



**West Wing,
Tshepong Hospital**



**East Wing,
Klerksdorp Hospital**

Does Test and Treat take attention from ill patients?

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Complex

FCP(SA), FRCP(Lon), DTM&H, Dip HIV Man(SA), DCH(SA)

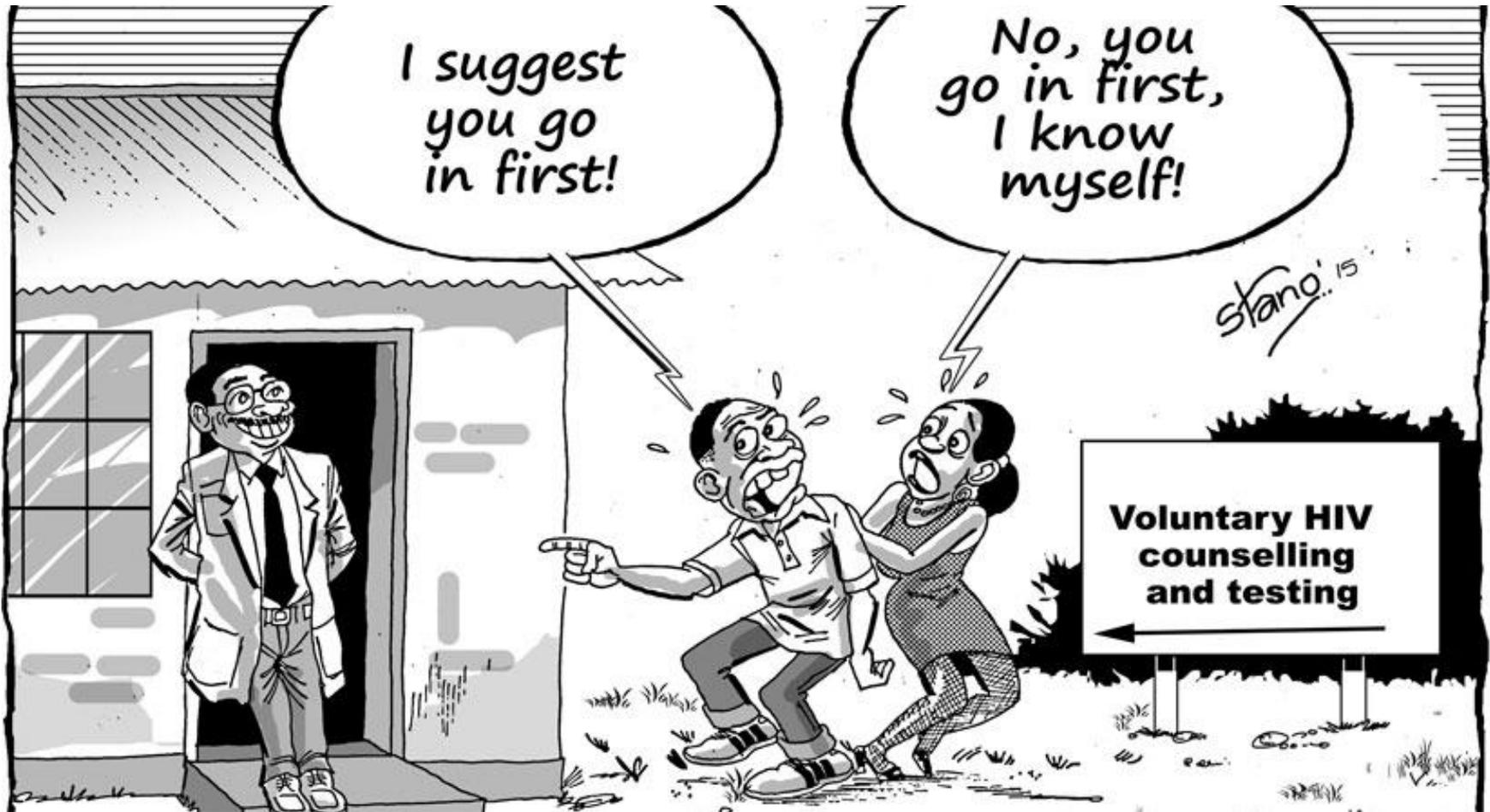
Disclosure

- Full time state employee
- Well paid (I think!)
- Not an ID, HIV, public health, community health specialist.
- A Clinician dabbling in most aspects of clinical care.
- No perverse incentives
- No pharmaceutical industry support.

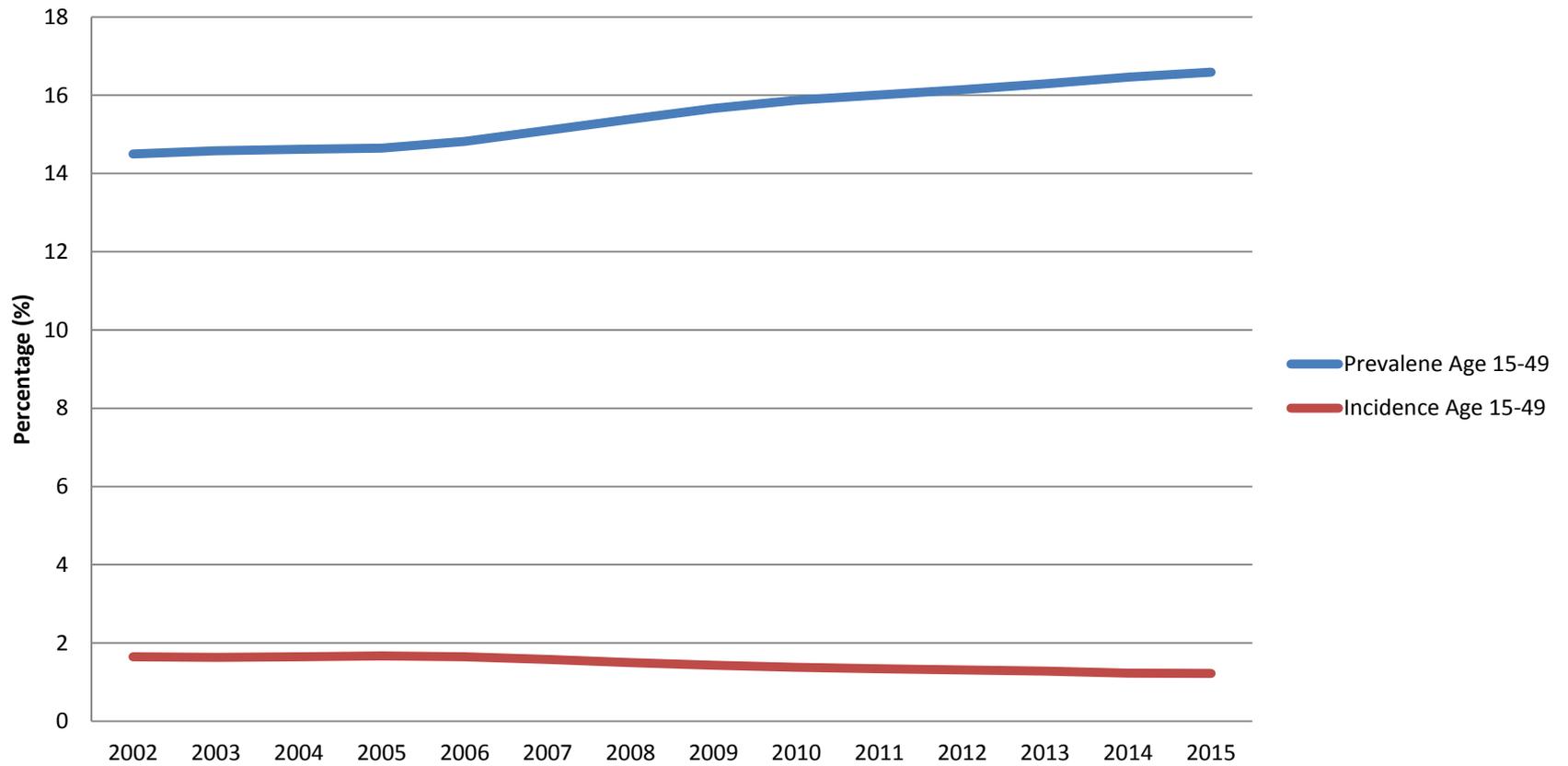
Overview

- Trends
- Test and Treat models
- HIV cascade
- 90/90/90 WHO targets
- Diagnosis
- Linkage to care
- Treatment
- Competing epidemics
- Conclusions

Are we winning?

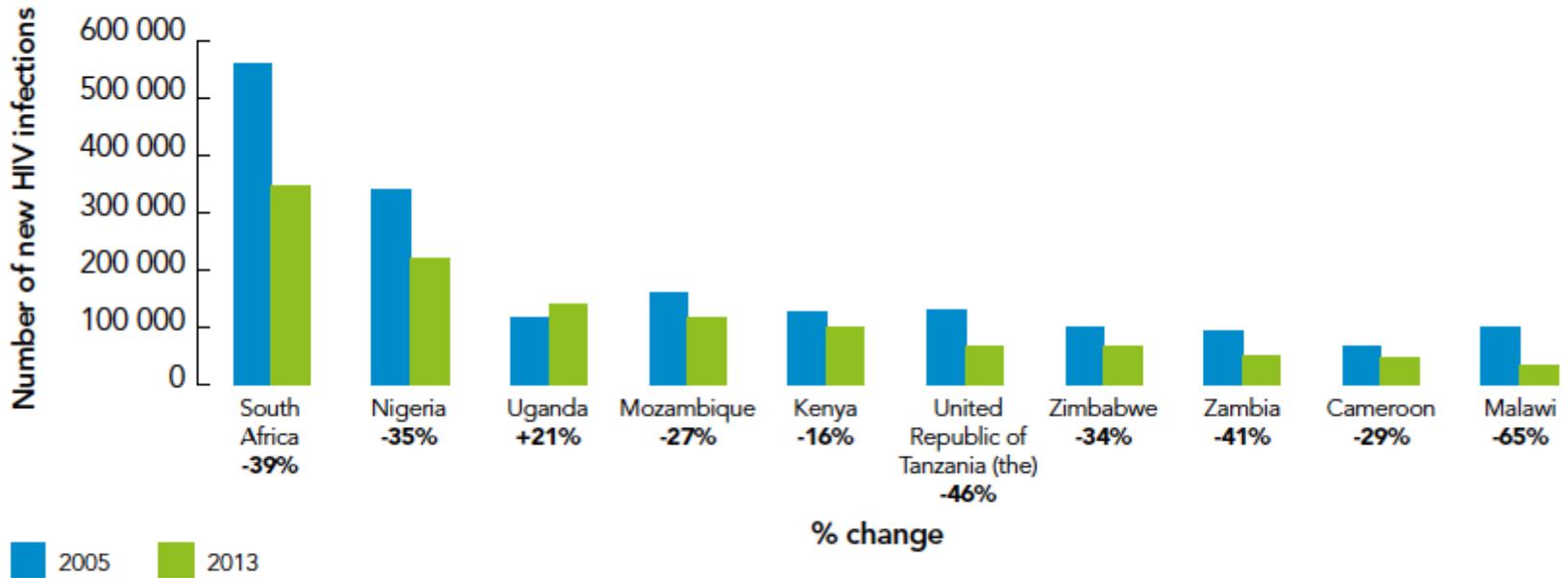


HIV Prevalence and Incidence 2002-2015



WHO Gap Report 2014

Trends in new HIV infections for top 10 countries in sub-Saharan Africa, 2005 and 2013



Source: UNAIDS 2013 estimates.

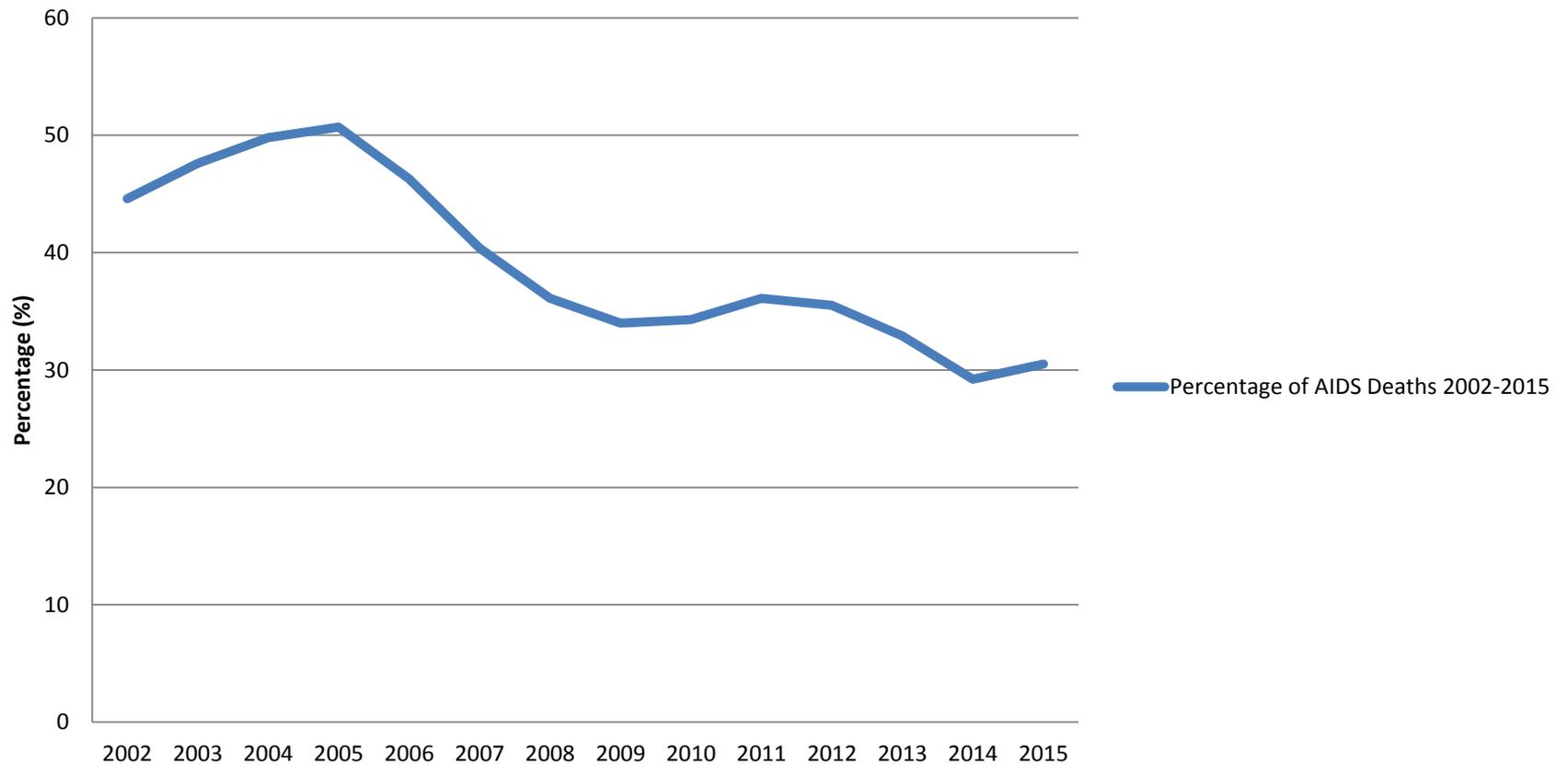


**Statistics
South Africa**



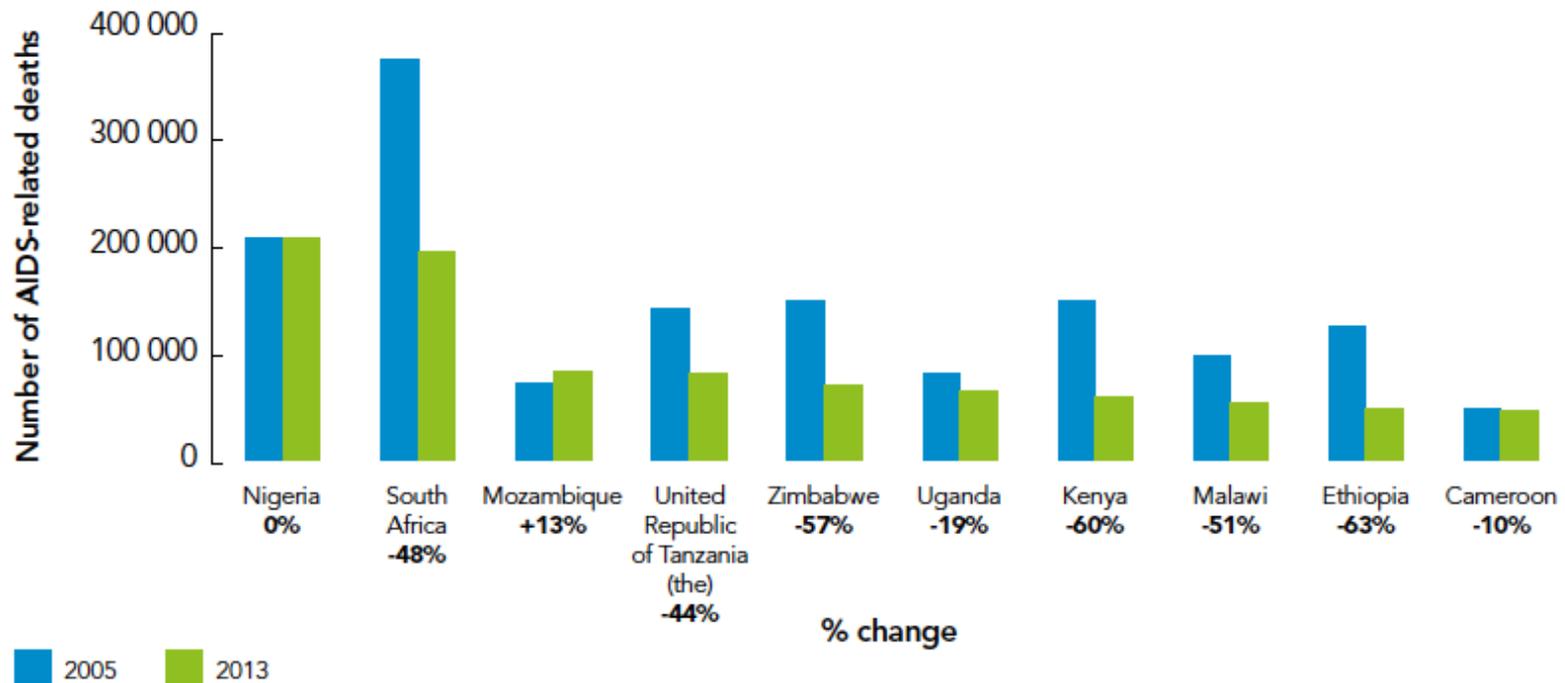
2015

Percentage AIDS Deaths of all deaths 2002-2015



WHO Gap Report 2014

Trends in AIDS-related deaths in sub-Saharan Africa, 2005 and 2013



Source: UNAIDS 2013 estimates.

Are we there yet?

- **Evolution of WHO ART guidelines**
 - 2006: <200 /stage 4/single agent/tail etc
 - 2009: <350 stage III/B—B+ option
 - 2013: consolidated guideline <500/all TB/all preg/hep B with severe liver disease
 - 2016: irrespective of CD4
 - 2 papers TEMPRANO & START support



HIV/AIDS Programme

GUIDELINES



CONSOLIDATED GUIDELINES ON
**THE USE OF
 ANTIRETROVIRAL DRUGS
 FOR TREATING AND
 PREVENTING HIV INFECTION**

RECOMMENDATIONS FOR A PUBLIC HEALTH APPROACH
 JUNE 2013



GUIDELINES



**GUIDELINE ON WHEN
 TO START ANTIRETROVIRAL
 THERAPY AND
 ON PRE-EXPOSURE
 PROPHYLAXIS FOR HIV**

SEPTEMBER 2015



World Health Organization

HIV/AIDS Programme
 Strengthening health services to fight HIV/AIDS

**ANTIRETROVIRAL THERAPY
 FOR HIV INFECTION IN ADULTS
 AND ADOLESCENTS:**
 Recommendations
 for a public health approach

2006 revision

HIV/AIDS Programme
www.who.int/hiv/aids

**ANTIRETROVIRAL THERAPY
 FOR HIV INFECTION IN ADULTS
 AND ADOLESCENTS**
 Recommendations for a public health approach
 2010 revision



What is Test and Treat?

- All HIV positive patients are started on ART irrespective of CD4. At time of first HIV diagnosis
- Early treatment → better outcomes-START and TEMPRANO studies reported in 2015.
- Various mathematical models predict reducing incidence of new infections—within 10-50 years from 2% to 0.3%

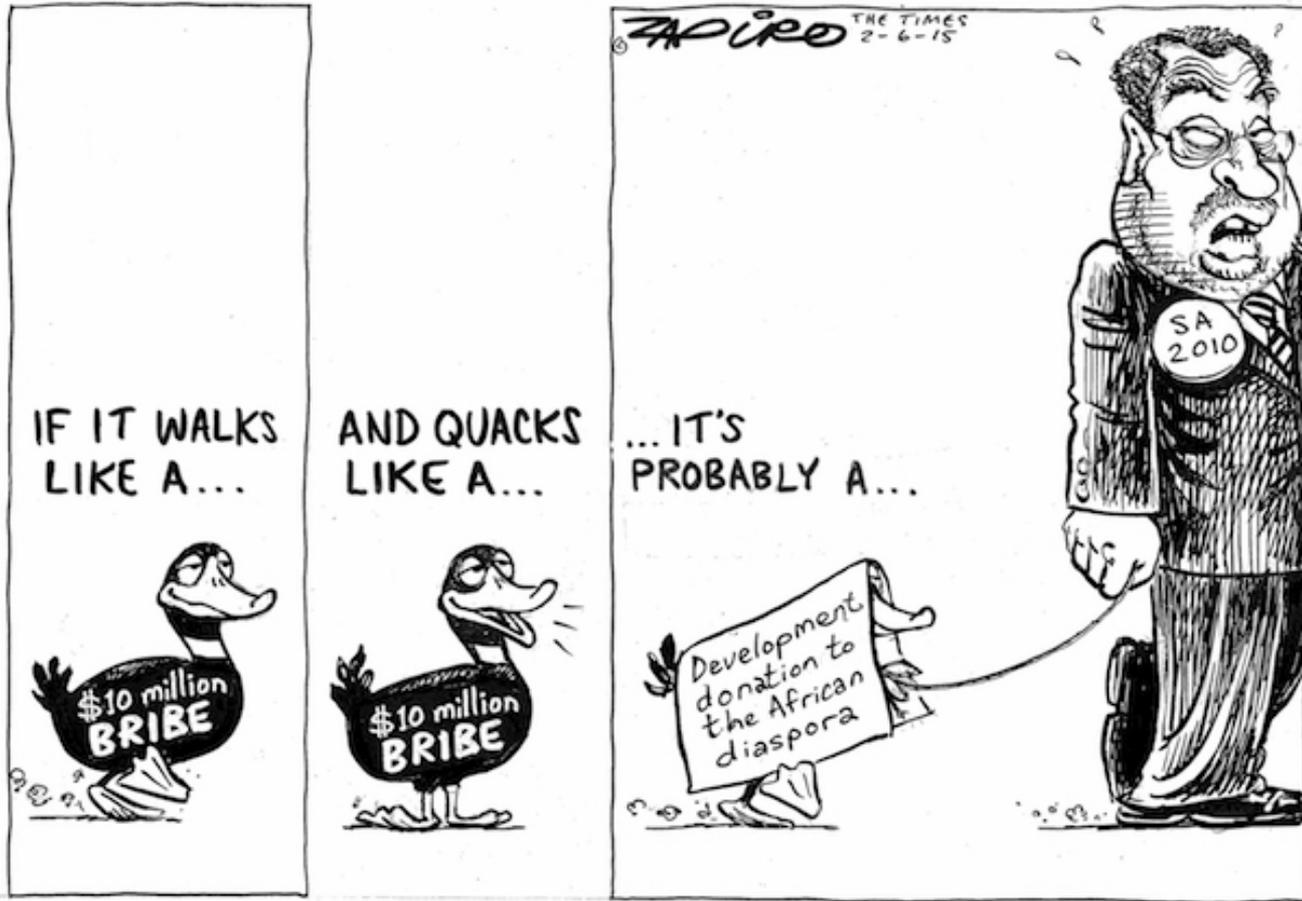
Before 2010



Before 2010

- During 2000- advent of Lop/rit. Blower et al developed a model that predicted if 90% of infected individuals in gay community of San Francisco were started on ART infection rates would be reduced by 2010—provided safe sex practices were maintained (Science Jan 28, 2000 Vol 287)
- In 2002 Hernandez, Blower et al concluded that combination ART can be used as preventative tool and a high prevalent epidemic could be eradicated. (Lancet Infect Dis 2002; 487-93)
- In 2009 Granich et al used data from SA and predicted that if universal testing and immediate ART could move the endemic to an elimination phase by 2016. (The Lancet. Vol 373 Jan 3, 2009)

After 2010



After 2010

- Safer ART (d4T removed and Tdf replaced) also fixed drug combinations became available
- Successes of MTCT and a land mark study *“Prevention of HIV-1 With Early Antiretroviral Therapy” HPTN 052* by Cohen et al in 2011
Showed a 96% reduction in HIV acquisition amongst discordant couples. *(NEJM Aug 2011, 11 vol 365 no.6)*
- Both led to further impetus in concept of test and treat to reduce new infections

- 2011 Gardener et al described the spectrum of care = cascade of care/continuum of care and used this model to the Test and Treat hypothesis”
(HIV/AIDS CID 2011, 15 Mar no:52)
- 2012 Hontelez et al developed 9 models using various data from SA to predict eradication *(PLoS Med 10(10): e1001534)*
- 2013 Kretzschmar et al maintained that elimination of HIV by Test-and-Treat strategy is only feasible with ongoing additional interventions
(PNAS Sept 23, 2013 vol. 110 no. 39)

Back to the future



Current trials

- Models are an abstraction of reality and never a mirror— trials test the hypothesis.
- Number of large randomized trials are and will examine the population effect of immediate ART on HIV incidence and mortality results expected in 2018 to 2019
 - Botswana Combination Prevention Trial
 - HPTN-071 (PopART) study,
 - 12249 ANRS TasP trial
 - MaxART

HIV care continuum

HIV treatment cascade

- Described by Gardener et al in 2011
- Useful for modeling purposes
- Now adapted by various agencies
- Used by WHO for 90/90/90

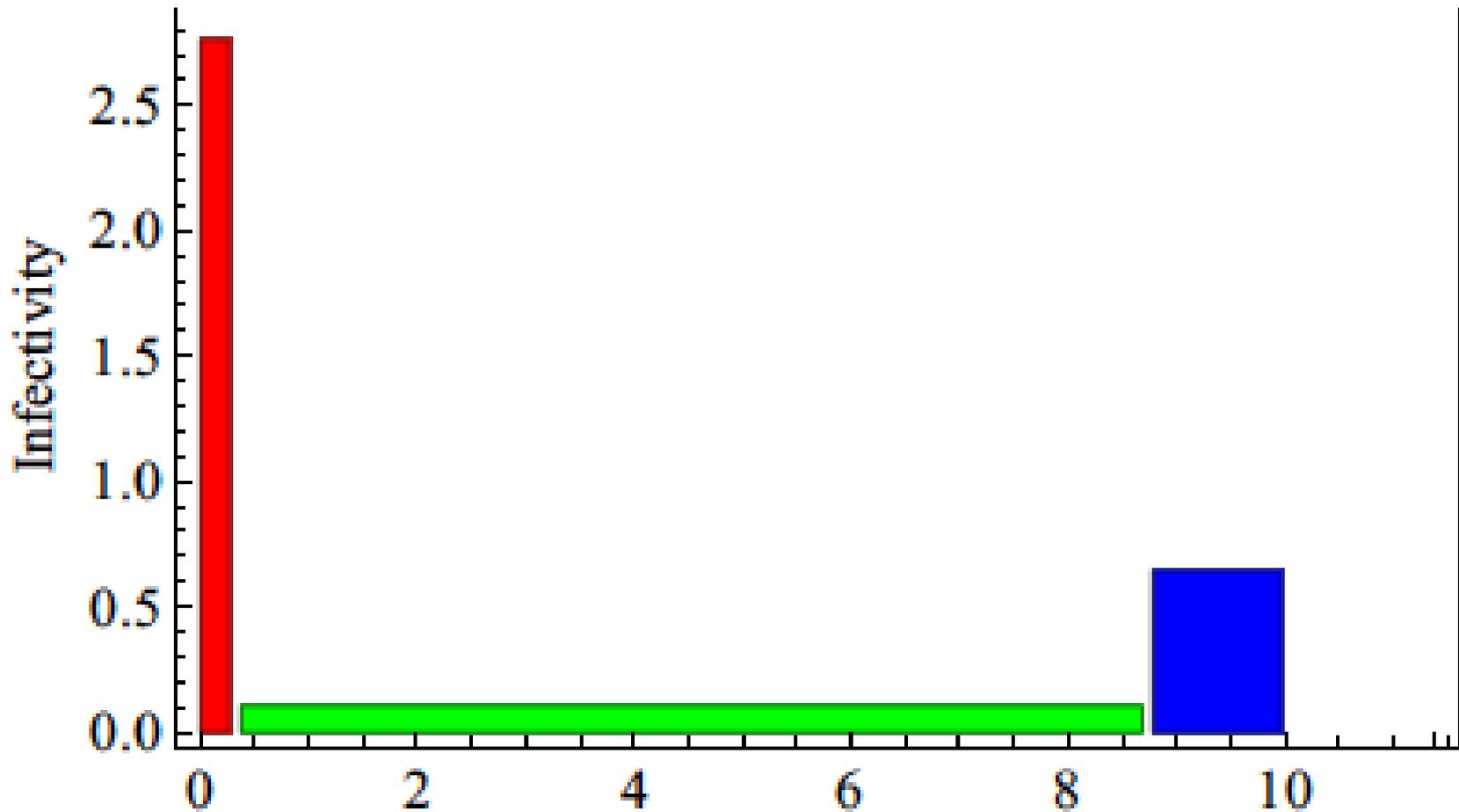
HIV CARE CONTINUUM:

THE SERIES OF STEPS A PERSON WITH HIV TAKES FROM INITIAL DIAGNOSIS THROUGH THEIR SUCCESSFUL TREATMENT WITH HIV MEDICATION



- Skarbinski et al looked at transmission risk at each stage within the continuum of care amongst HIV patients and found that risk for infection was highest amongst those in contact with undiagnosed HIV. *(JAMA Intern Med. Feb 23,2015;175(4):588-596).*
- For Test and treat strategy we must be aware of infectivity at each stage of HIV as highest risk for spread appears to be early HIV. *(pnas.130180111)*

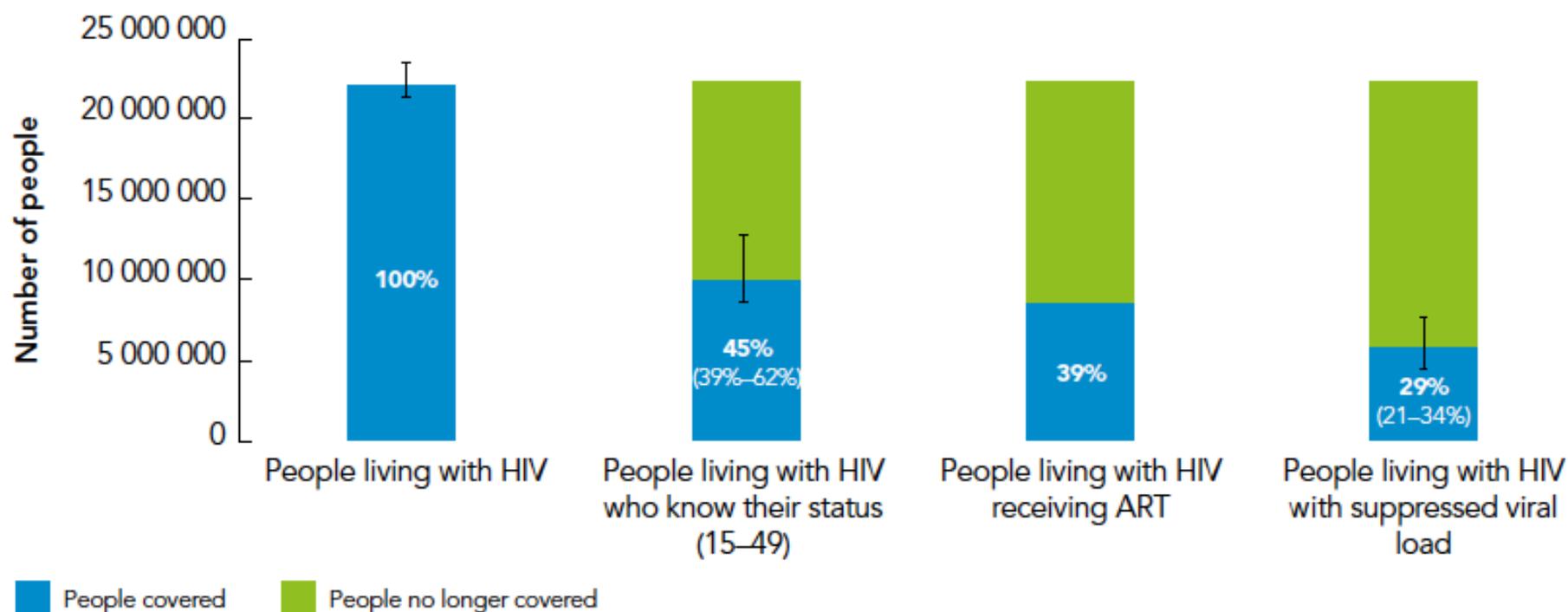
Infectivity of the different stages of infection.



Stage 1 (red): 2.76/y; stage 2 (green): 0.106/y; stage 3 (blue): 0.64/y; stage 4 (magenta): 0.0/y.

www.pnas.org/cgi/doi/10.1073/pnas.1301801111

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



Sources:

- UNAIDS 2013 estimates.
- Demographic and Health Surveys, 2007–2012 (www.measuredhs.com) and the South African National HIV Prevalence, Incidence and Behaviour Survey 2012: Shishana, O, Rehle, T, Simbayi, LC, Zuma, K, Jooste, S, Zungu, N, Labadarios, D, Onoya, D et al (2014) South African National HIV Prevalence, Incidence and Behaviour Survey, 2012. Cape Town, HSRC Press. 45% is the mid-point between the percentage of people living with HIV who are likely to know their status (tested positive in the survey and report receiving the results of an HIV test in the previous twelve months) and the percentage who tested positive in the survey who self-reported ever being tested for HIV (high bound, 62%). The low bound is denoted with 39% which is the percentage of people living with HIV receiving ART. Notes: The results of the HIV test during the survey are not known until the end of the survey process and thus are not disclosed to the respondents. Bounds do not include data from South Africa.
- Barth, RE, van der Loeff, MR, et al. (2010). Virological follow-up of adult patients in antiretroviral treatment programmes in sub-Saharan Africa: a systematic review. *Lancet Infect Disease* 10(3):155–166 and the Kenya AIDS Indicator Survey 2012: National AIDS and STI Control Programme, Ministry of Health, Kenya. September 2013. Kenya AIDS Indicator Survey 2012: Preliminary Report. Nairobi, Kenya., giving 50% weight to the work by Barth and 50% weight to KAIS 2012. Proportional bounds from Barth et al. were applied to combined value.



IAS 2015
vancouver, canada
8th IAS Conference on HIV Pathogenesis,
Treatment & Prevention 19-22 July 2015
IAS2015.ORG

Code: **MOAD01, MOAD0102**
Title: **90-90-90: Delivering on the Targets**
Date: **Monday, 20 July 2015**
Time: **16:30-18:00**
Room: **Ballroom C-D**

Can the UNAIDS 90-90-90 target be reached?

Analysis of national HIV treatment cascades

Jacob Levi¹ & Alice Raymond¹; Anton Pozniak²; Pietro Vernazza³; Philipp Kohler³; Andrew Hill²

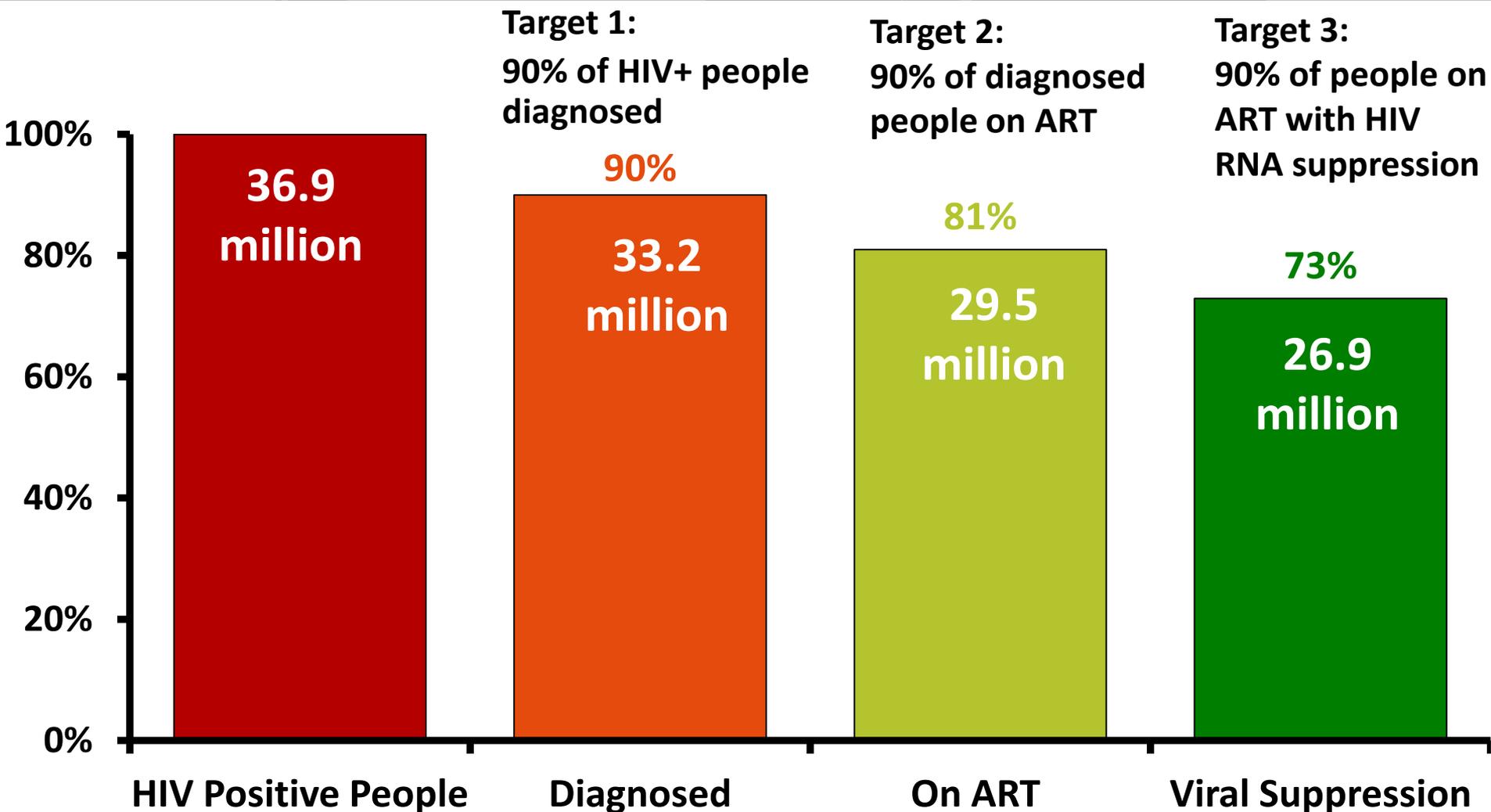
¹Imperial College London, Department of Public Health, London, United Kingdom

²St Stephens Centre, Chelsea and Westminster Hospital, London, UK

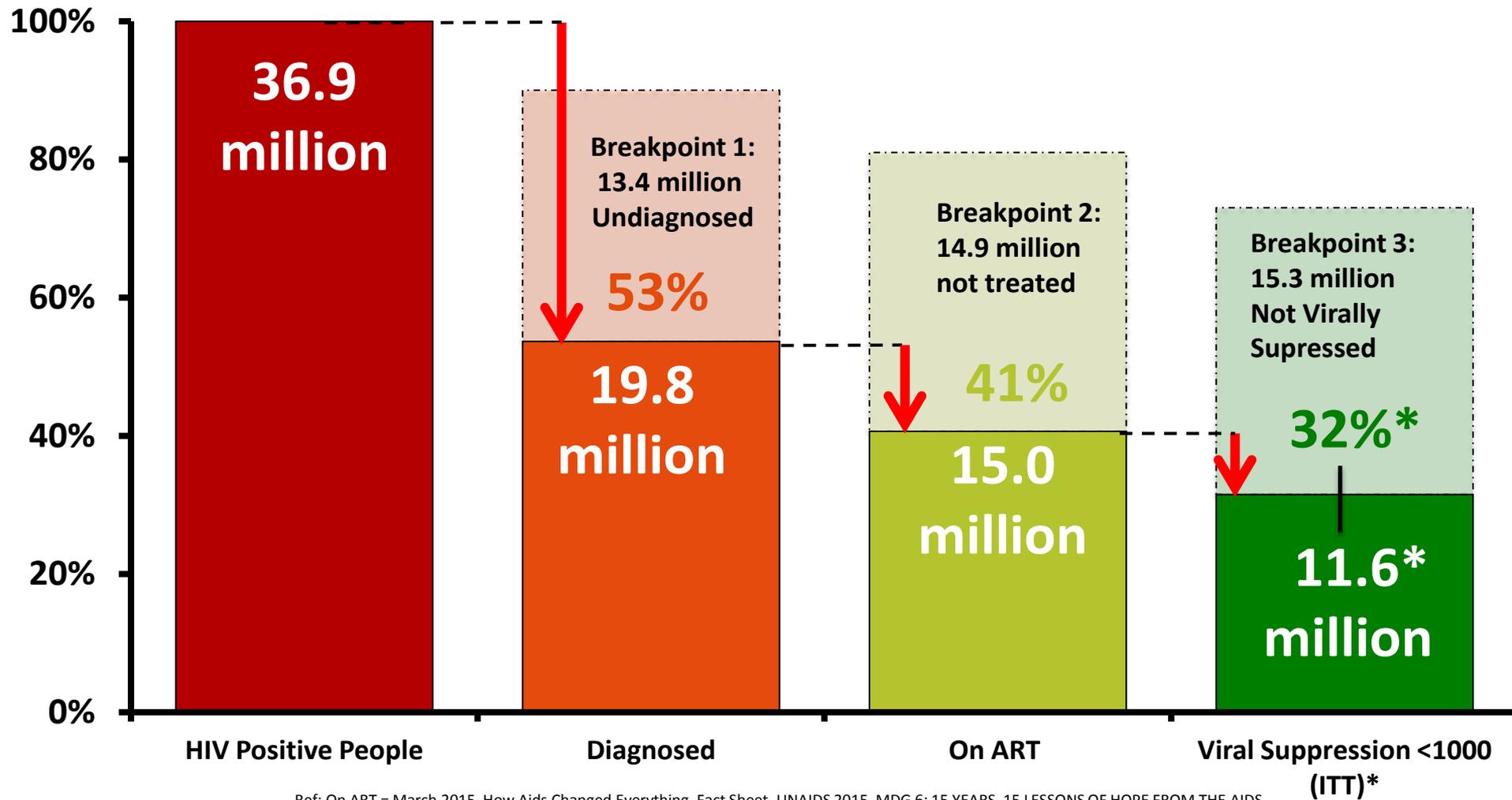
³Division of Infectious Diseases and Hospital Epidemiology, Cantonal Hospital of St. Gallen, Switzerland

UNAIDS 90-90-90:

HIV Treatment Targets for 2020 with Global Estimates (2014)

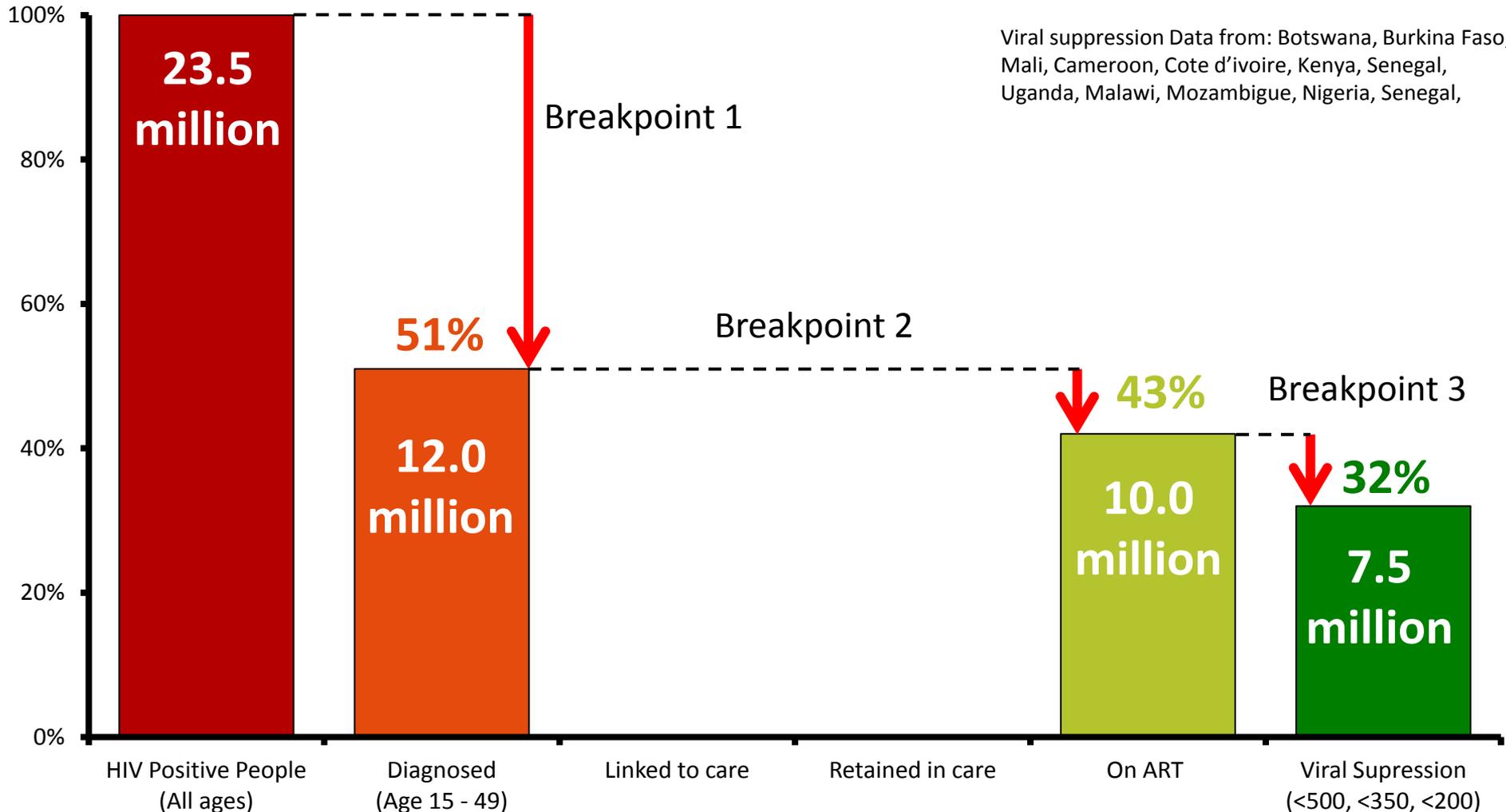


Global Estimates (2014-15) vs the Gap to reach 90-90-90 Targets



Ref: On ART = March 2015. How Aids Changed Everything. Fact Sheet. UNAIDS 2015. MDG 6: 15 YEARS, 15 LESSONS OF HOPE FROM THE AIDS RESPONSE July 2015. * Average viral suppression% Intention to Treat LMIC rate from a Systematic Review by McMahon J. et al. Viral suppression after 12 months of antiretroviral therapy in low-and middle-income countries: a systematic review." *Bulletin of the World Health Organization* 91.5 (2013): 377-385.

Cascade of HIV care – Sub-Saharan Africa 2013 (15 – 45 years old)



Diagnosis



Rates of HIV testing and diagnosis in South Africa: successes and challenges

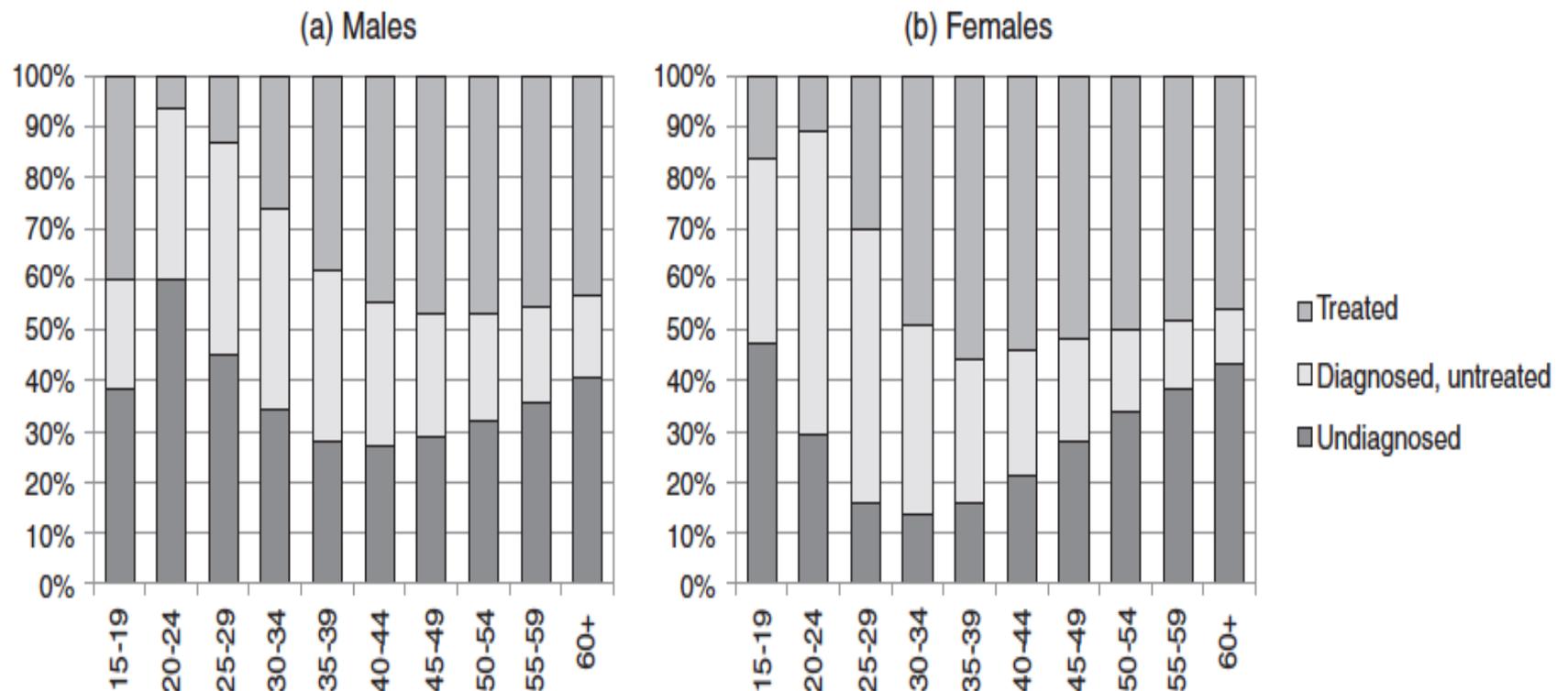


Fig. 2. Proportions of HIV-positive adults diagnosed and treated, by age and sex (2012).

Find them all!

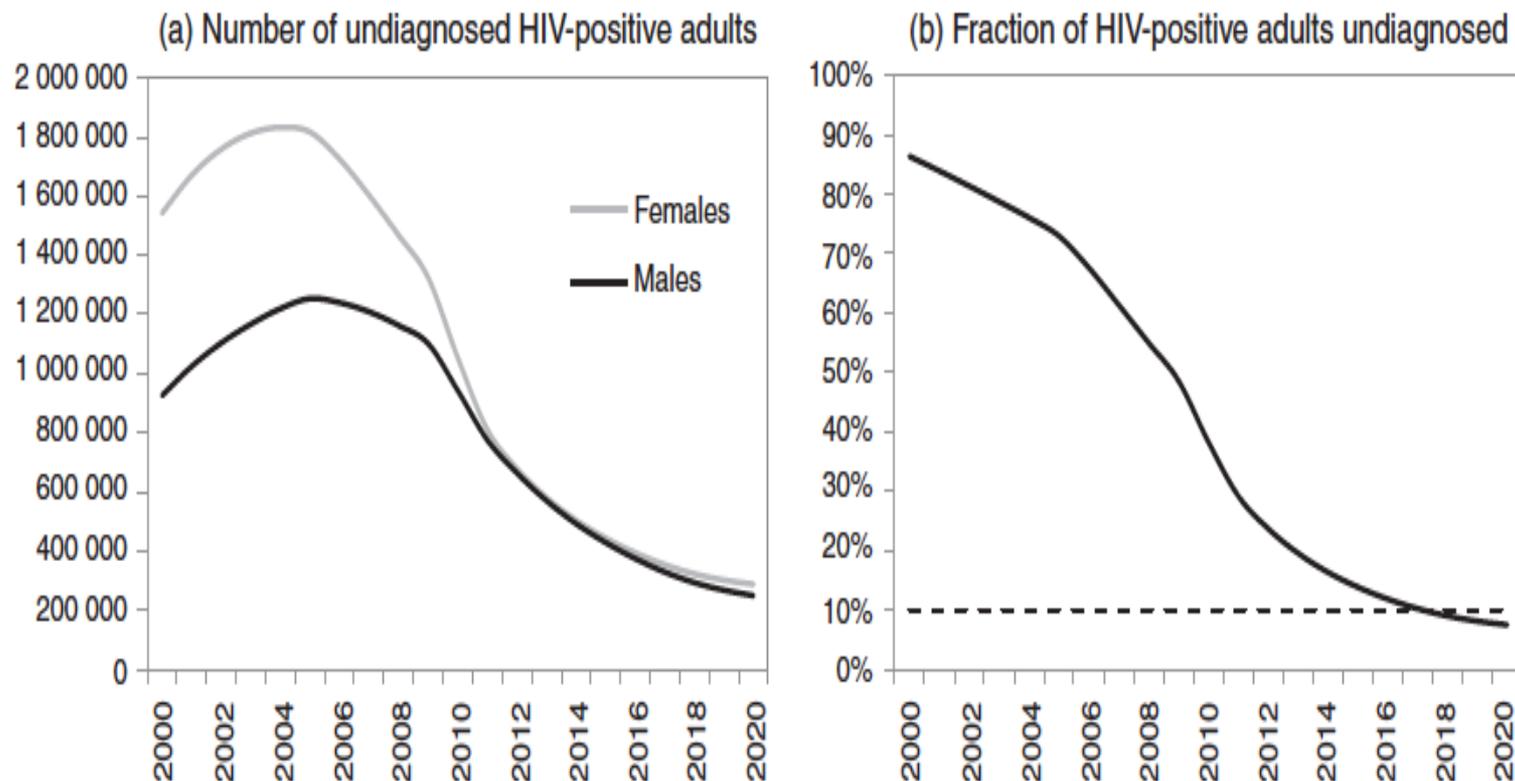


Fig. 4. Projected changes in undiagnosed HIV-positive adults. Projections are calculated assuming that the number of HIV tests performed is 10 million in each year after 2012. The dashed line in (b) represents the UNAIDS target (90% of HIV-positive adults diagnosed, equivalent to 10% undiagnosed).

Diagnosis

- Require to identify 90 % of the 6.1 million—
- Target high incidence/prevalent areas
- Lay counselors now provide HCT at clinics –few at hospital level—often volunteers “slave labor”
- Repeated testing required—yearly or biannually?
- Consider self testing.
- HCT great initiative as large numbers tested >13 million 2010-2011 –Should be ongoing and linked to treatment and—not a once off phenomena—
- PICT not done routinely at all institutions. More likely in medical wards and ante natal wards. Not routine for non-HIV diseases and less likely in surgical / trauma wards. Hospitals lack counselors in wards/poor interest among doctors.

- Although evidence for treatment of discordant couples exist---HIV is an STI---how often are partners tested?
- HIV exceptionalism—genetic disorders require entire families to be tested—yet for HIV?
- Do clinicians recommend testing of children of mothers who are HIV positive? Or mothers of children with HIV or TB?

Linkage to care

- Increased number of sites providing ART—with nurses trained on various programs
- Few new clinics—Matlosana with population of 470 000 and HIV prevalence of 14% has 16 clinics—only one new clinic built recently a few others renovated—
 - Anticipated number of HIV positive at each clinic 4000 which equates to 200 per day
- Larger skill network servicing the privileged - public vs private debate
- Poor use of Tech: No internet or electronic access—no unique identifier
- Simple tools like health passport may assist

Treatment



Trends in CD4 Count at Presentation to Care and Treatment Initiation in Sub-Saharan Africa, 2002–2013: Meta-analysis

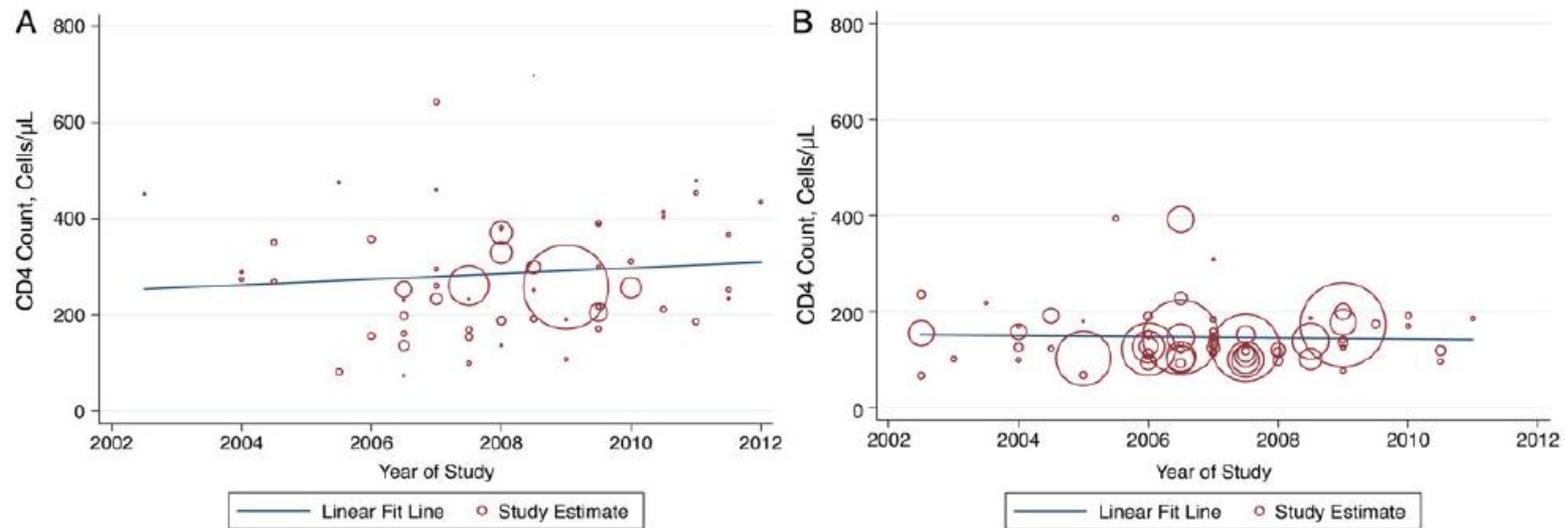
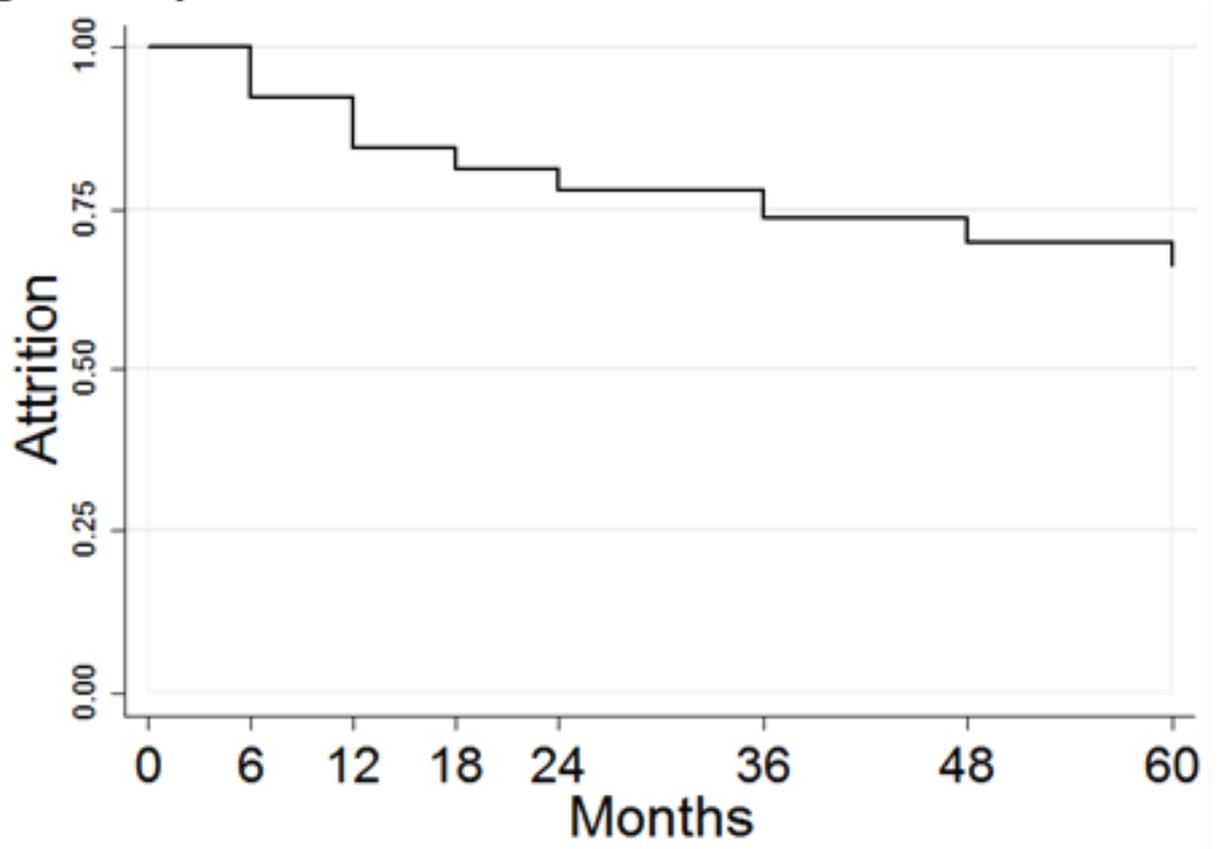


Figure 2. Temporal trends in CD4 count at presentation to care (A) and initiation of antiretroviral therapy (B) in sub-Saharan Africa during 2002–2013.

**RETENTION ON ANTIRETROVIRAL THERAPY IN SOUTH AFRICA:
 EVIDENCE FROM A SYSTEMATIC REVIEW 2008-2013**

Figure 2. Kaplan Meier curve of time to attrition



	0 mos	12 mos	24 mos	36 mos	48 mos	60 mos
N	214,088	196,835	122,967	102,143	93,046	86,746
Retention	1	0.8344	0.7661	0.7235	0.6862	0.6186

Treatment

- With new guideline 90% of 6 million must be started—took us 12 years to get 3 million and with lessons we learnt should take another 8 to reach target
- Ensure retention—seems that 30-40 % are lost at 5 years (HERO Policy Brief Jun 2014)
- Ensure adherence
- Risk of osteoporosis on Tdf? Crumbling bones in older patients?
- Reduce adverse effects—Efv was commonest reason for ART default/change in ART.

Virological suppression



Switching to second line most accurate if done with 2 repeated Viral loads

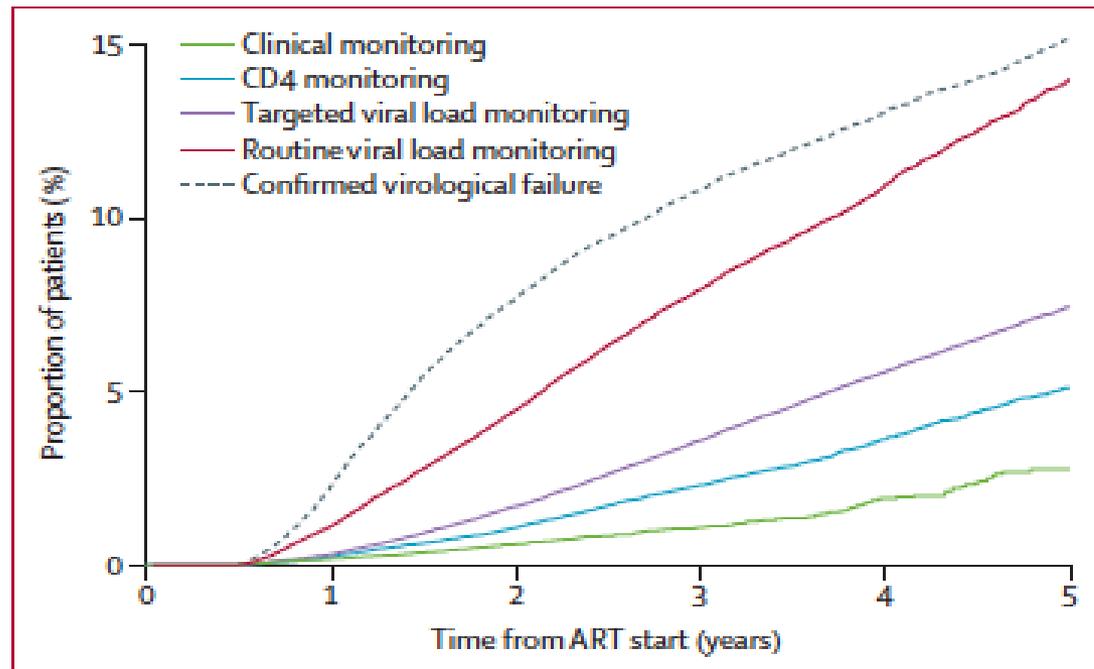


Figure 1: Cumulative probability of confirmed virological failure and switching to second-line ART

Confirmed virological failure was defined as two values above 1000 copies per mL within 1 year.

- *A D Haas et al Lancet HIV* 2015; 2: e271–78

Virological suppression

- Drugs with high threshold to resistance and minimal side effect profile to be used
- One size fit all strategy—need to identify those that may require different combination or dose adjustments. (Efv and slow metabolisers with low weight)
- Monitoring of viral load
 - Sentinel Surveillance data to see if resistance becomes a major issue in areas of high ART uptake
- Acting on viral loads— “Waiting for Godot”
- Need systems to identify and manage these and to consider Link results to m health—Ensure that patient directed action--

Competing epidemics will they be ignored?

- Violence/trauma
- Diabetes
- Obesity
- Hypertension
- Cardiovascular diseases
- Malignancies
- Chronic lung diseases
- Chronic liver diseases
- Neurological deterioration/diseases

- All (almost) HIV positive patients will require ART at some stage—avoid presentation when ill
- Delays result in admissions or other complications—more costly (numerous studies)
- Drug stock outs –multiple levels
- Treating all using reengineered PHC staff is possible—innovative drug distribution system reqd.
- Funding sources need co-ordination—ideally within a national body of various role players
 - In Dr KK have NGO providing MDR training—another secured funding to do the same.

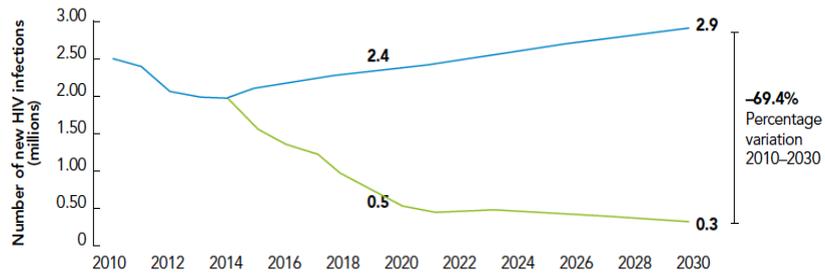
- With increased cost—other sources of funding required—the tendency with increased treatment cost—at the expense of prevention—this will be counterproductive
- With treating all HIV—will expansive treatments for other non HIV conditions be compromised?—interesting-- this was argument prior to ART amongst both clinicians and politicians.

Final word

- Treat Hard. Treat Now
 - Stop AIDS
 - Reduce new infections
 - Reduce disability
 - Prevent death
- Procrastination → those not on ART will attend a health center---ill and using resources, with social breakdown as more dysfunctional families may result.

WHO *and* Our Target

Ending AIDS scenario: new HIV infections (2010–2030)



— Constant coverage (%) — Expanded coverage (%)

Source: UNAIDS 2014 estimates.

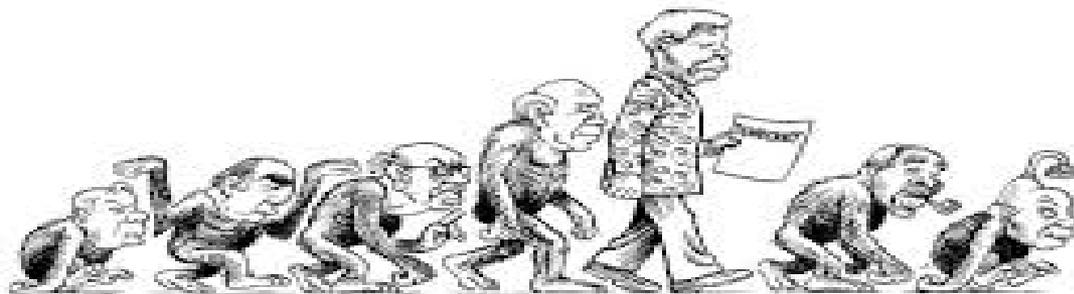
Ending AIDS scenario: AIDS-related deaths (2010–2030)



— Constant coverage (%) — Expanded coverage (%)

Our moral compass

Nelson Mandela said, "The more we lack the courage and the will to act, the more we condemn to death our brothers and sisters, our children and our grandchildren. When the history of our times is written, will we be remembered as the generation that turned our backs in a moment of a global crisis or will it be recorded that we did the right thing?"



..... ZAPIRO