How to estimate the size of the hidden HIV epidemic?

The case of France

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Background

❖ Many HIV positive individuals are unaware of their infection.

❖ Undiagnosed HIV infection has serious implications for both the individual and public health.

❖ Persons unaware of their HIV infection cannot benefit from timely treatment.

❖ Persons living with undiagnosed HIV infections may transmit HIV to others.

❖ Information on persons living with undiagnosed HIV infection is essential for guiding screening policy and resource allocation planning.

Methods to estimate the size of the hidden HIV epidemic

❖ Direct method

❖ Back-calculation method

❖ Methods based on CD4 cell count and simultaneous HIV/AIDS diagnosis

Estimated undiagnosed HIV prevalence in IDF and France in 2010 (using direct method)

IDF

Estimated undiagnosed prevalence:
0.14%* (95% CI: 0.08%-0.22%)

* d'Almeida KW *et al.* (2012) Modest Public Health Impact of Nontargeted Human Immunodeficiency Virus Screening in 29 Emergency Departments. *Arch Intern Med*, 172:12-20.

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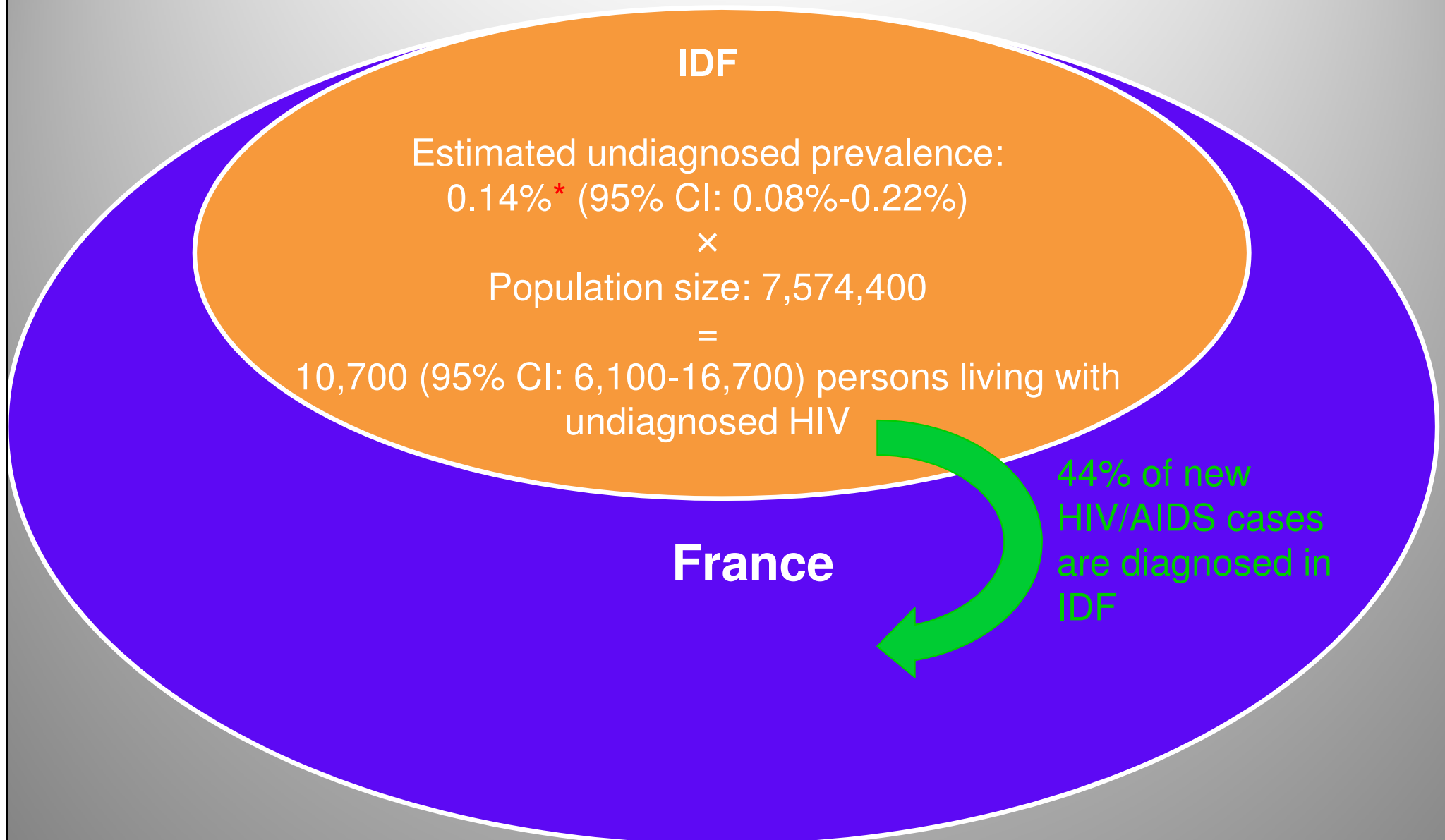0.14%* (95% CI: 0.08%-0.22%)
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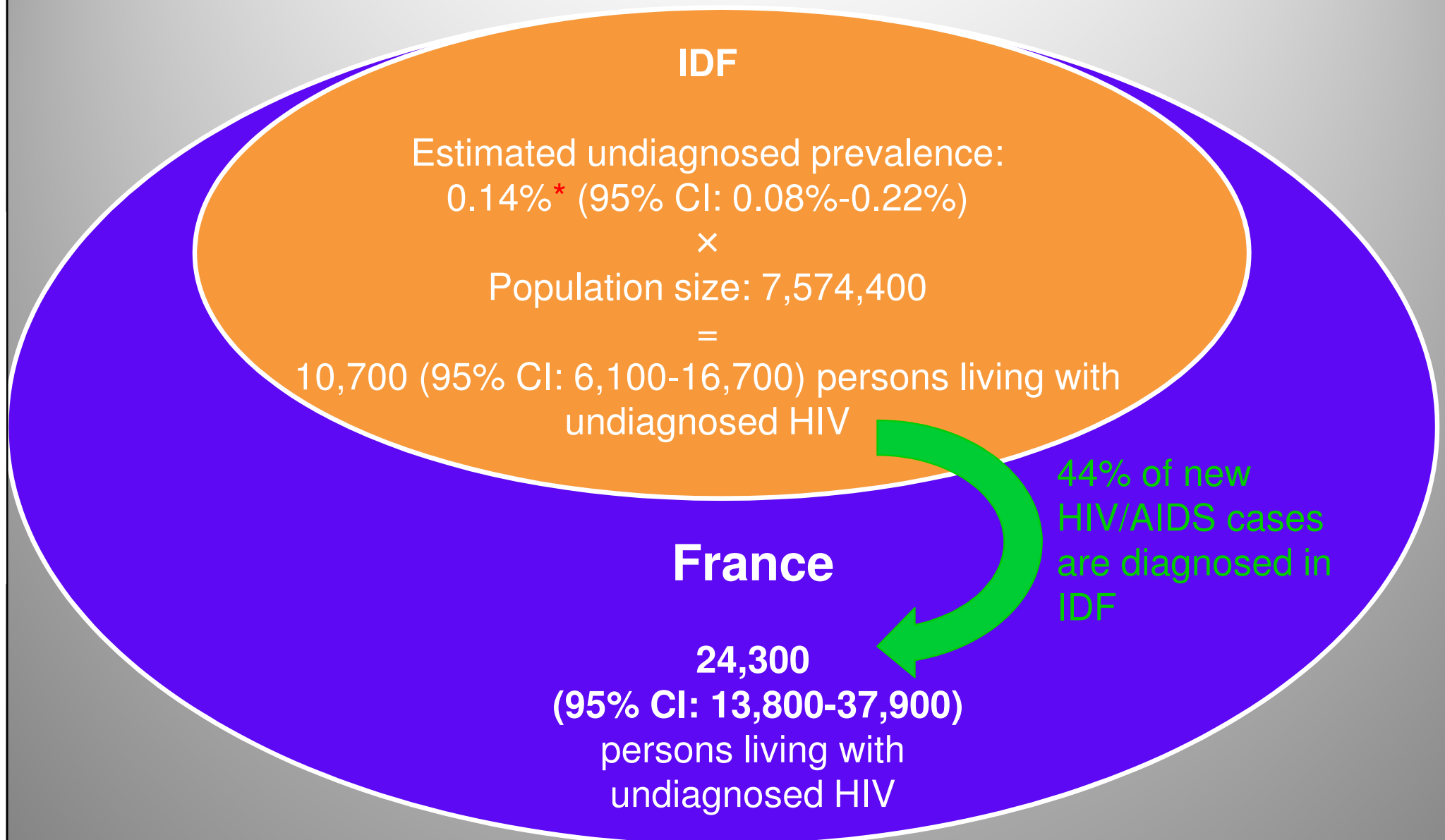
France?

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France

**24,300
(95% CI: 13,800-37,900)**
persons living with
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Estimated undiagnosed HIV prevalence in France in 2010 (using historical back-calculation model)

2000   88,300*   persons living with HIV
                (95% CI: 52,300-168,000)

*Deuffic-Burban S, Costagliola D. (2006) Including pre-AIDS mortality in back-calculation model to estimate HIV prevalence in France, 2000. *Eur J Epidemiol* 21:389-96.

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➔ prevalence has increased by 5,800 persons/year

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26% of persons newly enrolled in HIV care knew their HIV
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2010   **25,900**   persons living with
   **(95% CI: 0-84,900)**   undiagnosed HIV

*Deuffic-Burban S, Costagliola D. (2006) Including pre-AIDS mortality in back-calculation model to estimate HIV prevalence in France, 2000. *Eur J Epidemiol* 21:389-96.

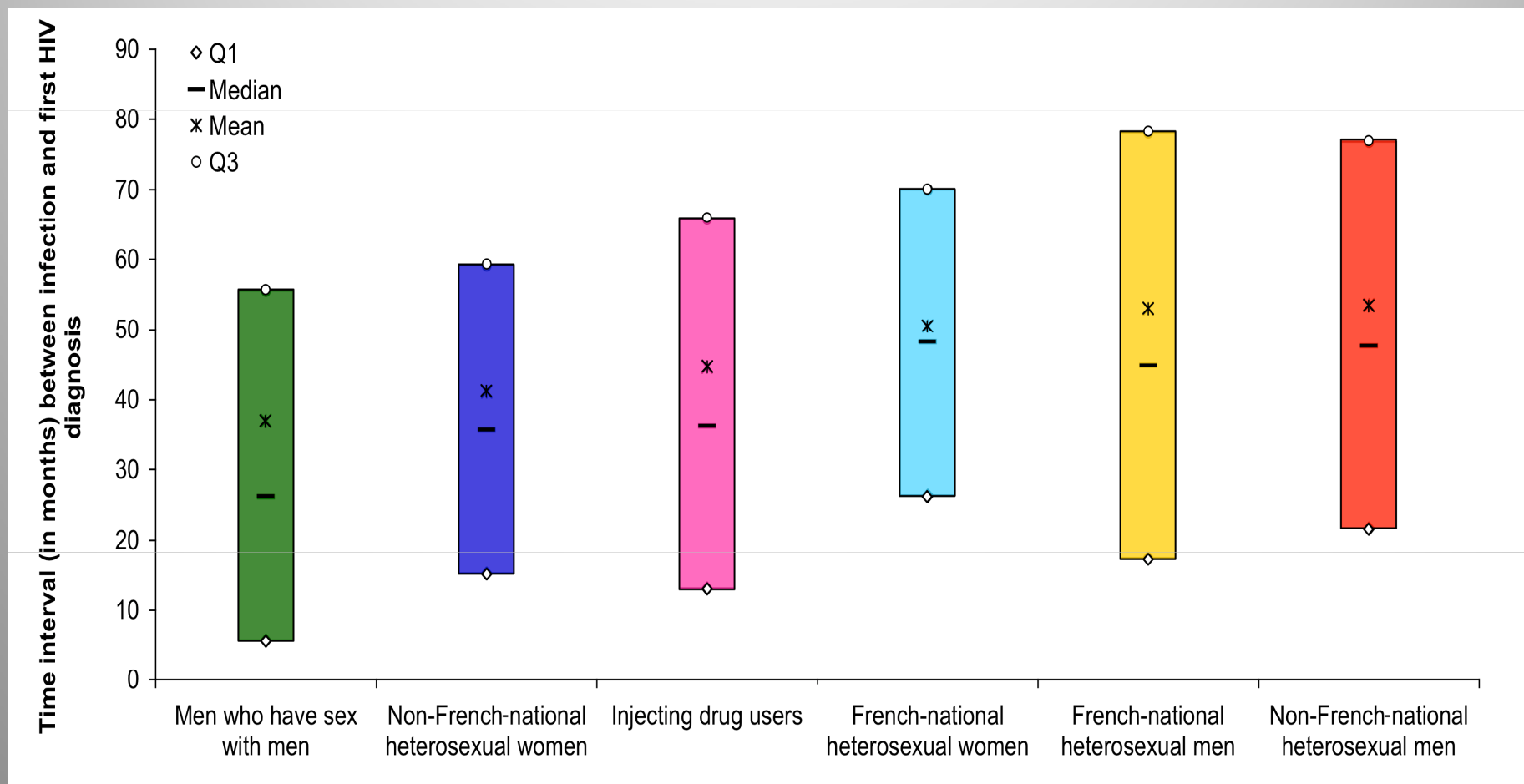# Estimated HIV incidence in France by transmission category (using new back-calculation model)
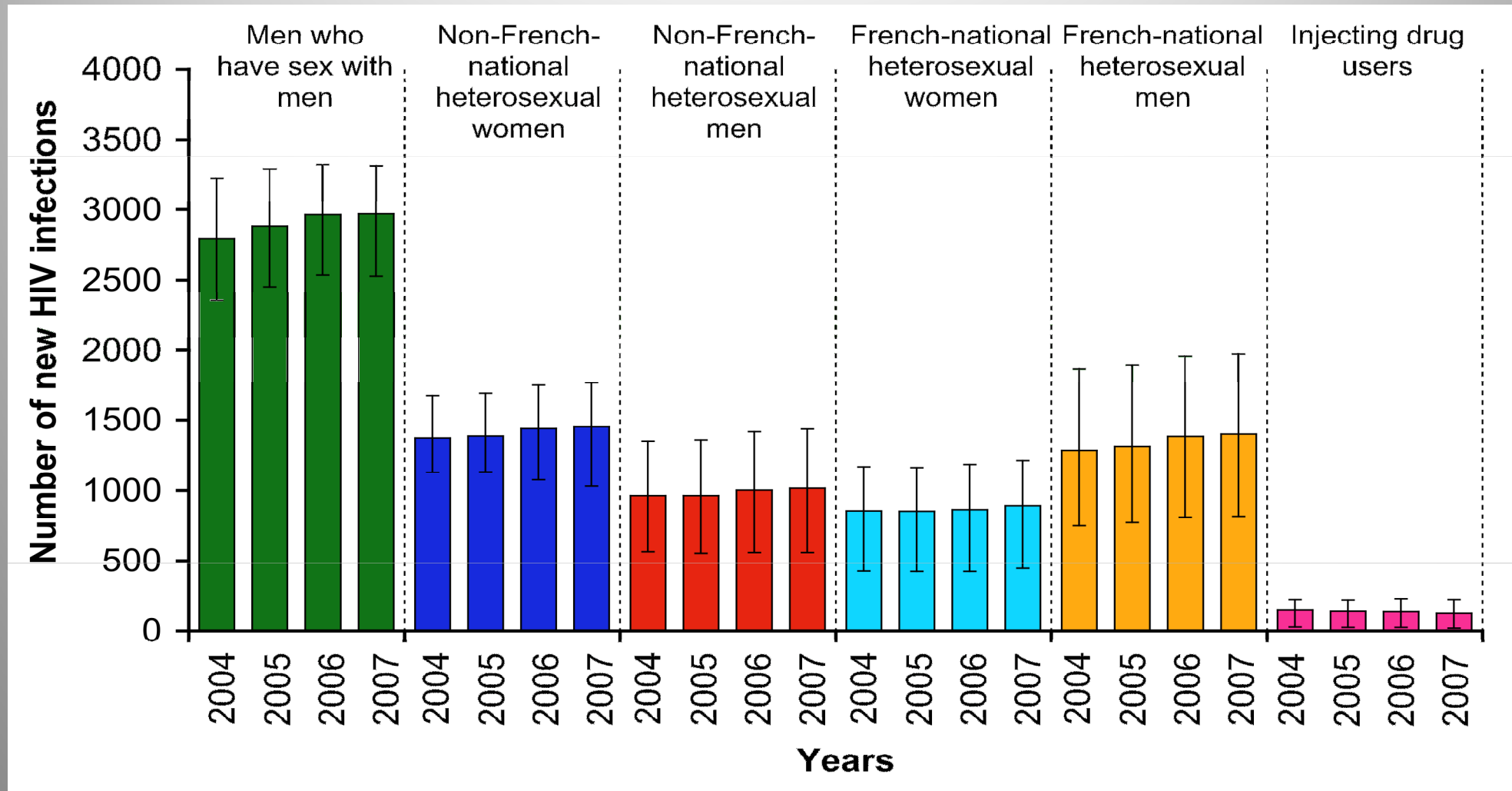
Ndawinz JD, Costagliola D, Supervie V. (2011) New method for estimating HIV incidence and time from infection to diagnosis using HIV surveillance data: results for France. *AIDS* 25:1905-13

Estimated distribution of time interval between infection and diagnosis by transmission category
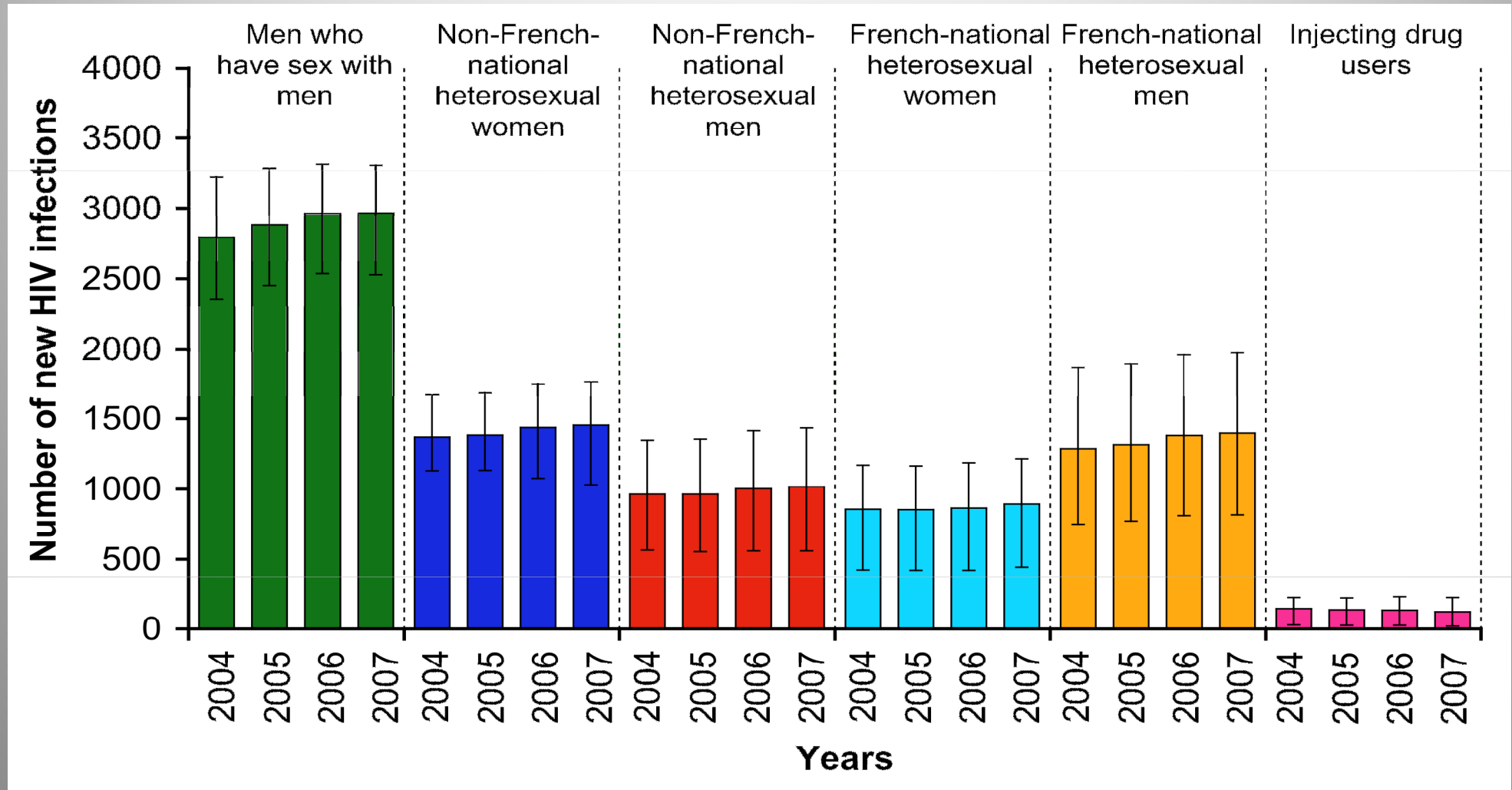(using new back-calculation model)
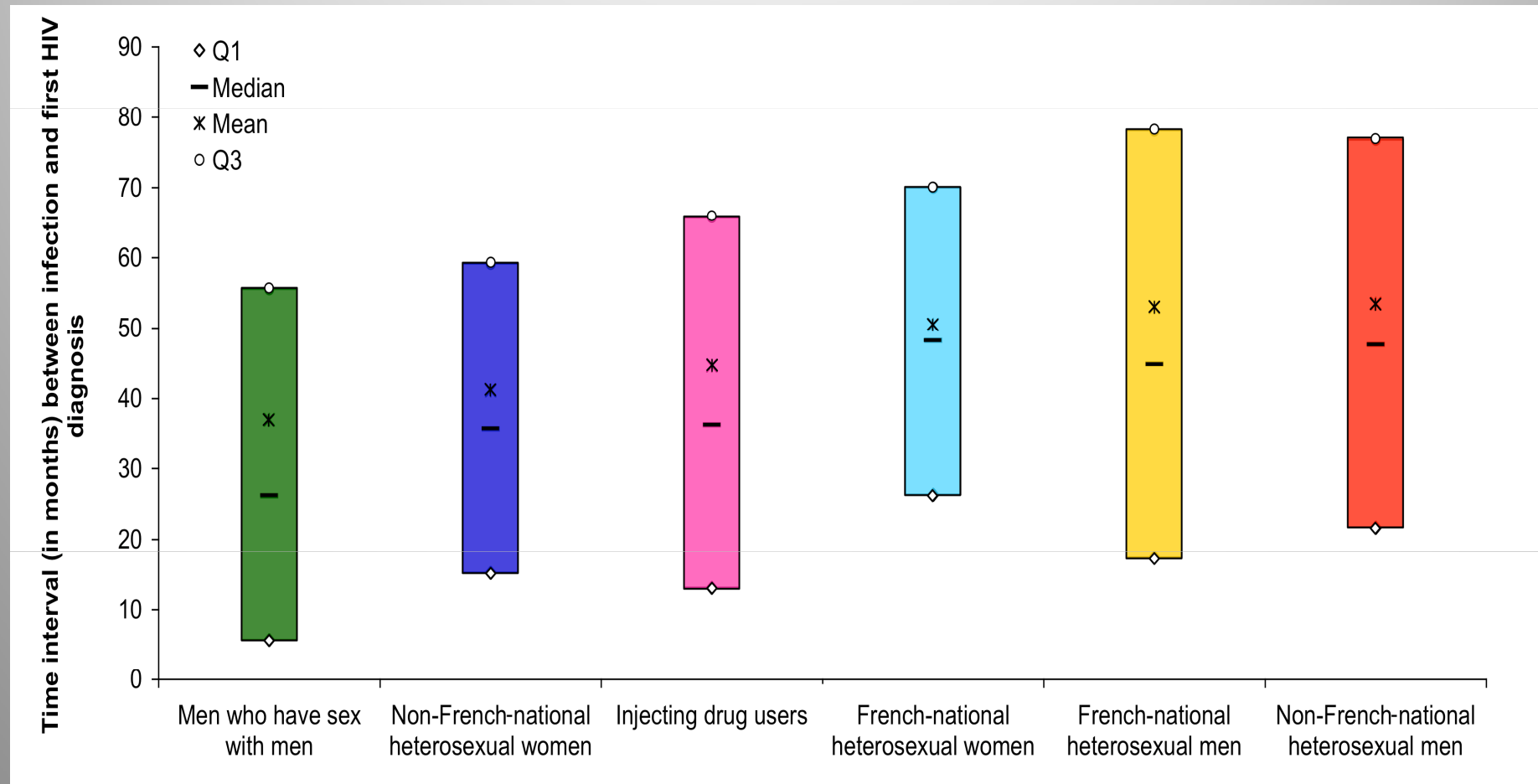
Estimated distribution of time interval between infection and diagnosis by transmission category
(using new back-calculation model)

The probability of not being diagnosed 10 years after the infection occurred is very small among each transmission group (<5%); therefore, most people infected before 2000 were aware of their HIV status at the end of 2010.

# Estimated HIV incidence in France by transmission category (using new back-calculation model)

Extrapolating our estimated curves of HIV incidence over the whole 2000-2010 period, and using our estimated distribution of times from infection to diagnosis, we obtained the size of the hidden epidemic in France in 2010.

Estimated undiagnosed HIV prevalence and rates in France by transmission category (using new back-calculation model)

	Persons living with undiagnosed HIV	Undiagnosed prevalence rate (per 10,000 population)
Overall	**28,800 (95% CI: 19,100-36,700)**	7 (5-9)
Men who have sex with men	9,000 (95% CI: 7,700-10,100)	314 (269-352)
Injecting drug users	500 (95% CI: 100-800)	70 (14-112)
French heterosexuals	9,800 (95% CI: 5,200-13,500)	3 (1-4)
Women	4,200 (95% CI: 1,800-5,100)	2 (1-3)
Men	5,600 (95% CI: 3,400-8,400)	3 (2-4)
Non French-national heterosexuals	9,500 (95% CI: 6,100-12,300)	26 (17-34)
Women	5,000 (95% CI: 3,600-6,000)	29 (21-34)
Men	4,500 (95% CI: 2,500-6,300)	24 (13-33)

Estimated number and percentage of HIV-infected persons engaged in selected stages of the continuum of HIV care
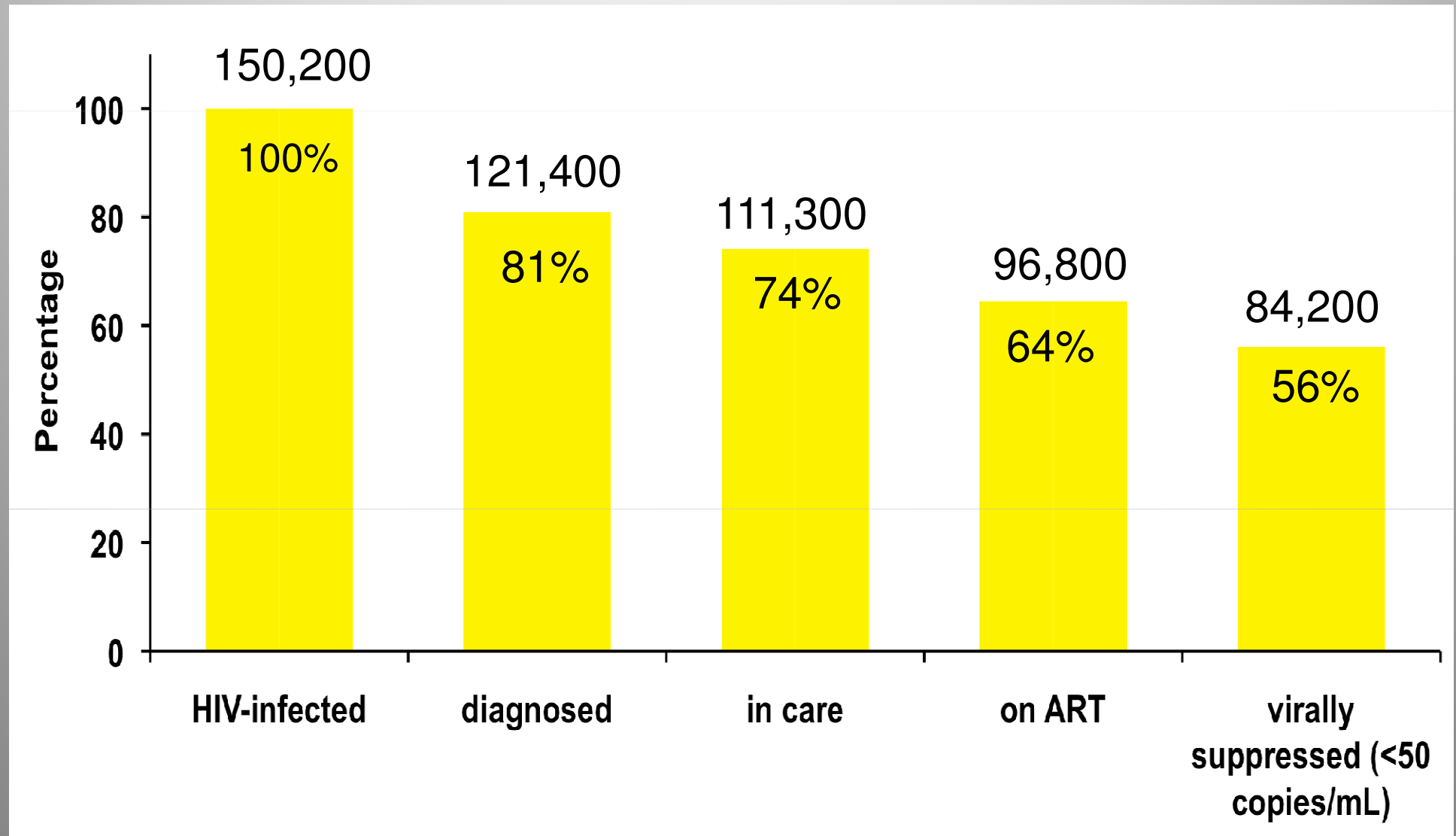
Awareness of HIV infection and transmission of HIV (Adapted from Marks G. *et al. AIDS* (2006) with French estimated data)

19%
unaware of HIV
infection

81%
aware of HIV
infection

Account for:

43%
of new HIV
infections

57%
of new HIV
infections

People living with
HIV/AIDS: 150,200

New infections
each year : 7,500
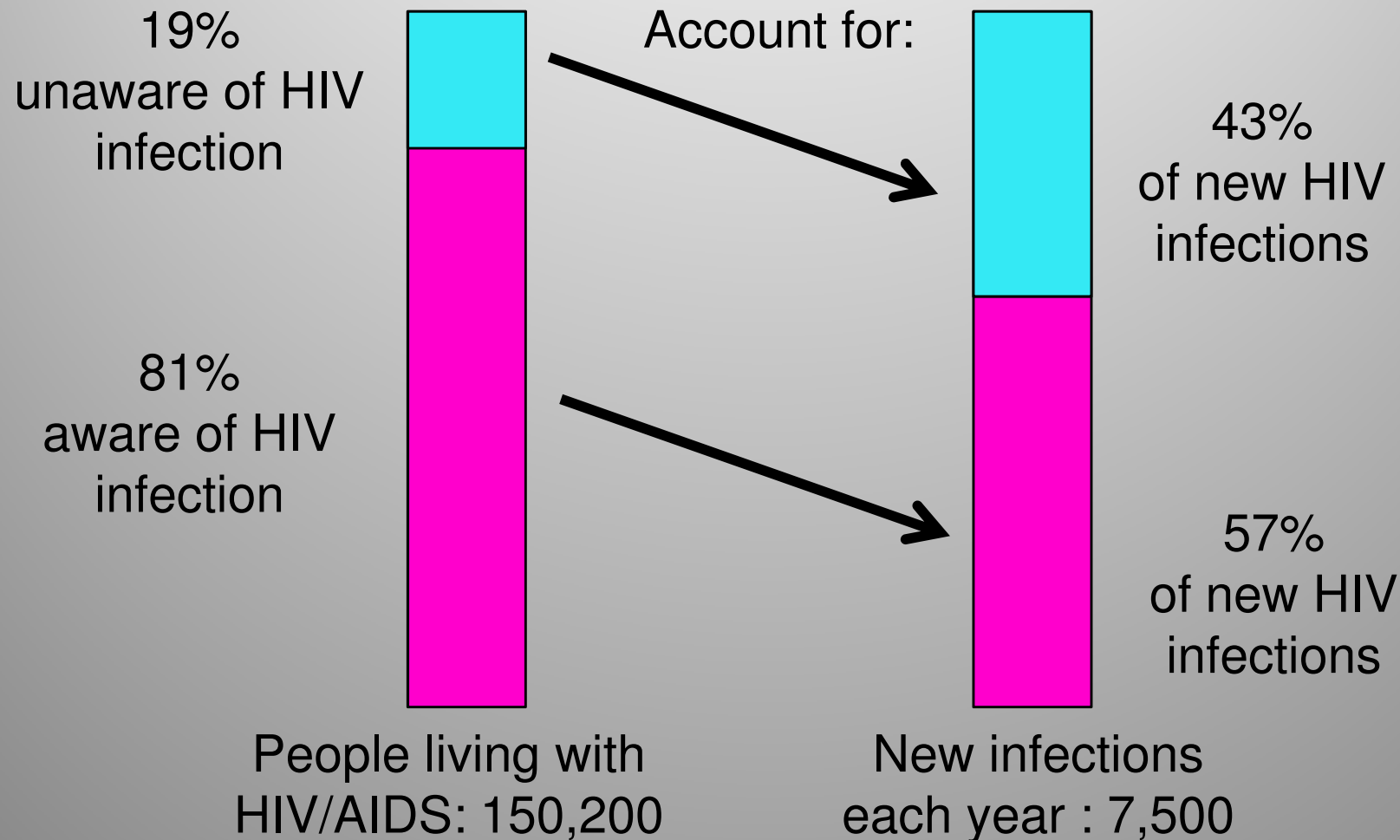
Conclusion

❖ The three methods gave similar results: between 24000 and 29000 individuals remain undiagnosed in France. This represents about 20% of HIV-infected people.

❖ Undiagnosed HIV people contribute for more than 40% of new infections.

❖ Although 56% of HIV-infected persons are virally suppressed, HIV incidence is not decreasing.

❖ Increasing HIV testing opportunities is thus essential.

Thanks for your attention!

New back-calculation model

Using HIV surveillance data
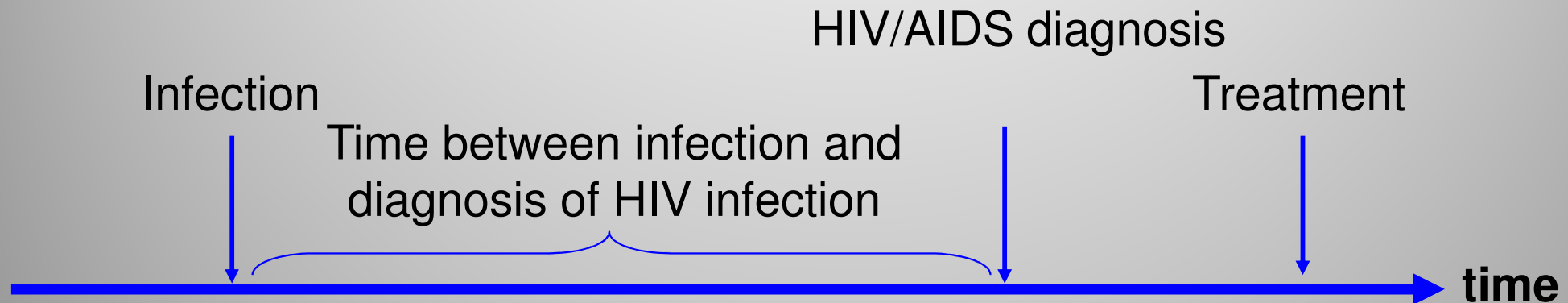
Provide information on times from infection to diagnosis of HIV diagnosis.

Times from infection to diagnosis of HIV diagnosis depend on HIV test-seeking behaviors.

New back-calculation model

Two different kinds of behaviors towards HIV testing

◆ **Diagnosed with symptoms of PHI:**
individuals decided to be tested because they experienced, and recognized, symptoms of PHI, or because they had recently been exposed to HIV

◆ **Diagnosed without symptoms of PHI :**
routine medical examination, onset of HIV symptoms that occur towards the end of the incubation period or AIDS

Provide information on times from infection to diagnosis of HIV diagnosis.

New back-calculation model

Times from infection to diagnosis of HIV diagnosis

◆ **Diagnosed with symptoms of PHI:**
Individuals diagnosed with PHI were assigned a short time between infection and initial diagnosis (3 months in median)

◆ **Diagnosed without symptoms of PHI:**
• natural AIDS incubation time (10 years in median)
• dependent on two unknown parameters that represent uptake of routine testing and onset of HIV symptoms that occur towards the end of the incubation period

Two unknown parameters and the annual HIV incidence were estimated by using respectively the Newton-Raphson method and the expectation-maximization-smoothing algorithm.

Interventional study conducted in 29 EDs of the metropolitan Paris region

Background: To lower the number of undiagnosed infections and to improve early detection, international health agencies have promoted nontargeted human immunodeficiency virus (HIV) screening in health care settings, including emergency departments (EDs). This strategy remains controversial and has yet to be tested on a large scale. We assessed the public health impact of nontargeted HIV–rapid test (RT) screening among ED patients in the metropolitan area of Paris (11.7 million inhabitants), where half of France's new HIV cases are diagnosed annually.

Methods: During a randomly assigned 6-week period for each of the 29 participating EDs, 18- to 64-year-old patients who were able to provide consent for HIV testing were offered a fingerstick whole-blood HIV RT. Main outcome measures were the number of patients tested for HIV and their characteristics vs those of the general metropolitan Paris population and the proportion of newly diagnosed HIV-positive patients among those tested and their characteristics vs those from the national HIV case surveillance.

Results: Among 138 691 visits, there were 78 411 eligible patients, 20 962 of whom (27.0%) were offered HIV RT; 13 229 (63.1%) accepted testing and 12 754 (16.3%) were tested. The ED patients' characteristics reflected the general population distribution. Eighteen patients received new HIV diagnoses (0.14%; 95% confidence interval, 0.08%-0.22%). Like national HIV case surveillance patients, they belonged to a high-risk group (n=17), were previously tested (n=12), and were either symptomatic or had a CD4 lymphocyte count lower than 350/μL, suggesting late-stage infections (n=8); 12 patients were linked to care.

Conclusions: Nontargeted HIV testing in EDs was feasible but identified only a few new HIV diagnoses, often at late stages, and, unexpectedly, most patients belonged to a high-risk group. Our findings do not support the implementation of nontargeted screening of the general population in EDs.

d'Almeida KW *et al.* (2012) Modest Public Health Impact of Nontargeted Human Immunodeficiency Virus Screening in 29 Emergency Departments. *Arch Intern Med*, 172:12-20.

Interventional study conducted in 29 EDs of the metropolitan Paris region

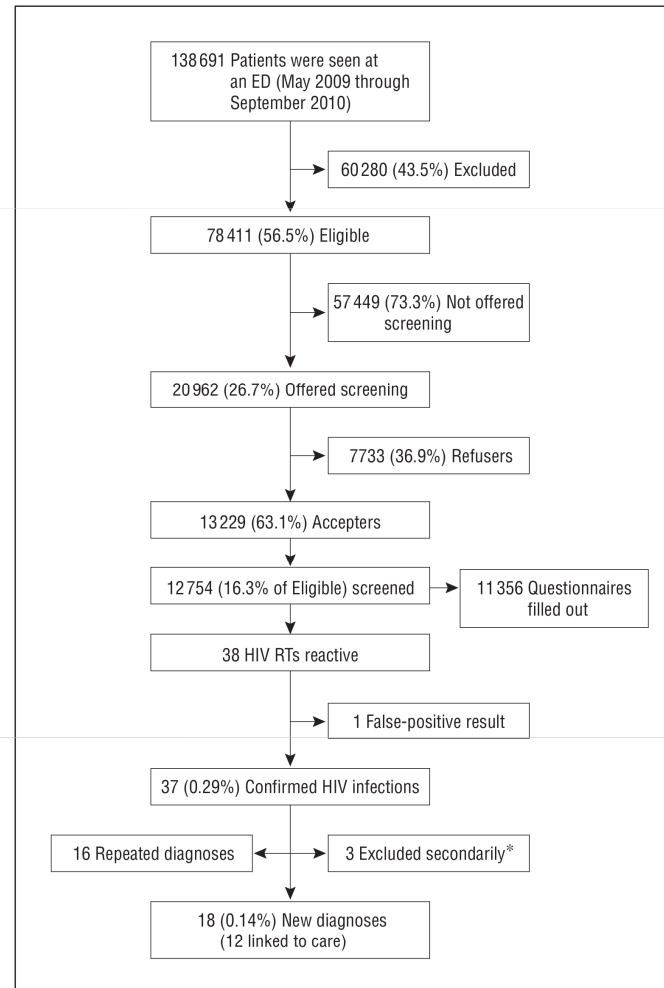**Figure.** Patient flow diagram. *Patients who were excluded because they were unable to give informed consent when human immunodeficiency virus (HIV) rapid tests (RTs) were performed (ordered for diagnostic purposes by emergency department [ED] physicians).

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Interventional study conducted in 29 EDs of the metropolitan Paris region

Table 1. Characteristics of Patients Who Were Tested for HIV in EDs and Who Completed Questionnaires Compared With a Reference General Population

Variable	ED-Tested Patients, No. (%) [95% CI] (n=11 356)[a]	General Population, %[b]
Sex		(1)[b]
Male	5928 (52.2) [51.3-53.1]	49.0
Female	5428 (47.8) [46.9-48.7]	51.0
Country of birth		(1)[b]
France	8666 (76.3) [75.5-77.1]	73.8
Born abroad	2690 (23.7) [22.9-24.5]	26.2
Sub-Saharan Africa	898 (7.9) [7.4-8.4]	6.6
Previous HIV test reported		(1)[b]
No	4860 (42.8) [41.8-43.7]	48.2
Yes in the past 5 y	4508 (39.7) [38.8-40.6]	29.6
Yes >5 y ago	1988 (17.5) [16.8-18.2]	22.2
Self-perceived HIV risk vs general population		(2)[b]
More risk	545 (4.8) [4.4-5.2]	4.0
Same risk	3562 (31.4) [30.5-32.2]	39.4
Less risk	2522 (22.2) [21.4-23.0]	42.2
No risk	2044 (18.0) [17.2-18.7]	14.4
Do not know	2683 (23.6) [22.8-24.5]	NA[c]
>1 Sexual partner during last 12 mo		(3)[b]
Among women	961 (17.7) [16.7-18.8]	13.8
Among men	1334 (22.5) [21.4-23.6]	22.1
Same-sex partner		(3)[b]
Among women	227 (4.2) [3.6-4.7]	4.0
Among men	268 (4.5) [3.9-5.1]	4.1

Abbreviations: CI, confidence interval; EDs, emergency departments; HIV, human immunodeficiency virus; MSM, men who have sex with men; NA, not available.

[a] Multiple imputation was used to estimate missing data from the questionnaires.

[b] Reference data for the metropolitan Paris region population was taken from 3 sources: (1) French national population census of 2006; (2) Knowledge, Attitudes, Behaviors, and Practice relating to AIDS in France (2004)[24]; and (3) Context of Sexuality in France (2004).[25]

[c] This response was NA in the questionnaire used to obtain the reference data.

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Interventional study conducted in 29 EDs of the metropolitan Paris region

Table 3. Proportion of New HIV Diagnoses in EDs According to Risk Group

Risk Group	New HIV Diagnoses	
	No.	No. (%) [95% CI]
All	18	12 754 (0.14) [0.08-0.22]
Heterosexuals born in sub-Saharan Africa	10	890 (1.12) [0.54-2.08]
Men	3	444 (0.68) [0.14-1.96]
Women	7	446 (1.57) [0.63-3.20]
Other heterosexuals born abroad	1	1768 (0.06) [0.001-0.31]
French heterosexuals	0	8430
MSM	7	268 (2.61) [1.06-5.31]

Abbreviations: HIV, human immunodeficiency virus; EDs, emergency departments; MSM, men who have sex with men.

d'Almeida KW *et al.* (2012) Modest Public Health Impact of Nontargeted Human Immunodeficiency Virus Screening in 29 Emergency Departments. *Arch Intern Med*, 172:12-20.

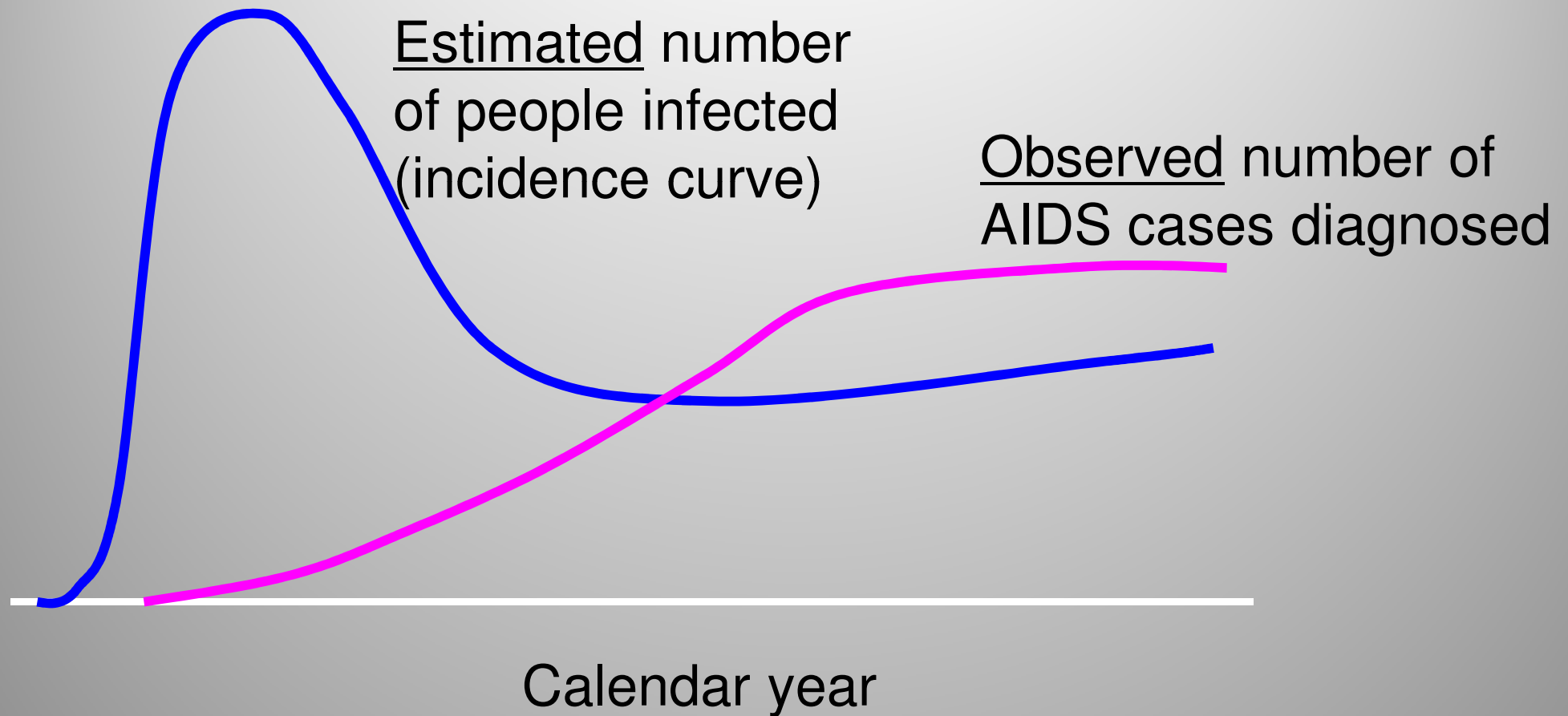# Interventional study conducted in 29 EDs of the metropolitan Paris region

Table 2. Characteristics of the 18 Patients With New HIV Diagnoses in the ED

Patient No./ Sex/Age, y	Country/ Region of Birth	Previous HIV Test (Year)	HIV-Related Symptoms at Presentation	Linked to Care[a]	Transmission Category	CD4 Lymphocyte Count, /μL
1/M/44	France	Yes (2008)	No	Yes	MSM	289
2/M/30	France	Yes (2007)	No	Yes	MSM	462
3/M/36	France	Yes (2010)	Fatigue, facial Kaposi sarcoma	Yes, hospitalized	MSM	27
4/M/25	France	Yes	No	Yes	MSM	532
5/M/18	France (Caribbean)	No	Fever, adenopathies, and pharyngitis (HIV primo-infection)	Yes, hospitalized	MSM	190
6/M/40	North Africa	Yes (2009)	No	Yes	MSM	688
7/M/29	Sub-Saharan Africa	Yes (2007)	Anal condyloma	Yes	MSM	217
8/M/38	Sub-Saharan Africa	Yes (2008)	Fever, weight loss	Yes, hospitalized	Heterosexual	6
9/M/43	Sub-Saharan Africa	Yes (2005)	No	Yes	Heterosexual	370
10/M/23	Sub-Saharan Africa	Yes (2009)	No	No	Heterosexual	NA
11/M/27	North Africa	Yes (2009)	No	No	Heterosexual	NA
12/F/37	Sub-Saharan Africa	No	*Candida* esophagitis	Yes, hospitalized	Heterosexual	53
13/F/27	Sub-Saharan Africa	Yes (2008)	Fatigue, cough	Yes	Heterosexual	207
14/F/29	Sub-Saharan Africa	NA	Headaches	Yes	Heterosexual	42
15/F/43	Sub-Saharan Africa	NA	No	No	Heterosexual	NA
16/F/52	Sub-Saharan Africa	NA	No	No	Heterosexual	NA
17/F/28	Sub-Saharan Africa	Yes (2007)	Zona	No	Heterosexual	NA
18/F/24	Sub-Saharan Africa	No	No	No	Heterosexual	NA

Abbreviations: ED, emergency department; HIV, human immunodeficiency virus; MSM, men who have sex with men; NA, not available.
[a] Defined as completing the first infectious disease follow-up visit after preliminary diagnosis in the ED.

d'Almeida KW *et al.* (2012) Modest Public Health Impact of Nontargeted Human Immunodeficiency Virus Screening in 29 Emergency Departments. *Arch Intern Med*, 172:12-20.

Original "back-calculation" approach, before availability of treatment

Estimated number
of people infected
(incidence curve)

Observed number of
AIDS cases diagnosed

Calendar year

From the incidence curve it was possible to work out the number estimated to be living with HIV by subtracting the number of deaths

Phillips, A. Estimation of the number of people with undiagnosed HIV infection in a country. HIV in Europe (2009), Stockholm.

Revised back-calculation approach

Question changes...

from: infection   ⟶   AIDS

How many people must be infected, and when must they have been infected, in order to produce the numbers of new AIDS we have observed ?

to: infection   ⟶   HIV diagnosis

How many people must be infected, and when must they have been infected, and what must the probability of getting diagnosed have been, in order to produce the numbers of new HIV diagnoses we have observed ?

Phillips, A. Estimation of the number of people with undiagnosed HIV infection in a country. HIV in Europe (2009), Stockholm.

Methods to estimate the size of the hidden HIV epidemic

❖ Direct method

❖ Back-calculation method

❖ Methods based on CD4 cell count and simultaneous HIV/AIDS diagnosis
- a proportion of the undiagnosed population is diagnosed with HIV infection and AIDS at the same time.
- the incidence of AIDS at a given CD4 cell count can be estimated from cohort studies.

Working Group on Estimation of HIV Prevalence in Europe (2011) HIV in hiding: methods and data requirements for the estimation of the number of people living with undiagnosed HIV. *AIDS* 25, 1017-1023.

Approach based on reported simultaneous HIV/AIDS cases

1000 people undiagnosed
CD4 count < 200

Phillips, A. Estimation of the number of people with undiagnosed HIV infection in a country. HIV in Europe (2009), Stockholm.

Approach based on reported simultaneous HIV/AIDS cases

1000 people undiagnosed
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Rate of development of AIDS for people with CD4 count < 200 ~ 25 per 100 person years

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250 people expected to develop AIDS over a 1 year period....

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Approach based on reported simultaneous HIV/AIDS cases

1000 people undiagnosed
CD4 count < 200

Rate of development of AIDS for people with CD4 count < 200 ~ 25 per 100 person years

250 people expected to develop AIDS over a
1 year period…..and hence present with simultaneous HIV/AIDS

Phillips, A. Estimation of the number of people with undiagnosed HIV infection in a country. HIV in Europe (2009), Stockholm.

Approach based on reported simultaneous HIV/AIDS cases

So if we observe 250 cases of simultaneous HIV/AIDS in people with CD4 count < 200 in a year then …..

Phillips, A. Estimation of the number of people with undiagnosed HIV infection in a country. HIV in Europe (2009), Stockholm.
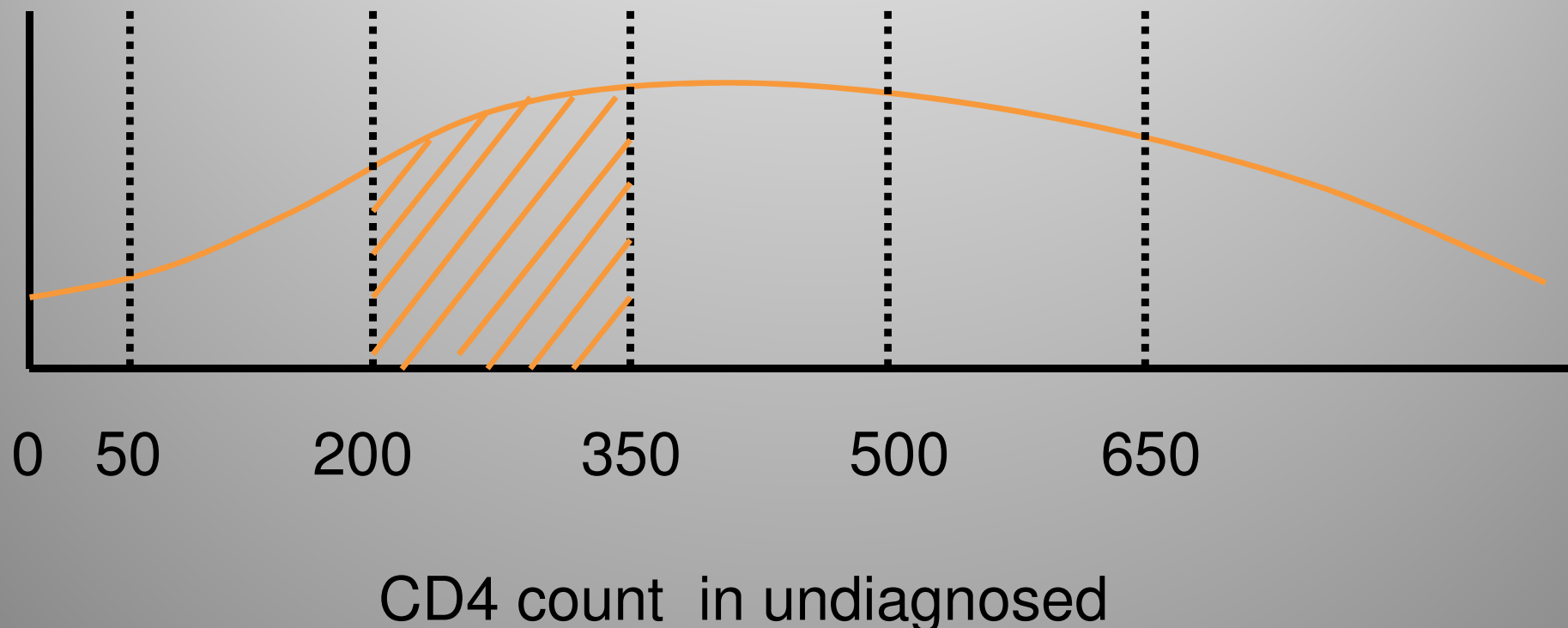
Approach based on reported simultaneous HIV/AIDS cases

…this implies there are 1000 people with undiagnosed HIV and CD4 count < 200

So if we observe 250 cases of simultaneous HIV/AIDS in people with CD4 count < 200 in a year then……..

Phillips, A. Estimation of the number of people with undiagnosed HIV infection in a country. HIV in Europe (2009), Stockholm.

Approach based on reported simultaneous HIV/AIDS cases

With knowledge of the distribution of CD4 count in undiagnosed people can use this approach to estimate total number of undiagnosed

CD4 count in undiagnosed

Phillips, A. Estimation of the number of people with undiagnosed HIV infection in a country. HIV in Europe (2009), Stockholm.
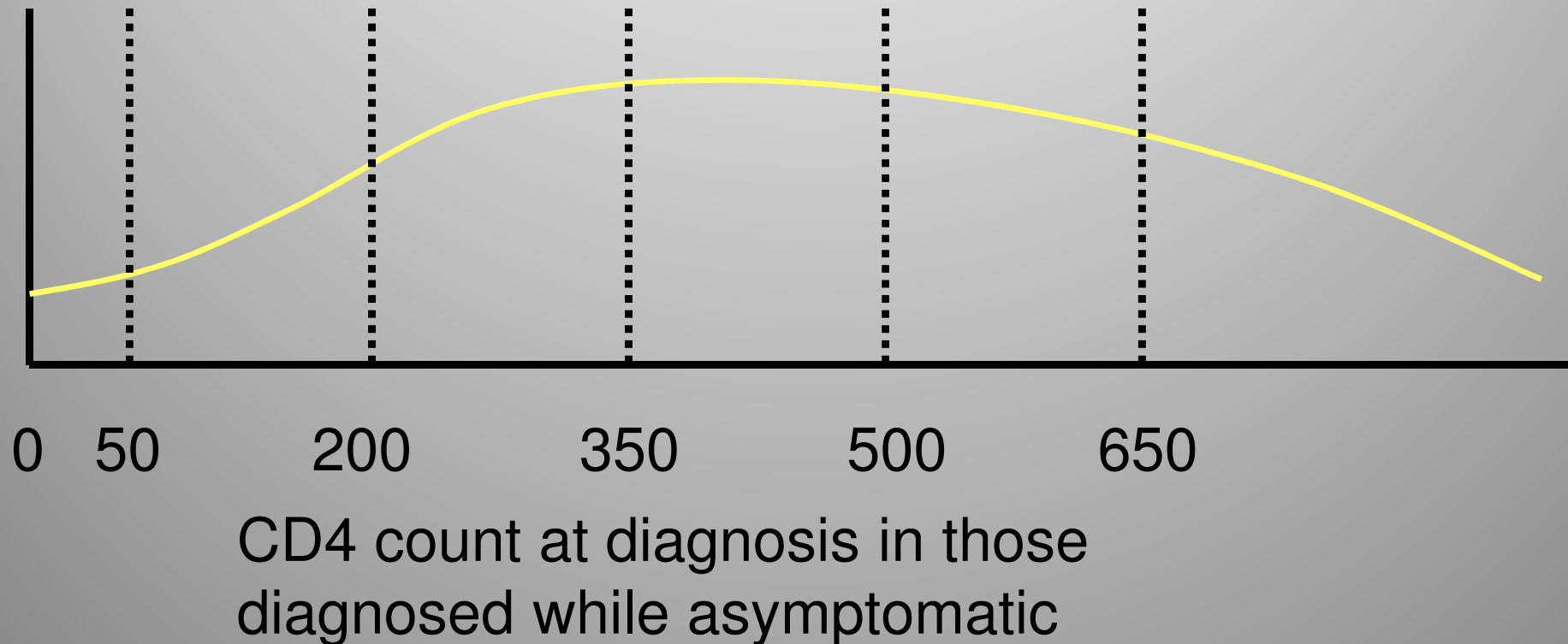
Approach based on reported simultaneous HIV/AIDS cases

With knowledge of the distribution of CD4 count in undiagnosed people can use this approach to estimate total number of undiagnosed

CD4 count at diagnosis in those diagnosed while asymptomatic

0   50   200   350   500   650

Phillips, A. Estimation of the number of people with undiagnosed HIV infection in a country. HIV in Europe (2009), Stockholm.
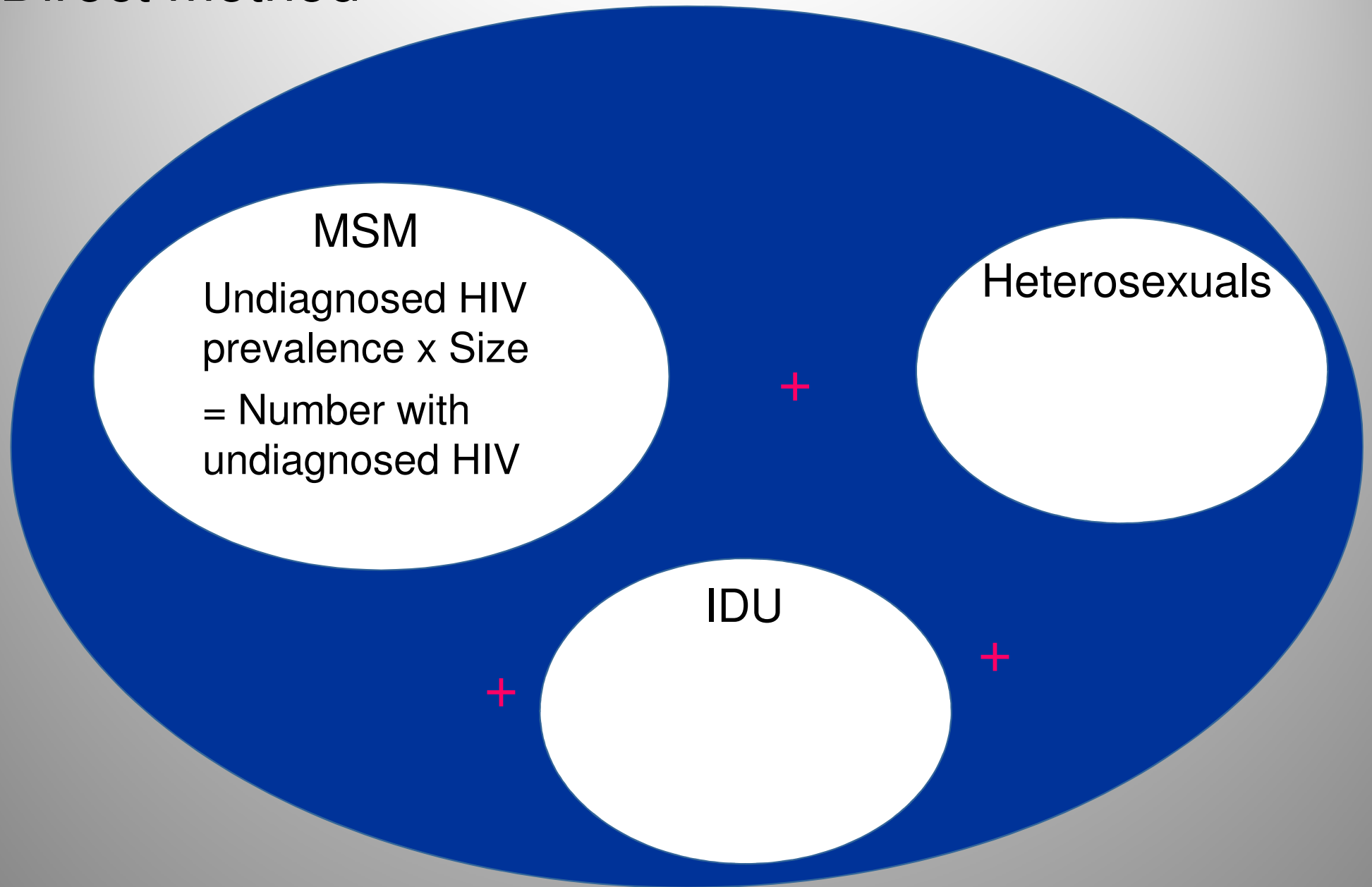
Approach based on reported simultaneous HIV/AIDS cases

Issues to consider

- Distribution of CD4 count in undiagnosed

- Under-diagnosis and under-reporting of AIDS

Phillips, A. Estimation of the number of people with undiagnosed HIV infection in a country. HIV in Europe (2009), Stockholm.

Direct method

MSM

Undiagnosed HIV prevalence x Size

= Number with undiagnosed HIV

Heterosexuals

IDU

+ + +

Phillips, A. Estimation of the number of people with undiagnosed HIV infection in a country. HIV in Europe (2009), Stockholm.

Approach based on prevalence surveys

Issues to consider

What risk categories to divide population into ?

How to estimate the size of each category ?

What prevalence to assume for those not falling into any of the selected 'risk' categories ?

Matching the populations sampled in the prevalence surveys with the populations for which size is estimated

Phillips, A. Estimation of the number of people with undiagnosed HIV infection in a country. HIV in Europe (2009), Stockholm.

Is prevalence survey based on representative sample of the risk group of the size estimated ?

Sexual risk activity in MSM

HIV prevalence

Low

High

Level of risk activity

Phillips, A. Estimation of the number of people with undiagnosed HIV infection in a country. HIV in Europe (2009), Stockholm.