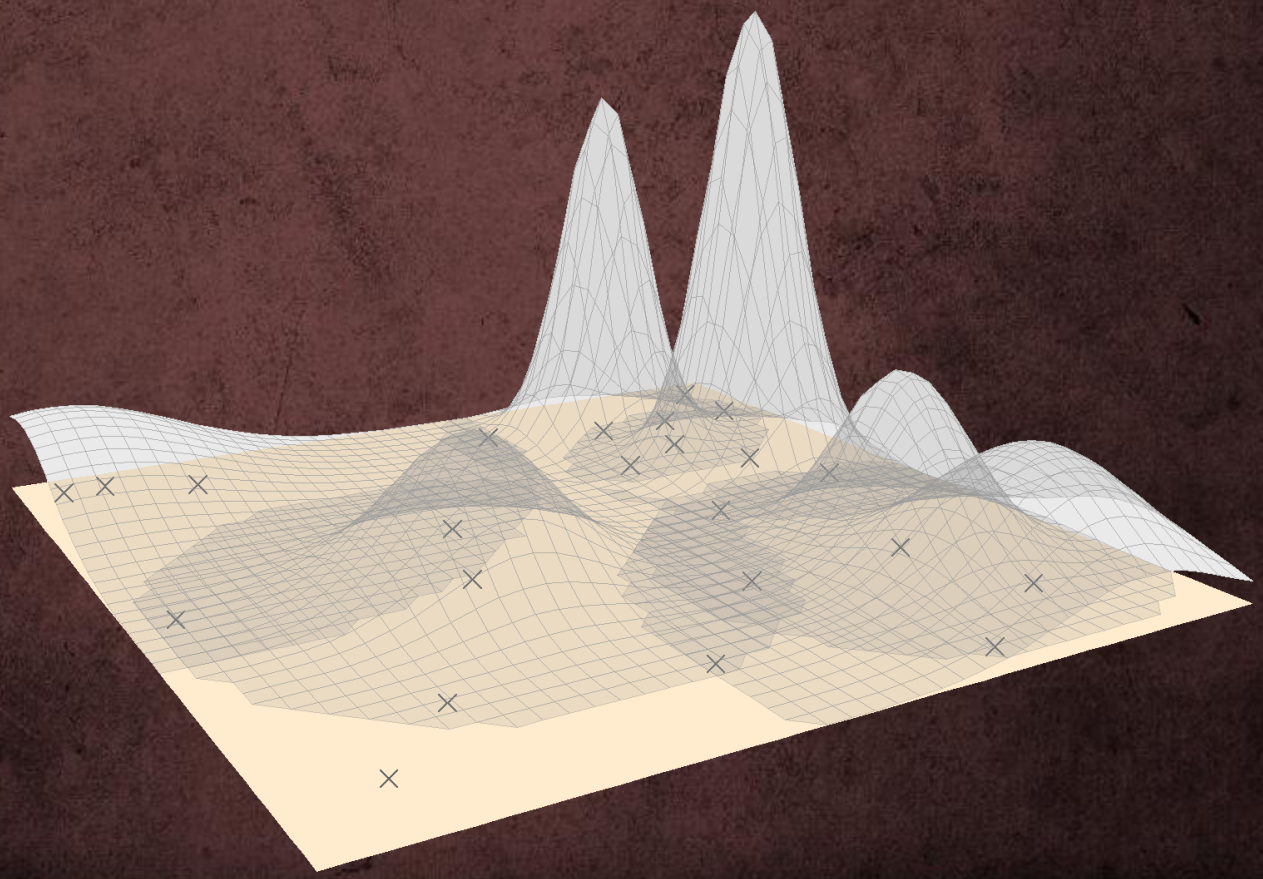
- The smoothing adapts to the local spatial distribution of the clusters.



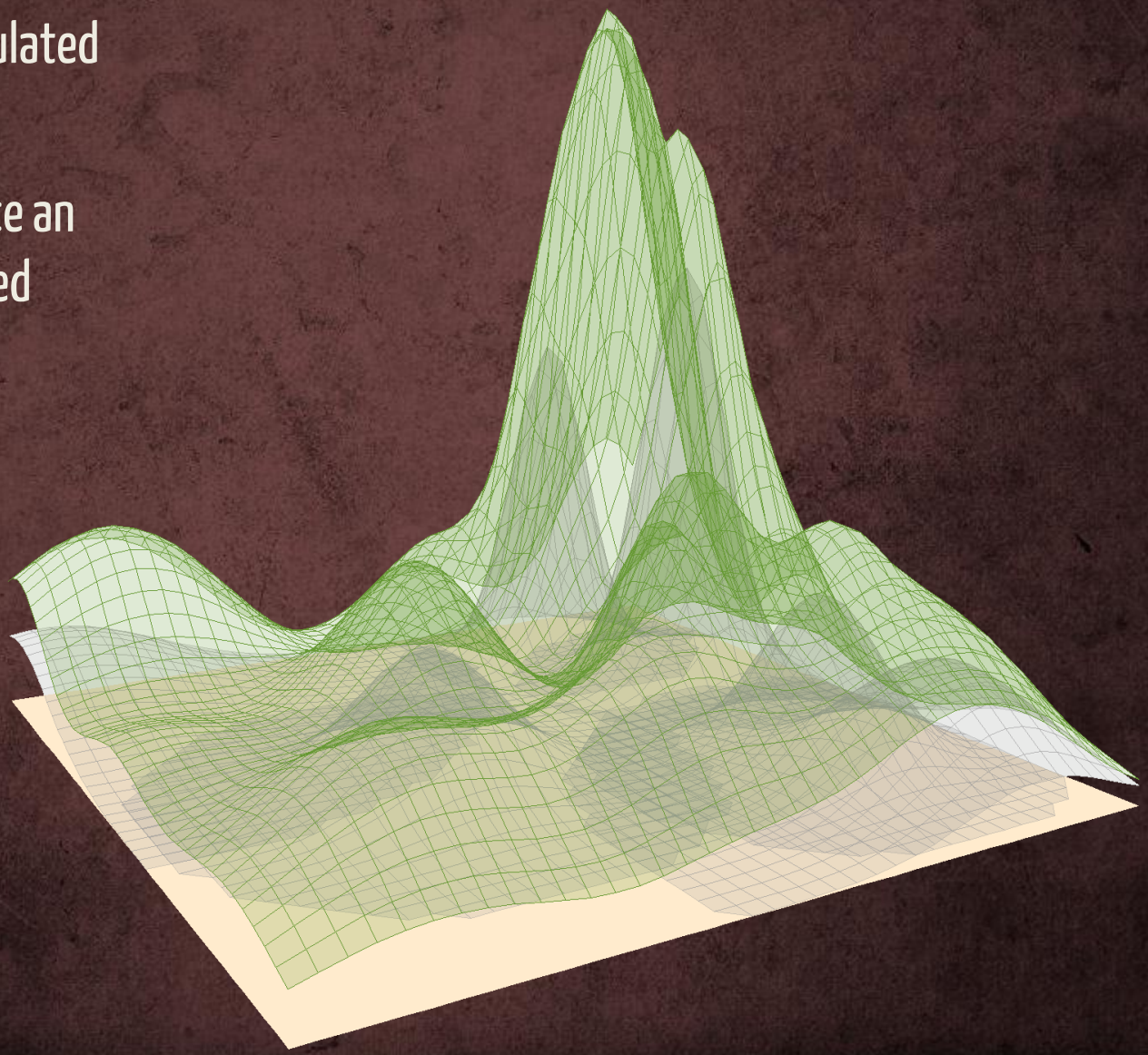
Calculating the surface of observations

» An intensity surface is calculated for each cluster.



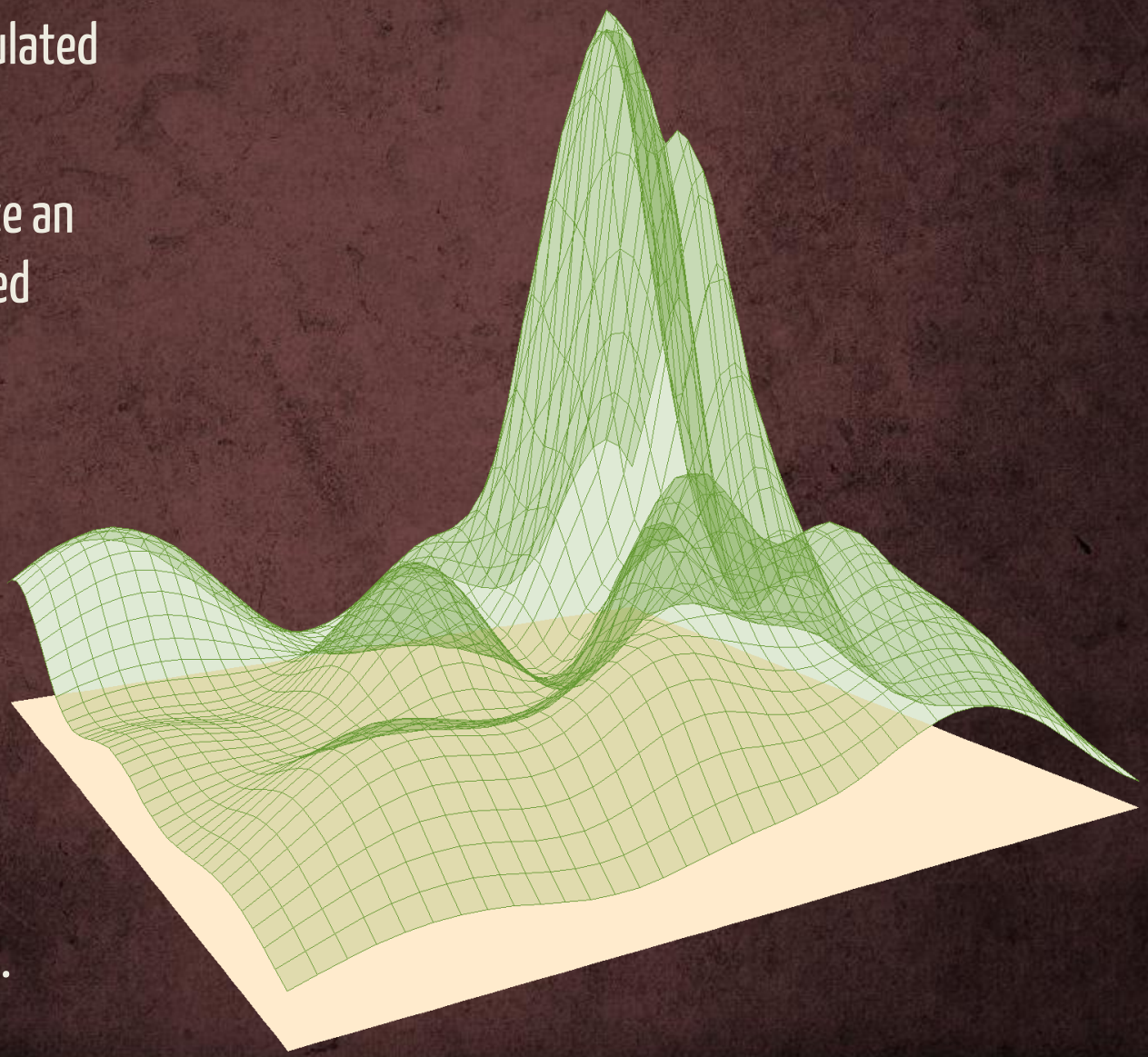
Calculating the surface of observations

- An intensity surface is calculated for each cluster.
- They are summed to produce an intensity surface of observed people.

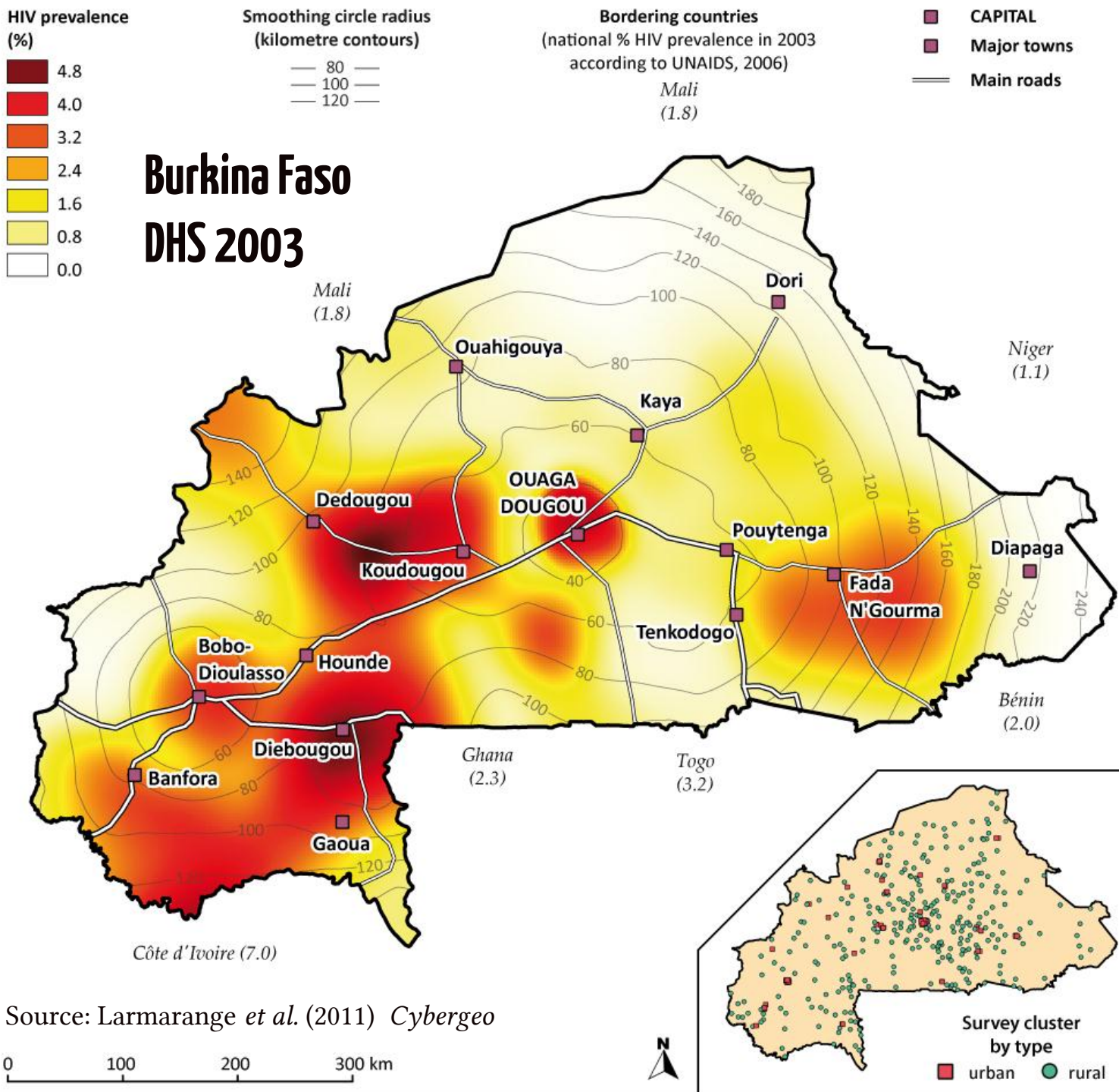


Calculating the surface of observations

- An intensity surface is calculated for each cluster.
- They are summed to produce an intensity surface of observed people.
- The same process is used to calculate the intensity surface of positive cases, using the same bandwidths.



- The ratio of the 2 surfaces (cases / observations) yields a prevalence surface.
- This map doesn't show accurate estimates of local prevalence, but regional trends.
- Interpretation needs to take into account the variations of the smoothing circle radius.



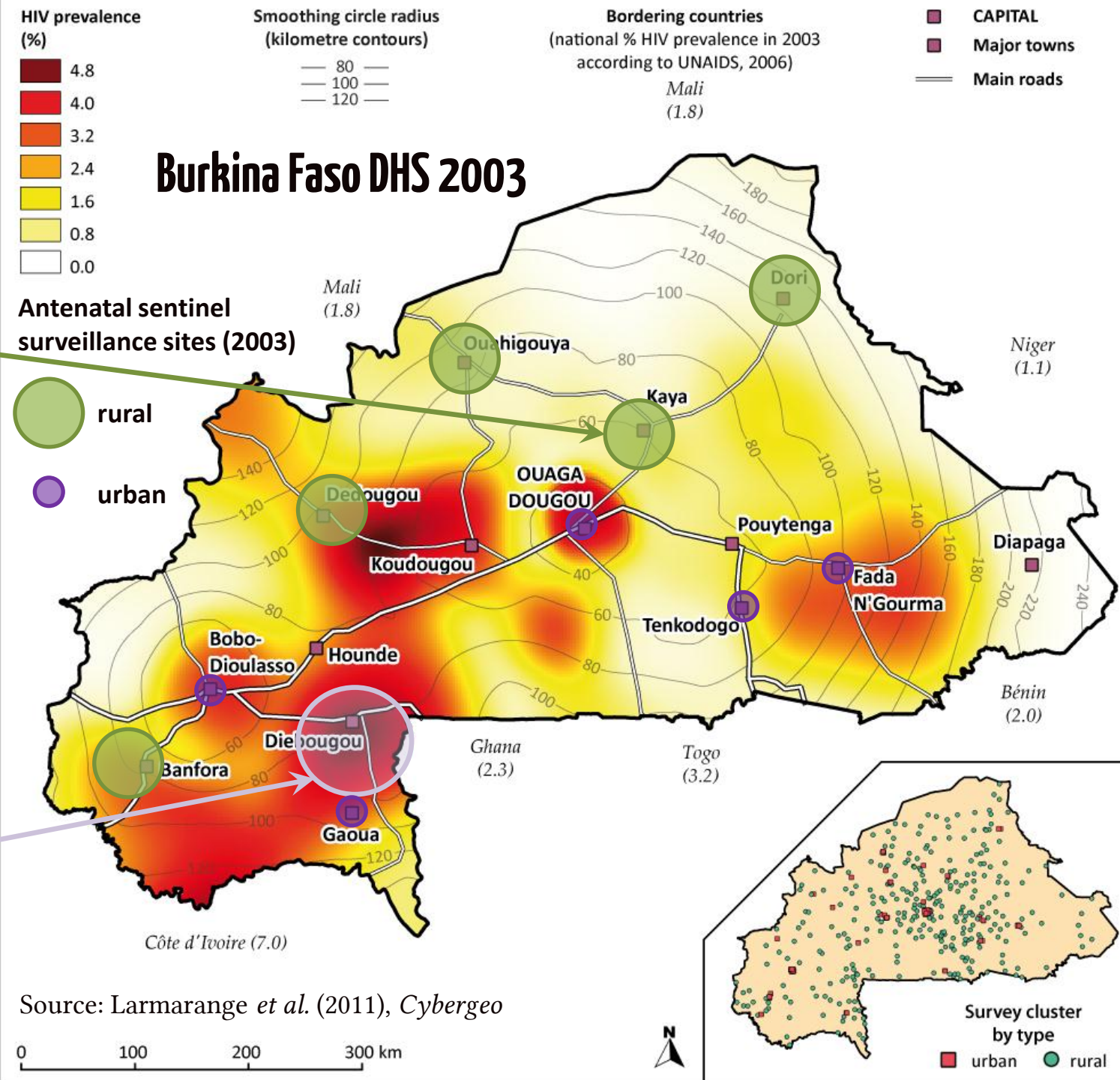
local comparison of DHS and prenatal surveillance

Prevalence of 3.6% in antenatal clinics.

Only 0.7 to 1.2% in DHS.

Gold mining, seasonally migrant males and sex workers.

Peak not measured by antenatal data.



Source: Larmarange *et al.* (2011), *Cybergeo*

Althougth local estimates from antenatal clinics are sometimes close to regional estimates from DHS (usually for small cities), they can differ greatly.

rural site of Kaya

It corresponds to 3 rural clinics.
In one of them, a high prevalence was measured (7.1%)
while it was lower in the two others (1.6 and 2.4%).
Estimated prevalence from DHS with a 60 km smoothing radius: 0.7 to 1.2%

big cities: the example of Douala (Cameroon)

In 2002, prevalence of 8.0% observed in 3 antenatal clinics:
3% (n=100), 6.5% (n=200) and 16% (n=100).
DHS 2004: prevalence of 4.4% (n=931 – 43 clusters).

Antenatal clinic estimates are very dependent on their *catchment area.*

new EPP approach since 2005/2006

DHS

- Representative at national and regional level.
- Possible biases (underestimation) but limited.
- Sample size too small for local estimates.
- Conducted **only every 5 to 10 years**.

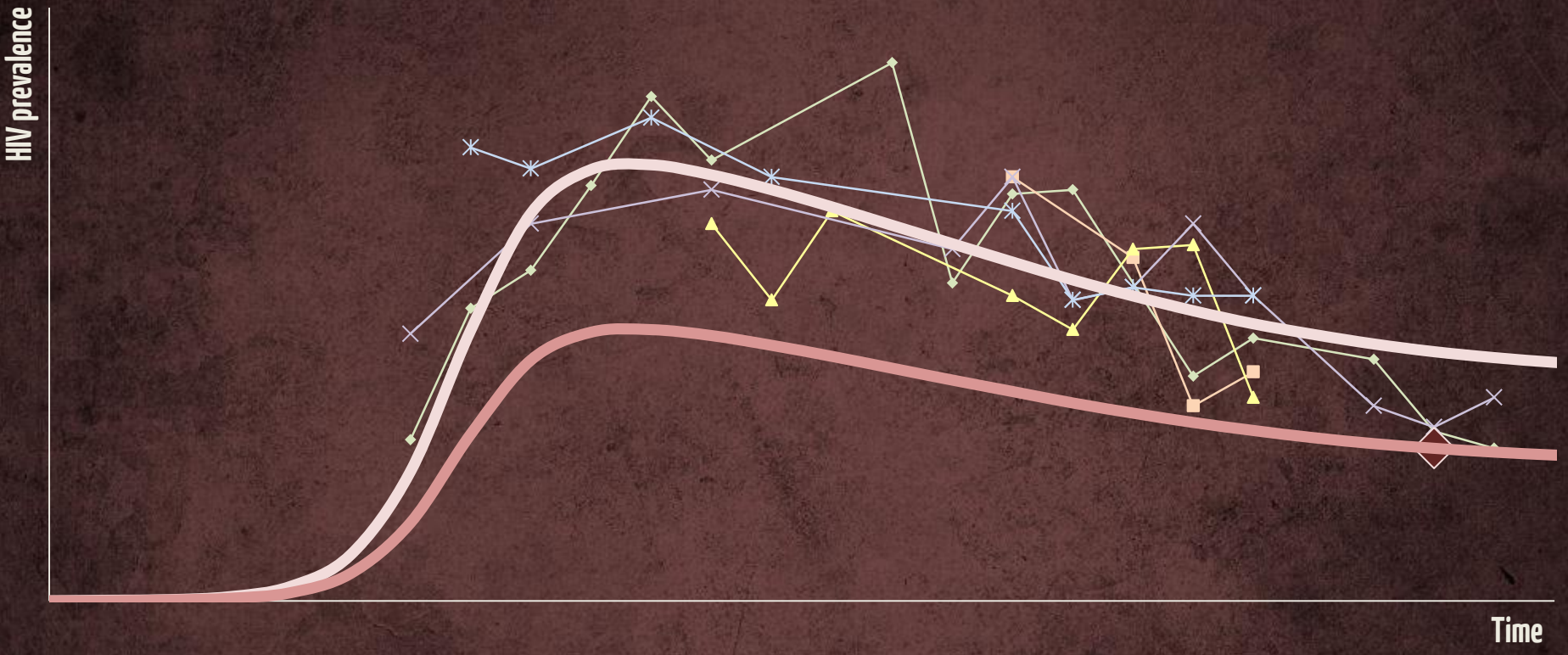
Sentinel surveillance in antenatal clinics

- Local indicator of the order of magnitude.
- Not representative at national level.
- Dependent on the clinics' catchment area.
- Usually **repeated every year**.
- Data available since the 90's

New approach used by EPP since 2005/2006

- Estimating the shape of the curve with antenatal data.
- Calibrating the curve using a population-based measure.

Calibrating the curve with a population-based measure



Data source: sentinel surveillance among pregnant women, by clinic

Fitting the curve to obtain its **shape**.

Population-based observed prevalence (usually from DHS) at a **specific date**.

Calibration: the DHS determines the **height** of the curve.

June 2006

UNAIDS Global Report estimates at end of 2005
integrates calibration using population-based surveys (if available).

June 2008

UNAIDS Global Report publishes estimates at
end of 2007 and end of 2001, giving trends.

November 2010

For the first time, the Global Report is not published before
the international AIDS conference.
The Report is completed by online *AIDS Info Database*
and *Country Fact Sheets* providing the complete
estimated prevalence curves with confidence intervals.

issues and perspectives

Complex epidemics

With uptake of ART, prevalence curves are more complex.
Possible shapes in EPP are limited and not able to fit complex trends like a second increase after a first decrease (as observed in Uganda).
➔ The 2011 version of EPP allows the r parameter (infection rate) to vary over time. The model is more flexible but uncertainty is higher.

Sub-group trends

In Western and Eastern Africa, while the epidemics are generalised, they are also concentrated in sub-groups (sex workers, men having sex with men or drug users…).
There is a need of specific estimates in these sub-groups, but data gap in Africa.

Are antenatal data a good indicator of trends?

Antenatal surveillance currently used to estimate trends.
There may be differences in trends in antenatal clinics compared to DHSs.
Catchment area of clinics could change over time, for example when a PMTCT program is implemented in a clinic.

Regional trends

More and more countries need regional trends to adapt their strategies accordingly.

➔ More frequent repeated DHS's are needed.

Correcting estimates from DHS for non participation

A paper published in 2011 by Bärnighausen *et al.* compares correction for non participation in the 2007 Zambia DHS using classic imputation models (as models presented before) and Heckman-type selection models (trying to take into account **unobserved factors**).

in % (95% CI)	Men	Women
Observed prevalence	12 (11-13)	16 (15-17)
Adjusted prevalence (imputation model)	12 (11-13)	16 (15-17)
Adjusted prevalence (selection model)	21 (20-22)	18 (17-19)

Further analyses are currently ongoing by the UNAIDS Reference Group (on 30 DHSs) to investigate this issue, identify the best model and selection variables to use.

Depending on results, implementation in EPP and Spectrum is planned for the 2013 round of estimates.

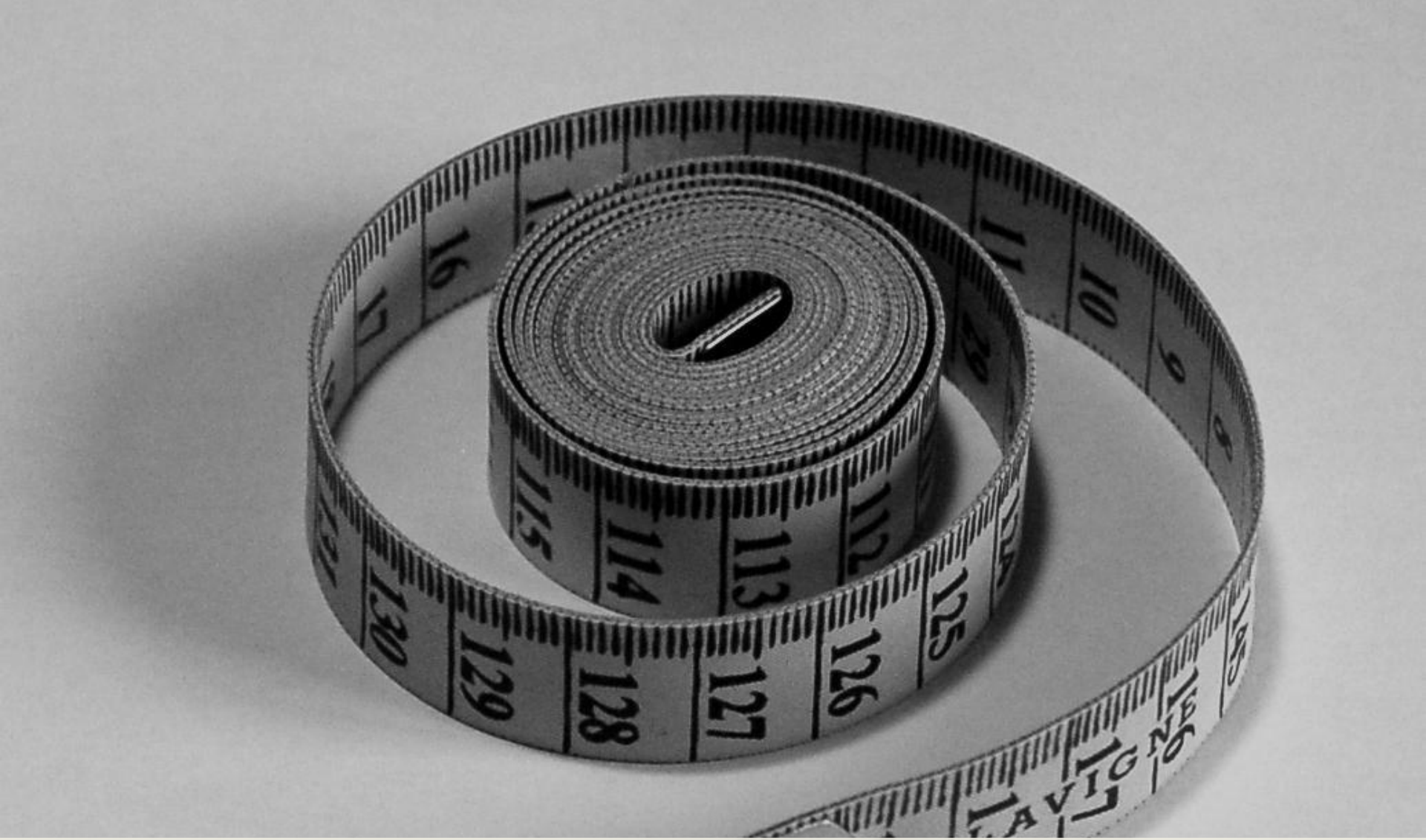
to conclude

UNAIDS estimates can't be compared from one Global Report to another.
Changes in estimates this last years are mainly explained by changes in methods rather than changes in the epidemiology.

For each new Global Report, the complete prevalence curve is re-estimated, giving trends.

Estimates are always imperfect, based on the available data. They should not be considered as a definitive fact. It's also important to keep in mind the uncertainty of the estimates.

Finally, HIV prevalence is only one indicator, which needs to be considered with others like incidence or mortality.



thank you for your attention