

30 years of HIV/AIDS Prevention in Western Industrialized settings: What have we learned, where should we be headed?

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Stockholm, Sweden, 8 November 2011

30 Years of AIDS

Pneumocystis Pneumonia — Los Angeles

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

Patient 1: A previously healthy 33-year-old man developed *P. carinii* pneumonia and oral mucosal candidiasis in March 1981 after a 2-month history of fever associated with elevated liver enzymes, leukopenia, and CMV viruria. The serum complement-fixation CMV titer in October 1980 was 256; in May 1981 it was 32.* The patient's condition deteriorated despite courses of treatment with trimethoprim-sulfamethoxazole (TMP/SMX), nystatin, and fluconazole. He died May 3, and postmortem examination showed residual *P. carinii* and CMV pneumonia, but no evidence of neoplasia.

Patient 2: A previously healthy 30-year-old man developed *P. carinii* pneumonia in April 1981 after a 5-month history of fever each day and of elevated liver-function tests, CMV viruria, and documented seroconversion to CMV, i.e., an acute-phase titer of 16 and a convalescent-phase titer of 28⁺ in anticomplement immunofluorescence tests. Other features of his illness included leukopenia and mucosal candidiasis. His pneumonia responded to a course of intravenous TMP/SMX, but, as of the latest reports, he continues to have a fever each day.

Patient 3: A 30-year-old man was well until January 1981 when he developed esophageal and oral candidiasis that responded to Amphotericin B treatment. He was hospitalized in February 1981 for *P. carinii* pneumonia that responded to oral TMP/SMX. His esophageal candidiasis recurred after the pneumonia was diagnosed, and he was again

Number of people living with HIV and scientific breakthroughs, 1981–2011

15 Years of HIV/AIDS in Eurosurveillance



175 articles on HIV/AIDS topics, including:

- **66 on general surveillance/epi topics, such as**
 - **5 in 1998-2002 on transitioning to HIV surveillance**
 - **10 on tests for recent infection to estimate incidence (STARHS), mostly in 2008**
 - **Monitoring increases in HIV Eastern Europe since beginning of publication**
- **16 on coinfection**
- **14 on perinatal AIDs or Mother-to-child transmission, especially in 1998-2004**
- **23 on MSM, especially in 2008-2011**

Overview

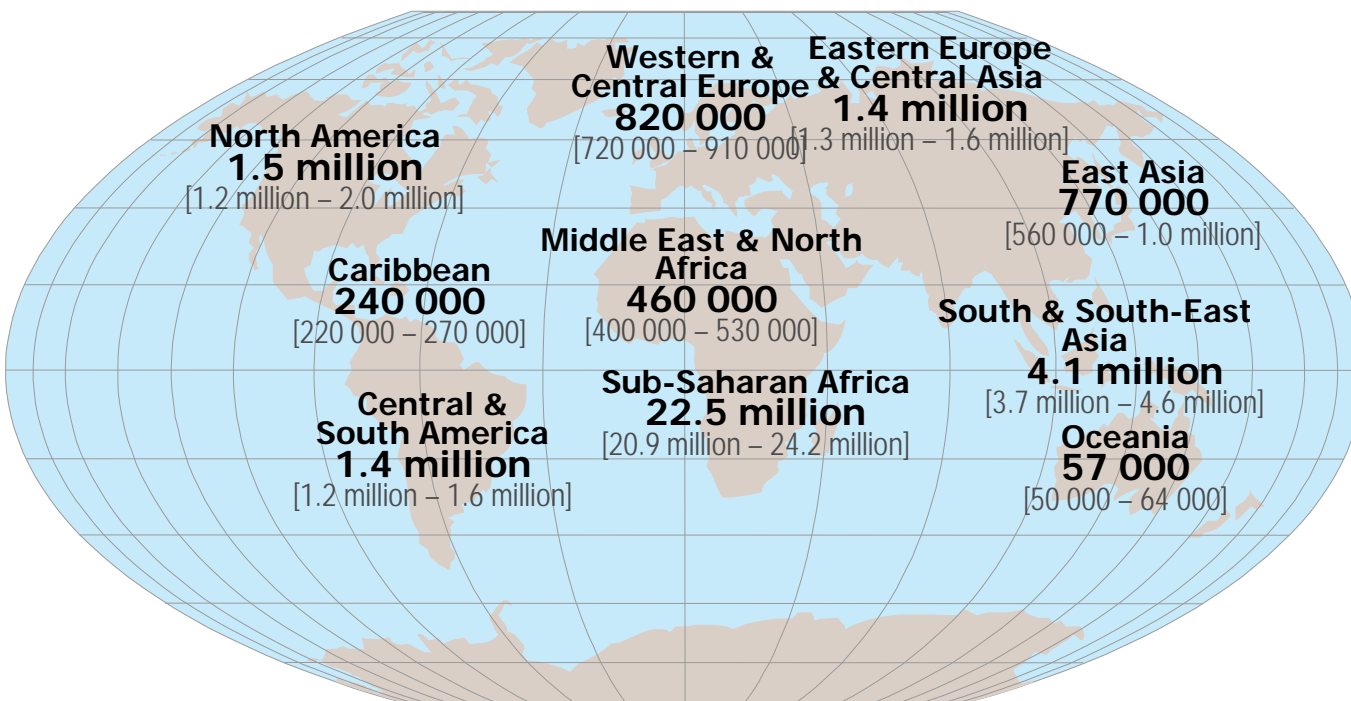


- **Overview of the global and European HIV/AIDS Epidemic: Where are we now?**
- **Advances in HIV prevention, 1995-2011: What have we learned?**
- **Looking to the future: New tools and new approaches to improve impact**
- **Summary**



Global View of the HIV Epidemic

Adults and children estimated to be living with HIV: 2009



Total: 33.3 million [31.4 million – 35.3 million]

New HIV infections in 2009 : 2.6 million

Deaths due to AIDS in 2009: 1.8 million

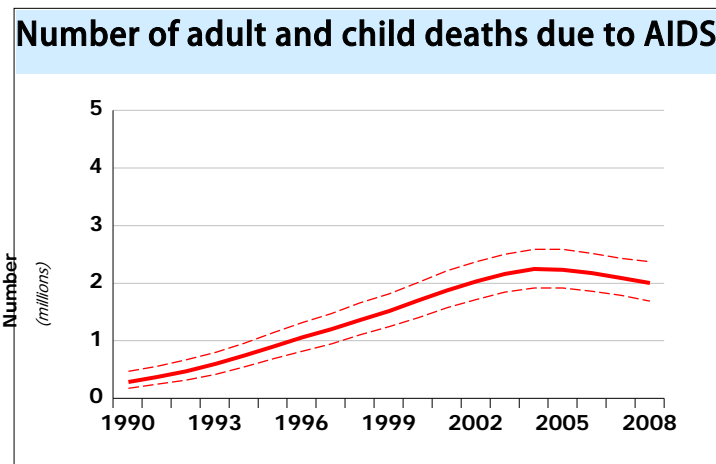
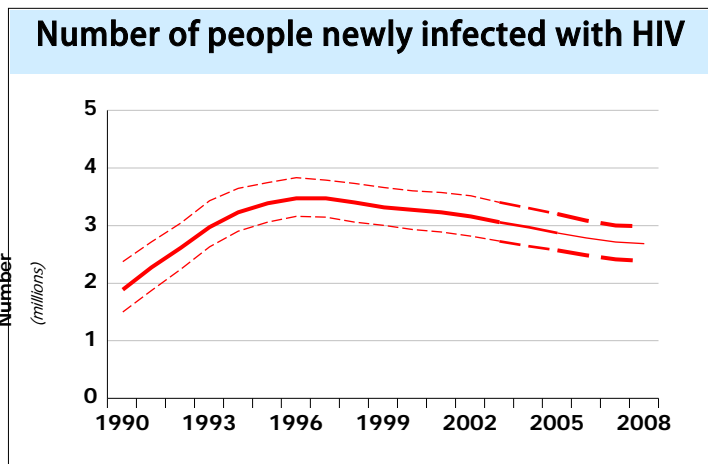
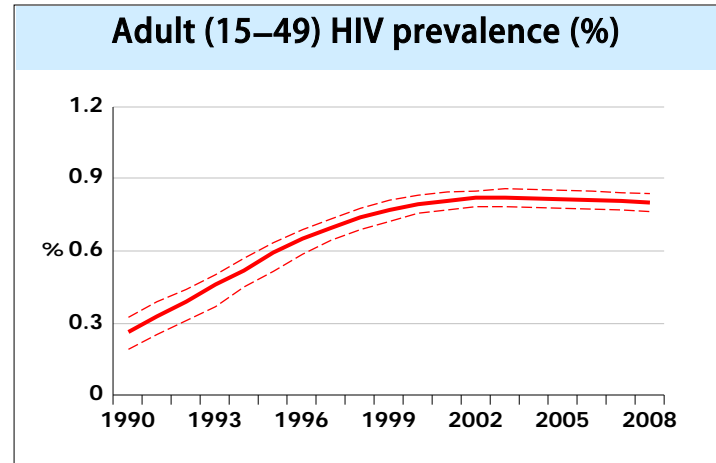
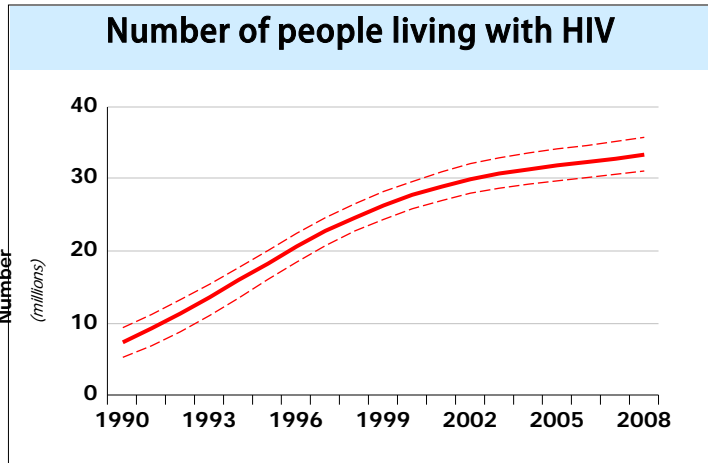
Over 7000 new HIV infections a day in 2009

About 97% are in LMI countries

About 1000 are in children under 15 years of age

**About 6000 are in adults aged 15 years and older, of whom:
51% are women
41% youth**

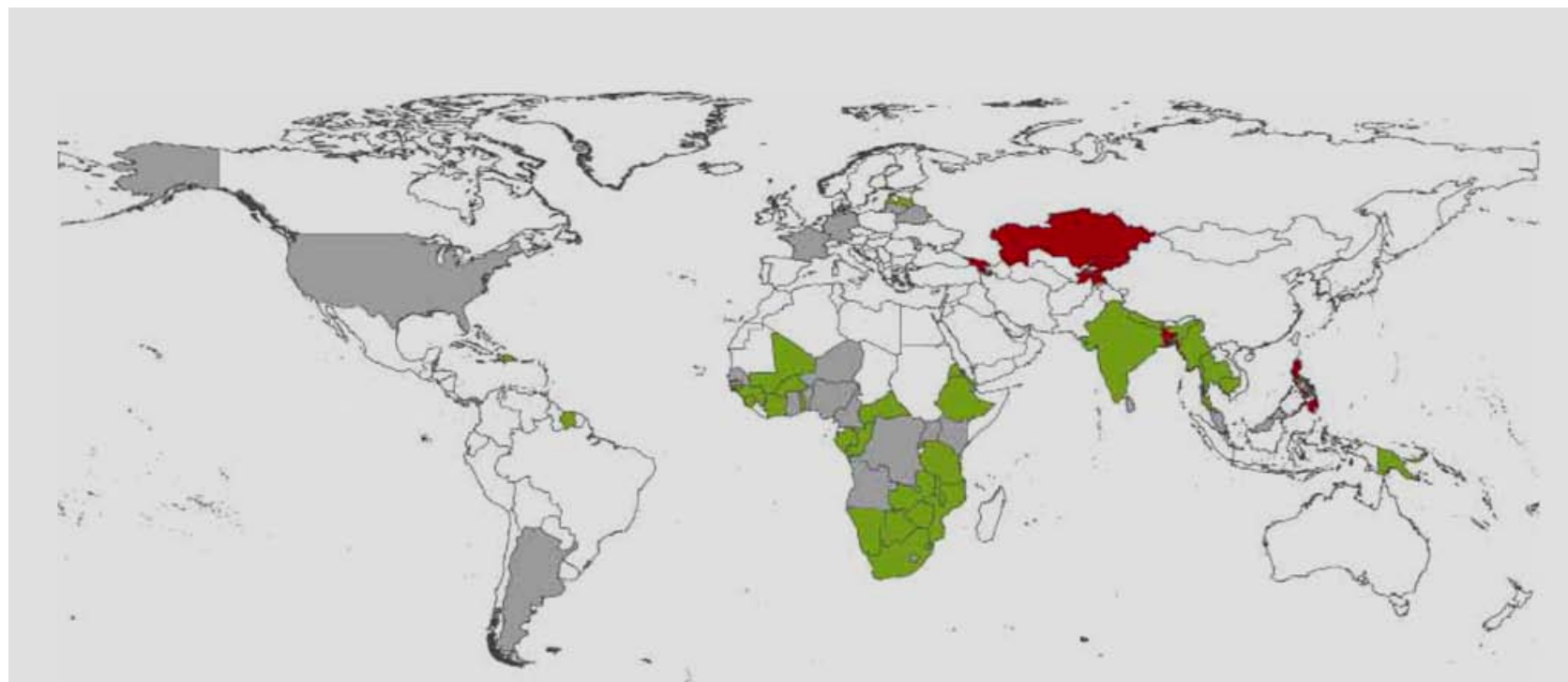
Global estimates 1990–2008







— Estimate - - - High and low estimates

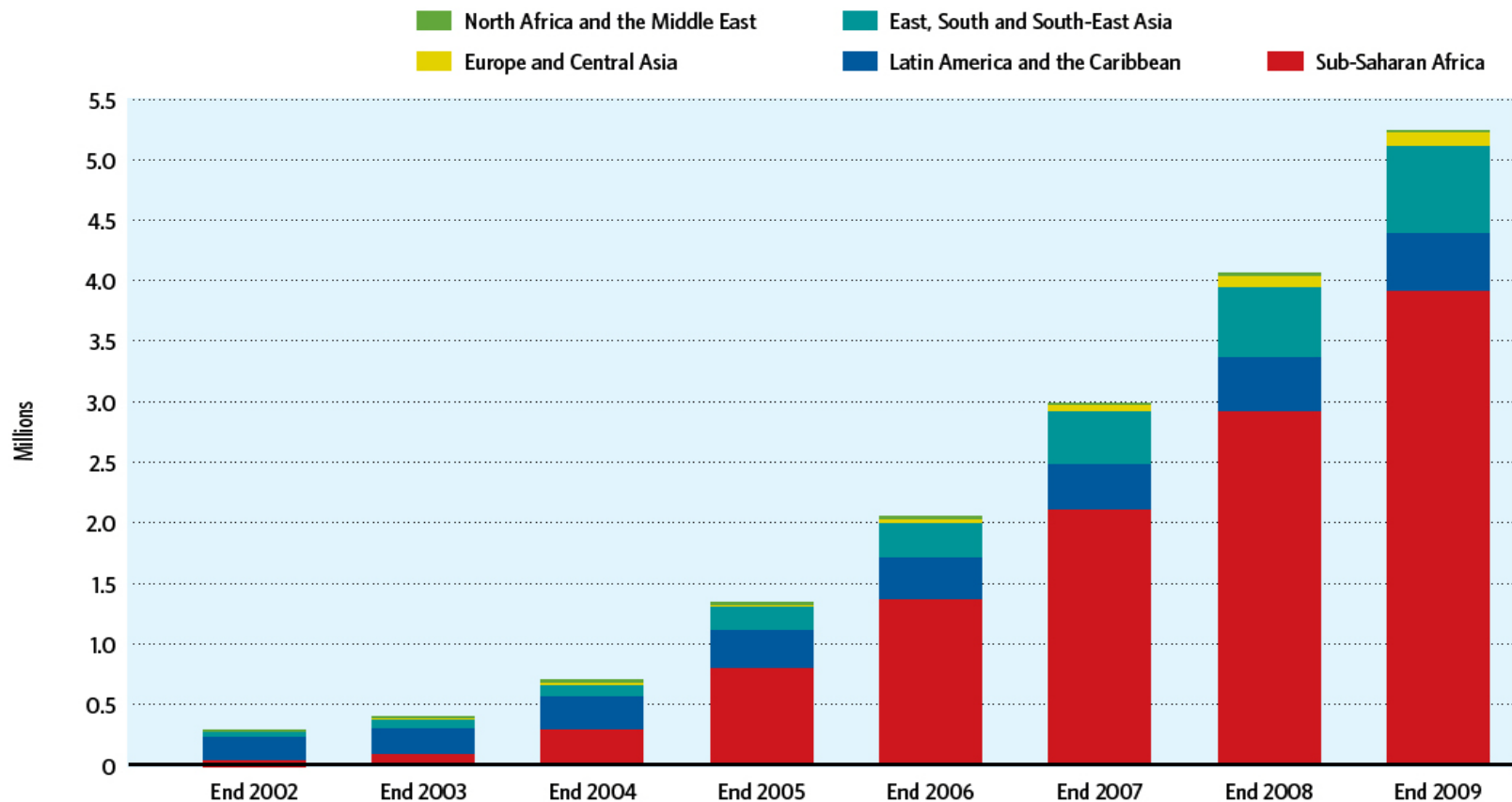
Source: UNAIDS/WHO

Change in HIV Incidence, 2001 - 2009



-  Increasing >25%
-  Stable
-  Decreasing >25%
-  Not included in analysis

Towards universal treatment access



6.6 million on ART by end of 2010
> 13 fold increase in six years
Global coverage ~ 35%

Coverage of antiretroviral therapy at the end of 2009 (WHO 2010 Guidelines, CD4 < 350)



21-40%

Algeria	Kazakhstan
Angola	Lithuania
Armenia	Malaysia
Azerbaijan	Mauritania
Bangladesh	Mauritius
Belarus	Morocco
Belize	Mozambique
Bulgaria	Nicaragua
Cameroon	Niger
Chad	Nigeria

0-20%

Bolivia	Madagascar
Bhutan	Maldives
Burundi	Mongolia
CAR	Myanmar
Colombia	Nepal
DR Congo	Pakistan
Djibouti	Moldova
Egypt	Russian Fed
Gambia	Sierra Leone
Iran	Somalia
Kyrgyzstan	Sri Lanka
Latvia	Sudan
Lebanon	Tajikistan
Liberia	Ukraine

China	Panama
Congo	Paraguay
Côte d'Ivoire	Peru
Ecuador	Philippines
Eq Guinea	Poland
Eritrea	Serbia
Fiji	South Africa
Ghana	Togo
Guinea	Uganda
Guinea-Bissau	UR Tanzania
Honduras	Uzbekistan
Hungary	Viet Nam
India	Zimbabwe
Indonesia	

41-60%

Benin	Lesotho
Brazil	Malawi
Burkina Faso	Mali
Dominican Rep	Mexico
El Salvador	PNG
Ethiopia	Senegal
Gabon	Suriname
Guatemala	Swaziland
Haiti	Tunisia
Jamaica	Uruguay
Kenya	Venezuela

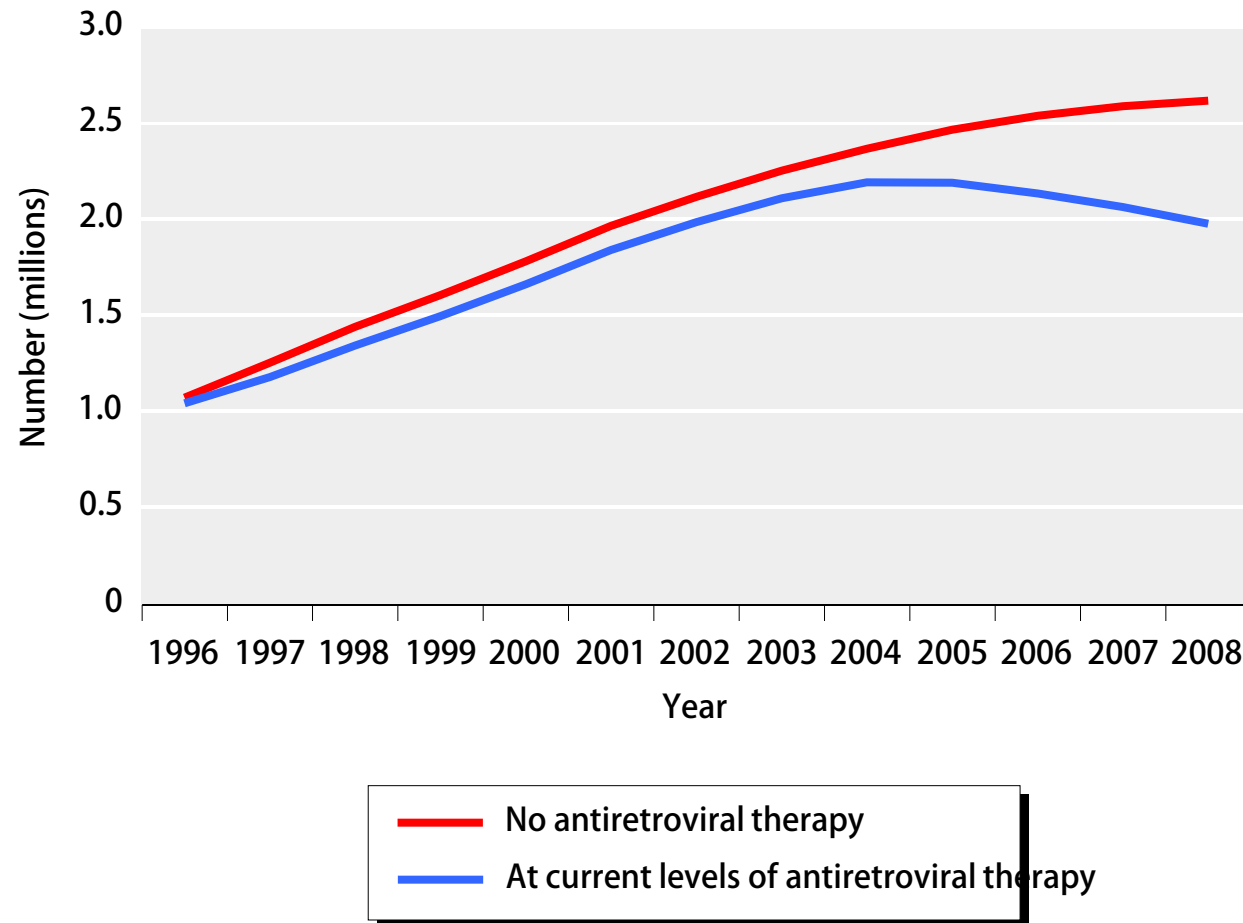
61-80%

Argentina	Namibia
Chile	Slovakia
Costa Rica	Thailand
Croatia	Turkey
Georgia	Zambia
Lao PDR	

>80%

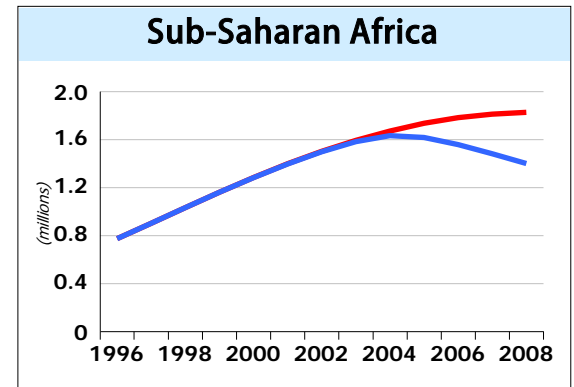
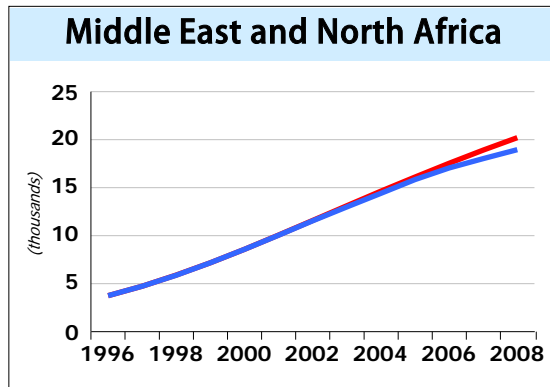
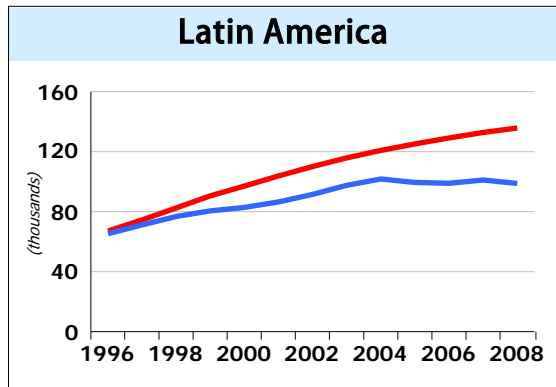
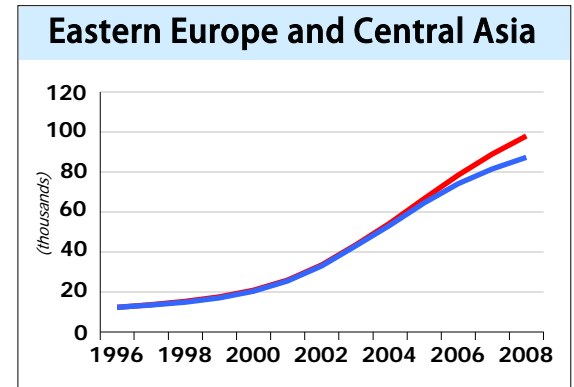
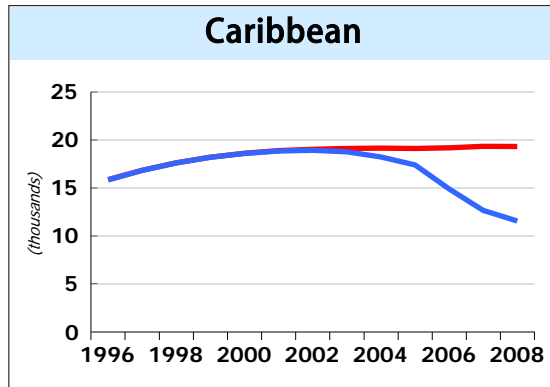
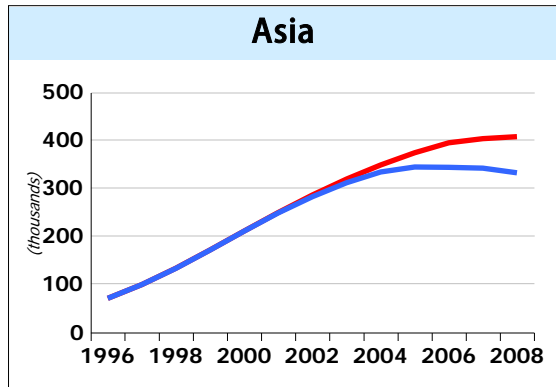
Botswana	Oman
Cambodia	Romania
Cuba	Rwanda
Guyana	

Estimated number of AIDS-related deaths with and without antiretroviral therapy, globally, 1996–2008



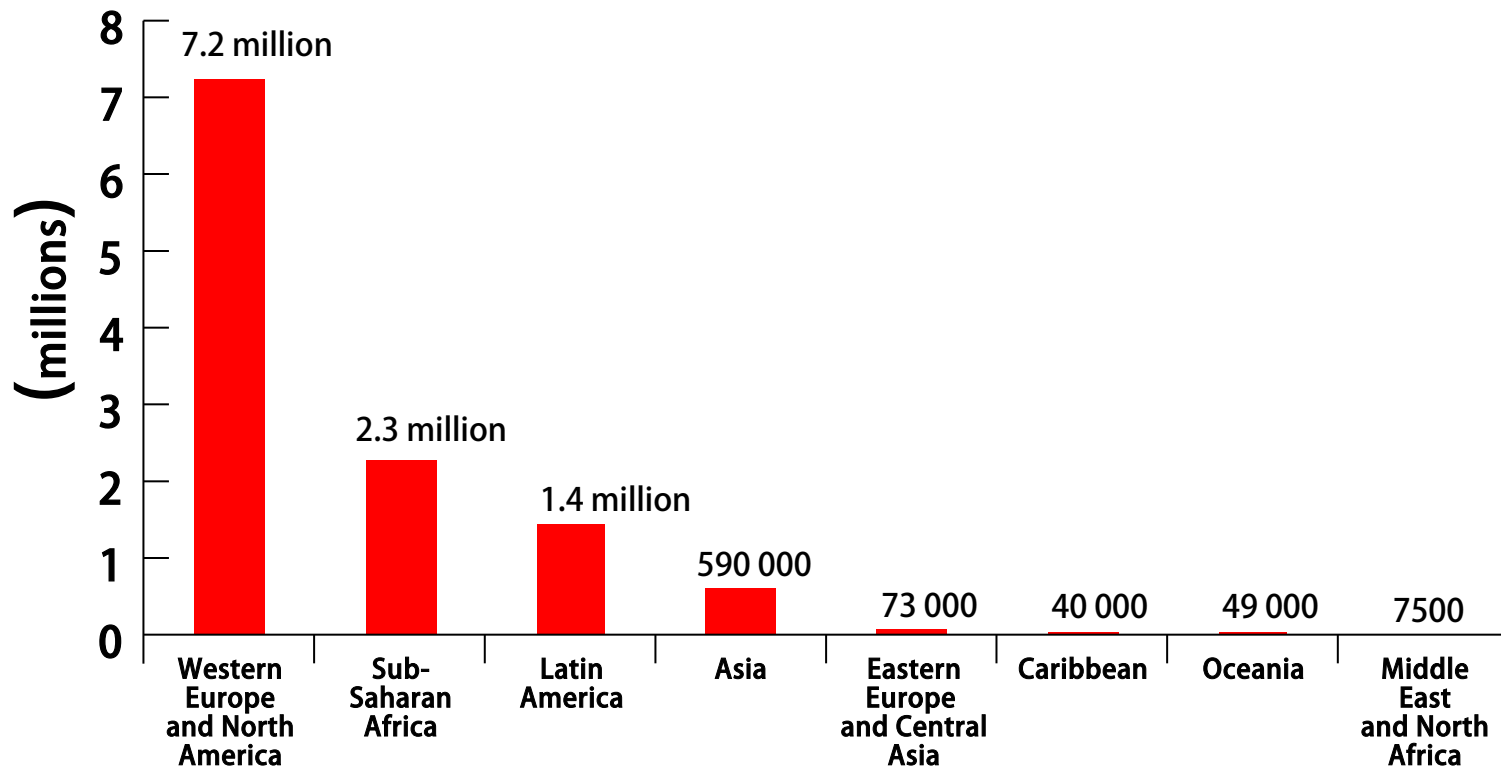
The number of AIDS-related deaths has declined by over 10% over the past five years...

Estimated number of AIDS-related deaths with and without antiretroviral therapy, by region, 1996–2008



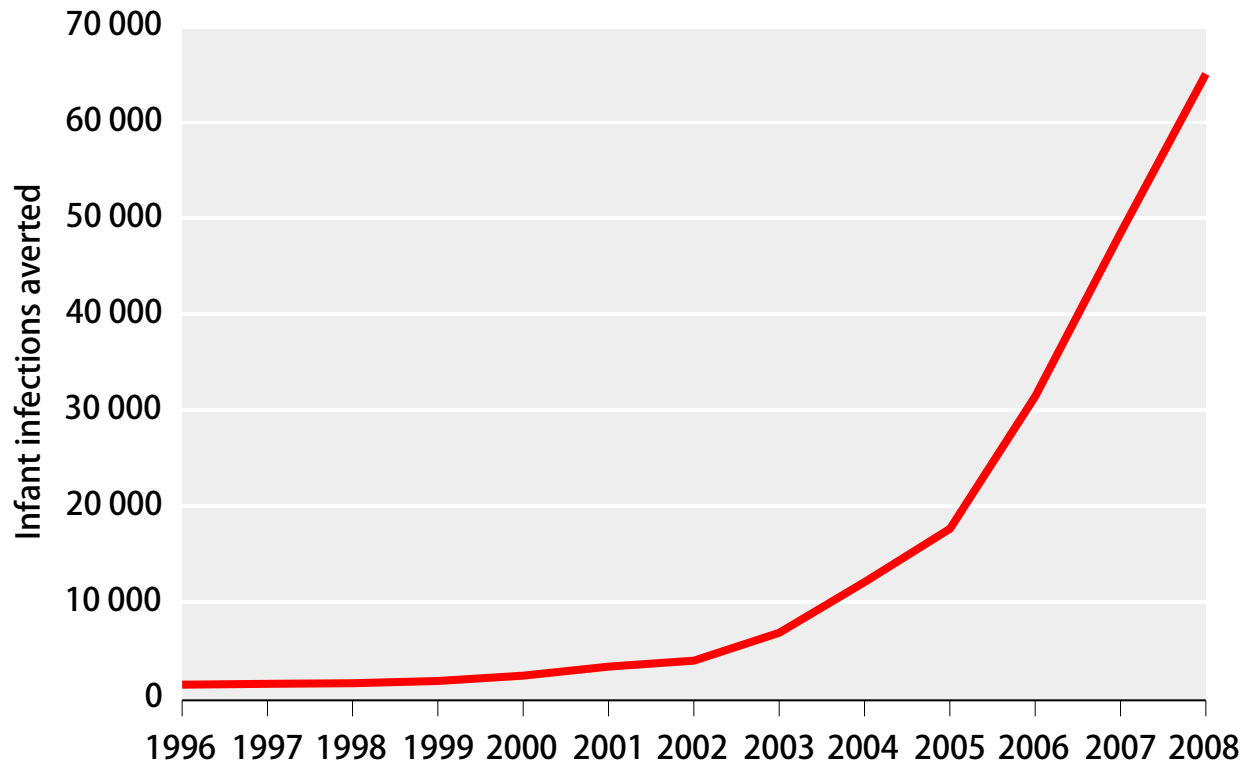
— No antiretroviral therapy — At current levels of antiretroviral therapy

Estimated number of Life-years added due to antiretroviral therapy, by region, 1996–2008



Since 1996 the availability of effective treatment, has saved some 2.9 million lives...

Estimate of the annual number of infant infections averted through the provision of antiretroviral prophylaxis to HIV-positive pregnant women, globally, 1996–2008



HIV in Europe

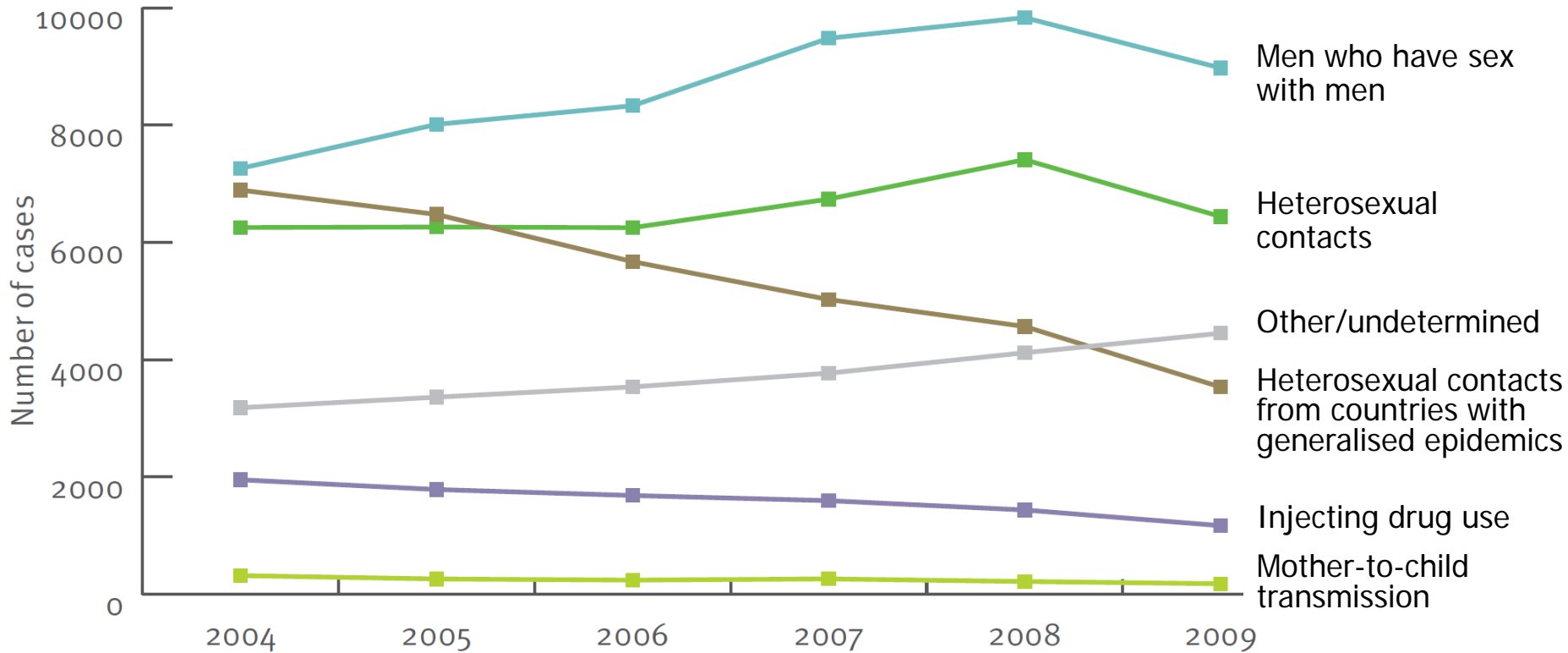


HIV infection is of major public health importance in Europe, with evidence of continuing transmission and no clear signs of decrease.

Large heterogeneity exists in HIV epidemics in the EU/EEA:

- Predominant mode of transmission is sex between men.**
- Considerable proportion among heterosexually acquired cases comes from countries with a generalised epidemic.**
- Continued HIV transmission among IDUs in eastern EU countries.**

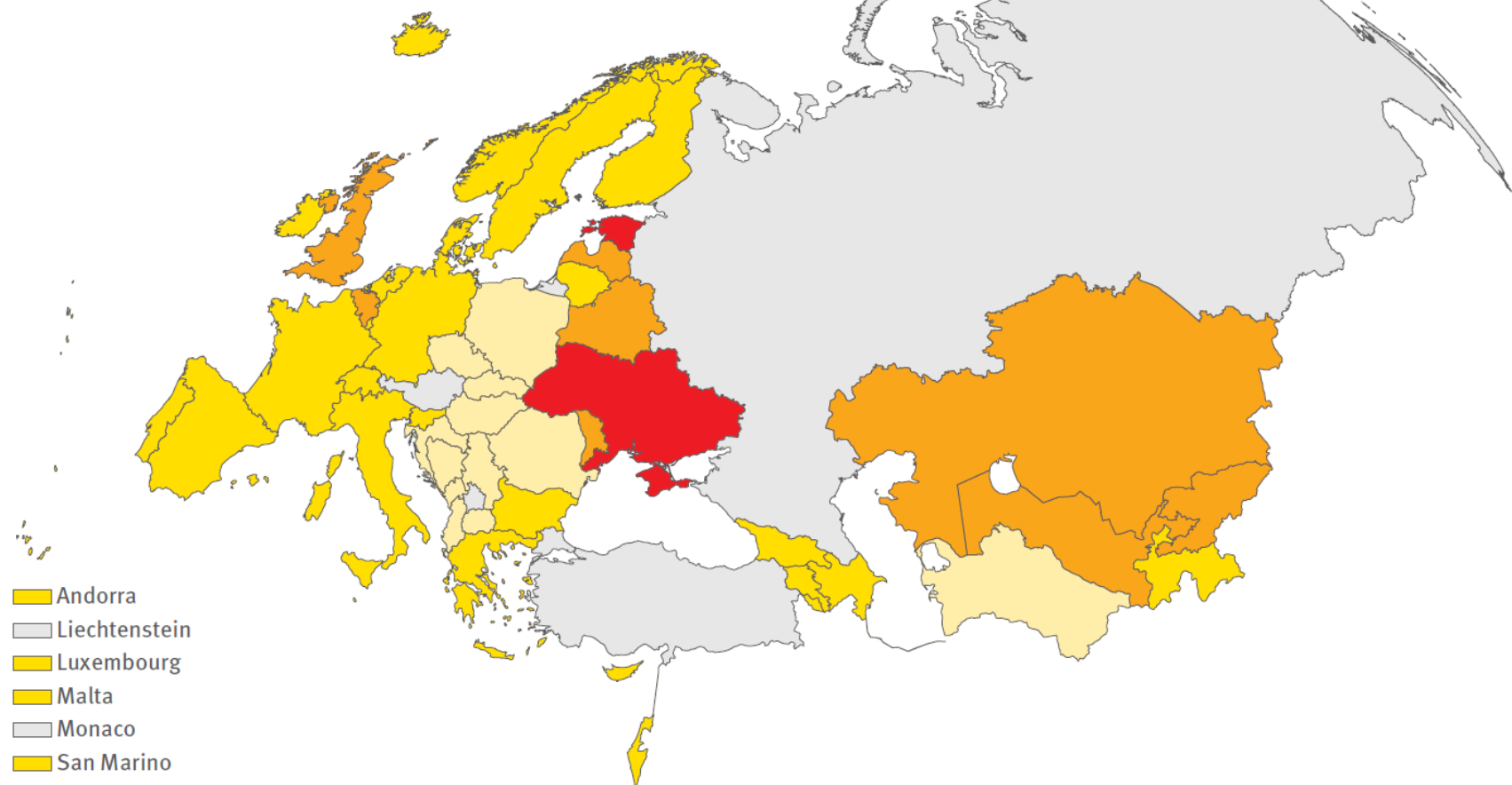
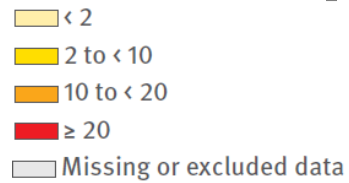
HIV infection by transmission group and origin in EU/EEA countries, 2004–09



Predominant transmission group: men who have sex with men

Data were not included from: Austria, Estonia and Poland.

HIV infections diagnosed in 2009 per 100 000 population: all cases



21st Century HIV prevention challenges in Western Countries



Dynamic: Changing demography, patterns and distribution of risk behavior, disease epidemiology, cultural norms and values

Disparities: Among the worst health inequities observed for sexual and reproductive health

Concentration: Increasing concentration of issues among the socio-economically disadvantaged, minorities, migrants, and those with poor healthcare access

Interconnectedness: Overlapping epidemics or "syndemics" require a systemic change in our health care delivery system

Contexts: Challenging policy and fiscal environments require increased efficiency, harmonization and minimize duplication



Advances in HIV Prevention, 1995 - 2011

High likelihood of exposure

High prevalence
Untested partners
Inconsistent/incorrect condom use
Multiple partners
(relatively) closed community

Interconnected networks

Exposure

Condoms  **Behavior Change**

Individual-level Determinants

Rapid spread
Ongoing transmission

ART

PrEP, PEP, MC

Infectivity

STI Rx

Susceptibility

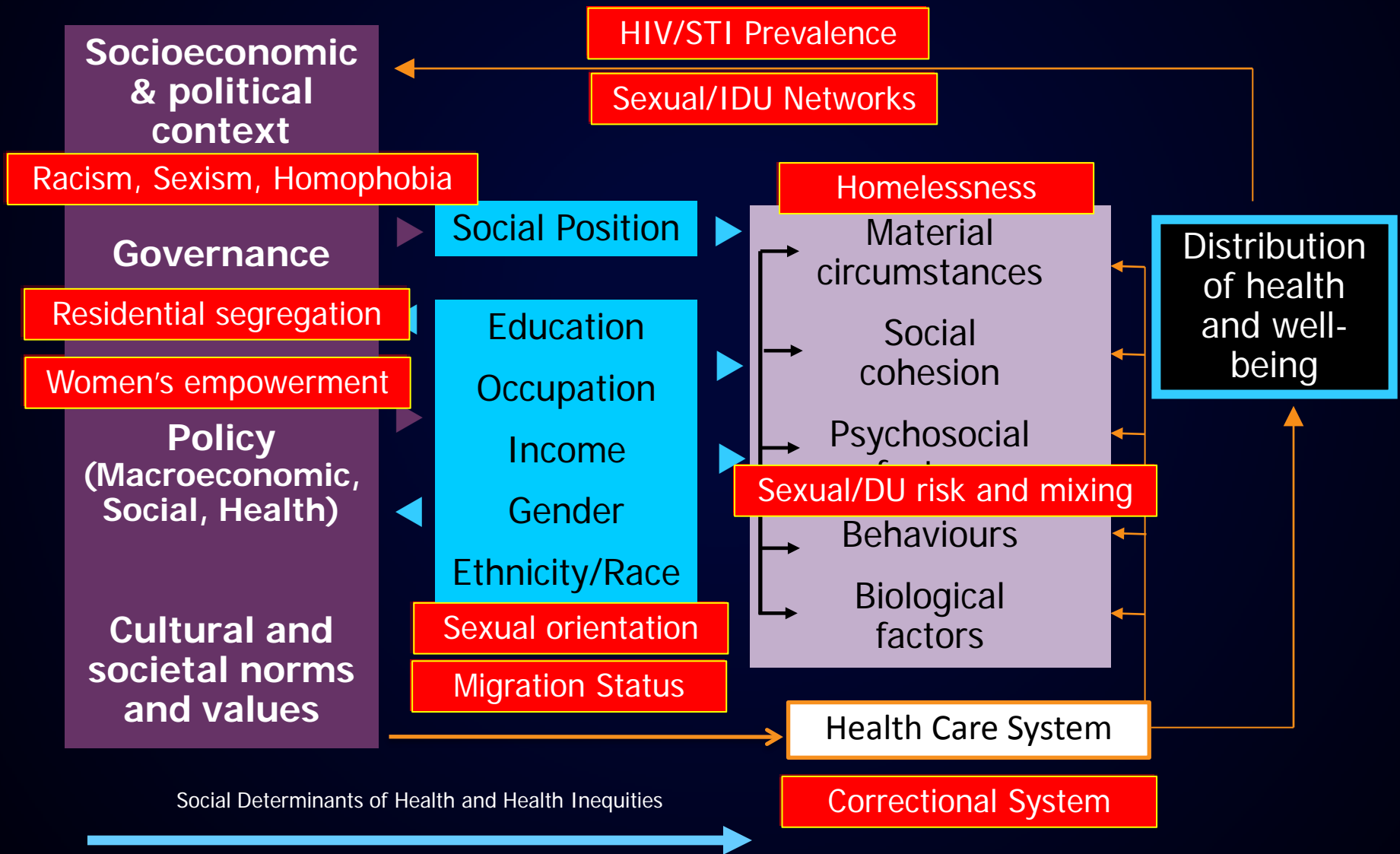
High viral load in genital tract secretions

High incidence
Untreated late infection
Co-occurring STI

Lack of circumcision
Early sexual debut
(ectopy, trauma)
Co-occurring STI

Social and Structural Determinants:

Adapting the WHO SDH Model to understand HIV Inequalities



What works for HIV prevention? RCT Results: Data to June 2010



Review: 37 HIV prevention RCTs on 39 interventions:

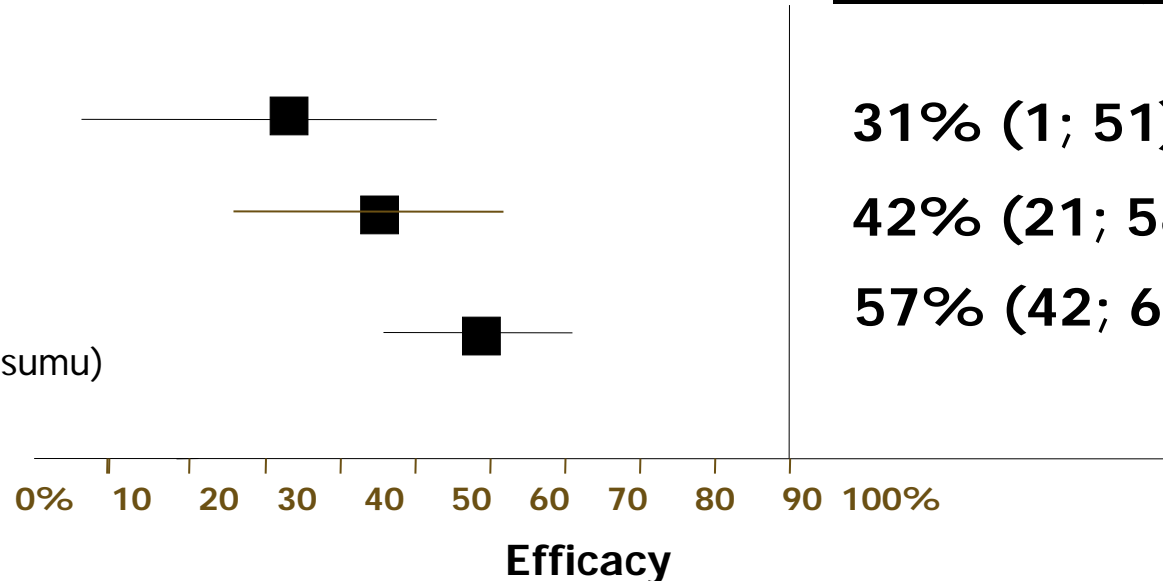
- PrEP : 1
- Behavioural: 7
- Microbicides: 12
- Microfinance: 1
- Diaphragm: 1
- Male circumcision: 4
- STI treatment: 9
- Vaccines: 4

Study

HIV Vaccine
(Thai RV144)

STD treatment
(Mwanza)

Circumcision
(Orange Farm, Rakai, Kisumu)



Effect size (CI)

31% (1; 51)

42% (21; 58)

57% (42; 68) : M-A

0% 10 20 30 40 50 60 70 80 90 100%

Efficacy

July 2010: ARV microbicide (topical PrEP) prevents HIV & HSV-2 in women - CAPRISA 004



RESEARCH ARTICLES

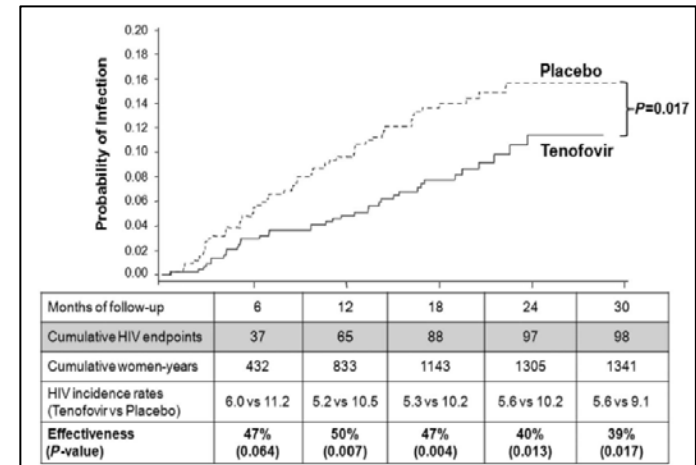


3 SEPTEMBER 2010 VOL 329 SCIENCE

Effectiveness and Safety of Tenofovir Gel, an Antiretroviral Microbicide, for the Prevention of HIV Infection in Women

Quarraisha Abdool Karim,^{1,2*}† Salim S. Abdool Karim,^{1,2,3*} Janet A. Frohlich,¹ Anneke C. Grobler,¹ Cheryl Baxter,¹ Leila E. Mansoor,¹ Ayesha B. M. Kharsany,¹ Sengeziwe Sibeko,¹ Koleka P. Mlisana,¹ Zaheen Omar,¹ Tanuja N. Gengiah,¹ Silvia Maarschalk,¹ Natasha Arulappan,¹ Mukelisiwe Mlotshwa,¹ Lynn Morris,⁴ Douglas Taylor,⁵ on behalf of the CAPRISA 004 Trial Group†

The Centre for the AIDS Program of Research in South Africa (CAPRISA) 004 trial assessed the effectiveness and safety of a 1% vaginal gel formulation of tenofovir, a nucleotide reverse transcriptase inhibitor, for the prevention of HIV acquisition in women. A double-blind, randomized controlled trial was conducted comparing tenofovir gel (*n* = 445 women) with placebo gel (*n* = 444 women) in sexually



39% protection against HIV overall
54% effective against HIV in high adherers
51% reduction in HSV-2

May 2011: ART prevents HIV transmission from infected partners (HPTN 052)

THE LANCET

Editorial

HIV treatment as prevention—it works

Last week any doubts around treatment as an approach to halt the spread of the HIV epidemic were allayed. An international study showed that antiretroviral treatment can prevent the sexual transmission of HIV among heterosexual couples in whom one partner is HIV-infected and the other is not. UNAIDS described the result as a “serious game changer” for HIV prevention.

The phase 3 clinical trial, HPTN 052, was done by the HIV Prevention Trials Network and funded by the US National Institutes of Health. It was due to run until 2015, but

group versus three cases in the immediate group. Study participants and investigators have been informed of the results and all participants offered the appropriate care. All study participants will be followed for at least 1 more year.

Clearly, treating sooner rather than later results in both a clinical benefit for the individual and has a potentially enormous public health benefit in slowing the spread of infection. These results are likely to provide a new level of dialogue between physician and patient. Besides emphasising the benefit of medication adherence to the



RCT enrolled 1763 HIV sero-discordant couples

Index member of the couple had CD4 cell counts between 350-550 cells per μL .

Couples randomly assigned to immediate vs. deferred HAART for infected partner.

Study found a 96% decrease in the risk of HIV transmission with immediate HAART.

- HAART associated with a 30% decrease in disease progression and death
- Immediate HAART was also associated with an 83% reduction in extra-pulmonary TB

HIV prevention interventions shown to be effective in reducing HIV incidence rates in RCTs – July 2011

Study

Effect size (95% CI)

Antiretroviral treatment for prevention
(HPTN 052 - Africa, Asia, Americas¹)

PrEP for discordant couples
(PartnersPrEP - Uganda, Kenya²)

PrEP for heterosexuals
(TDF2 - Botswana³)

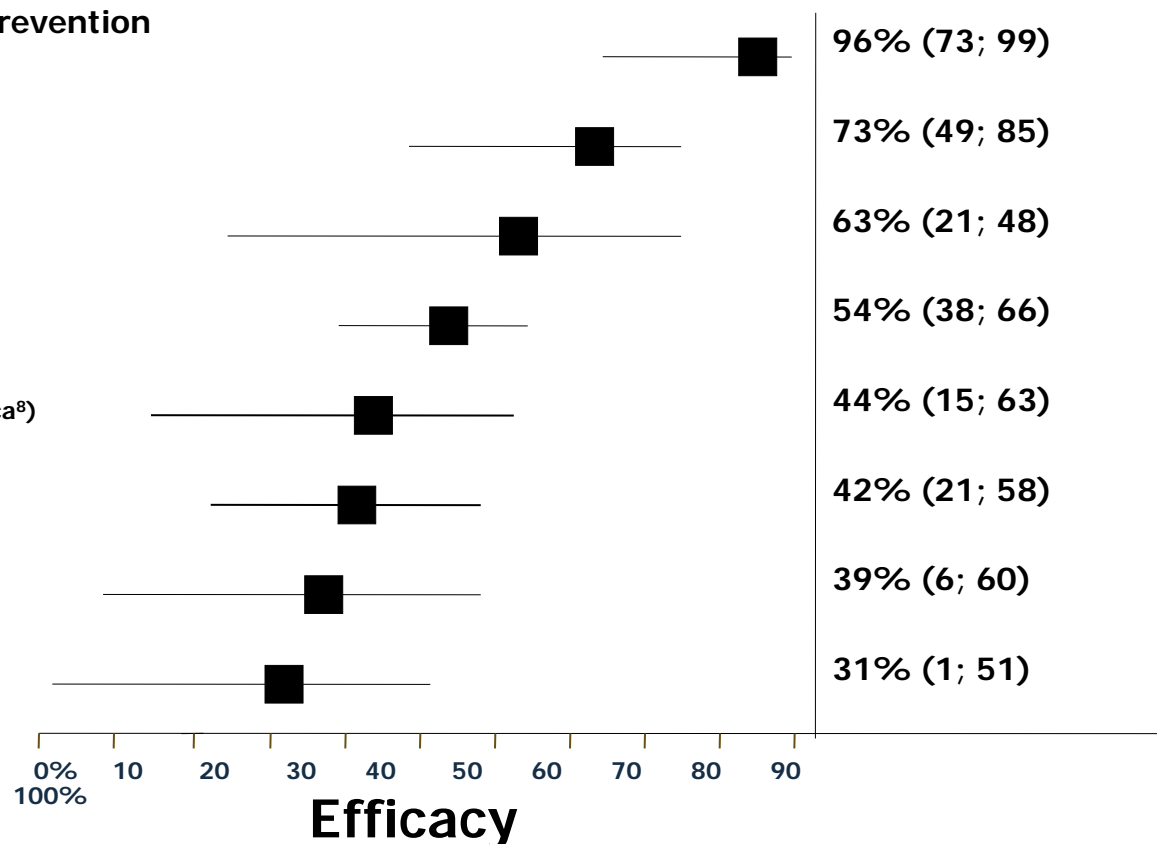
Medical male circumcision
(Orange Farm⁴, Rakai⁵, Kisumu⁶)^{*7}

PrEP for MSMs
(iPrEX - Americas, Thailand, South Africa⁸)

STD treatment
(Mwanza - Tanzania⁹)

Microbicide
(CAPRISA 004 – South Africa¹⁰)

HIV Vaccine
(RV144 - Thailand¹¹)



Convergence around ARVS



Microbicides for women

Abdool Karim Q, Science 2010

Male circumcision



Auvert B, PLoS Med 2005
Gray R, Lancet 2007
Bailey R, Lancet 2007



Treatment of STIs

Grosskurth H, Lancet 2000



Treatment for prevention

Donnell D, Lancet 2010
Cohen M, NEJM 2011



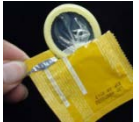
Female Condoms

Behavioural positive prevention



Fisher J, JAIDS 2004

Male Condoms



Oral pre-exposure prophylaxis

Grant R, NEJM 2010 (MSM)
Baeten J, 2011 (Couples)
Paxton L, 2011 (Heterosexuals)

HIV Counselling and Testing

Coates T, Lancet 2000



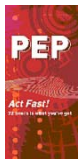
Behavioural Intervention

- **Abstinence**
- **Be Faithful**



Post Exposure prophylaxis (PEP)

Scheckter M, 2002



Vaccines

Rerks-Ngarm S, NEJM 2009

Note: PMTCT, Screening transfusions, Harm reduction, Universal precautions, etc. have not been included – this is focused on reducing sexual transmission

New hope in HIV prevention

- Until 2010, skepticism in HIV prevention
- Little evidence that prevention can change the epidemic

The new technologies provide new hope for women

- Gender dynamic is key to controlling HIV in Africa
- TFV gel - new target population for women
- Role of oral PrEP in women remains uncertain
- ?Implications of HPTN 052 for women

New HIV prevention is fundamentally dependent on HIV status

- Pre-circumcision, HIV messages were generic
- HIV testing now a key to HIV prevention
- Tailored, sero-status approach to HIV prevention



Looking to the Future

Getting to Zero
Combination Prevention
Implementation Science
Program Science
High Impact Prevention

UNAIDS Strategy: Getting to Zero

Vision and goals:

Zero new infections

Zero AIDS-related deaths

Zero discrimination

Strategic directions:

Revolutionize prevention

Catalyze the next phase of treatment, care and support

Advance human rights and gender equality for the HIV response

Core Themes



People

Inclusive responses reach the most vulnerable, communities mobilized, human rights protected



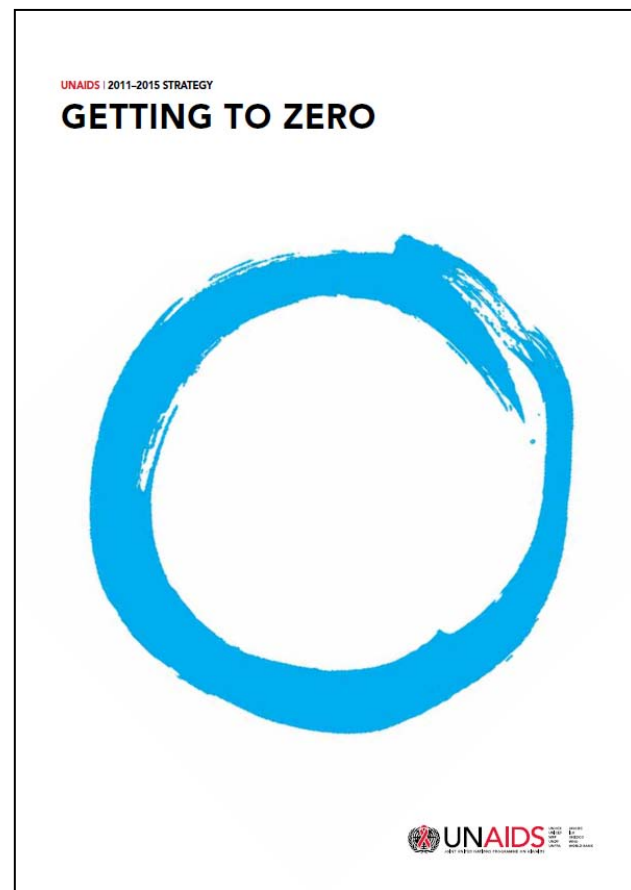
Countries

Nationally owned sustainable responses, financing diversified, systems strengthened



Synergies

Movements united, services integrated, efficiencies secured across Millennium Development Goals



UNAIDS
JOINT UNITED NATIONS PROGRAMME ON HIV/AIDS

UNHCR
UNICEF
WFP
UNDP
UNFPA
UNODC
ILO
UNESCO
WHO
WORLD BANK

HIV prevention today: The imperative for urgent action



Stable HIV incidence is not acceptable

- To prevent increasing prevalence, need to decrease new infections more aggressively
- Too many at risk individuals are not being reached

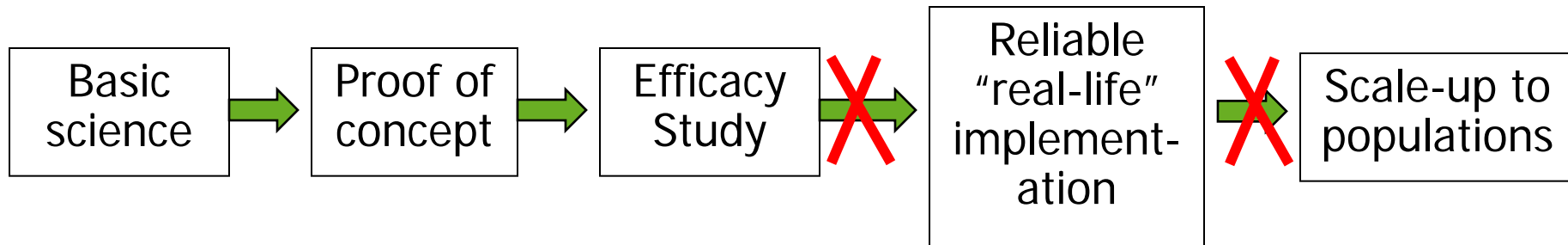
Combination prevention now offers hope

- Always had combination prevention - now targeted combinations
- Will require new partnerships and strong health care systems
- Must incorporate context, epidemic phase, target populations, implementation, quality, impact
- Limited resources are available and we need to prioritize

Applying the science of implementation and program to maximize impact, and improve quality



Improving Implementation: Bridging the Efficacy – Effectiveness Gap



We will never be able to leverage the full potential of HIV prevention or treatment if we fail to target appropriately, implement effectively, and bring to scale what we know works

Program Science



Programme Science is defined as the systematic application of scientific knowledge to improve the design, implementation and evaluation of public health programs.

Programme Science is concerned with three aspects of prevention programs:

- Strategic planning of programs (who to target, when and for how long);**
- Implementation of interventions to achieve the best outcomes;**
- Program management processes that are necessary for scaling up and optimizing program quality.**

High Impact Prevention

CDC's new strategic approach to HIV prevention, developed in response to the new National HIV/AIDS Strategy

High Impact Prevention encourages us to model, implement, and evaluate the highest impact biomedical, behavioral, and structural interventions together. Key components:

- Effectiveness and cost-effectiveness of the intervention
- Address the social, structural and political contexts
- Prioritization of populations and interventions
- Feasibility of full-scale implementation
- Coverage of targeted populations
- Interaction, combination and targeting of interventions
- Implementation and Program Science

What's different about these approaches?



- 1. Focuses on packages of interventions, and the synergies and antagonisms across interventions**
- 2. Considers the combination, differential uptake and sustainability of interventions**
- 3. Includes interventions that modify social determinants of morbidity**
- 4. Includes planning, modeling and research into “required and achievable coverage” or reach of interventions**
- 5. Prioritizes evaluation and operational research on implementation of interventions**
- 6. Considers issues of resource expansion, advocacy, and mobilization**

Summary



Major advances in treatment and prevention over the past 30 years, with early signals of impact. Despite this more needs to be done, and a sense of urgency remains

Now, more than ever, it is possible to change the course of the HIV epidemic, by combining HIV prevention interventions, including ART for treatment and prevention

Future success will depend on our ability to implement and bring to scale what we know works, for those at risk

- **Knowledge of the epidemiology and ability to choose & target efficacious combinations for synergy against specific risks**
- **Robust engagement with affected communities**
- **Strong health care delivery systems**
- **Ability to enrol, retain and maintain adherence**

Thank you

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STD and TB Prevention**

Centers for Disease Control and Prevention

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