The public health impact of TasP, models of its effect and implications for ART access

EATG New Developments in Prevention Meeting
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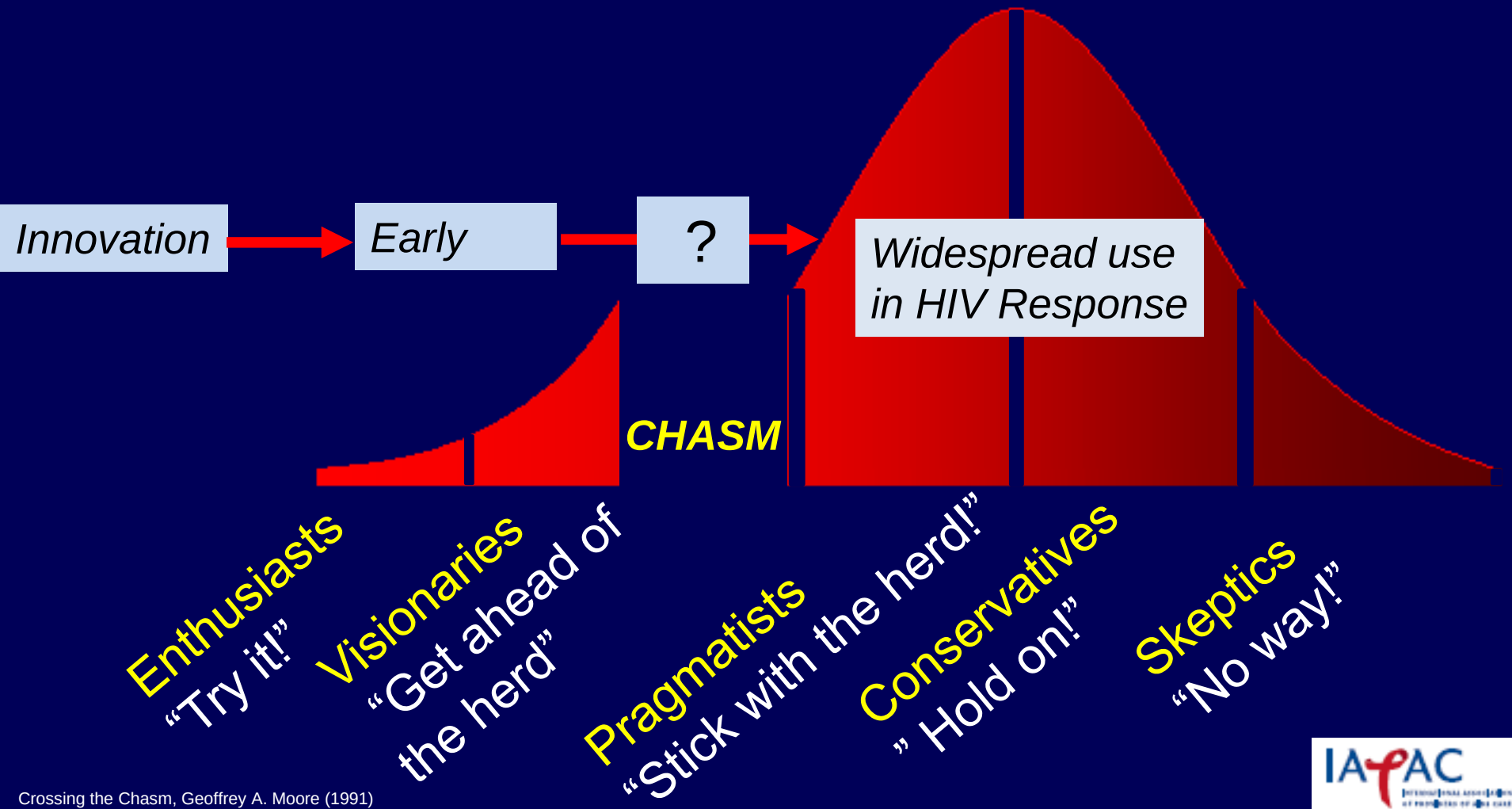
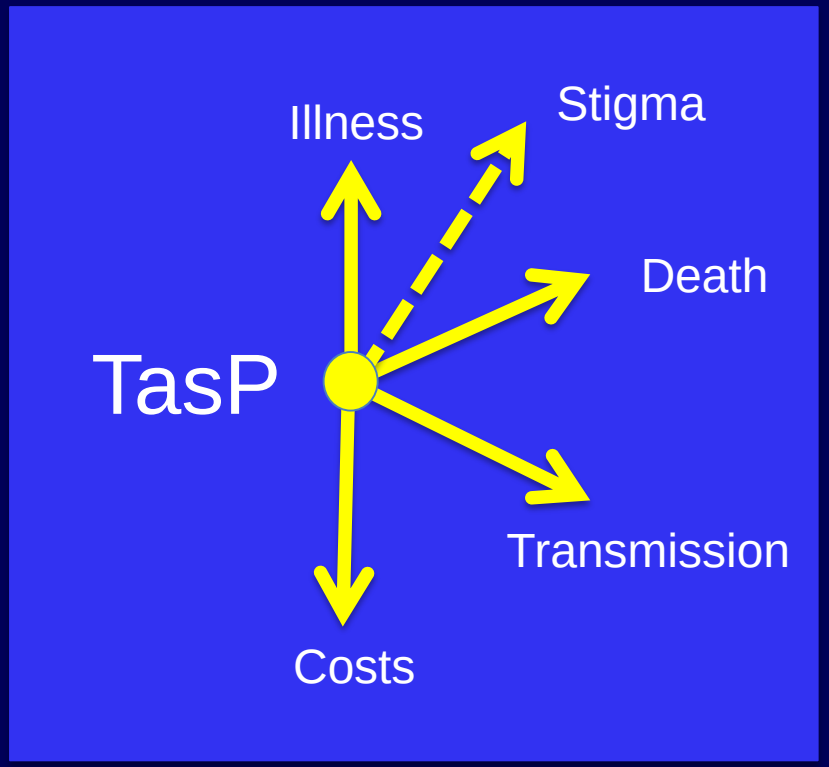
To end AIDS we will need to bridge the "innovation to scale" chasm



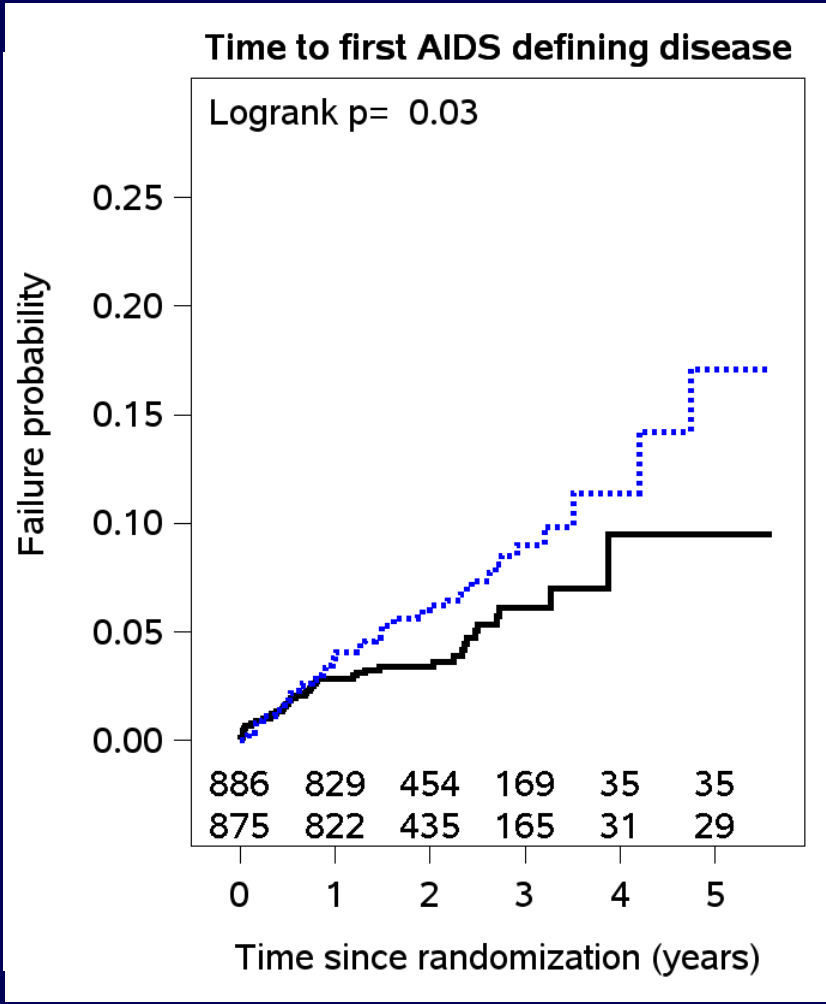
Crossing the Chasm, Geoffrey A. Moore (1991)

Treatment as prevention

- Re-conceptualizing treatment
  - Prevention of illness (keeping people healthy)
  - Prevention of death (keeping people alive)
  - Prevention of transmission (keeping partners and children safe from HIV)
  - Preventing costs for individuals, governments and society
  - Prevent denial of human rights including right to health
- Transmission benefit is secondary to helping people stay healthy



HPTN 052 showed clinical benefit for earlier ART at <550 CD4 cell count

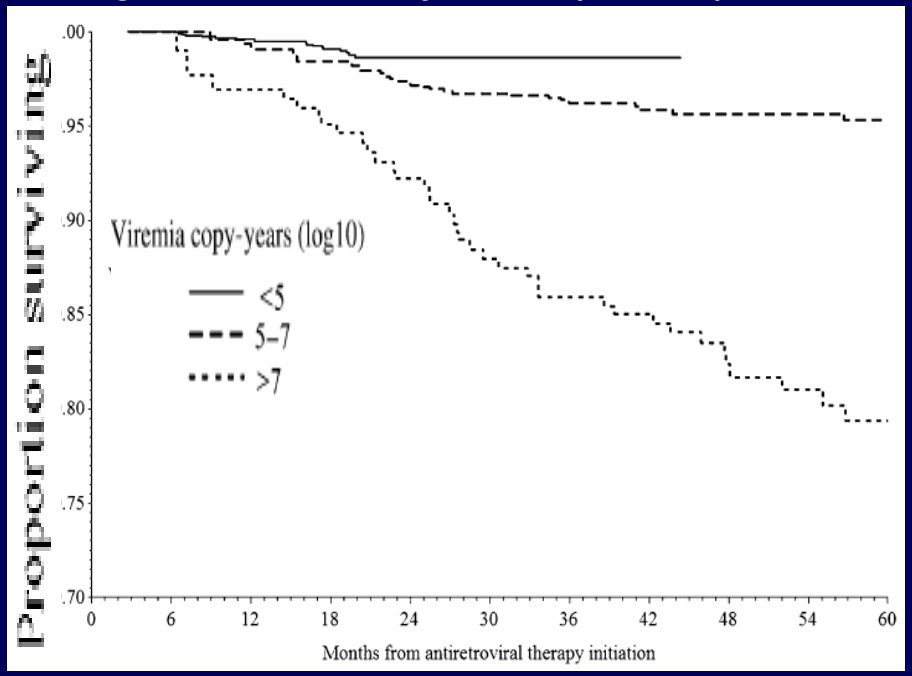


Number of subjects experiencing ≥1 event	Delayed	Immediate
Tuberculosis	**34 (4%)**	**17 (2%)**
Serious bacterial infection	**13 (1%)**	**20 (2%)**
WHO Stage 4 event	**19 (2%)**	**9 (1%)**
Oesophageal candidiasis	2	2
Cervical carcinoma	2	0
Cryptococcosis	0	1
HIV-related encephalopathy	1	0
Herpes simplex, 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

Source: Grinsztejn B, et al, Lancet Infectious Diseases, 4 March 2014

Unchecked viral replication impacts disease progression independent of CD4 count

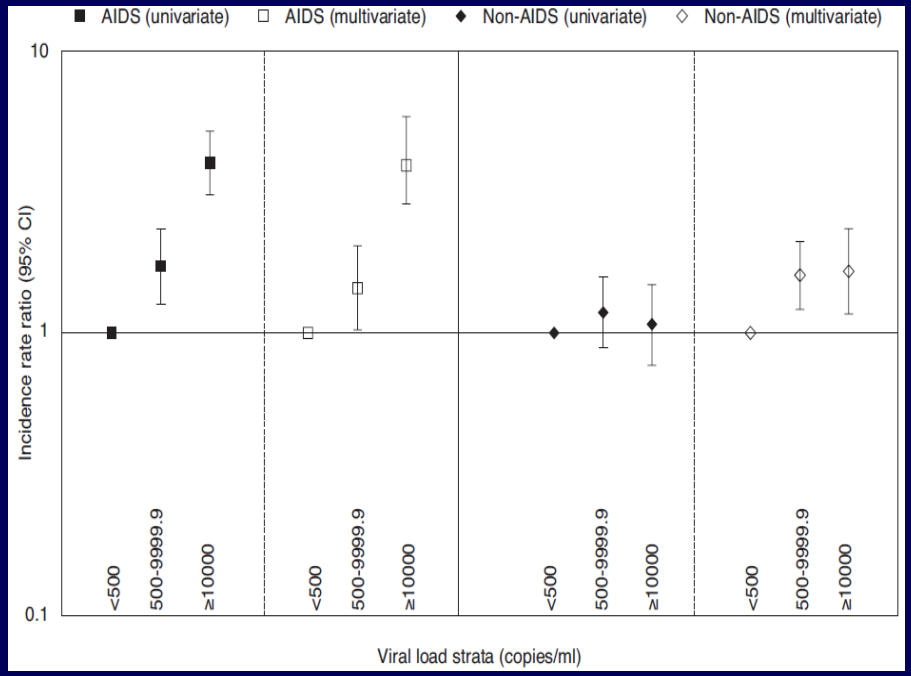
Centers for AIDS Research Network of Integrated Clinical Systems (CNICS) cohort



- 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

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.

Reekie et al. AIDS 2011

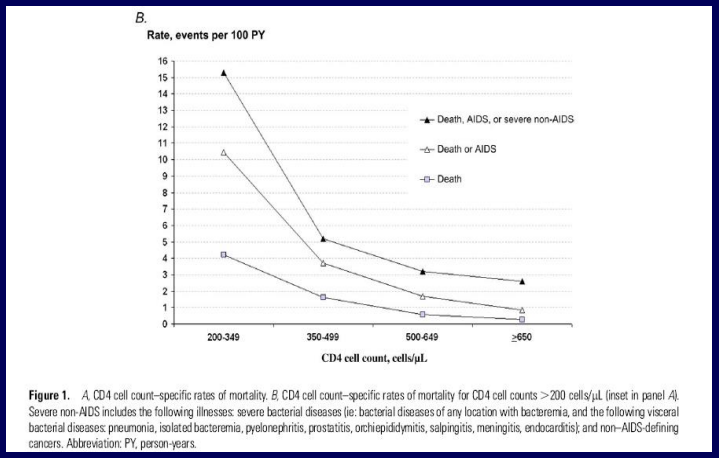


Figure 1. *A*, CD4 cell count–specific rates of mortality. *B*, CD4 cell count–specific rates of mortality for CD4 cell counts >200 cells/μL (inset in panel *A*). Severe non-AIDS includes the following illnesses: severe bacterial diseases (ie: bacterial diseases of any location with bacteremia, and the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

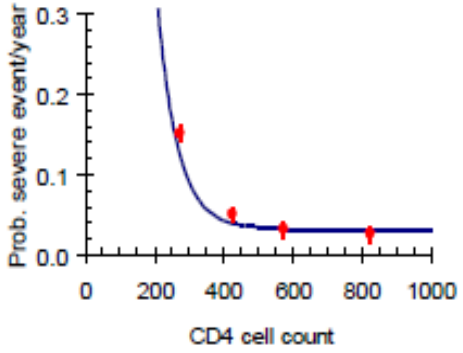


Figure 1. Line fitted to the risk of a severe event.

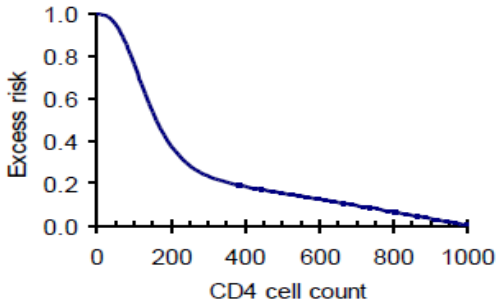


Figure 2. Excess risk of AIDS and non-AIDS morbidity and mortality as a function of the $CD4^+$ cell count at which people start treatment.

Significant cumulative risk?

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

Fitted risk of event to CD4 data

Cumulative risk of adverse events while Waiting to be eligible:

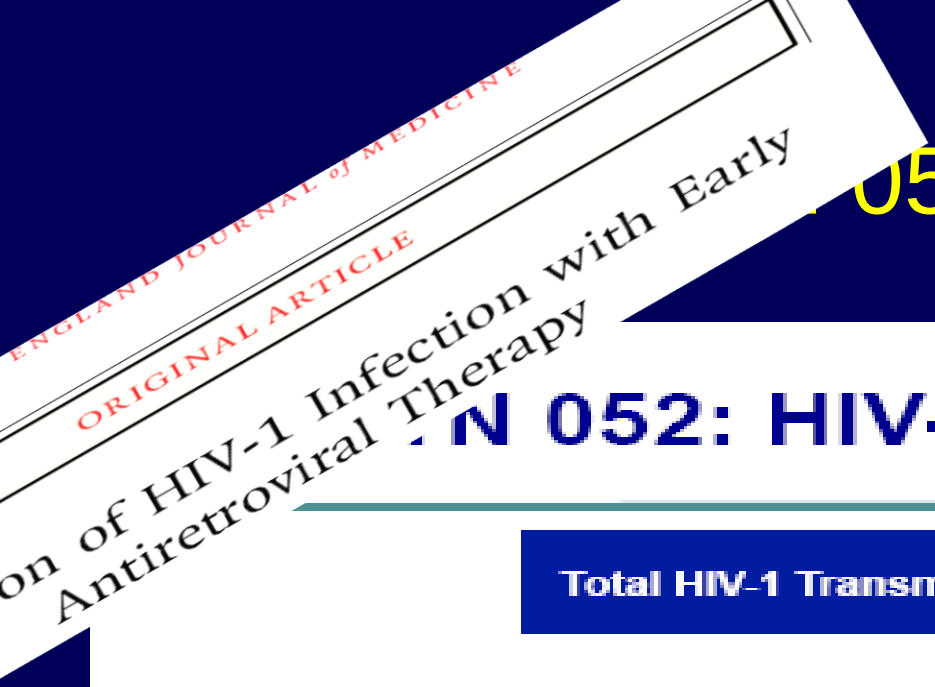
<200 38%

<350 21%

<500 15%

<950 2%

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



052 Results

N 052: HIV-1 Transmission

Total HIV-1 Transmission Events: 39

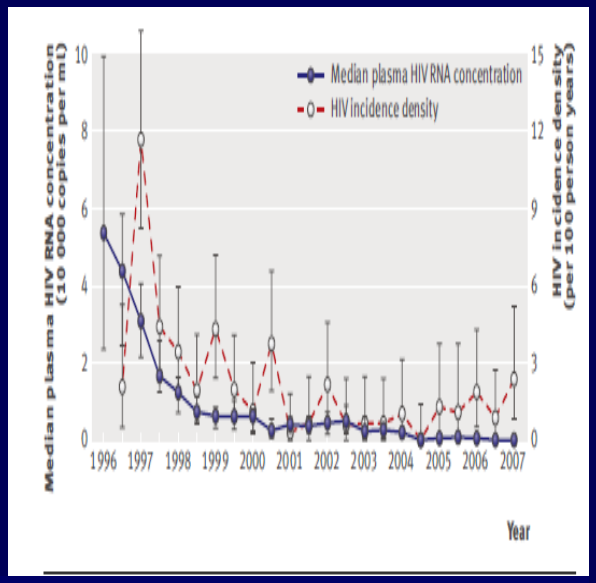
- **Linked Transmissions: 28**
  - **Immediate Arm: 1**
  - **Delayed Arm: 27**
  - $p < 0.001$
- **Unlinked or TBD Transmissions: 11**

- 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

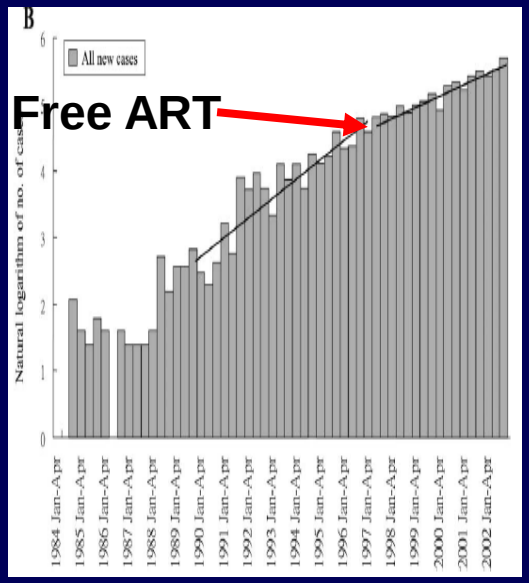
Cohen NEJM 2011

Scaling treatment has an impact on community HIV transmision

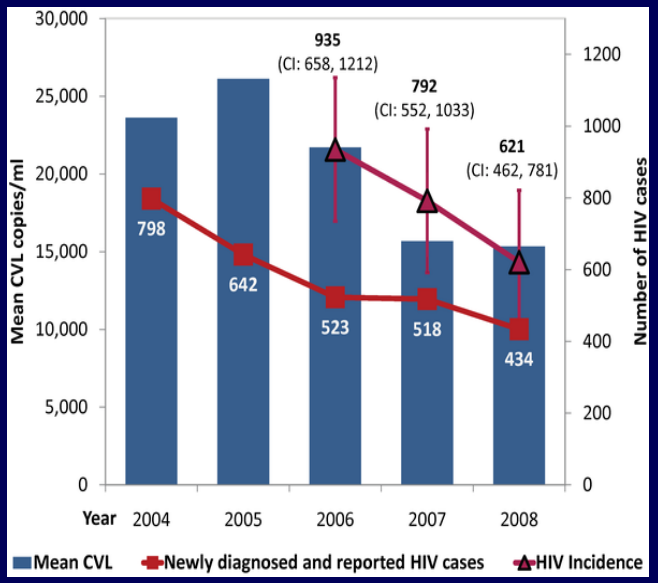
BC Canada



Taiwan



San Francisco

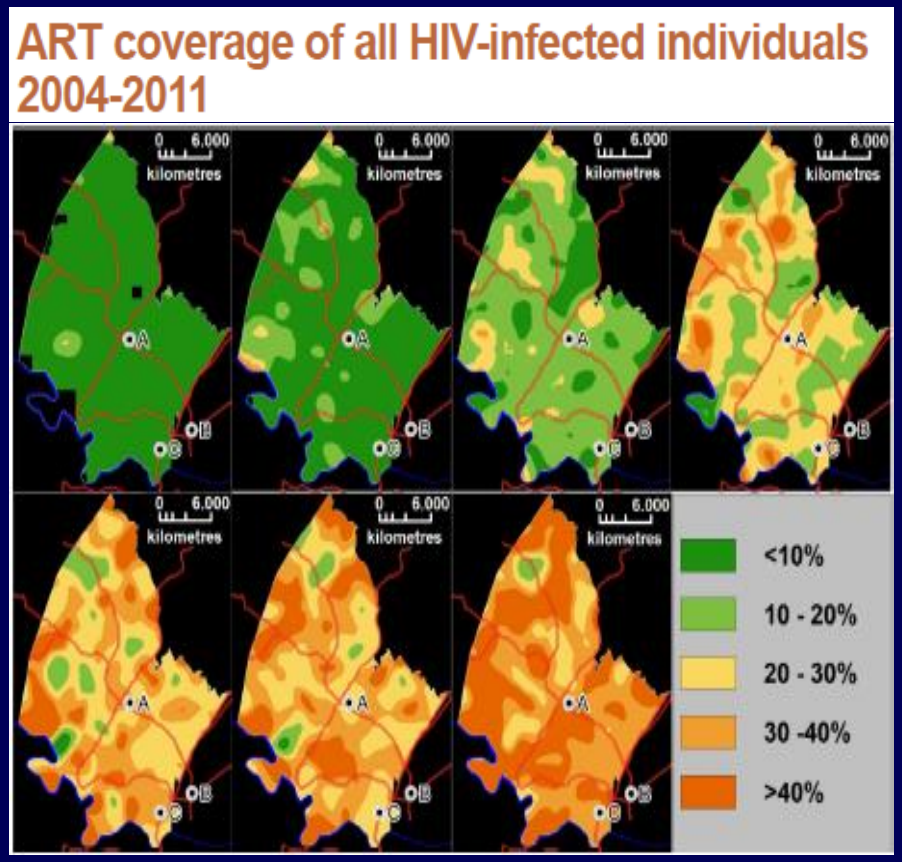


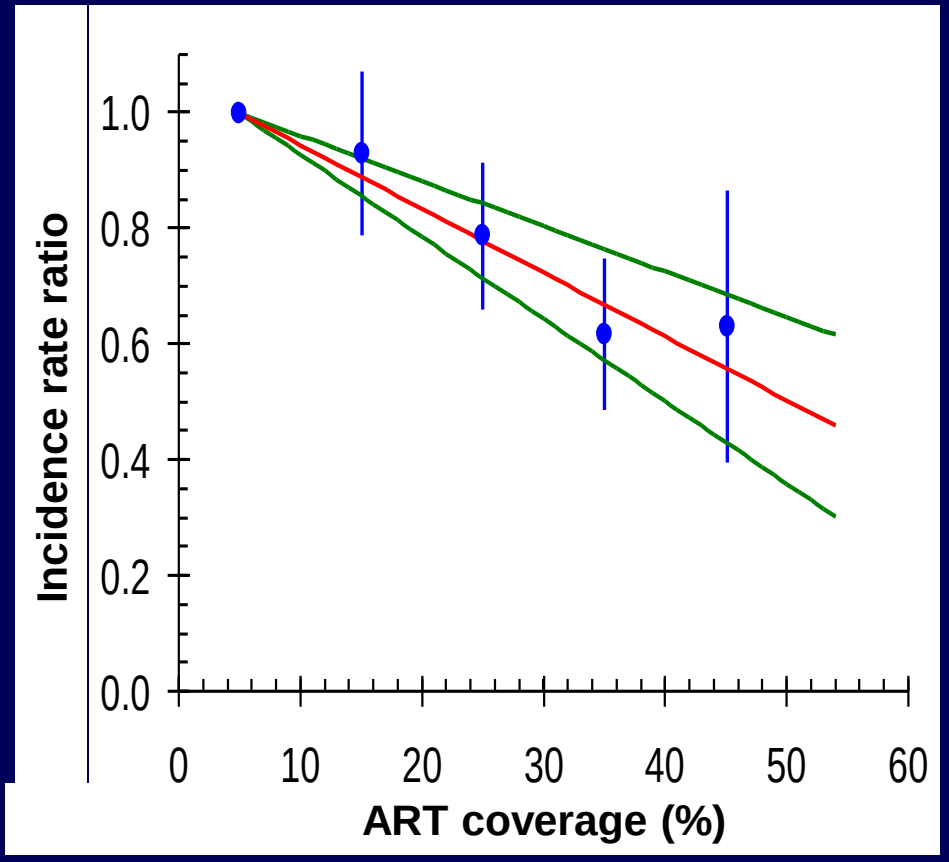
Wood et al. BMJ 2009;338b:1649

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

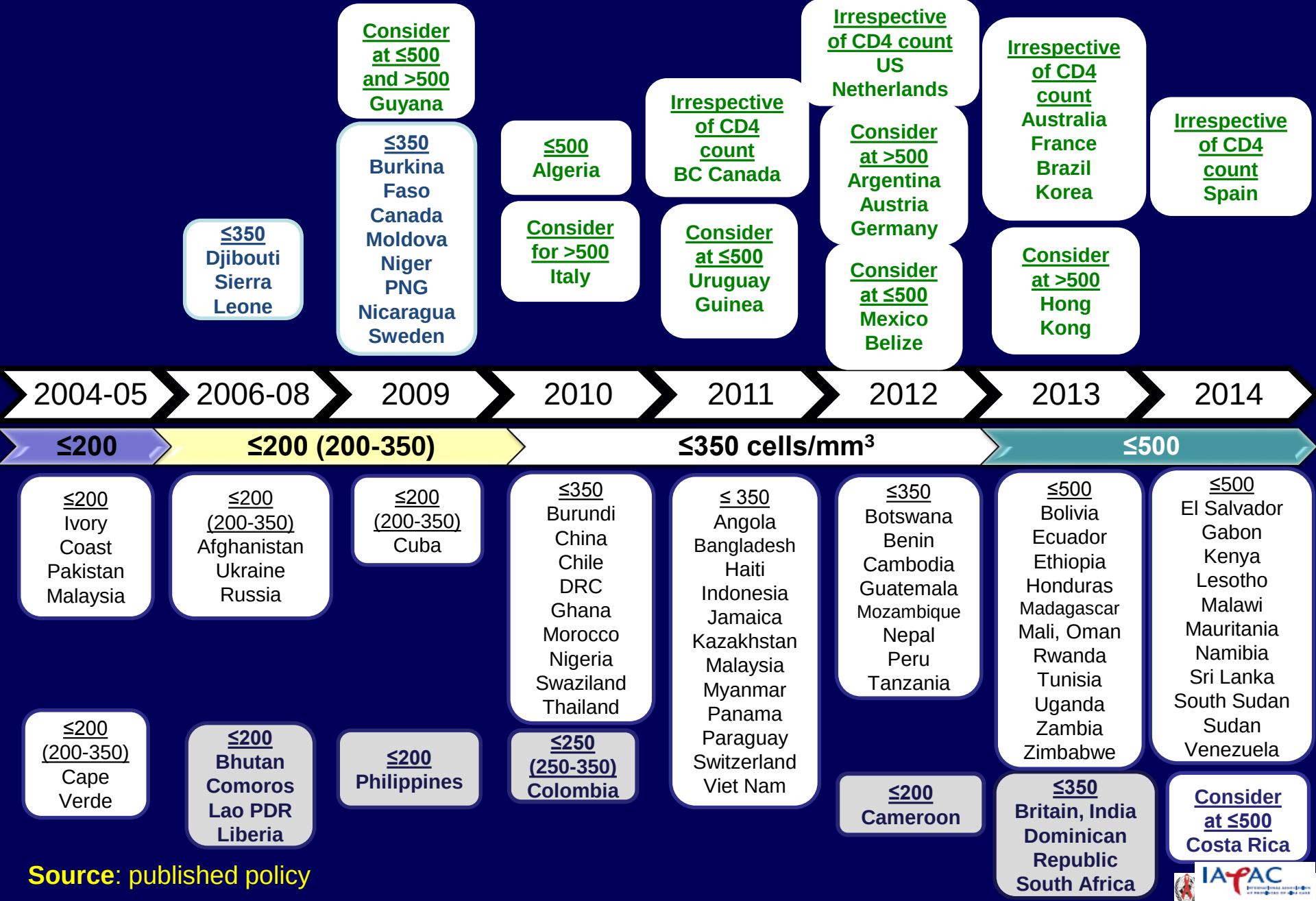




Incidence falls by 1.1% (0.8%-1.4%) for each 1% increase in coverage

Tanser Science 2013; Williams 2013

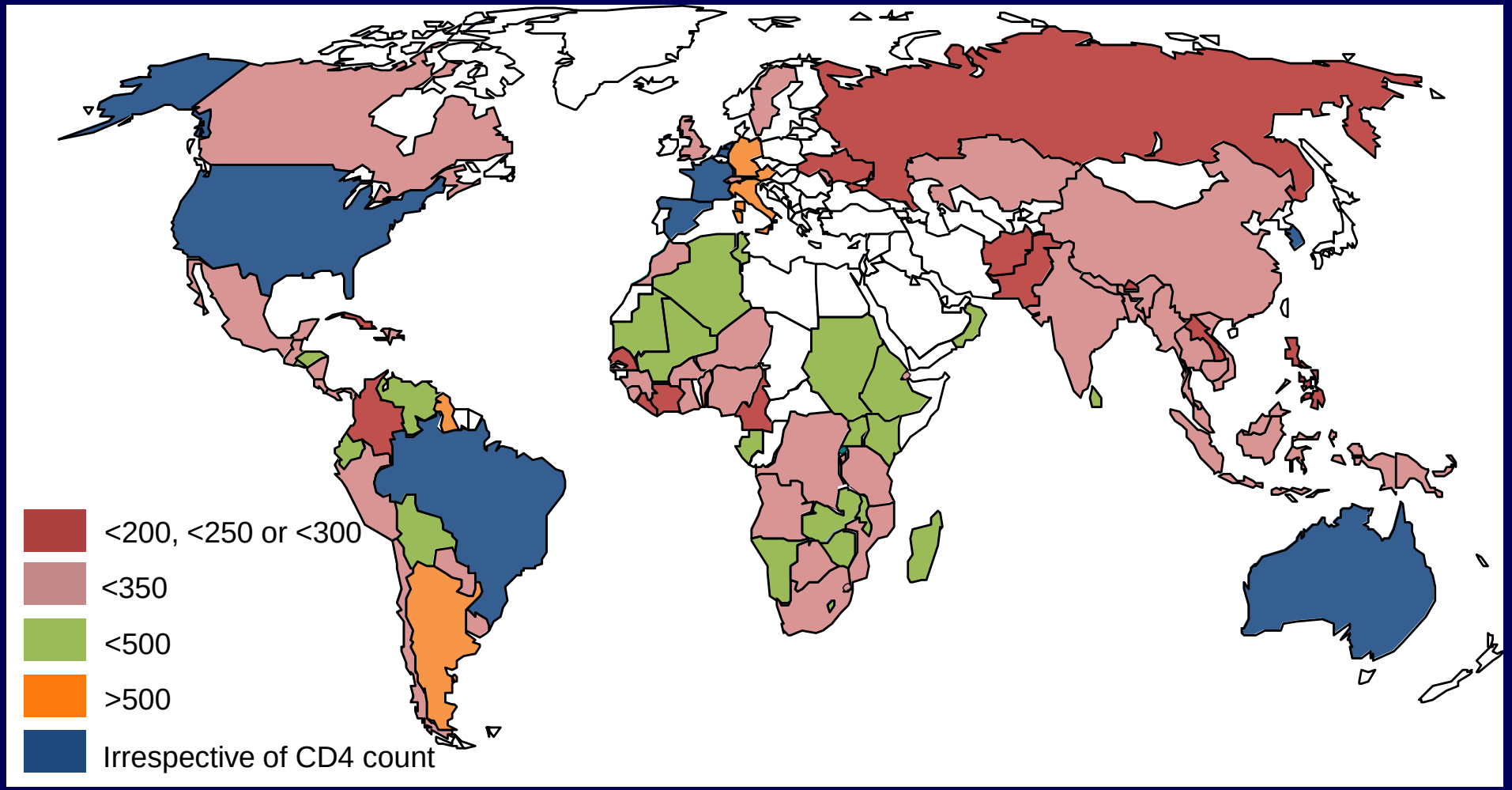
National ART policy: CD4 cell count criteria



Source: published policy

ART initiation for asymptomatic people

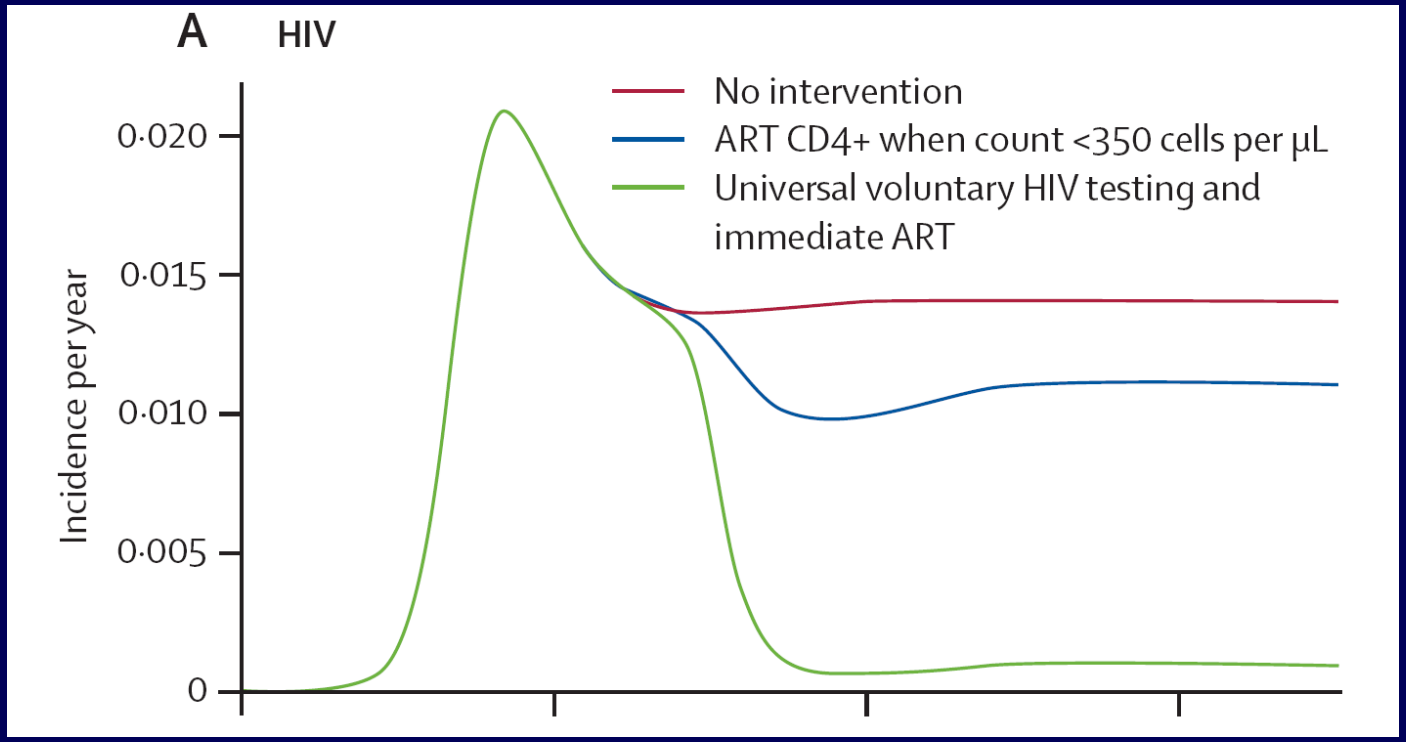
2013 WHO Recommendation : CD4 count ≤ 500 cells/mm^3



Source: published policy from 120 countries as of Nov 2014

IAPAC

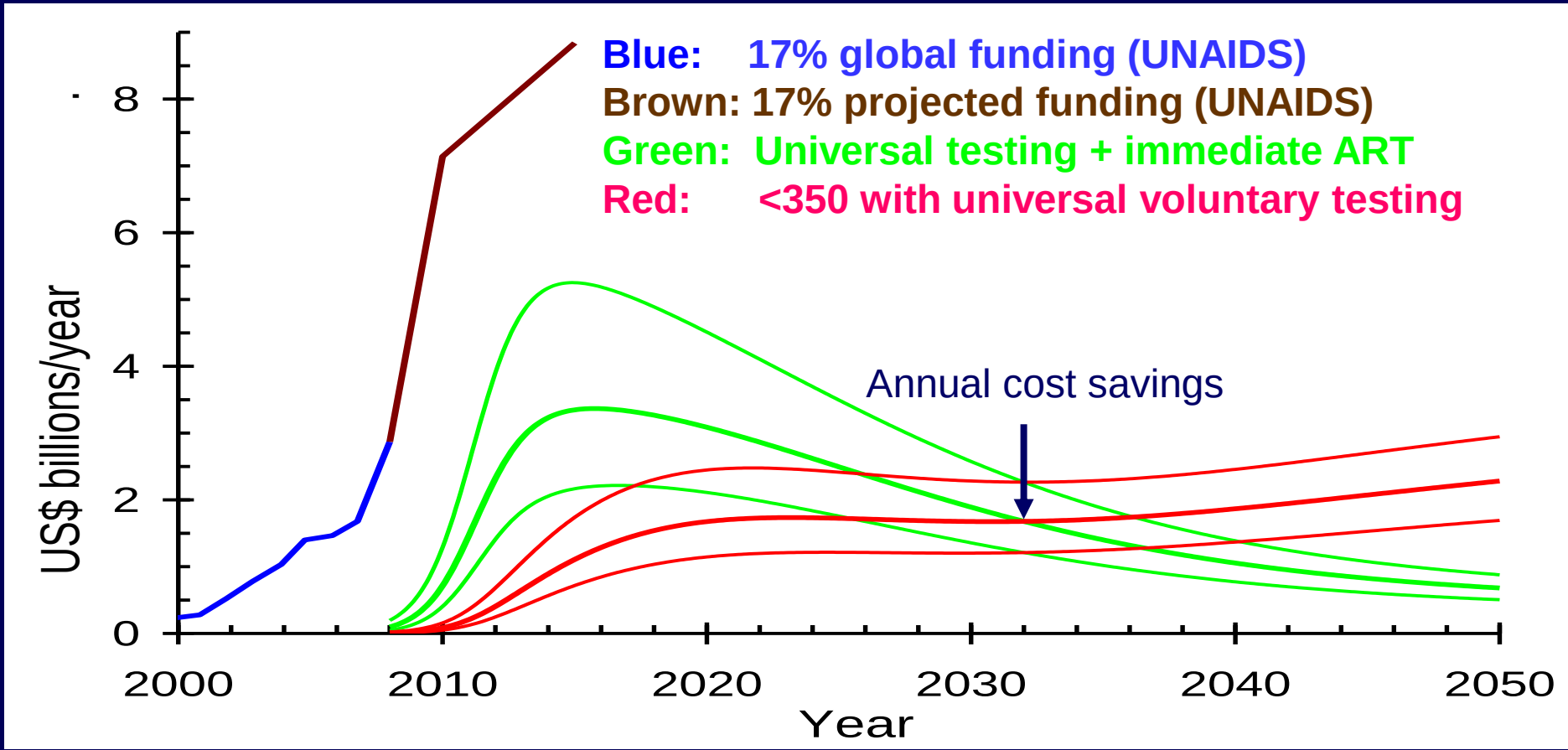
ART as prevention: 90-90 impact



- Testing and ART impacts HIV incidence and survival
- Elimination is feasible
- Consider potential role for treatment as part of solution to ending HIV epidemic

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

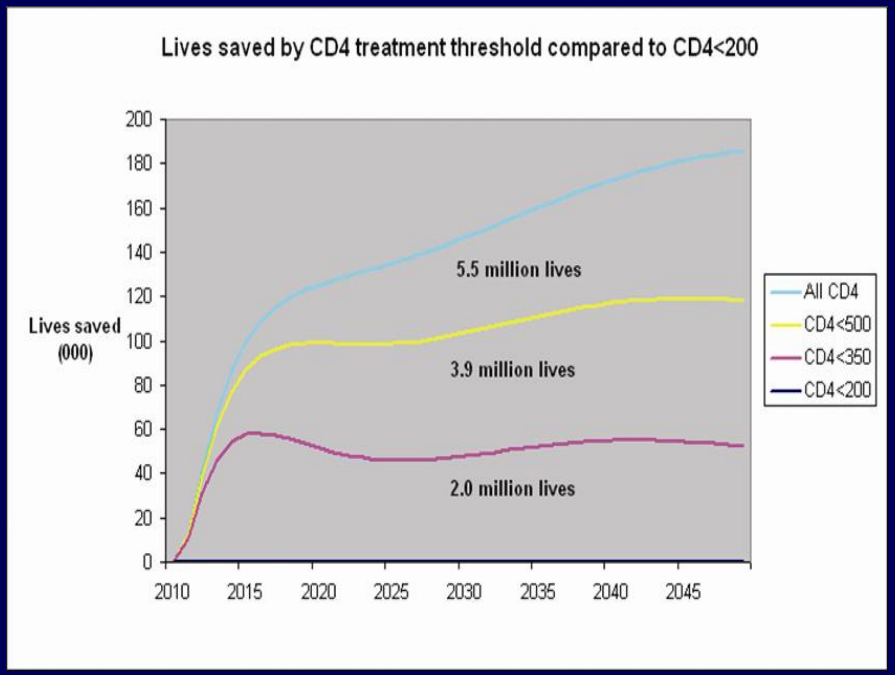
Available funding and costs: We appear to be in the right ball park….



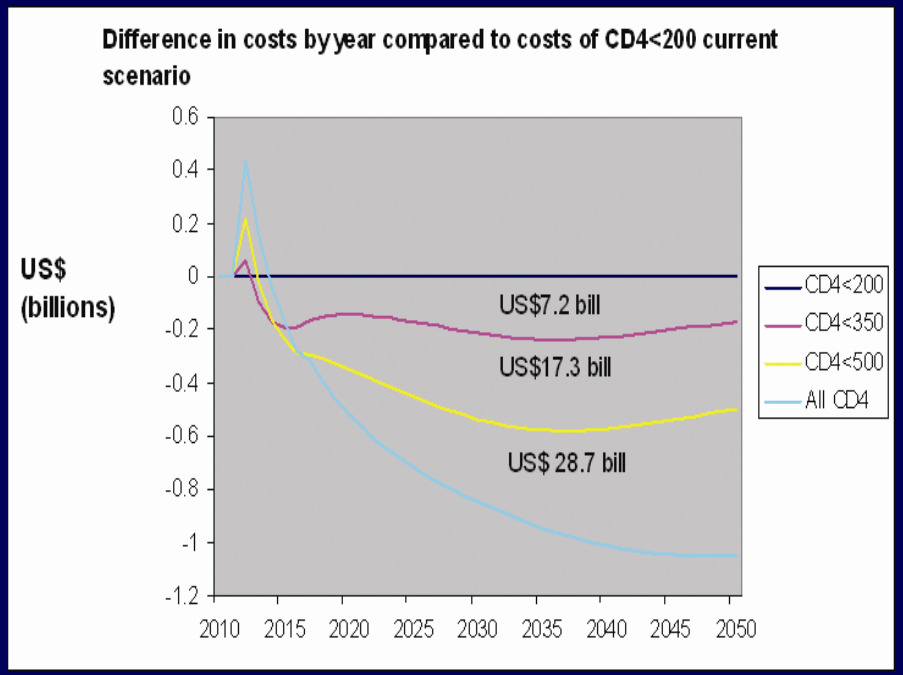
Cohen J. HIV/AIDS. The great funding surge. Science **2008** Jul 25;321(5888):512-9.

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.

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



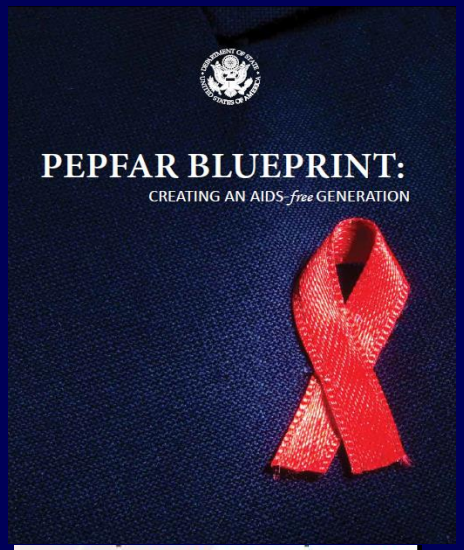
Lives saved (millions)

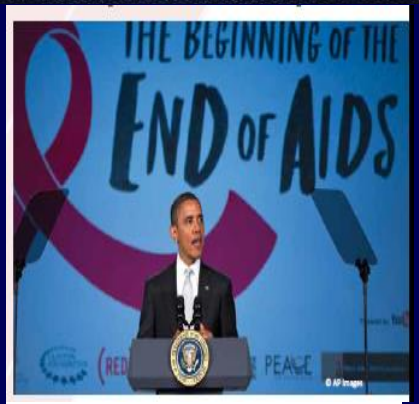


Cost savings (billions)

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

PEPFAR 2012 Blueprint: modelling end of AIDS





November 29, 2012

As a nation, we are firmly committed to turning the tide on the 30-year-old fight against AIDS. That's why I proudly announced last year that creating an AIDS-free generation is a new policy imperative for the United States.

To be clear, we still face enormous challenges. Far too many people are dying from this disease. We need to reach more people with both prevention and treatment services. But today, thanks to remarkable scientific discoveries and the work of countless individuals, organizations and governments, an AIDS-free generation is not just a rallying cry—it is a goal that is within our reach.

At the International AIDS Conference this past July, I asked our Global AIDS Coordinator, Ambassador Eric Goosby, to prepare this blueprint outlining our path to helping create an AIDS-free generation. I want the next Congress, the next Secretary of State, and all of our partners here at home and around the world to understand everything we've learned and to have a road map for how the United States will contribute to an AIDS-free generation.

This blueprint should make one thing clear: the United States is and will continue doing our part. But creating an AIDS-free generation is too big a task for one government or one country. It requires the world to share in the responsibility. We call on partner countries, other donor nations, civil society, faith-based organizations, the private sector, foundations, multilateral institutions and people living with HIV to join us as we each do our part.

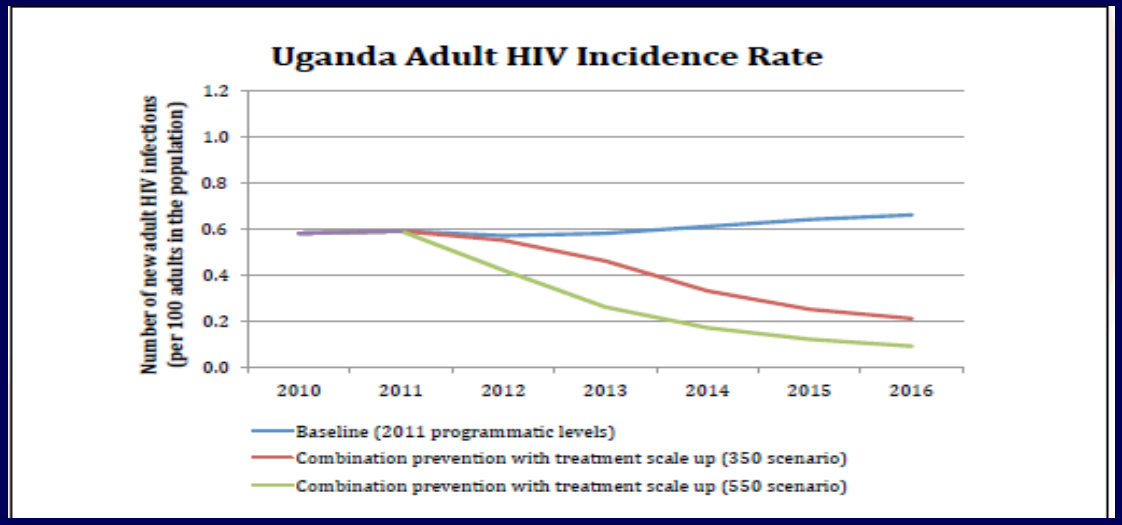
Together, we can deliver a better future to millions across the globe. A future where children are not born with HIV… where teenagers and adults are at far lower risk of contracting the virus… where those who do have the virus get lifesaving treatment. A future where every child has the chance to live up to his or her God-given potential.

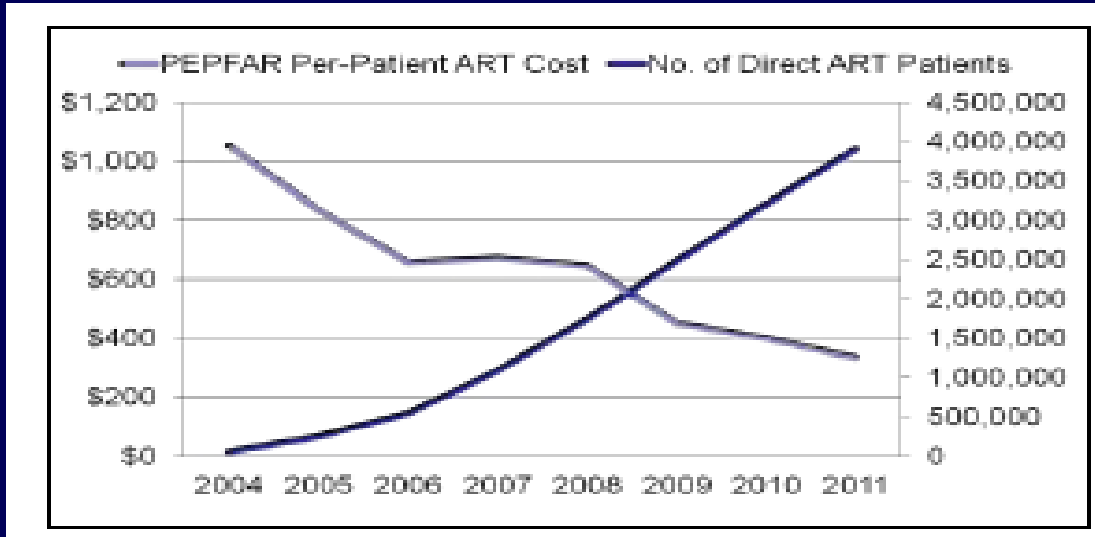
That's a future worth fighting for, together.

Sincerely,

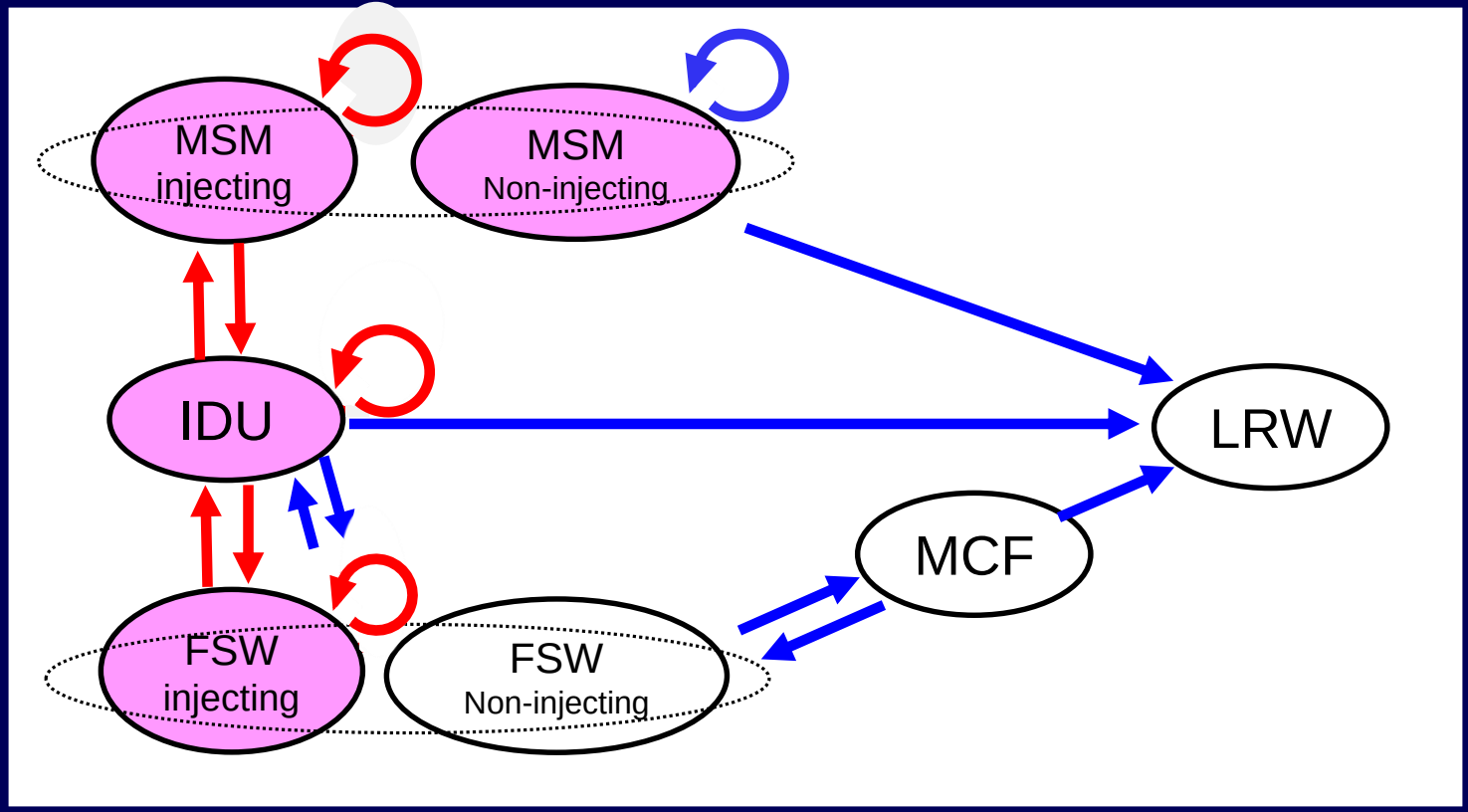
Hillary Rodham Clinton

Hillary Rodham Clinton
Secretary of State





7 sub-populations in the Viet Nam model



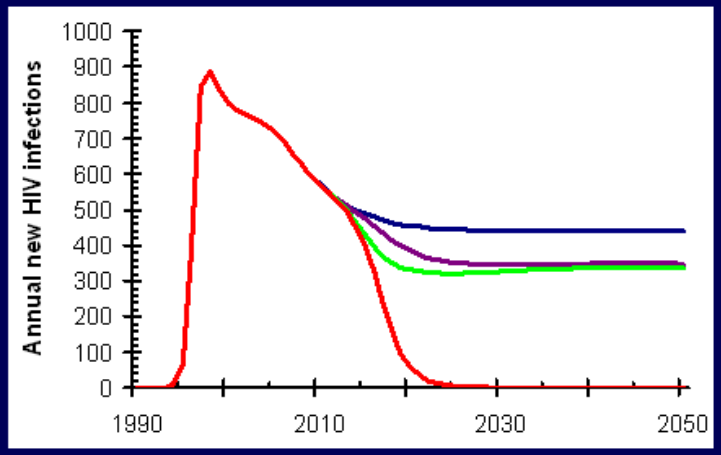
IDU: Injection drug users
MSM: Men having sex with men
FSW: Female sex workers
MCF: Male clients of FSW
LRW: Low risk women

Red arrow: Transmission via needle sharing
Blue arrow: Sexual transmission
Pink circle: Transmission within group

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

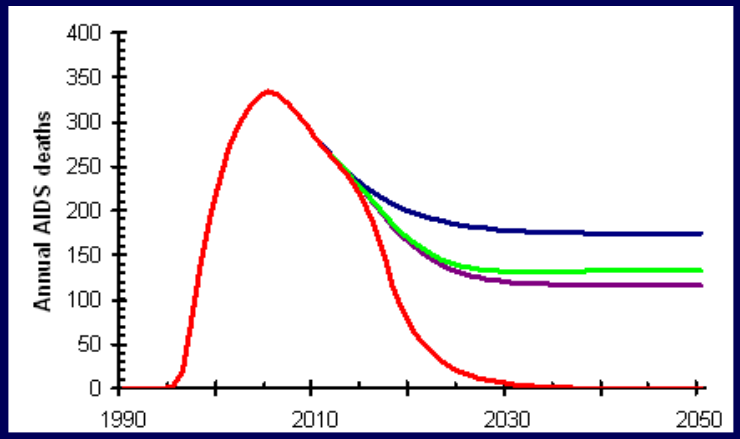
Annual new HIV infection

A



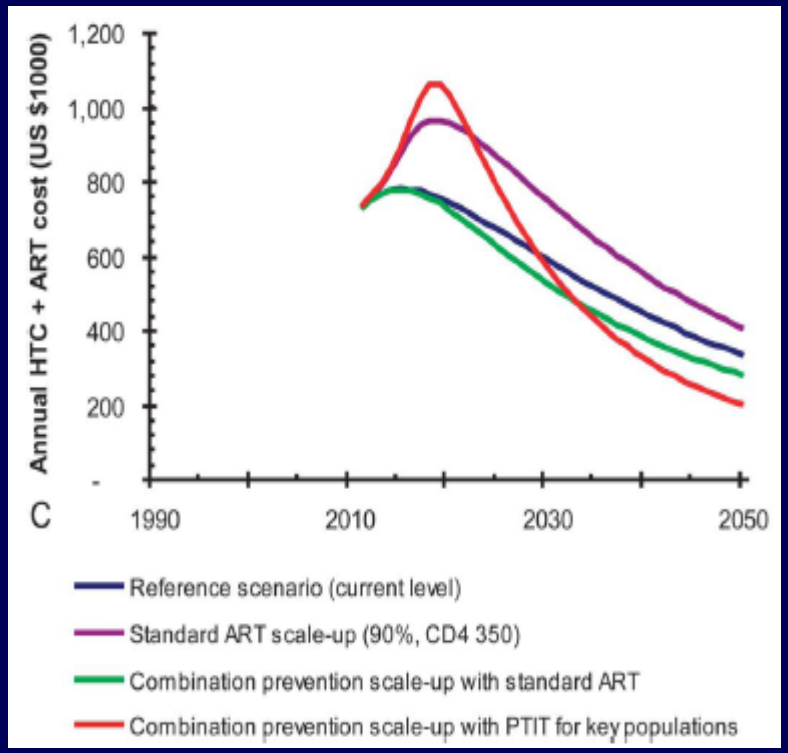
Annual AIDS death

B



ART and HTC cost

C

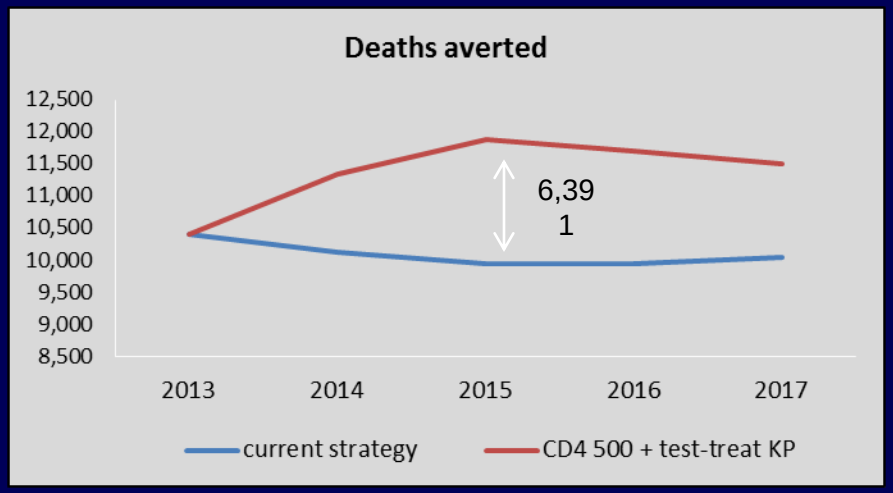


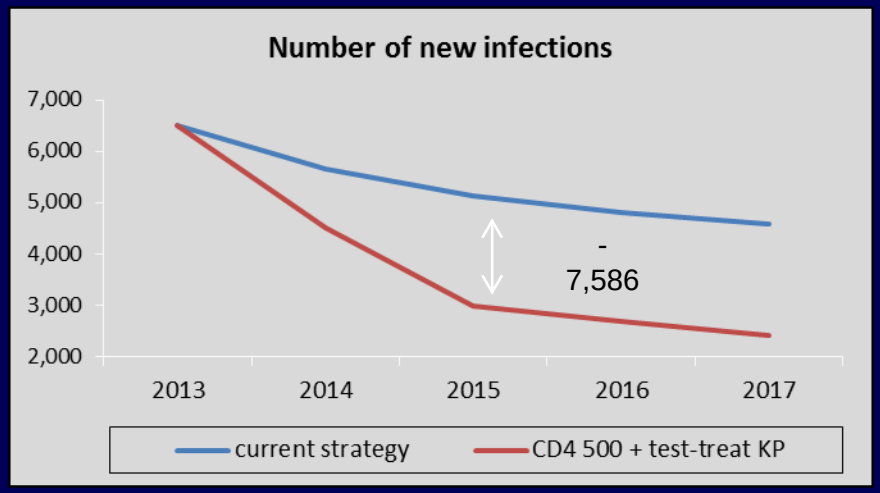
Periodic testing and immediate treatment (PTIT)

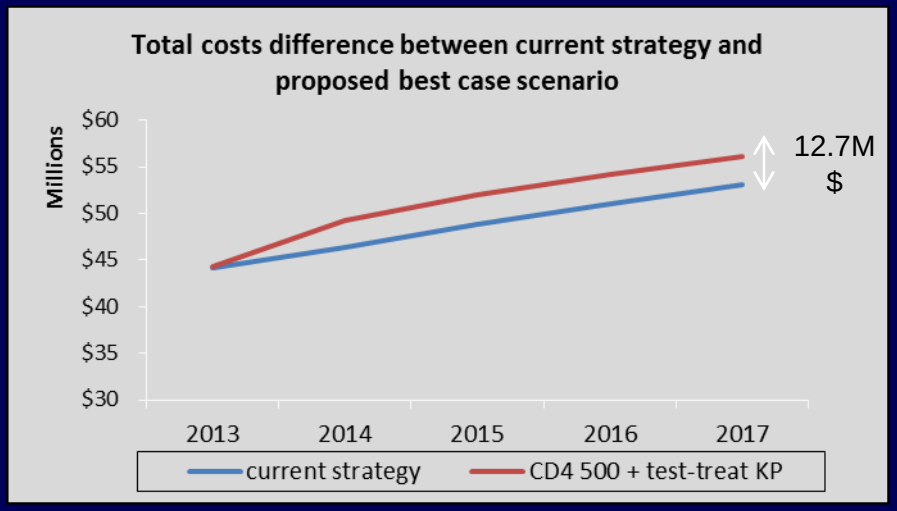
Kato M et al . JAIDS Vol 63(5) 2013

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

Are we on track to scale?

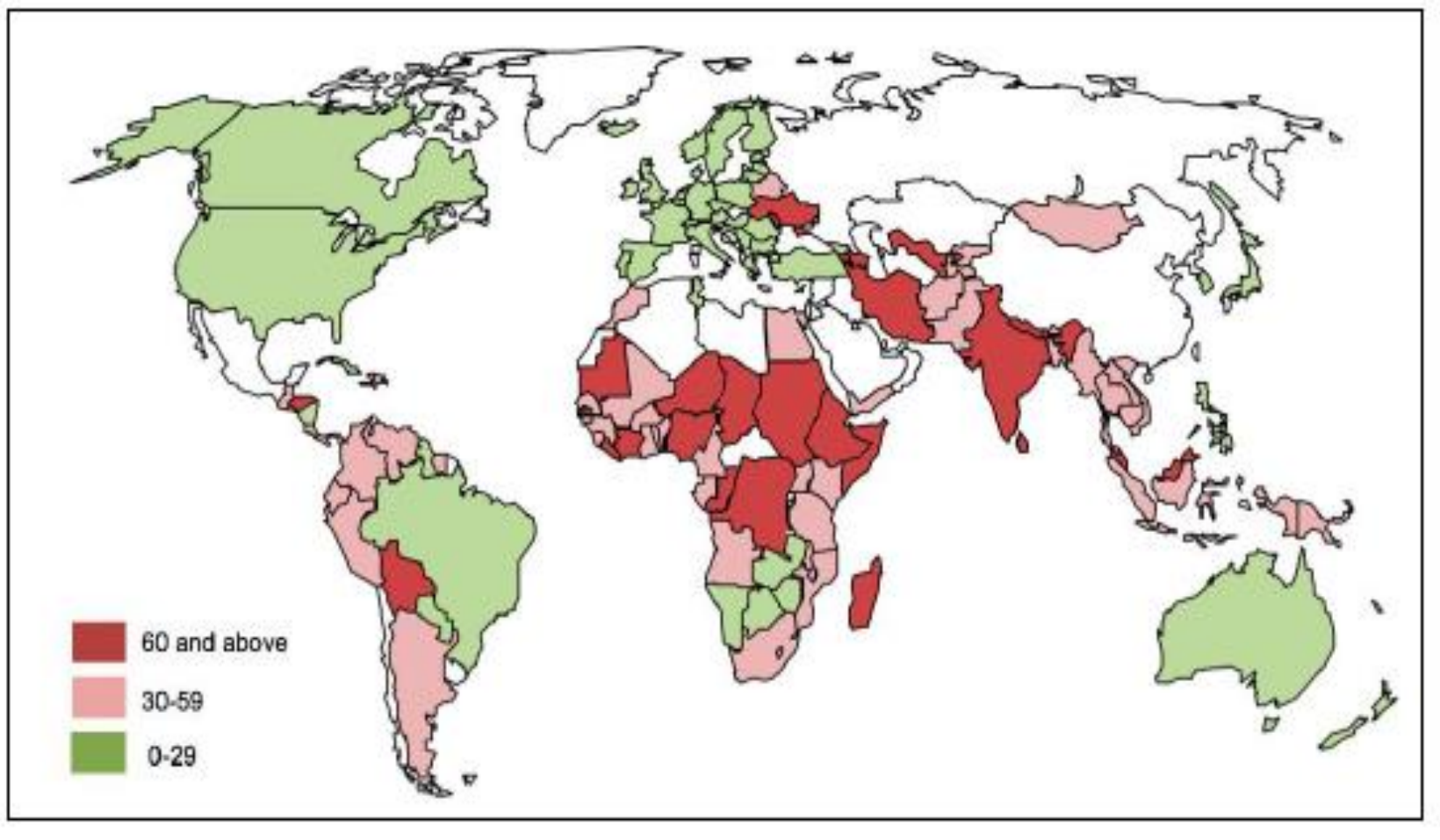
By end of 2013:

- ~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)

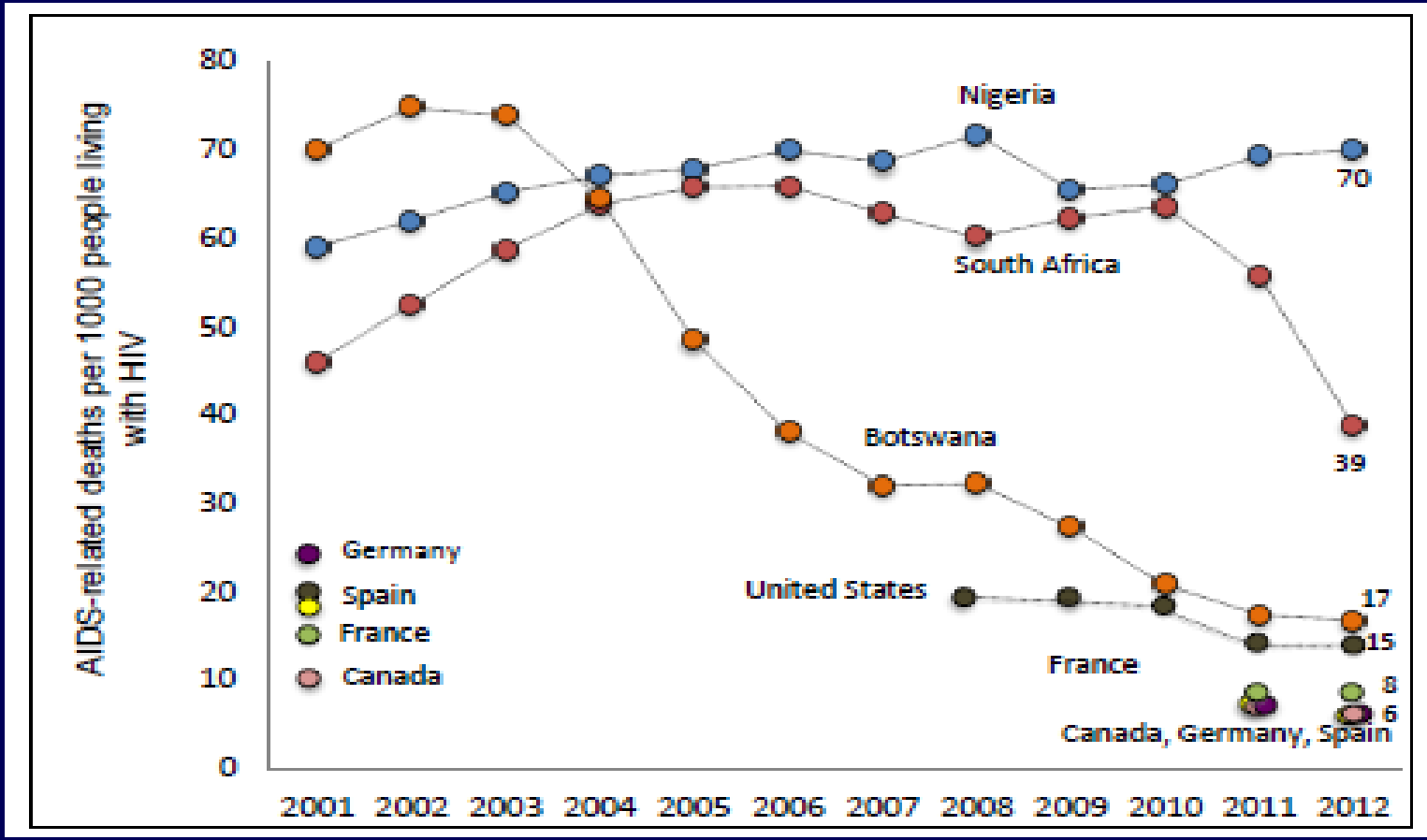
Bottom line:

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

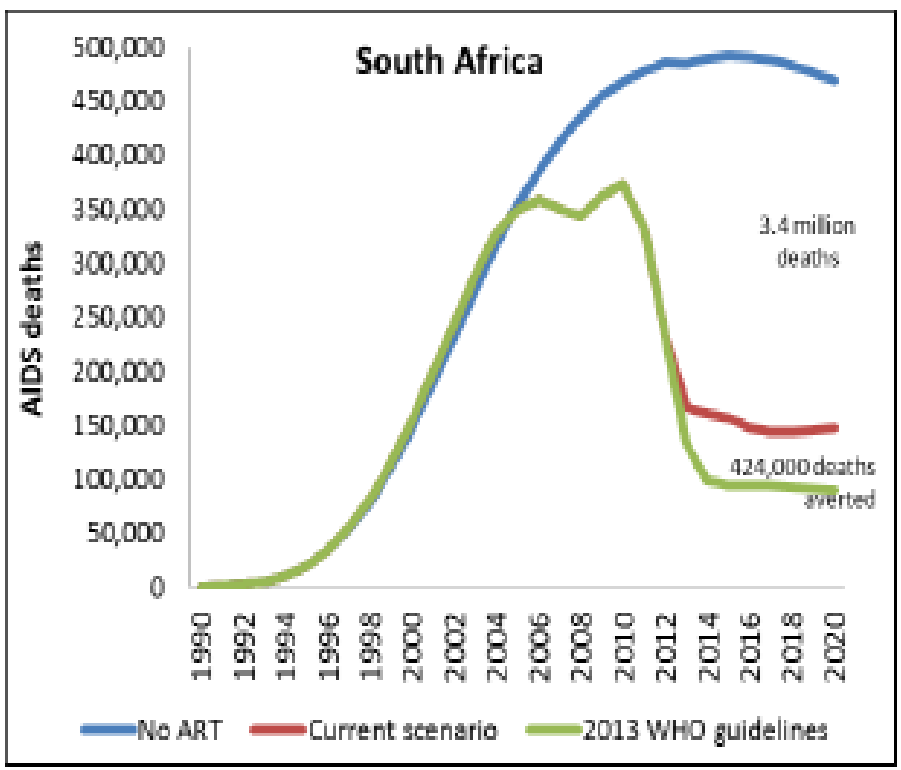
Global AIDS related deaths per 1000 people living with HIV, 2012

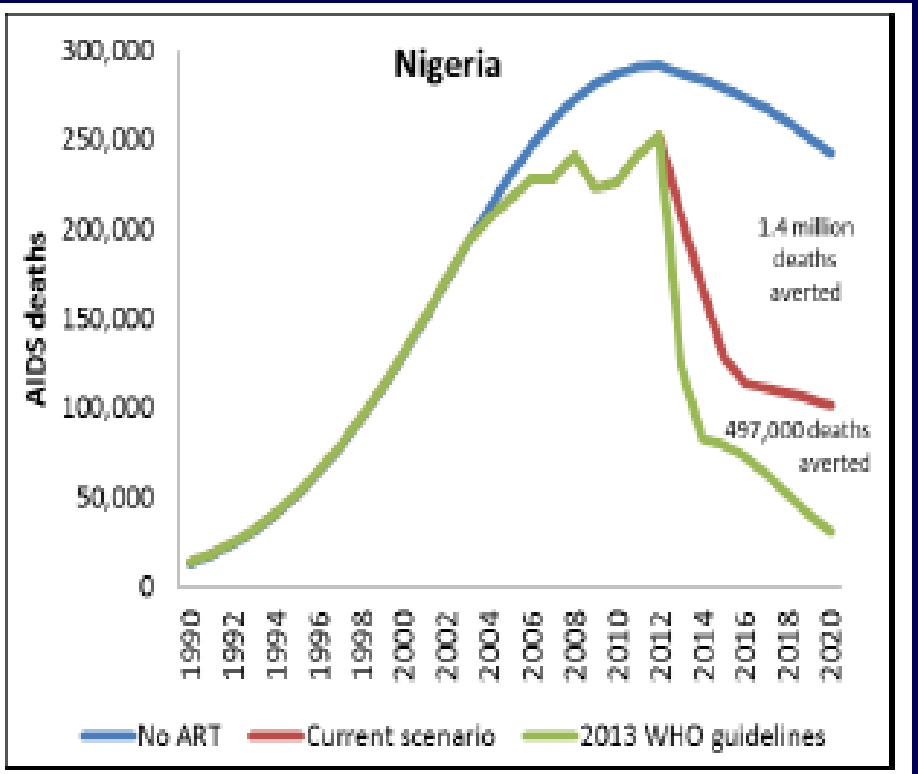


Estimated AIDS related deaths per 1000 people living with HIV, 2012

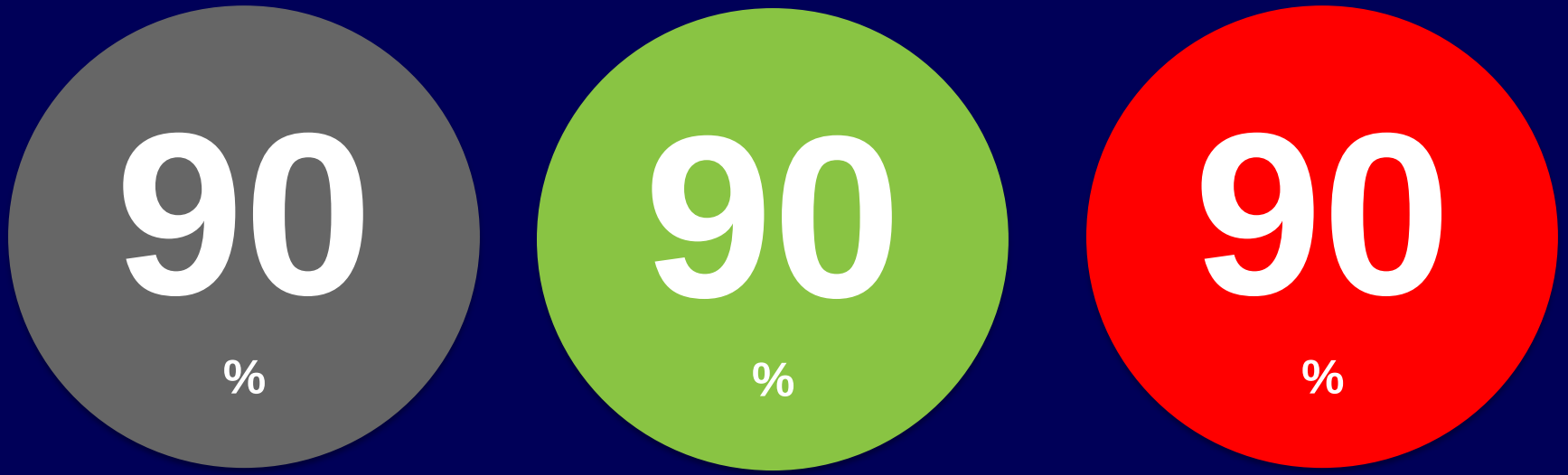


Expansion scenarios: no ART, current coverage, expansion to 90% WHO 2013 by 2020





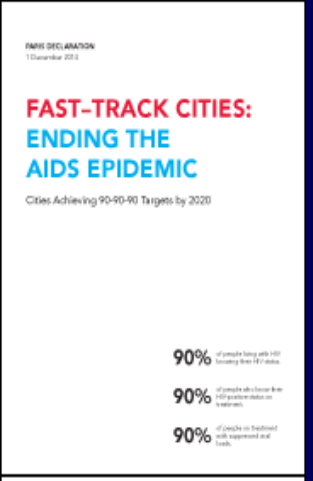
UNAIDS treatment targets: getting to scale



tested

on treatment

virally suppressed



Fast Track Cities: Ending the AIDS Epidemic

- IAPAC-UN HABITAT-UNAIDS initiative
- Cities achieving 90-90-90 targets by 2020
- Cities are pioneers in our response
- Paris Declaration (December 1st 2014)
  - End AIDS epidemic
  - Put people at center
  - Address causes of risk, vulnerability, and transmission
  - Use AIDS response for social transformation
  - Build and accelerate appropriate local response
  - Mobilize resources for integrated public health and development
  - Unite as leaders

IAPAC

Thank You

Biomedical interventions for the prevention of HIV transmission