IS THE END OF AIDS IN SIGHT?

Joseph LARMARANGE (Ceped, IRD / Africa Centre, UKZN)
François DABIS (ISPED, Inserm)

Colloque « En Afrique, accoucher après la fin de l'exceptionnalité du sida »
Bordeaux, 14 avril 2015

CePeD
Centre Population & Développement

AFRICA CENTRE
FOR HEALTH AND POPULATION STUDIES

Bordeaux school of public health
ISPED
Institut de Santé Publique d'Epidémiologie et de Développement

JUNE 2011


The Economist
The trap for Turkey
Wall Street's plumbing problem
Lady Gaga, Mother Teresa and profits
Brazil's boiling economy
The farce that is FIFA
JUNE 4TH–10TH 2011
Economist.com
The end of AIDS?
How 5 million lives have been saved, and a plague could now be defeated
£4.00
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The NEW ENGLAND JOURNAL of MEDICINE

Perspective

AUGUST 23, 2012

The Beginning of the End of AIDS?

Diane Havlir, M.D., and Chris Beyrer, M.D., M.P.H.

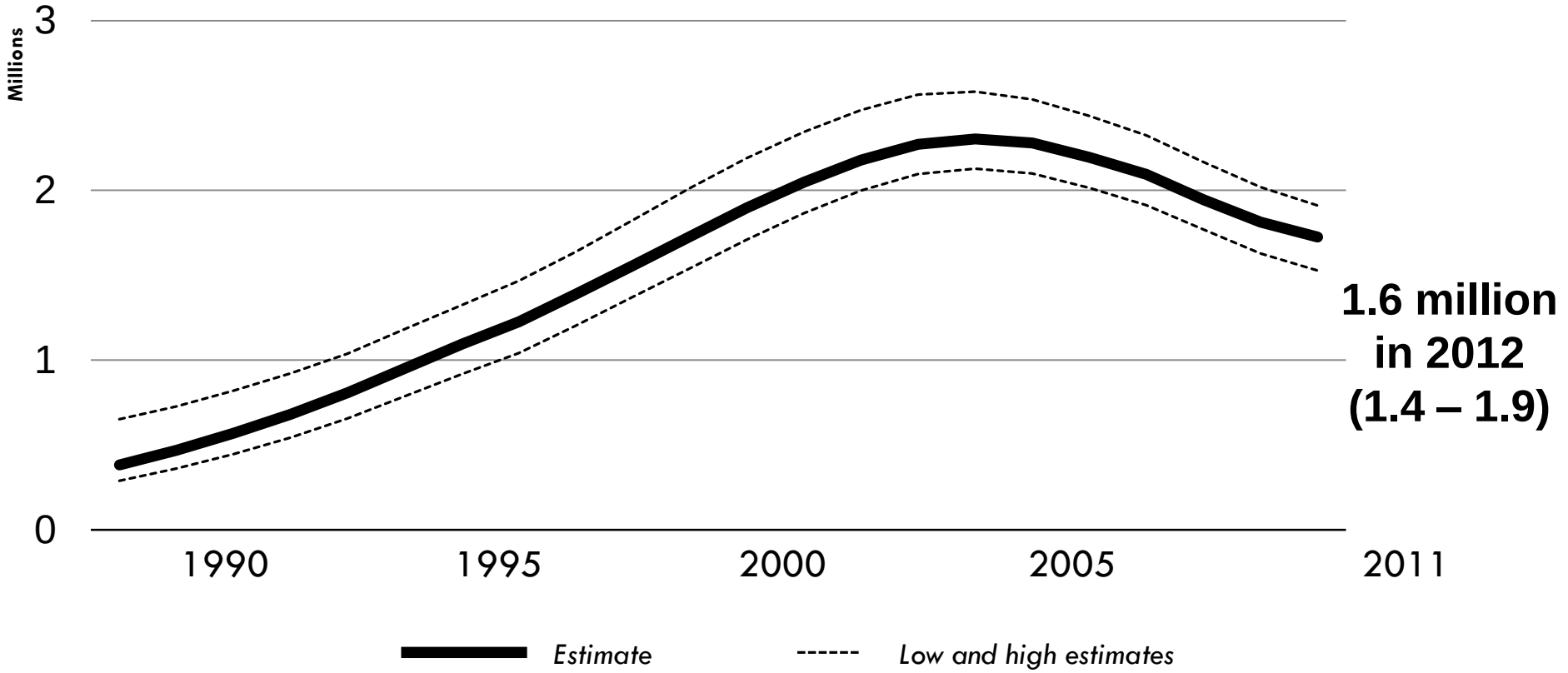
ENDING THE AIDS EPIDEMIC IS POSSIBLE

UNAIDS, The Gap Report, July 2014

GLOBAL TRENDS OF THE PANDEMIC

THE BEGINNING OF THE END?

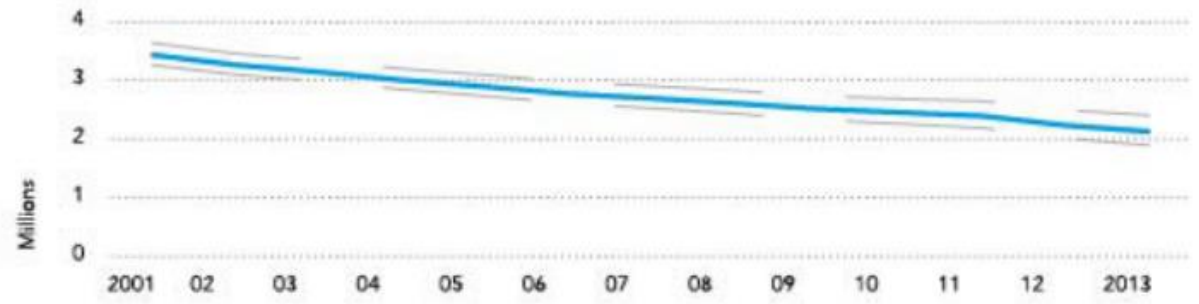
ADULT AND CHILD DEATHS DUE TO AIDS



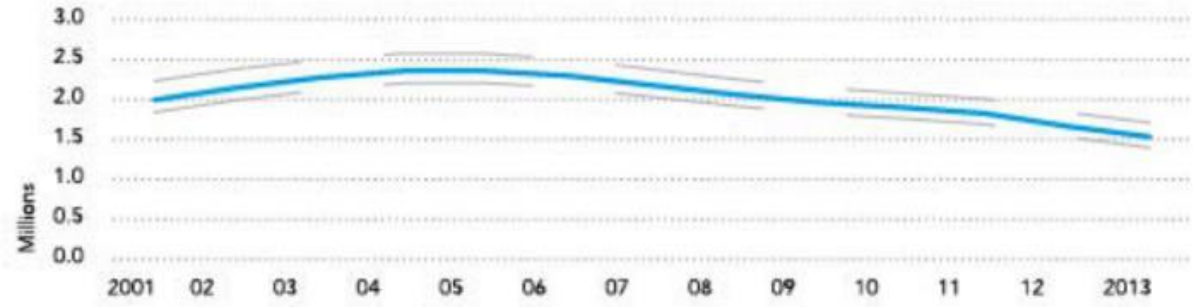
World Health Organization

UNAIDS

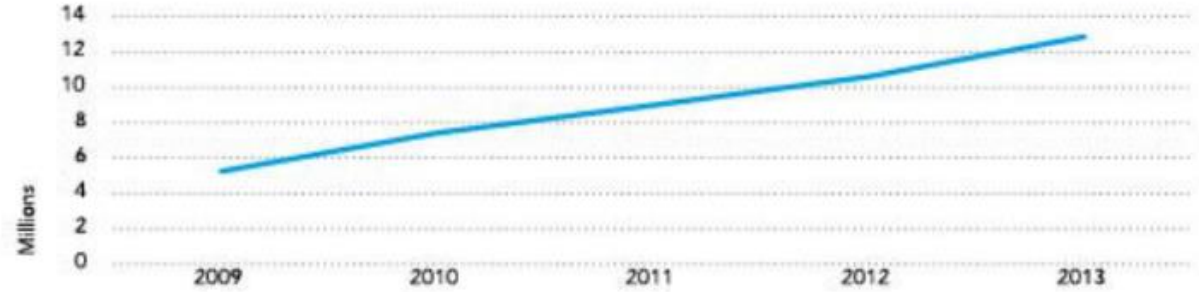
GLOBAL TRENDS (WORLD)



Number of new HIV infections – global



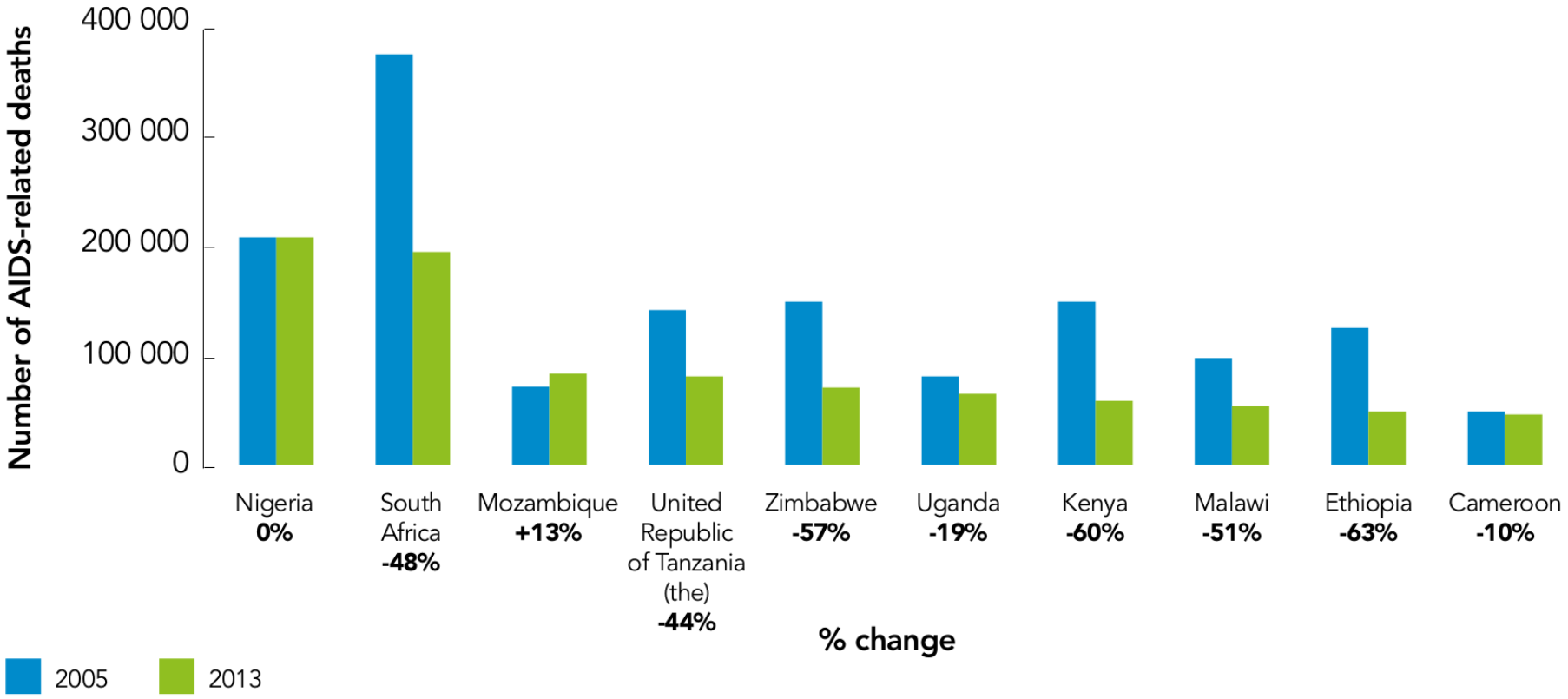
Number of AIDS-related deaths – global



Number of people receiving ART – global

AIDS-RELATED DEATHS

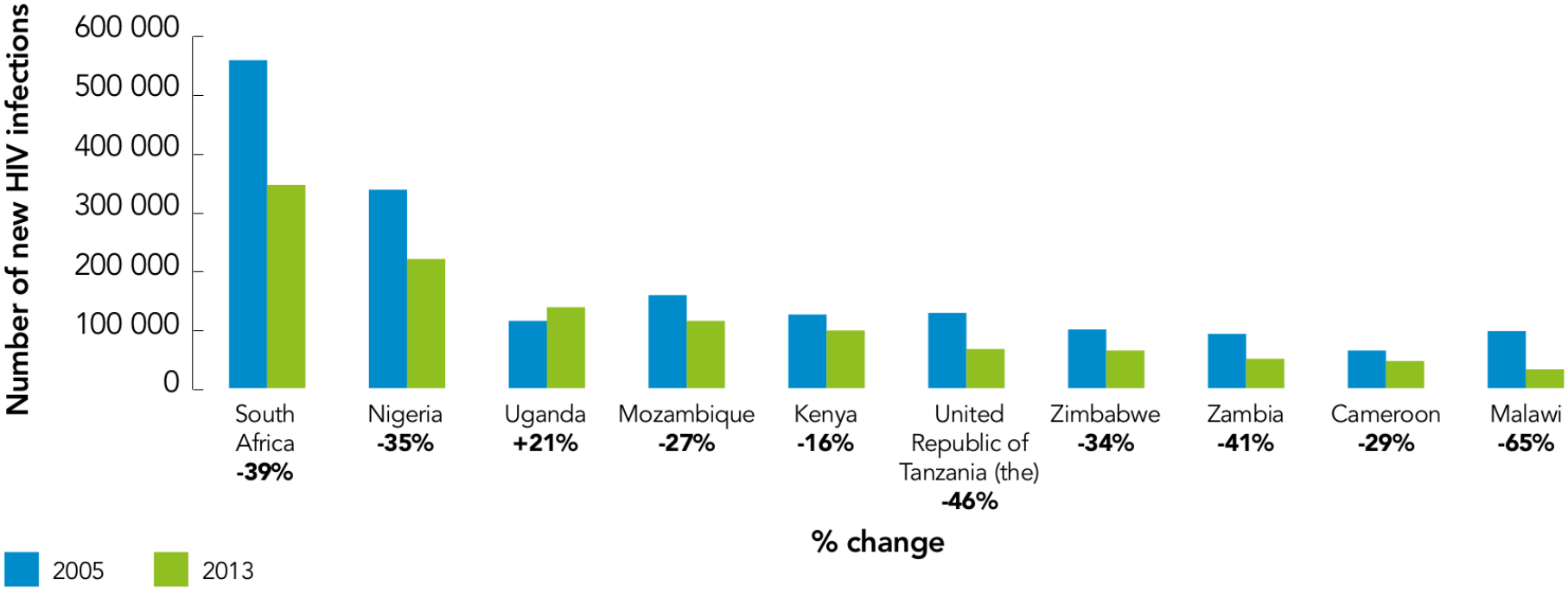
trends for top 10 countries in sub-Saharan Africa, 2005 and 2013



Source: UNAIDS 2013 estimates.

NEW HIV INFECTIONS

trends for top 10 countries in sub-Saharan Africa, 2005 and 2013



Source: UNAIDS 2013 estimates.

WHAT DO WE MEAN BY THE END OF AIDS?

PROPOSED DEFINITION

- No new AIDS-defining events and deaths (including TB-HIV deaths)
  - HIV = chronic disease

- No new HIV infections among adults and children
  - the promise of an AIDS-free generation
  - Elimination at population-level is often defined by modellers as an incidence below 1 per 1000 person-years

PREVENTING HIV TRANSMISSION

- Sexual transmission
  - Heterosexual women and men
  - Homosexual men
- Mother to Child
  - during pregnancy, delivery and breastfeeding
- Blood transmission
  - Intravenous drug use
  - Blood donation

THE HIV TOOLKIT

SEXUAL TRANSMISSION

1981 – 2012: A LIMITED ALPHABET

- Abstinence
- Be faithful
- Condom

EVALUATION OF "ABC" POLICIES

- **A**bstinence
  - At best a short term strategy
  - "What do we do for the rest of our lives"

CRITIQUES OF U.S. ABSTINENCE-ONLY POLICIES AND PROGRAMS (PEPFAR = US-SUPPORTED)

- Not medically accurate, promote misinformation
- Poorly designed, lack program efficacy
- Inconsistent with demographic realities

- A "moral" agenda, not a public health agenda

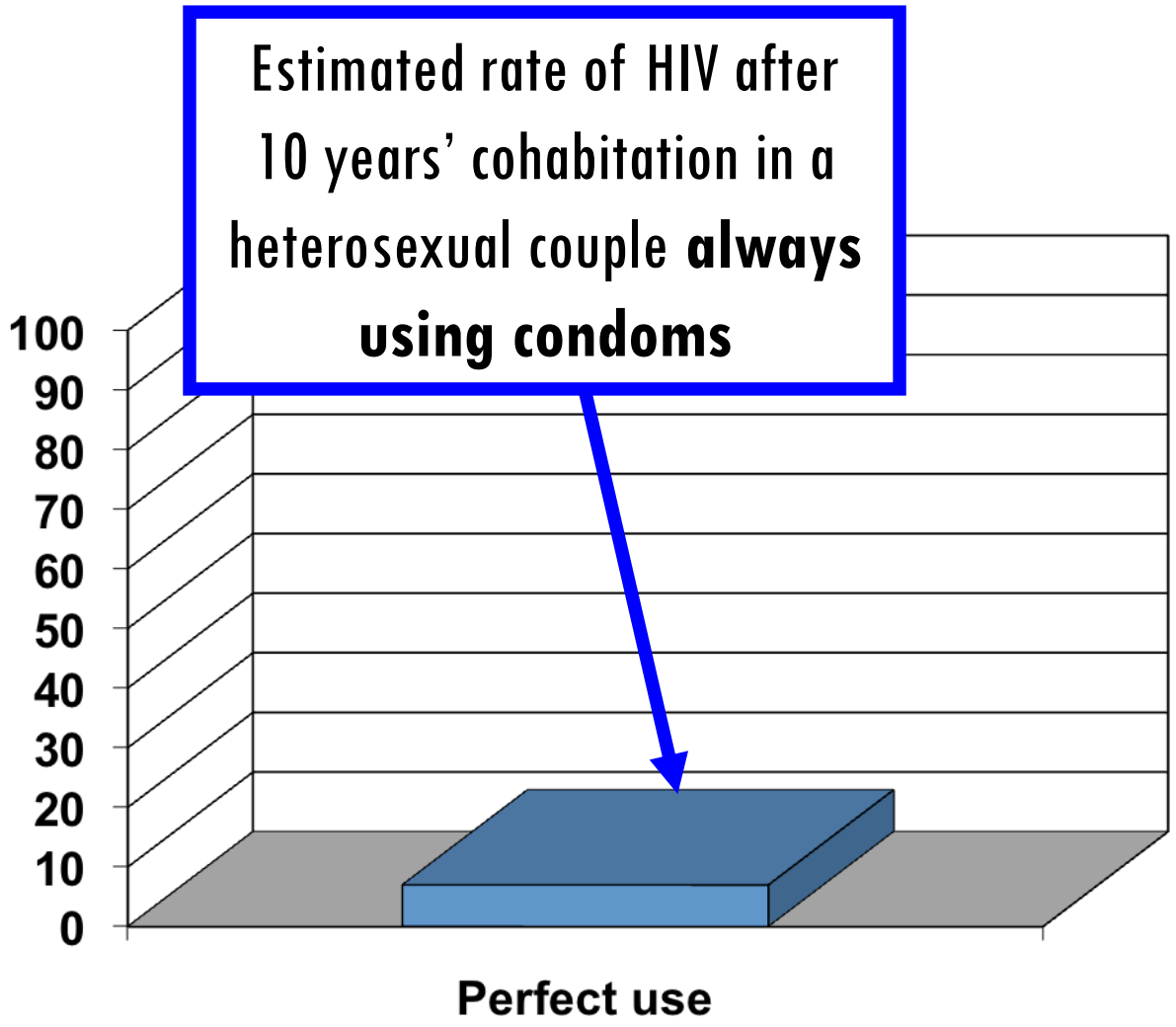
- Harm to public health (foreign aid) programs

EVALUATION OF "ABC" POLICIES

- **A**bstinence
  - At best a short term strategy
  - "What do we do for the rest of our lives"

- **B**e faithful (monogamy)
  - Risk for many married woman is her husband
  - Unilateral monogamy ineffective
  - Real issue is concurrency and interconnected sexual networks

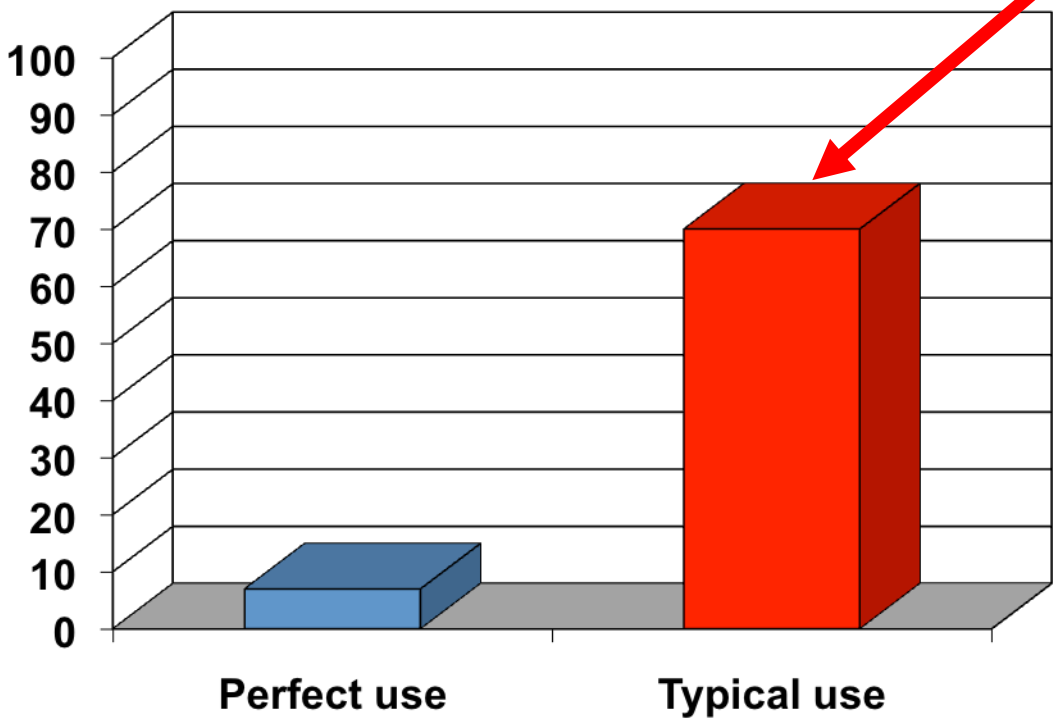
THE THEORY IS JUST FINE…



Adapted from W. Cates, FHI

PRACTICE RATHER LESS SO…

Estimated rate of HIV after 10 years' cohabitation in a heterosexual couple **at typical rates of condom use**



Adapted from W. Cates, FHI

EVALUATION OF "ABC" POLICIES

- **A**bstinence
  - At best a short term strategy
  - "What do we do for the rest of our lives"
- **B**e faithful (monogamy)
  - Risk for many married woman is her husband
  - Unilateral monogamy ineffective
  - Real issue is concurrency and interconnected sexual networks
- **C**ondoms
  - Effective if used consistently and correctly
  - Limited acceptance in many countries and relationships
  - Interferes with childbearing

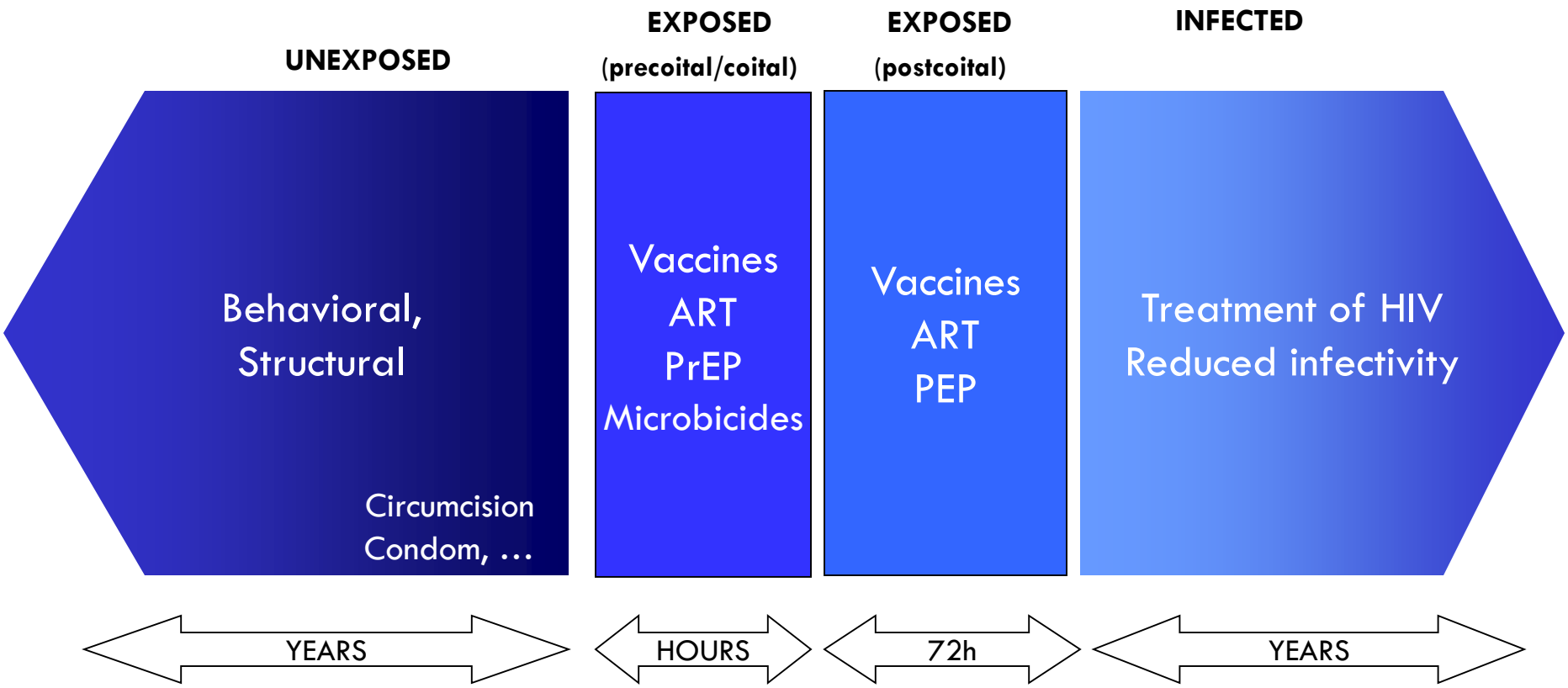
FROM

- Abstinence
- Be faithful
- Condom

TO

- Abstinence
- Be faithful
- Condom
- (male) Circumcision
- Counselling & Testing
- Microbicides
- Post-exposure prophylaxis
- Pre-exposure prophylaxis
- Sexually transmitted infections control
- (antiretroviral) Treatment (TasP)
- Vaccine

4 PREVENTION OPPORTUNITIES



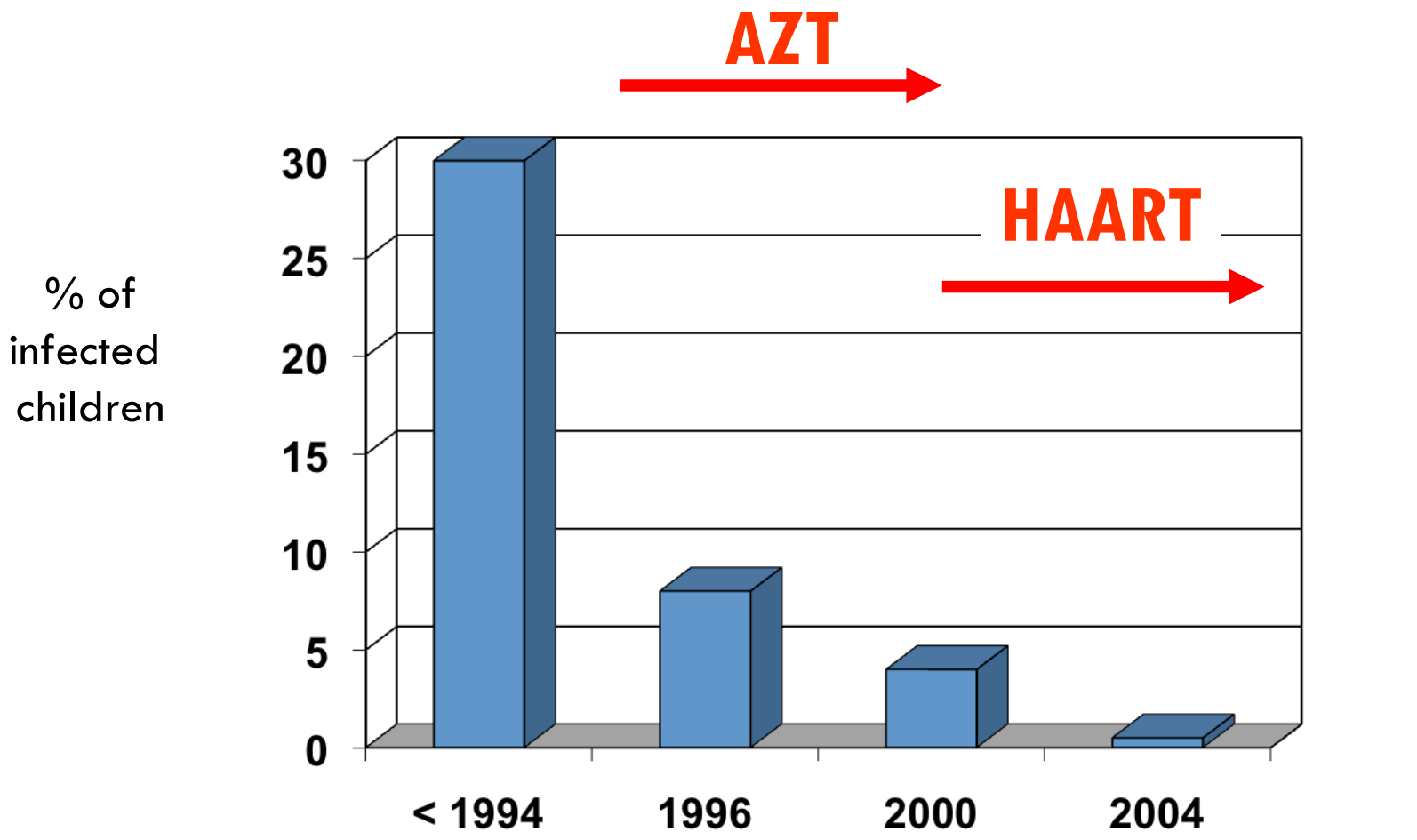
Adapted from Cohen , IAS 2008

TREATMENT

&

PREVENTION

MOTHER-TO-CHILD TRANSMISSION



Adapted from Coovadia and Lallemant, NEJM 2004

MTCT IN EUROPE

"Virtual elimination" of MTCT in Europe

Country	MTCT	Time period
France	**1.0%**	2005-2009
Italy	**1.0%**	2005-2010
Denmark	**0.5%**	2000-2008
Sweden	**0.6%**	1999-2003
Spain	**1.6%**	2000-2007
Ukraine	**4.1%**	2008-2010
Russia	**3-4%**	2010
UK	**0.57%**	2007-2011

Jasseron et al 2011, von Linstow et al 2010, Naver et al 2006, Chiappini et al 2011, Prieto et al 2012, ECS unpublished data, Personal comm. Inga Latysheva

UK and Ireland

National Study of HIV in Pregnancy and Childhood NSHPC

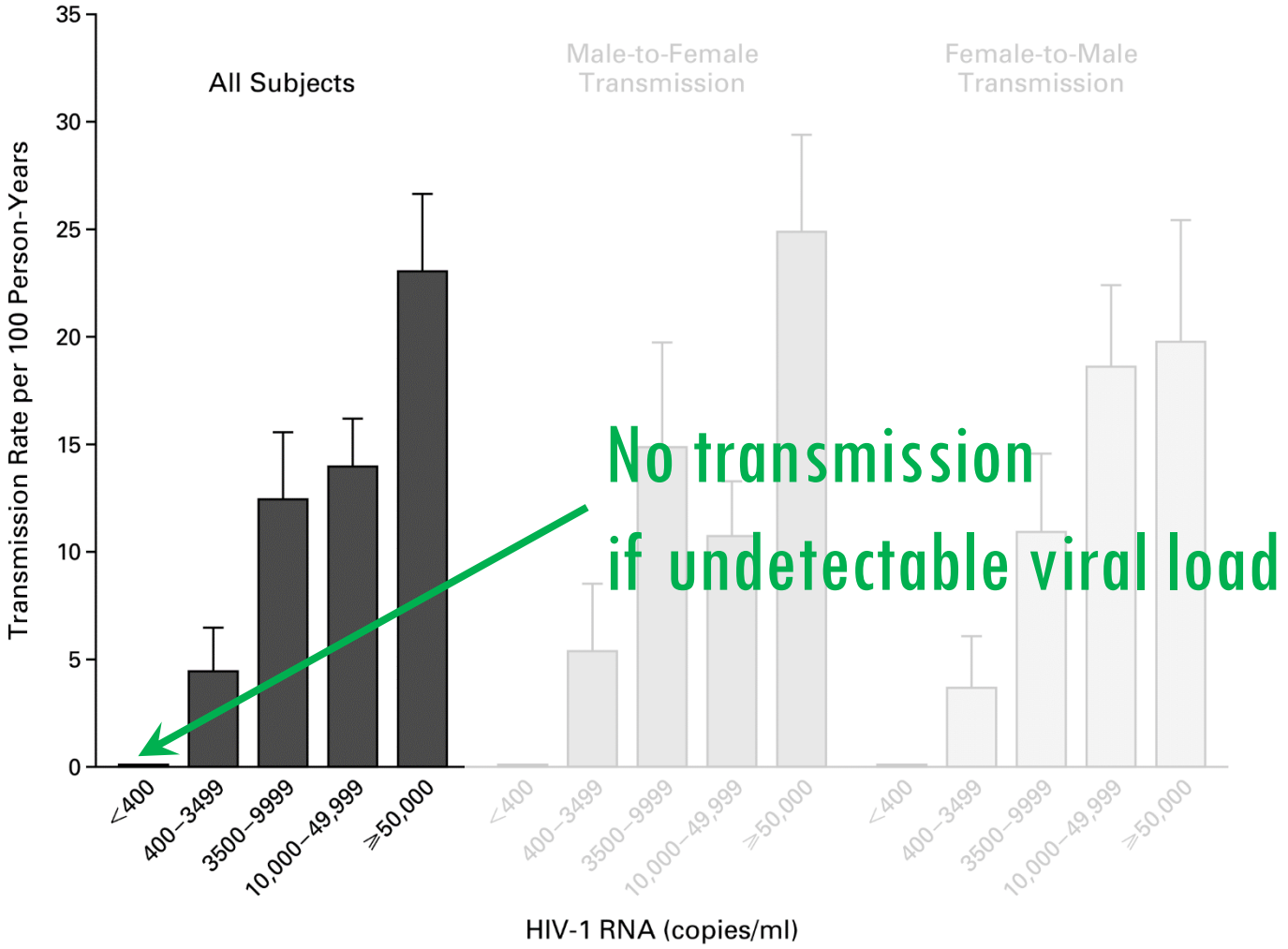
MTCT rates 2000-2011

- 33 infected infants among 5788 singleton live births

Source: Diana M. Gibb, CROI 2015

2000: THE "RAKAI" STUDY

Transmission risk as function of plasma viral load



Source:
Quinn et al.
NEJM
2000

Figure 1. Mean (+SE) Rate of Heterosexual Transmission of HIV-1 among 415 Couples, According to the Sex and the Serum HIV-1 RNA Level of the HIV-1–Positive Partner.

2008: THE SWISS STATEMENT

HIV-infected individuals on ART with undetectable viral load for 12 months and no other IST don't transmit HIV sexually anymore and could stop using a condom within a stable couple

CFS

AUTRES GROUPEMENTS ET INSTITUTIONS

Les personnes séropositives ne souffrant d'aucune autre MST et suivant un traitement antirétroviral efficace ne transmettent pas le VIH par voie sexuelle

Could ARV treatment contribute to reduce HIV transmission at individual and population levels?

2011: HPTN 052 STUDY

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 AUGUST 11, 2011 VOL. 365 NO. 6

Prevention of HIV-1 Infection with Early Antiretroviral Therapy

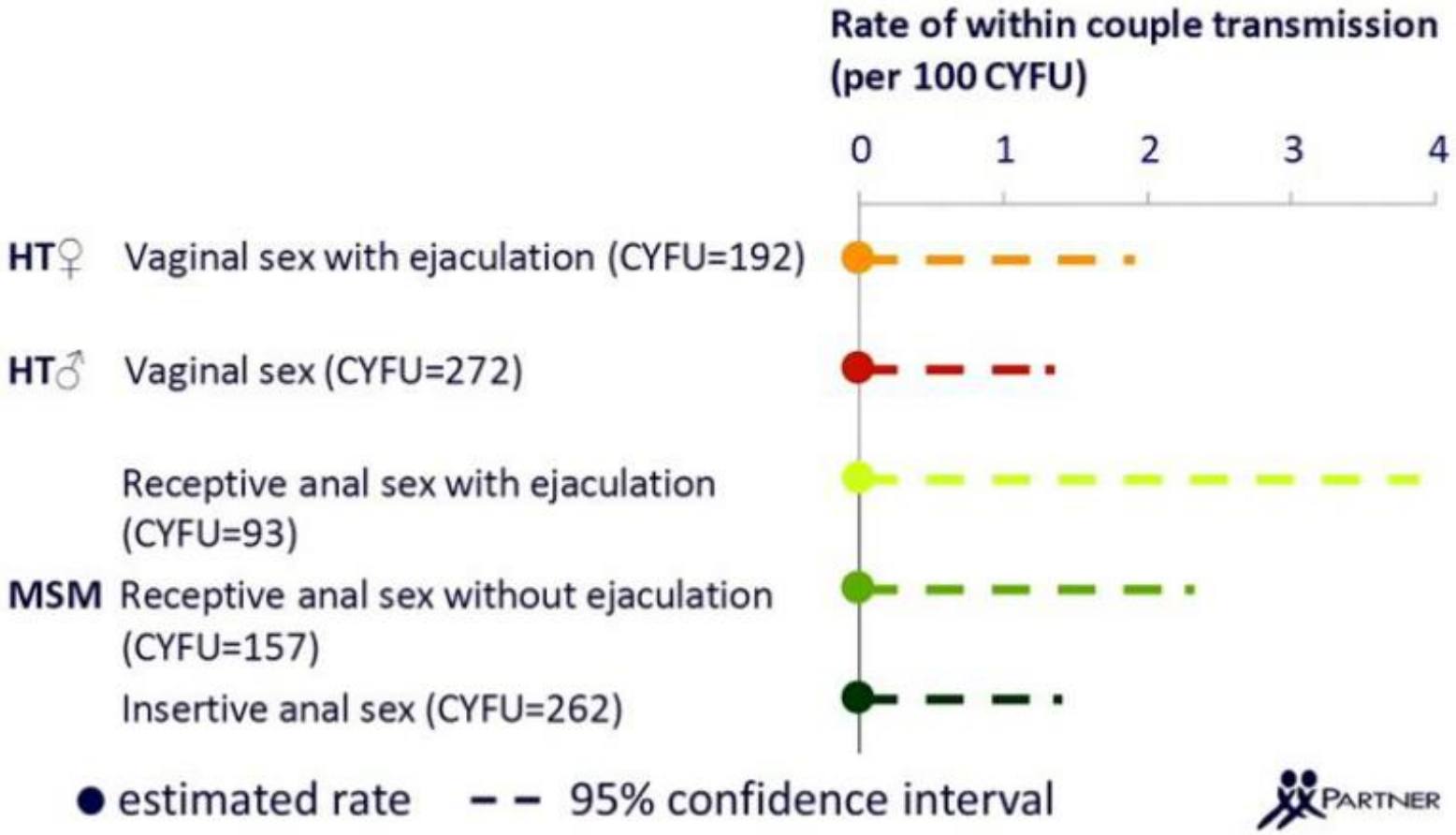
Myron S. Cohen, M.D., Ying Q. Chen, Ph.D., Marybeth McCauley, M.P.H., Theresa Gamble, Ph.D., Mina C. Hosseinipour, M.D., Nagalingeswaran Kumarasamy, M.B., B.S., James G. Hakim, M.D., Johnstone Kumwenda, F.R.C.P., Beatriz Grinsztejn, M.D., Jose H.S. Pilotto, M.D., Sheela V. Godbole, M.D., Sanjay Mehendale, M.D., Suwat Chariyalertsak, M.D., Breno R. Santos, M.D., Kenneth H. Mayer, M.D., Irving F. Hoffman, P.A., Susan H. Eshleman, M.D., Estelle Piwowar-Manning, M.T., Lei Wang, Ph.D., Joseph Makhema, F.R.C.P., Lisa A. Mills, M.D., Guy de Bruyn, M.B., B.Ch., Ian Sanne, M.B., B.Ch.,

The early initiation of antiretroviral therapy reduces rates of sexual transmission of HIV-1 by 96%

2015: THE PARTNER STUDY (IN EUROPE)

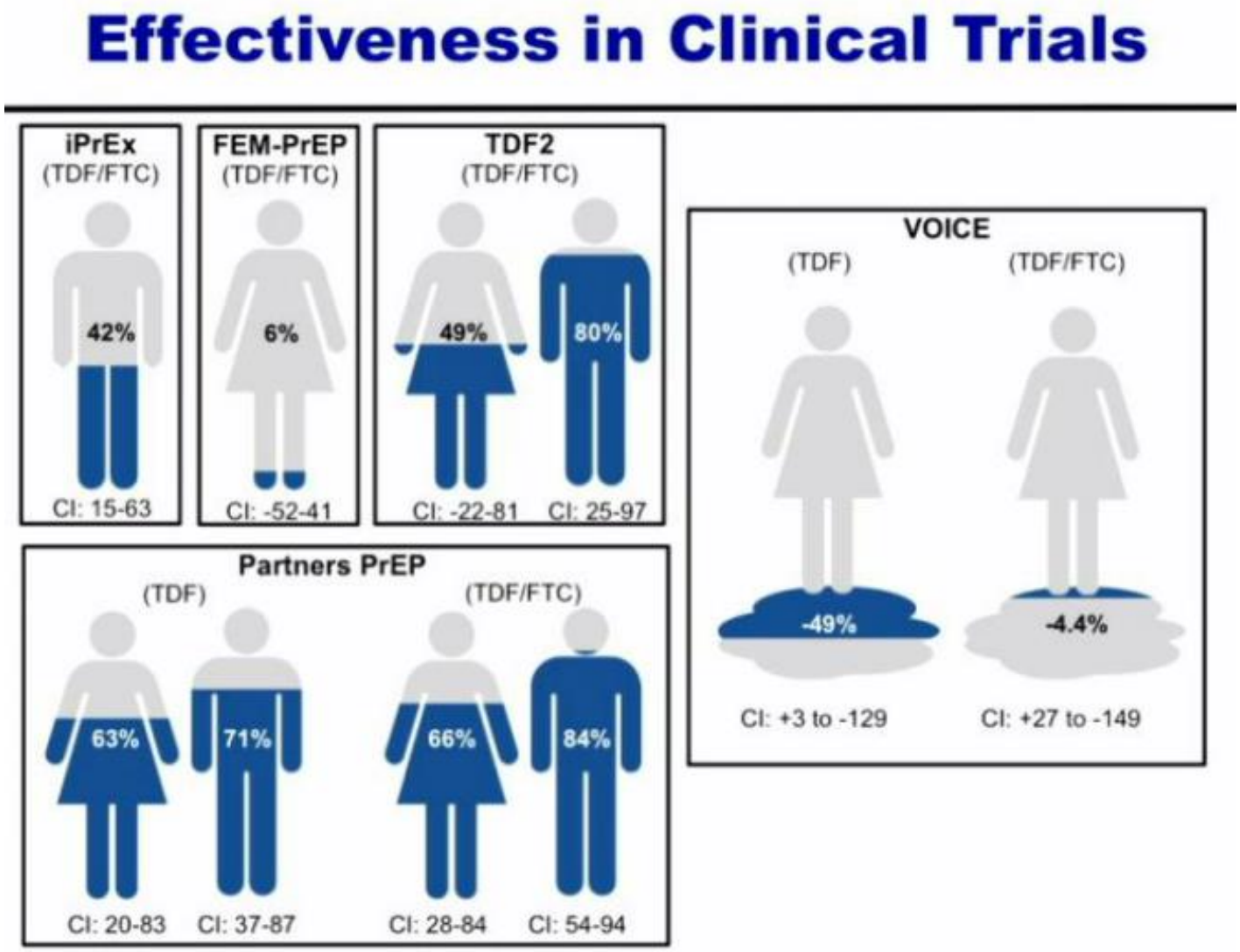
HIV+ partner on ART and virologically suppressed

Rate of HIV transmission according to sexual behavior reported by HIV- partner



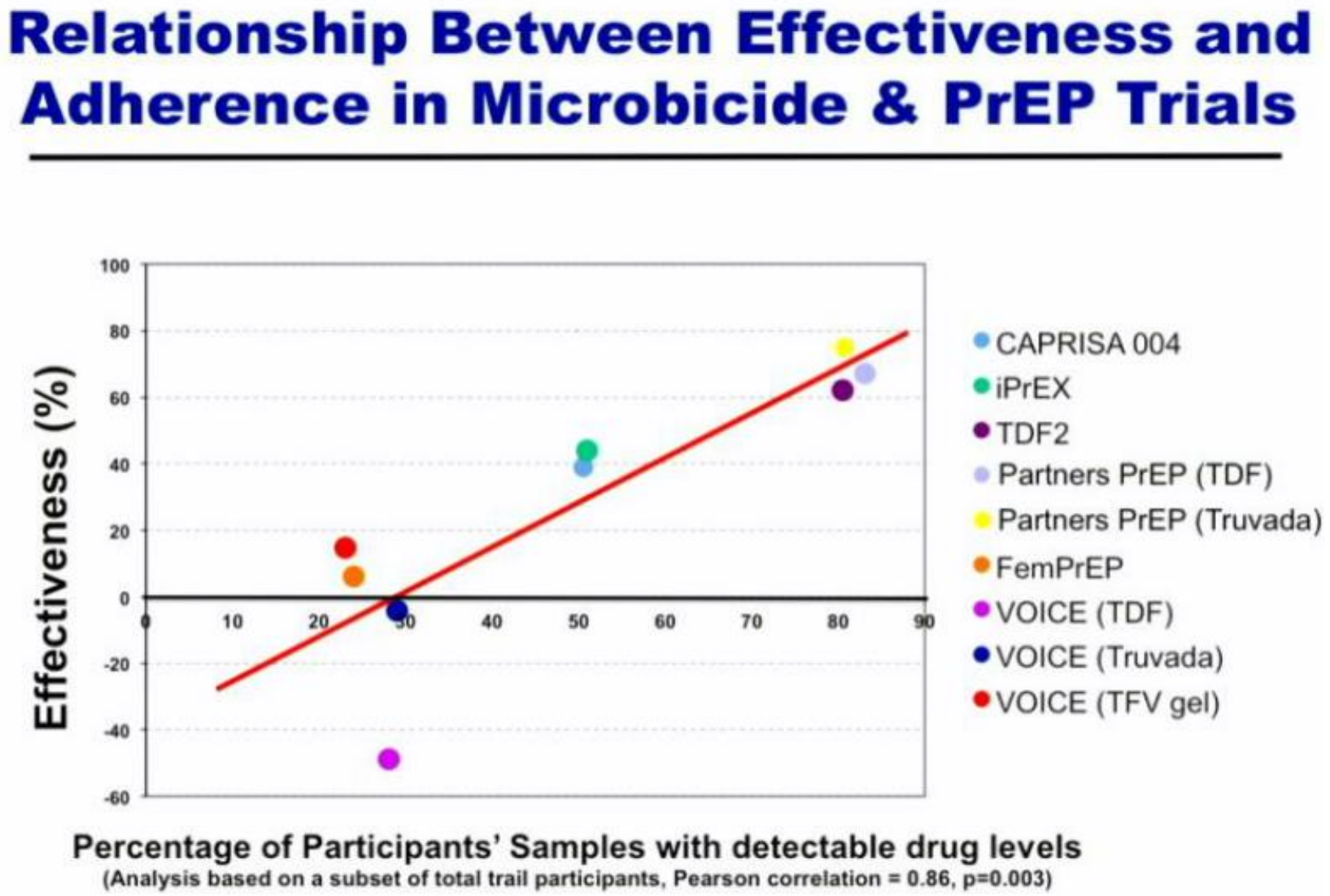
Source: Alison Rodger, CROI 2015

PRE-EXPOSURE PROPHYLAXIS (PREP)



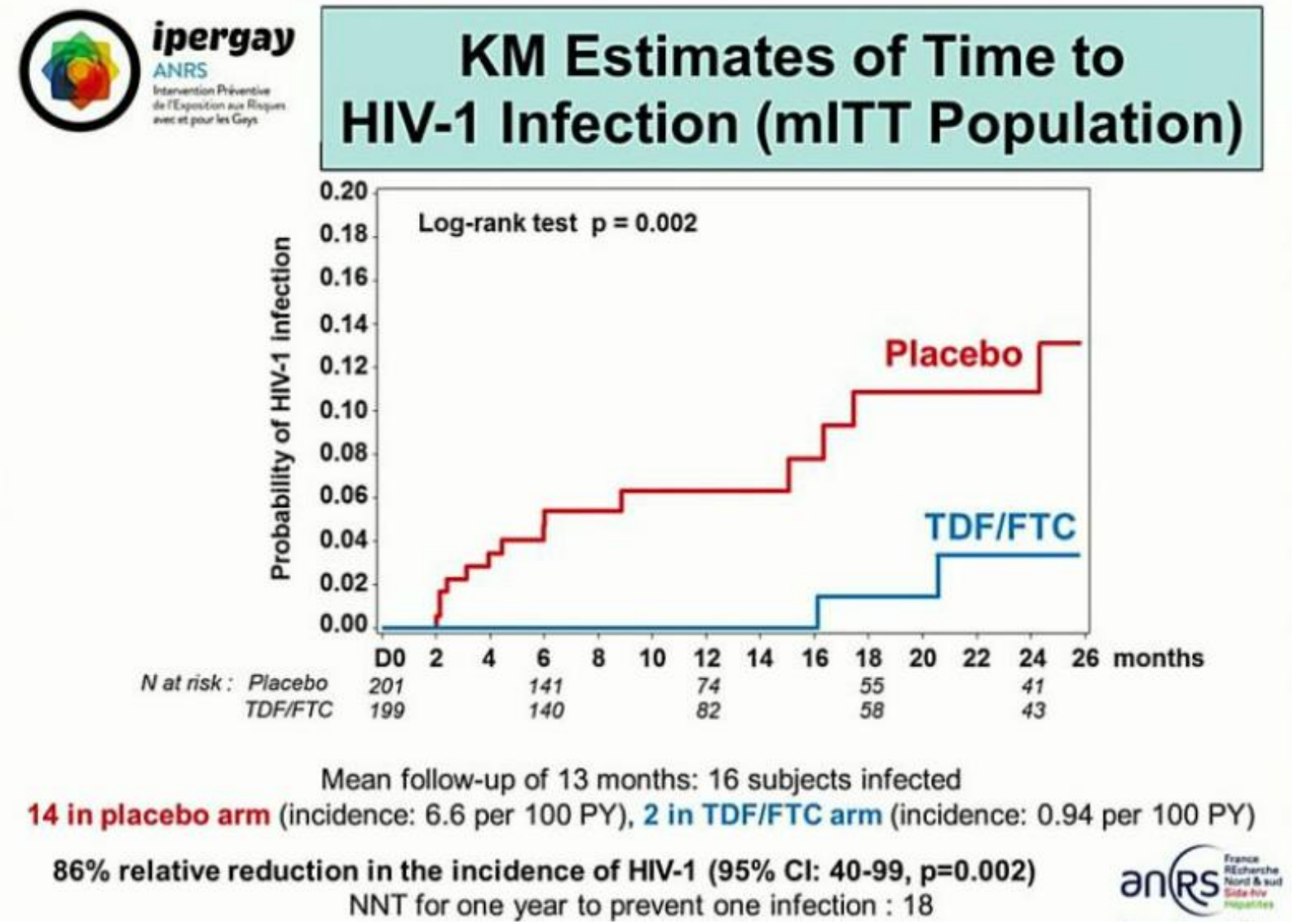
Source: Raphael Landovitz, CROI 2015

PRE-EXPOSURE PROPHYLAXIS (PREP)



Source: Raphael Landovitz, CROI 2015

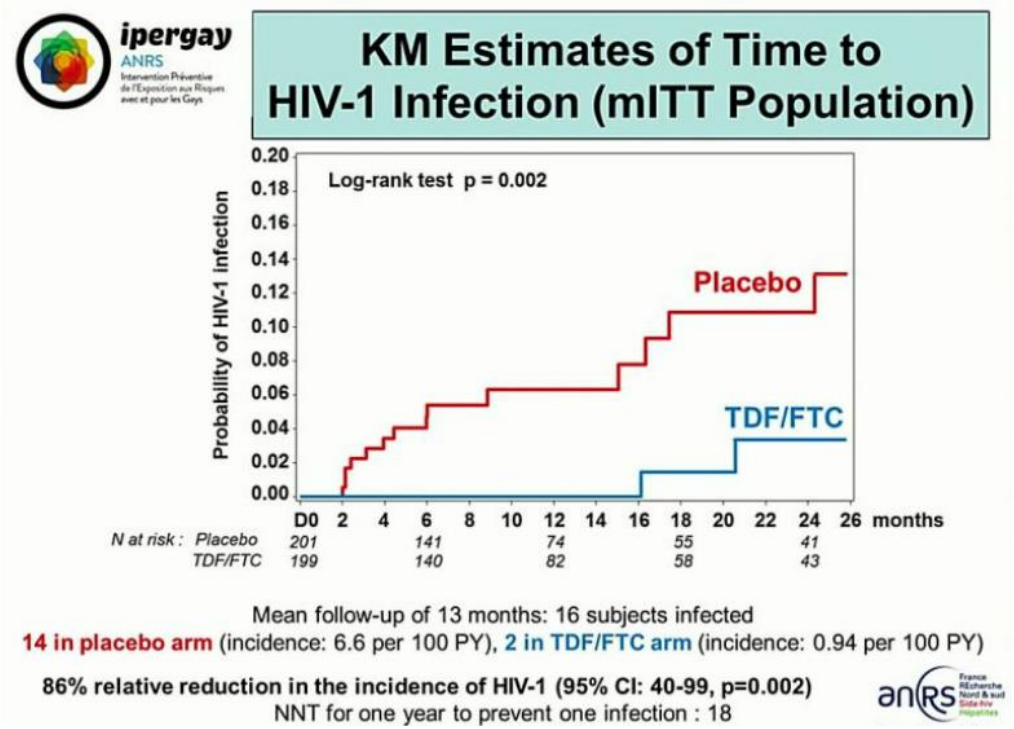
PREP AMONG GAY MEN IN EUROPE: THE IPERGAY TRIAL



Source: Jean-Michel Molina, CROI 2015

PREP AMONG GAY MEN IN EUROPE: IPERGAY & PROUD TRIALS

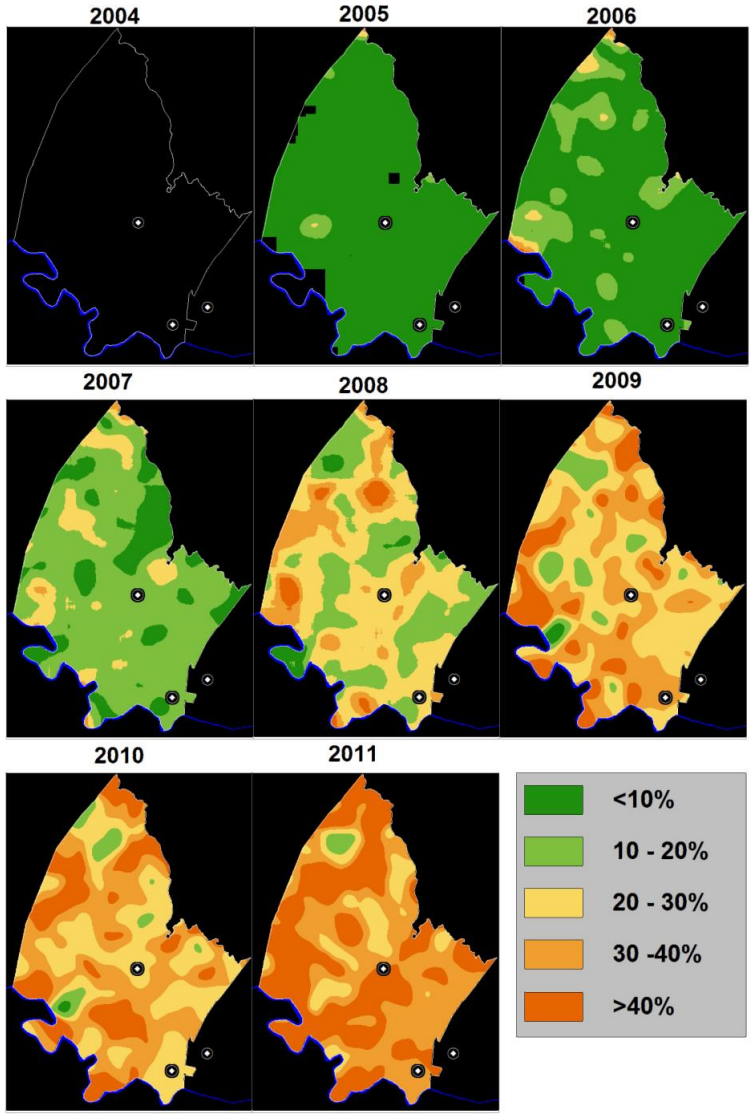
- Efficacy: 86%
- Similar result observed in the PROUD trial among gay men in UK



Source: Jean-Michel Molina, CROI 2015

IMPACT OF ART AT POPULATION LEVEL

ART COVERAGE 2004-2011
HLABISA SUB-DISTRICT, RURAL SOUTH AFRICA



- ART coverage 2004-2011
- ART coverage = proportion of the total HIV-infected population receiving ART at <200 then <350 CD4 cells/µl
- >20 000 patients initiated ART

Source:
Tanser et al.
Science 2013

IMPACT OF ART ON MORTALITY

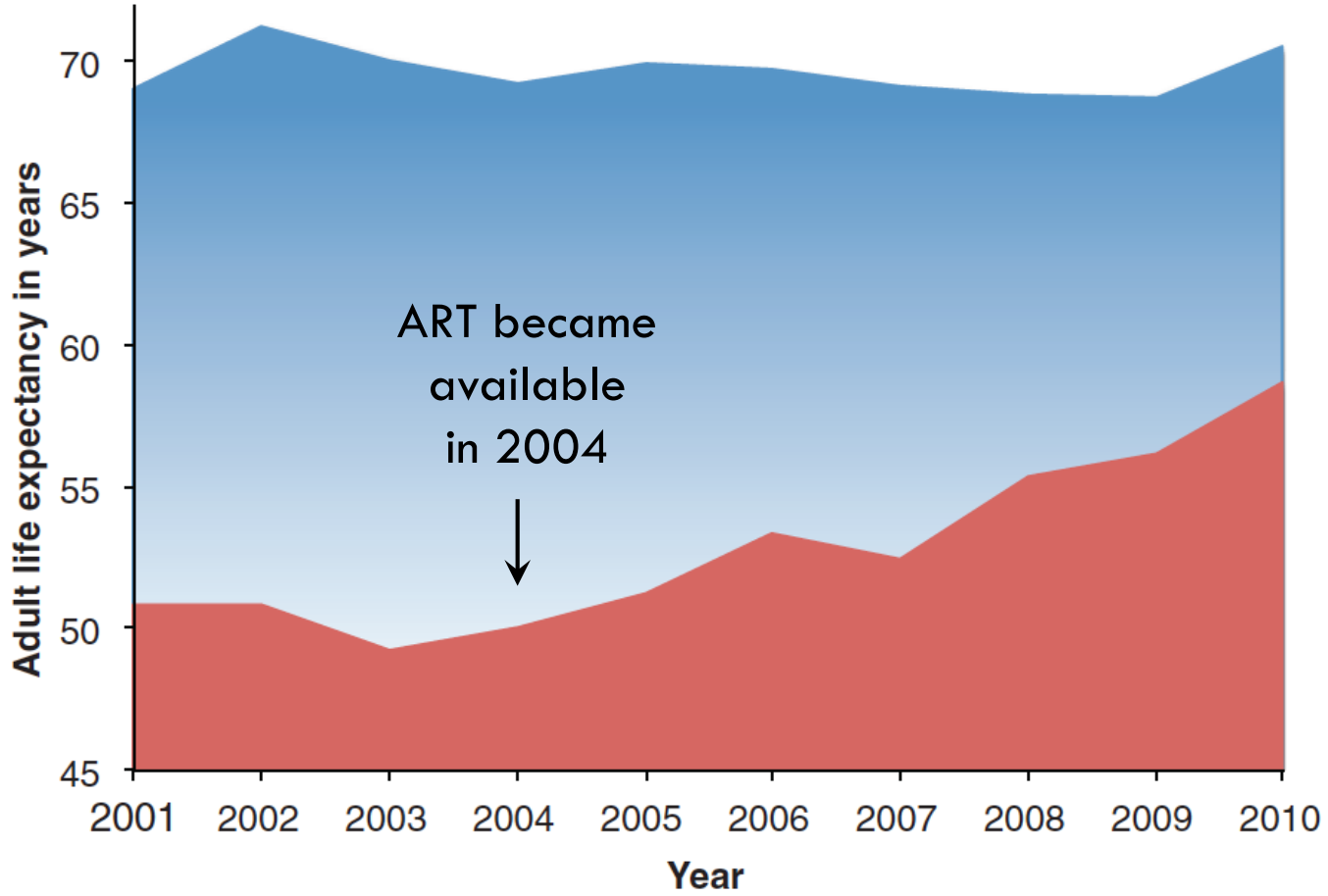
Increases in Adult Life Expectancy in Rural South Africa: Valuing the Scale-Up of HIV Treatment

Jacob Bor,[1,2*] Abraham J. Herbst,[1] Marie-Louise Newell,[1,3] Till Bärnighausen[1,2]

www.sciencemag.org SCIENCE VOL 339 22 FEBRUARY 2013

IMPACT OF ART ON MORTALITY

- Adult life expectancy (red line) increased from 49.2 years (2003) to 60.5 years (2011)



Rural South Africa

Source: Bor et al. *Science* 2013

IMPACT OF ART ON INCIDENCE

REPORTS

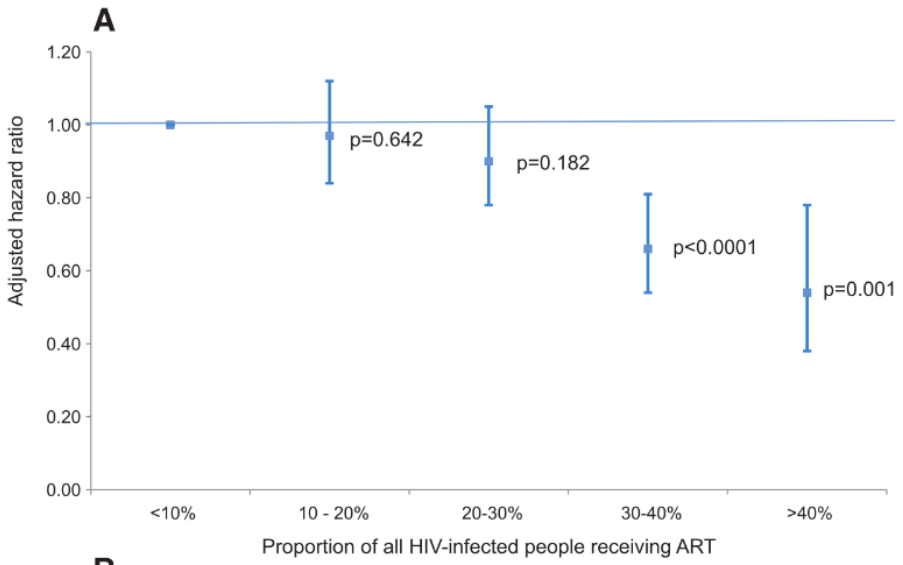
High Coverage of ART Associated with Decline in Risk of HIV Acquisition in Rural KwaZulu-Natal, South Africa

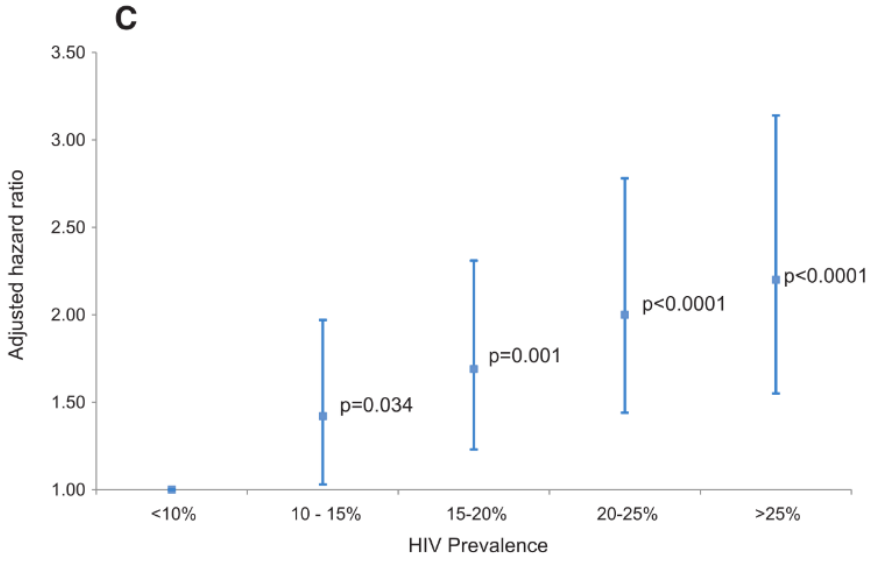
Frank Tanser,[1*] Till Bärnighausen,[1,2] Erofili Grapsa,[1] Jaffer Zaidi,[1] Marie-Louise Newell[1,3]

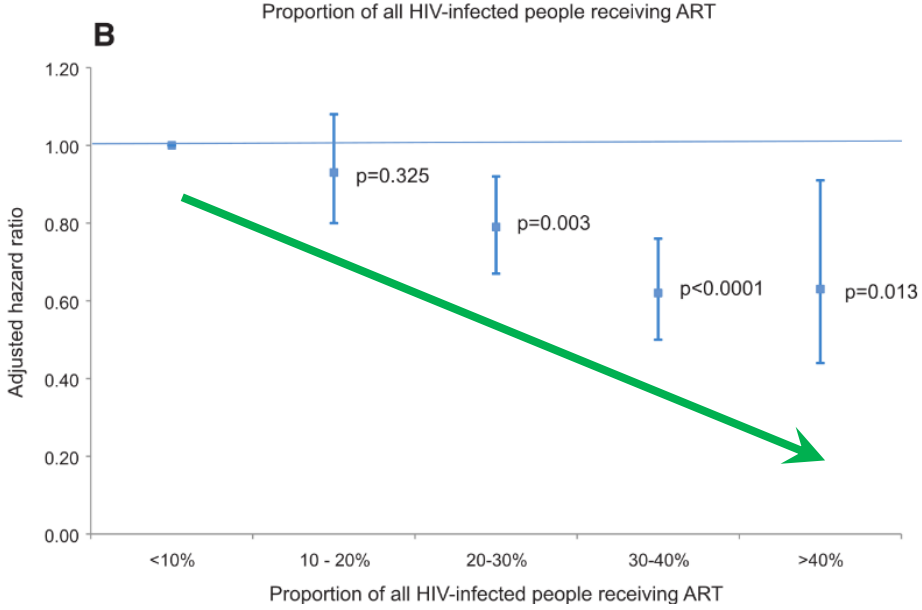
www.sciencemag.org SCIENCE VOL 339 22 FEBRUARY 2013

IMPACT OF ART ON INCIDENCE

Adjusted HIV acquisation hazard ratio by ART coverage







The risk of acquiring HIV is reduced when ART coverage increases at population level

Source:
Tanser et al.
Science 2013

WHAT WOULD HAPPEN TO THE EPIDEMIC IF MORE INFECTED PERSONS WERE TREATED?

2009: THE "GRANICH MODEL"

Universal voluntary HIV testing with immediate antiretroviral therapy as a strategy for elimination of HIV transmission: a mathematical model

Reuben M Granich, Charles F Gilks, Christopher Dye, Kevin M De Cock, Brian G Williams

Lancet 2009; 373: 48–57

Published Online November 26, 2008 DOI:10.1016/S0140-6736(08)61697-9

See Comment pages 7 and 9

Department of HIV/AIDS (R M Granich MD, Prof C F Gilks DPhil, Prof K M De Cock MD) **and Stop TB Department** (Prof C Dye DPhil, B G Williams PhD), **WHO, Geneva, Switzerland**

Summary

Background Roughly 3 million people worldwide were receiving antiretroviral therapy (ART) at the end of 2007, but an estimated 6·7 million were still in need of treatment and a further 2·7 million became infected with HIV in 2007. Prevention efforts might reduce HIV incidence but are unlikely to eliminate this disease. We investigated a theoretical strategy of universal voluntary HIV testing and immediate treatment with ART, and examined the conditions under which the HIV epidemic could be driven towards elimination.

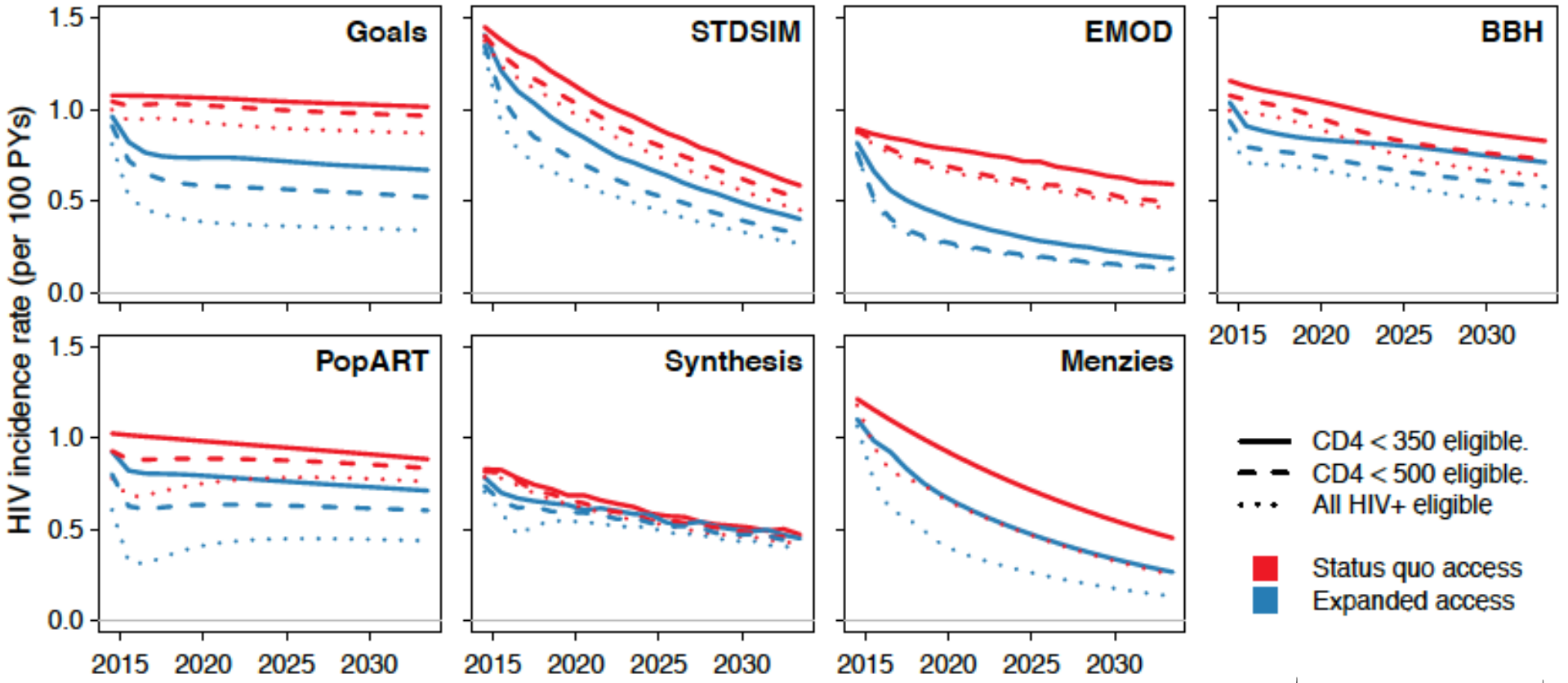
Methods We used mathematical models to explore the effect on the case reproduction number (stochastic model) and long-term dynamics of the HIV epidemic (deterministic transmission model) of testing all people in our test-case community (aged 15 years and older) for HIV every year and starting people on ART immediately after they are diagnosed HIV positive. We used data from South Africa as the test case for a generalised epidemic, and assumed that all HIV transmission was heterosexual.

Universal testing with immediate antiretroviral therapy could eliminate HIV transmission

(model calculated in the context of South Africa)

MODELING THE IMPACT OF ART

HIV incidence rate according to CD4 eligibility thresholds and ART uptake
South Africa case study – Seven models



Status quo: continuation of patterns of testing and ART uptake

HIV Modelling Consortium

CAN WE REACH HIV ELIMINATION?

Table 3. Year of HIV elimination (incidence <1/1,000 person-years) under universal testing and immediate ART for all HIV-infected patients (UTT) and number of life-years saved through UTT compared to the baseline of no UTT.

Model	Sub-Model	Year of Elimination[a] (Range)	Life-Years Saved per ART Treatment Year in 2050 (Range)
Model A		2019 (2018; 2021)	5.7 (4.7; 7.2)
	+ Age structure (B1)	2019 (2018; 2020)	3.8 (3.1; 4.3)
	+ Heterogeneity in HIV transmission by disease stage[b] (B2)	2053 (2048; >2060)	2.6 (2.1; 3.3)
Model B (B1 and B2 combined)		2053 (2042; >2060)	3.0 (2.6; 3.5)
	+ Sexual network (C1)	>2060 (2058; >2060)	2.6 (1.8; 2.9)
	+ Background prevention interventions (C2)	2042 (2037; 2050)	2.8 (2.1; 3.2)
	+ Up-to-date ART assumptions (C3)	>2060 (2054; >2060)	2.9 (2.5; 3.1)
Model C (C1, C2, and C3 combined)		2032 (2030; 2041)	1.8 (1.1; 2.0)
Model D (STDSIM)		2029 (2027; 2034)	1.7 (1.2; 2.6)
Model D baseline (ART at CD4 count ≤350 cells/μl)		2041 (2037; 2047)	N/A

UTT is scaled up linearly, starting in 2012 and reaching 90% coverage in 2019. Ranges reflect the variation in outcome due to the uncertainty in the parameter values that were quantified based on fitting the model to the data.

[a]Incidence below 1/1,000 person-years.

[b]We assumed four different stages: acute, asymptomatic, symptomatic, and AIDS.

N/A, not applicable.

doi:10.1371/journal.pmed.1001534.t003

Source:
Hontelez et al.
PLoS Med 2013

“ALL MODELS ARE WRONG, BUT SOME ARE USEFUL”

quoted by Thiébaut R. & May MT. *AIDS*, 2013

UNIVERSAL TEST & TREAT HYPOTHESIS

HIV testing of all members of a community,
followed by immediate ART initiation
of nearly all HIV-infected individuals
regardless of immunological / clinical stage

i.e. Universal Test & Treat (UTT)

will prevent onward transmission and
reduce HIV incidence in this population

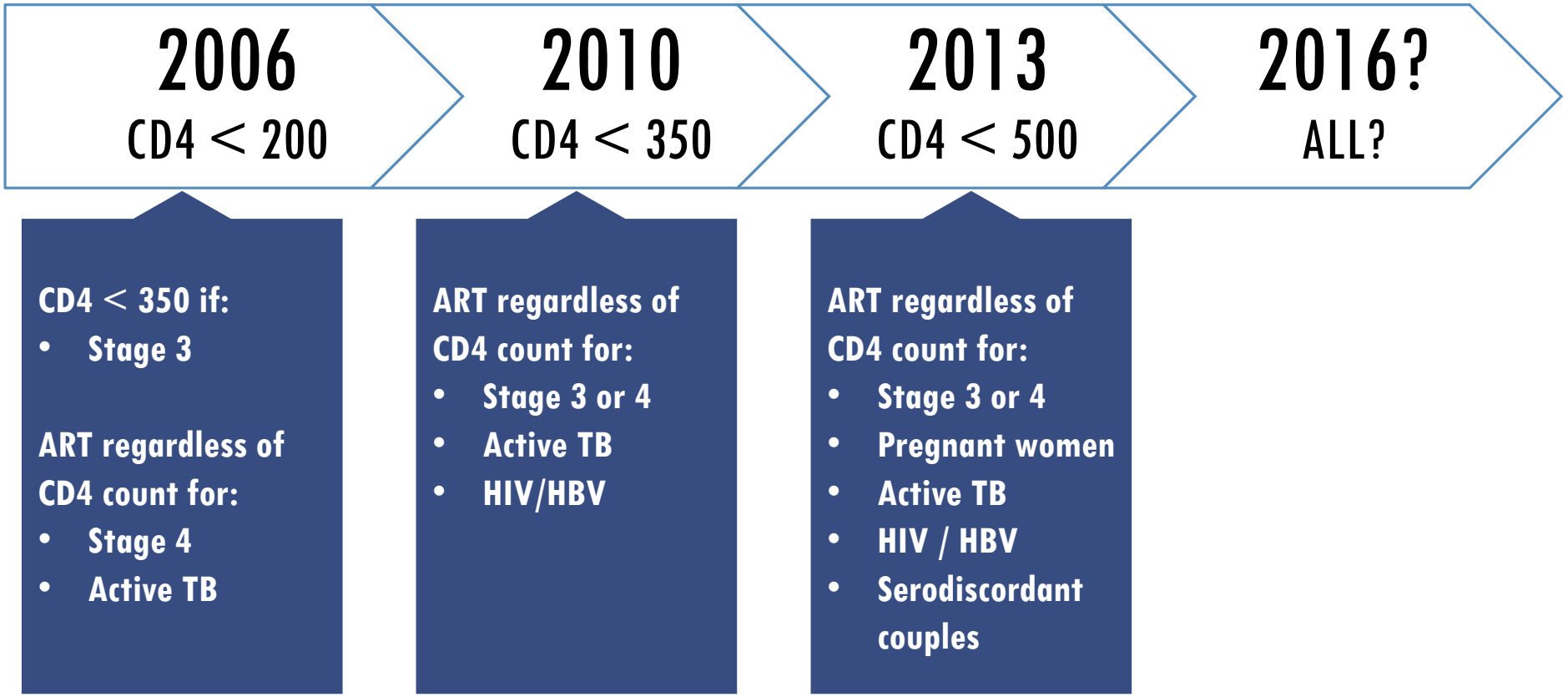
UTT CLUSTER RANDOMIZED TRIALS

- 4 on-going in Africa
  - ANRS 12 249 TasP (South Africa)
  - HPTN 071 PopART (South Africa & Zambia)
  - CDC BCPP (Bostwana)
  - SEARCH (Uganda & Kenya)

- 1 on-going in the US
  - HPTN 065 TLC-Plus (Washington DC & Bronx NY)

TREATING EARLIER

EVOLUTION OF WHO GUIDELINES

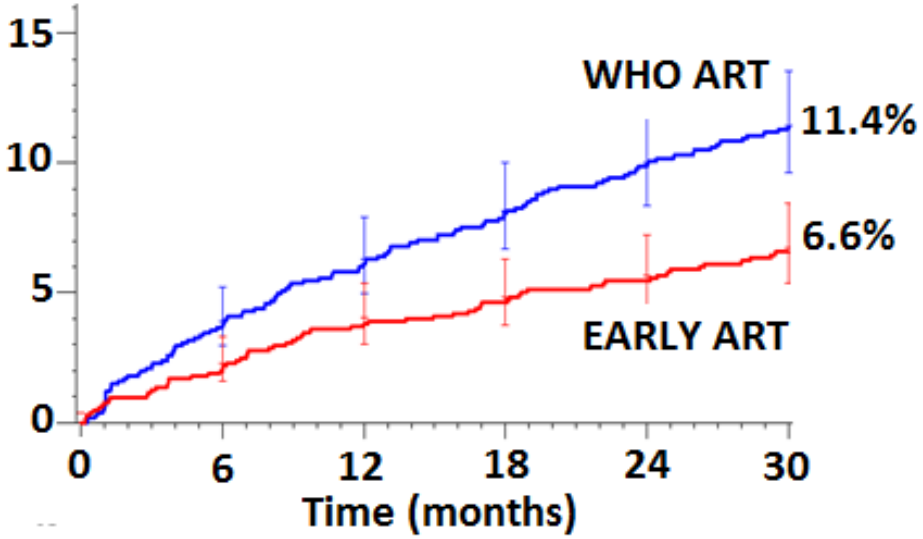


INDIVIDUAL BENEFIT OF EARLY TREATMENT: TEMPRANO RESULTS

- ANRS 12136
- Côte d'Ivoire
- Early ART (CD4<800) vs. WHO guidelines

- 44% reduction in severe HIV morbidity (all cause mortality, any AIDS defining-event, severe bacterial diseases, and non AIDS cancers)

Severe HIV morbidity



	n	Rate /100 PY	aHR	*p*
WHO ART	111	4.9		
Early ART	64	2.8	0.56	*0.0002*

aHR: adjusted Hazard Ratio

Source: Christine Danel, CROI 2015

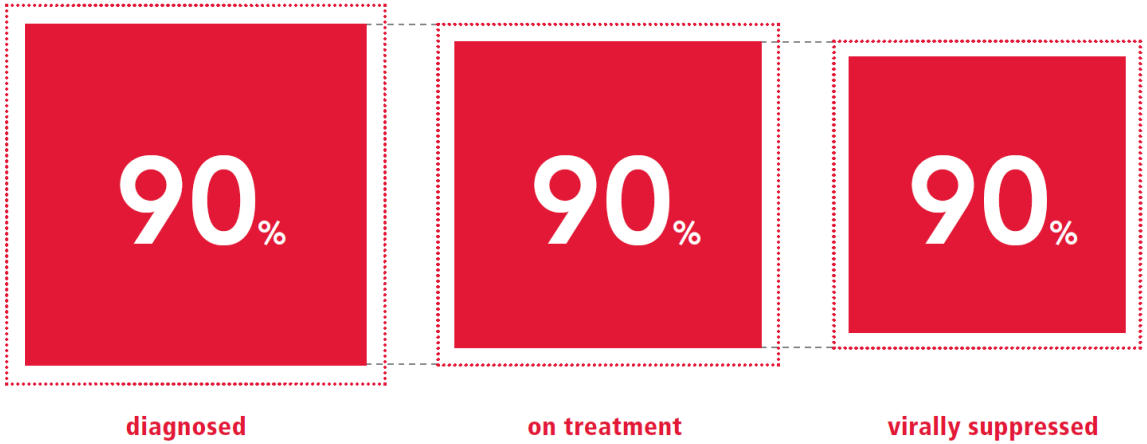
TREATING ALL

GRANICH'S MODEL ASSUMPTIONS

- 90% of all individuals ever tested
- 90% of those diagnosed on ART

➔ 81% of all HIV+ on treatment

NEW UNAIDS OBJECTIVES (2014)



by 2020

90-90-90

Treatment

500 000

New infections among adults

ZERO

Discrimination

by 2030

95-95-95

Treatment

200 000

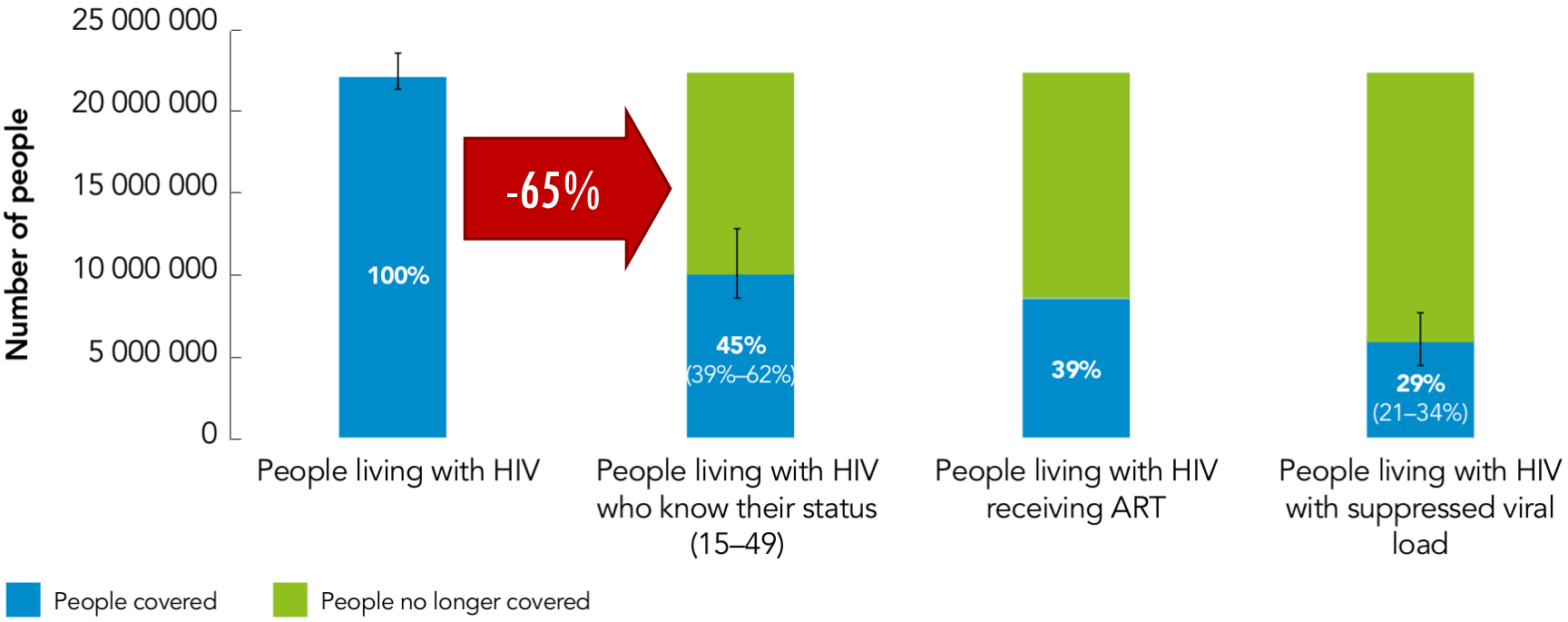
New infections among adults

ZERO

Discrimination

THE TREATMENT "CASCADE"

Abbreviated HIV treatment cascade for adults in sub-Saharan Africa aged 15 years or more, 2013

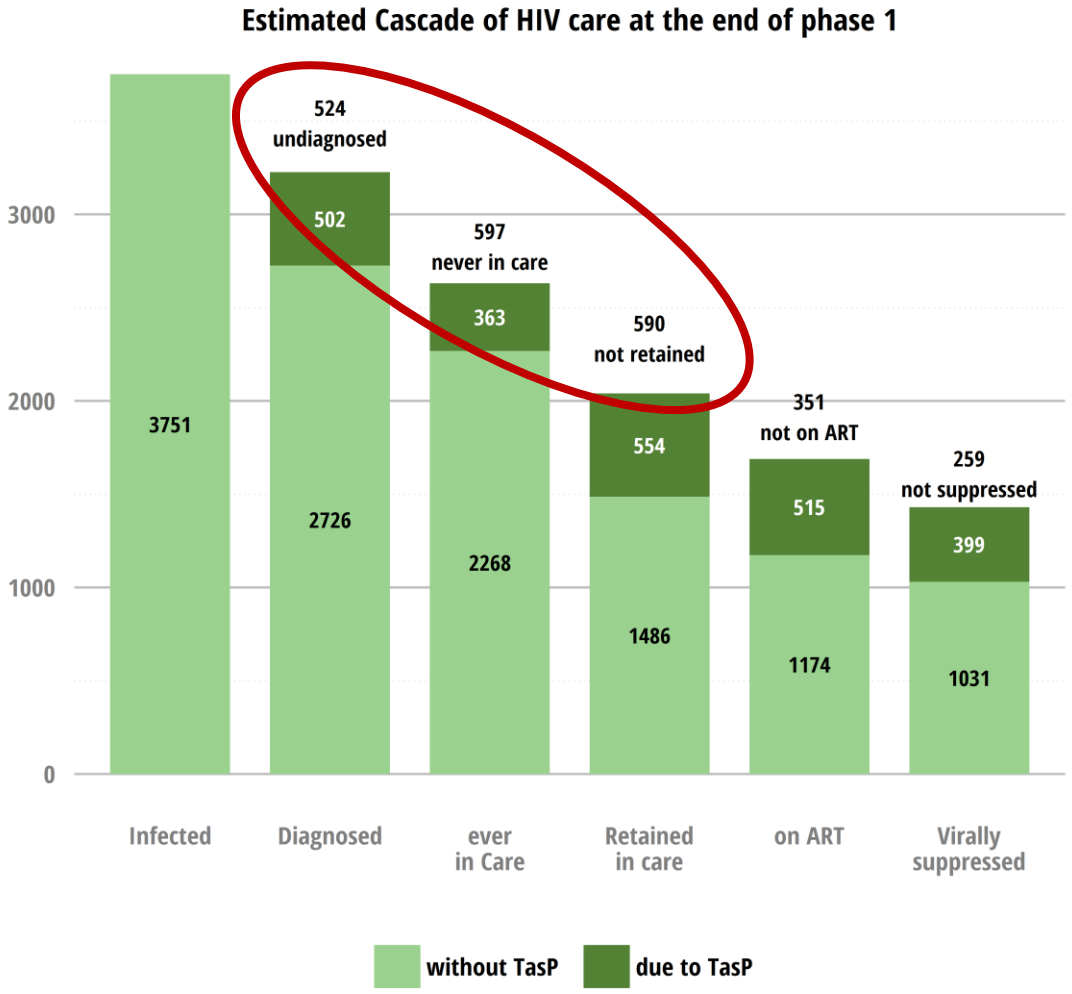


Source: UNAIDS, The Gap Report, 2014

WE CAN'T REACH
UNIVERSAL TREATMENT
WITHOUT
UNIVERSAL TESTING
AND LINKAGE TO CARE

CHALLENGE FOR UTT TRIALS

- Example of TasP ANRS 12249
  - repeat home-based testing twice a year
  - local dedicated clinic
  - rural South Africa
  - HIV prevalence >30%
- Preliminary results
  - 10 clusters
  - End of May 2014



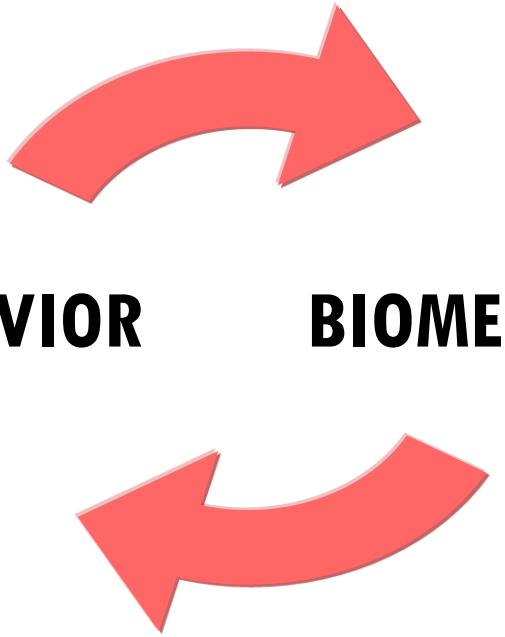
TasP

NEXT STEP FOR TASP ANRS 12249 TRIAL

- New combination interventions package:
  - *Community level:* community engagement and mobilization package
  - *HIV testing:* combination of repeat home-based testing, mobile testing and clinic testing
  - *Linkage to care:* SMS reminders, counselling and motivational support (phone calls, face-to-face visits), escort to clinics, health navigators, clinical assessment at home, option between home-based or clinic-based ART initiation
  - *Retention in care:* SMS reminders, phone calls and home visits in case of missed appointment, simplified ART care for stable patients, additional health services in clinics

TasP

BIOMEDICAL INTERVENTIONS & BEHAVIORS



The success of biomedical interventions will depend on behavioral changes.

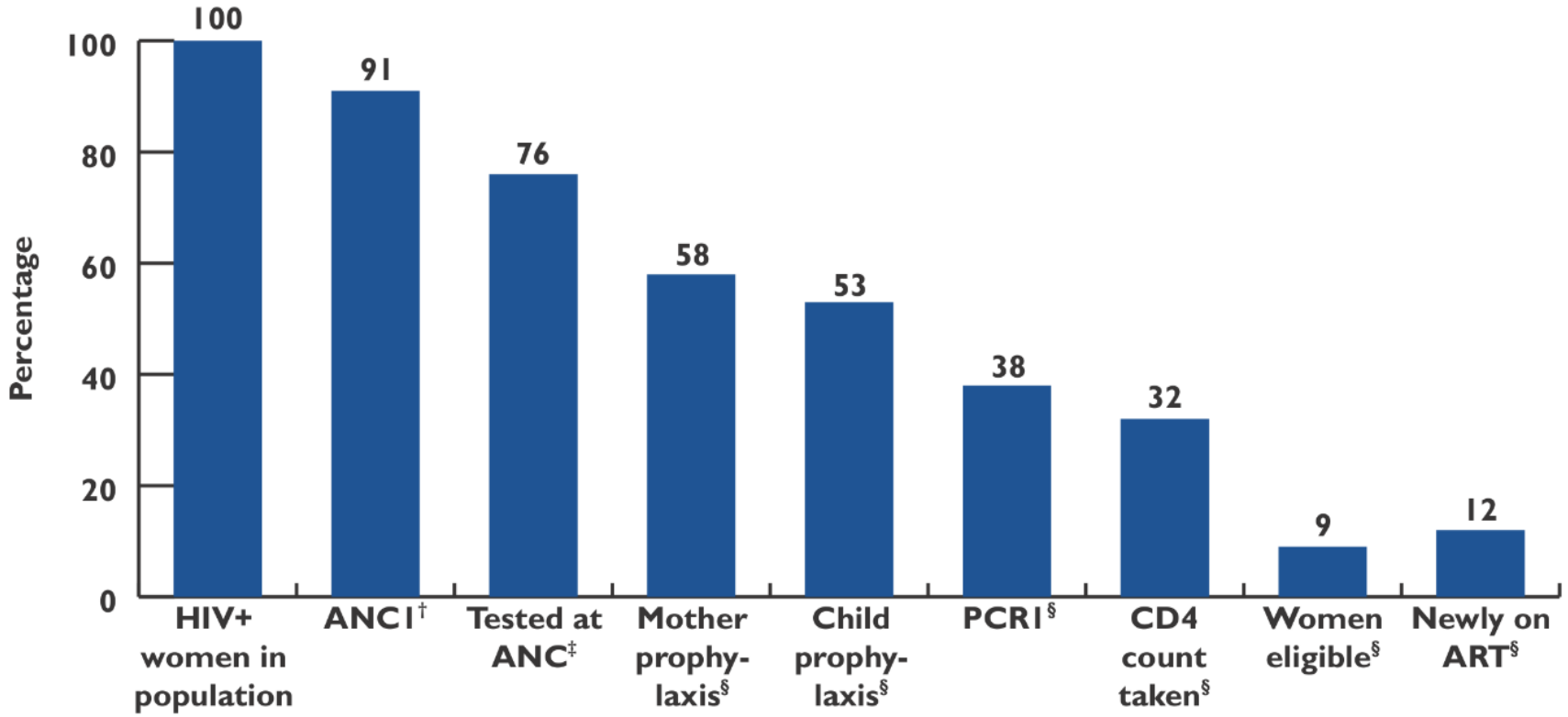
IMPLEMENTATION & BEHAVIORAL SCIENCE IS CRUCIAL

“ONE SIZE DOESN’T FIT ALL”

How best to combine a full set of different kind of interventions?

PMTCT CASCADE IN CÔTE D'IVOIRE

Figure 6 Estimated PMTCT cascade by proportion of all HIV+ pregnant women in population



†DHS 2011 data, ‡Carnet data, §Registry data

Source: Gloyd et al., 2014, HIVCore

TREATING EVEN EARLIER

BACK TO GRANICH'S MODEL

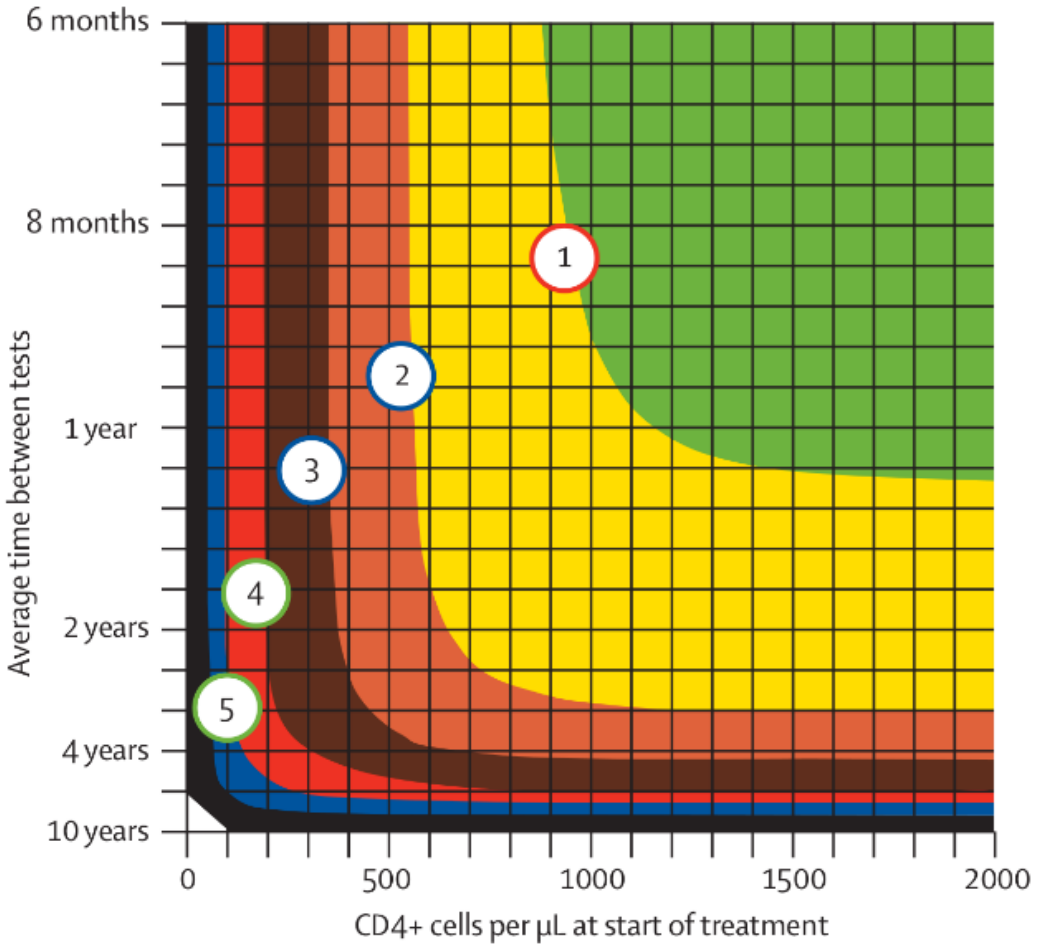


Figure 3: **Relation between HIV testing frequency, CD4+ cell count, and R_0**

R0 (the number of secondary infections resulting from one primary infection in an otherwise susceptible population) plotted against the CD4+ cell count at which treatment starts for different frequencies of HIV testing (average time between HIV tests represented in years and months). Numbers in circles represent R0 values. Green shading: R0<1; yellow: 1<R0<2; orange: 2<R0< 3; brown: 3<R0< 4; red: 4<R0<5; blue: 5<R0<6; and black: 6<R0< 7.

Source: Granich et al. *Lancet* 2009

BACK TO GRANICH'S MODEL

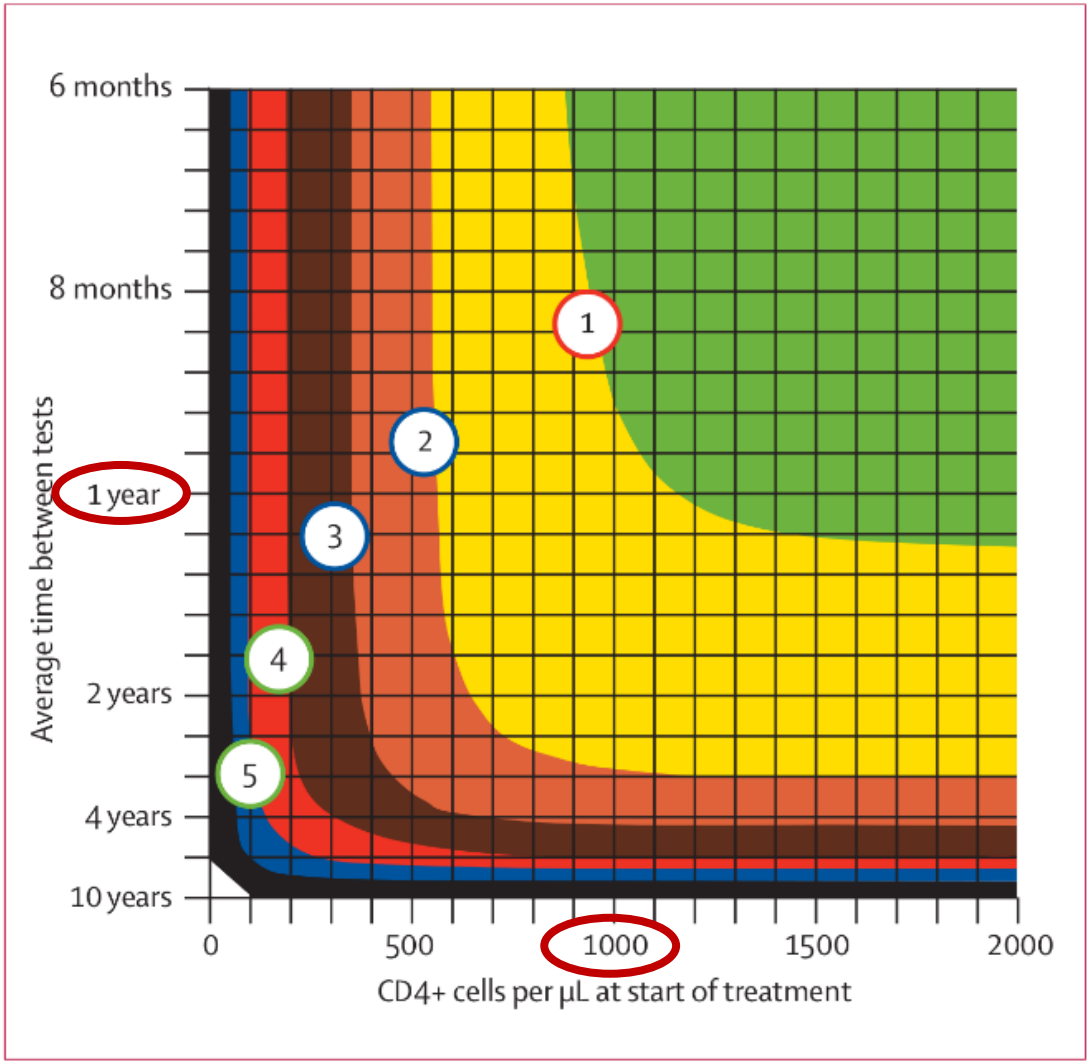


Figure 3: Relation between HIV testing frequency, CD4+ cell count, and R_0

To achieve elimination:

- ART should be initiated at >800 CD4
- HIV negative should be retested at least once a year

HIV TRANSMISSION AFTER ACQUISITION

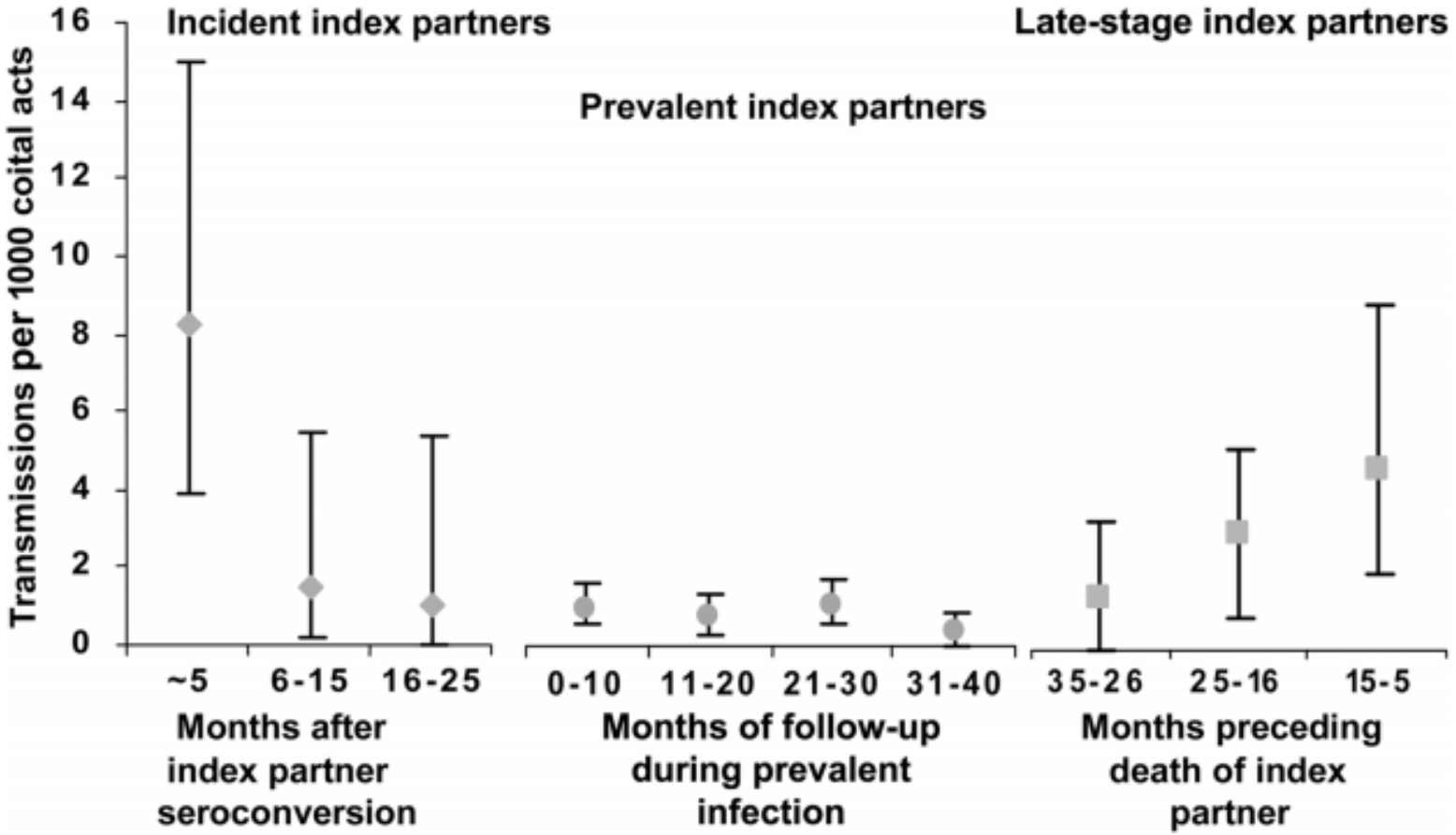


Figure 1. HIV transmission per coital act, and 95% confidence intervals, by follow-up interval

Source: Wawer et al. *JID* 2005

INCIDENT CASES DUE TO EARLY HIV

in Malawi

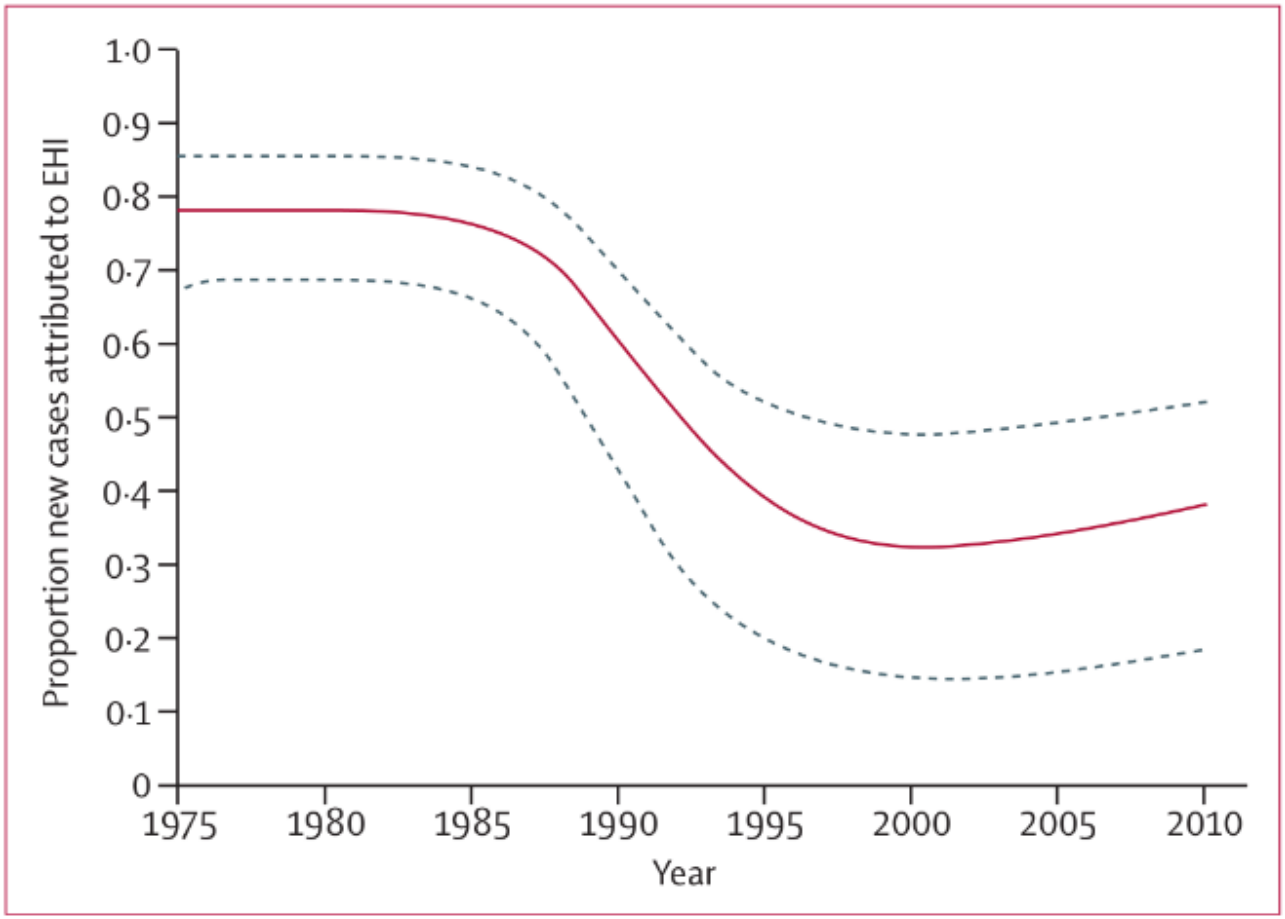
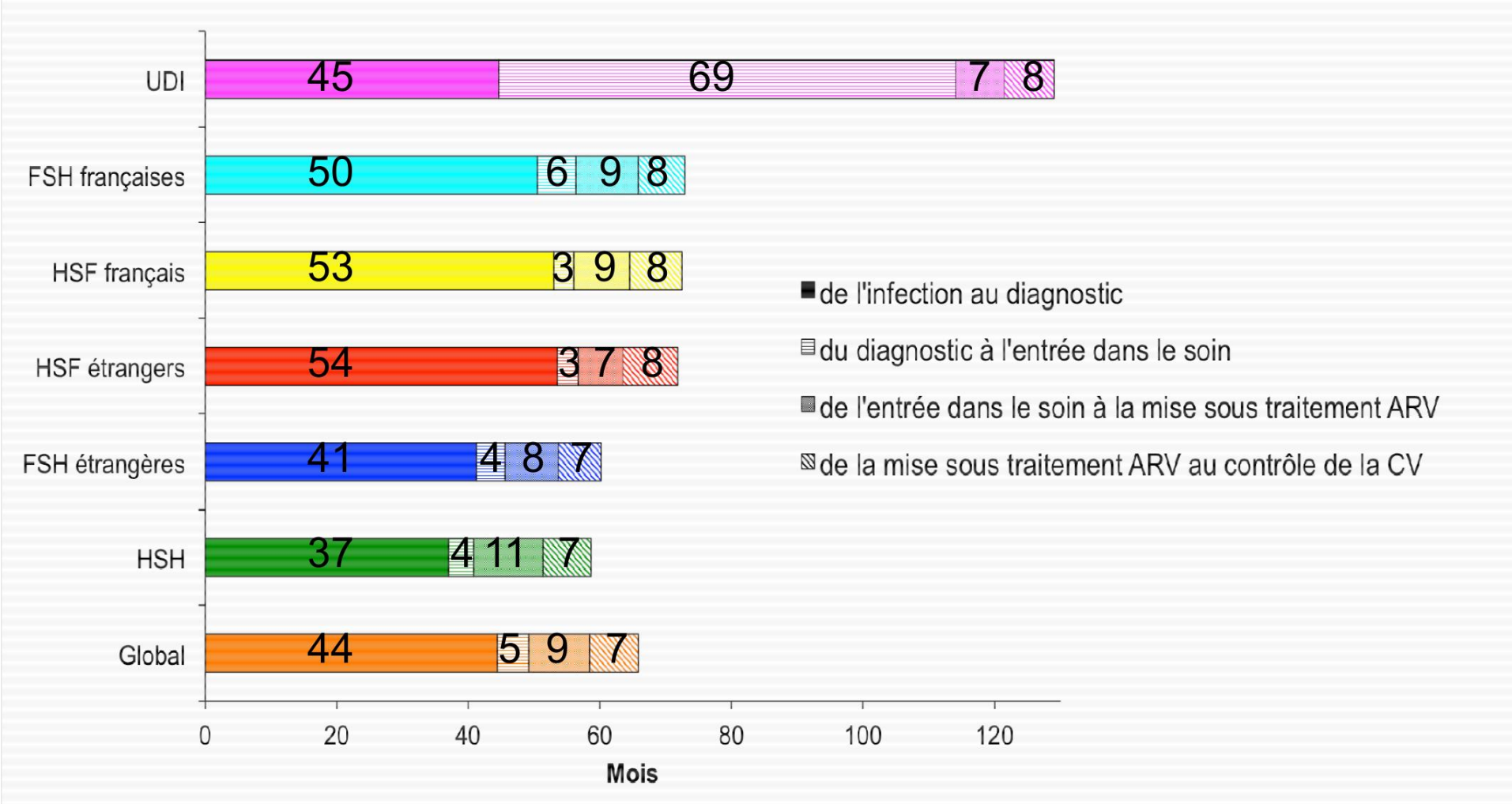


***Figure 4*: Estimated proportion of incident HIV infections attributable to contact with individual with early HIV infection**

Source: Powers et al. *Lancet* 2011

ESTIMATED DELAY WITHIN THE CASCADE

in France



Source: Supervie & Brouard, XVème congrès de la SFLS, octobre 2014

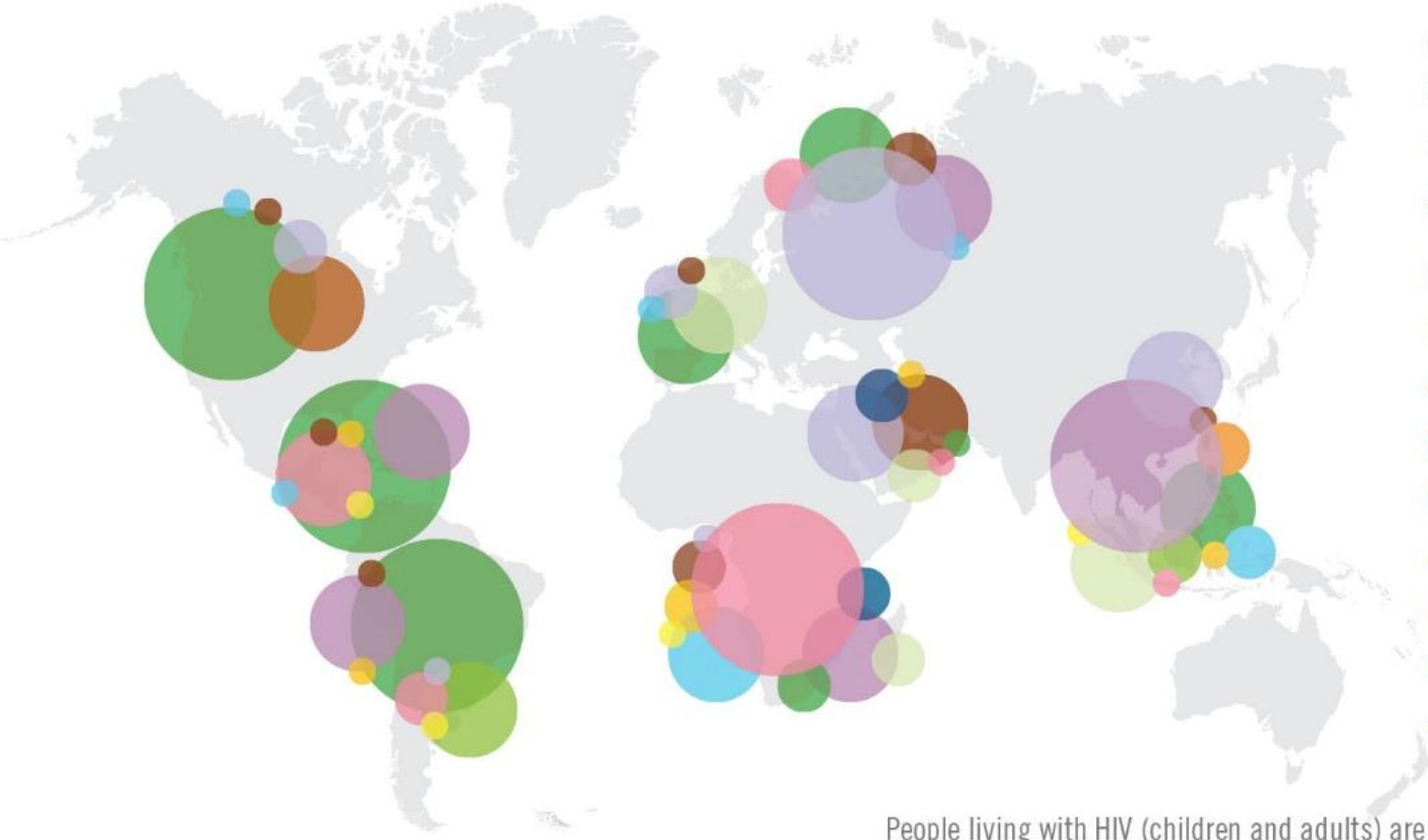
WE NEED TO TEST PEOPLE
AS SOON AS POSSIBLE
AFTER HIV ACQUISITION

REPEAT TESTING

FOR POPULATIONS WITH HIGH INCIDENCE

TO CONCLUDE

THE IMPORTANCE OF LOCATION AND POPULATION



Adapted from 2013 data from UNAIDS 2014 Gap Report

People living with HIV (children and adults) are included as members of all of the featured populations. They are implicitly included in this map as they must have universal access to services.

30+ YEARS OF SCIENCE

have helped us to

- understand the epidemiology
- understand the virus
- design, evaluate and implement solutions for prevention and treatment
- build a global response

but not to control the pandemic

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WE HAVE THE TOOLS TO END AIDS IF

- Political will
- Appropriate funding
- Contextualized interventions
- Continuous scale-up of programs
- Decentralization
- Integrate HIV with other health & development programs
- On-going research agenda on implementation science

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INTEGRATION, EFFICIENCY, RESOURCES, EQUITY

THE LONG AND WINDING ROAD
TO HIV PREVENTION, CARE AND TREATMENT

SPECIAL THANKS

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Collins Iwuji, Joanna Orne-Gliemann

THANK YOU FOR YOUR ATTENTION

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