State-of-the-Science: Treatment as Prevention and/or Treatment for Treatment?

IAPAC London 2014

Reuben Granich, MD, MPH
Senior Advisor, Care and Treatment
UNAIDS

State-of-the-Science:
Treatment is prevention (not all of it but a lot of it):

Prevention of:
Illness, death, transmission, costs, loss of social capital, loss of human rights (fill in blank)

IAPAC London 2014

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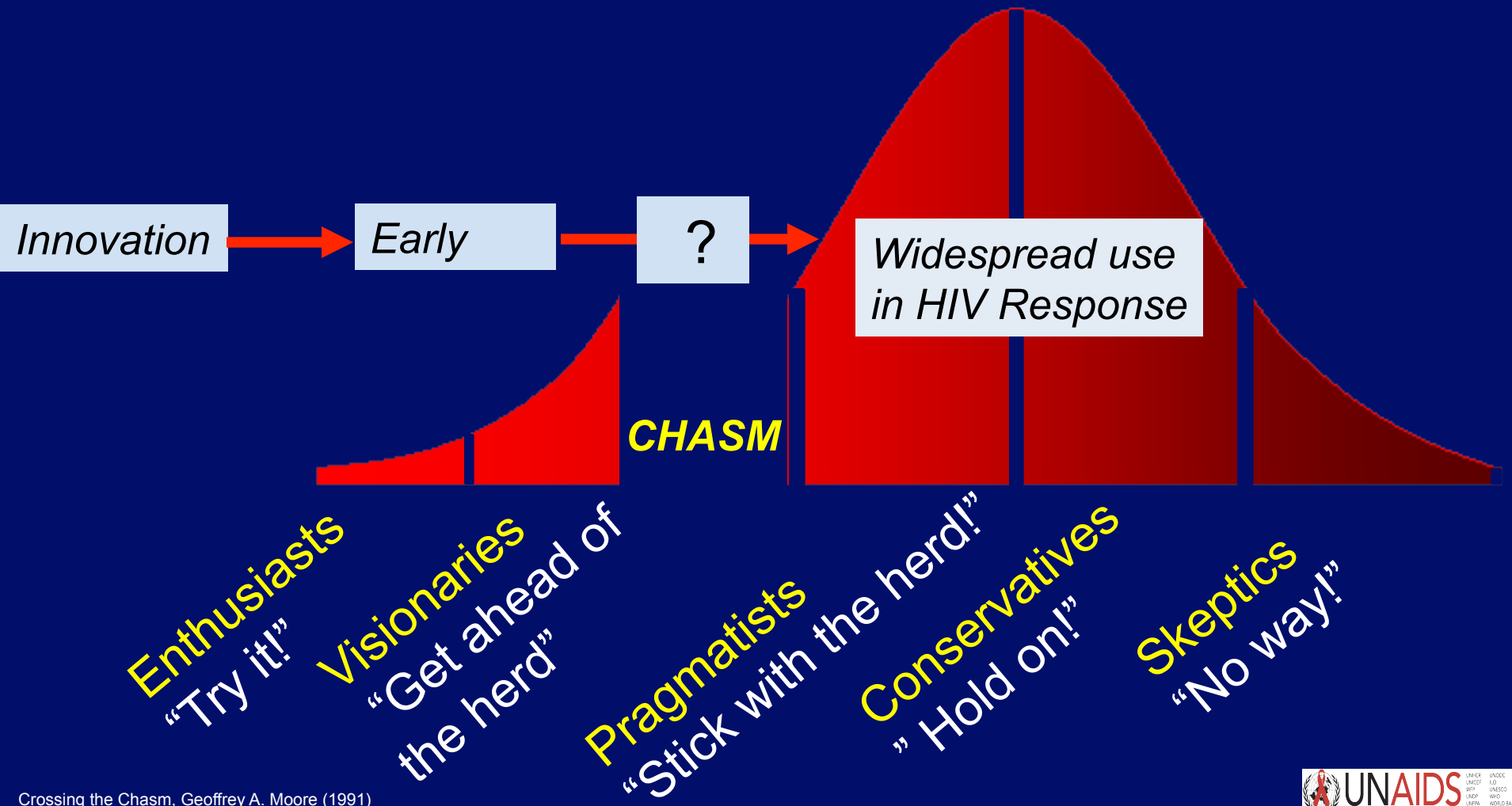
To end AIDS we will need to bridge the "innovation to scale" chasm



Crossing the Chasm, Geoffrey A. Moore (1991)

UNAIDS treatment targets: getting to scale

tested

on treatment

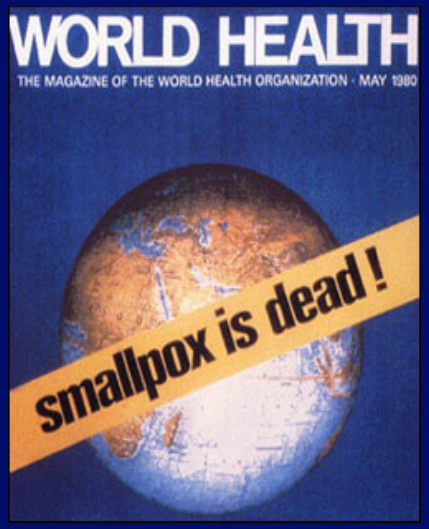
virally suppressed

Ending AIDS as a major public health problem

Feasible:

"capable of being done or carried out"

--Merriam-Webster's Dictionary



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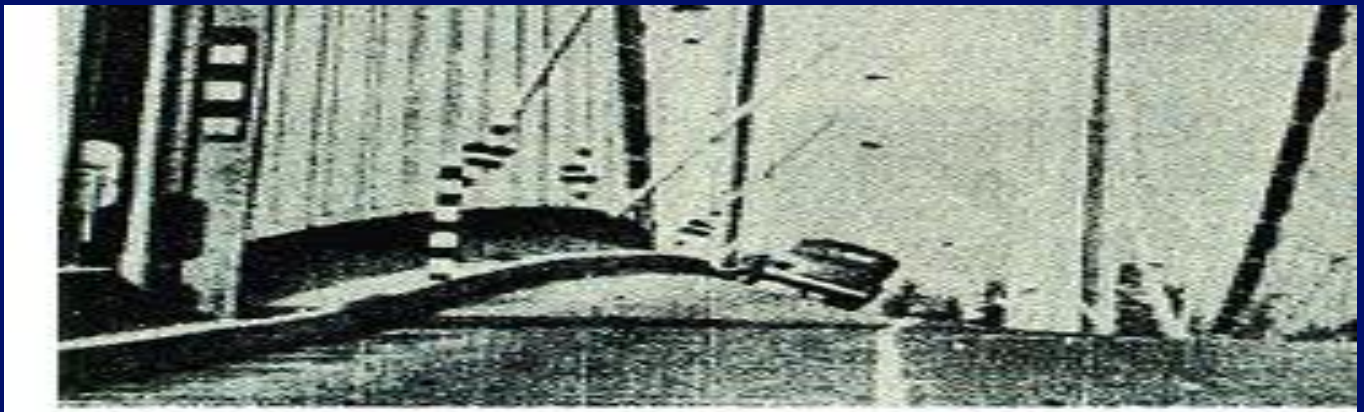
Bridging the chasm: can we scale innovations to get to 90-90-90?

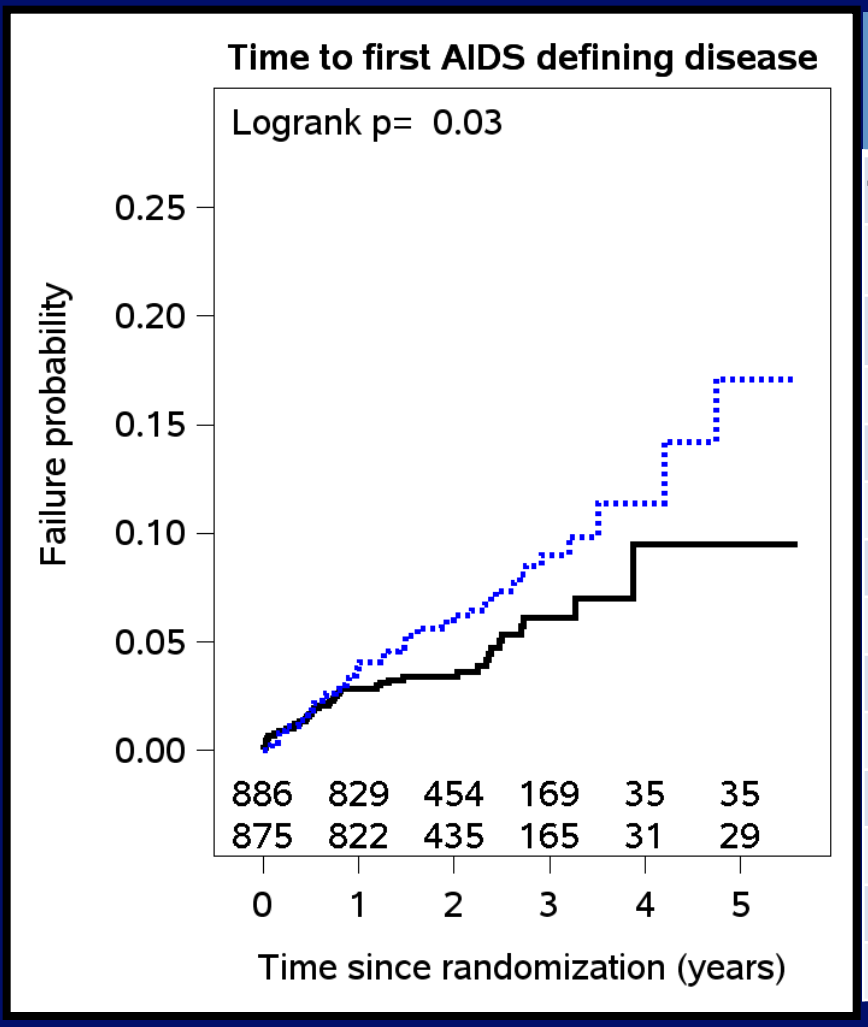


The Tacoma Narrows Bridge literally twisted apart on Nov. 7, 1940.

Treatment works--*Lazarus effect*

…after 90 days of ARV treatment

Early treatment makes sense and works better



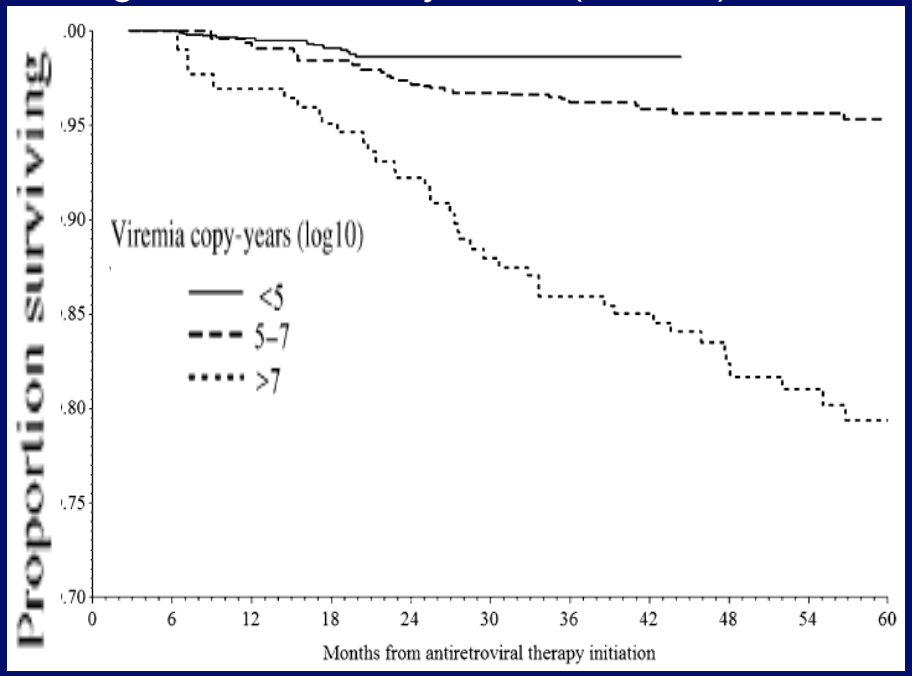
Number of subjects experiencing ≥1 event	Delayed	Immediate
Tuberculosis	**34 (4%)**	**17 (2%)**
Serious bacterial infection	**13 (1%)**	**20 (2%)**
WHO Stage 4 event	**19 (2%)**	**9 (1%)**
Oesophageal candidiasis	2	2
Cervical carcinoma	2	0
Cryptococcosis	0	1
HIV-related encephalopathy	1	0
Herpes simplex, chronic	8	2
Kaposi's sarcoma	1	1
CNS Lymphoma	1	0
Pneumocystis pneumonia	1	0
Septicemia	0	1
HIV Wasting	2	0
Bacterial pneumonia	1	2

Grinsztejn et al (in review)

UNAIDS

Unchecked viral replication impacts disease progression independent of CD4 count

Centers for AIDS Research Network of Integrated Clinical Systems (CNICS) cohort

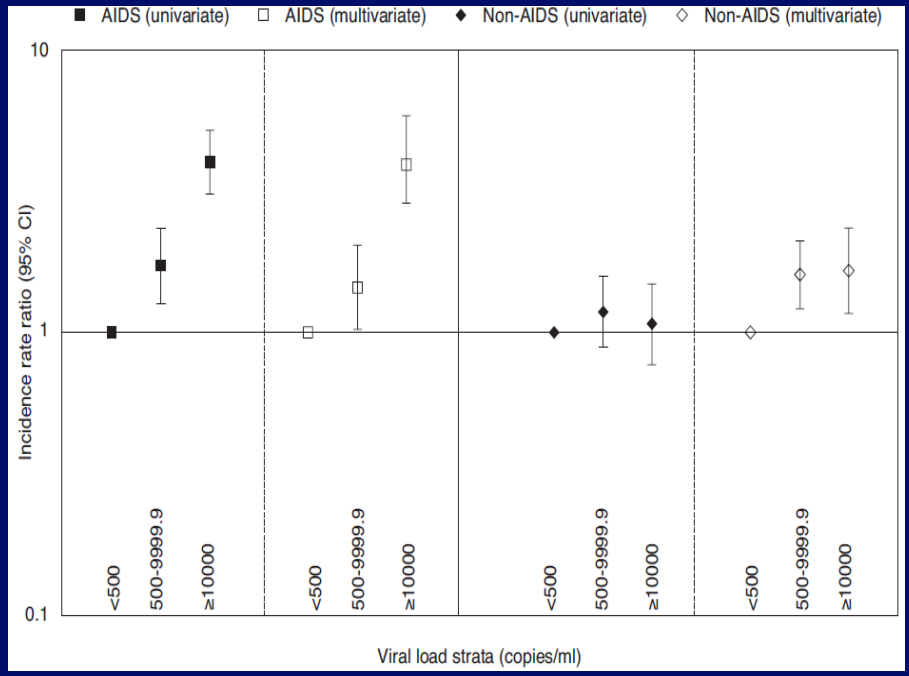


- Cumulative exposure to replicating virus independently associated with mortality.
- Multivariable model (HR 1.44 per log10 copy-year/mL; 95% CI: 1.07–1.94).

Mugavero et al. Clin Infect Dis. 2011

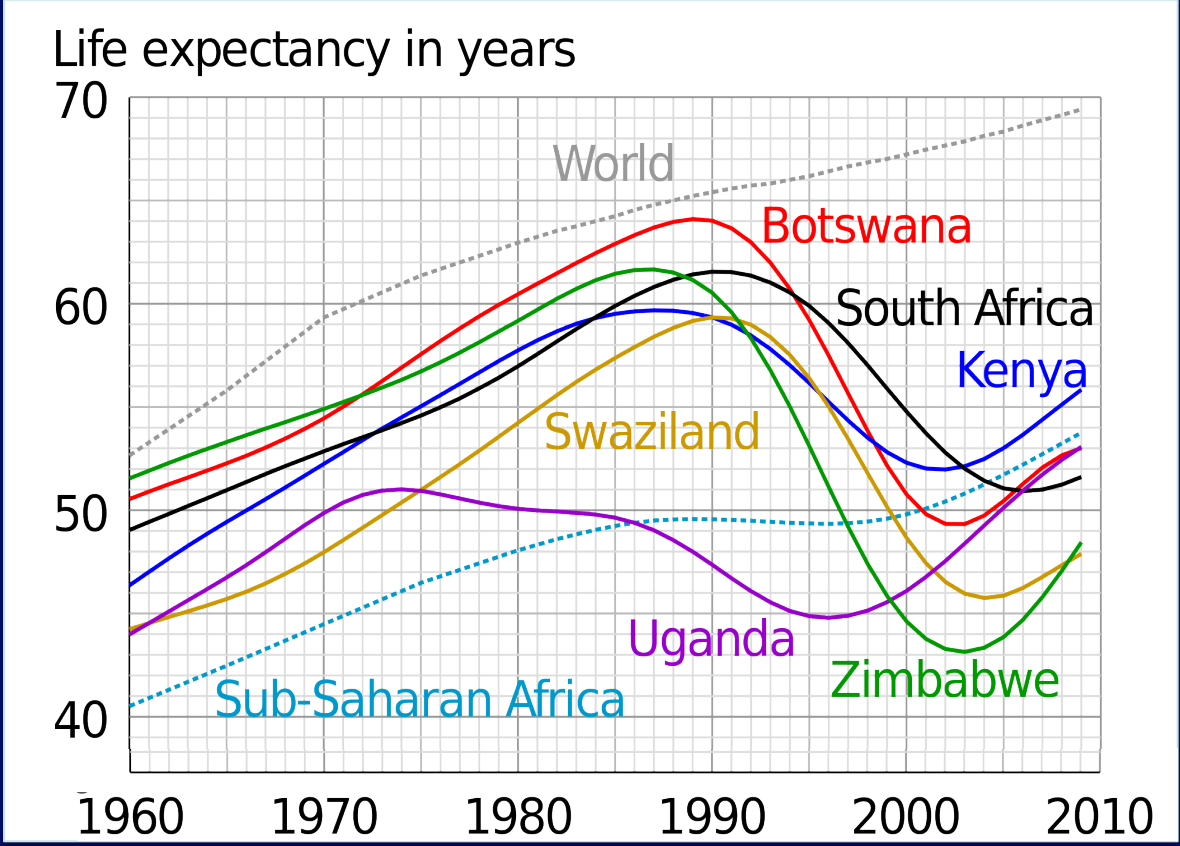
Reekie et al. AIDS 2011

EURO SIDA



- Impact of VL on fatal and non-fatal AIDS-related and non-AIDS-related events.
- After adjustment, **rates of non-AIDS events were 61% (*P*=.001) and 66% (*P*=.004) higher** in those with VLs 500-9,999 and >10,000, respectively, than in those with VLs <500.

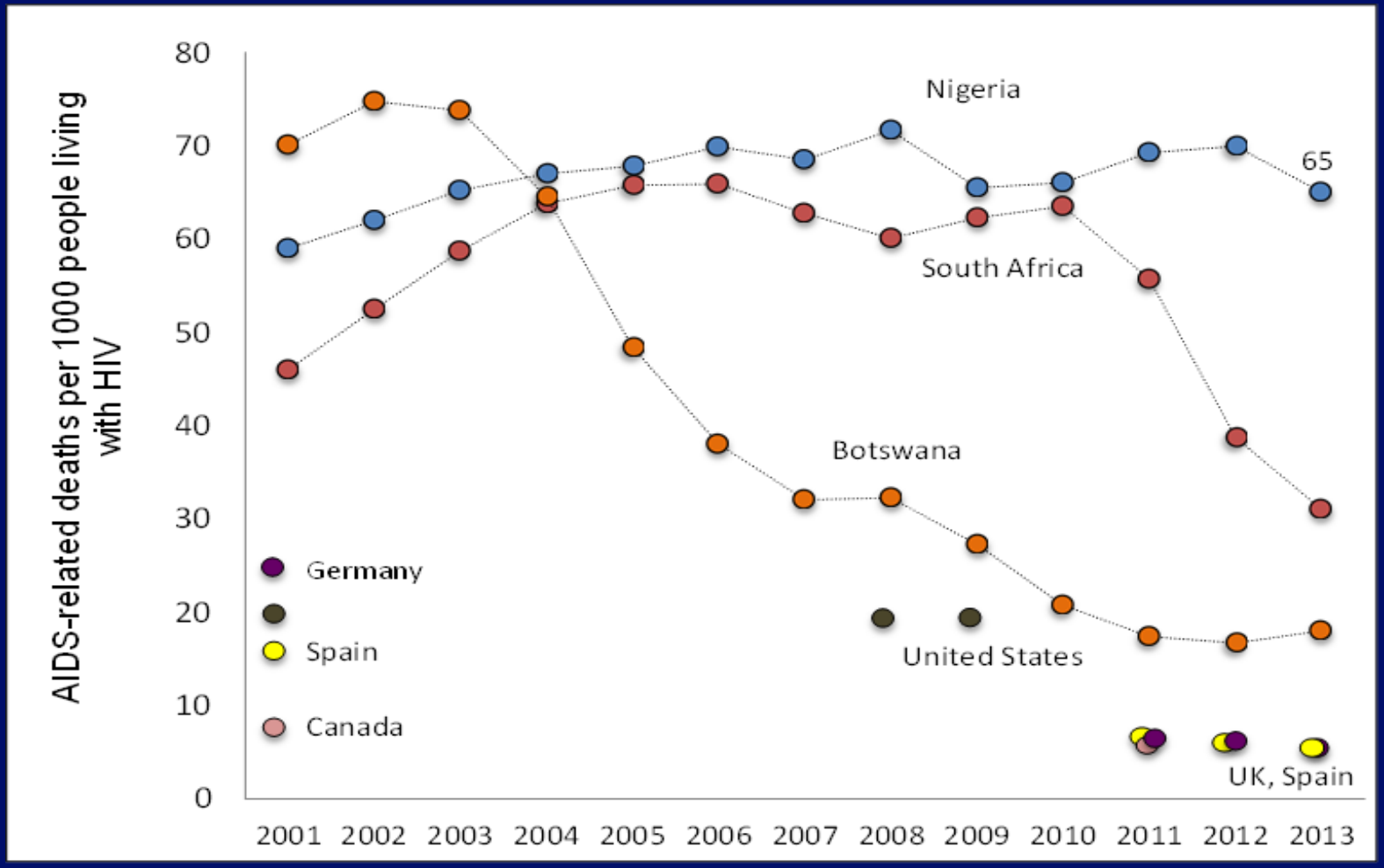
Scale matters: access to treatment has a dramatic impact on life expectancy



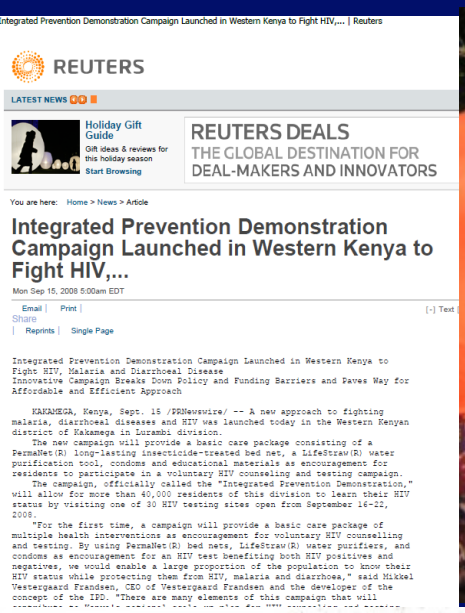
World Bank life expectancy data

Slide courtesy D Birx, PEPFAR

Estimated annual AIDS deaths per 1000 people living with HIV



We can deliver services at scale in ways that respect and engage end-users: HIV testing


Integrated Prevention Demonstration Campaign Launched in Western Kenya to Fight HIV,... | Reuters

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Integrated Prevention Demonstration Campaign Launched in Western Kenya to Fight HIV,...

Mon Sep 15, 2008 5:00am EDT

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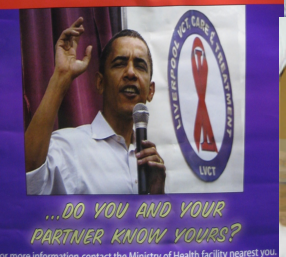
Integrated Prevention Demonstration Campaign Launched in Western Kenya to Fight HIV, Malaria and Diarrhoeal Disease
Innovative Campaign Breaks Down Policy and Funding Barriers and Paves Way for Affordable and Efficient Approach

KAKAMEGA, Kenya, Sept. 15 /PRNewswire/ -- A new approach to fighting malaria, diarrhoeal diseases and HIV was launched today in the Western Kenyan district of Kakamega in Lurambi division.

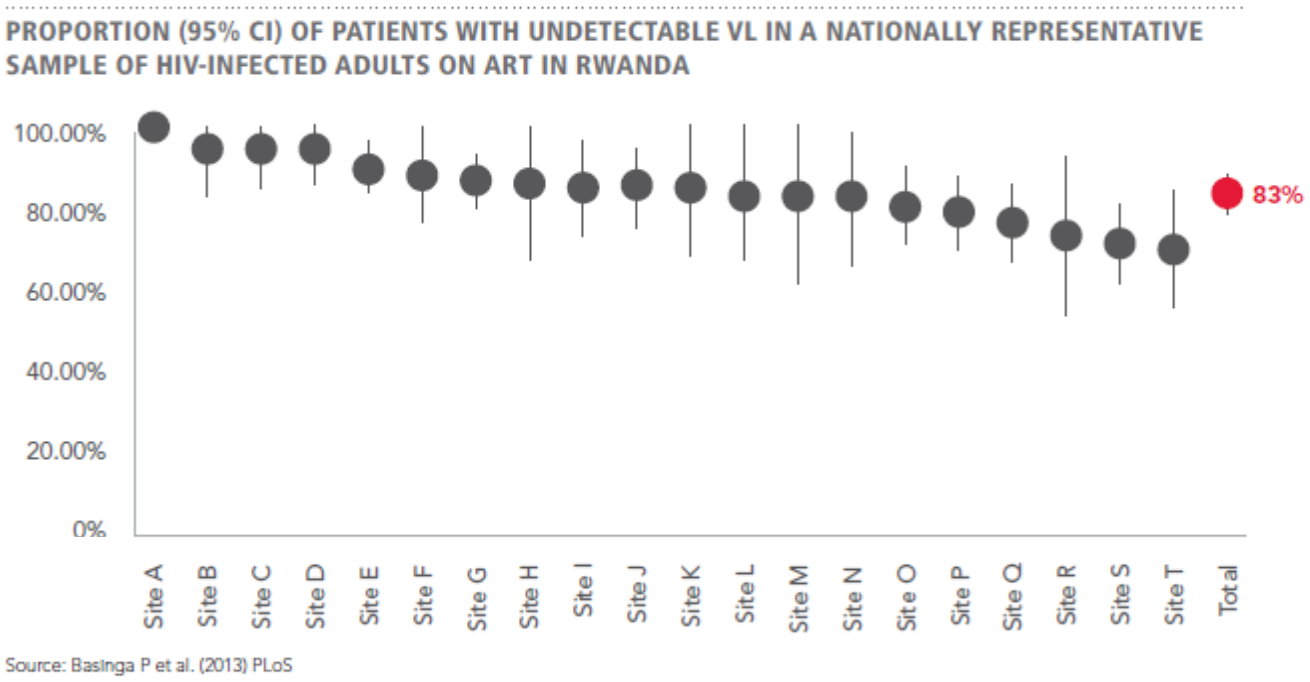
The new campaign will provide a basic care package consisting of a PermaNet(R) long-lasting insecticide-treated bed net, a LifeStraw(R) water purification tool, condoms and educational materials as encouragement for residents to participate in a voluntary HIV counseling and testing campaign.

The campaign, officially called the "Integrated Prevention Demonstration," will allow for more than 40,000 residents of this division to learn their HIV status by visiting one of 30 HIV testing sites open from September 16-22, 2008.

"For the first time, a campaign will provide a basic care package of multiple health interventions as encouragement for voluntary HIV counselling and testing. By using PermaNet(R) bed nets, LifeStraw(R) water purifiers, and condoms as encouragement for an HIV test benefiting both HIV positives and negatives, we would enable a large proportion of the population to know their HIV status while protecting them from HIV, malaria and diarrhoea," said Mikkel Vestergaard Frandsen, CEO of Vestergaard Frandsen and the developer of the concept of the IPD. "There are many elements of this campaign that will



Scaling high viral suppression is feasible: population based data from Rwanda



Basina P, Plos 2013

HIV treatment reduces viral load and heterosexual transmission (2003)

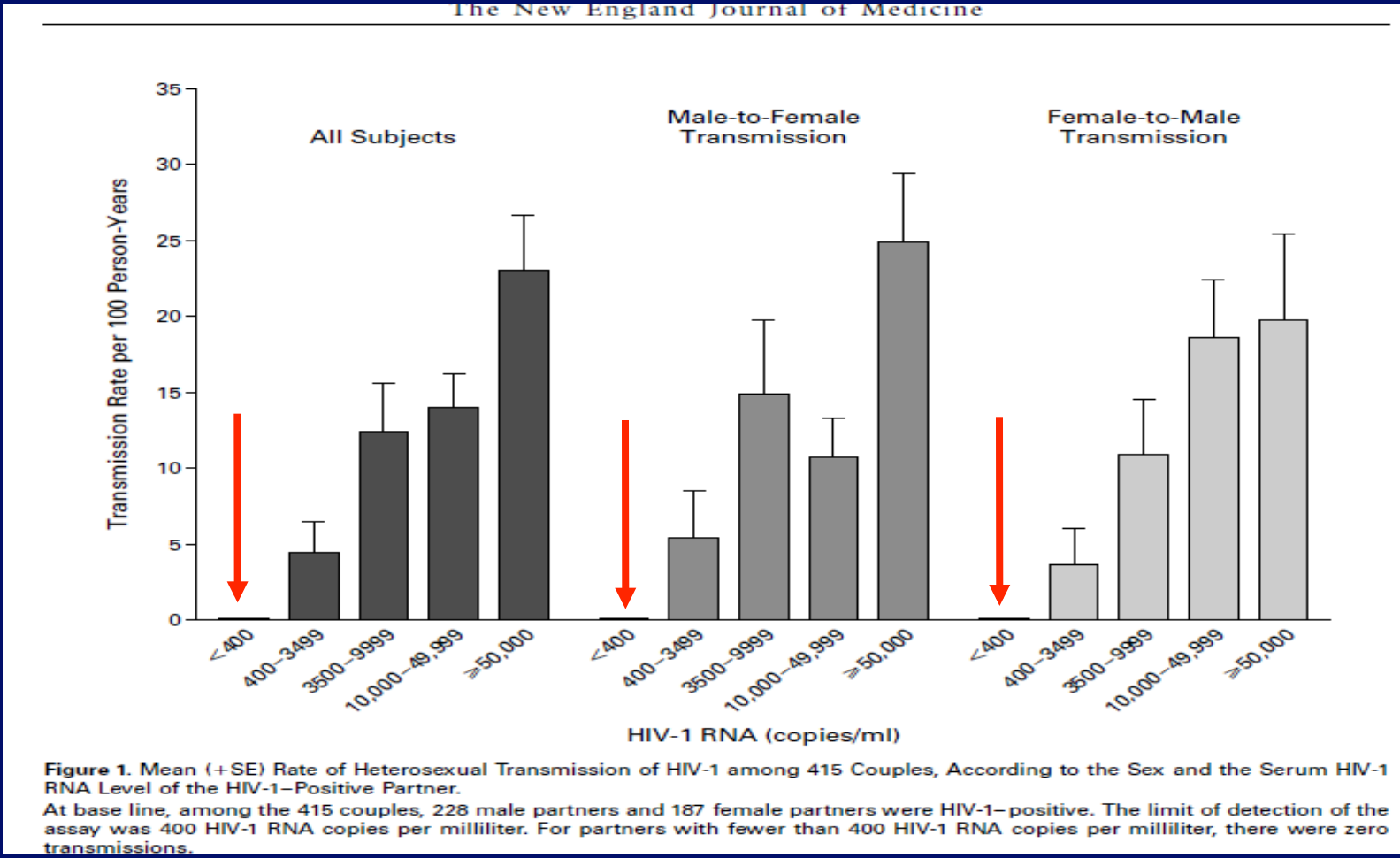


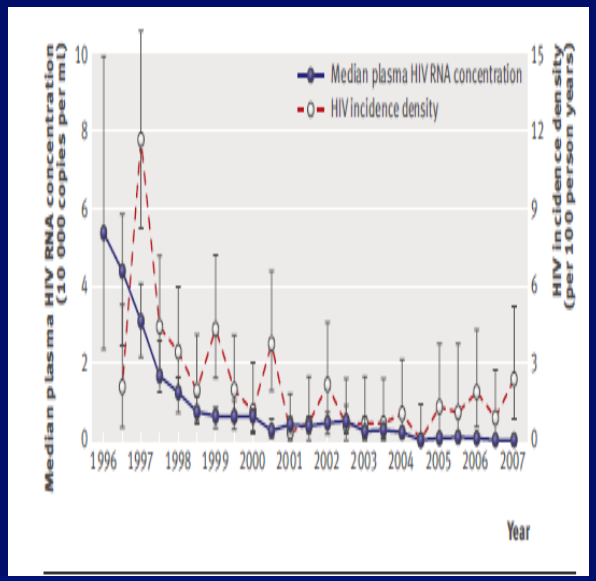
Figure 1. Mean (+SE) Rate of Heterosexual Transmission of HIV-1 among 415 Couples, According to the Sex and the Serum HIV-1 RNA Level of the HIV-1–Positive Partner.

At base line, among the 415 couples, 228 male partners and 187 female partners were HIV-1–positive. The limit of detection of the assay was 400 HIV-1 RNA copies per milliliter. For partners with fewer than 400 HIV-1 RNA copies per milliliter, there were zero transmissions.

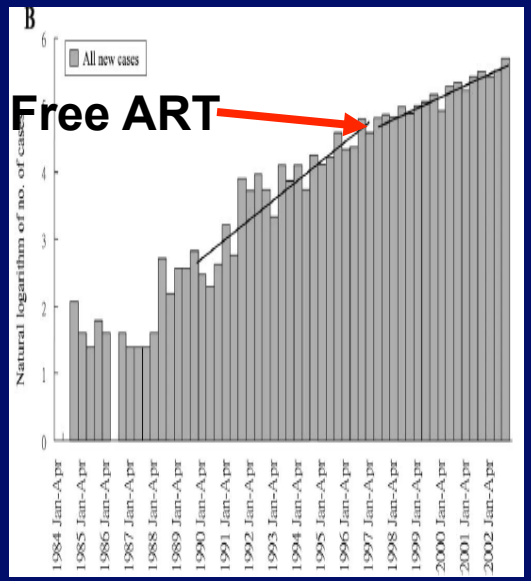
Quinn et al. NEJM. 2003;342(13):921-929.

Scaling treatment has an impact on community HIV transmision

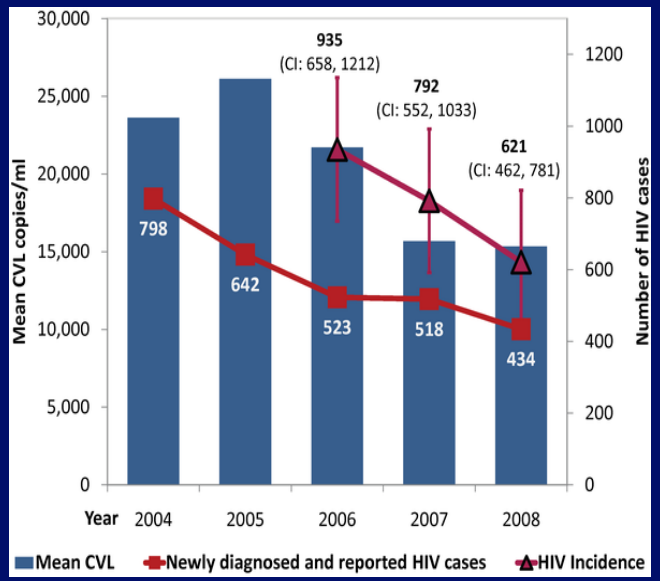
BC Canada



Taiwan



San Francisco

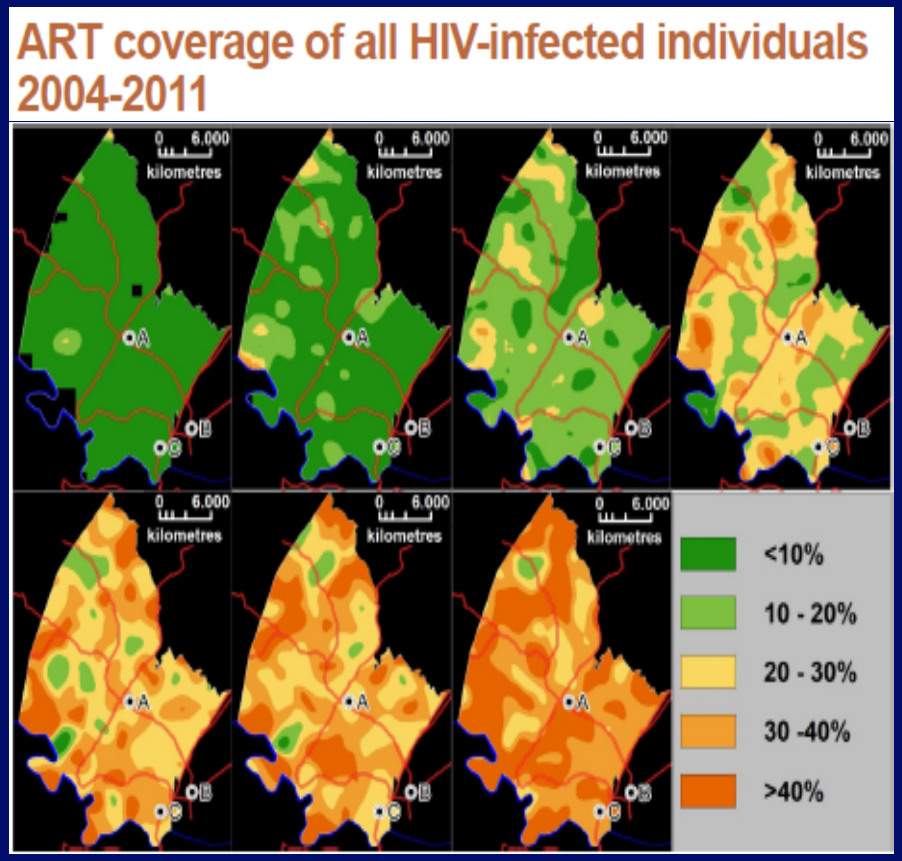


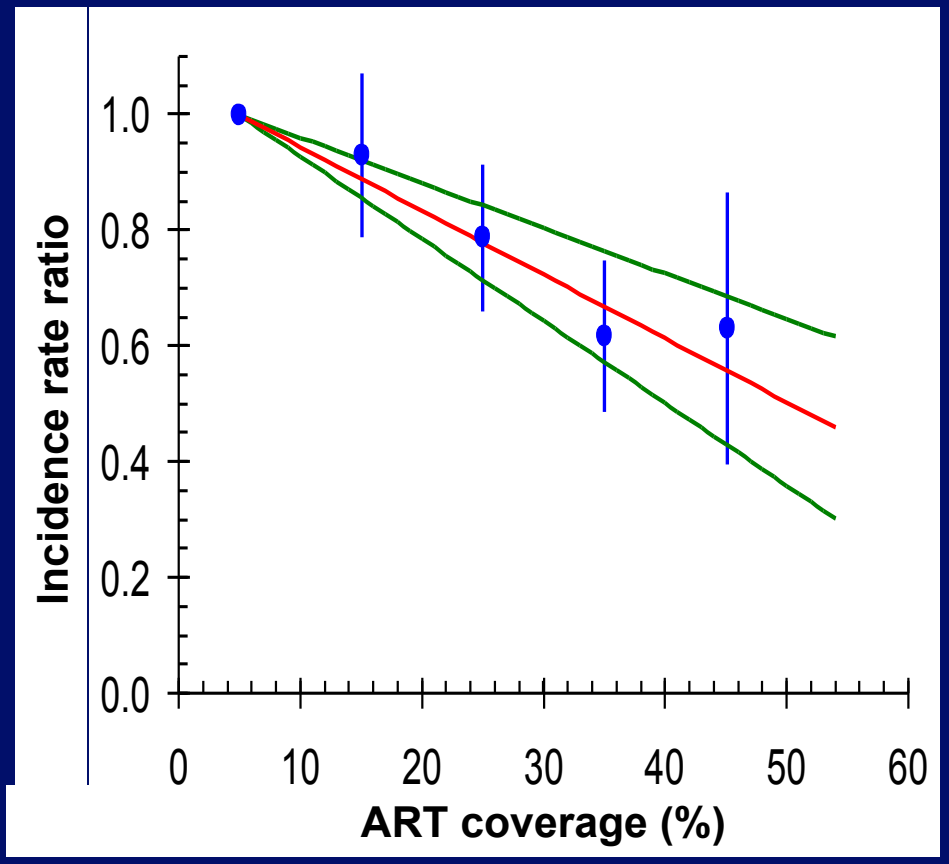
Wood et al. BMJ 2009;338b:1649

Fang et al. JAIDS 2004;190:879-85

Das et al. PlosOne 2010

Community scaling of ART coverage reduces individual risk of transmission: KZN South Africa

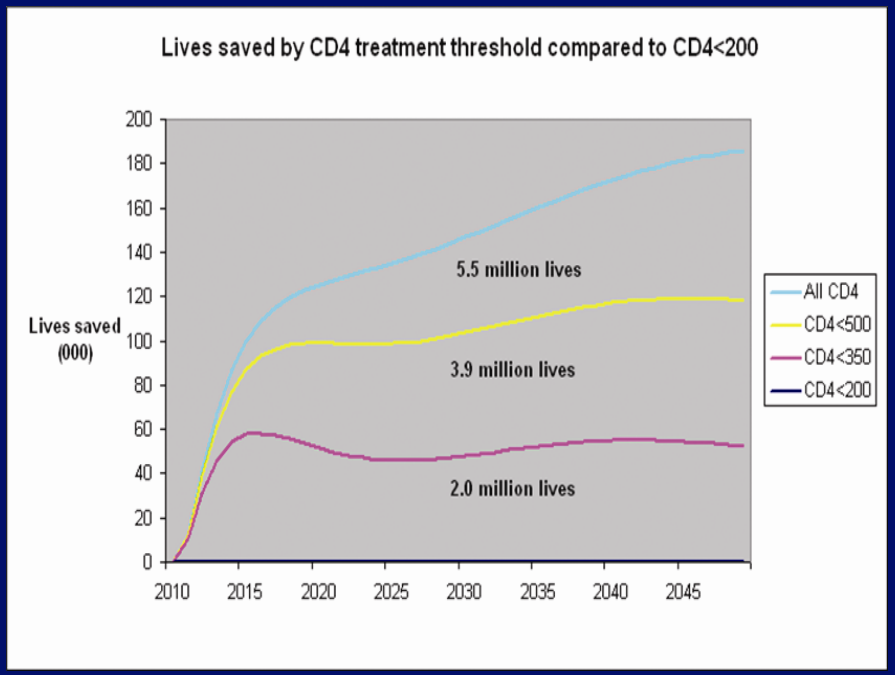




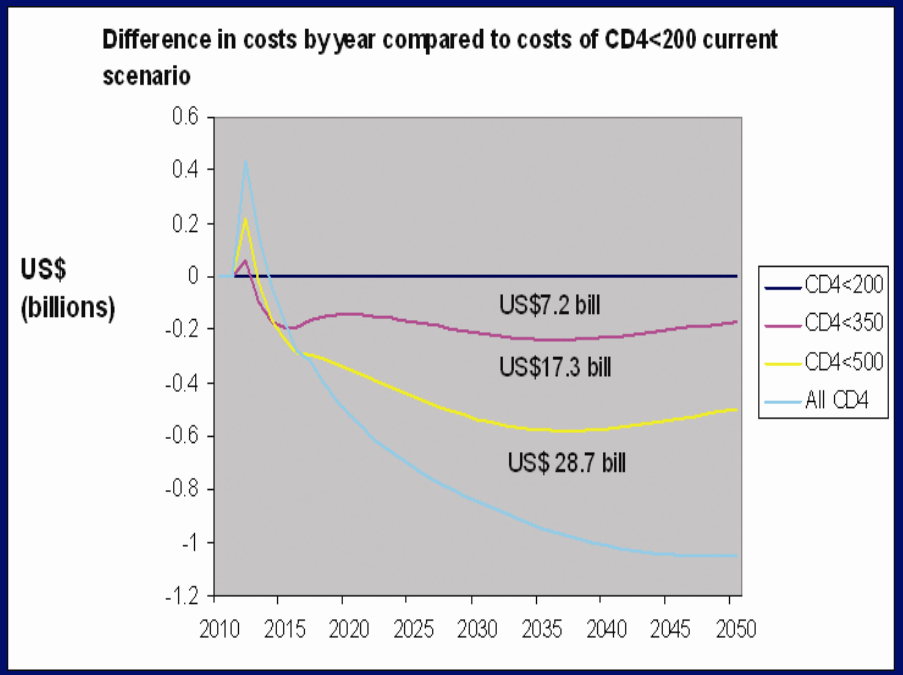
Incidence falls by 1.1% (0.8%-1.4%) for each 1% increase in coverage

Tanser Science 2013; Williams 2013

Projected impact of scaling ART access suggests that it would save lives and costs



Lives saved (millions)



Cost savings (billions)

Granich et al. Expanding ART for Treatment and Prevention of HIV in South Africa: Estimated Cost and Cost-Effectiveness 2011-2050. Plos Med

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Tracking 90-90-90 progress

tested on treatment virally suppressed

Are we on track to scale?

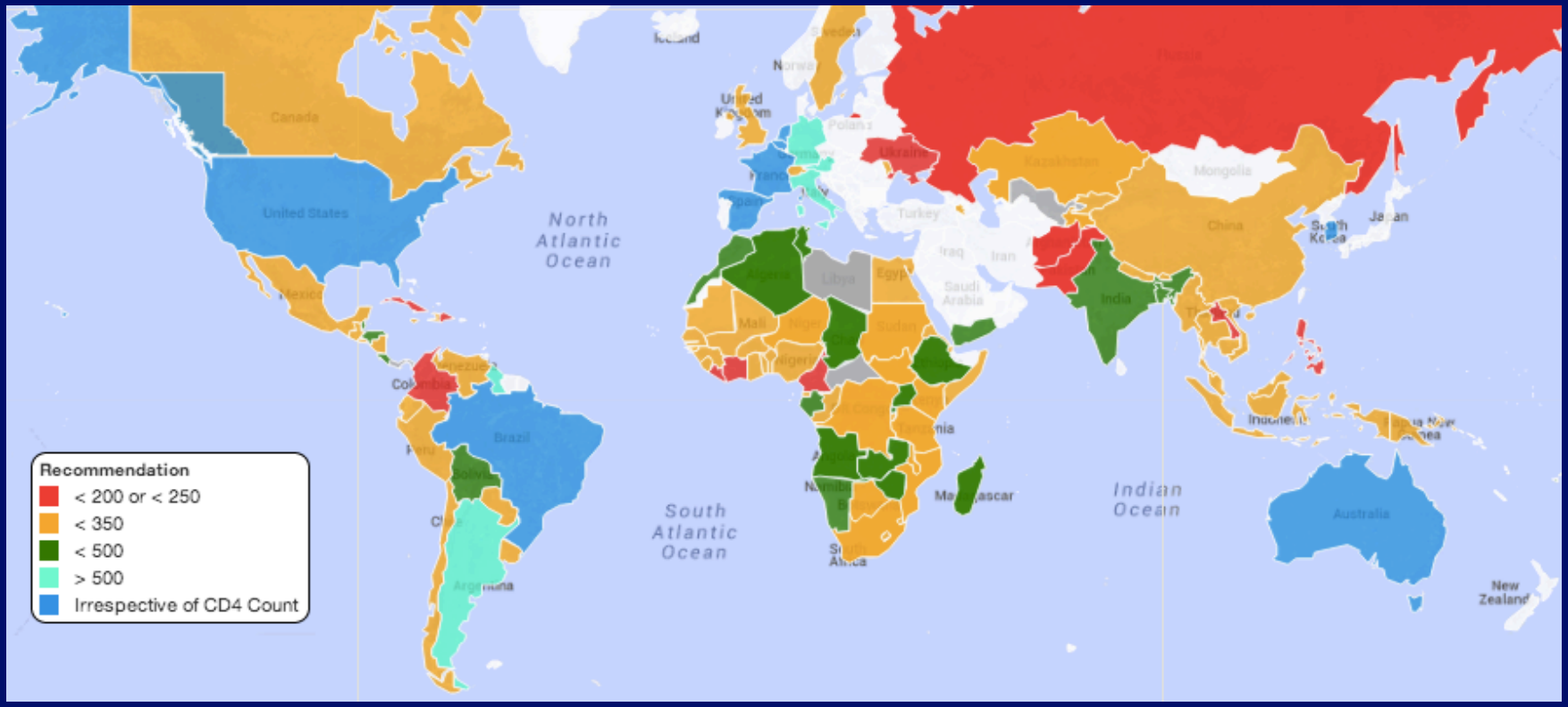
By end of 2013:

- ~52% of people living with HIV do not know their status
- ~22 million (63%) are not on treatment (76% for children)
- ~1.5 million deaths
- ~2.1 million new infections (5753 per day; 240 per hour)

Bottom line:

- Everyone living with HIV will need ART to survive
- Treatment expansion is part of solution to preventing illness, death, transmission, and costs.

Scaling treatment policy: ART CD4 initiation criteria for asymptomatic people



94 published policies:
26 countries (27% HIV burden) are at <500 or above

August, 2014

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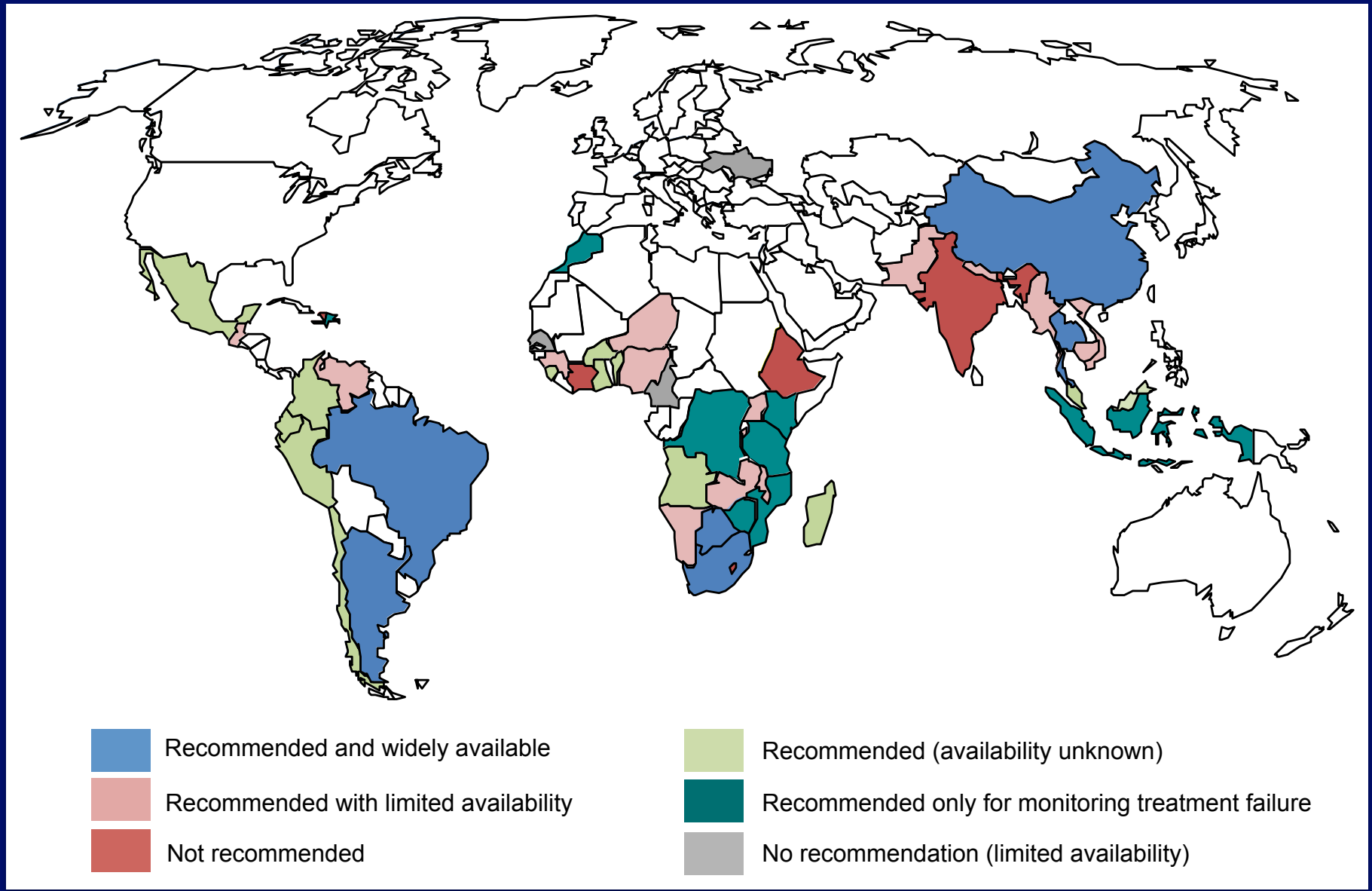
Scaling viral load for ART monitoring (51 countries)



Source: MSF Issue Brief: Getting to Undetectable

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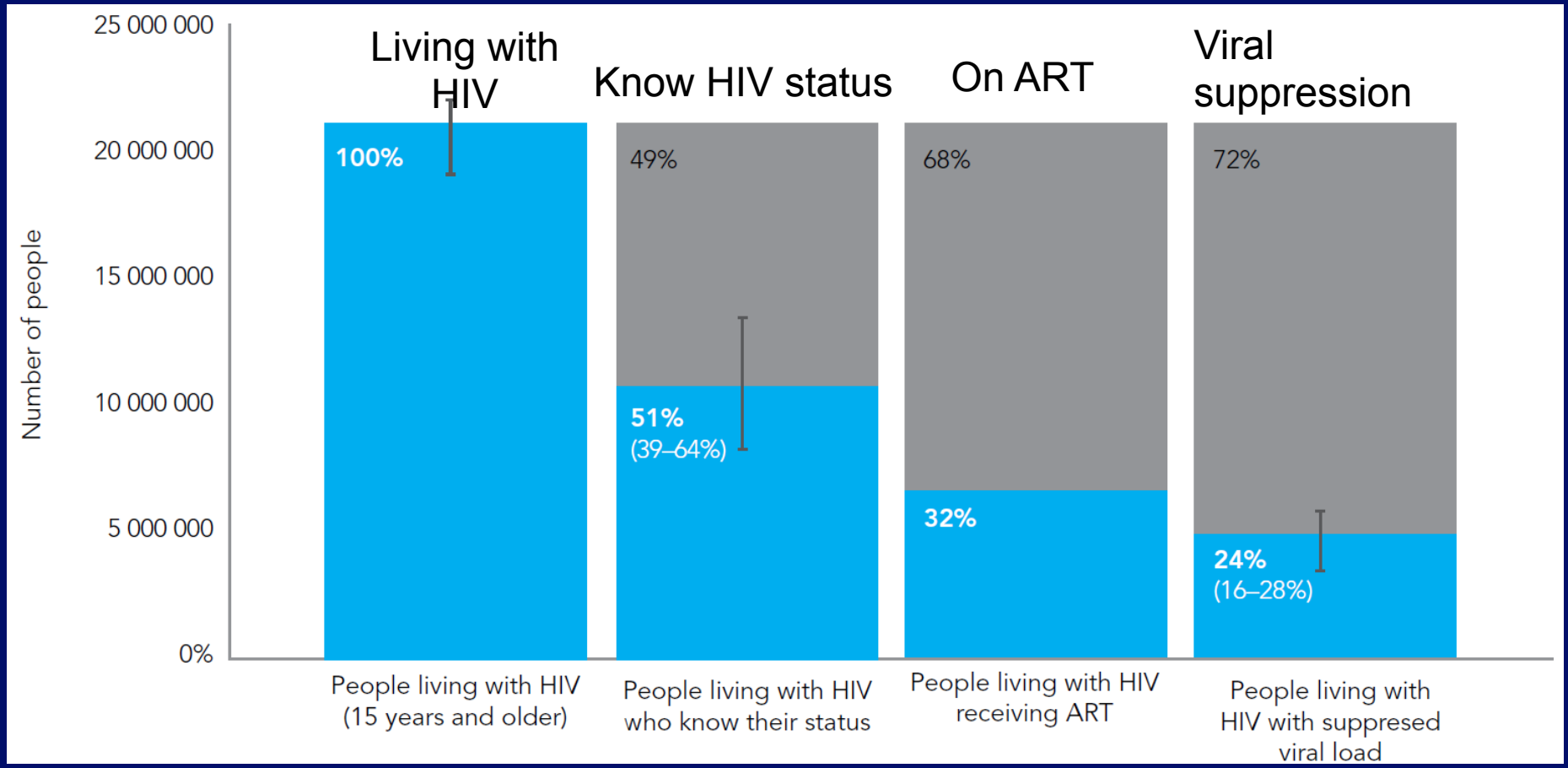
Accountability: measuring diffusion and scale

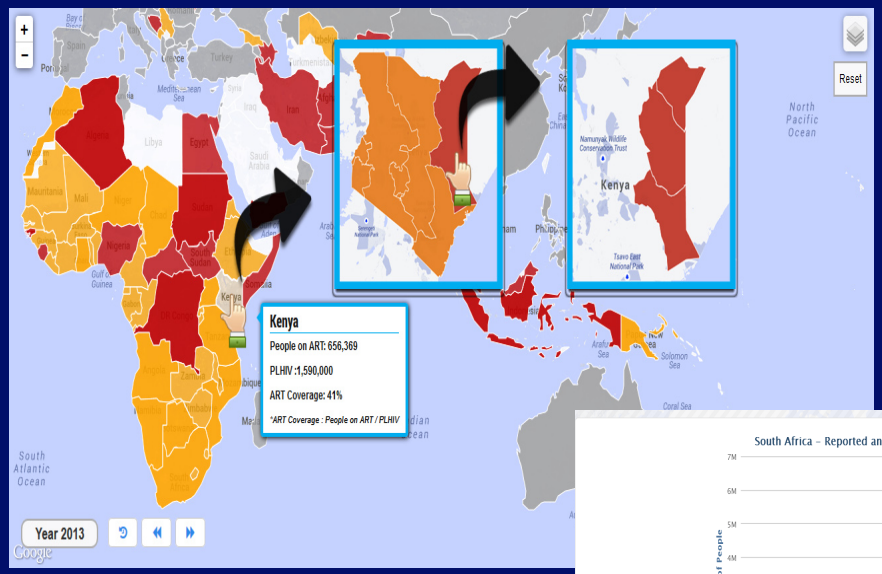


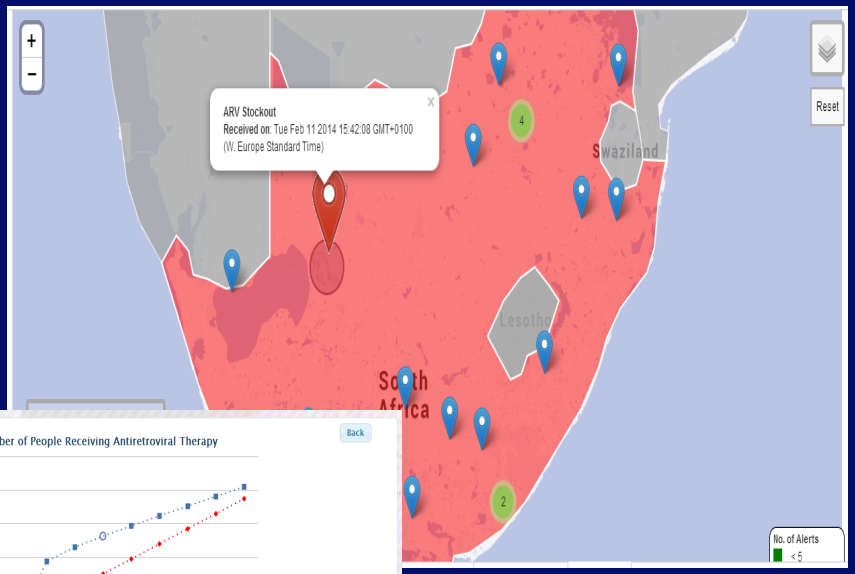
HIV treatment cascade for sub-Saharan Africa, 2012

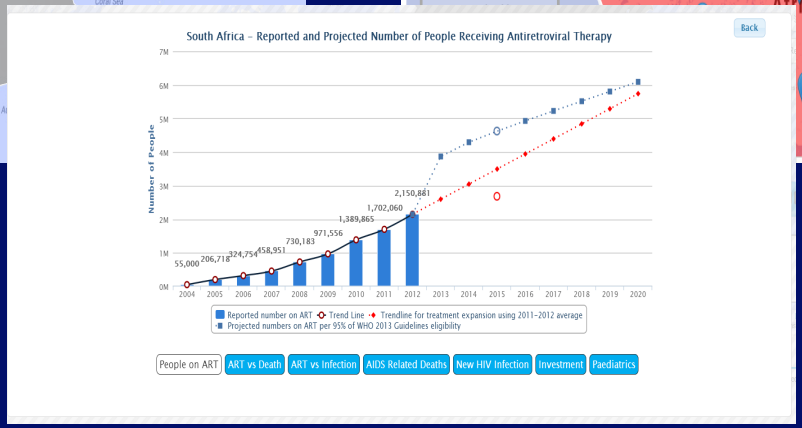
Notes: No systematic data are available for the proportion of people living with HIV who are linked to care, although this is a vital step to ensuring viral suppression in the community.

Sources: 1. UNAIDS 2012 estimates; 2. Demographic and Health Surveys, 2007–2011 (www.measuredhs.com); 3. Kranzer, K., van Schaik, N., et al. (2011), PLoS ONE; 4. CARPP 2012; 5. Barth R E, van der Loeff MR, et al. (2010), Lancet Infect Disease.

Scaling the use of data for transparency, accountability, progress:
UNAIDS Treatment Situation Room







Real-time mapping local epidemiology, interventions and financing to monitor impact

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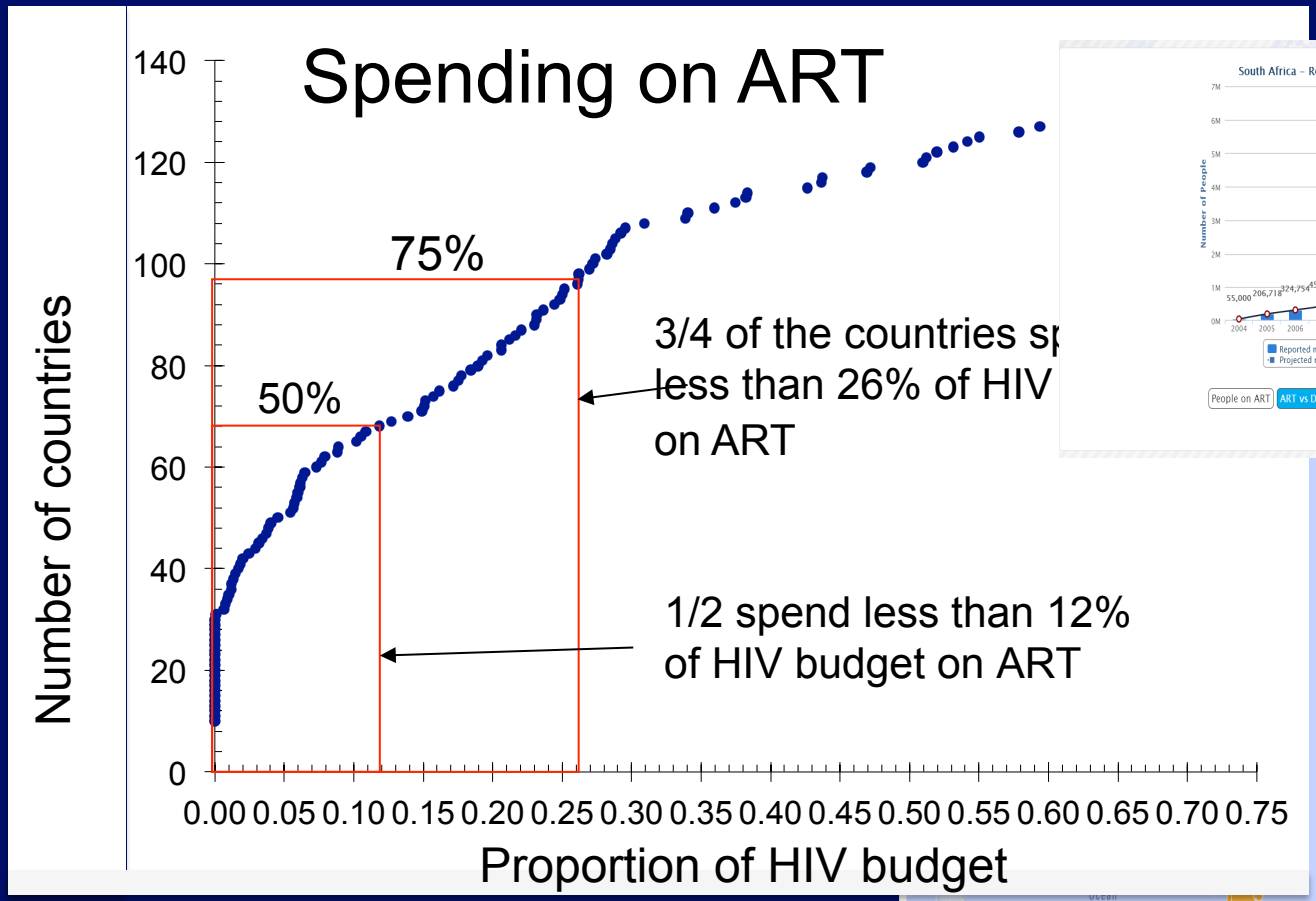
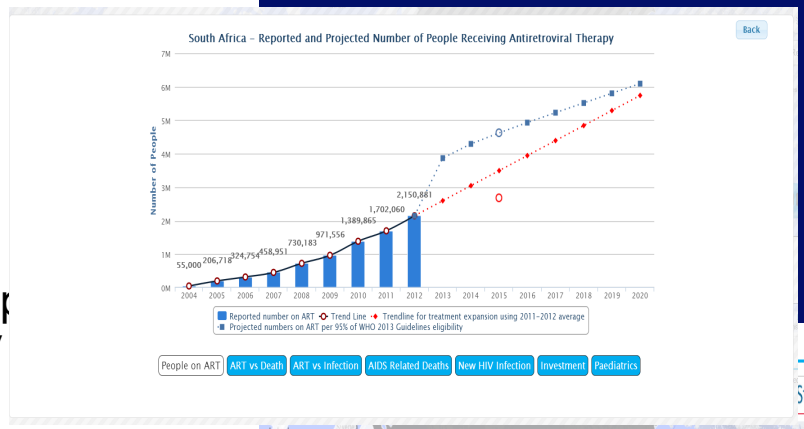
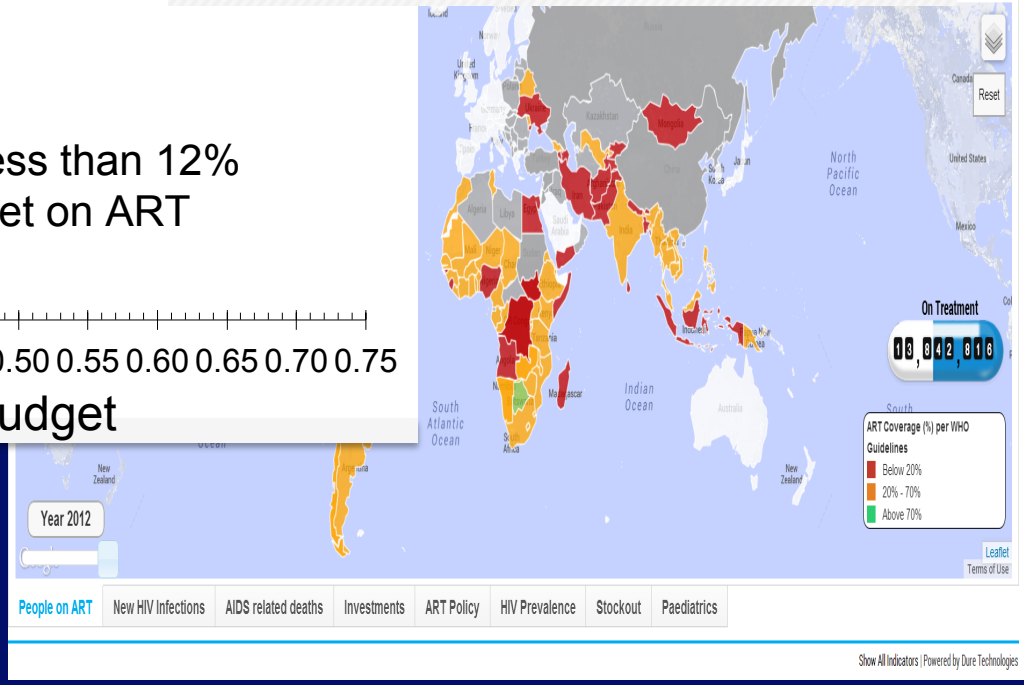
Scale requires break from business as usual: More public domain mashups please

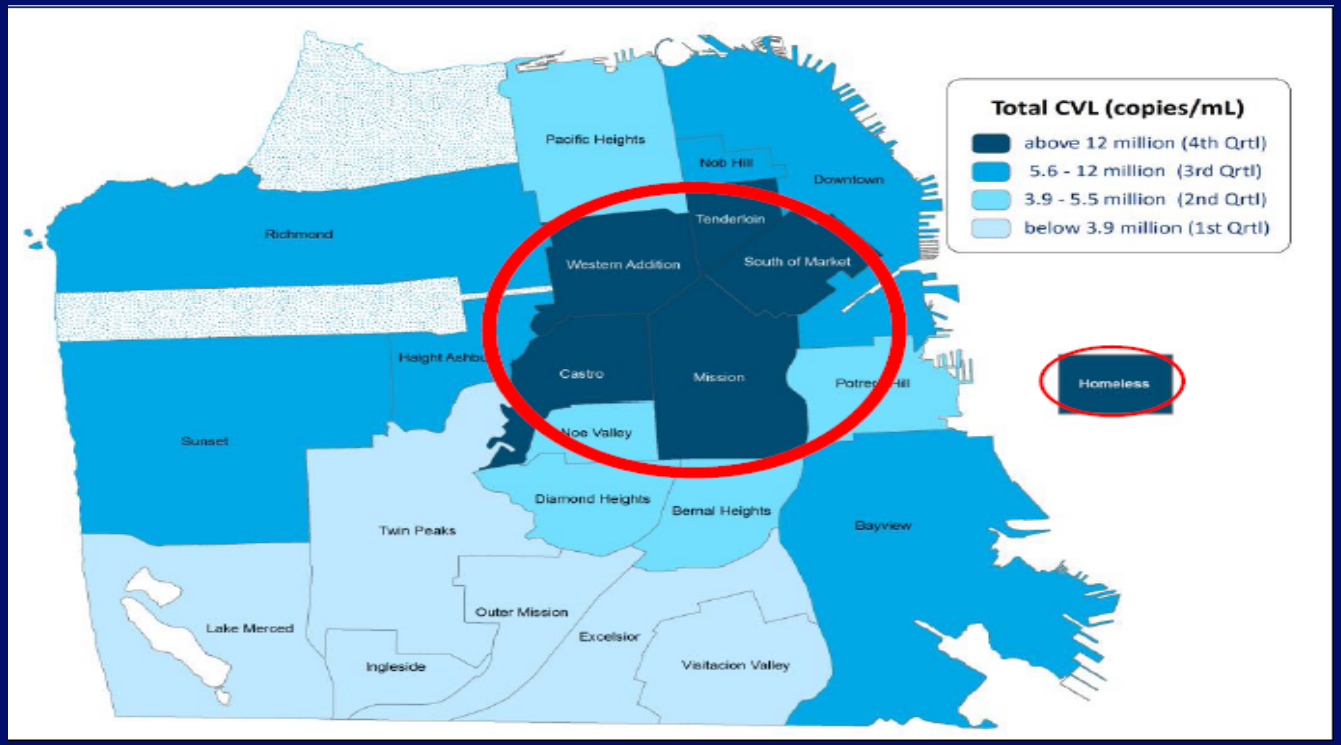


Williams, unpublished data, UNAIDS GARPR database 2014





Cities matter—scale requires focus: Mashup to drive 90-90-90?



Spatial distribution of total community viral load by San Francisco Neighborhood, 2005-2008

Grant Colfax, HIV Prevention and Mapping Community Vital Load
http://www.princeton.edu/cbli/student-projects-1/PPT-Colfax-HIV-Prevention-and-Mapping-Community-ViralLoad.pdf September 2014

Scaling innovations to end AIDS is feasible:

- Think big--set ambitious targets to realize potential
- We have the tools—scaling testing and treatment is fundamental to our response
- Scale by working with community to reach everyone living with HIV to prevent illness, death, transmission, costs…
- Global solidarity to finance scale up—focus resources to ensure efficiency and impact
- Scale data sharing and encourage *wisdom of crowds*—liberate the data and ”just say no” to hoarding behavior
- Mind the Innovation Chasm—we will need to understand the *behavioral economics* to ensure that innovations can go to scale

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Thank You

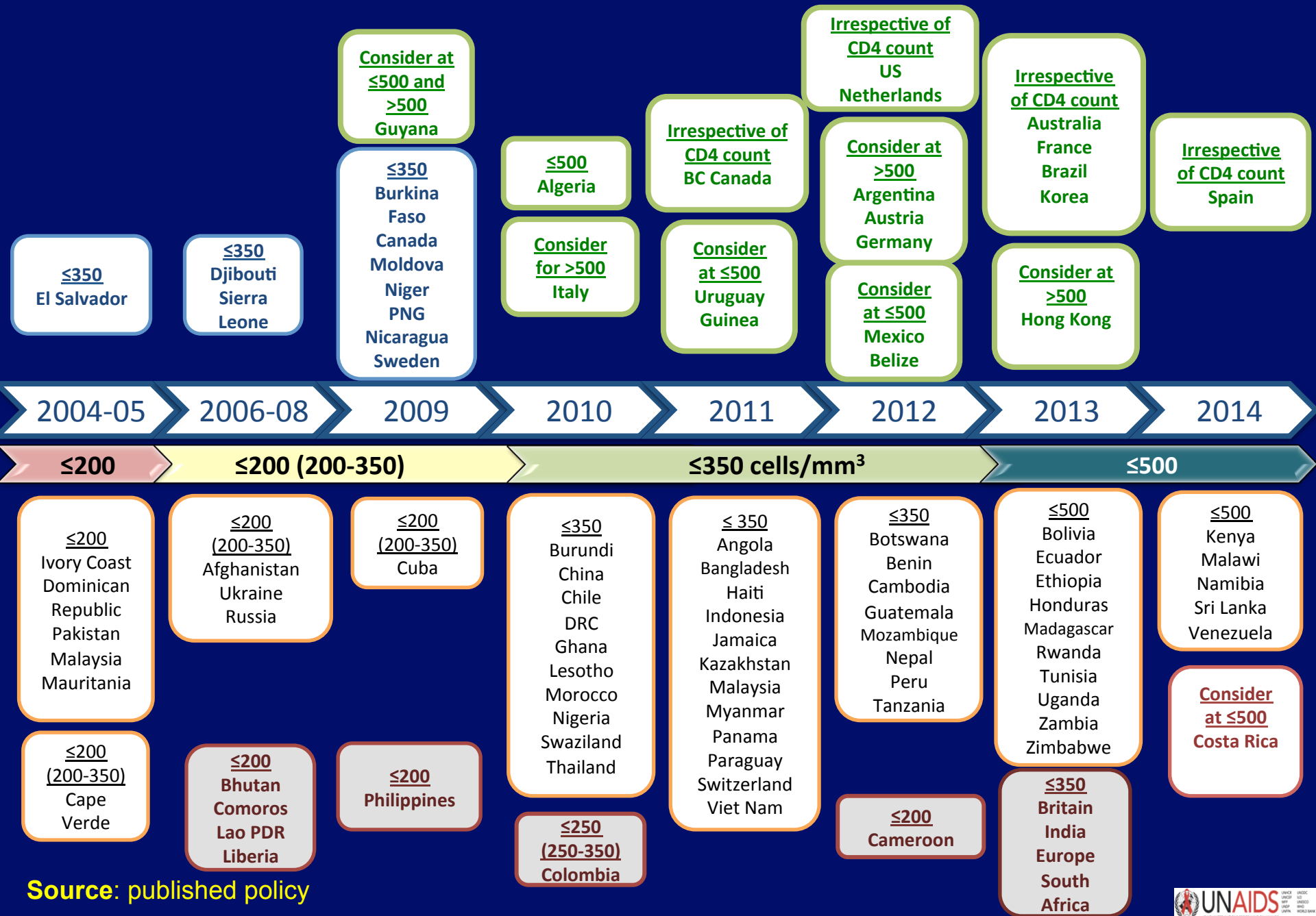
Views expressed in this presentation are those of the author and do not necessarily represent the views of the Joint United Nations Programme on HIV/AIDS (UNAIDS).

“Tear down that data wall”

- Findable
- Standardized
- Trustworthy
- Narrative (why was the data collected and why it matters)

Get the right people in the room with the right data…

ART for asymptomatic people living with HIV



Source: published policy

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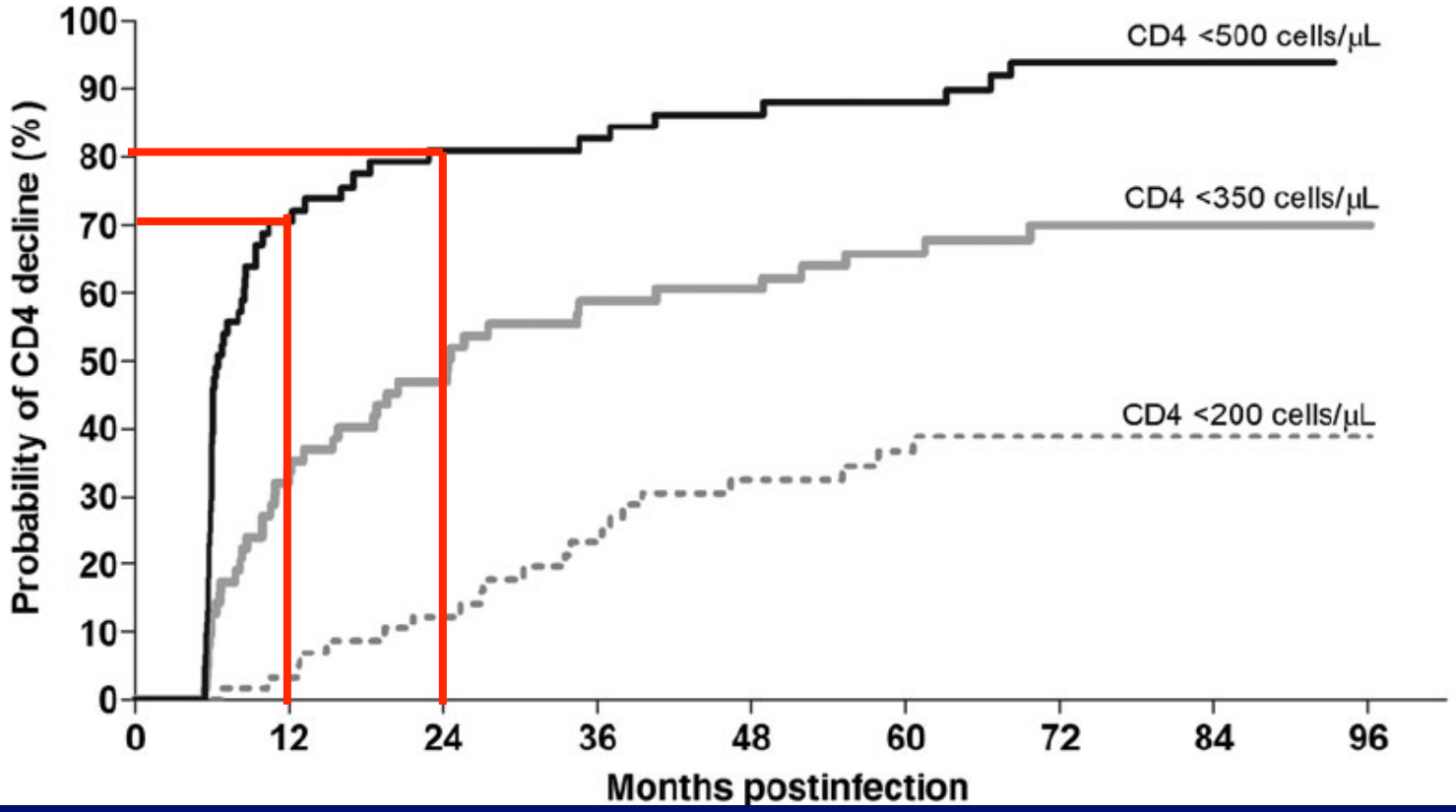
Time to CD4 cell count: South African women infected with sub-type C



Mlisana CID 2014

Global solidarity has resulted in remarkable progress

- By end of 2013
  - New HIV infections are down by 38% since 2001
  - Over 12.9 million persons are on treatment for HIV
  - HIV deaths are down by 35% since 2005
  - We are on a trajectory to eliminate new HIV infections in children globally

Community based delivery can lead to high uptake of ART (83%)

OPEN ACCESS Freely available online

PLOS | ONE

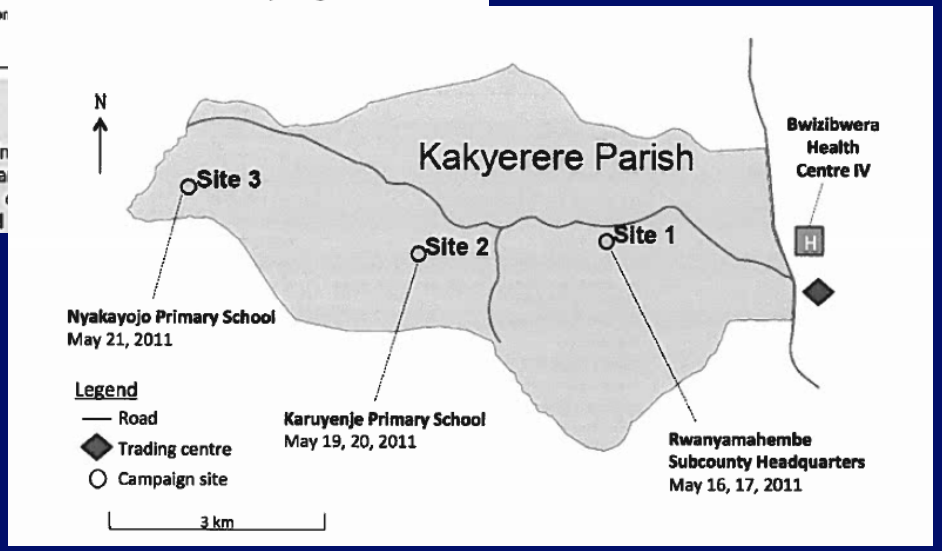
Leveraging Rapid Community-Based HIV Testing Campaigns for Non-Communicable Diseases in Rural Uganda

Gabriel Chamie[1,2]*, Dalsone Kwarisiima[3], Tamara D. Clark[1,2], Jane Kabami[2], Vivek Jain[1,2], Elvin Geng[1,2], Maya L. Petersen[4], Harsha Thirumurthy[5], Moses R. Kamya[2,6], Diane V. Havlir[1,2], Edwin D. Charlebois[2,7], and the SEARCH Collaboration

1 HIV/AIDS Division, Department of Medicine, San Francisco General Hospital, University of California San Francisco, San Francisco, California, United States of America, 2 Makerere University-University of California San Francisco (MU-UCSF) Research Collaboration, Mbarara, Uganda, 3 Mulago-Mbarara Joint AIDS Program, Kampala and Mbarara, Uganda, 4 School of Public Health, University of California, Berkeley, California, United States of America, 5 Gillings School of Global Public Health, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina, United States of America, 6 Department of Medicine, School of Medicine, Makerere University College of Health Sciences, Kampala, Uganda, 7 Center for AIDS Prevention Studies, Department of Medicine, University of Califor
of America

Abstract

Background: The high burden of undiagnosed HIV in sub-Saharan Africa lin
Community-based HIV testing campaigns can address this challenge and provide a
communicable diseases (NCDs). We tested the feasibility and diagnostic yield
diseases into a rapid HIV testing and referral campaign for all residents of a rural



Chamie Plos One 2012

Re-think delivery: SEARCH Uganda community trial of test and treat

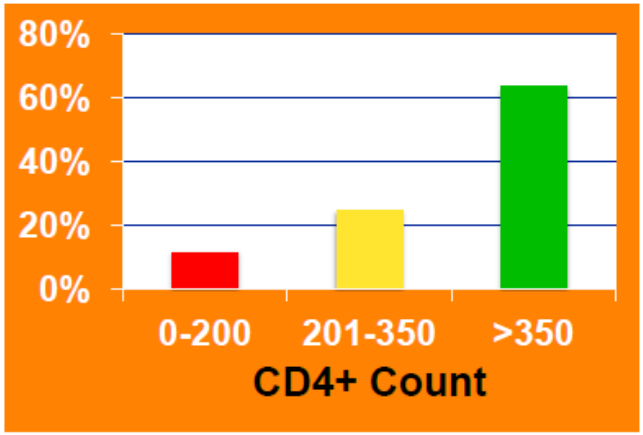
Approach: Multidisease "Community Health Campaign" HIV + other diseases

Principles:

- community led
- high throughput
- health services for children/ adults

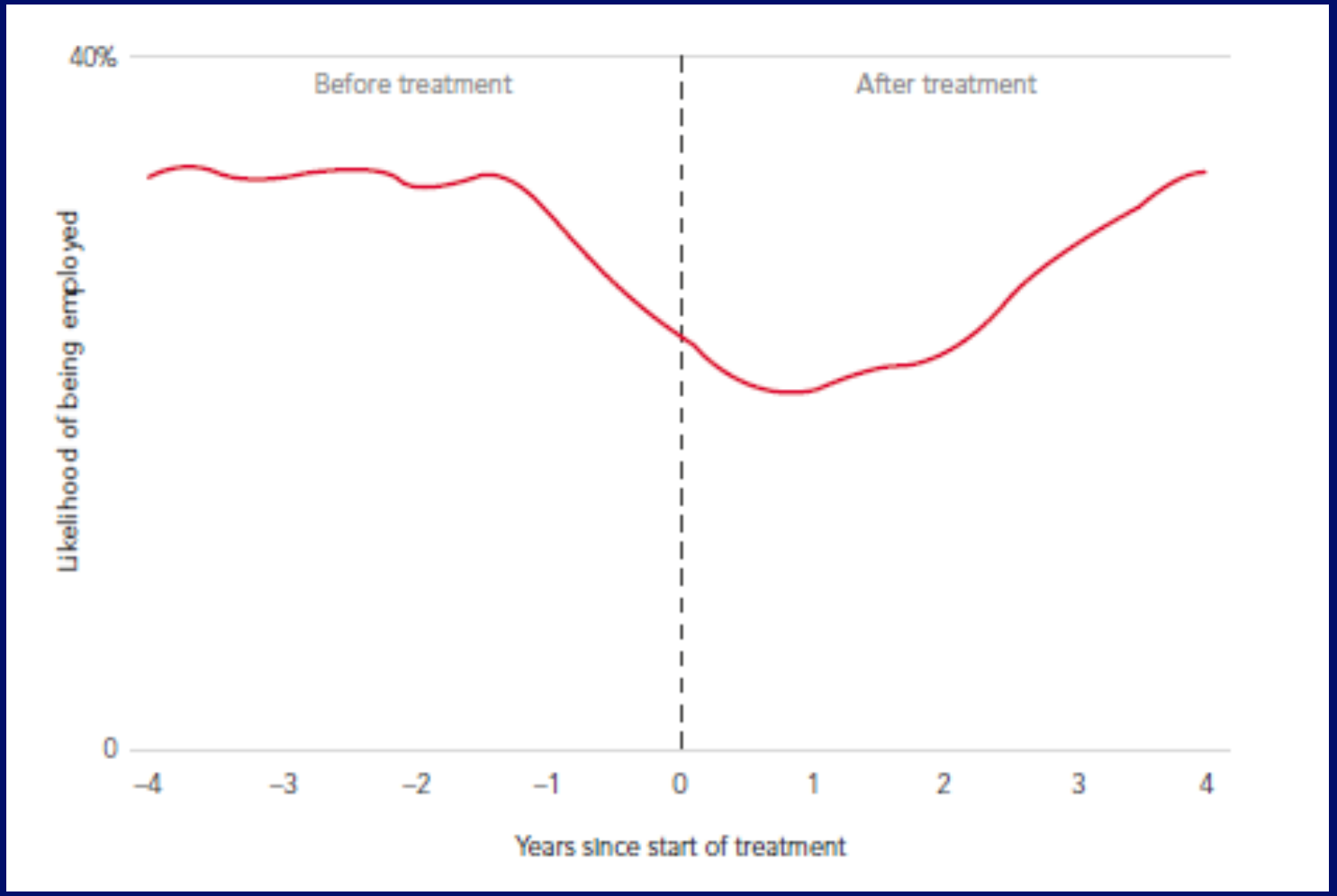
Findings:

- Adults with HIV 8%
- Hypertension 12%
- Diabetes 3.5%



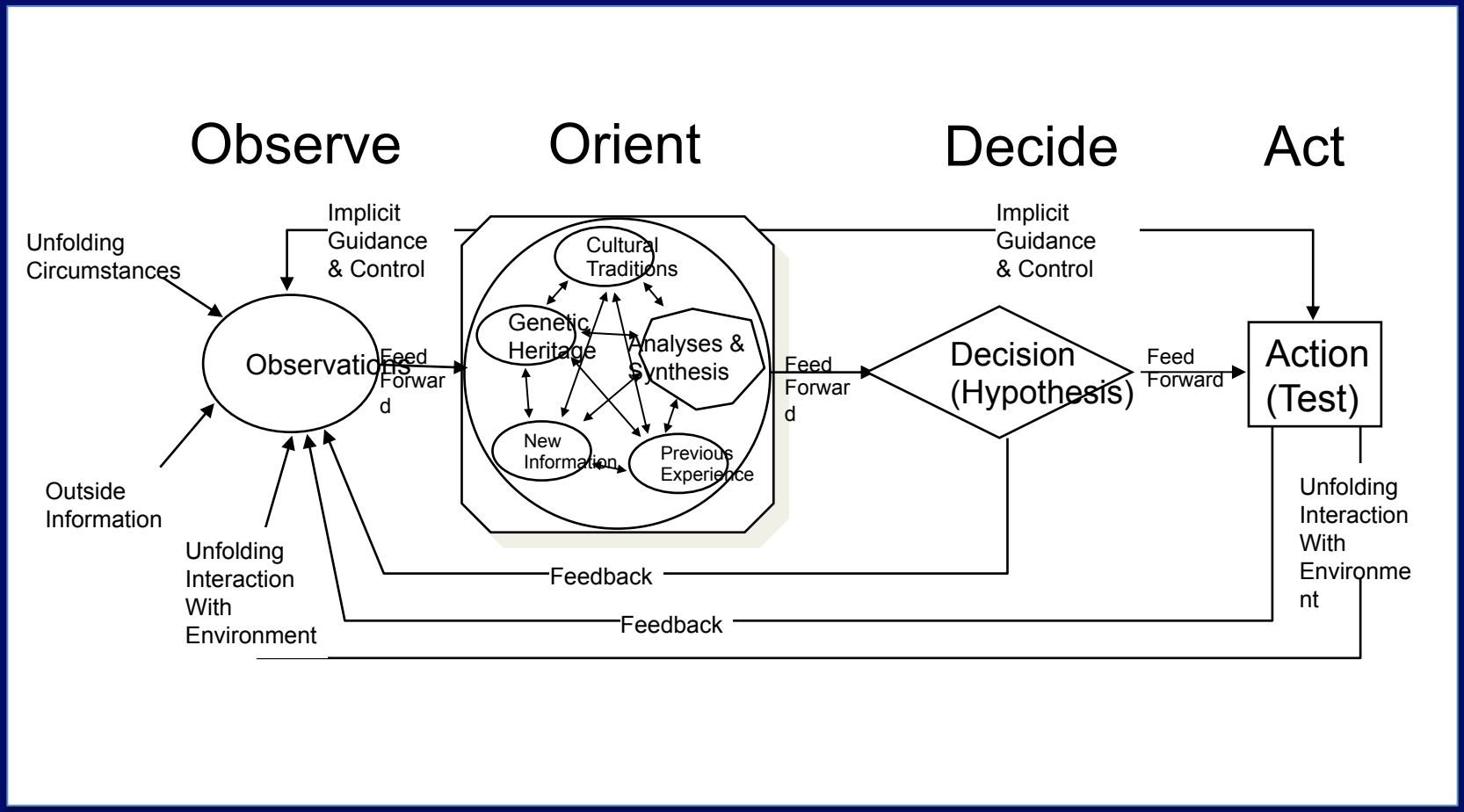
Chamie, PLOS Med, 2012

Treatment has a positive economic impact: healthy people go back to work



Source: Bärnighausen T et al. The economic benefits of ART: evidence from a complete population cohort in rural South Africa. *2nd International HIV Workshop on Treatment as Prevention, Vancouver, Canada, 22–25 April 2012.*

Shorten OODA loop



increase *anti-fragility*

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“Kahneman Gamble”

We cannot predict your viral load or how long before you become ill from HIV. We do know that there are some downsides of waiting and for starting ART. At what level of cumulative risk of adverse outcomes of AIDS, serious non-AIDS or death would you want to start ART? At what point would adverse drug risks outweigh the risk of illness from HIV?

- 1% risk of AIDS, serious non-AIDS or death;
- 5% risk of AIDS, serious non-AIDS or death
- 10% risk of AIDS, serious non-AIDS or death
- Over 10% risk of AIDS, serious non-AIDS or death

Significant cumulative risk?

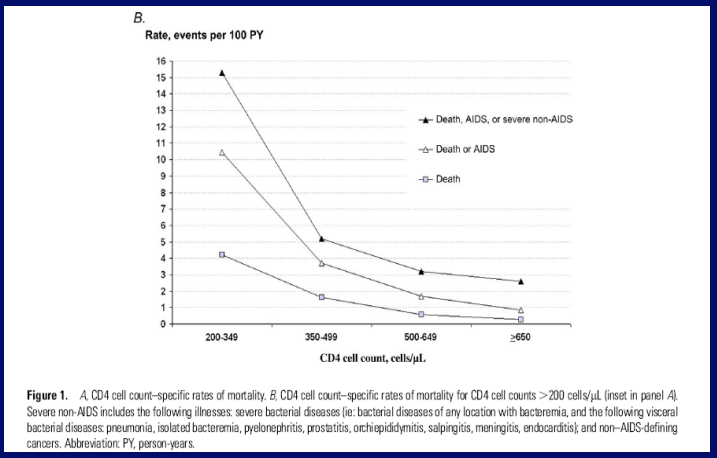


Figure 1. *A*, CD4 cell count–specific rates of mortality. *B*, CD4 cell count–specific rates of mortality for CD4 cell counts >200 cells/μL (inset in panel *A*). Severe non-AIDS includes the following illnesses: severe bacterial diseases (ie: bacterial diseases of any location with bacteremia, and the following visceral bacterial diseases: pneumonia, isolated bacteremia, pyelonephritis, prostatitis, orchiepididymitis, salpingitis, meningitis, endocarditis); and non–AIDS-defining cancers. Abbreviation: PY, person-years.

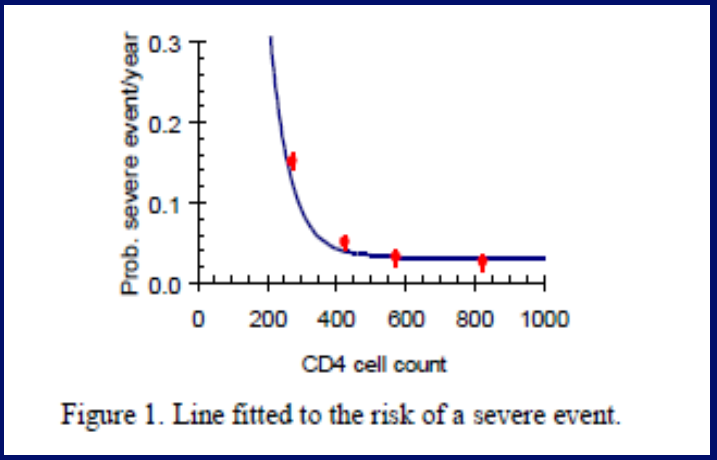


Figure 1. Line fitted to the risk of a severe event.

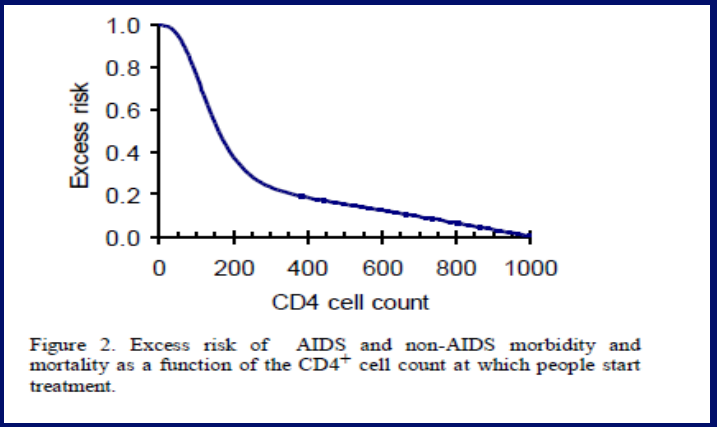


Figure 2. Excess risk of AIDS and non-AIDS morbidity and mortality as a function of the $CD4^+$ cell count at which people start treatment.

Risk of AIDS, serious non-AIDS or death (Anglaret 2012)

Fitted risk of event to CD4 data

Adverse events:

<200 38%

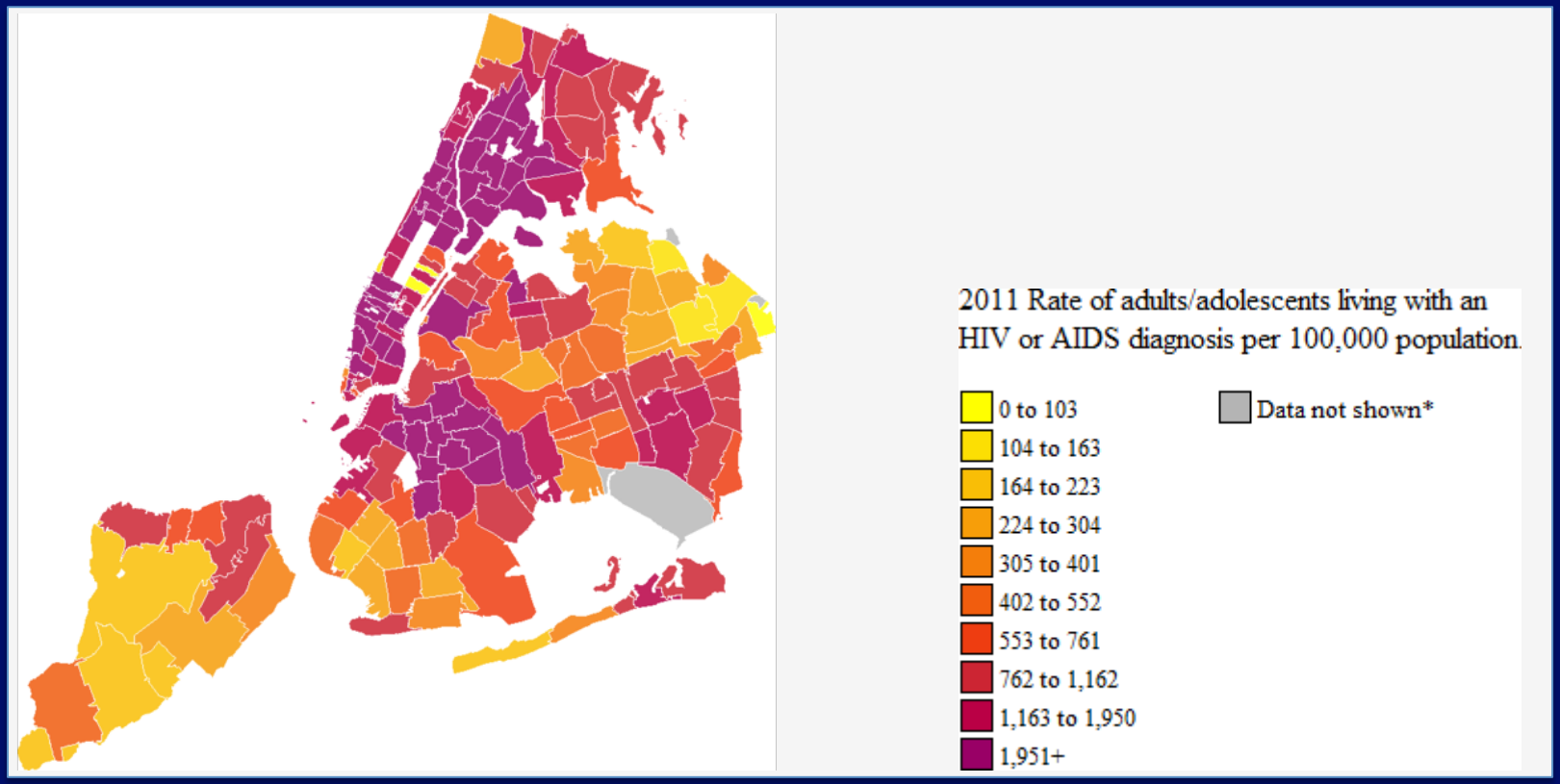
<350 21%

<500 15%

<950 2%

Anglaret, et al, CID 2012; Williams, Archives 2013

Mash-up to drive implementation and health outcomes: 90-90-90



Rates of people living with HIV or AIDS diagnosis by zip code, New York City 2011

AIDSVu http://aidsvu.org/resources/downloadable-maps-and-resources/ Sept 11 2014

WHO 2013 Guidelines
Using new science to optimize TasP

- Earlier Initiation of ART (CD4 ≤ 500):
  - Strategic use to maximize treatment & prevention benefits
  - Symptomatic and CD4 ≤ 350 as a priority
  - CD4-independent situations for ART initiation:
    - TB-HIV and HBV-HIV
    - pregnant women (*Option B+*)
    - sero-discordant couples
    - children < 5 years of age
- No specific recommendations for key populations

Conceptual diagram of CD4+ response on ART: starting later translates in lower CD4 levels (and higher risk)

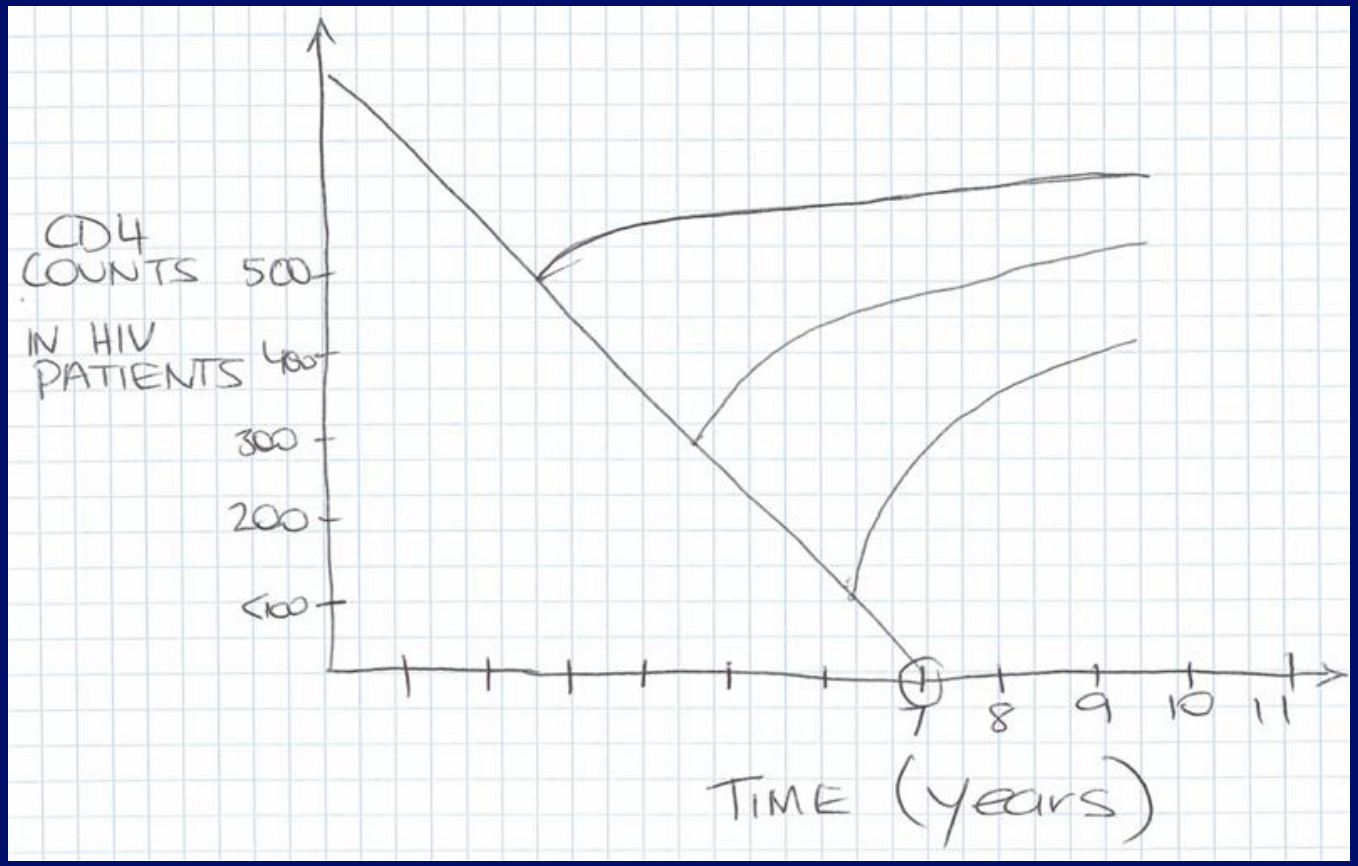
5-7 YEARS

Le Moing et al. HIV Med 2007;8:156.

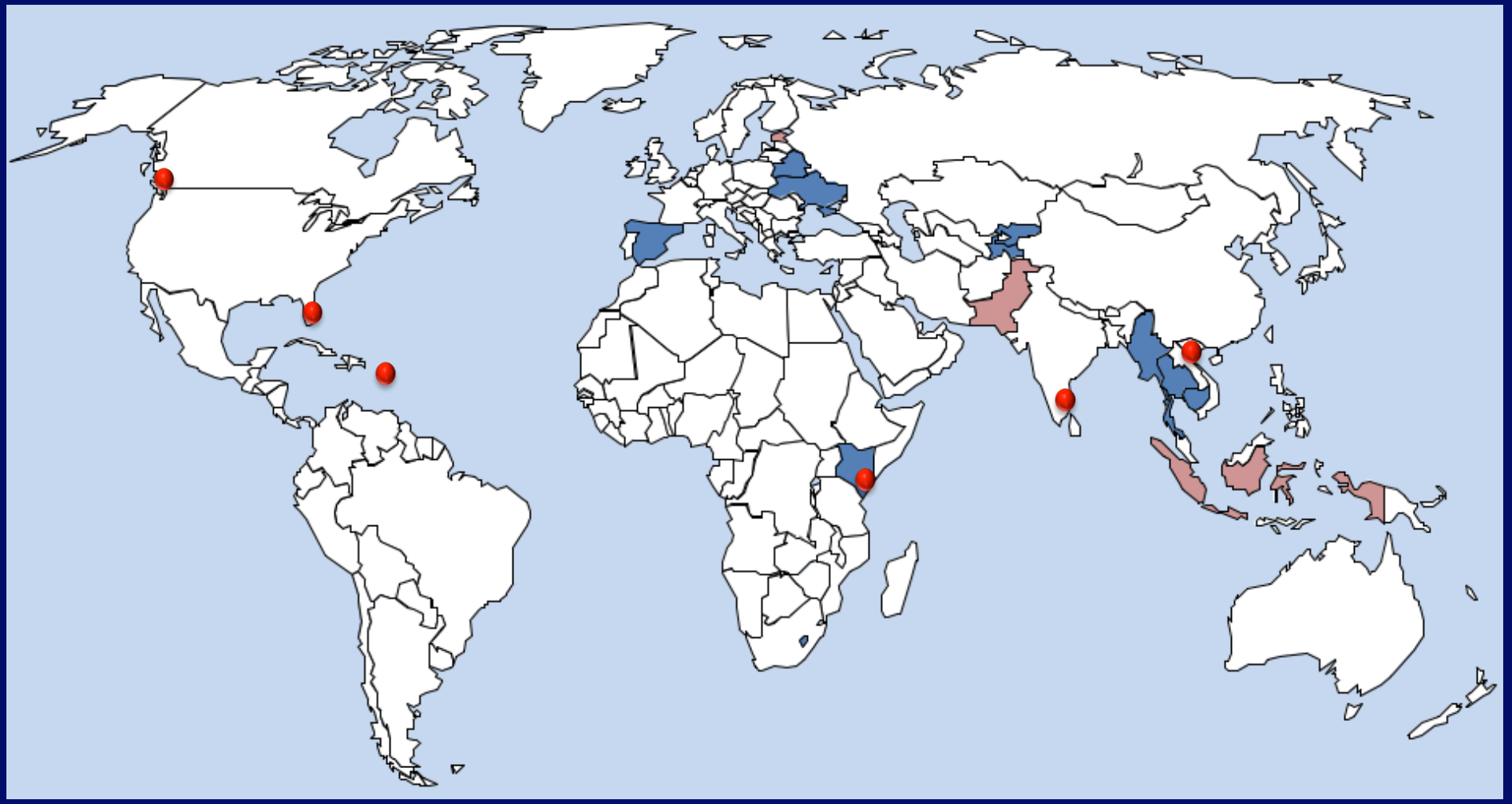
Micheloud et al. J Infection 2008;56:130.

Mocroft et al. Lancet 2007;370:407.

Vrisekoop et al. J Immunol 2008;181:1573.



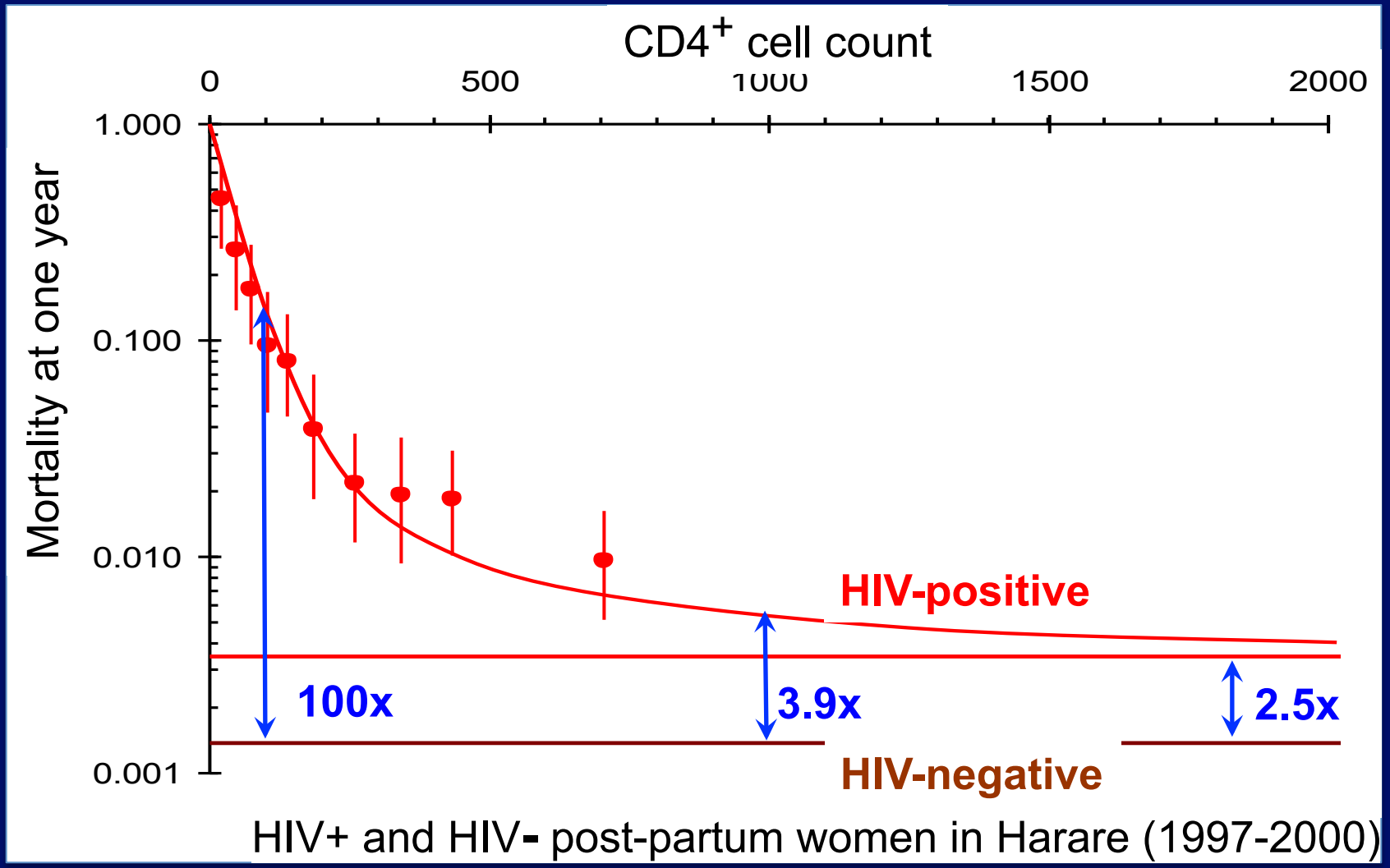
Countries with studies on TasP for PWID



Dark blue represents countries where 15-25% of IDUs are living with HIV (2011); pink represents countries where >25% of IDUs are living with HIV (2011) and the red dots represent countries conducting research

UNAIDS

Higher mortality for mothers in Zimbabwe even when their CD4 cell counts are at higher level (ZIVTAMBO study)

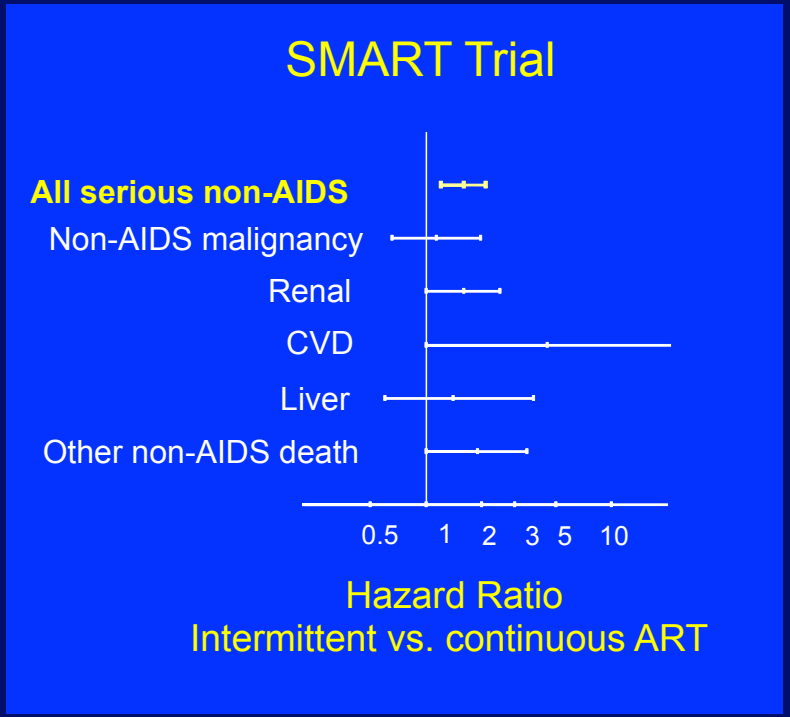


Data: Hargrove *AIDS* 2010; Model: Williams *JID 2006*

UNAIDS

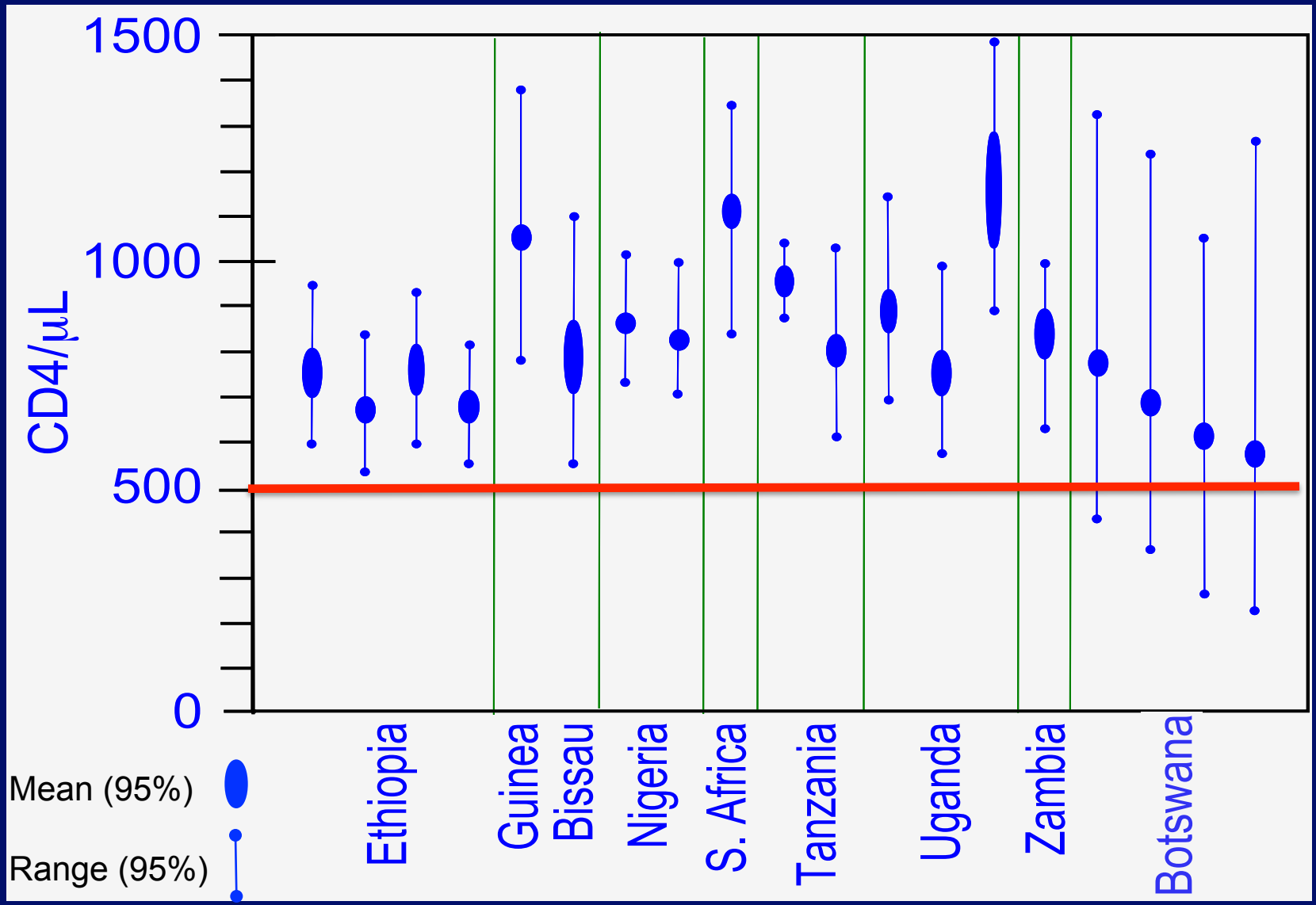
Risk of non-AIDS morbidity and mortality

- HIV may be associated with serious non-AIDS defining events
  - Cardiovascular
  - Renal
  - Liver
  - Non-AIDS malignancies
- At higher CD4 counts non-AIDS events are much more common than AIDS events
- Does ART use reduce risk of some serious non-AIDS events?



SMART Study Group, NEJM 2006 & Neaton et al, Current Opinion in HIV/AIDS 2008
Slide courtesy of A Phillips

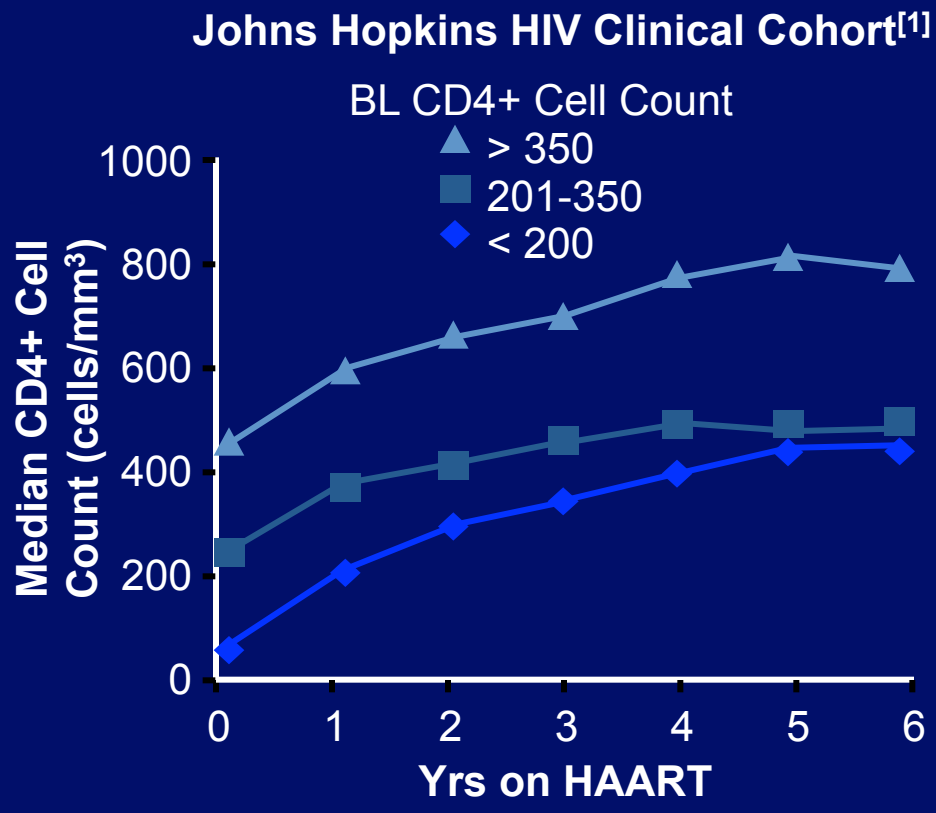
CD4 highly variable in **HIV-negative** people

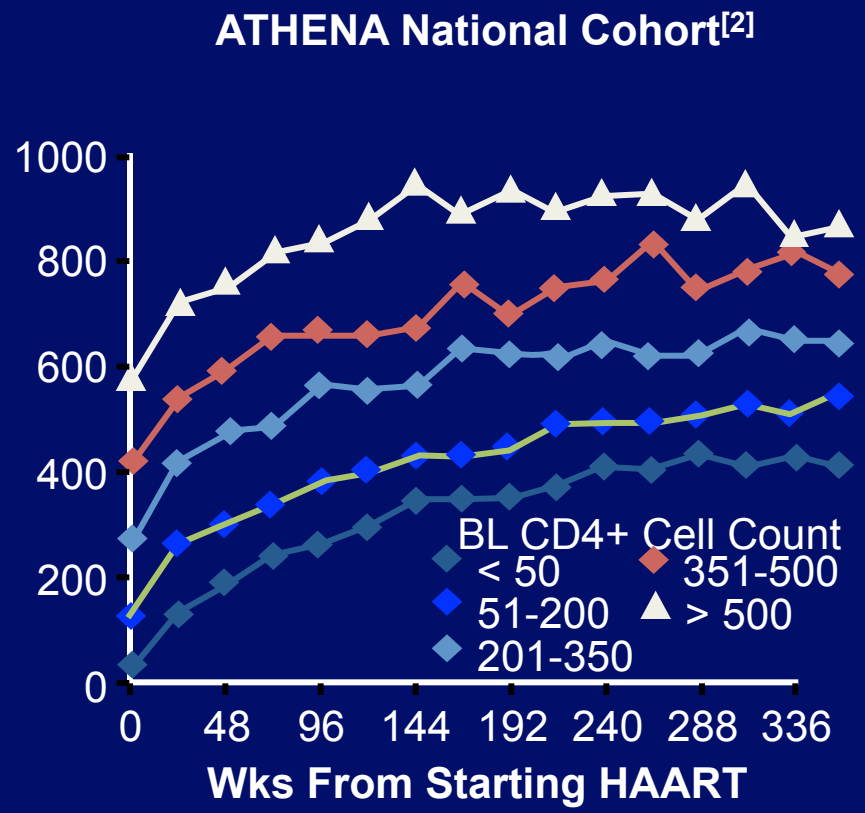


Williams *et al. J Infect Dis.* 2006; 194: 1450-8; Bussman *et al. Clinical and Diagnostic Laboratory Immunology* 2004

UNAIDS

Likelihood of achieving normal CD4+ cell count on ART depends on baseline level



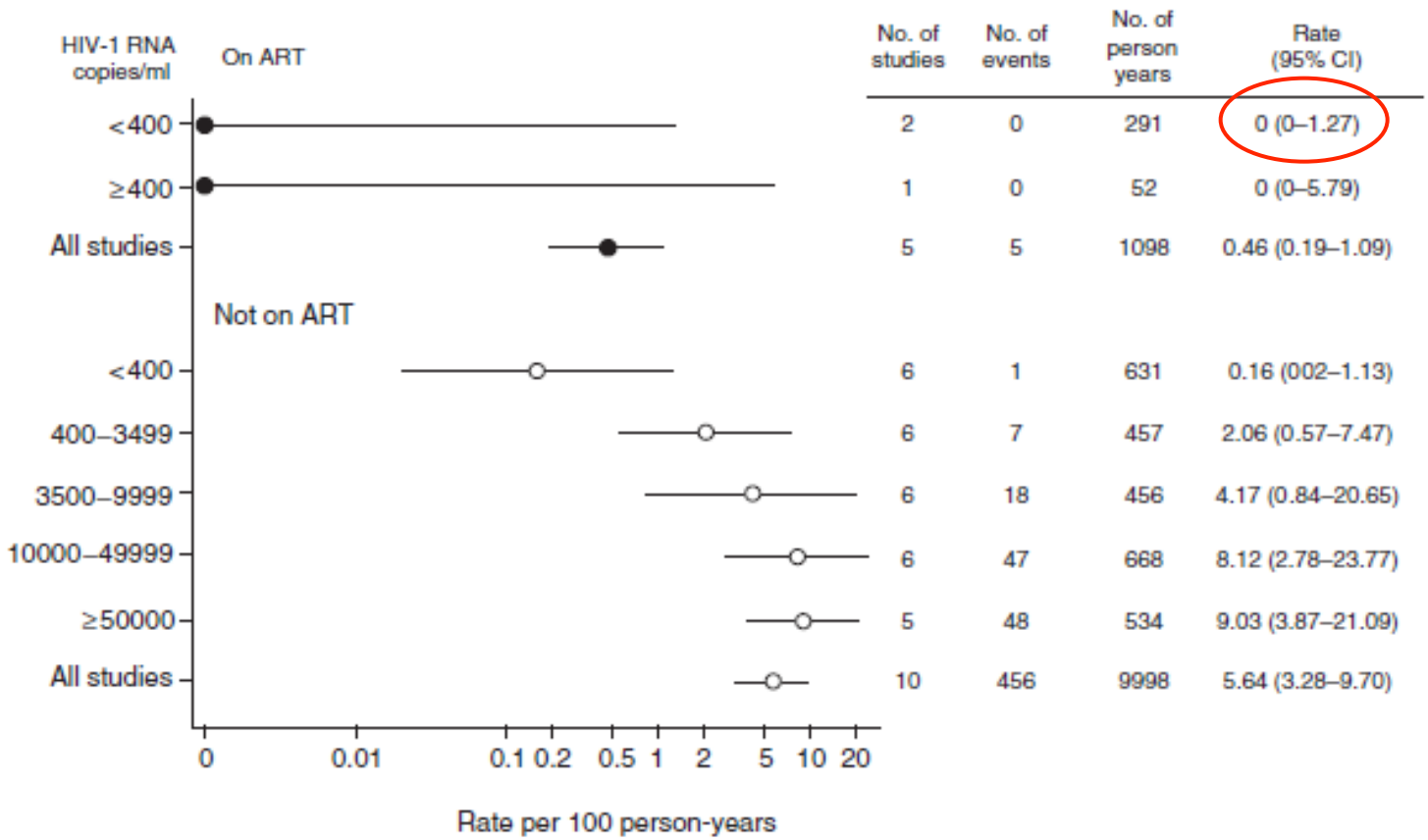


1. Moore RD, et al. Clin Infect Dis. 2007;44:441-446. Published by The University of Chicago Press. Copyright ©2009. University of Chicago Press. All rights reserved. http://www.journals.uchicago.edu/toc/cid/current.
2. Gras L, et al. J Acquir Immune Defic Syndr. 2007;45:183-192. Reproduced with permission.

ART reduces sexual transmission of HIV: meta-analysis shows no transmission <400 copies per ml

2009

Sexual transmission of HIV Attia *et al.*

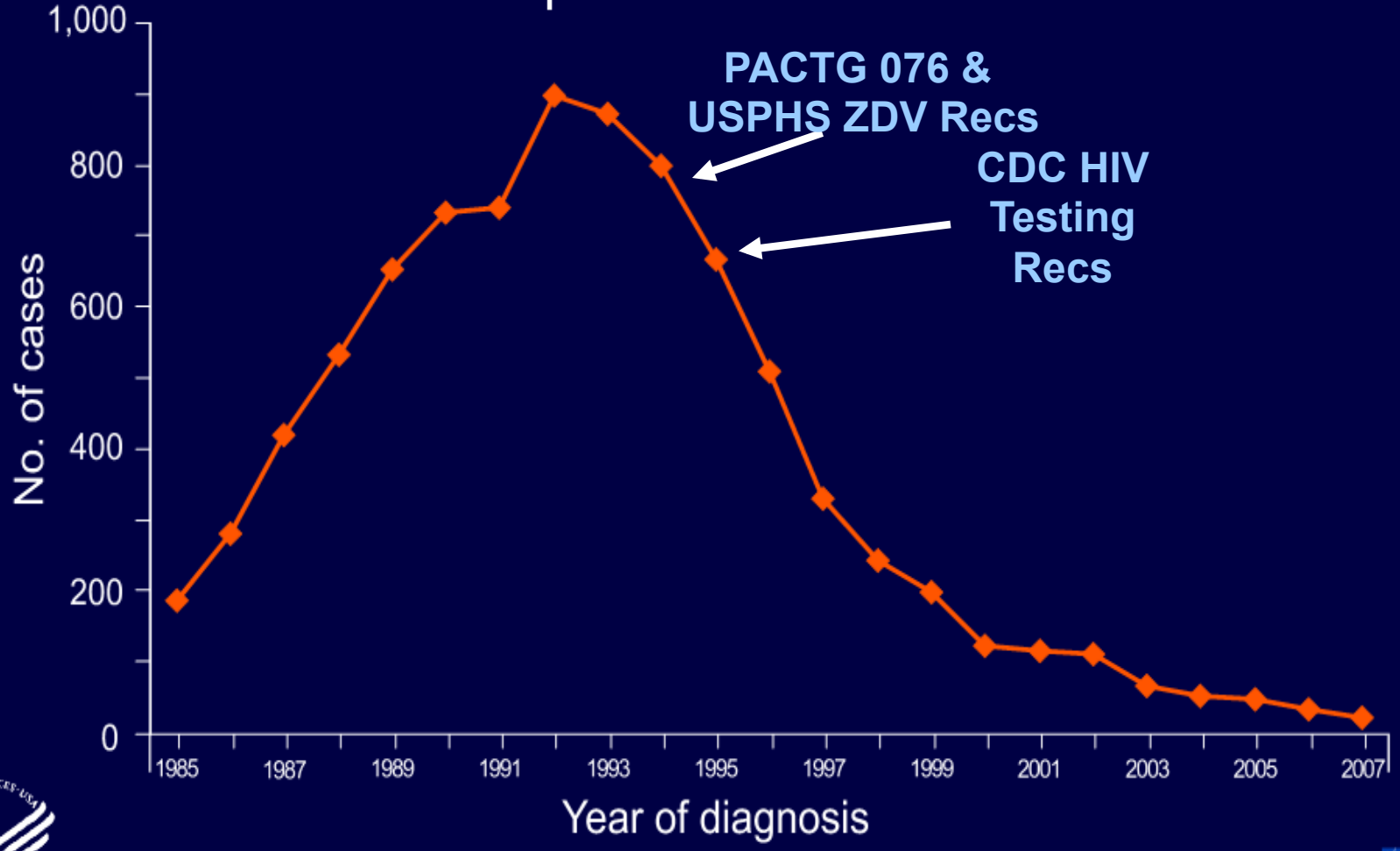


	No. of studies	No. of events	No. of person years	Rate (95% CI)
On ART				
<400	2	0	291	0 (0–1.27)
≥400	1	0	52	0 (0–5.79)
All studies	5	5	1098	0.46 (0.19–1.09)
Not on ART				
<400	6	1	631	0.16 (002–1.13)
400–3499	6	7	457	2.06 (0.57–7.47)
3500–9999	6	18	456	4.17 (0.84–20.65)
10000–49999	6	47	668	8.12 (2.78–23.77)
≥50000	5	48	534	9.03 (3.87–21.09)
All studies	10	456	9998	5.64 (3.28–9.70)

Attia S, et al.AIDS 2009 Jul 17;23(11):1397-404.

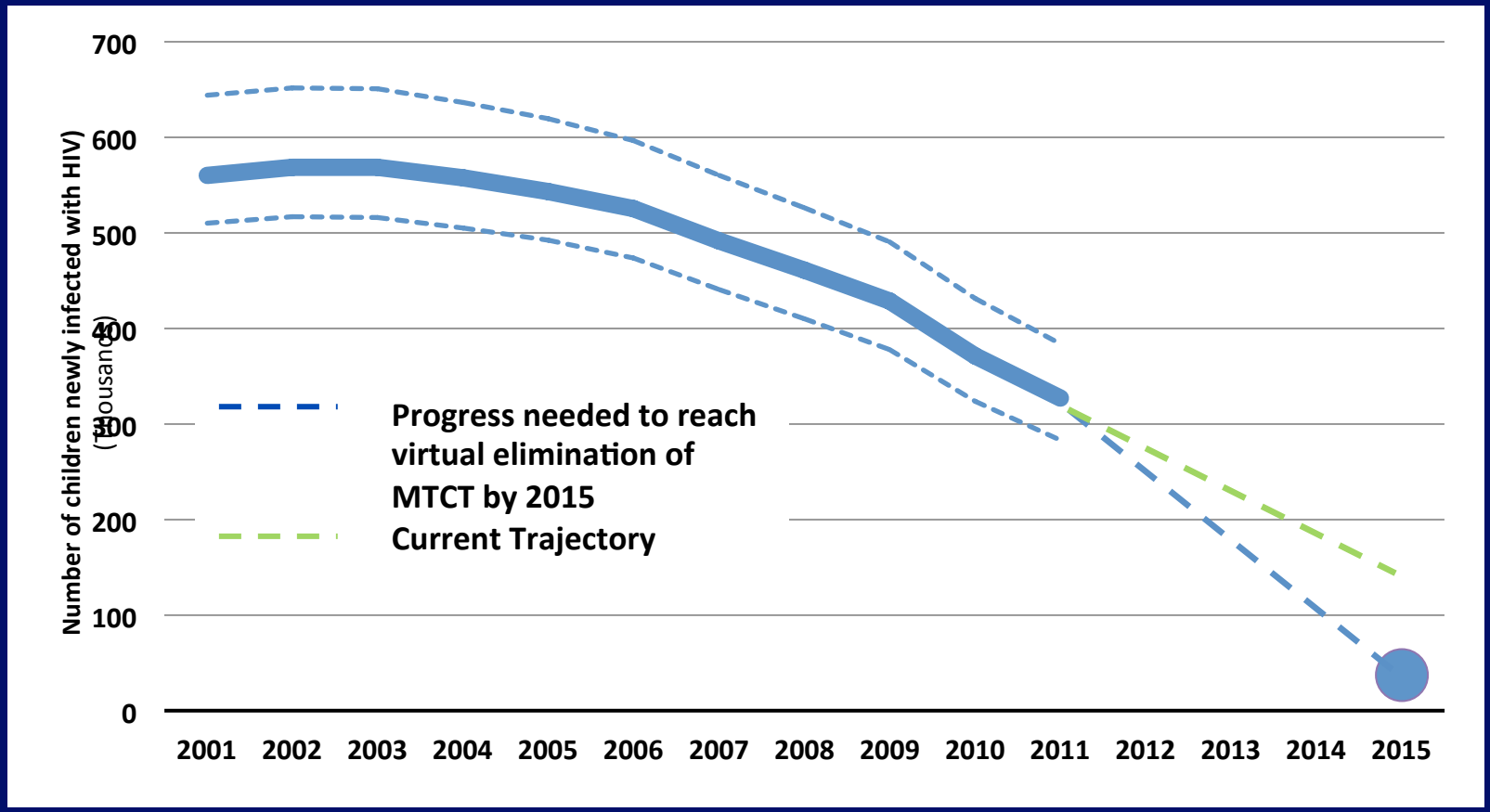
UNAIDS

Estimated Numbers of Perinatally Acquired AIDS Cases by Year of Diagnosis, 1985–2007—United States and Dependent Areas



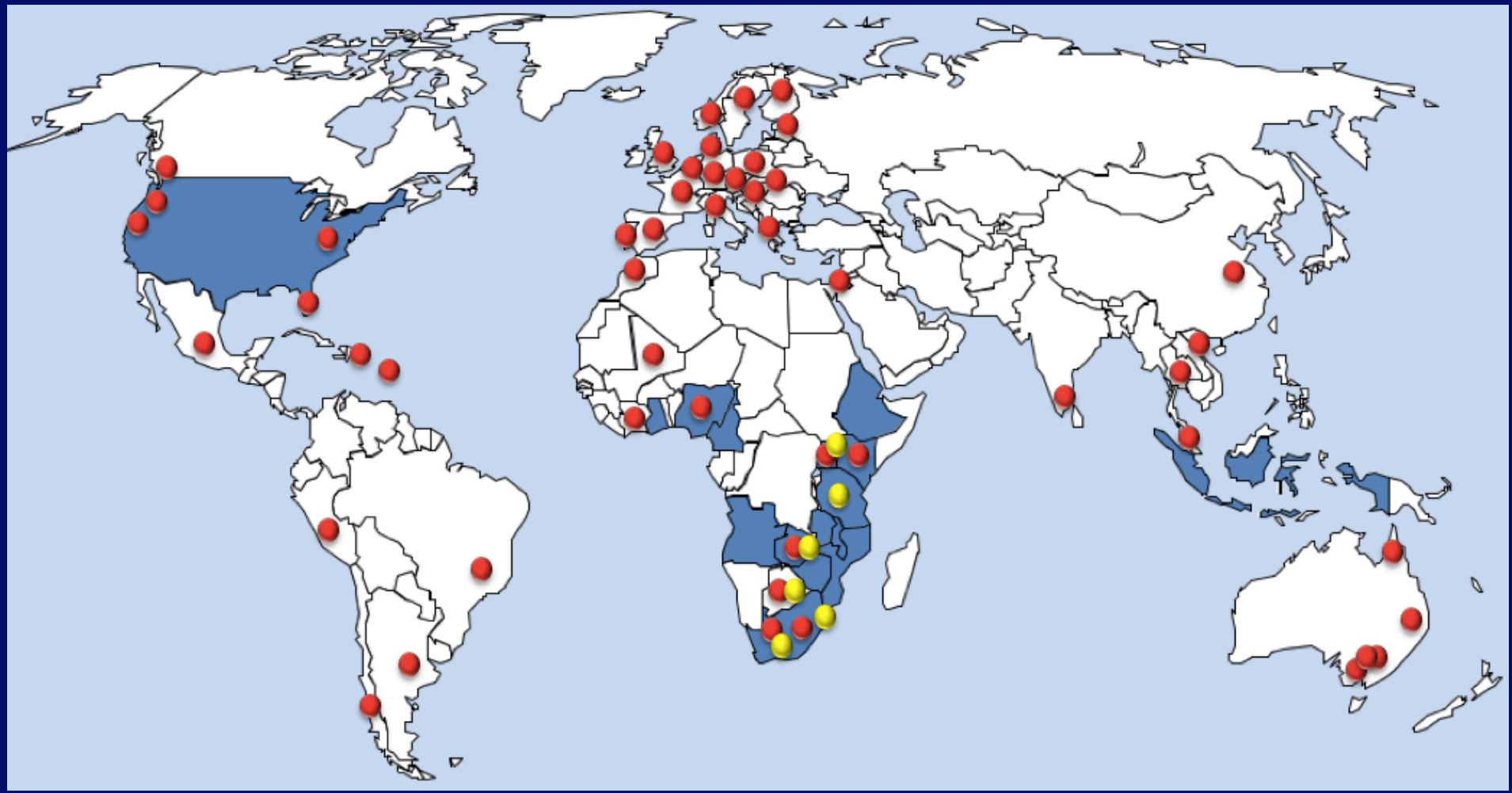
Note. Data have been adjusted for reporting delays and missing risk-factor information.

Impact of ART: Significant Decrease in Mother-to-Child Transmission of HIV since 2010



UNAIDS Global Report 2012

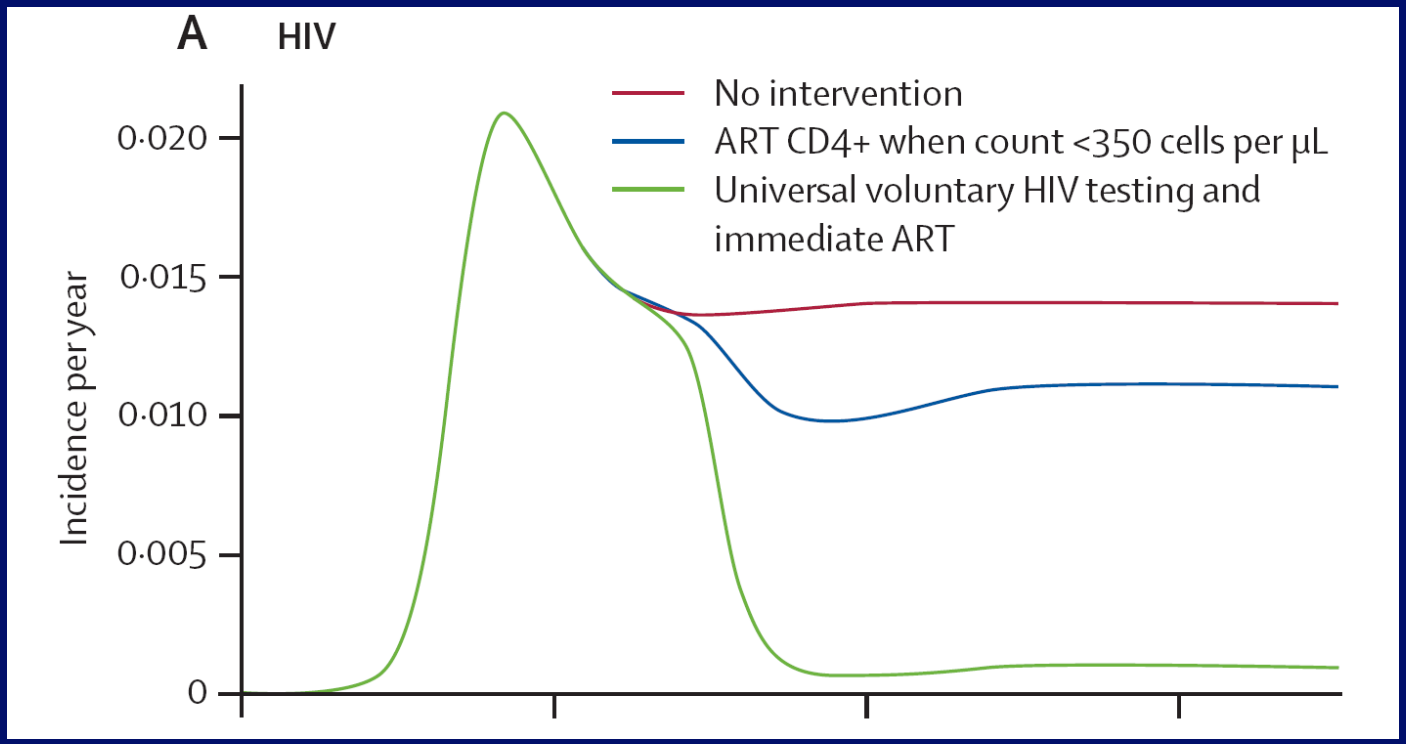
Ongoing and planned TasP studies: feasibility, impact and key populations



- Countries in blue are high HIV incidence countries (2011)
- Red dots represent countries with ongoing/planned research on early ART and the yellow dots represent countries with research on combination HIV prevention strategies

UNAIDS

ART as prevention

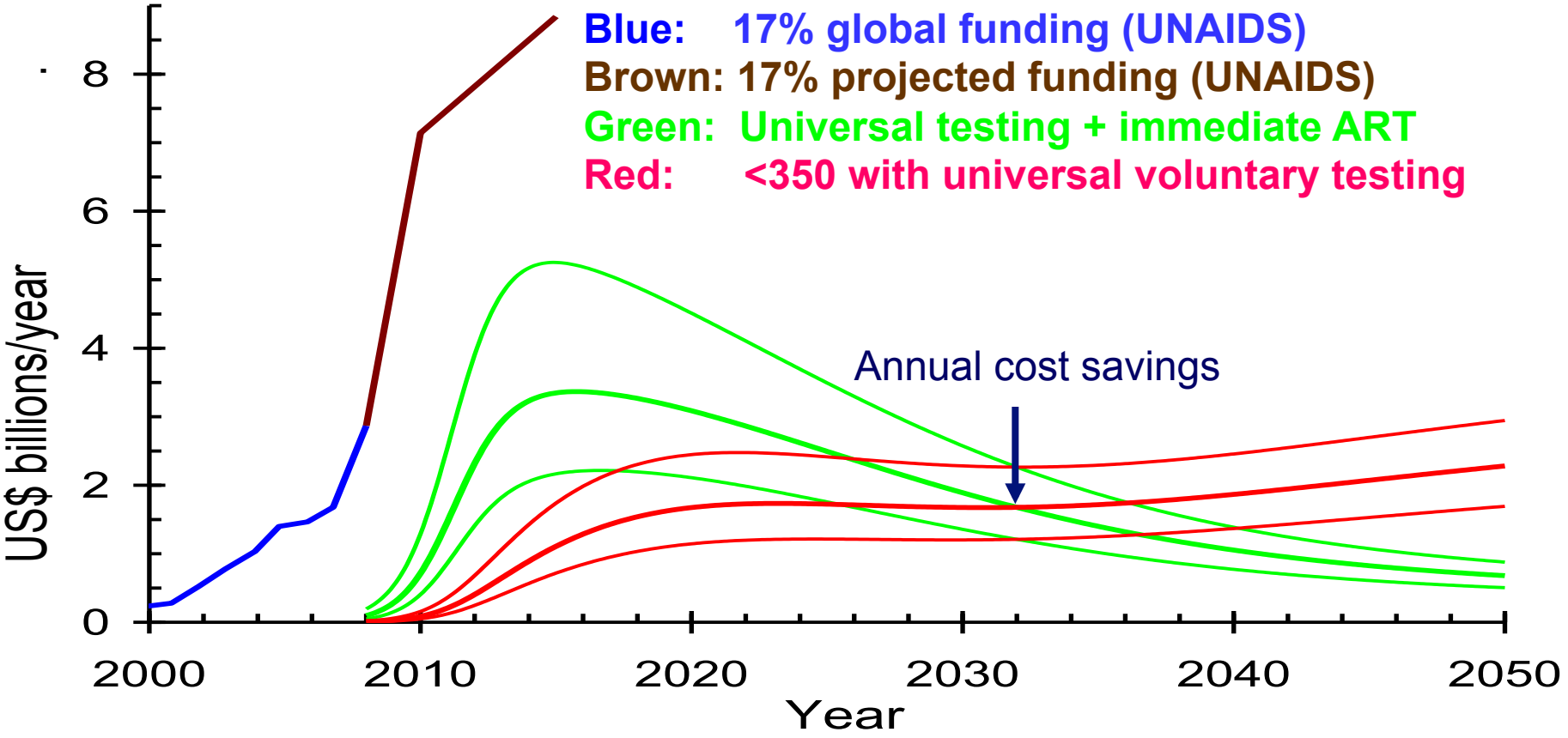


- Testing and ART impacts HIV incidence and survival
- Elimination is feasible

Granich, Gilks, Dye, De Cock, Williams *Lancet* 2008

UNAIDS

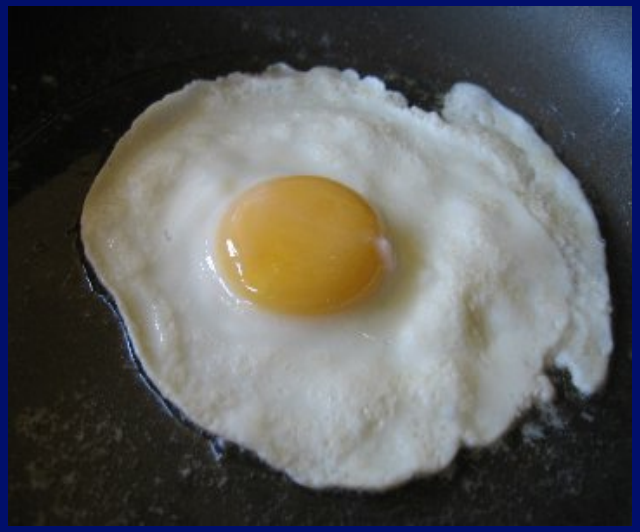
Available funding and costs: We appear to be in the right ball park….



Cohen J. HIV/AIDS. The great funding surge. Science **2008** Jul 25;321(5888):512-9.

UNAIDS. Financial resources required to achieve universal access to HIV prevention, treatment, care and support. UNAIDS Report (2007). http://data.unaids.org/pub/Report/2007/20070925_advocacy_grne2_en.pdf.

ART policy vs. funding conundrum



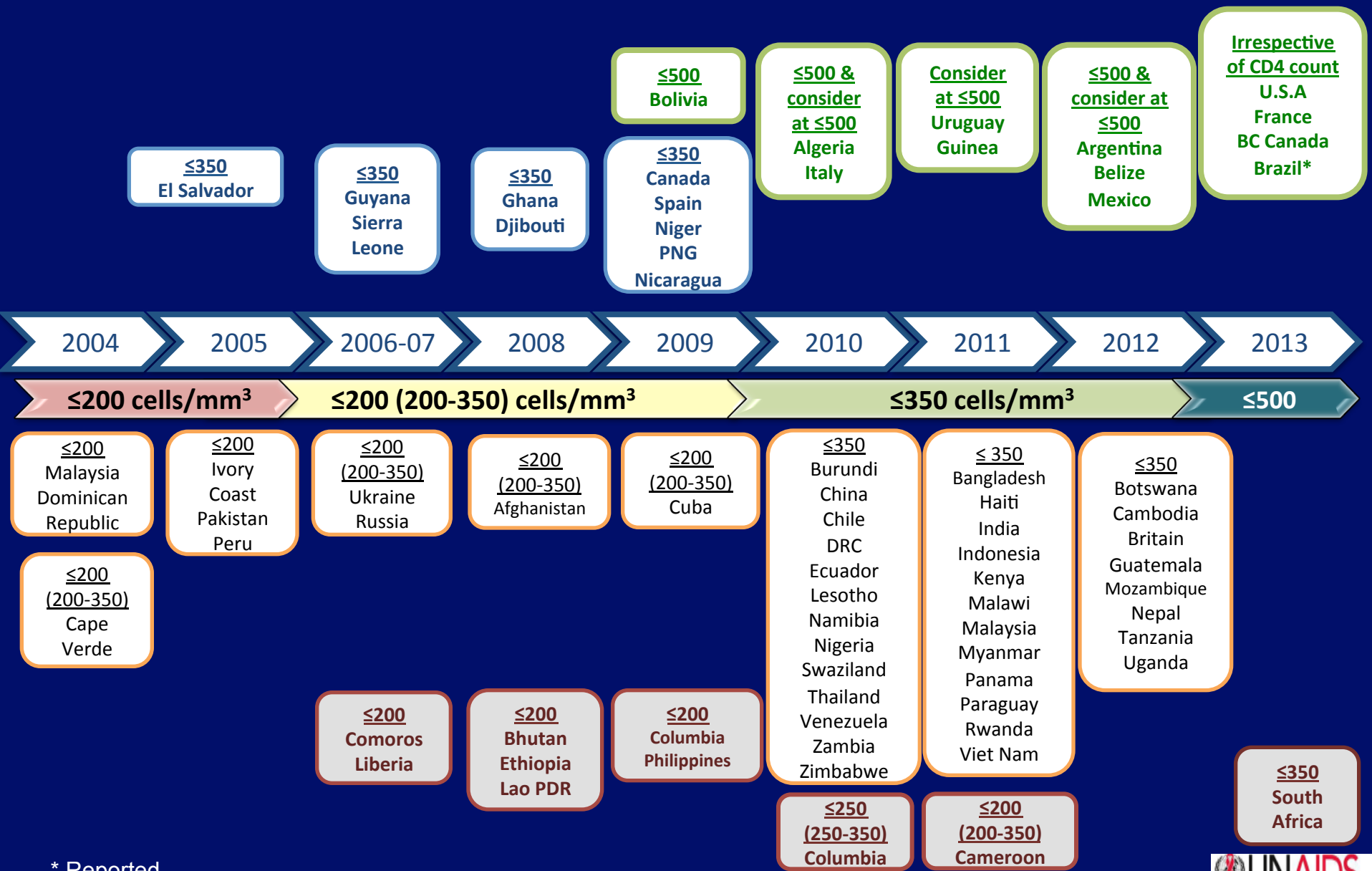
Can we afford to shift policy to provide earlier ART ?

Can we afford not to?

WHO 2013 Guidelines
Using new science to optimize TasP

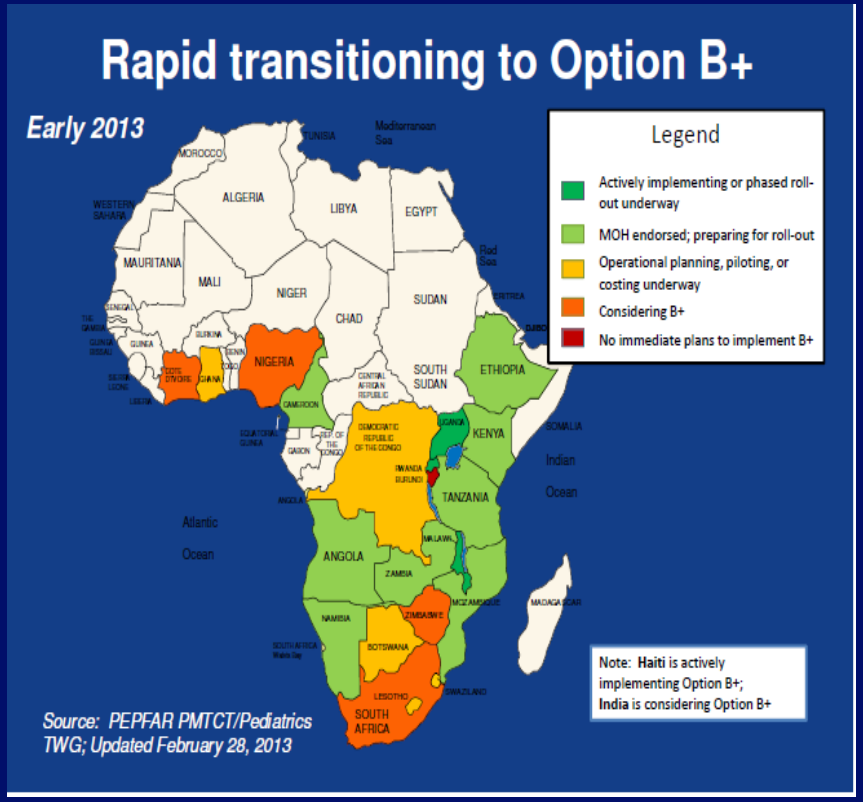
- Earlier Initiation of ART (CD4 ≤ 500):
  - Strategic use to maximize treatment & prevention benefits
  - Symptomatic and CD4 ≤ 350 as a priority
  - CD4-independent situations for ART initiation:
    - TB-HIV and HBV-HIV
    - pregnant women (*Option B+*)
    - sero-discordant couples
    - children < 5 years of age
- No specific recommendations for key populations

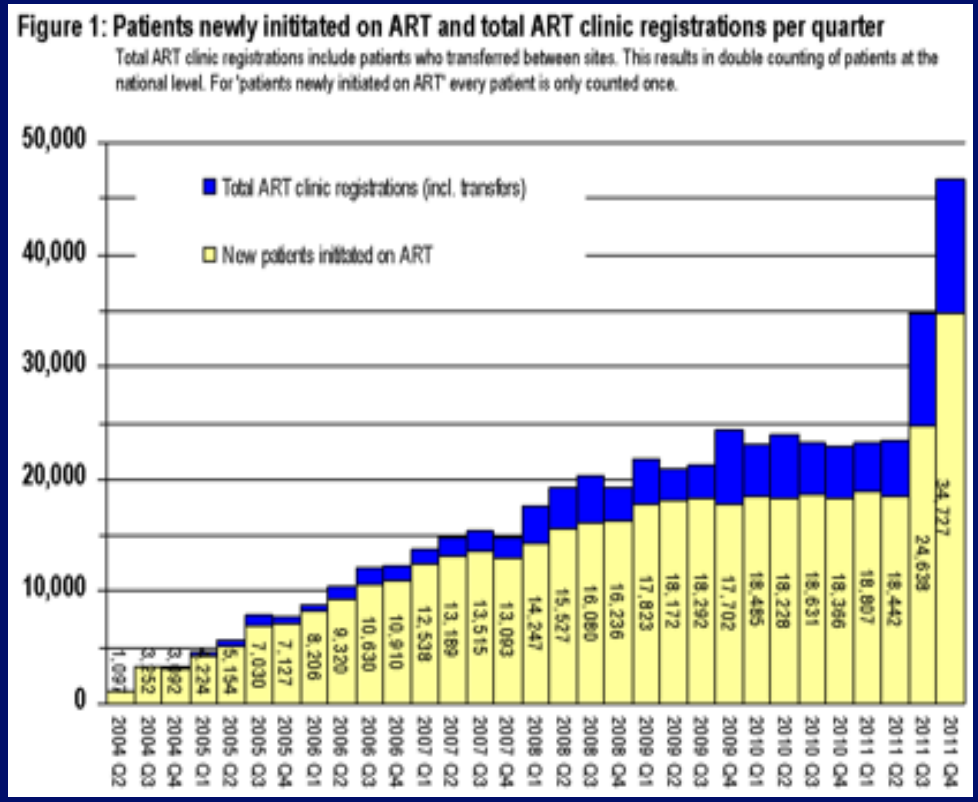
Early ART for asymptomatic people living with HIV



* Reported

One size does not fit all….





Option B+: early 2013

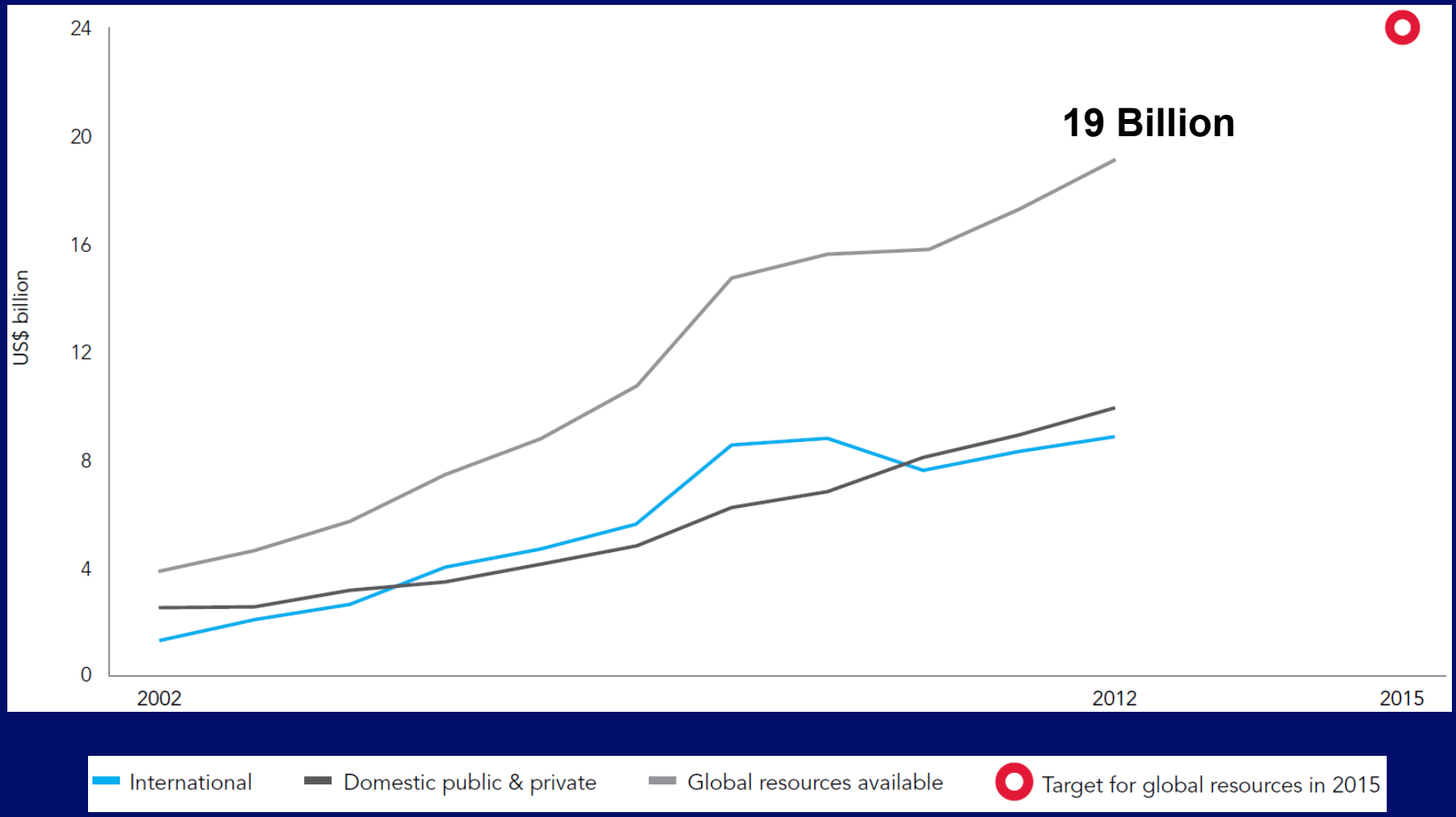
Slide courtesy of CDC

UNAIDS

However beautiful the strategy, you should occasionally look at the results

--Winston Churchill

Resources available for HIV in low- and middle-income countries, 2002–2012 and 2015 target*

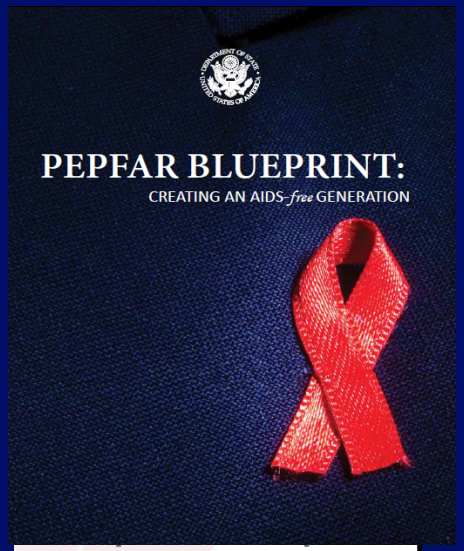


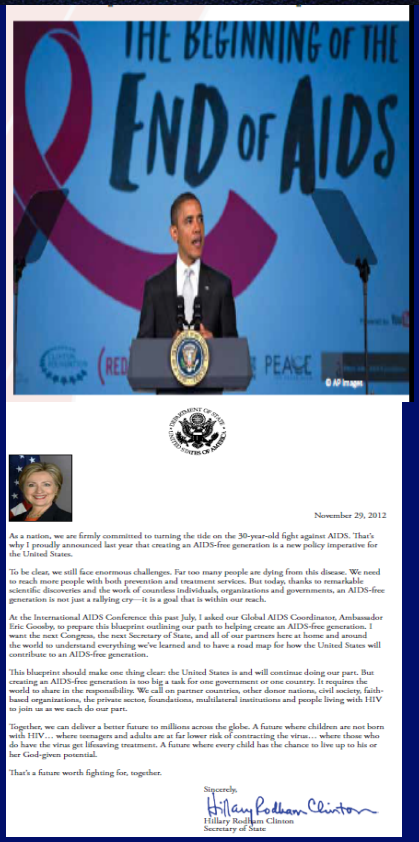
* The UN General Assembly 2011 Political Declaration on HIV and AIDS set a target of US$ 22bn – 24bn by 2015.

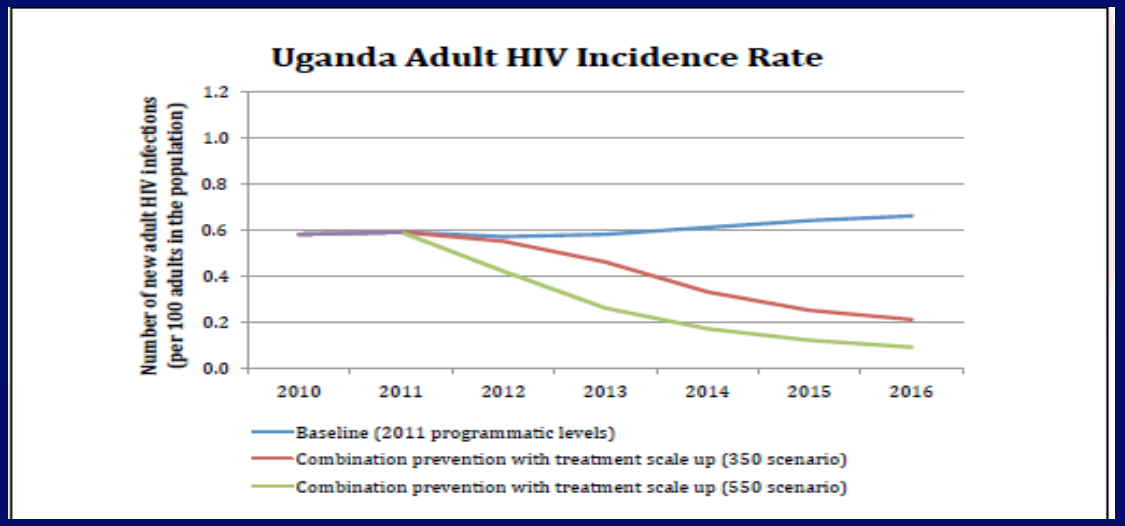
Source: UNAIDS estimates.

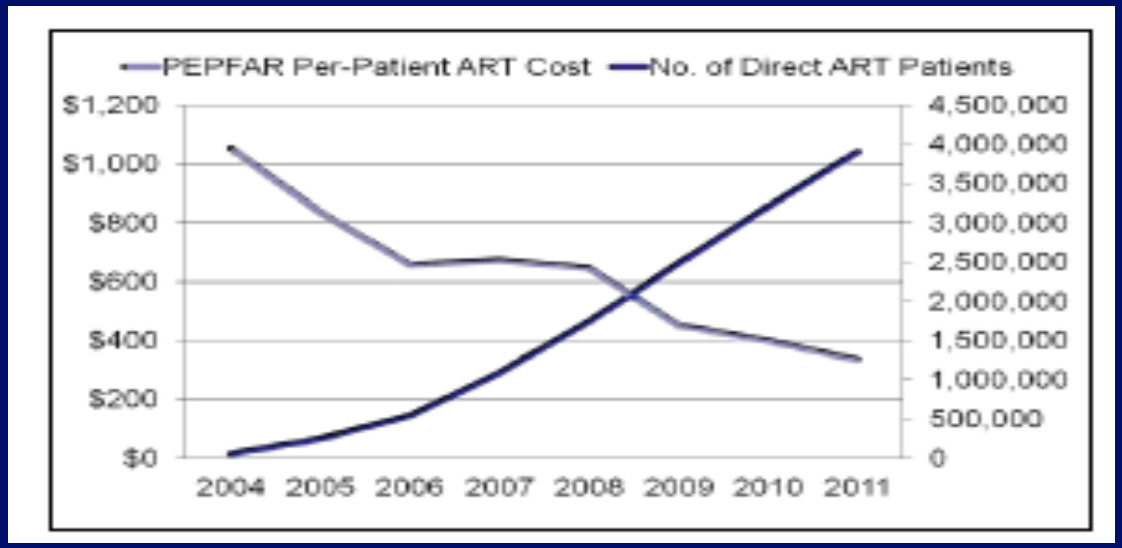
Re-think how we spend the money

Re-think focus:
eMTCT, Testing. ART, VMMC



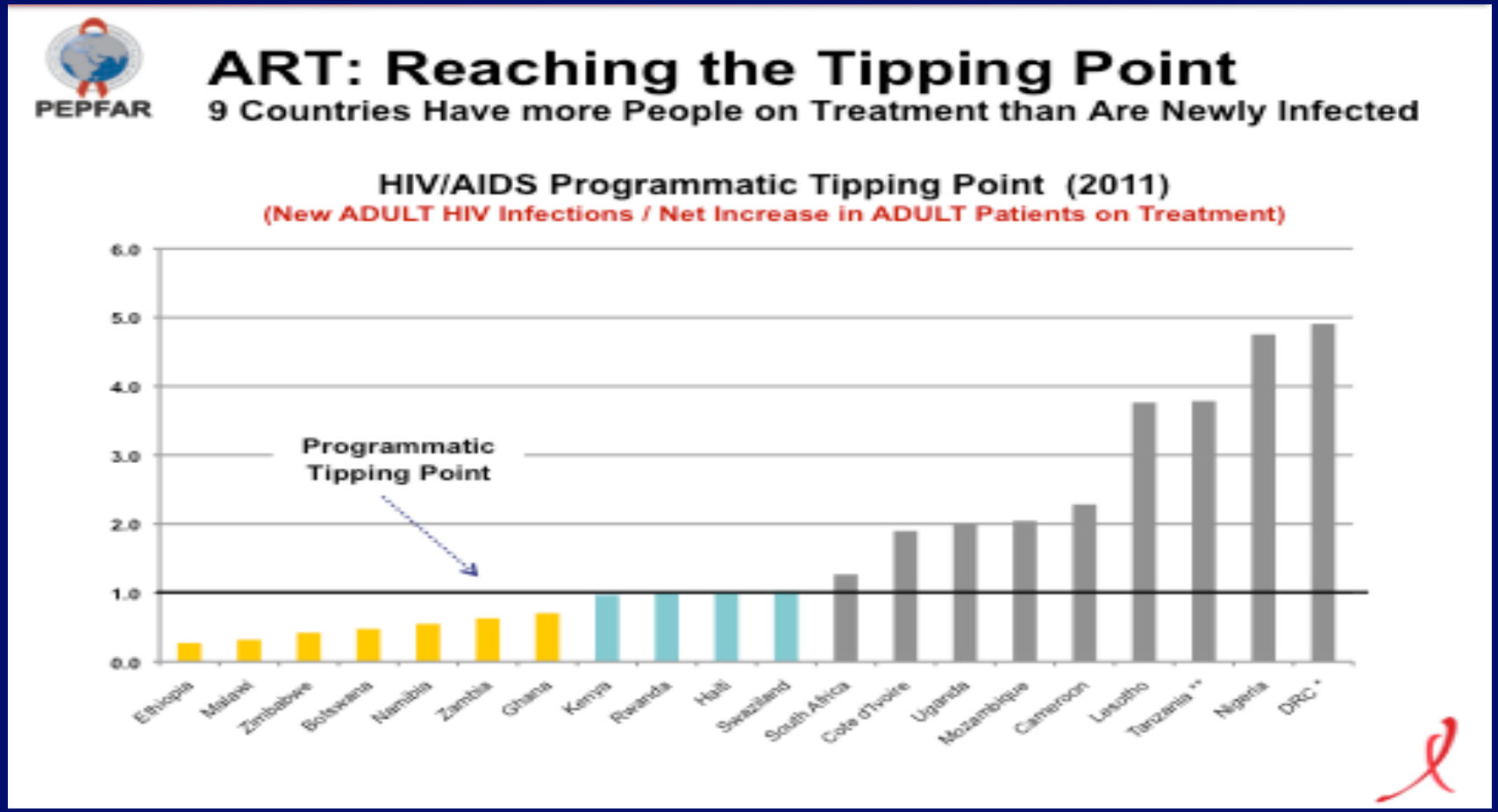






UNAIDS

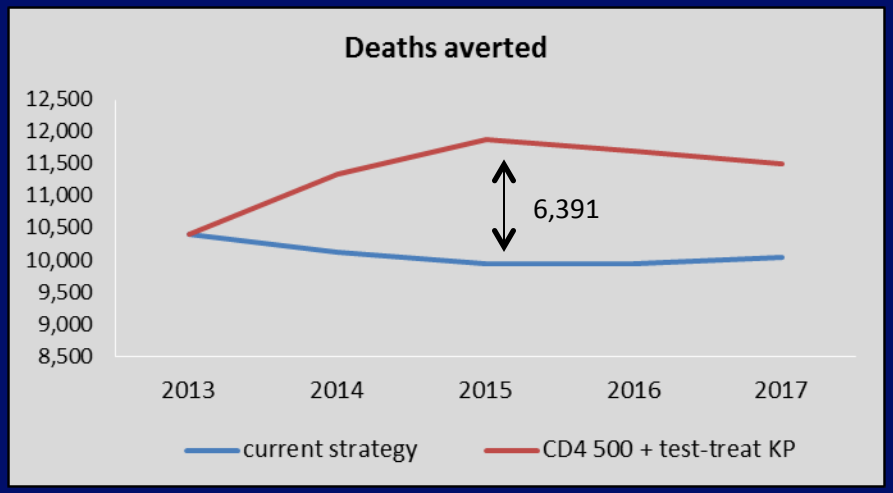
Re-think targets*: programmatic tipping point*: on treatment equals new infections

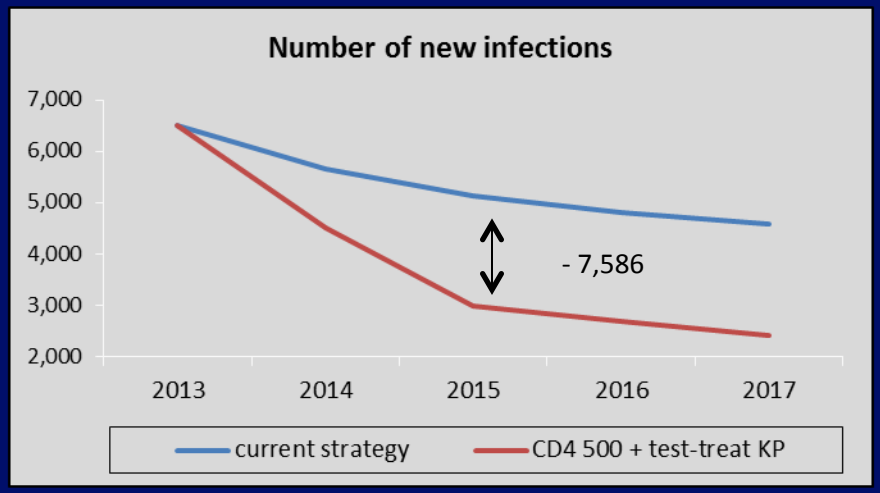


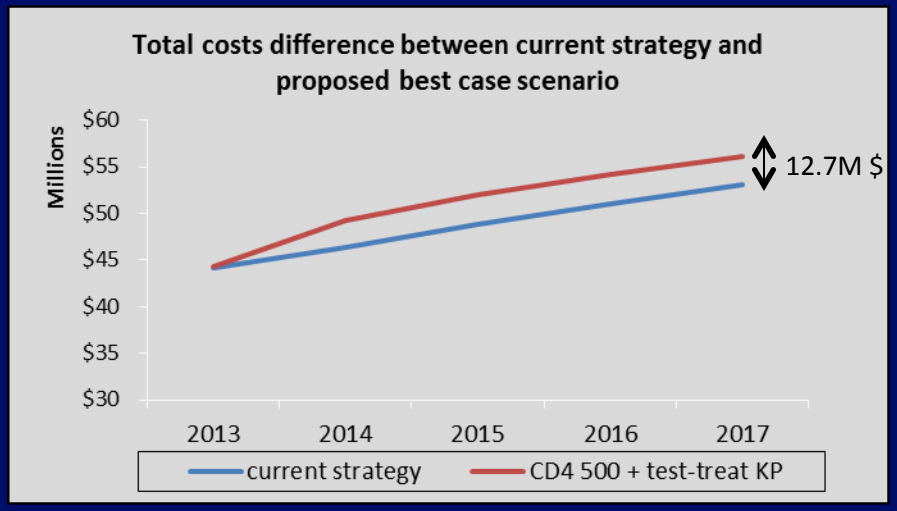
Slide courtesy of PEPFAR

Re-think when to start ART: test and treat for key populations or everyone?

Over a 5 year period, a 5.2% increase in costs* would results in 12.7% additional deaths averted and a 28.4% decrease in new infections**







Investing an additional 12.7M $ would results in

6,391 deaths averted and

7,586 fewer new infections

- Additional costs may be underestimated as current resources were assumed to be able to absorb the new ART and pre-ART patients. *
- * EPI impact calculated with Spectrum, with conservative assumptions

UNAIDS

Re-think delivery: SEARCH Uganda community trial of test and treat

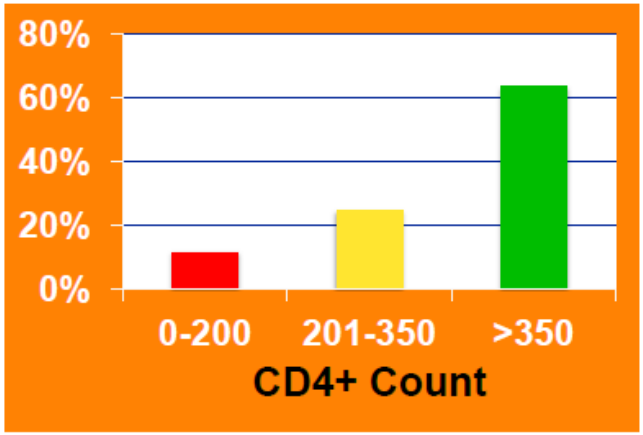
Approach: Multidisease "Community Health Campaign" HIV + other diseases

Principles:

- community led
- high throughput
- health services for children/ adults

Findings:

- Adults with HIV 8%
- Hypertension 12%
- Diabetes 3.5%

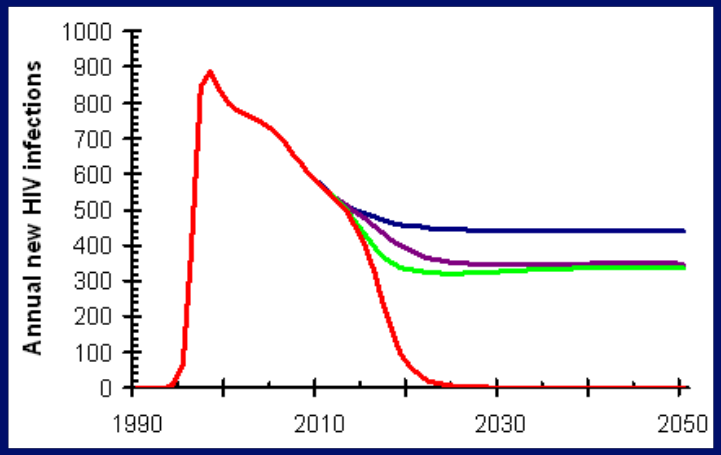


Chamie, PLOS Med, 2012

Re-think strategy for “concentrated epidemics” and key populations

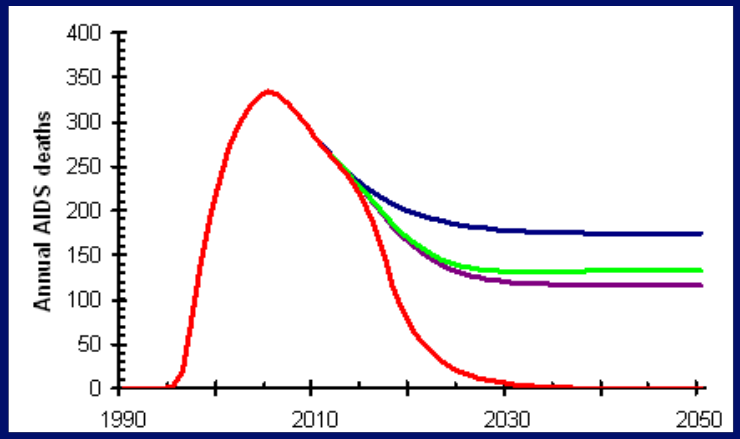
A

Annual new HIV infection



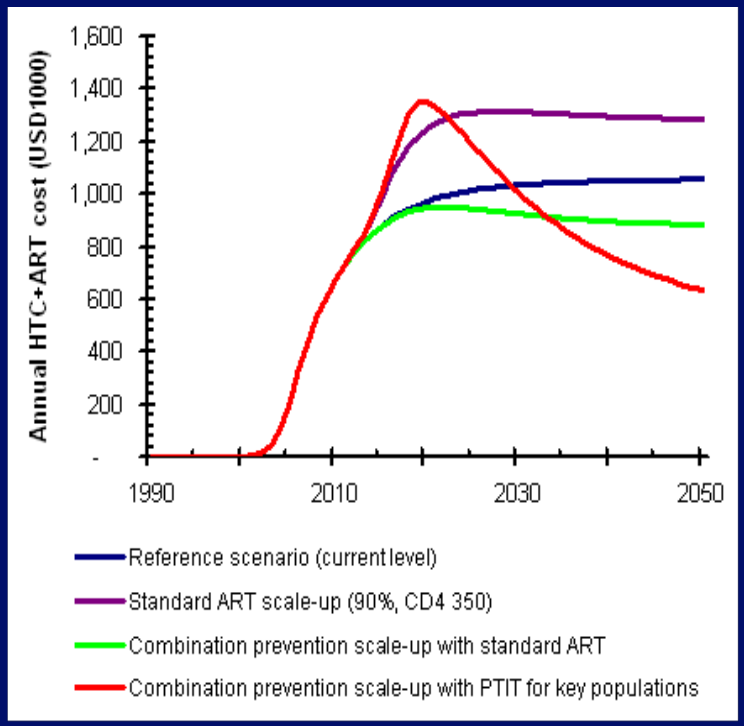
B

Annual AIDS death



C

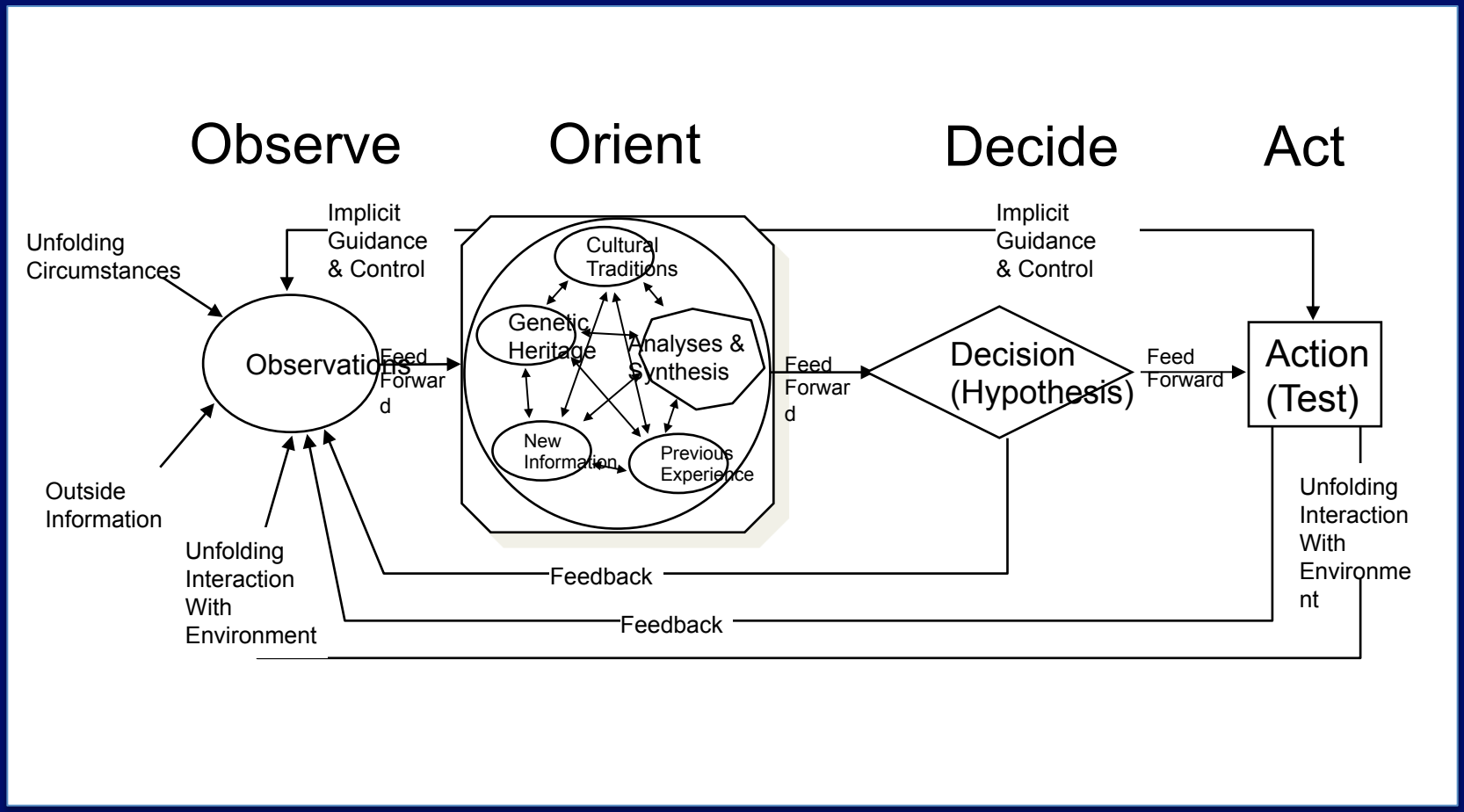
ART and HTC cost



Periodic testing and immediate treatment (PTIT)

Kato M et al . Unpublished data

Re-think M and E strategy: the OODA Loop



Speed matters…and our feedback loop is slow

Fail fast vs. global consensus

UNAIDS

Conclusion

- Prevention matters—combination will be required
- Treatment prevents illness, death, transmission
- Global testing and treatment scale-up plan with practical measurable milestones (think end game)
- Speed—slow scale up is not an option for millions, remove complexity and barriers to access
- Innovation—community delivery, consider standardized franchise model
- People first, community engagement

Public health is purchasable. Within a few natural and important limitations any community can determine its own health.

--Hermann M. Biggs

(29 Sep 1859 - 28 Jun 1923)
New York City's Public Health Officer and public health pioneer

Policy matters

PARTNERS Study: CROI 2014

Press conference at CROI 2014.

Photo by Liz Highleyman, hivandhepatitis.com.

- 16,400 occasions of sex in the gay men and 28,000 in the heterosexuals
- Zero transmissions within couples from a partner with an undetectable viral load
- Upper bounds of confidence intervals suggest that risk is not zero

Rodger A et al. *HIV transmission risk through condomless sex I f HIV+ partner on suppressive ART: PARTNER study.* 21st CROI, Boston, abstract 153LB, 2014.

Significantly higher employment at CD4≥500 among adults

- Compared to CD4<200, CD4≥500 associated with
  - 5.8 more days/month
  - 2.2 more hours/day (40% more than ref. mean of 5.5)

Regression model coefficients		
	(1)	(2)
Outcome:	Days worked in the past month	Hours worked on usual day in past
CD4<200	Reference	Reference
CD4 200-349	2.7	1.8
CD4 350-499	4.8	0.9
CD4 ≥500	5.8**	2.2*
Observations	107	107

- Linear regression model with age, age-squared, and sex included as controls
- ** p<0.05, * p<0.10
- Reference group has CD4<200

Those with CD4≥500 worked nearly 1 week/month more than those with CD4<200, and as much as HIV-uninfected adults

Thirurmurthy, Health Affairs, 2012

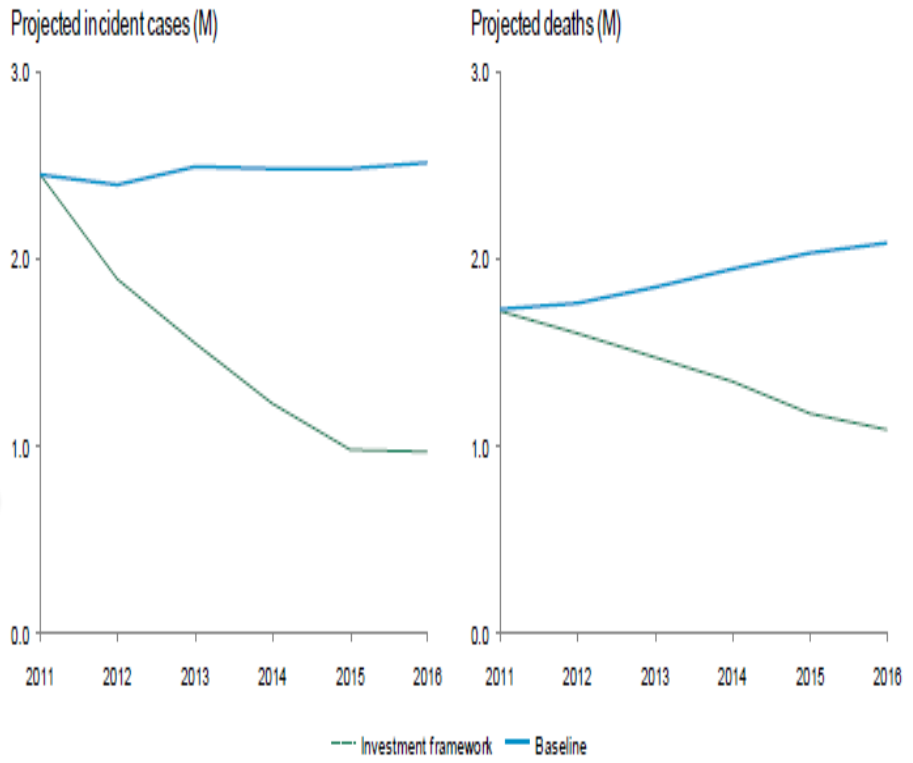
The Global Fund
To Fight AIDS, Tuberculosis and Malaria

REVIEW OF HIV/AIDS, TUBERCULOSIS AND MALARIA LANDSCAPE FOR THE GLOBAL FUND STRATEGY 2012-2016

Exhibit 5: HIV/AIDS – Likelihood and impact of new interventions[12]

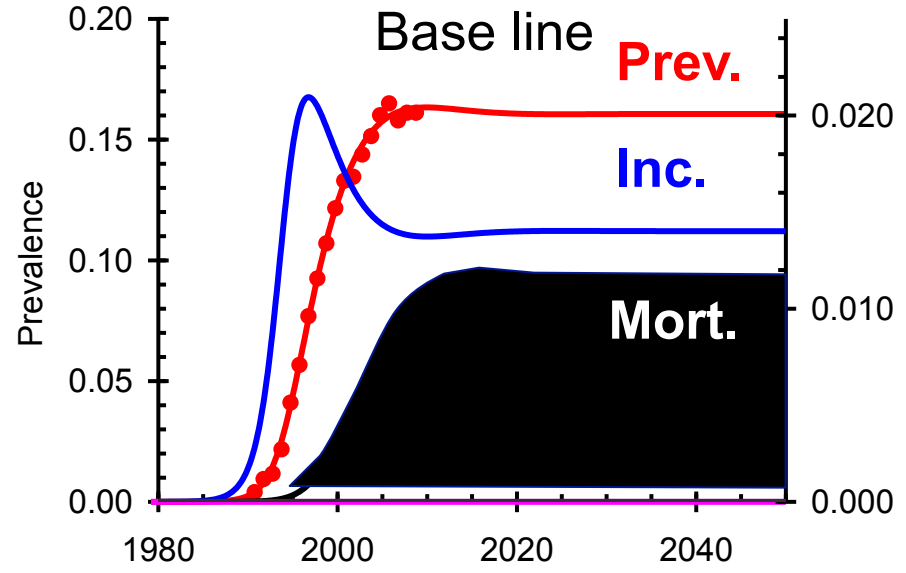
Type	Existing	Anticipated	Timing	Likelihood	Impact
Vaccine	N/A	RV144, HVTN 505	2020+		
Prevention	Condoms, Male Circumcision	Treatment as Prevention (discordant couples)	2011		
		Oral PReP (for MSMs)	2011		
		Male circumcision devices	2012		
Treatments	ARV	Treatment. 2.0	2011		
Diagnostics	CD4, viral load	Point of care	2011		
		Couples testing	2011		

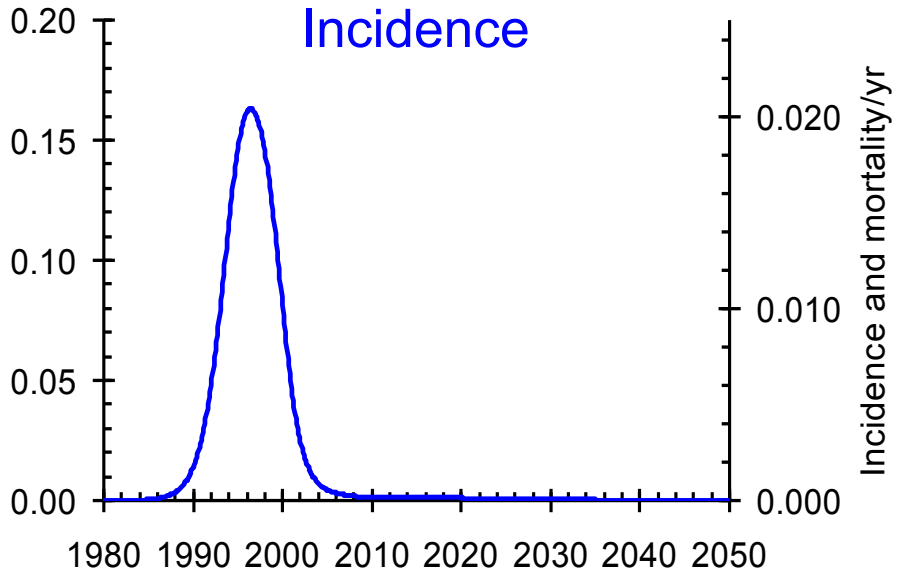
Exhibit 3: *HIV/AIDS – Projected incidence and deaths (2011-2016)*[6]

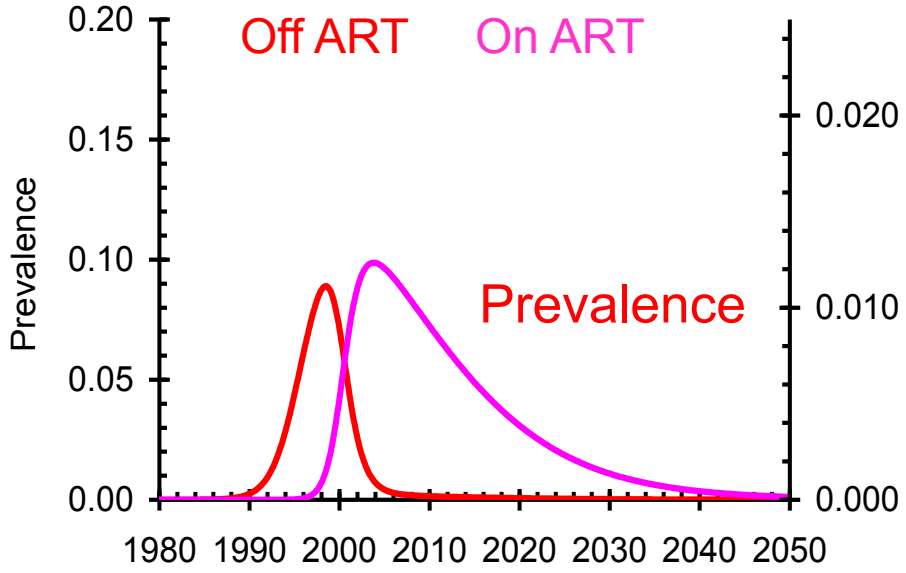


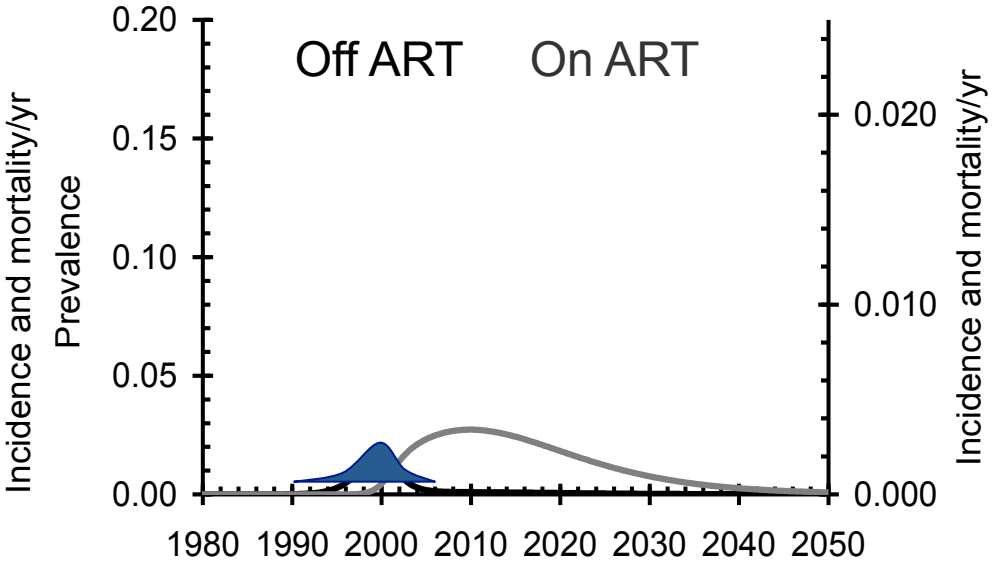
Global Fund website http://www.theglobalfund.org/en/about/strategy/ accessed September 19th 2013

Accountability and the dreaded retrospectoscope









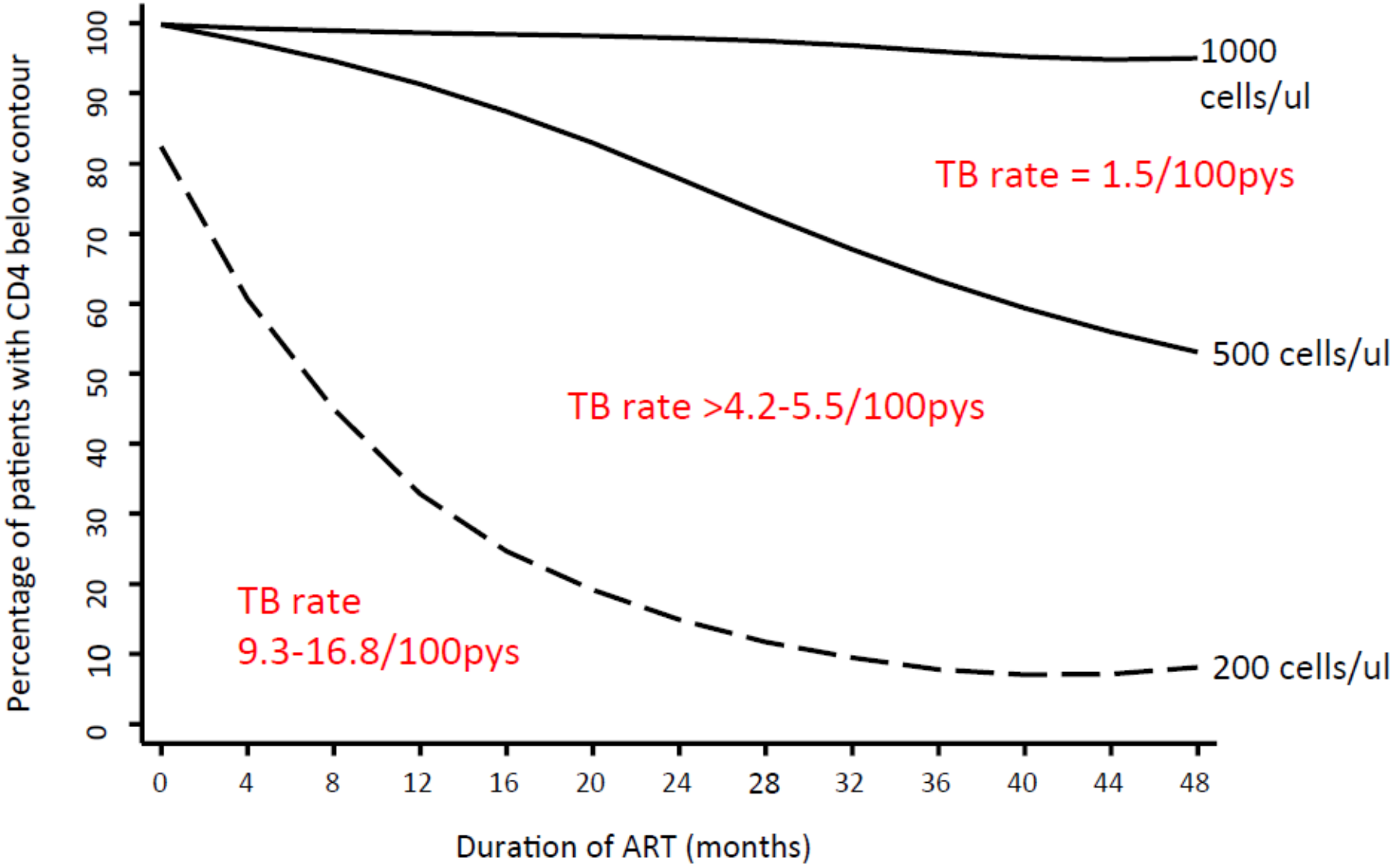
HIV in South Africa: test and treat starting in 1995

Williams 2010

HIV control: challenges

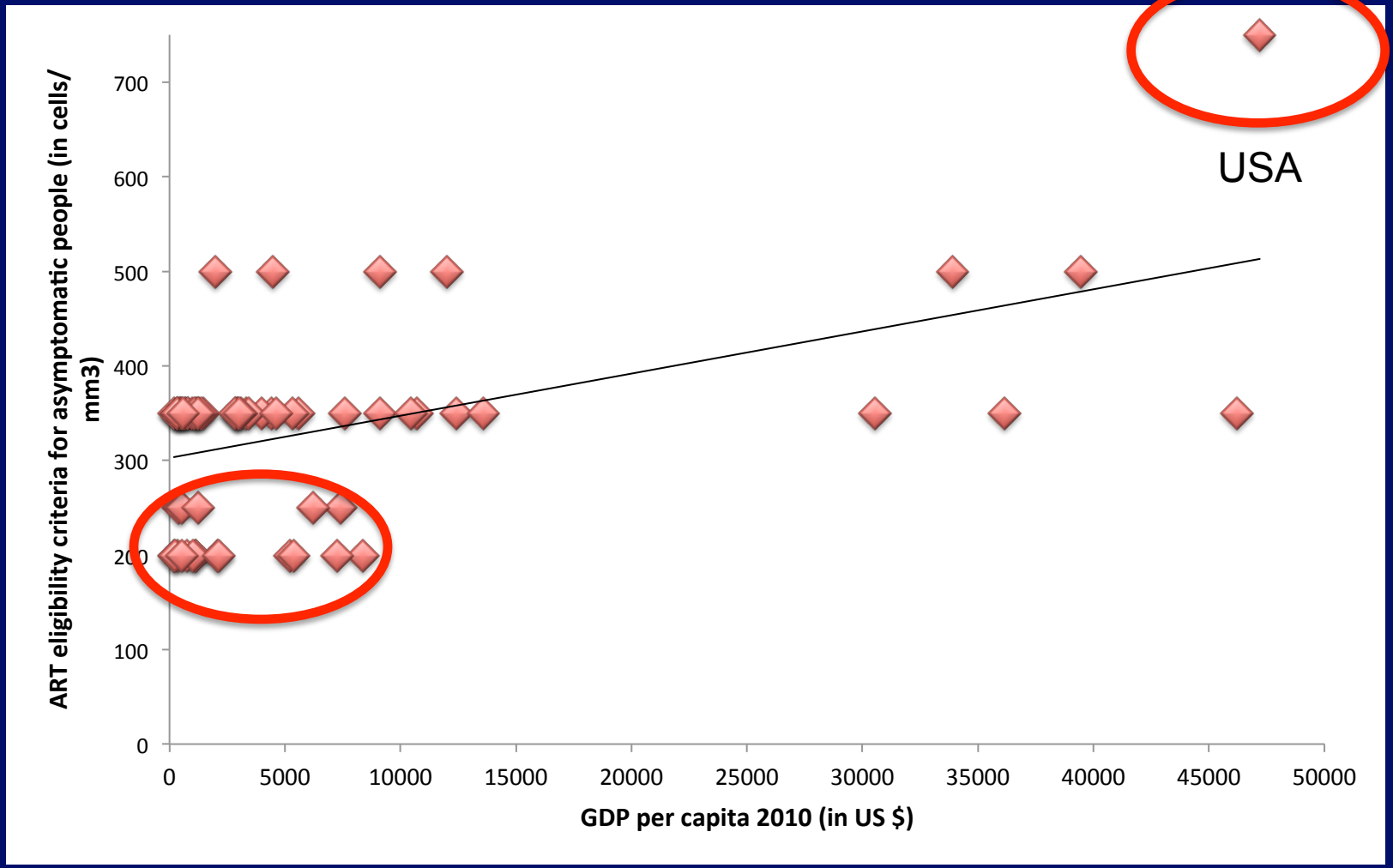
- Political will—leadership and funding
  - "Coordination"—simplify current complexity
- Scale-up plan with practical measurable milestones
- Focus—prioritize interventions, geography/people
- Speed—slow scale up is not an option for millions
- Innovation—private sector, community delivery, franchise model
- Delivery—standardized approach, clear practical guidelines, people first, community engagement
- Robust supply chain, simplify commodities
- Better M and E and surveillance

CD4 Count Profile of Cohort and TB Risk



Slide courtesy of Steve Lawn

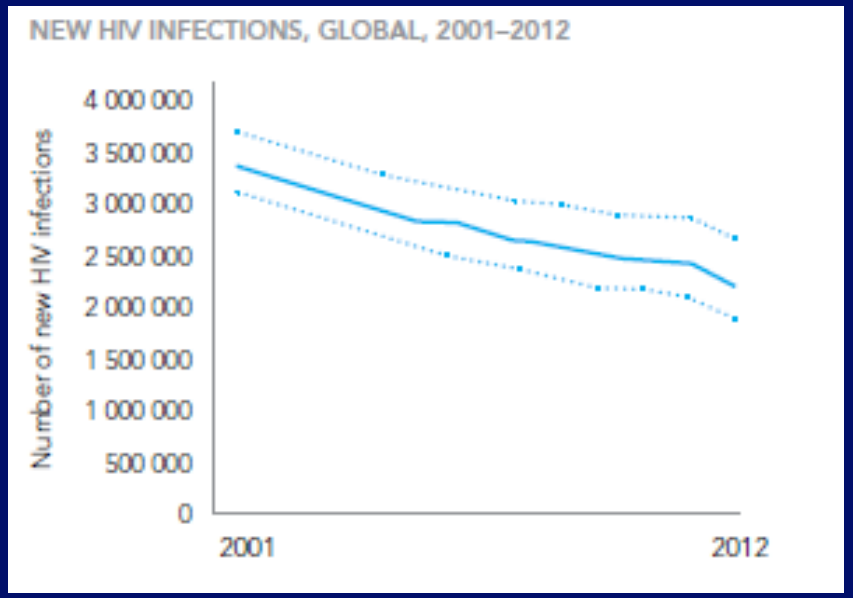
2010 GDP per capita and ART eligibility for asymptomatic people living with HIV



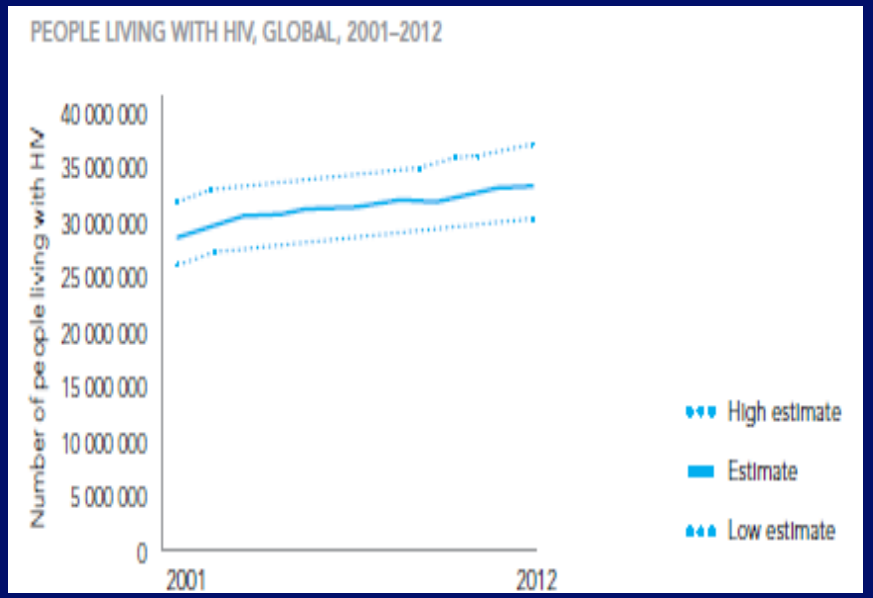
Positive but low correlation between GDP per capita and ART eligibility criteria for asymptomatic people

World Health Organization

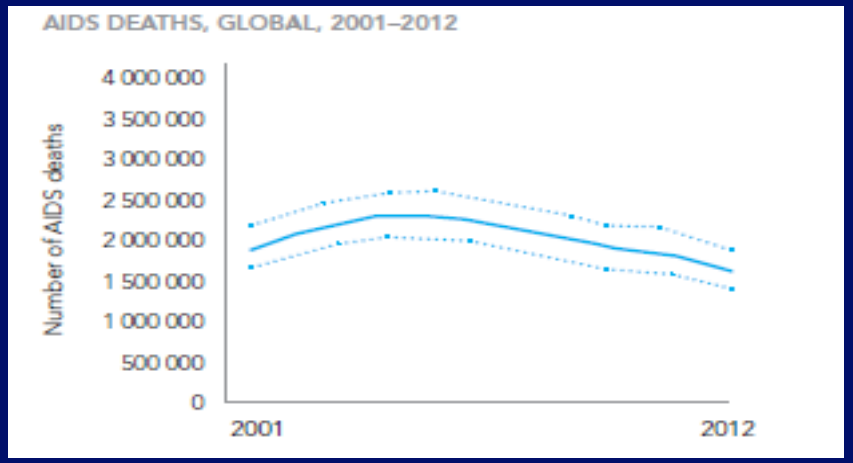
Numbers of people living with HIV, new HIV infections, and AIDS deaths, 2001-2012



New infections

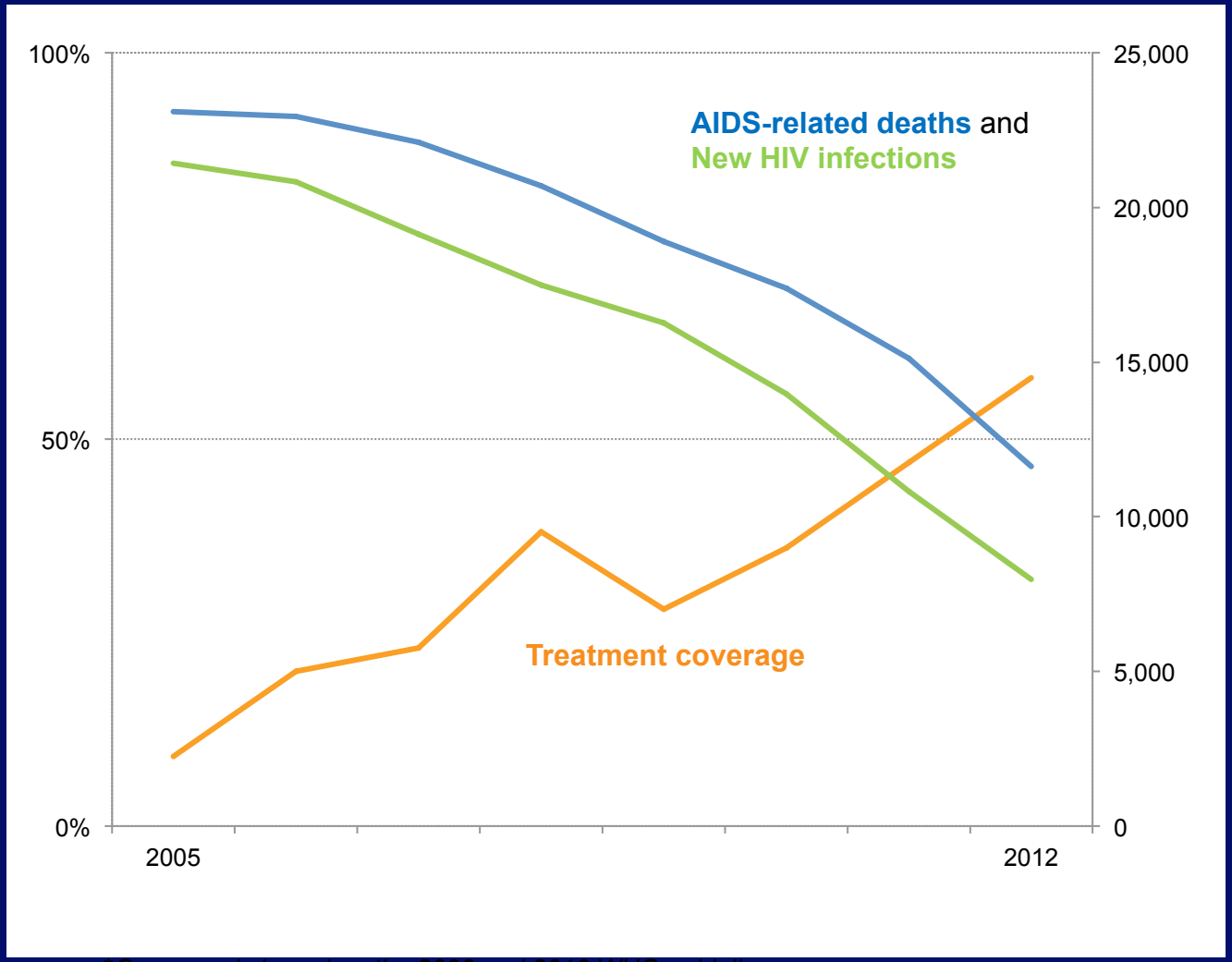


People living with HIV



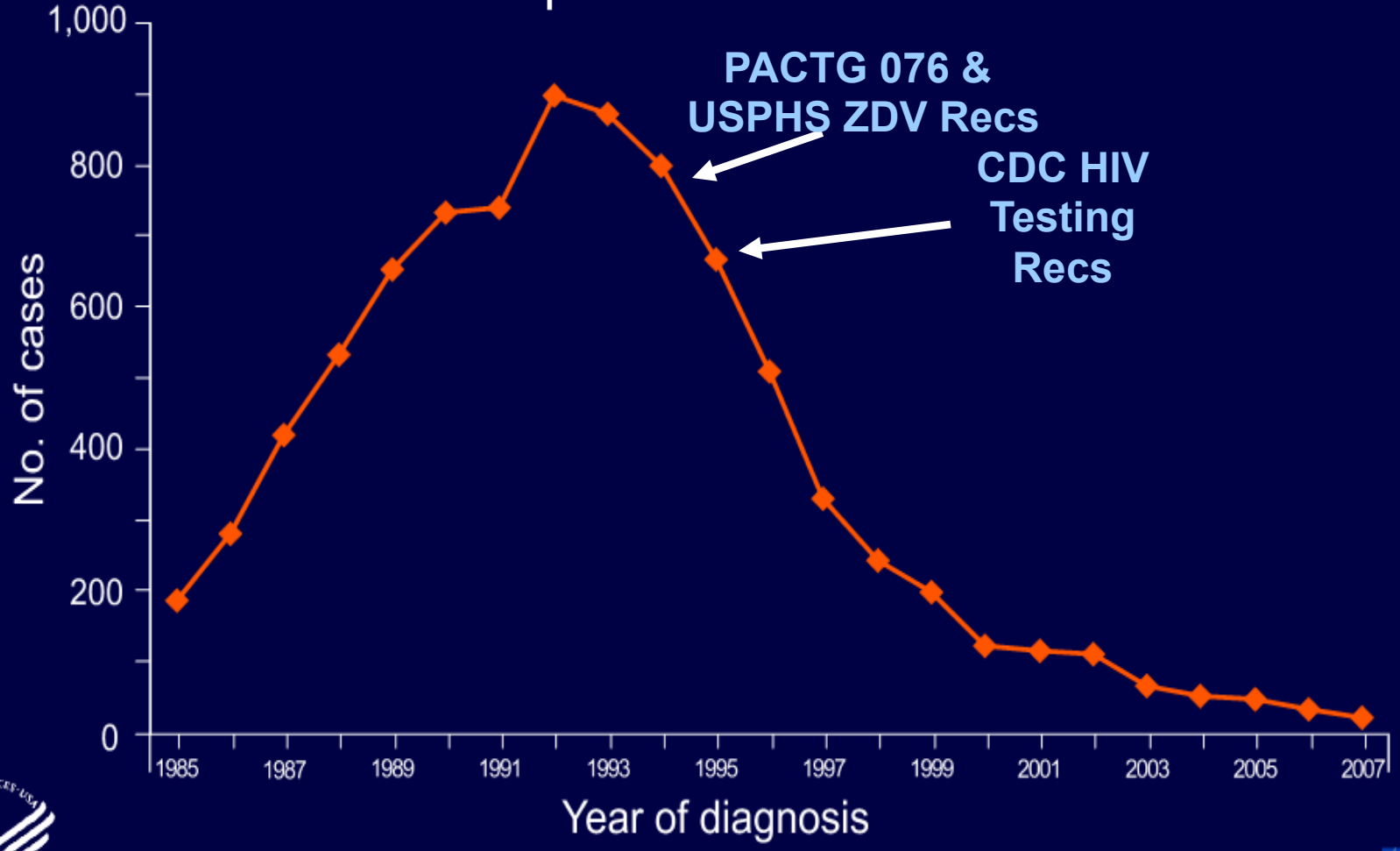
Deaths

Ghana: As HIV treatment coverage rose, new HIV infections and AIDS-related deaths fell, 2005-2012



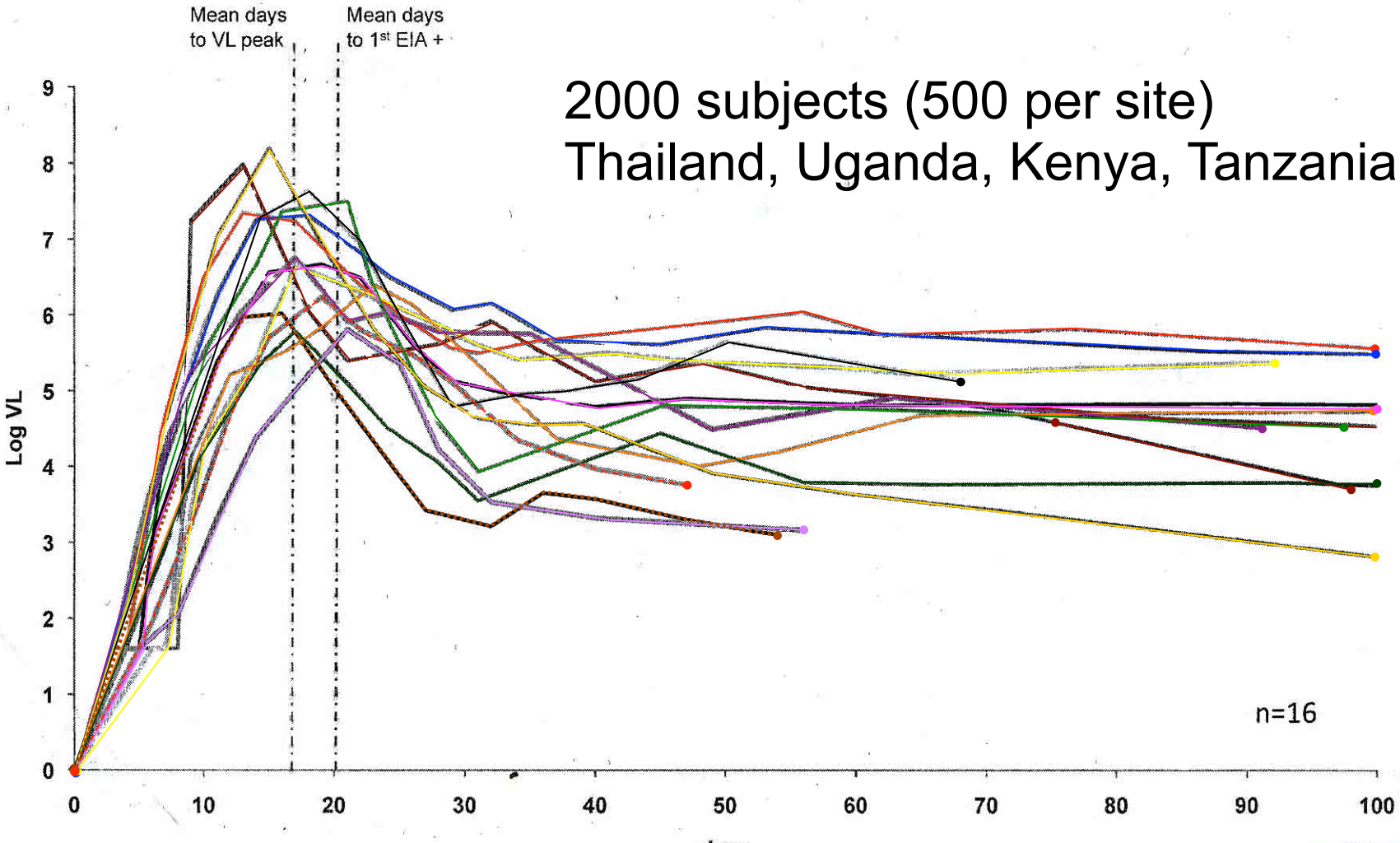
*Coverage is based on the 2006 and 2010 WHO guidelines

Estimated Numbers of Perinatally Acquired AIDS Cases by Year of Diagnosis, 1985–2007—United States and Dependent Areas



Note. Data have been adjusted for reporting delays and missing risk-factor information.

Aggregate Priority 1 Viral Loads- 1st 100 days

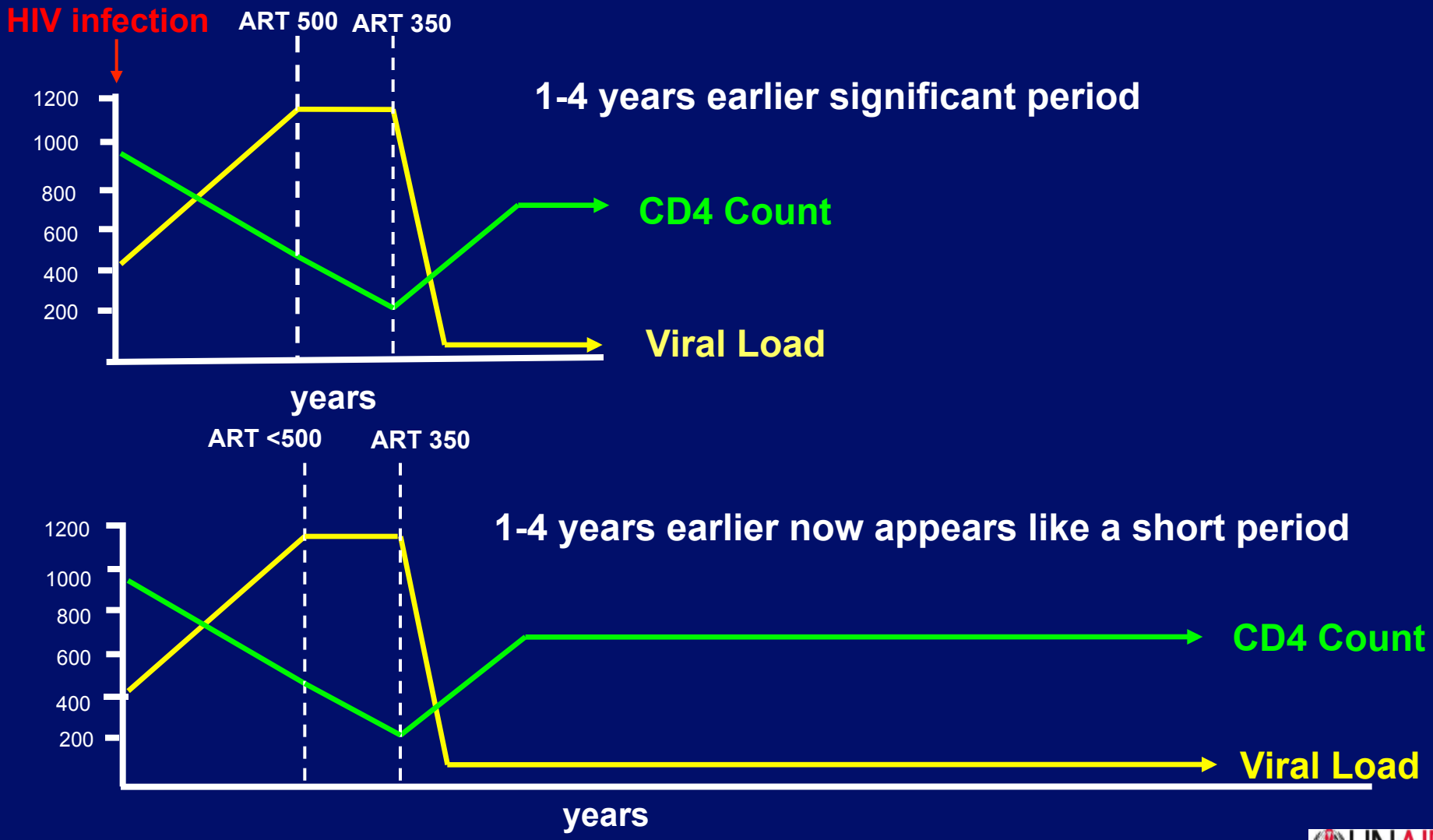


2000 subjects (500 per site)
Thailand, Uganda, Kenya, Tanzania

Mean # timepoints before peak = 4 (range: 3-6)
Mean # timepoints after peak = 8 (range: 6-11)

Robb ML. AIDS Vaccine 2012 Conference; 2012

When to start ART?
A matter of perspective



Slide adapted from Julio Montaner

UNAIDS

When to start?

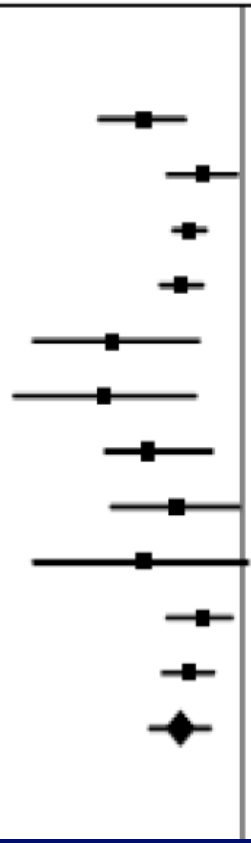
- **Advantages**:
  - Reduces mortality and extends lifespan
  - Prevents AIDS-related events and OIs
  - Reduces non-AIDS related events
  - Improves immune function
  - Reduces transmission
- **Disadvantages**:
  - Does not cure HIV
  - Side effects and toxicity
  - Pill burden/quality of life
  - Lifelong adherence
  - Resistance may develop
  - Cost ($$) – for drugs and for monitoring

Slide courtesy of D. Riedel

Morbidity prevention: Providing ART decreases the risk of TB by 65% across all CD4 levels

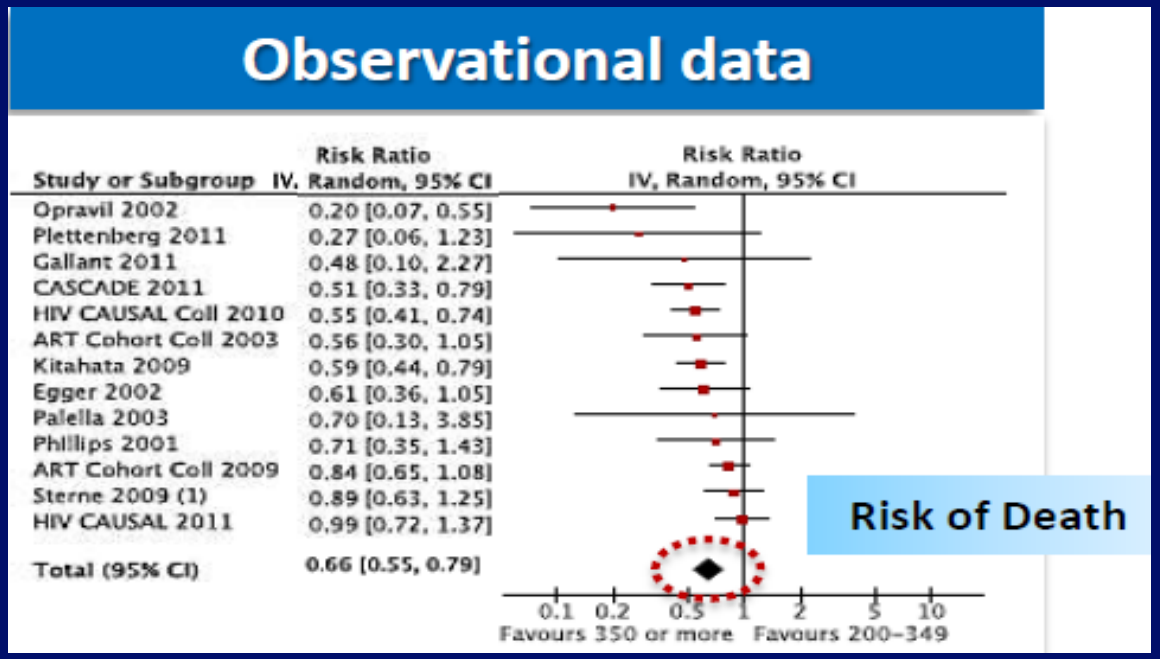
	ART		Control		IRR (95% CI)
	TB cases	PY at risk	TB cases	PY at risk	
All baseline CD4 counts					
Badri (2002)	9	375.1	82	848.2	0.19 (0.09 - 0.38)
Cohen (2011)	17	1661.9	33	1641.8	0.51 (0.28 - 0.91)
Golub (2007)	221	11627	155	3865	0.41 (0.31 - 0.54)
Golub (2009)	44	952	200	2815	0.36 (0.25 - 0.51)
Jerene (2006)	6	162.6	9	80.9	0.11 (0.03 - 0.48)
Lannoy (2008)	-	-	-	-	0.10 (0.02 - 0.45)
Miranda (2007)	-	-	-	-	0.20 (0.10 - 0.60)
Samandari (2011)	-	-	-	-	0.33 (0.11 - 0.94)
Santoro-Lopes (2002)	1	-	42	-	0.19 (0.03 - 1.09)
Severe (2010)	18	-	36	-	0.50 (0.28 - 0.83)
Zhou (2009)	57	5186	40	985	0.40 (0.26 - 0.61)
All studies					**0.35 (0.28 - 0.44)**

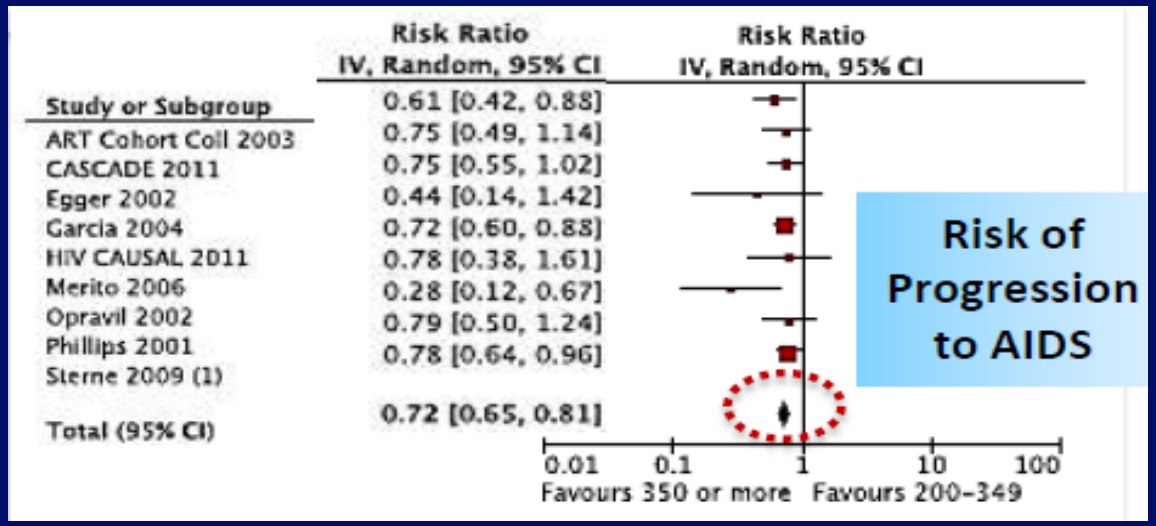
Effect: Z = 9.19, p < 0.001; Heterogeneity: I^2 = 31% (22% - 44%) , p = 0.151



Suthar et al 2012 ,Plos Med

When to start ART….or how late is too late?





KL 2013 Critical issues for Adults with HIV: Presentation of Systematic reviews and Main recommendations. Doherty. WHO 2013 ARV Guidelines Launch

When to start?

- **Advantages**:
  - Reduces mortality and extends lifespan
  - Prevents AIDS-related events and OIs
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  - Reduces transmission
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  - Does not cure HIV
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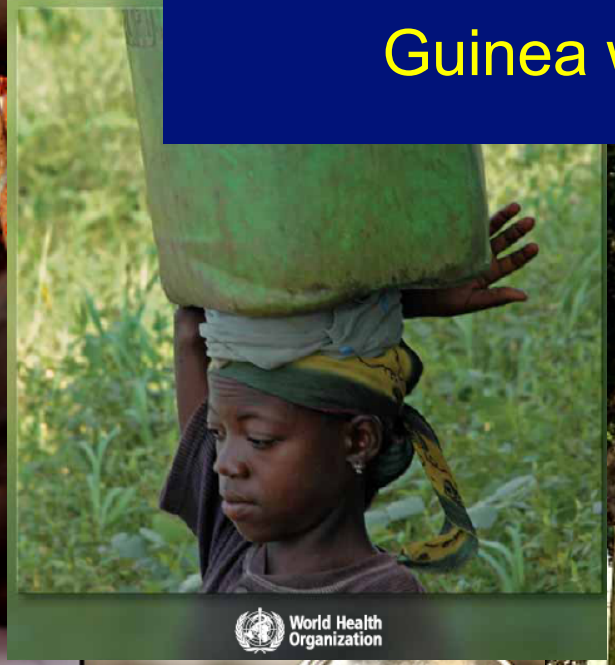
  - Lifelong adherence
  - Resistance may develop
  - Cost ($$) – for drugs and for monitoring

Slide courtesy of D. Riedel

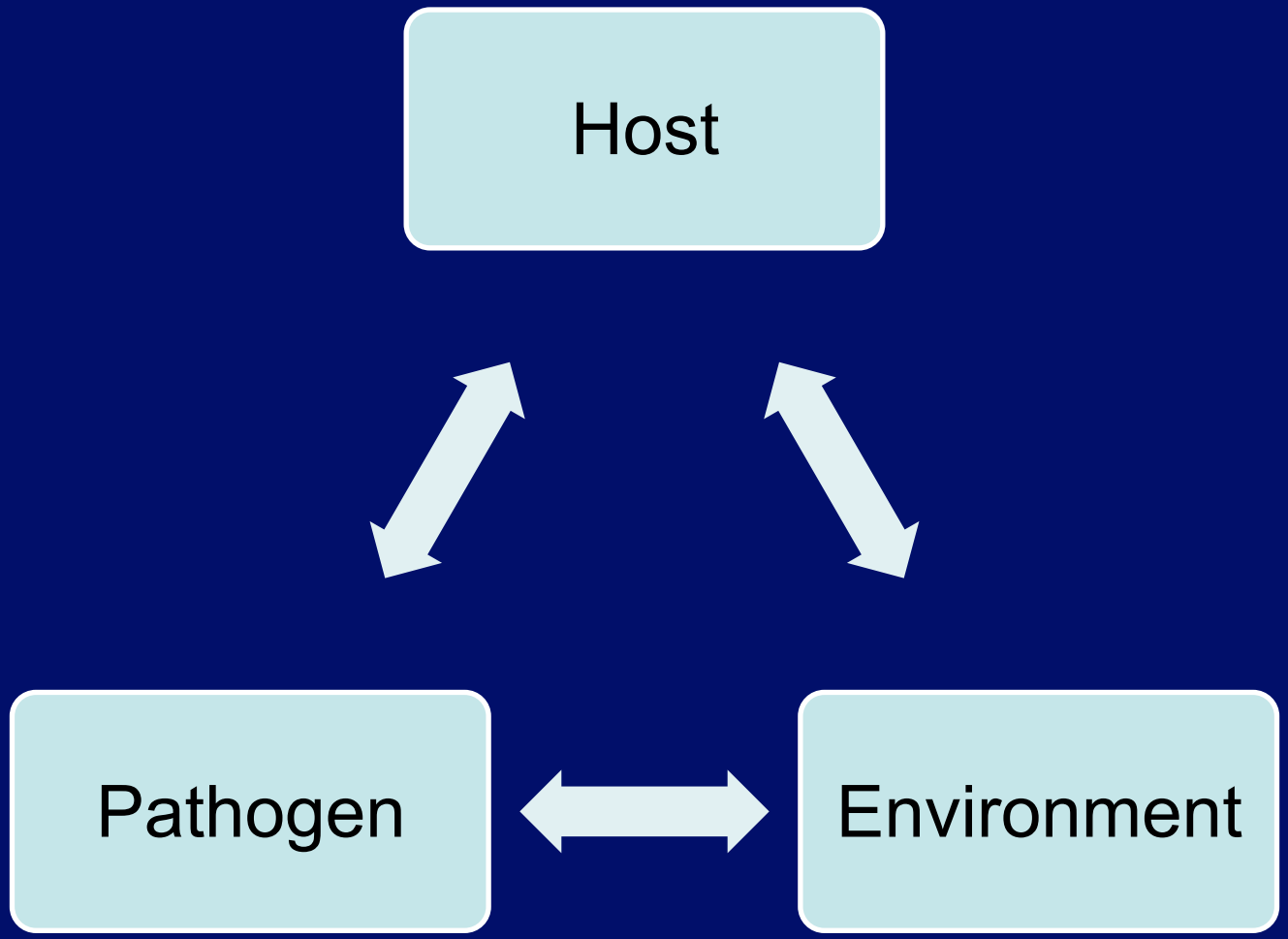
Guinea worm eradication



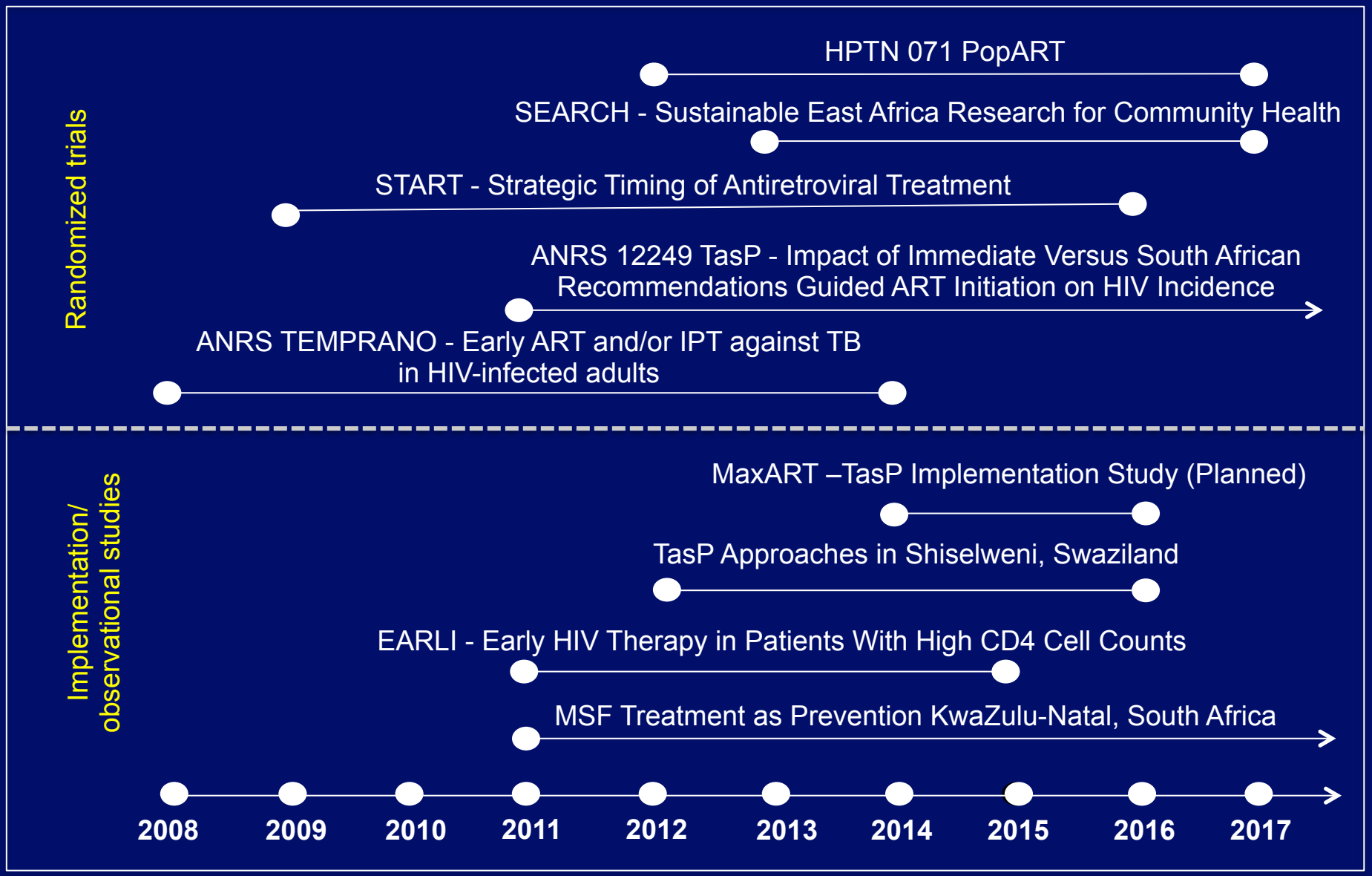
Preventable blindness

UNAIDS

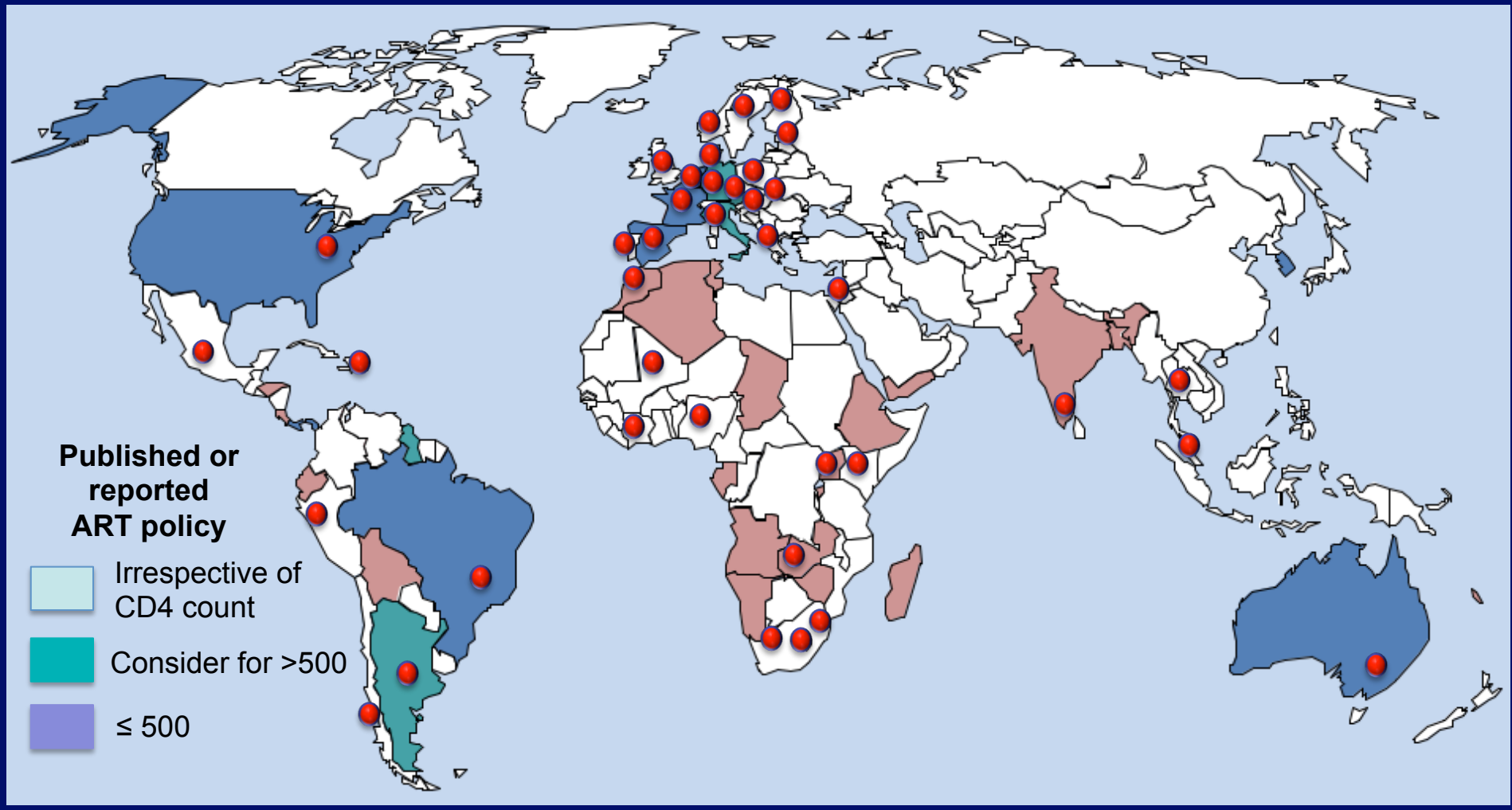
ART addresses all parts of classic infectious disease triangle



Timeline on projects with early ART (≥500)



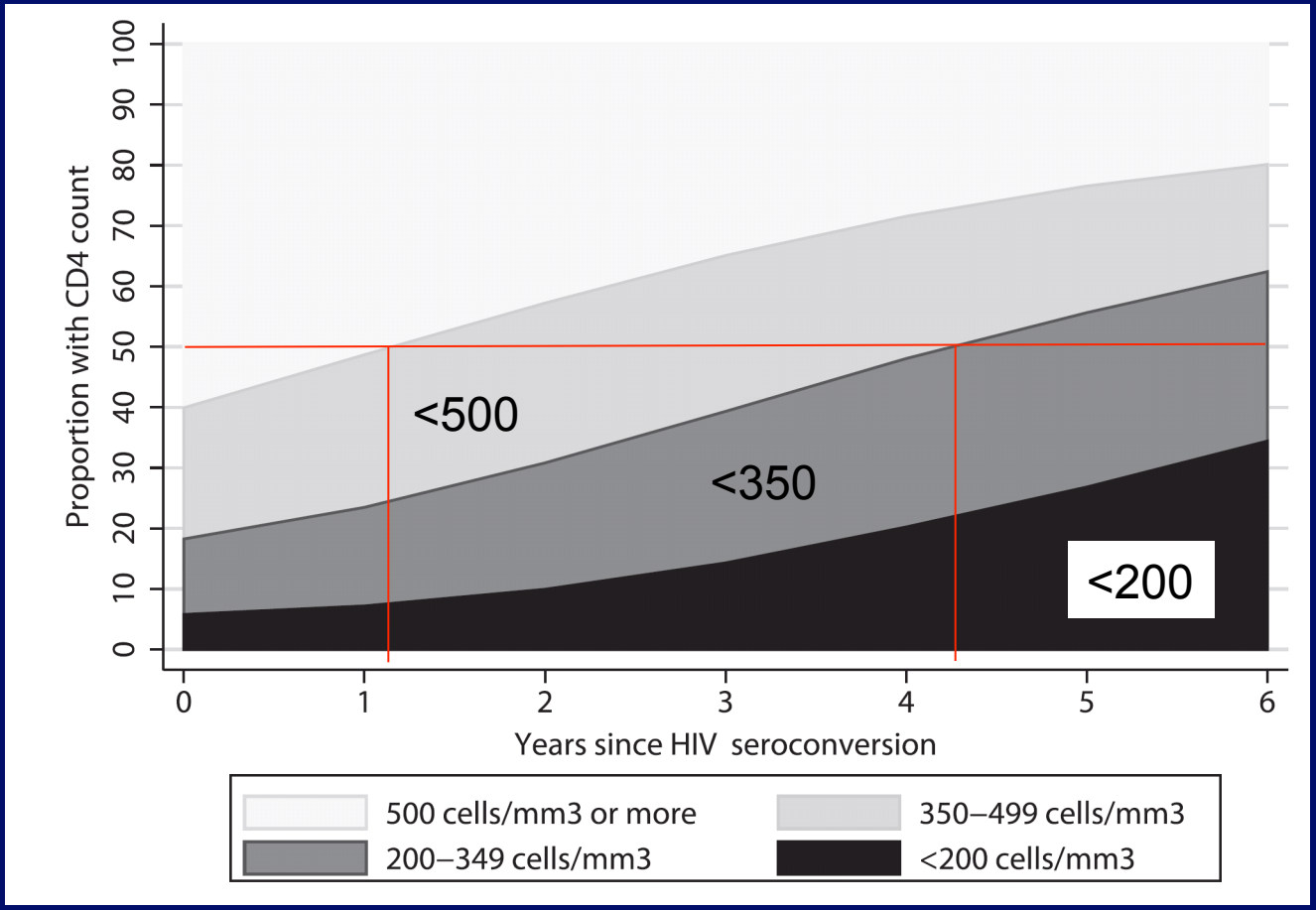
Countries with studies on early ART (≥ 500)



Red dots represent the countries with research on early ART

UNAIDS

Time from HIV seroconversion to CD4 <500 is median of 1.2 years

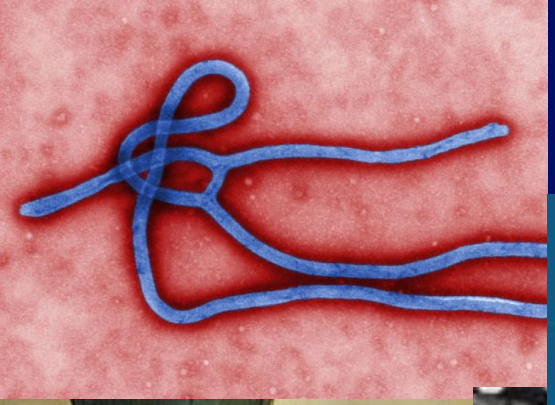


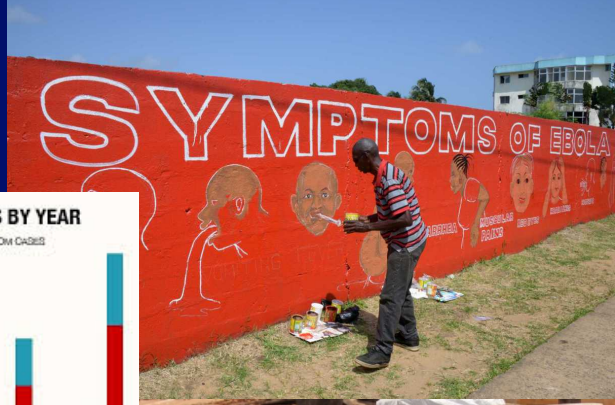
Median year (95% CI):
< 500: 1.19 (1.12-1.26)
<350: 4.19 (4.09-4.28)
<200 : 7.93 (7.76-8.09)

CASCADE: Lodi *et al*, CID 2011

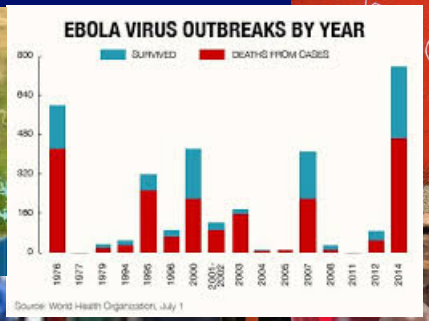
UNAIDS

Ebola




SYMPTOMS OF EBOLA

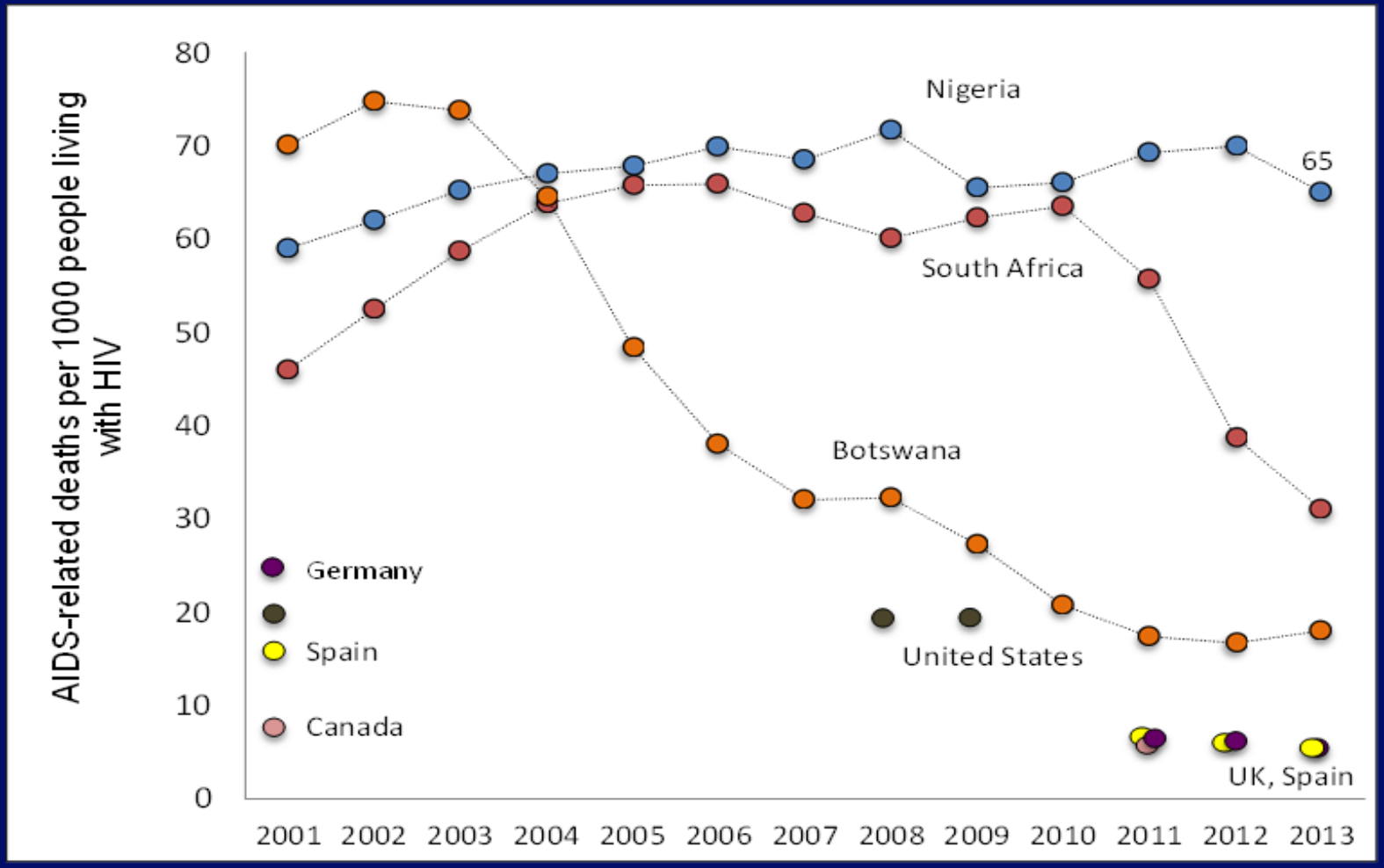

SENEGAL
MALI
GUINEA-BISSAU
GUINEA
Conakry
Dabakedou
SIERRA LEONE
IVORY COAST
LIBERIA


EBOLA VIRUS OUTBREAKS BY YEAR
SURVIVED
DEATHS FROM CASES
800
640
480
320
160
0
1976
1977
1979
1994
1995
1996
2000
2001
2002
2003
2004
2005
2007
2008
2011
2012
2014
Source: World Health Organization, July 1

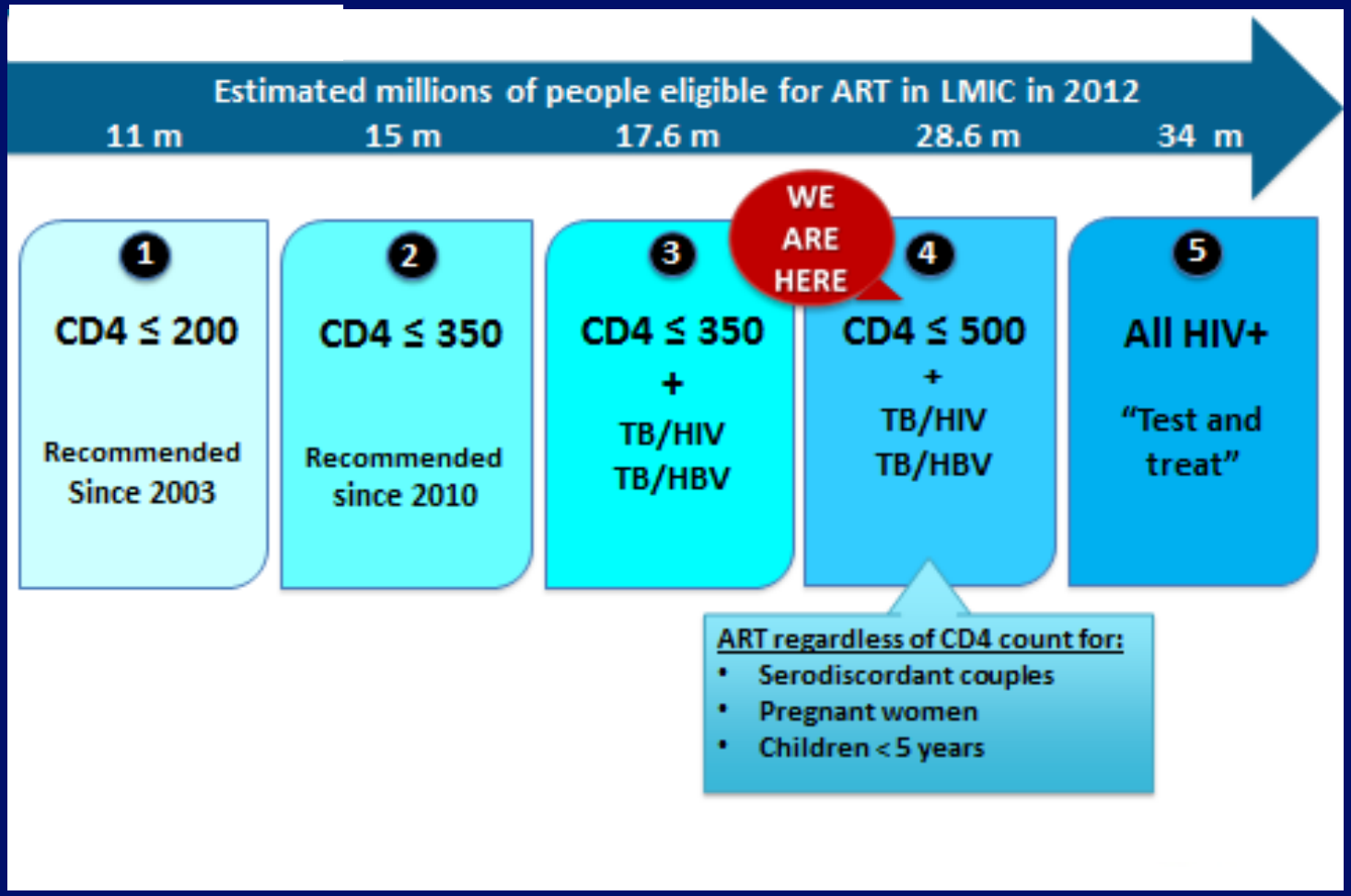

CONSULTATION ROOM


GUINEA
319
Deaths
SIERRA
LEONE
224
Deaths
LIBERIA
129

Estimated annual AIDS deaths per 1000 people living with HIV

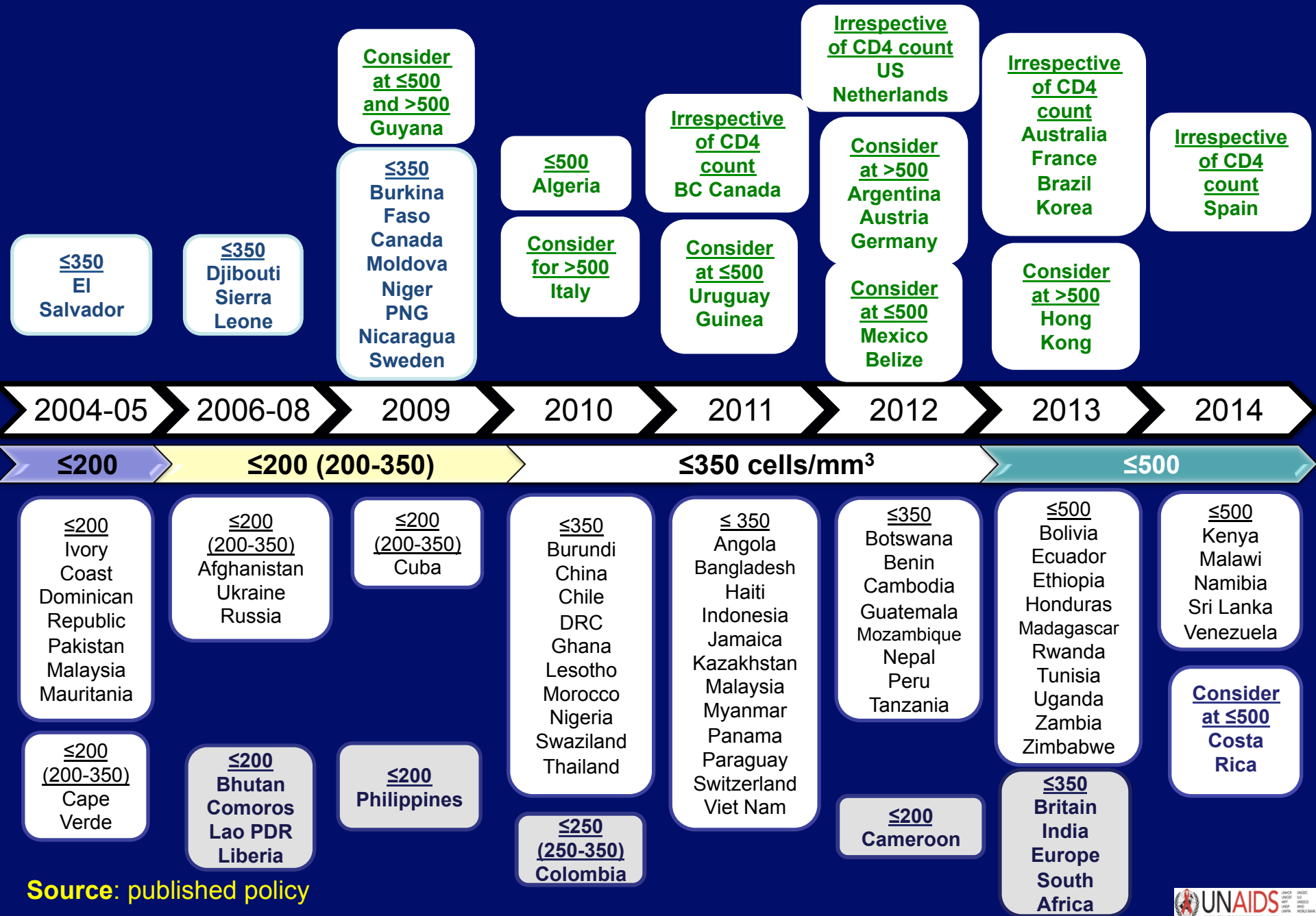


Scenarios of ARV eligibility: WHO vision



Source: WHO 2014

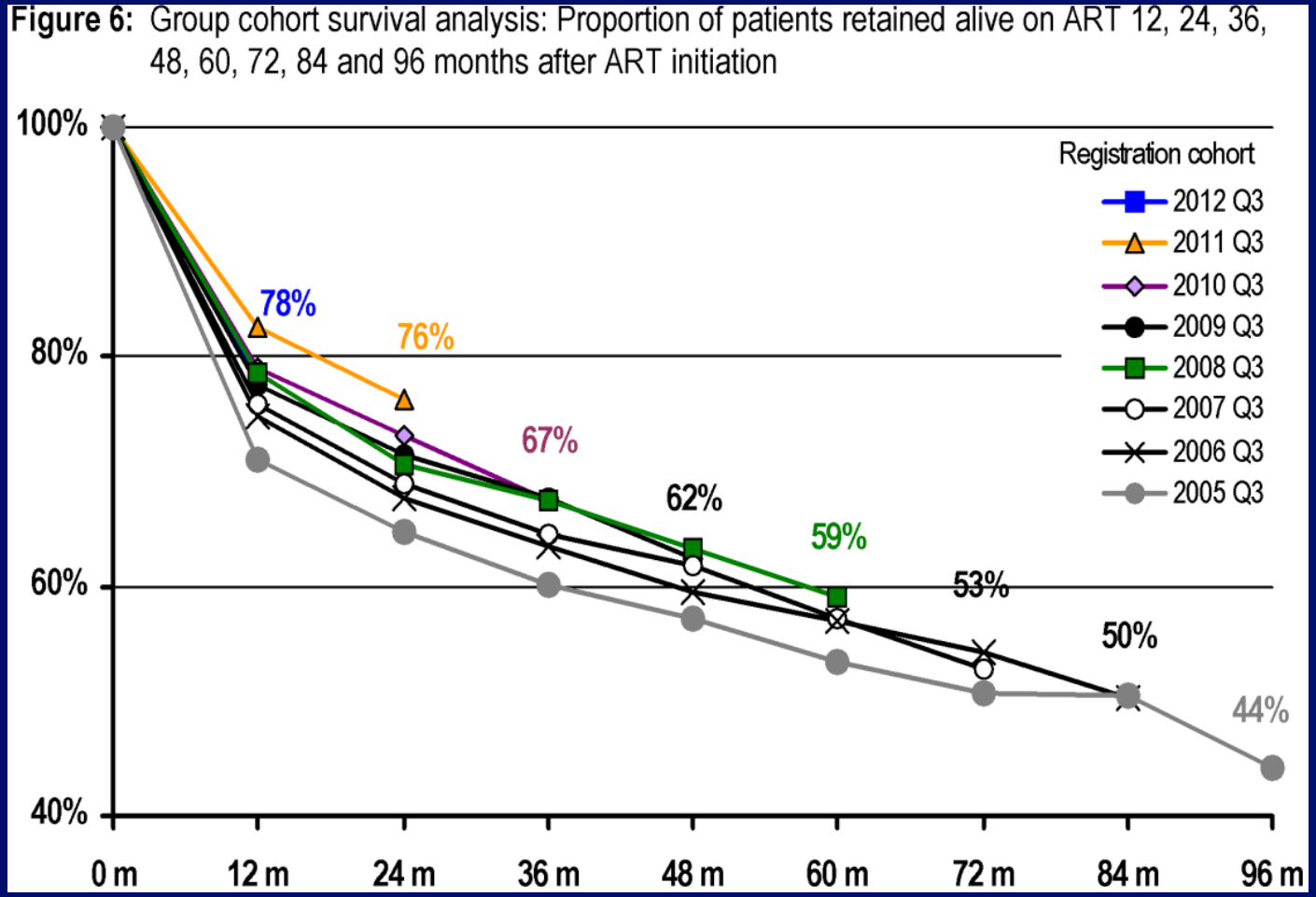
Early ART for asymptomatic people living with HIV



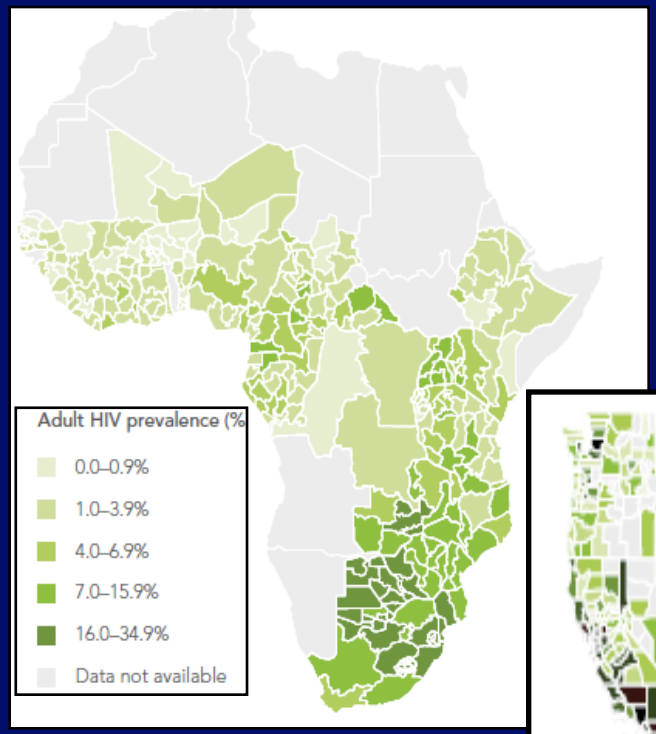
Source: published policy

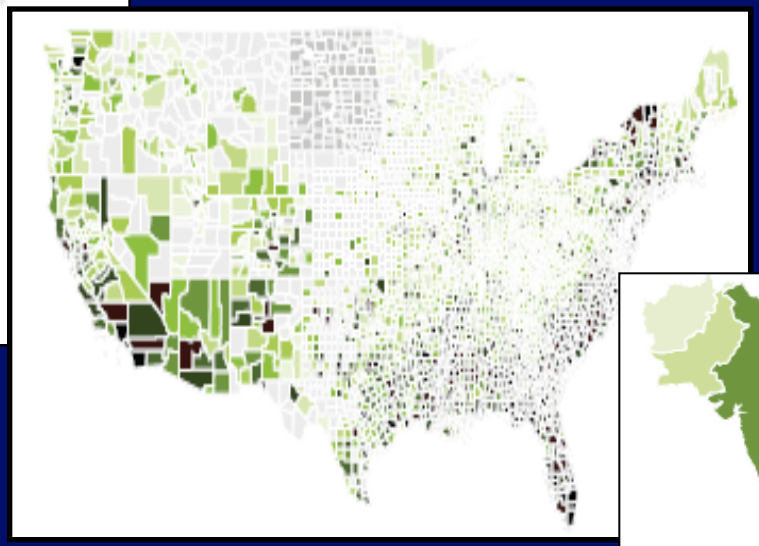
UNAIDS

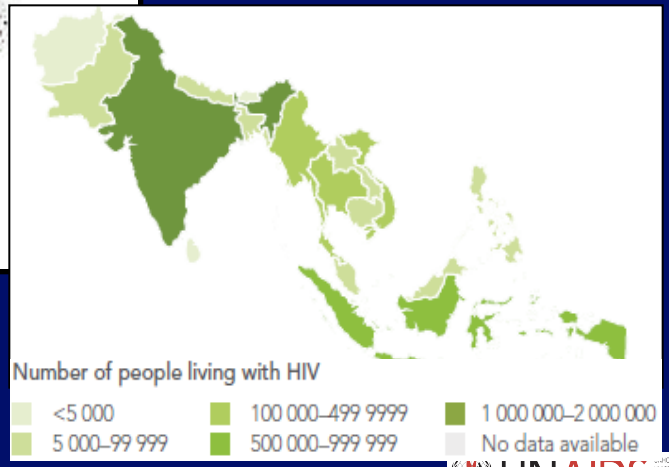
Malawi: each cohort is doing better than the last



Mapping local epidemiology, interventions and financing to monitor impact

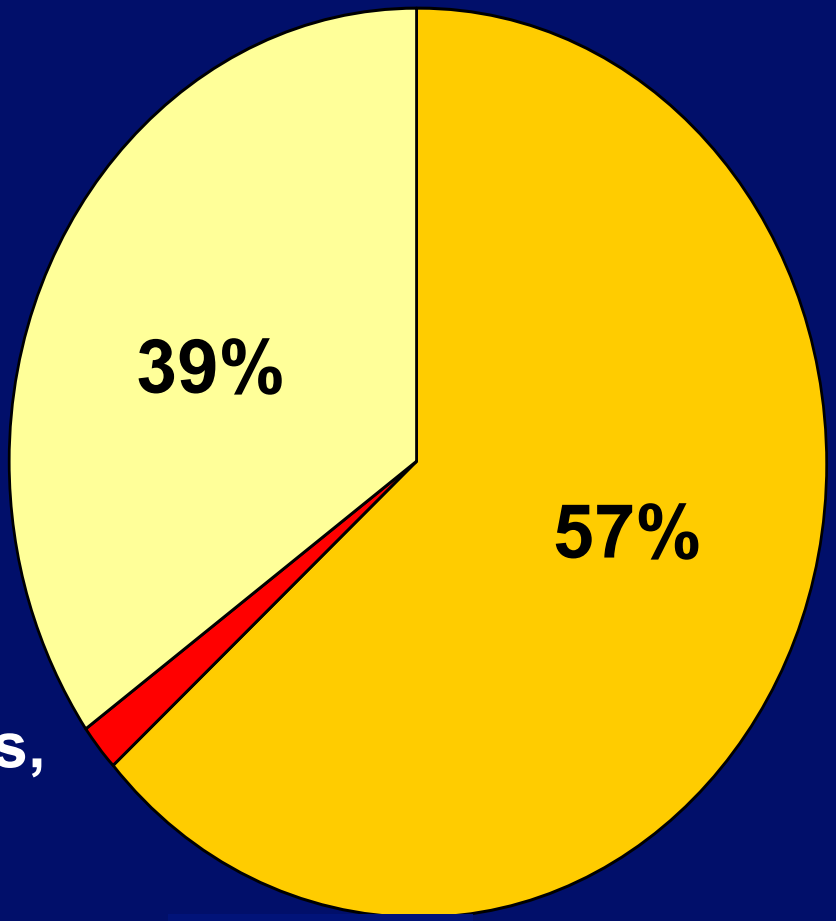






UNAIDS

Coverage of ART among eligible people living with HIV Kenya (2007 KAIS)

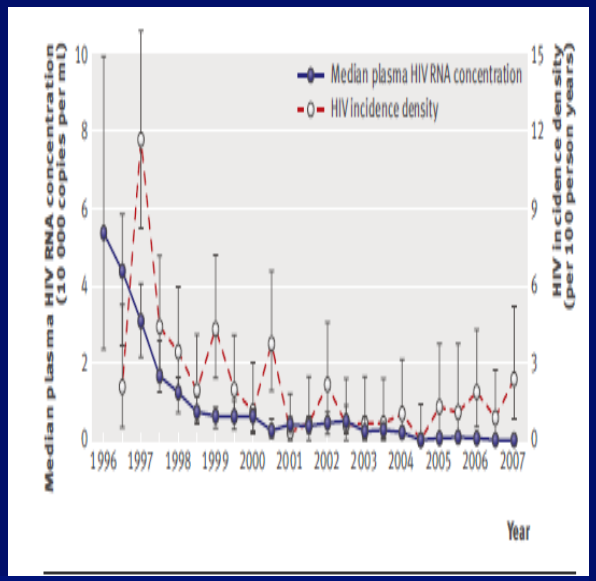


Among those who knew status and were eligible 92% were on ART

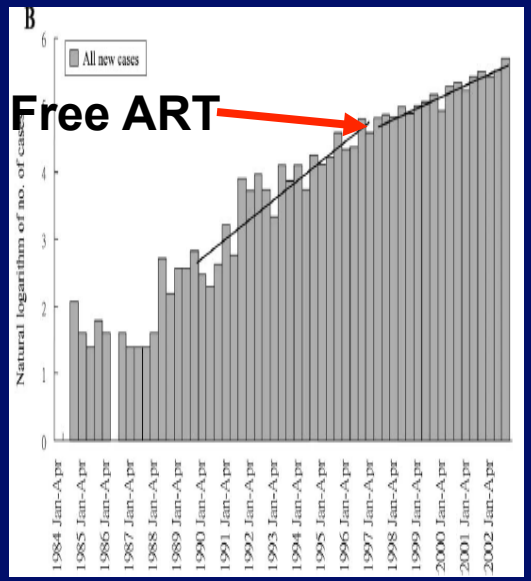
Mohammed, CROI 2009

Community studies suggest population-level impact of ART

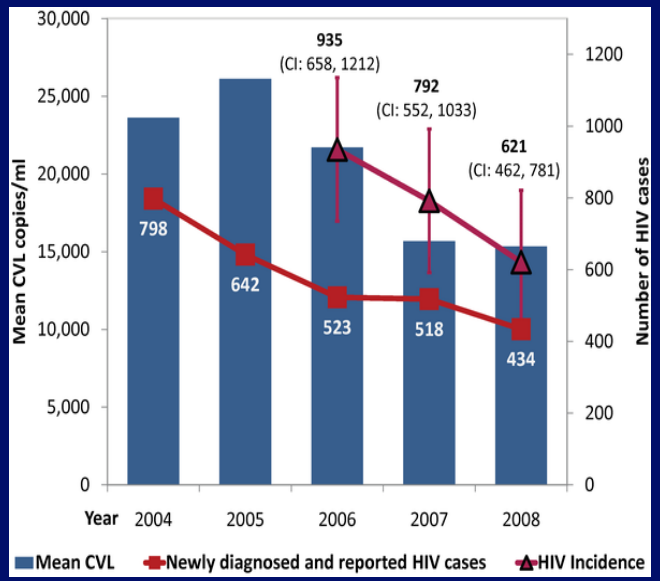
BC Canada



Taiwan



San Francisco

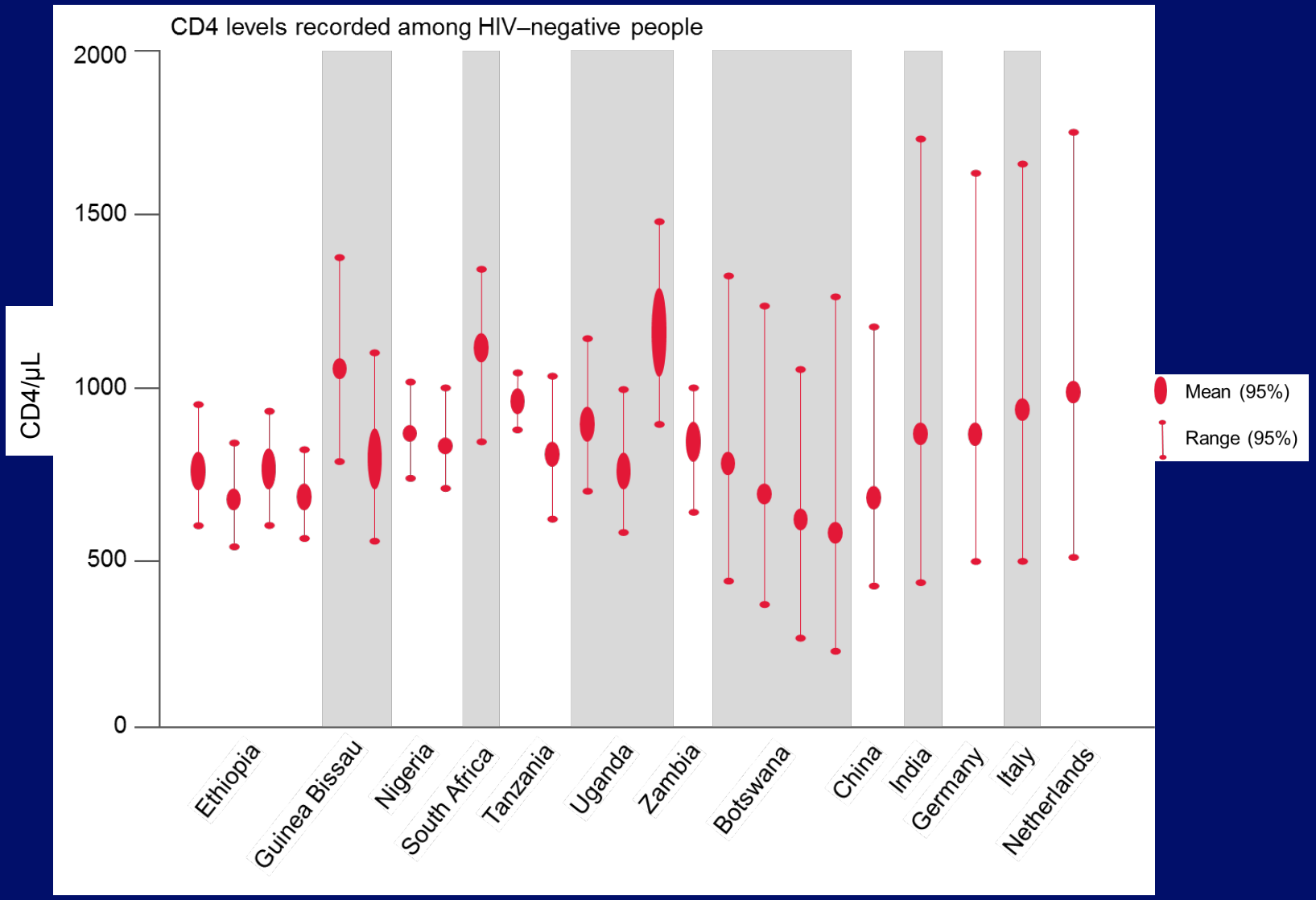


Wood et al. BMJ 2009;338b:1649

Fang et al. JAIDS 2004;190:879-85

Das et al.

Mean CD4 is highly variable across populations

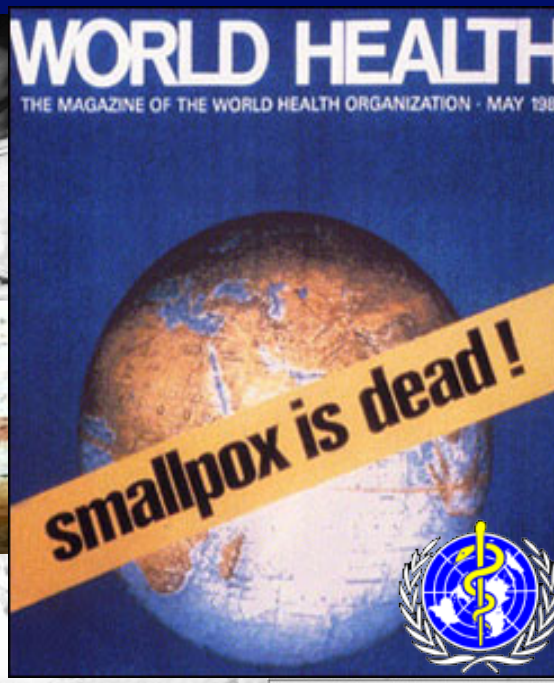


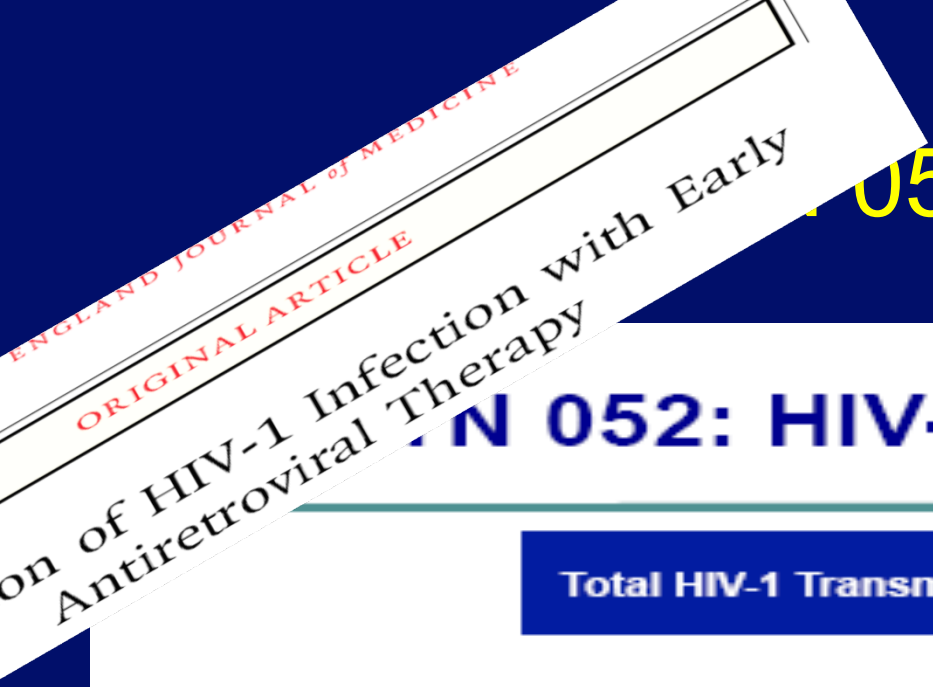
Sources: Williams *et al.* 2006; 194: 1450-8; Bussman *et al.* 2004; Messele *et al*, 1999; Levin *et al*, 1996; Aina *et al*, 2005; Zekeng *et al*, 1997; Jiang *et al*, 2004; Uppal *et al*, 2003; Jentsch-Ullrich *et al*, 2005; Santagostino *et al*, 1999; Tsegaye *et al*, 1999.

Kenya Multidisease Prevention Campaign

September 16-22, 2008

Smallpox eradication 1796 to 1977: Edward Jenner to Merca Town, Somalia





052 Results

N 052: HIV-1 Transmission

Total HIV-1 Transmission Events: 39

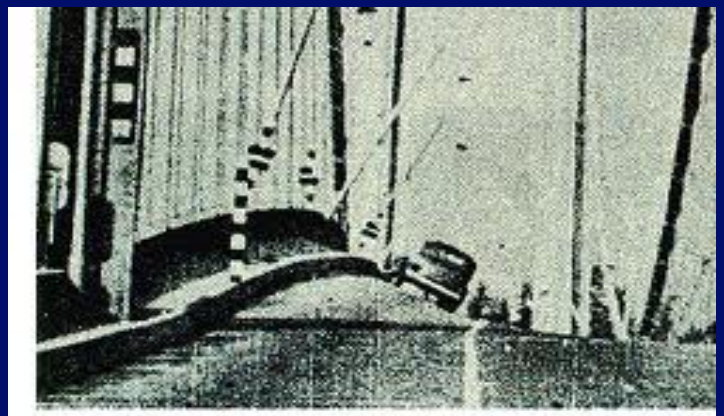
- **Linked Transmissions: 28**
  - **Immediate Arm: 1**
  - **Delayed Arm: 27**
  - $p < 0.001$
- **Unlinked or TBD Transmissions: 11**

- 18/28 (64%) transmissions from infected participants with CD4 >350 cells/mm^3 and VL >50,000 copies/ml at transmission
- 23/28 (82%) transmissions in sub-Saharan Africa
- 18/28 (64%) transmissions from female to male partners

Cohen NEJM 2011

UNAIDS

Bridging the chasm: can we scale to 90-90-90?



The Tacoma Narrows Bridge literally twisted apart on Nov. 7, 1940.

- Science
- Policy
- Technology
- Service delivery
- Getting into the cloud and crowd sourcing data
- Community and behavioral economics

Kenya Multi-disease Prevention Campaign

September 16-22, 2008

Over 7 day period more than 47,000 (80%) of the 15-49 population attended the campaign and 41,040 were tested for HIV. Over 18,000 men received an HIV test….

PARTNERS Study: CROI 2014

Press conference at CROI 2014.

Photo by Liz Highleyman, hivandhepatitis.com.

- 16,400 occasions of sex in the gay men and 28,000 in the heterosexuals
- Zero transmissions within couples from a partner with an undetectable viral load
- Upper bounds of confidence intervals suggest that risk is not zero

Rodger A et al. *HIV transmission risk through condomless sex I f HIV+ partner on suppressive ART: PARTNER study.* 21st CROI, Boston, abstract 153LB, 2014.