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Global health: infectious disease and AIDS: history and progression

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November 2012

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Learning outcomes

To define and distinguish

- incidence
- prevalence
- mortality

To describe the global epidemiology of HIV/AIDS

To reflect on the dramatic impact of an emerging infectious disease

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Manchester, 1959

David Carr admitted to hospital

age 25

symptoms

- tired
- night sweats
- breathless
- loss of weight

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Mystery illness

Doctors could find no cause for his condition, and continued testing and trying various treatments

He died after 20 weeks in hospital

The post mortem showed:

- *Pneumocystis carinii* pneumonia (PCP)
- cytomegalovirus (CMV) infection

These conditions had never been previously reported in adults

The case was reported as a rare condition and never referred to for more than 20 years

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Los Angeles, 1980

a previously fit and healthy debilitated 33 year old man was admitted to hospital with *Pneumocystis carinii* pneumonia

He died a few months later.

The doctor said at the time,
"This is a red flag for something. This patient has no prior history of illness that should predispose him to PCP. It makes no sense".

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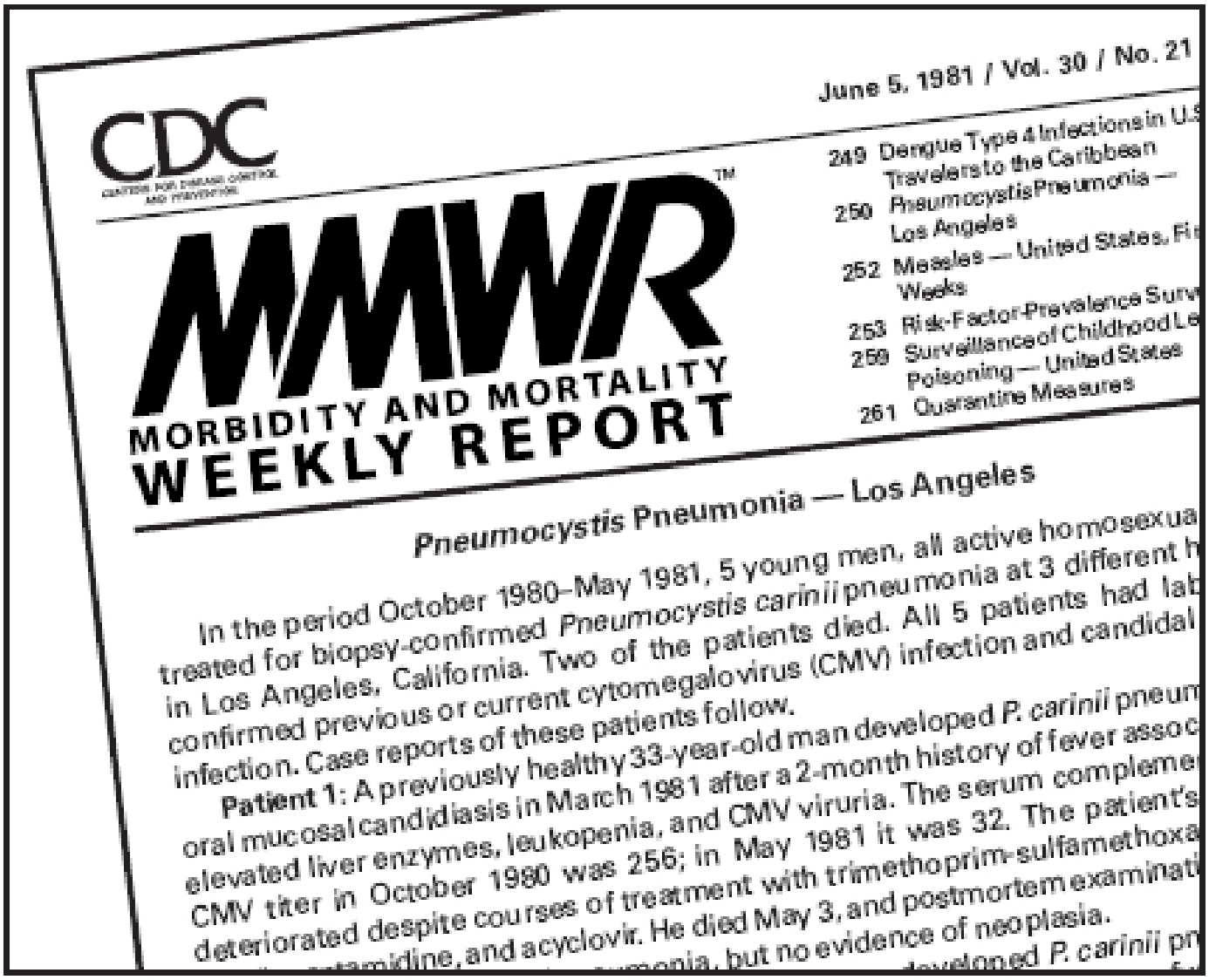
“Gay Related Immune Deficiency” - G.R.I.D.

By April 1981 the doctor had seen 5 men with a similar illness.

They were all in their early 30s, white and gay.

By June a report was published about this curious new health problem among homosexual men

FIGURE. *MMWR* report on *Pneumocystis* pneumonia in five previously healthy young men in Los Angeles — June 5, 1981



June 5, 1981 / Vol. 30 / No. 21

CDC

MMWR™

MORBIDITY AND MORTALITY WEEKLY REPORT

Pneumocystis Pneumonia — Los Angeles

In the period October 1980–May 1981, 5 young men, all active homosexua treated for biopsy-confirmed *Pneumocystis carinii* pneumonia at 3 different h in Los Angeles, California. Two of the patients died. All 5 patients had lab confirmed previous or current cytomegalovirus (CMV) infection and candidal infection. Case reports of these patients follow.

Patient 1: A previously healthy 33-year-old man developed *P. carinii* pneum oral mucosal candidiasis in March 1981 after a 2-month history of fever assoc elevated liver enzymes, leukopenia, and CMV viruria. The serum compleme CMV titer in October 1980 was 256; in May 1981 it was 32. The patient's deteriorated despite courses of treatment with trimethoprim-sulfamethoxa pentamidine, and acyclovir. He died May 3, and postmortem examinati pneumonia, but no evidence of neoplasia. developed *P. carinii* pn

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Initial hypotheses

An environmental factor?

- bad batch of drugs
- inhaled nitrates (poppers)

An infectious disease

- a new virus
- a strange combination of existing agents

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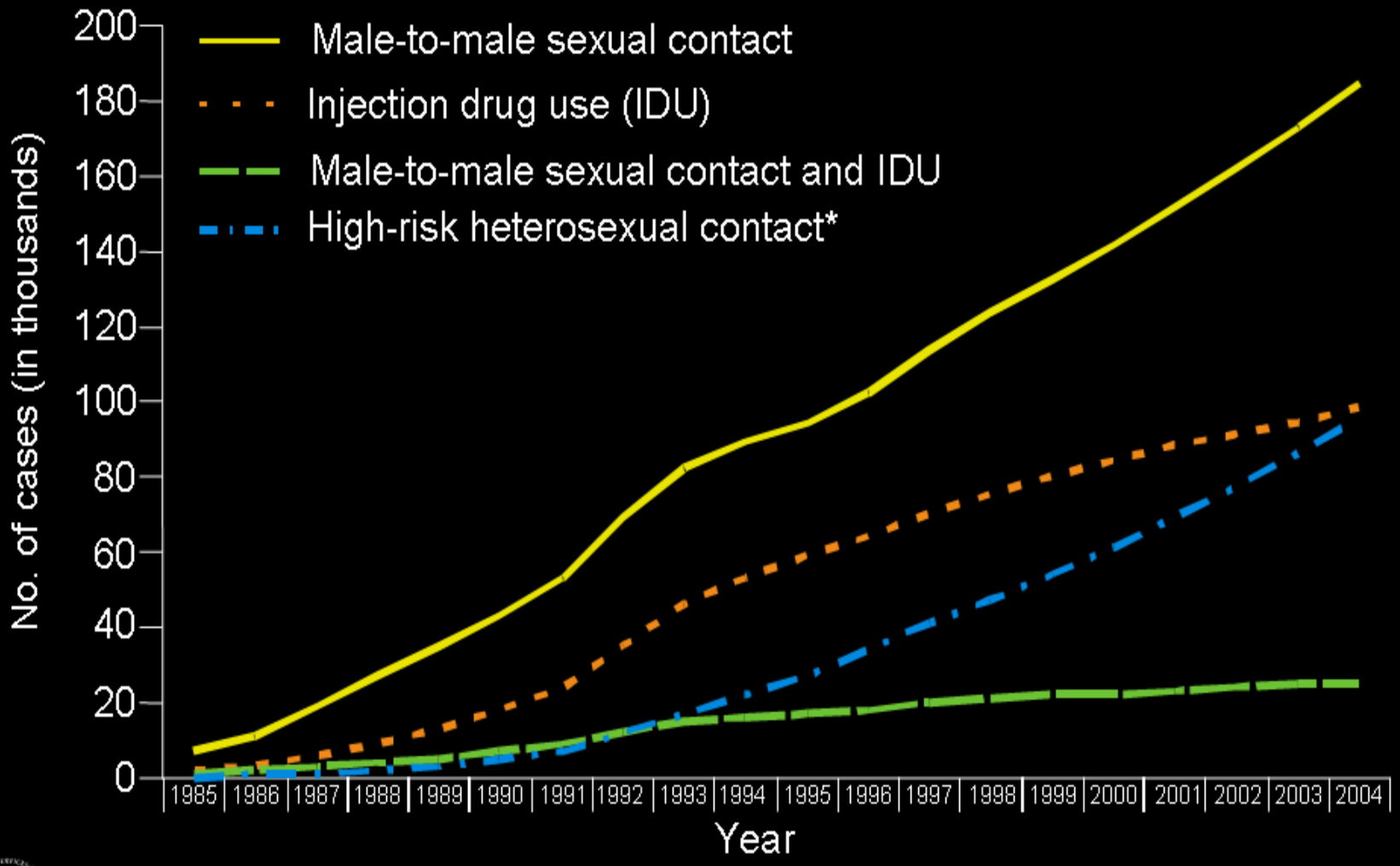
The growth of the epidemic in the USA

June 1981 - 5 cases of PCP
July 1981 - 26 cases of Kaposis Sarcoma
Dec 1981 - 180 cases
March 1982 - 285 cases
Jan 1983 - >1000 cases
1993 - 79,000 cases
2006 – 1.3 million people living with HIV (40,000 newly acquired)

Adults and Adolescents Living with AIDS by Transmission Category,1985-2004, United States



Note. Data have been adjusted for reporting delays and cases without risk factor information were proportionally redistributed.
* Heterosexual contact with a person known to have or at high risk for HIV infection.

http://www.youtube.com/watch?v=1LKJ5ZzzL0w&feature=related

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What has happened since?

Global disease

Transmission through body fluids: sexual contact , breast feeding or blood

90% of disease in developing countries

Research

- epidemiology (distribution)
- natural history
- treatment

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World Health Organization

UNAIDS

Over 7400 new HIV infections a day in 2007

- More than 96% new infections are in low and middle income countries
- About 1000 are in children under 15 years of age
- About 6300 are in adults aged 15 years and older of whom:
  - almost 50% are among women
  - about 45% are among young people (15-24)

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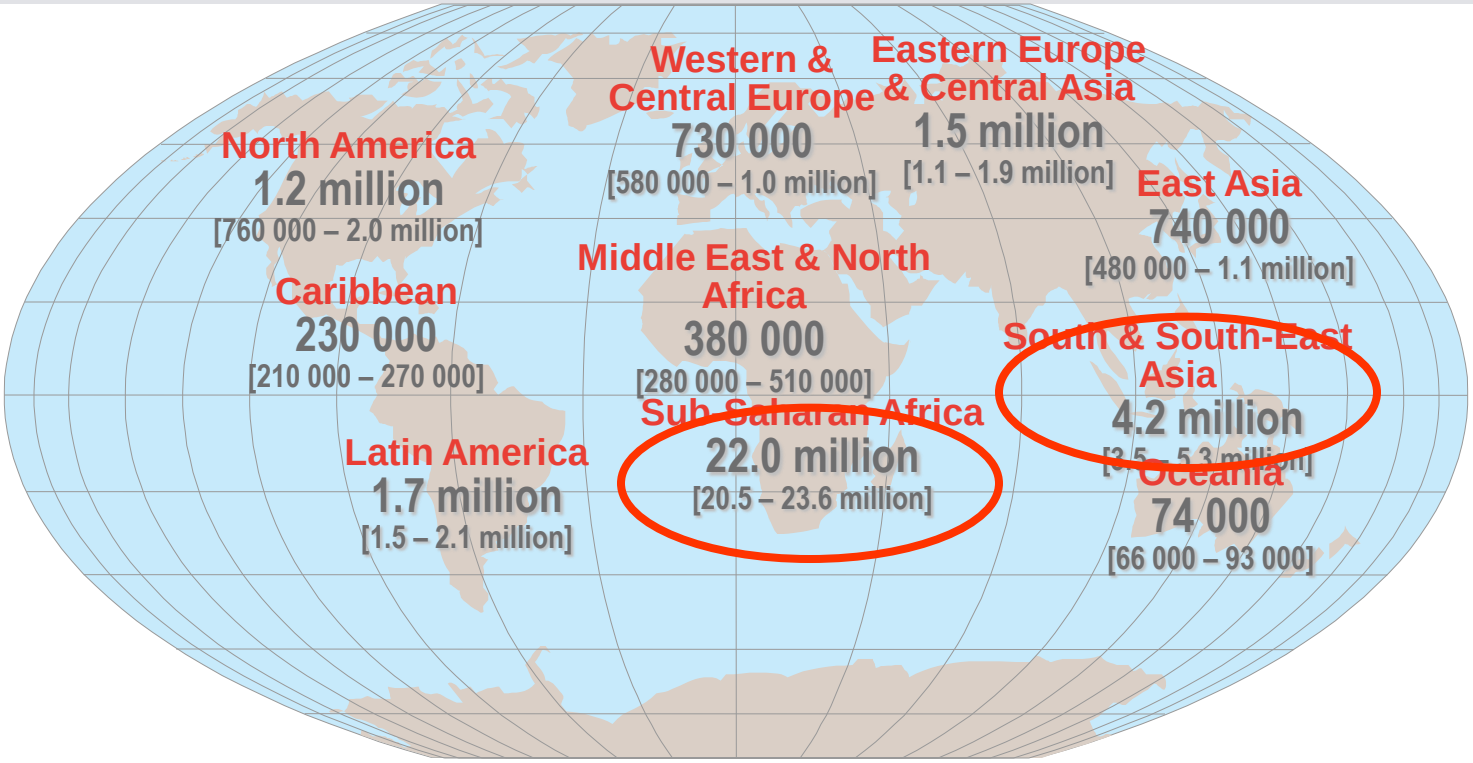
World Health Organization

UNAIDS

Adults and children estimated to be living with HIV, 2009



Total: 33 million (30 – 36 million)

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World Health Organization

UNAIDS

Global estimates for adults and children, 2009

- **People living with HIV** — **33** million [30 – 36 million]
- **New HIV infections in 2009** — **2.7** million [2.2 – 3.2 million]
- **Deaths due to AIDS in 2009** — **2.0** million [1.8 – 2.3 million]

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Prevalence

The frequency of a disease in a population at a point in time

$$= \frac{\text{number of cases in population}}{\text{number of people in population}}$$

- Prevalence measures burden of disease in a population
- It is useful for planning
- It can be used to compare burden of chronic disease between populations

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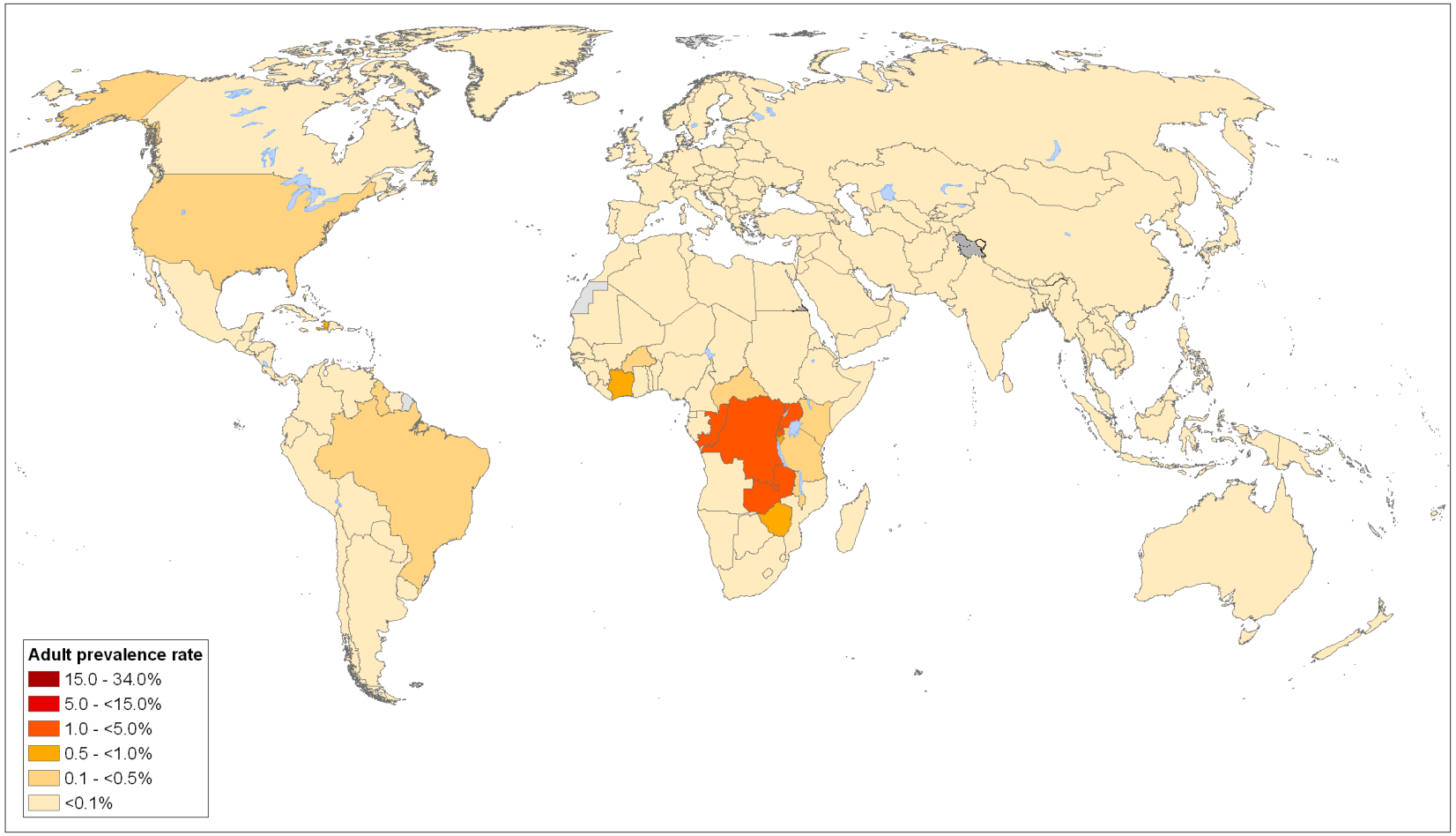
Global HIV prevalence in adults, 1985



UNAIDS/WHO, 2006

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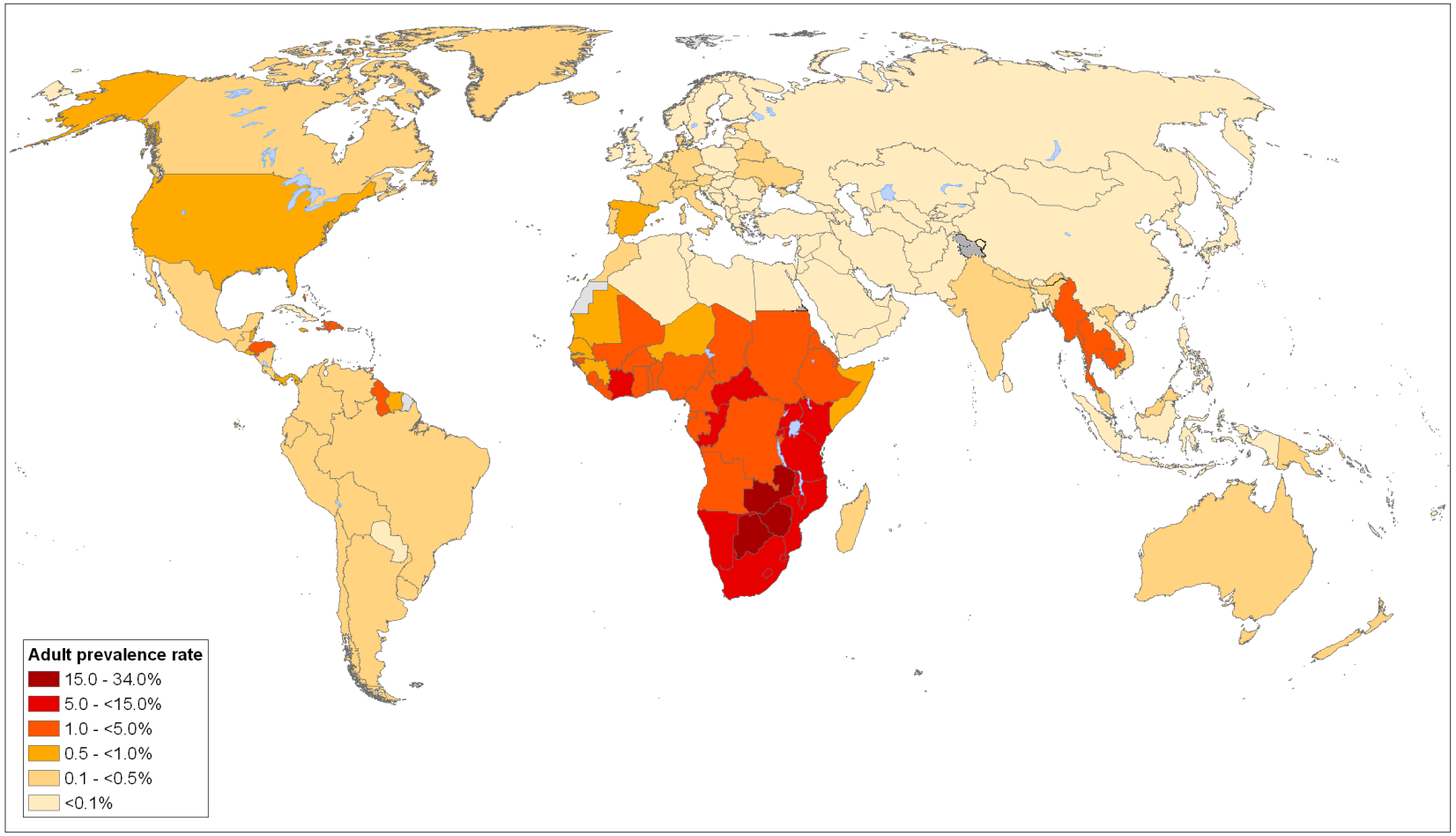
Global HIV prevalence in adults, 1995



UNAIDS/WHO, 2006

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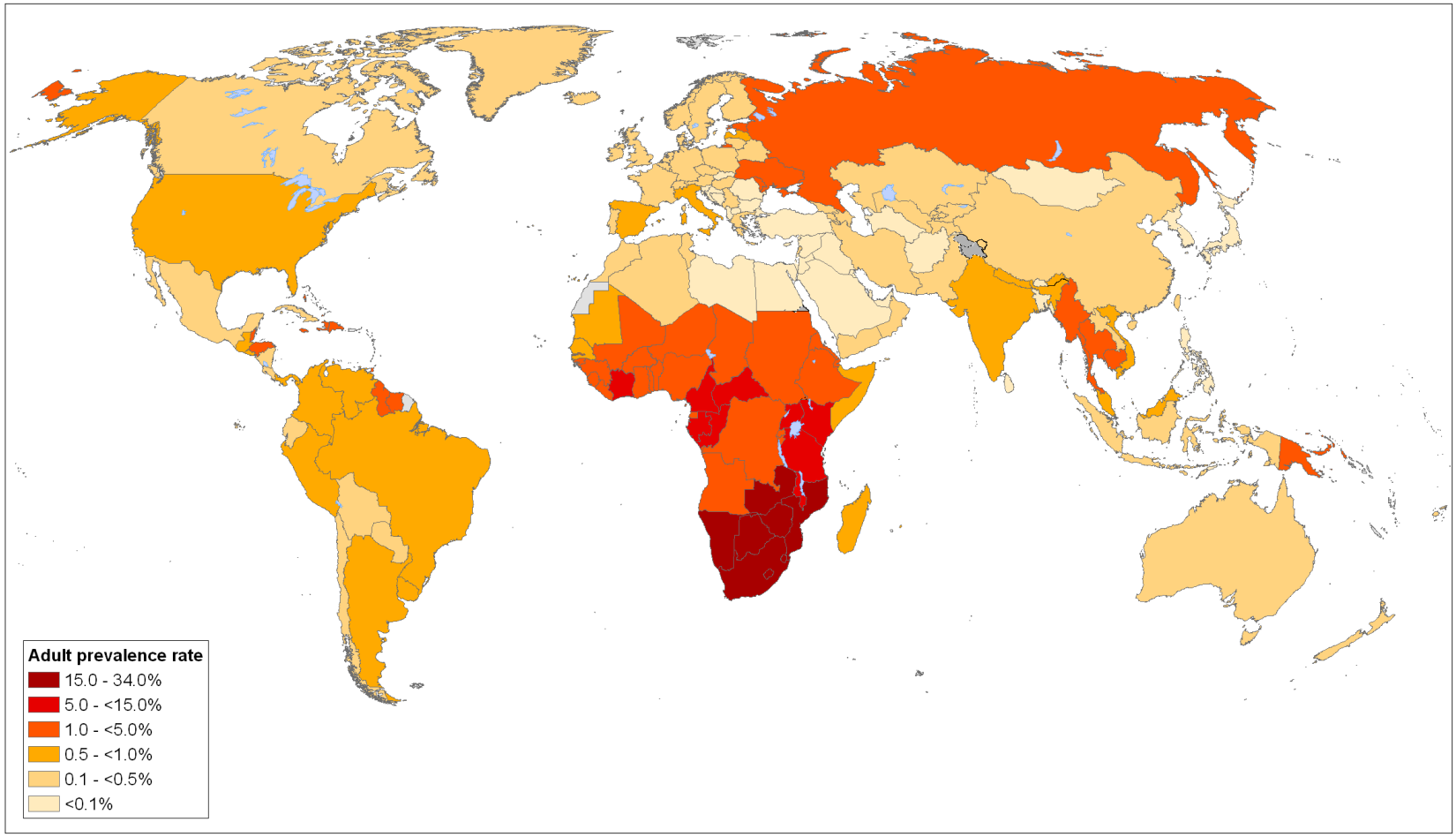
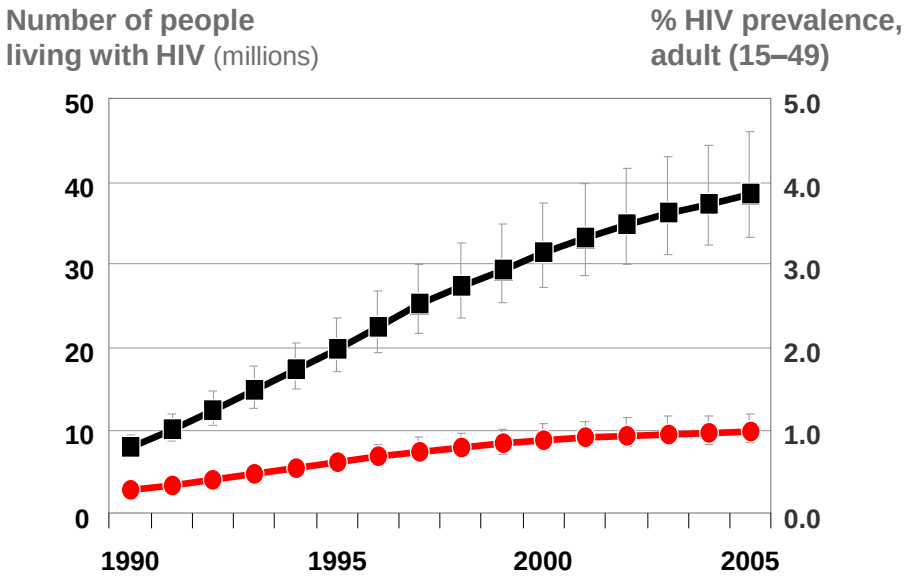
Global HIV prevalence in adults, 2005



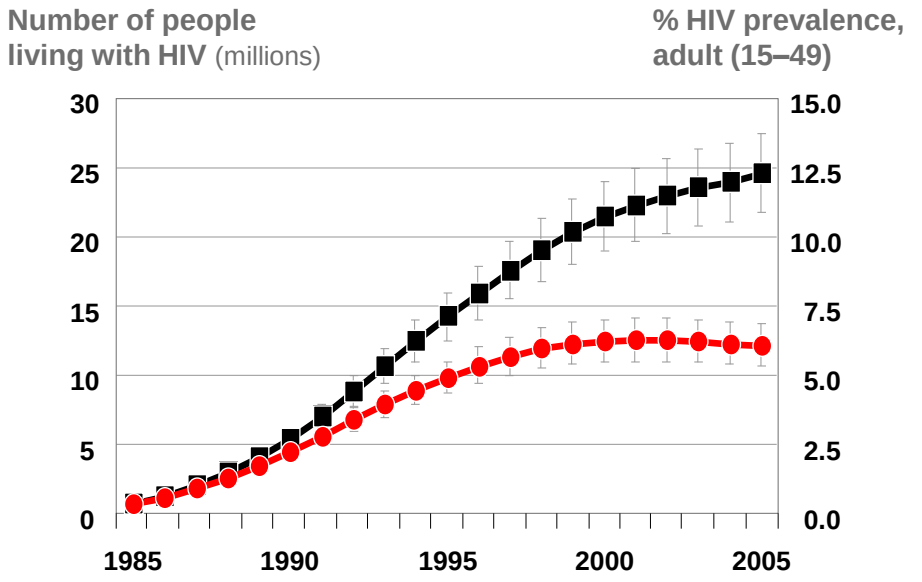
UNAIDS/WHO, 2006

Estimated number of people living with HIV, and adult HIV prevalence

Global HIV epidemic, 1990–2005*



HIV epidemic in sub-Saharan Africa, 1985–2005*



Number of people living with HIV

% HIV prevalence, adult (15-49)

This bar indicates the range around the estimate

*Even though the HIV prevalence rates have stabilized in sub-Saharan Africa, the actual number of people infected continues to grow because of population growth. Applying the same prevalence rate to a growing population will result in increasing numbers of people living with HIV.

Incidence

The number of new infections within a population over time

Incidence

Number of new cases of disease in a population over a given time

- cumulative incidence (risk)

$$\frac{\text{new cases of disease in a given time period}}{\text{number of disease free people at start of time period}}$$

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World Health Organization

UNAIDS

Estimated number of adults and children newly infected with HIV, 2007

Total: 2.7 million (2.2 – 3.2 million)

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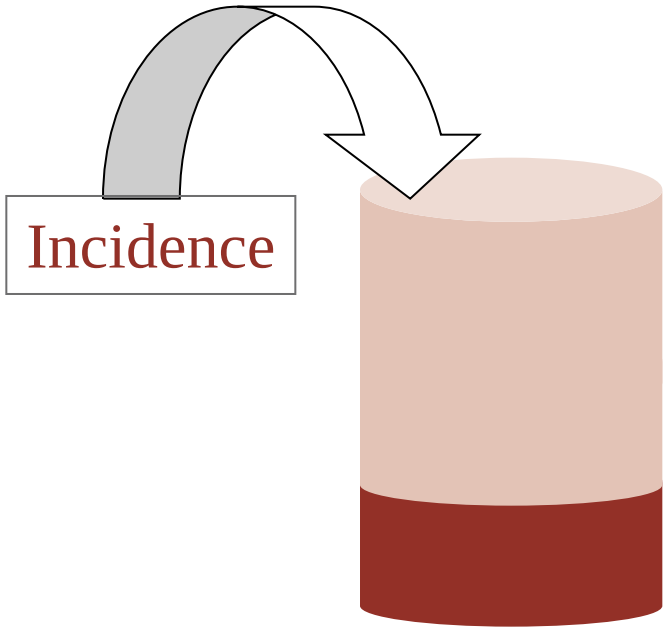
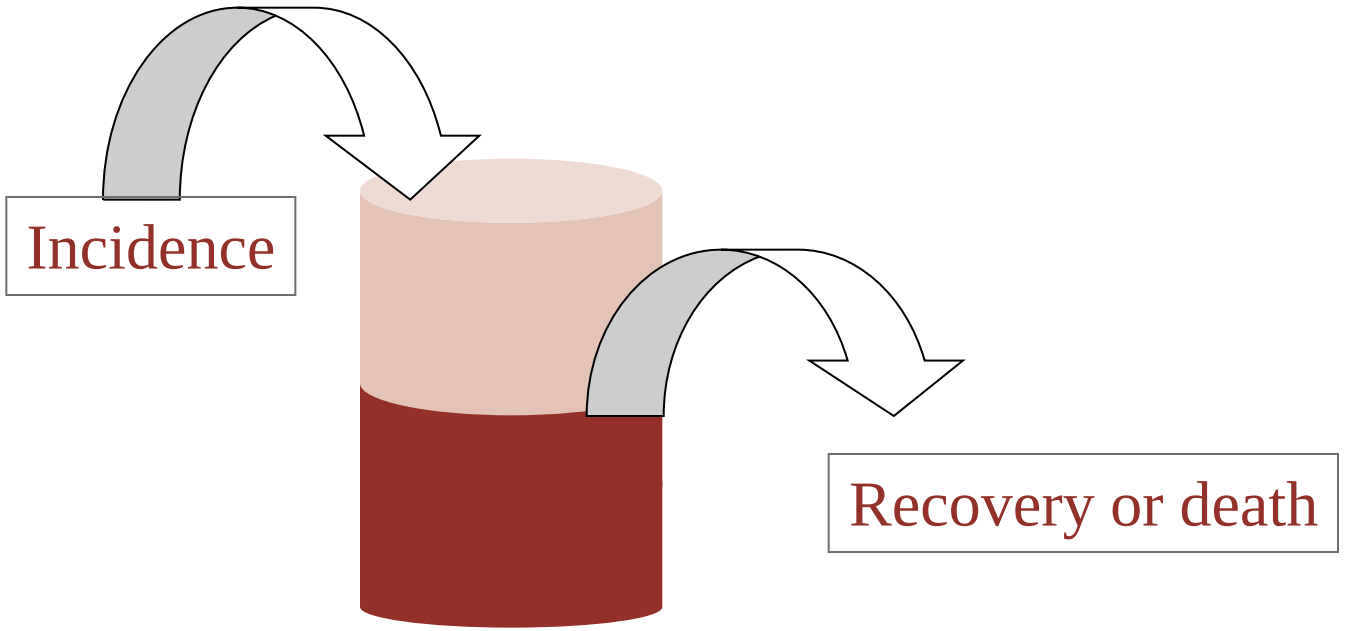
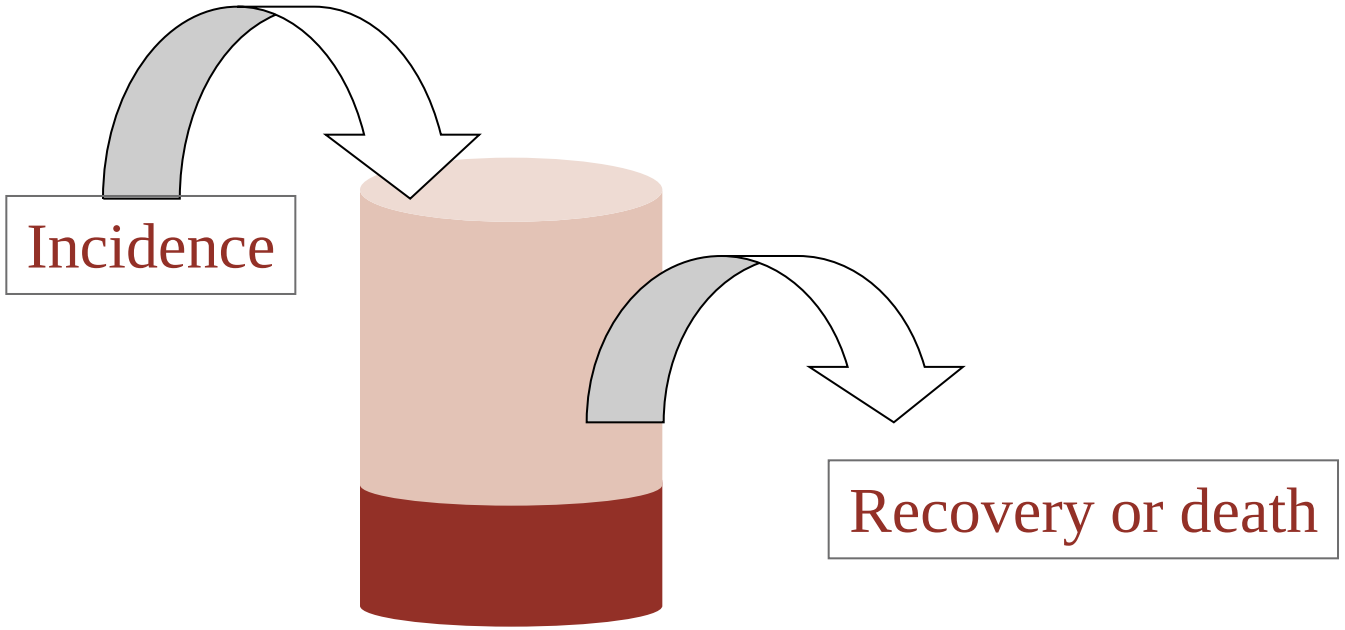
Relationship of prevalence and incidence



Relationship of prevalence and incidence



Relationship of prevalence and incidence



Prevalence = incidence x duration of infection

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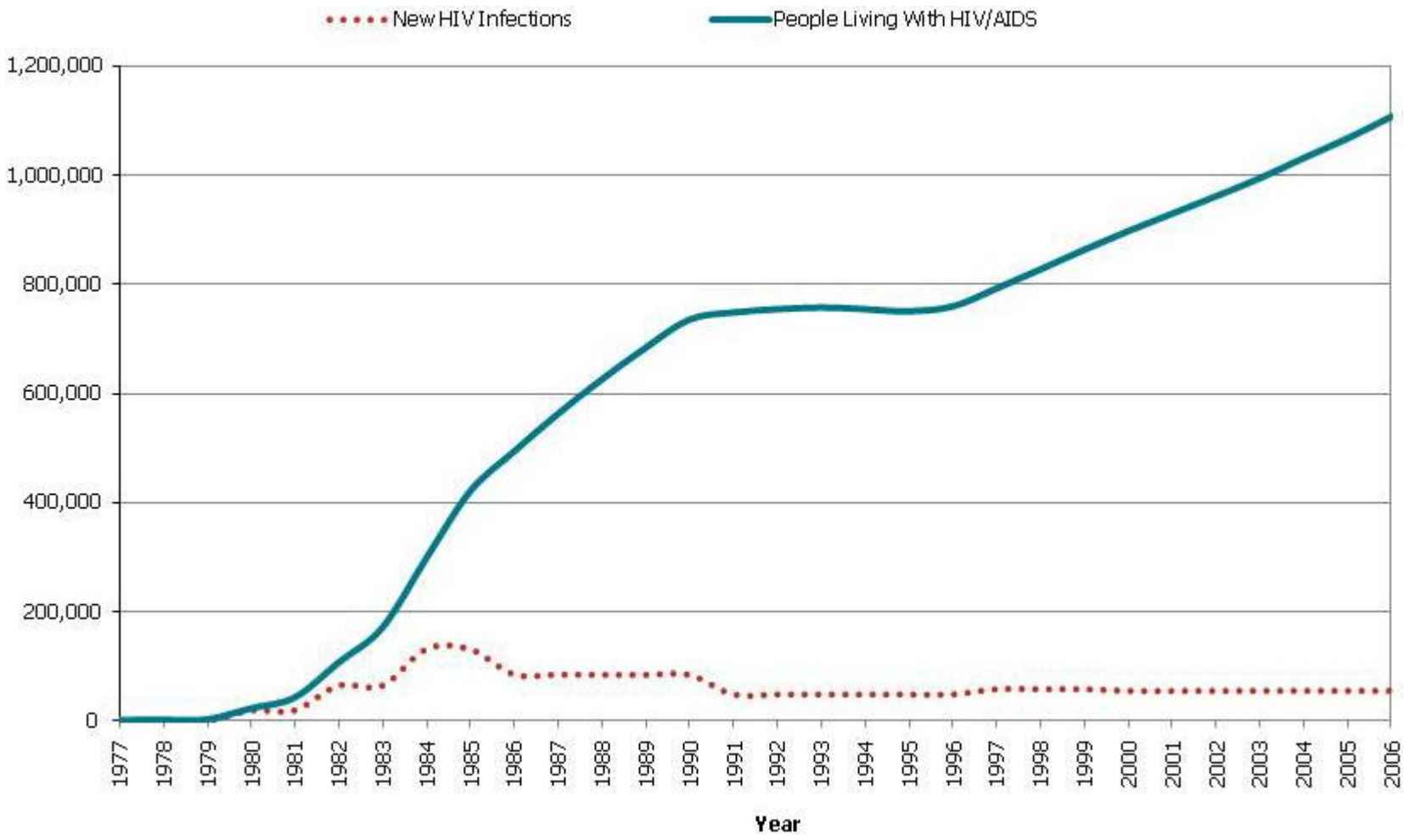
Incidence and prevalence of HIV in USA 1997-2006

Hall HI, Song R, Rhodes P, et al. Estimation of HIV Incidence in the US. *JAMA* 2008;300: 520–529.



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Mortality

Number of deaths from a disease in a population over a given time

$$= \frac{\text{Deaths from disease in a given time period}}{\text{population at start of time period}}$$

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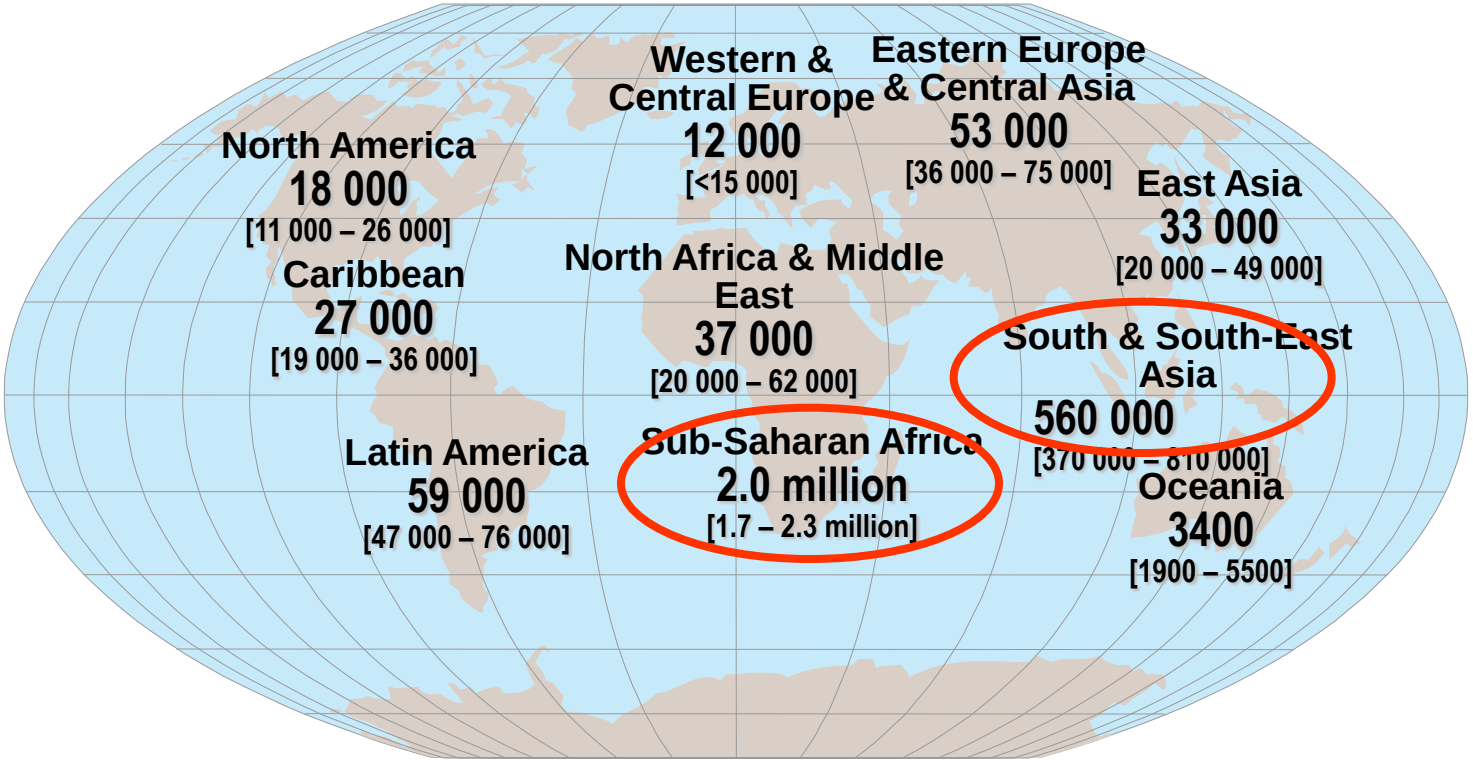
Estimated adult and child deaths from AIDS, 2005



Total: 2.8 (2.4 – 3.3) million

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Deaths due to HIV AIDS 2010

Since the beginning of the epidemic almost 60 million people have been infected with HIV

Estimated 25 million people have died from HIV related causes

2.7 million new infections/year (40% in ages 15-24 years)

2 million deaths/year

67% of all HIV cases are in Sub-Saharan Africa, 91% of all new infections in children are in SSA

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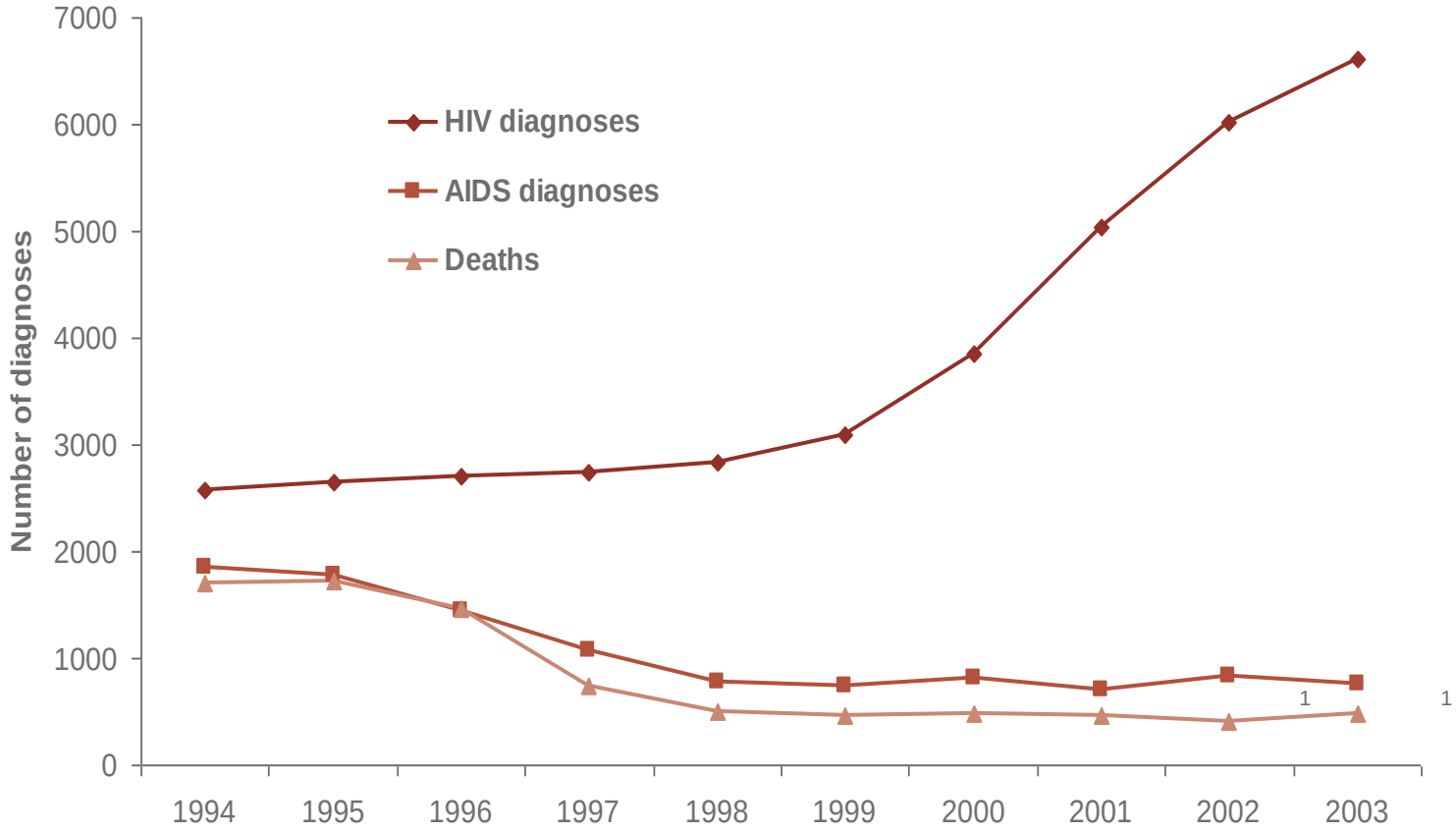
HIV and AIDS diagnoses and deaths in HIV-infected individuals by year of diagnosis, United Kingdom, 1994-2003



[1] Numbers will rise, for recent years, as further reports are received.

Data Source: HIV/AIDS reports. Reports received by the end of June 2004.

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What is it like to live in a high prevalence (26%) HIV area- Swaziland

http://www.youtube.com/watch?v=3r9jFwCyW6k

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Antiretroviral treatment (ART)

Its impact on mortality incidence and prevalence

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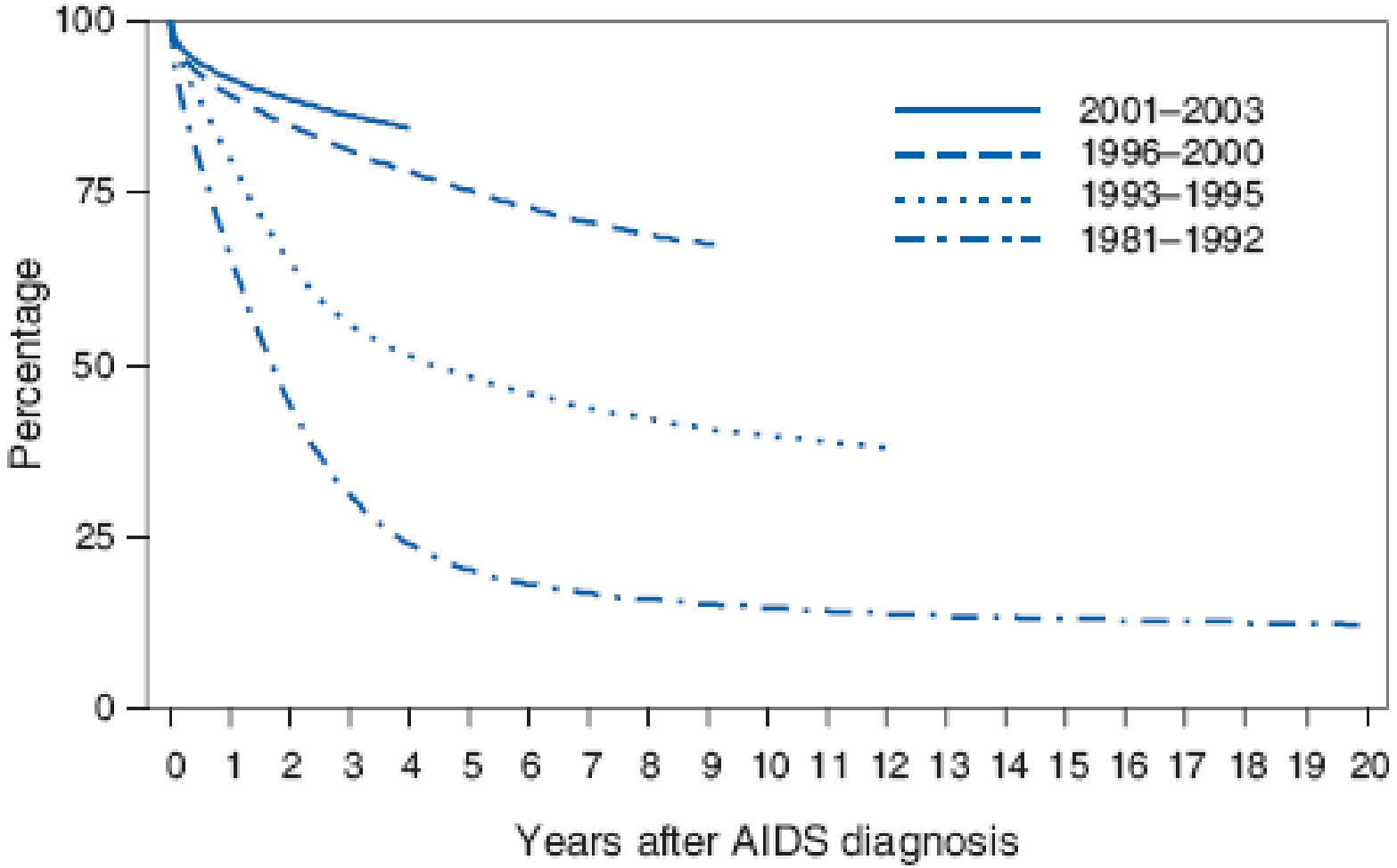
Antiretroviral treatment (ART) works!!

Haitian Patient, before and after Receiving Free Treatment for HIV Infection and Tuberculosis.

The photograph on the left was taken in March 2003, and that on the right in September 2003. Many impoverished patients in rural Haiti and Rwanda now receive comprehensive medical care through public–private partnerships.

FIGURE 2. Percentage of persons surviving through June 2005, by years after acquired immunodeficiency syndrome (AIDS) diagnosis cohorts during 1981–2003 and by year of diagnosis — United States



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Annual incidence 2.7 million
Annual mortality 2.8 million

If mortality = incidence the epidemic is stable

BUT

If we keep more people alive with ART then the mortality reduces and potentially people are alive longer

As mortality goes down more people are alive and live longer they can:

transmit virus to sexual partners and their babies and incidence may go up

prevalence increases as more cases are transmitted as well as people not dying

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How do we measure incidence

A measure of the number of new infections

What is the denominator?

How do we chose a sample of the denominator?

Need to know pervious uninfected individuals who BECOME infected in a given time period

- Need to serially repeat test
- Need a specific blood test that can not only identify those people who are infected but also tell if the infection is recent

•What confounds the measures?

- How many people CHOSE to accept a test
- How do we extrapolate the data we have to a whole population?
- Are the people we are testing representative of the whole population?

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2006 High Level Meeting on AIDS

2. Note with alarm that we are facing an unprecedented human catastrophe; that a quarter of a century into the pandemic, AIDS has inflicted immense suffering on countries and communities throughout the world; and that more than 65 million people have been infected with HIV, more than 25 million people have died of AIDS, 15 million children have been orphaned by AIDS and millions more made vulnerable, and 40 million people are currently living with HIV, more than 95 per cent of whom live in developing countries;

3. Recognize that HIV/AIDS constitutes a global emergency and poses one of the most formidable challenges to the development, progress and stability of our respective societies and the world at large, and requires an exceptional and comprehensive global response;

UN General Assembly, 2 June 2006

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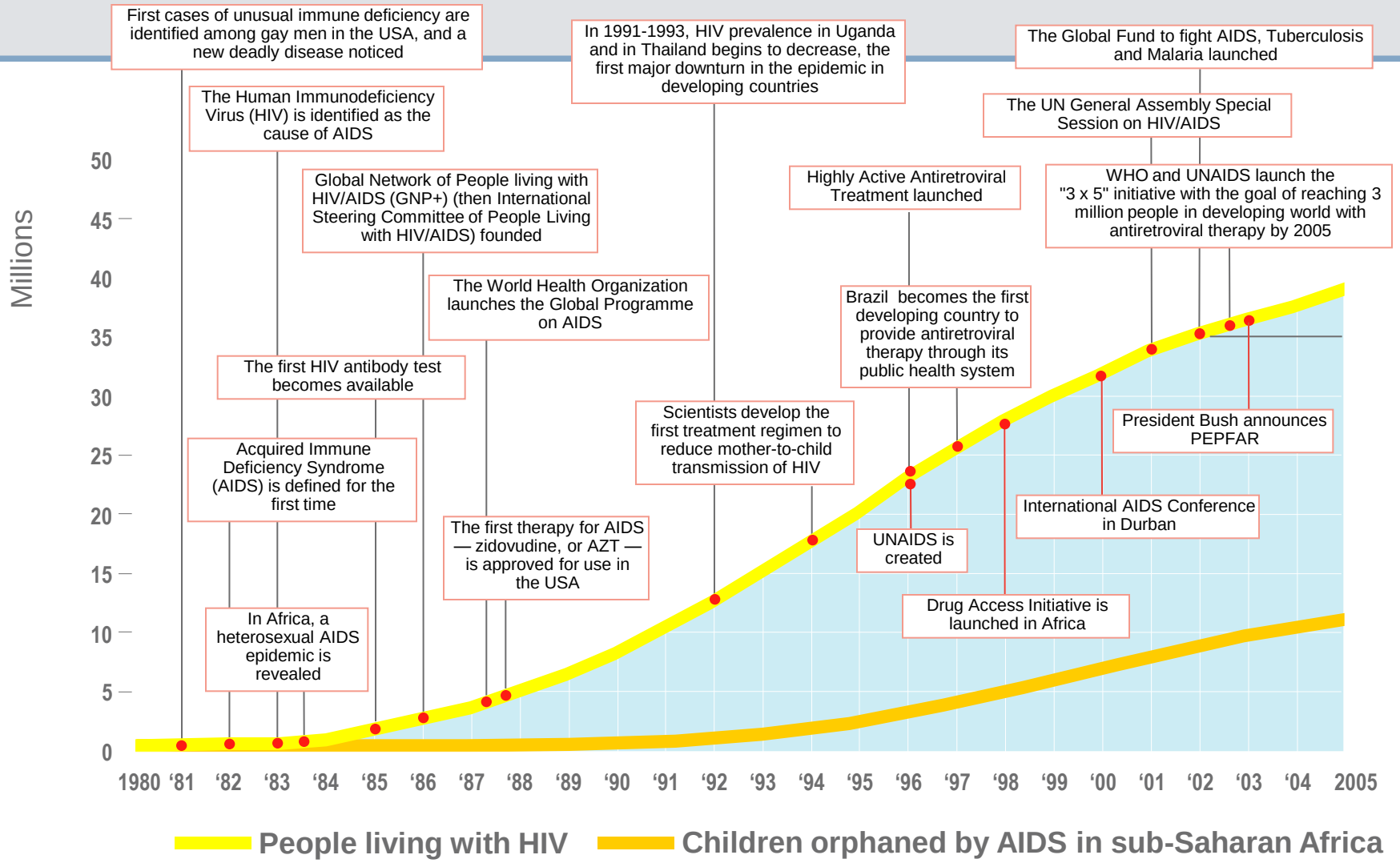
25 years of responding to AIDS



2006 Report on the global AIDS epidemic (UNAIDS, 2006)

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A world apart - 2005

USA

1.3 million with HIV

43,000 new cases

18,000 deaths

Mortality in people with HIV = 1.4% per year

Sub Saharan Africa

24.5 million with HIV

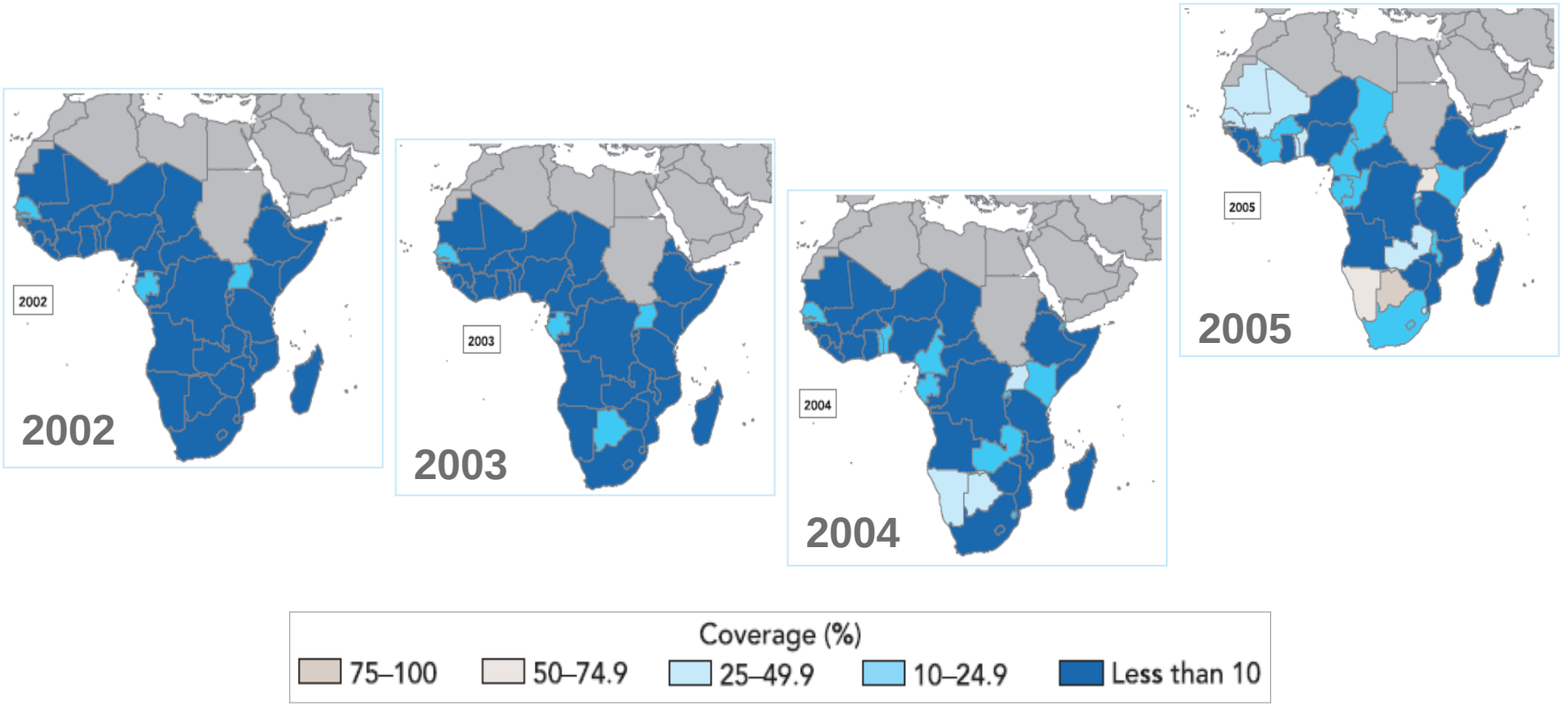
2.7 million new cases

2 million deaths

Mortality in people with HIV = 8.2% per year

New infections outstrip Treatment by 5:2

People in sub-Saharan Africa on antiretroviral treatment as percentage of those in need, 2002–2005



Source: WHO/UNAIDS (2005). Progress on global access to HIV antiretroviral therapy: An update on "3 by 5."

World AIDS Day
1988-2008

IAS 2010 Treatment 2.0

i) Recognize and use HIV treatment as a tool for preventing new infections

ii) Develop better combination antiretroviral medications and cheaper diagnostics tools

iii) Find ways to lower other HIV-related costs

iv) Expand the availability of HIV testing and build stronger links between HIV testing and care

v) Encourage and support community leadership in expanding and improving local HIV responses.

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Funding

At the current rate of infection the projected costs of delivering and maintaining “universal ART access” is;

$42 billion in 2010

$54 billion by 2015

Preventing the 3,550 HIV infections that were probably acquired, and subsequently diagnosed in the UK in 2008, would have reduced future HIV-related costs by more than **£1.1 billion.**

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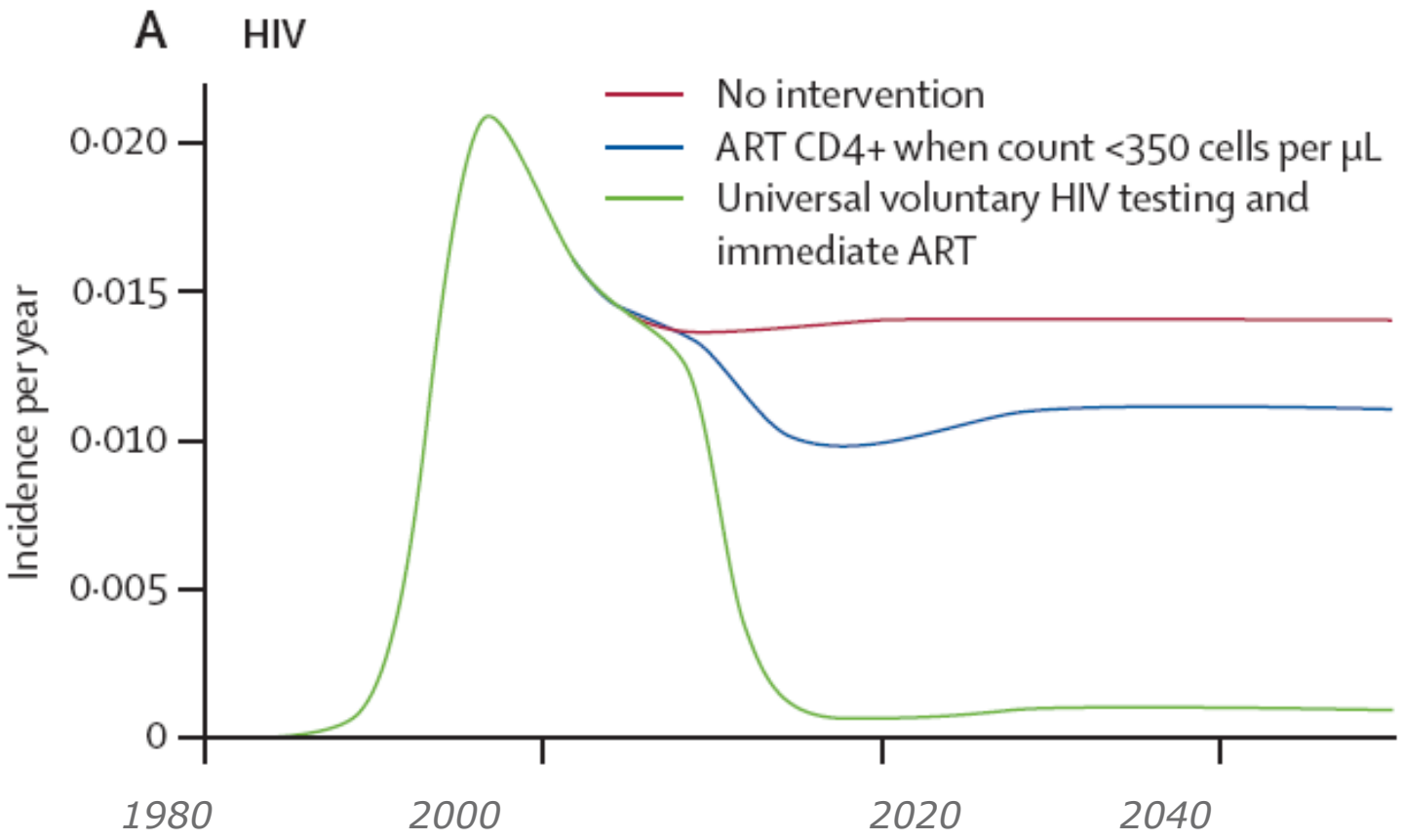
HIV Universal test and Treat



BALANCE BETWEEN INCREASING PREVALENCE AND REDUCING INCIDENCE

Can ART prevent transmission?

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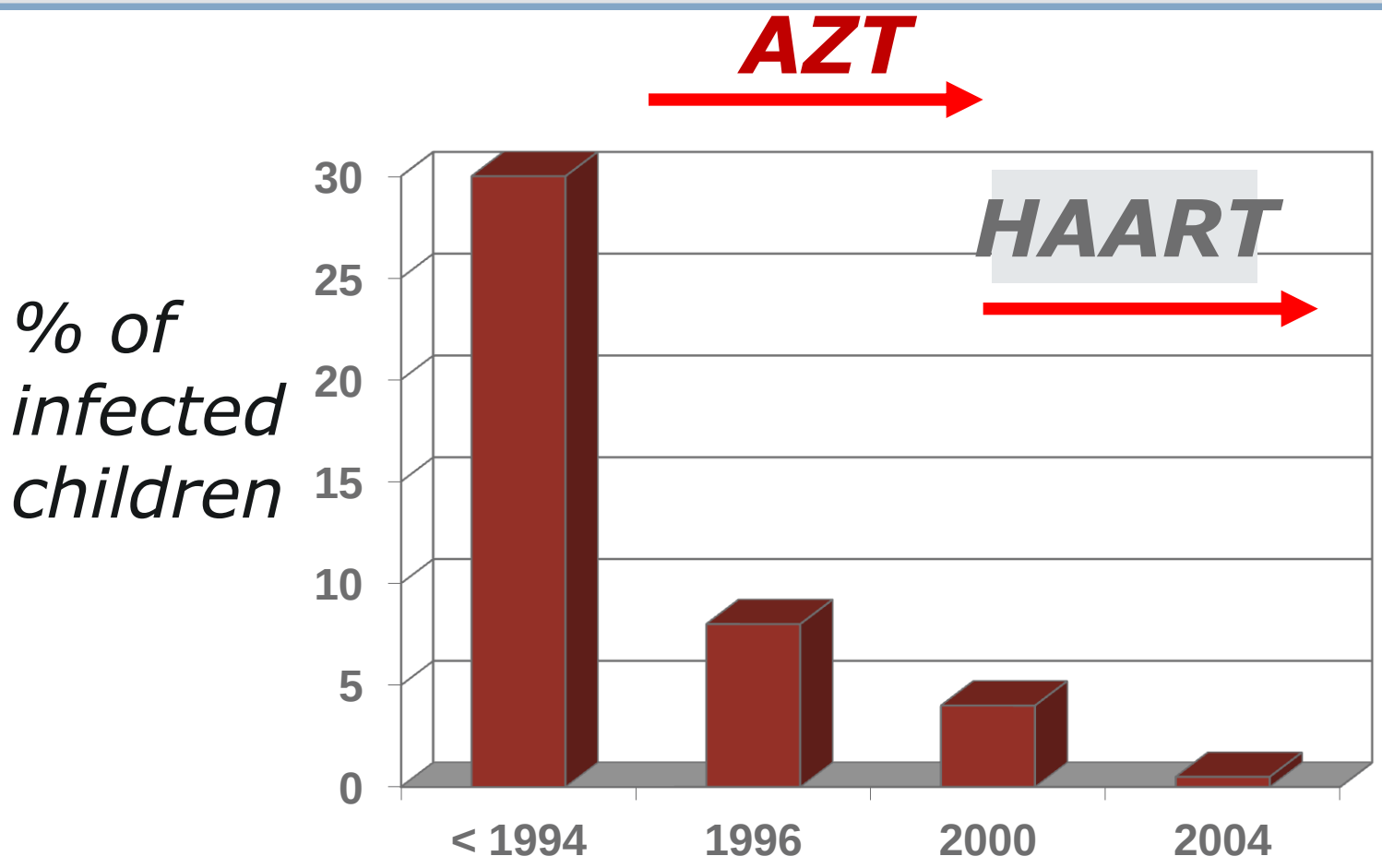
Mother to Child Transmission



Adapted from Coovadia and Lallemant, NEJM 2004

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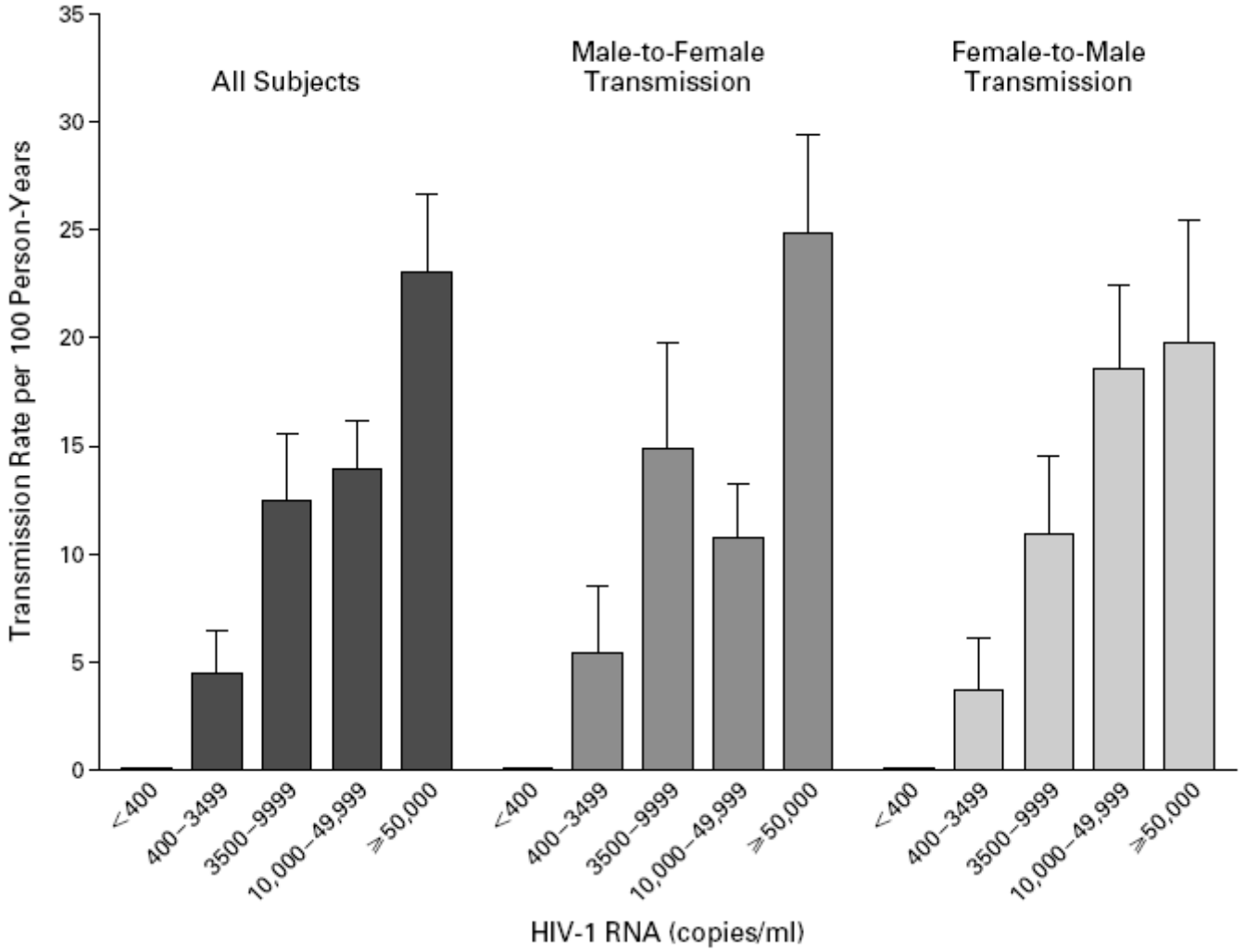
Rakai Study: Transmission risk = viral load

Quinn et al. N Engl J Med 2000;342:921-9



HPTN 052 Study Design

Stable, healthy, serodiscordant couples, sexually active

CD4 count: 350 to 550 cells/mm^3

Primary Transmission Endpoint

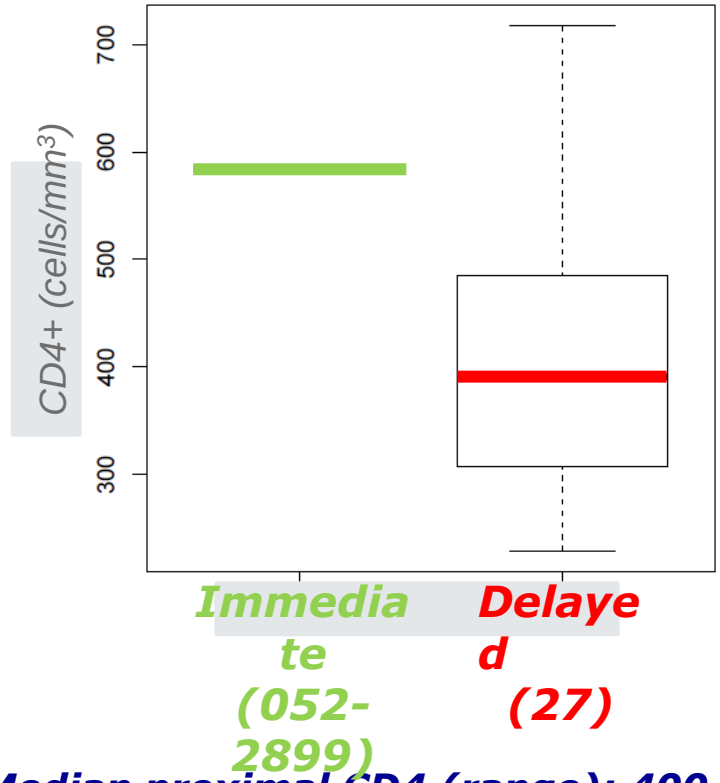
Virally linked transmission events

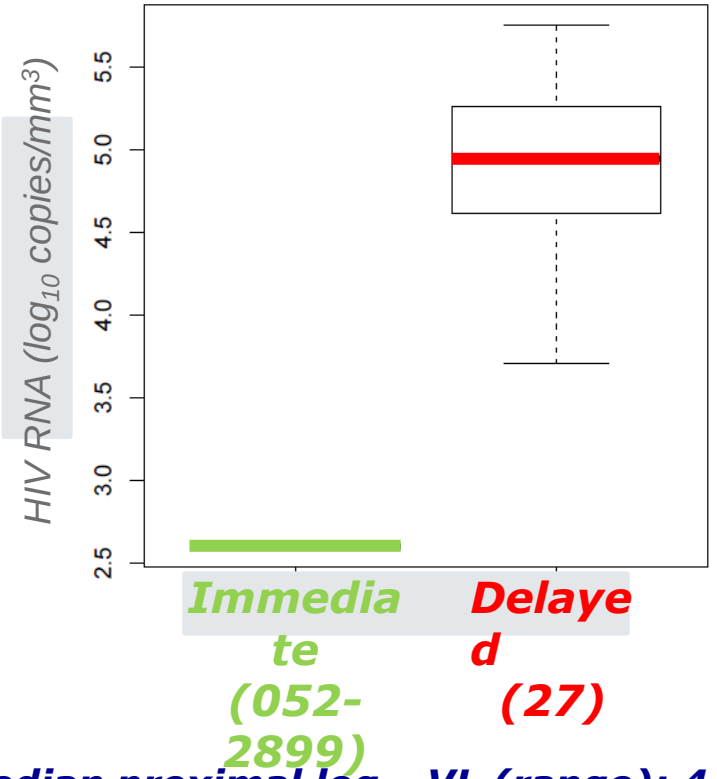
Primary Clinical Endpoint

WHO stage 4 clinical events, pulmonary tuberculosis, severe bacterial infection and/or death

HIV sexual Transmission and Viral Load HPTN 052

28 Linked Transmissions





Median proximal CD4 (range): 400 (229-858)

Immediate arm: 584 (584-584)

Delayed arm: 391 (229-858)

Median proximal log_{10} VL (range): 4.9 (2.6-5.8)

Immediate arm: 2.6 (2.6-2.6)

Delayed arm: 4.9 (2.6-5.8)

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BUT.....Global access to treatment

45% of all HIV infected women have access to treatment to prevent transmission to their babies

Less than 40% of people living with HIV know their status

More than 4 million people (36%) increase over the past year, and a 10 fold increase over the past 5 years

2008 42% of people in need of therapy had access (CD4 <200 cells/cc^3)

6.7 million people need ART 2.9 million on ART

Global total of number of people on ART 4.7 million

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Comparison of mortality in low and high income countries

57 million people die each year

Cardiovascular diseases kill more people each year than any others. In 2008, 7.3 million people died of ischaemic heart disease, 6.2 million from stroke or another form of cerebrovascular disease.

In high-income countries

- **> 66%** of all people live beyond the age of 70
- Predominant cause of death is chronic diseases: cardiovascular disease, chronic obstructive lung disease, cancers, diabetes or dementia.

In low-income countries

- **<20%** reach the age of 70,
- **>30%** of all deaths are among children under 15.
- Predominant cause of death is infectious diseases: lung infections, diarrhoeal diseases, HIV/AIDS, tuberculosis, and malaria.
- Other causes: Complications of pregnancy and childbirth together continue to be leading causes of death, claiming the lives of both infants and mothers.

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Causes of death lower income countries WHO figures June 2011

Causes of death	Deaths in millions	% of deaths
Lower respiratory tract infection	1.05	11.3%
Diarrhoea	0.75	8.2%
HIV/AIDS	0.72	7.8%
Ischaemic heart disease	0.57	6.1%
Malaria	0.48	5.2%
Stroke CVD	0.45	4.9%
TB	0.40	4.3%

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The Economist June 4, 2011

" Thirty years on, it looks as though the plague can now be beaten, if the world has the will to do so"

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BUT where is the money?

http://www.youtube.com/watch?v=MkWoKgLhDVs