



Antiretroviral Treatment in South Africa (Immediate vs Delayed Initiation)

South African Medical Association Conference

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NDOH Consolidated HIV Guidelines on your mobile or tablet!!!

- Download for iPhone/iPad on App Store
 - Search '**HIV Clinical Guide**'
 - Add 'South Africa' 'TOMPSA'
- Download for Android
 - Search '**HIV Clinical Guide**'
 - Add 'South Africa' 'Open Medicine Project'





Outline

- HIV Epidemiology
 - Global
 - South Africa
- HIV response
 - Fast Track 90-90-90
 - South Africa
- Rationale for ART scale up
 - Public health benefit - Treatment as prevention
 - Individual benefit - Immediate vs Delayed ART – Test and Treat
 - Challenges for Test and Treat
 - Global and national policy
 - WHO guidelines, Vancouver statement, SA guidelines
- NDOH Consolidated HIV Clinical Guidelines & App
- Conclusion & Take Home Messages





HIV EPIDEMIOLOGY





Global estimates for adults & children living with HIV - 2014

People living with HIV	37 million [34.3 million – 41.4 million]
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New HIV infections	2 million [1.9 million – 2.2 million]
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Deaths due to AIDS	1.2 million [1.0 million – 1.5 million]
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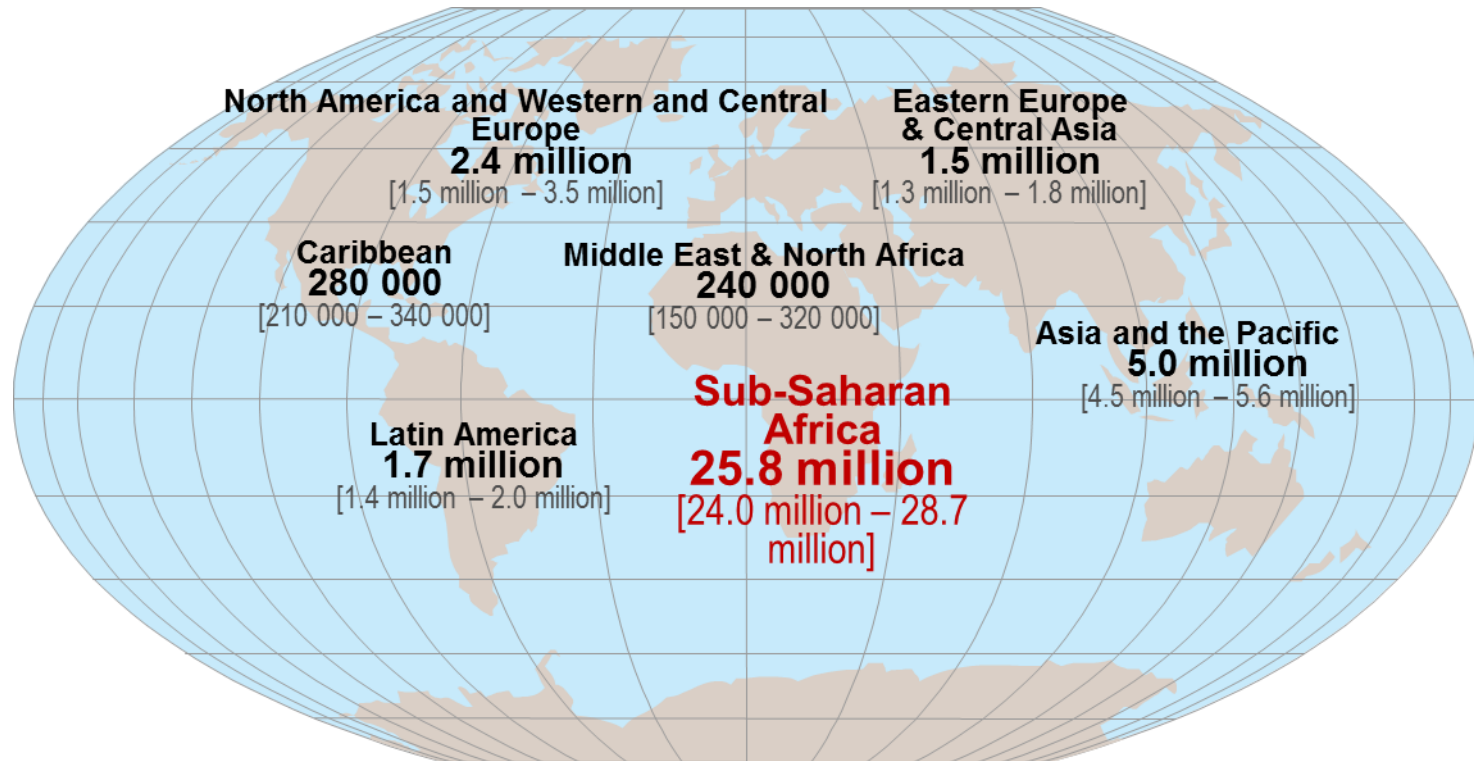
This means approximately:

- 5,600 new HIV infections a day
- 66% are in sub-Saharan Africa
- 600 are in children <15 years of age
- 5,000 are in adults 15+ years of age, of whom:
 - 48% are among women
 - 30% are among young people (15-24)





Adults and children estimated to be living with HIV - 2014



Total: 37 million [34.3 million – 41.4 million]

HIV prevalence rising as a result of ART & reduced mortality and continuing HIV transmission (HIV incidence falling slowly)

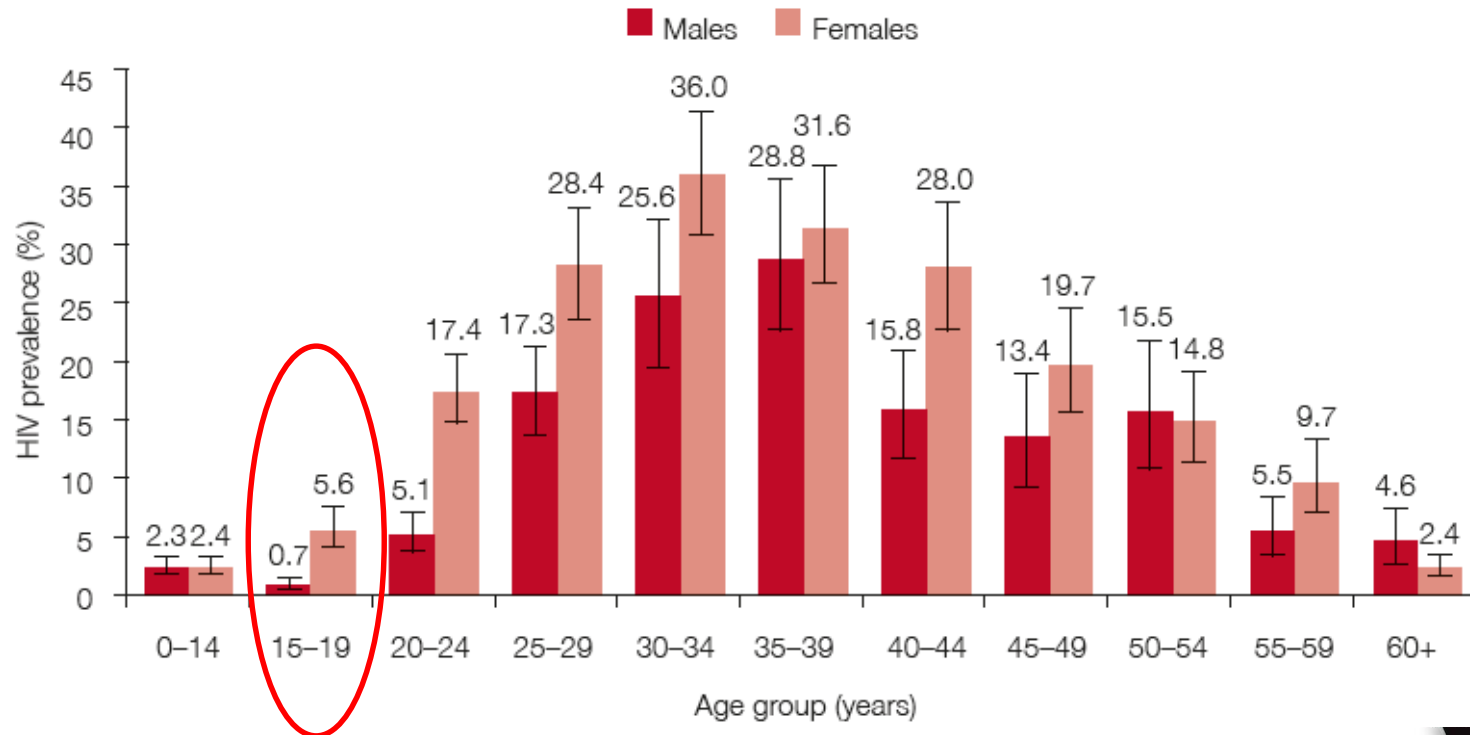




National HIV Prevalence

- Men: 9.9% (est. 2,531,000)
- Women: 14.4% (est. 3,873,000)

HIV prevalence by sex and age, South Africa 2012

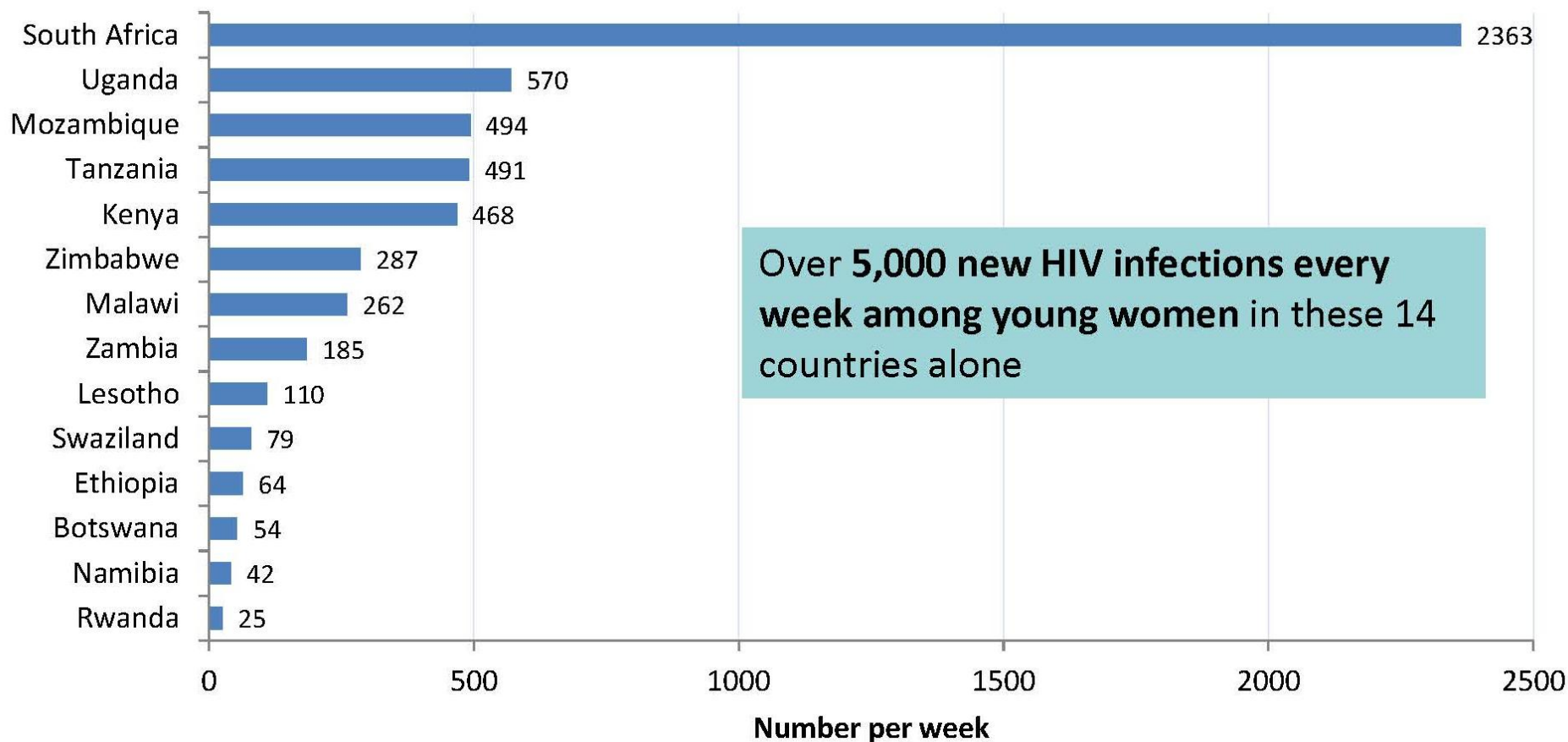


HIV prevalence up to 8 times higher in adolescent girls 15-19 compared to boys the same age





Estimated new HIV infections *per week* in young women (aged 15-24) in East and Southern Africa - 2012



Source: UNAIDS 2013





Overall Context

- 6.4 million PLHIV – 12% of population in 2013
- 74,083 teenage pregnancies per year
- 2.4 million children orphaned due to AIDS
- Largest ART programme in the world – over 3 million people on treatment
- Over 600,000 people initiated on ART annually, but LTFU rate is 30-40%
- In FY 15/16, over 80% of funding for HIV came from government; rest is from development partners (PEPFAR, GFATM...)
- Strong political leadership on HIV
 - President Zuma lists HIV & TB top of health & development priorities
 - Deputy President Ramaphosa Chair of SANAC
 - Minister Motsoaledi first to adopt 90-90-90 for HIV & TB

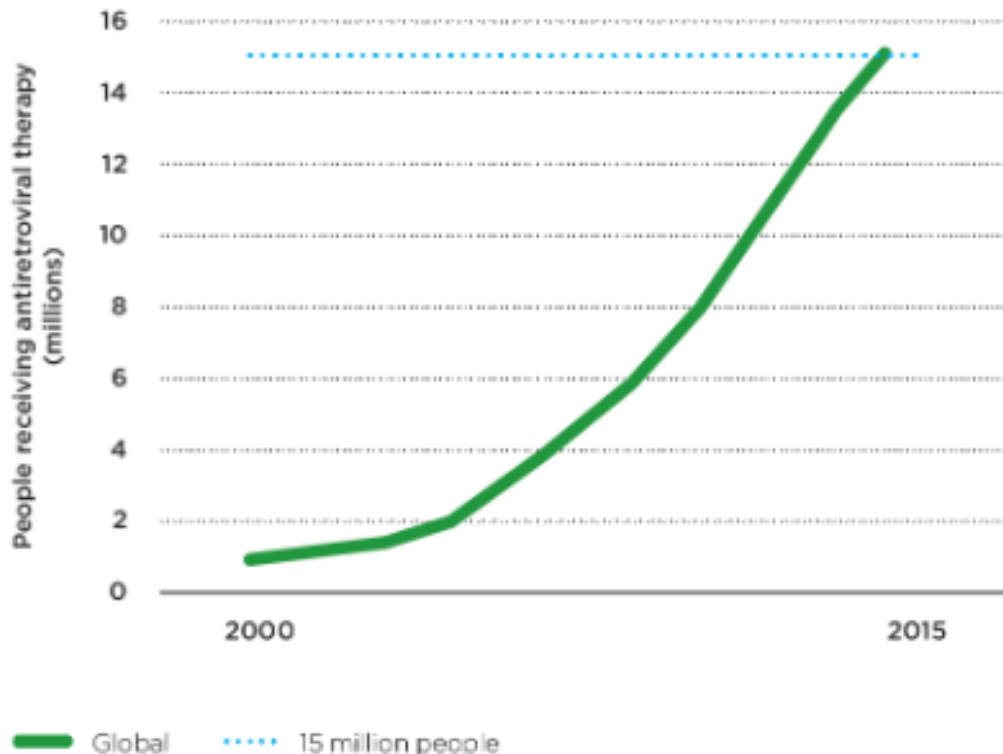






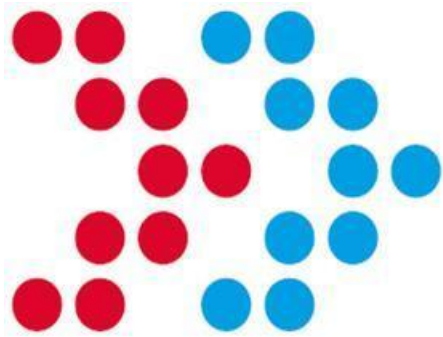
Global ART coverage - 2015

Number of people receiving antiretroviral therapy, 2000–2015



Great success story but how do we take it forwards?





FAST-TRACK

ENDING THE AIDS EPIDEMIC BY **2030**





Fast Track Targets

Ending the AIDS epidemic by 2030

by 2020

90-90-90

Treatment

500 000

New infections among adults

ZERO

Discrimination

by 2030

95-95-95

Treatment

200 000

New infections among adults

ZERO

Discrimination





Ambitious, but achievable, new targets

90%

diagnosed

90%

on treatment

90%

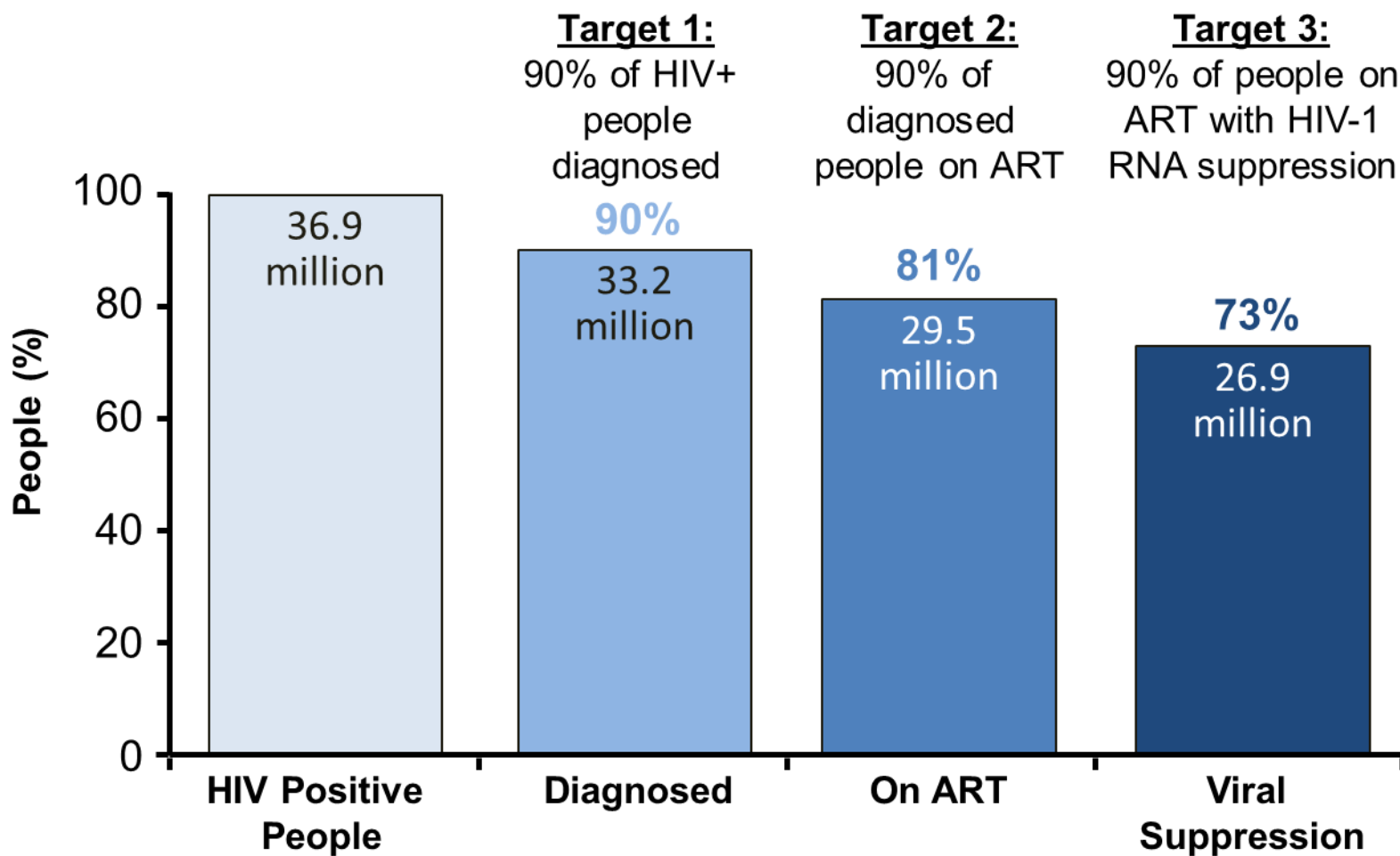
virally suppressed

Combines HIV counselling & testing; access to combination prevention; treatment & treatment success



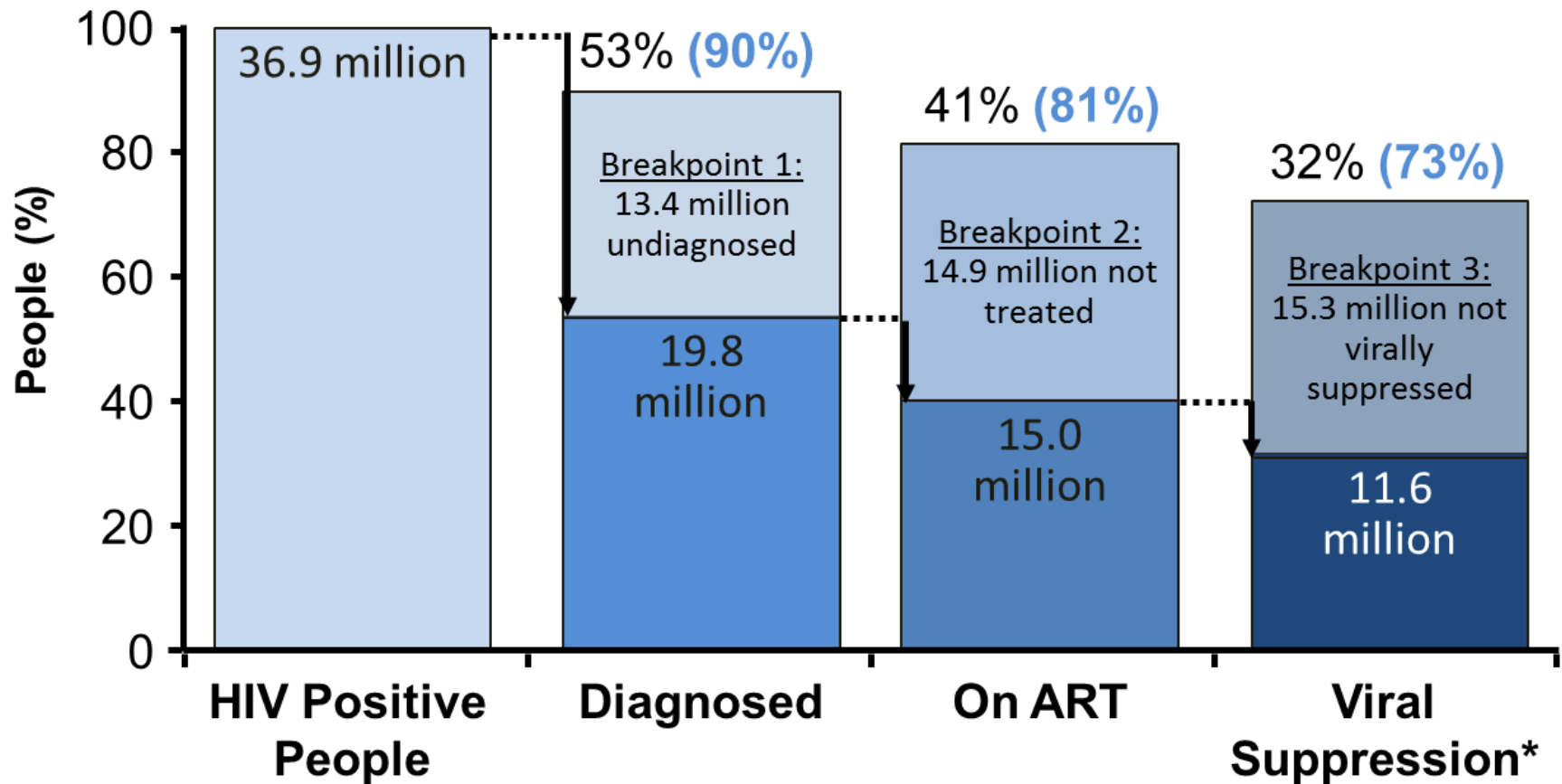


Global Fast Track 90-90-90 Treatment Cascade Targets





UNAIDS: 90-90-90 Global Estimated Gaps



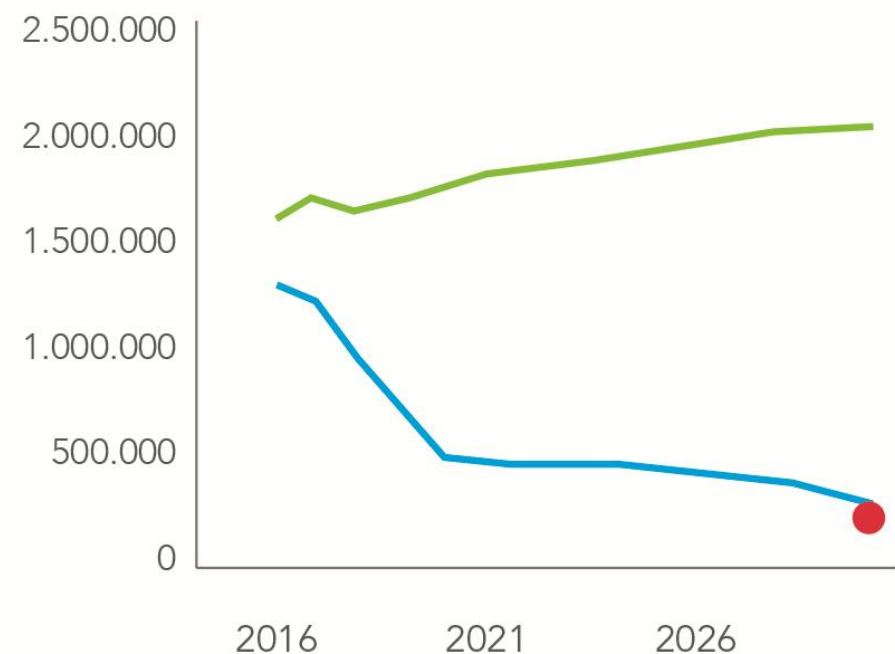
*HIV-1 RNA < 1000 copies/mL.





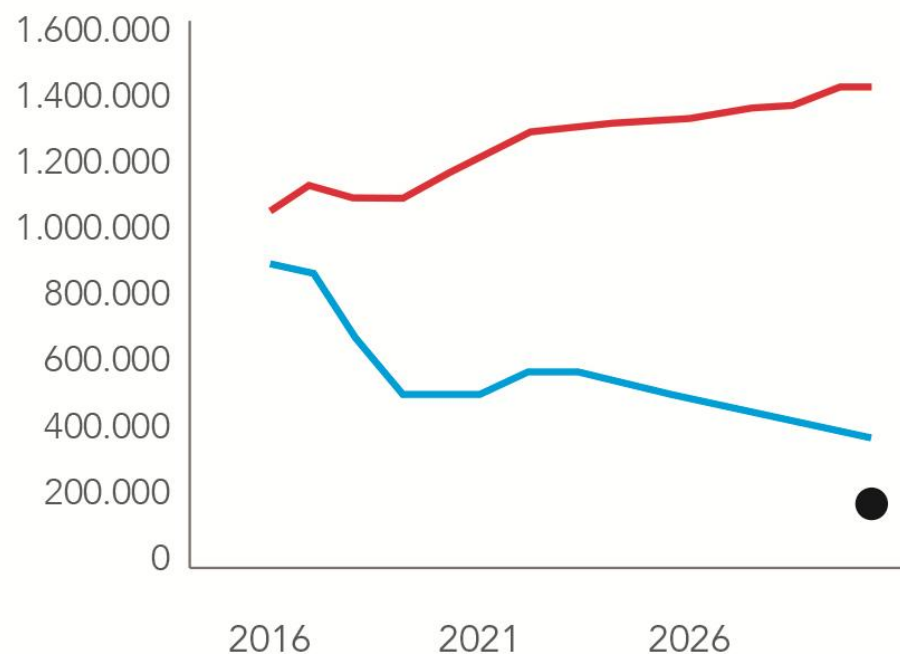
Impact of ambitious new targets on HIV infections and AIDS-related deaths, 2016-2030

New HIV infections



— 2020 Goal — Constant Coverage
● Goal

AIDS-related deaths



— 2020 Goal — Constant Coverage
● Goal



What Fast Track by 2020 means in South Africa

90-90-90 for HIV:

- 6.4 million PLHIV
- **1st 90** - 5.7 million PLHIV know their HIV status
- **2nd 90** - 4.1 million PLHIV who know their status & *who are eligible* are on treatment
- **3rd 90** - 3.7 million PLHIV on treatment with suppressed viral loads

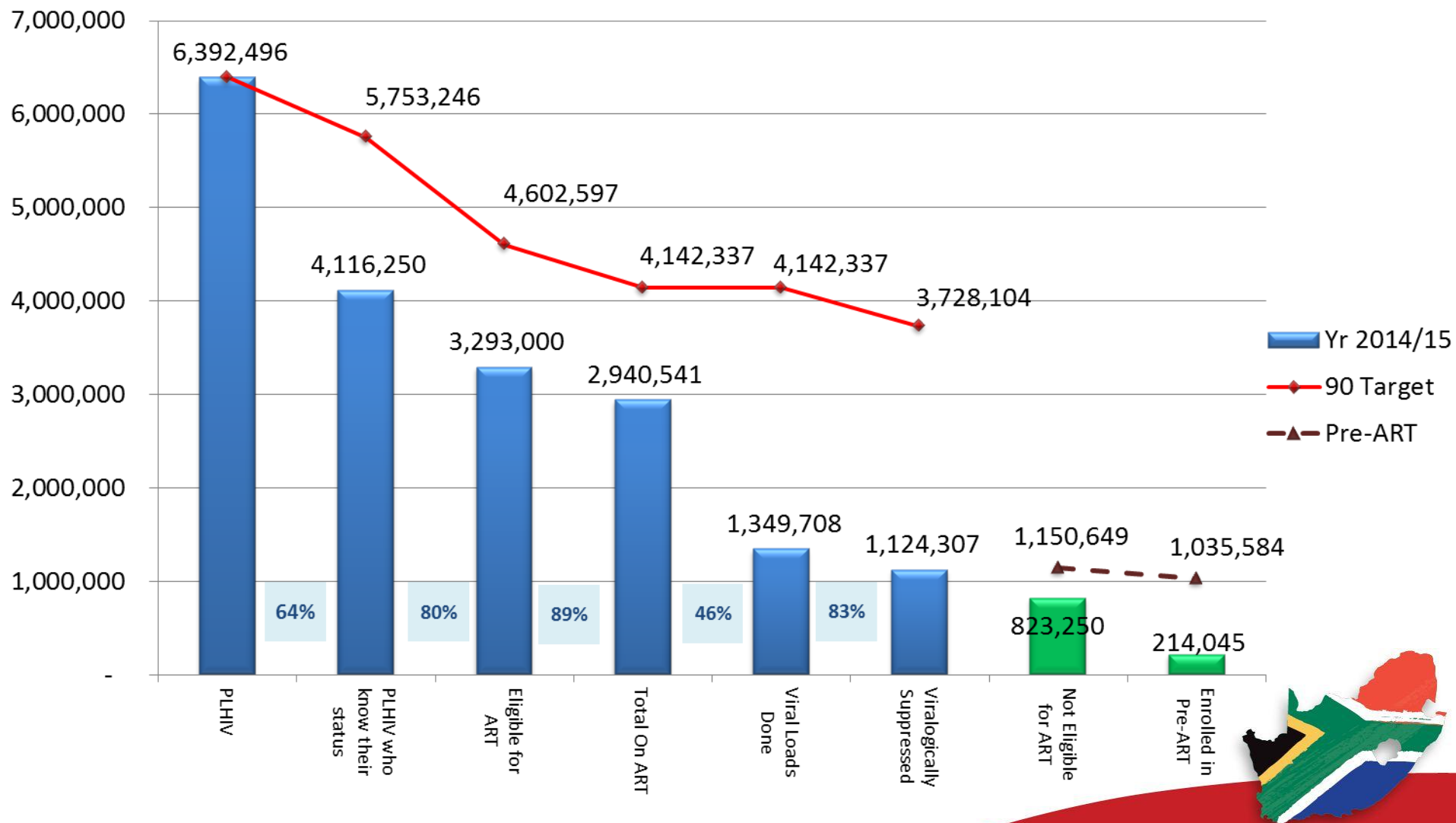
Reduce the annual number of new HIV infections by 150,000





What Fast Track by 2020 means in South Africa

Adult (15 years and older) HIV Care and Treatment Cascade

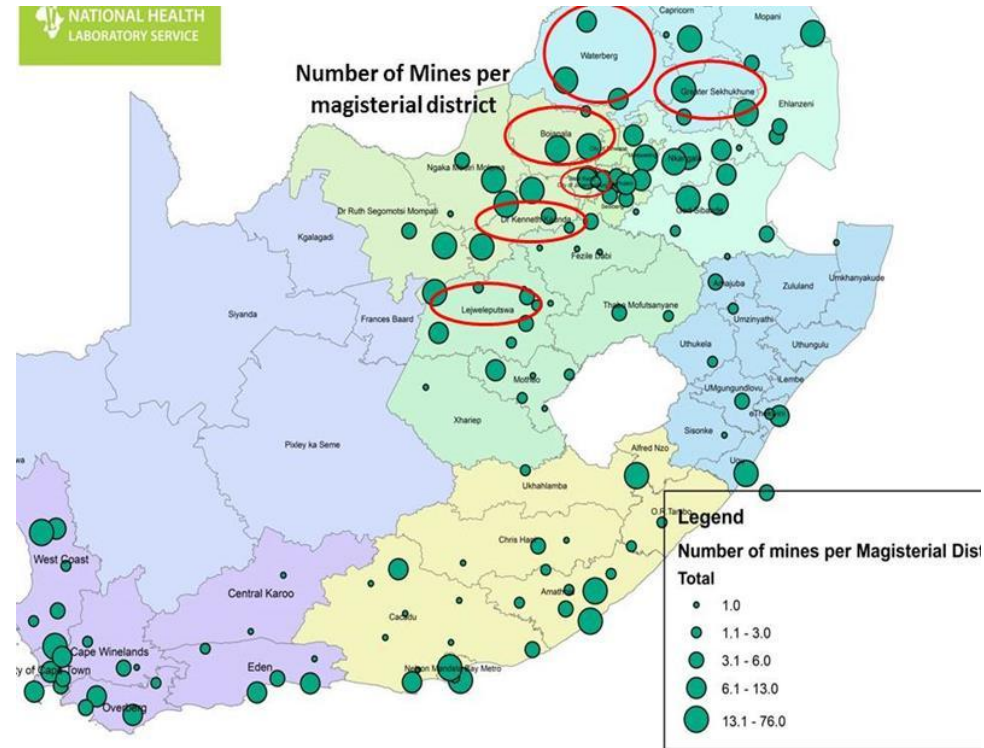




What Fast Track by 2020 means in South Africa

90-90-90 for TB

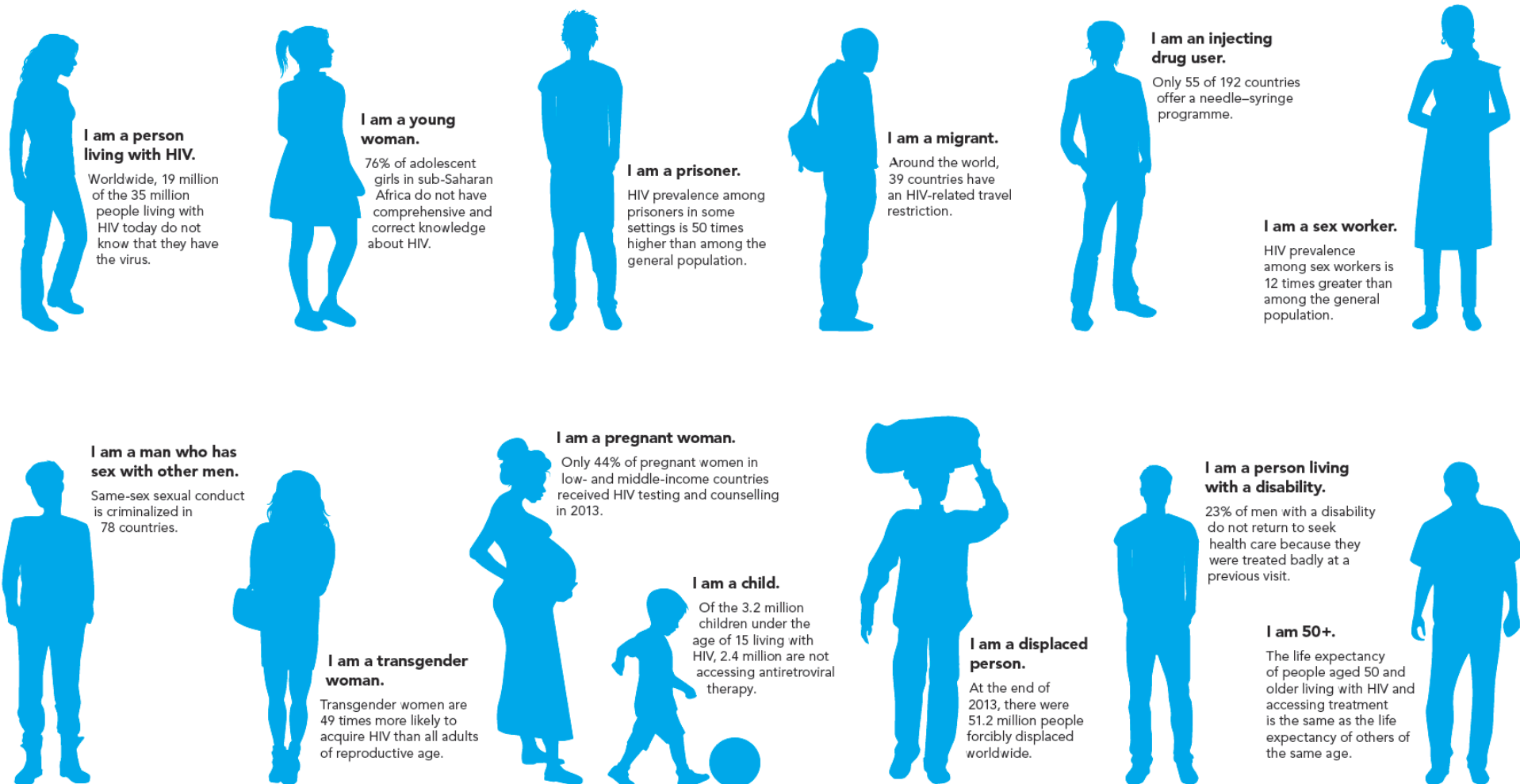
- **1st 90** - 90% of vulnerable people screened for TB
 - PHC attendees
 - inmates in correctional facilities
 - miners & peri-mining communities
- **2nd 90** - 90% of people with TB diagnosed & treated
- **3rd 90** - 90% treatment success





CAUTION – before we start something new!!

12 populations being left behind







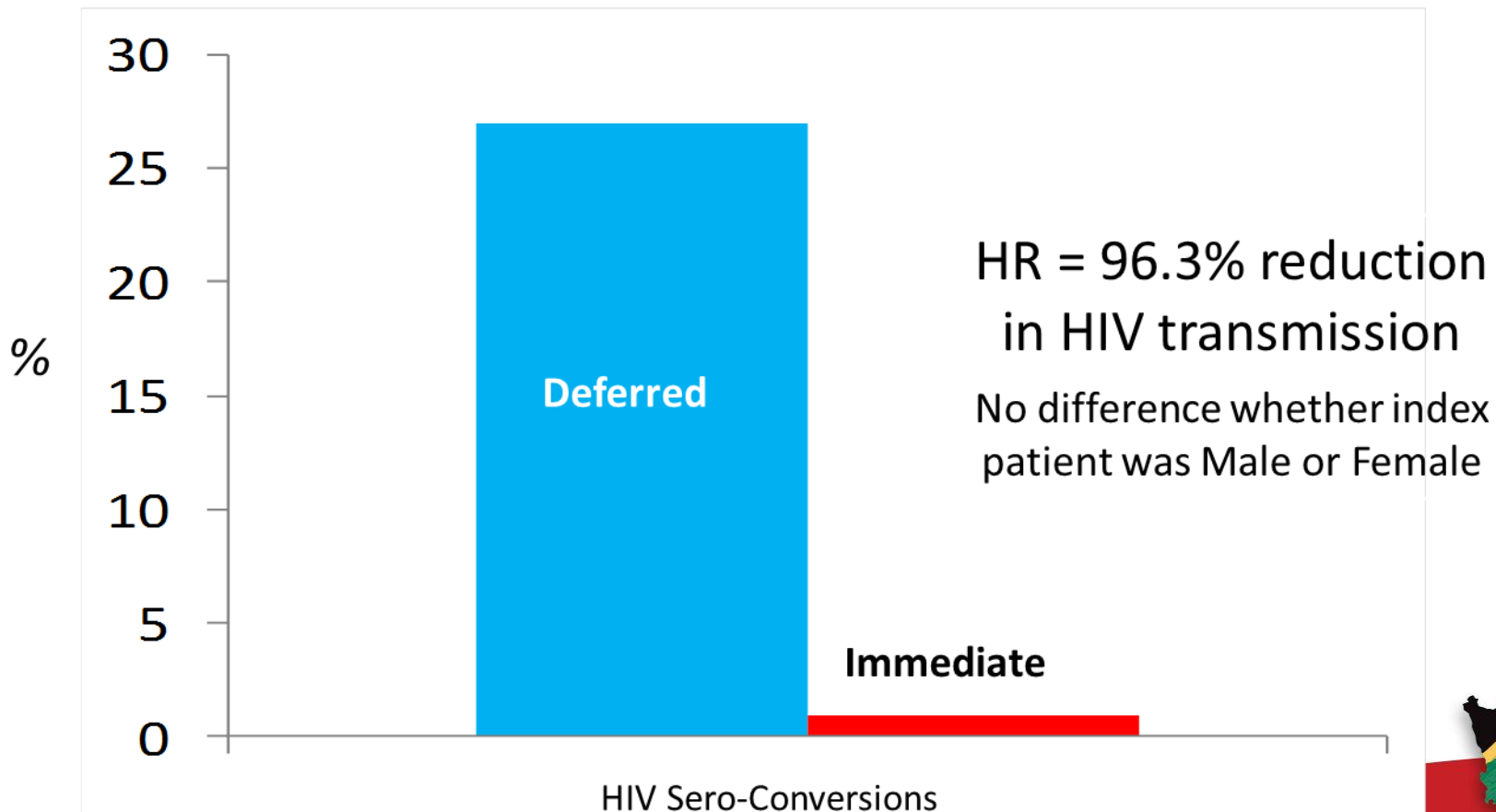
PUBLIC HEALTH IMPACT OF EARLY ART 'TREATMENT AS PREVENTION'





HPTN 052 trial highlighted the effectiveness of 'treatment as prevention'

- 1736 sero-discordant couples (one partner HIV+) in Botswana, Brazil, India, Kenya, Malawi, SA, Thailand, Zimbabwe, USA
- Immediate vs. Delayed ART for HIV+ partner





HPTN052 results show dramatic reduction in HIV transmission

- But these were couples in a clinical trial!
- Is this generalizable at a community level?
- Could early HIV treatment (regardless of CD4) on a mass scale reach enough discordant couples to prevent HIV at population level – Treatment as Prevention?

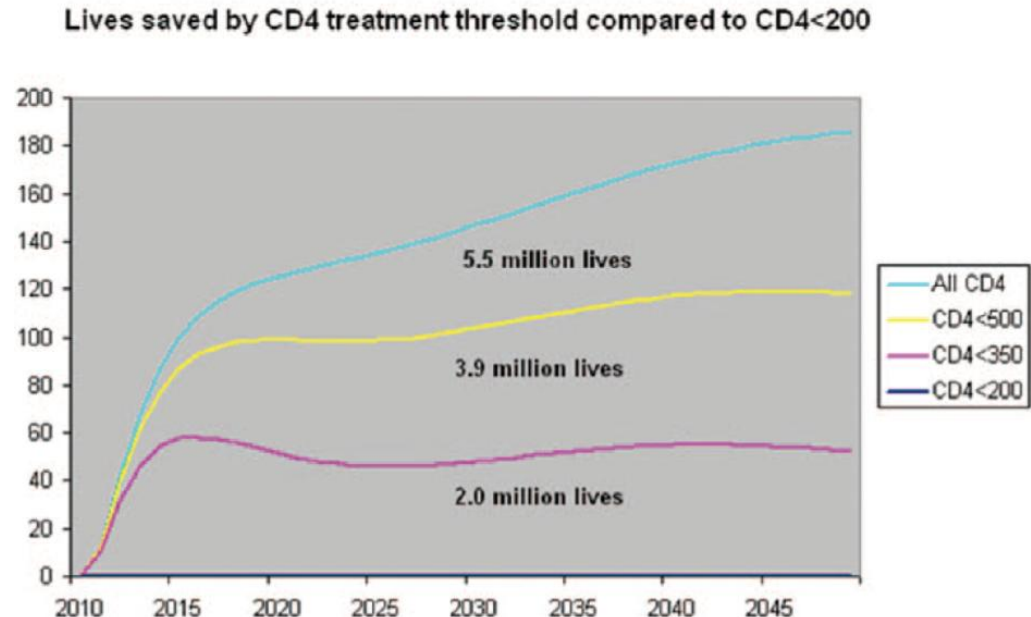




Modelling scale up of 'Treatment as Prevention' strategy

Expanding ART for Treatment & Prevention of HIV in South Africa: Estimated Cost and Cost-Effectiveness 2011-2050

- Assume 90% annual HIV testing (15-49 yrs)
- Expanding eligibility to all CD4 counts compared to CD4<350, would by 2050:
 - Reduce HIV infections by 3.3m
 - Reduce deaths by 3.5m
 - Reduce costs by US\$10bn
- Costs break even in 2022





‘Real life’ ART scale-up reduces HIV incidence

Hlabisa district KZN – Africa Centre

- 16,667 HIV-negative adults followed 2004-2011
- HIV prevalence & ART coverage calculated for 3km circle around each adult - *clever maths & mapping*
- Risk of HIV seroconversion in relation to ART coverage calculated
- 1,413 HIV seroconversions over 53,605 years of observation





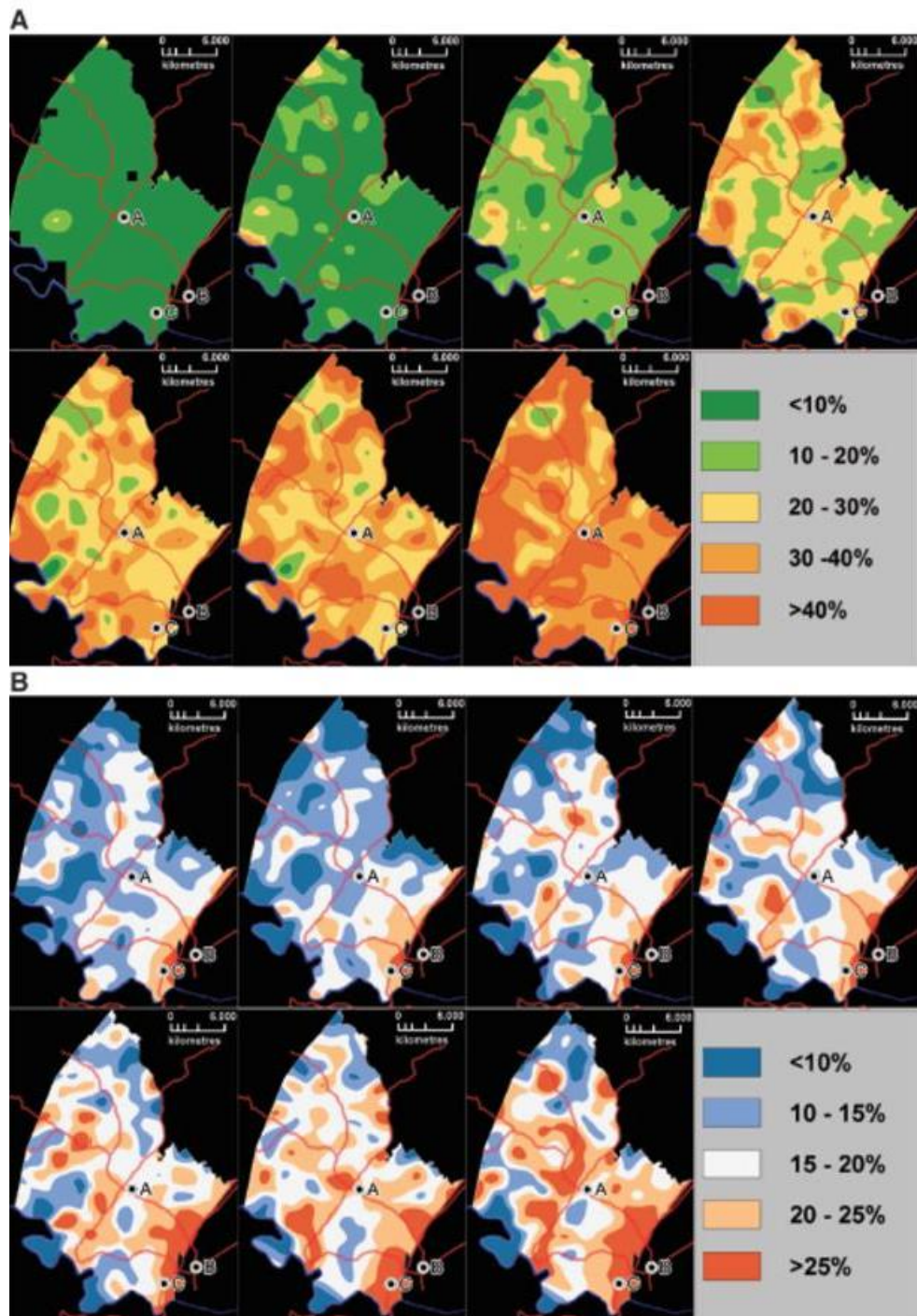
Hlabisa, Africa Centre

ART coverage
2005 - 2011

Researchers linked:
HIV surveillance database
ART clinic database

HIV prevalence
2005 - 2011

Tanser, Science 2013;339:966

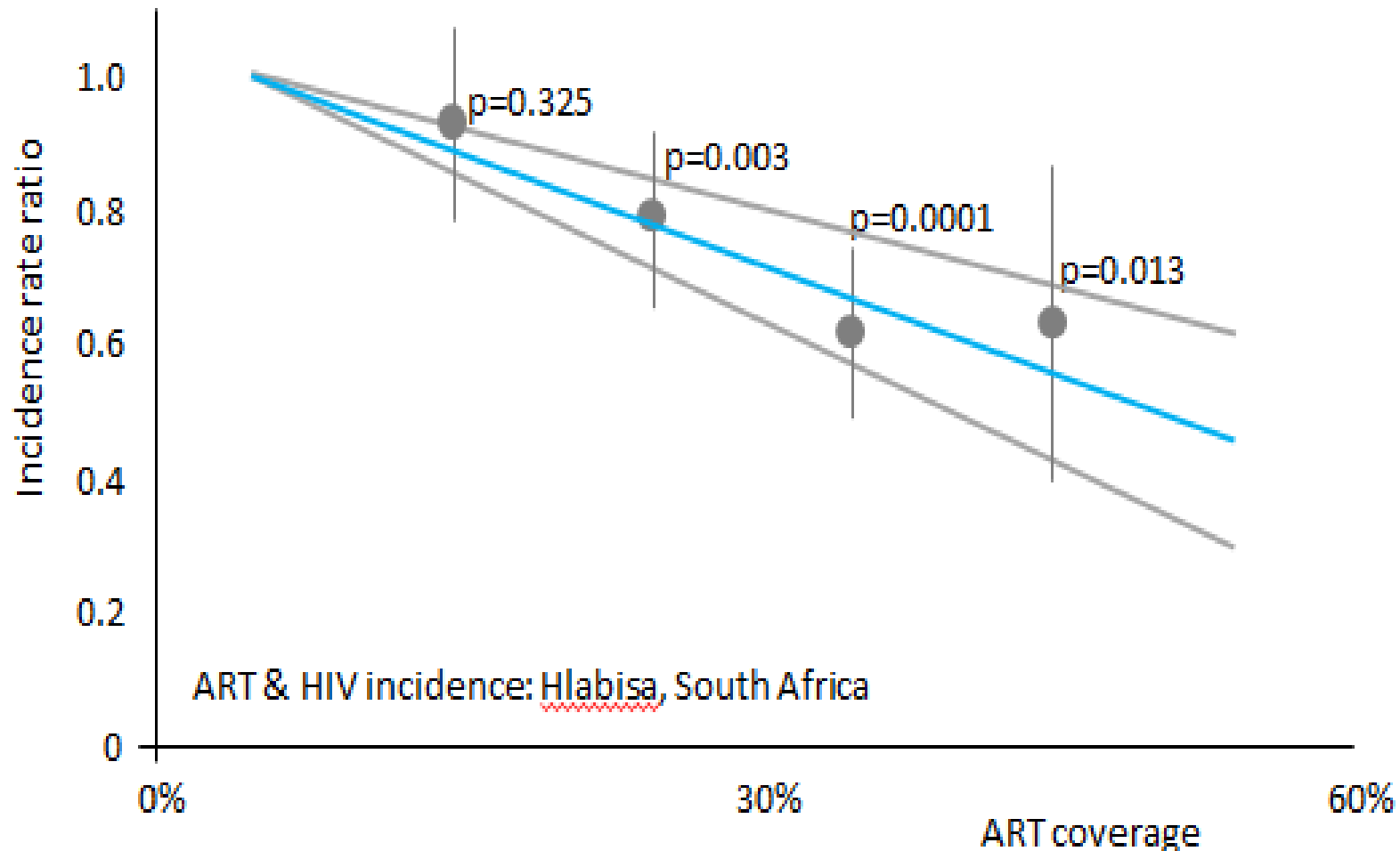




Direct relation between ART coverage & HIV incidence

Treatment as Prevention - Hlabisa, Africa Centre

1.1% (0.8%-1.4%) reduction in HIV incidence, for each 1.0% increase in treatment coverage.





Early ART – the story so far

Treatment as Prevention (TasP)

- Evidence base for efficacy (from clinical trials) is persuasive
 - Public health benefit
 - Reduced HIV transmission in couples & communities
 - Reduced HIV incidence
- Public health benefit alone does not justify “treatment as prevention” if it means potential harm to healthy individuals
- HPTN 052 not convincing re data on individual benefits of early treatment





Recently published START & TEMPRANO studies demonstrate individual benefit

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Initiation of Antiretroviral Therapy in Early Asymptomatic HIV Infection

The INSIGHT START Study Group*

ABSTRACT

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

A Trial of Early Antiretrovirals and Isoniazid Preventive Therapy in Africa

The TEMPRANO ANRS 12136 Study Group*

ABSTRACT





INDIVIDUAL BENEFIT OF EARLY ART 'TEST & TREAT'

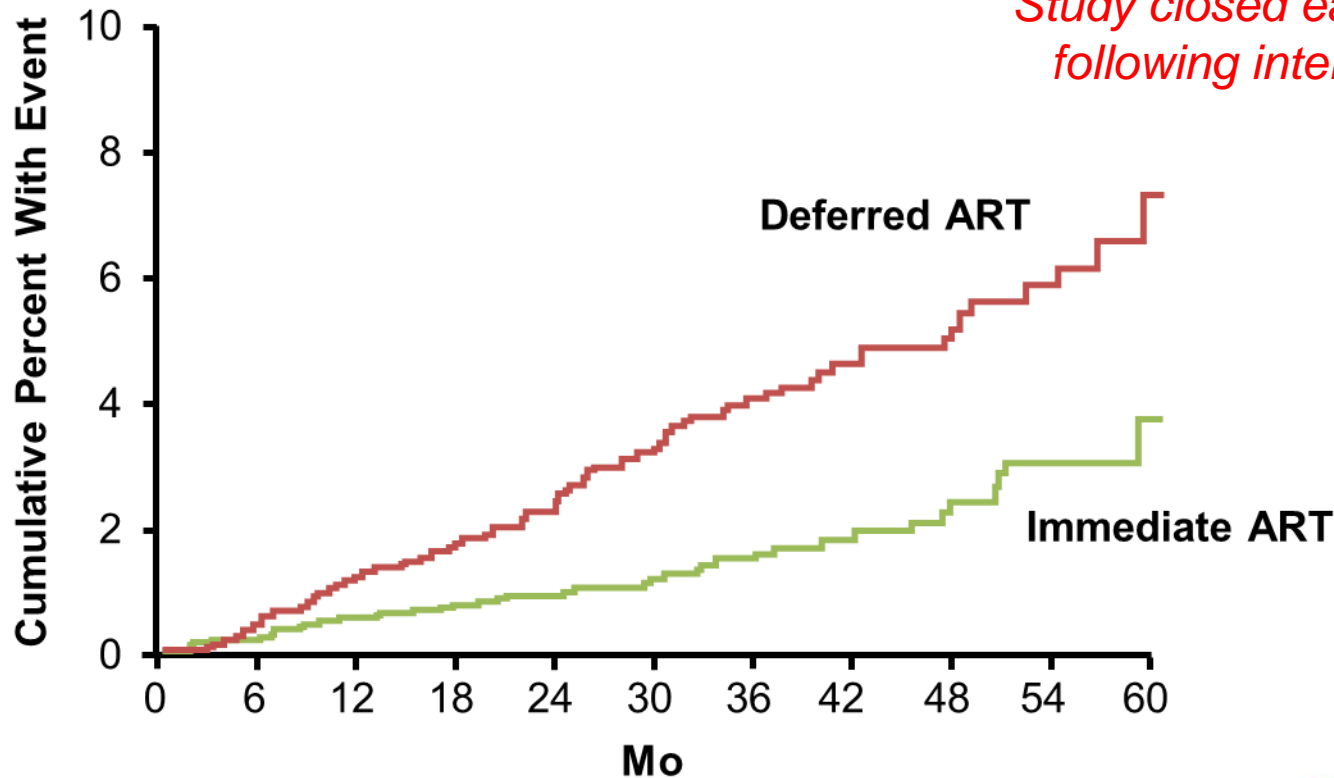




New Evidence START Study

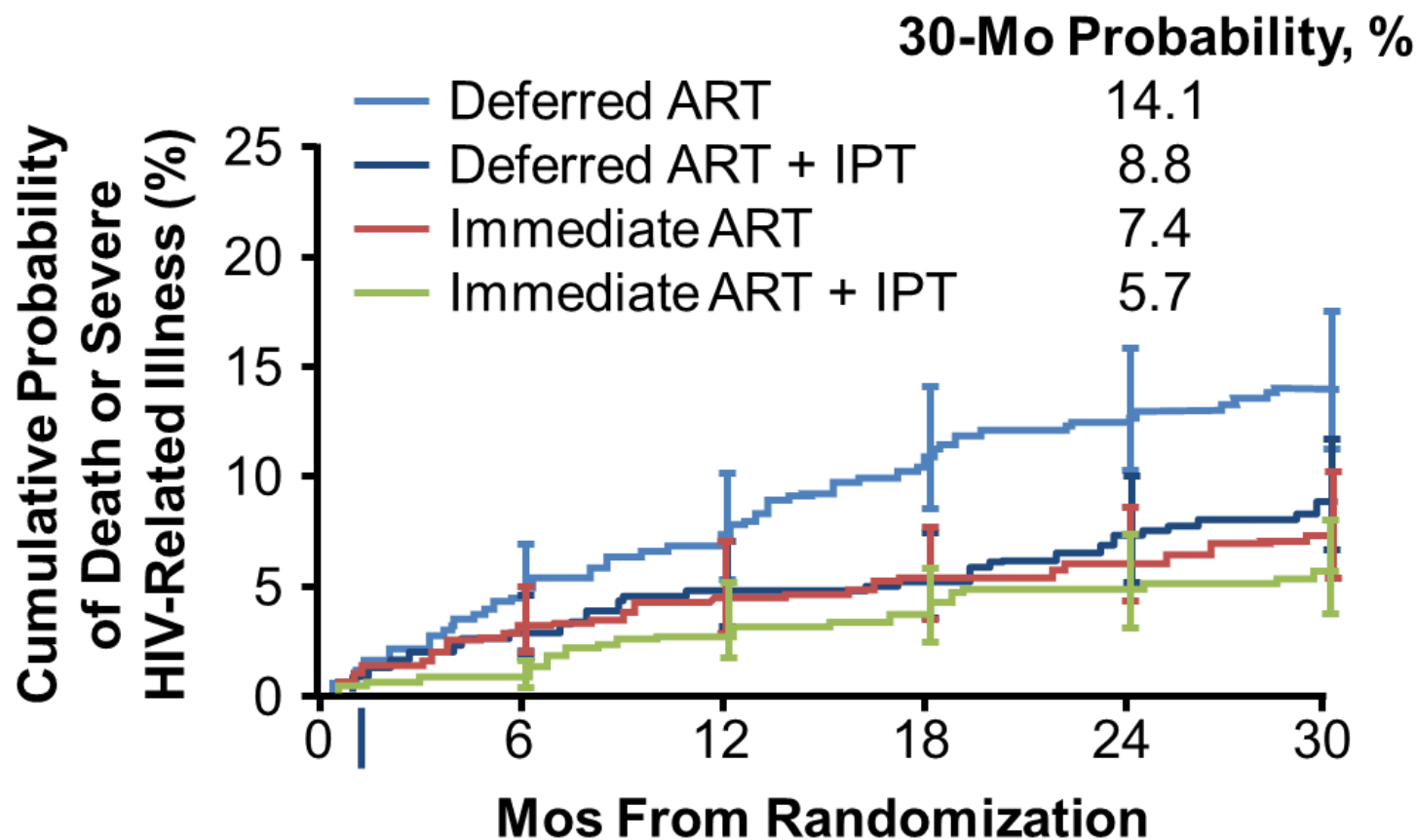
57% reduced risk of serious events/death with immediate ART

- 4.1% vs 1.8% in deferred vs immediate arms had serious AIDS or non-AIDS-related event or death (HR: 0.43; 95% CI: 0.30-0.62; $P < .001$)





New Evidence TEMPRANO Study: Immediate vs Deferred ART Initiation &/or IPT Delivery for PLHIV in Cote d'Ivoire





Summary of evidence-base for early ART (test & treat) updated...

- Evidence base for efficacy is persuasive
 - Public health
 - Reduced HIV transmission in couples & communities
 - Reduced HIV incidence
 - Individual health
 - Reduced mortality
 - Reduced morbidity
 - TB and other HIV related conditions
- Challenge will be effectiveness - taking to massive scale under programmatic conditions
 - Real life South Africa!





Achilles heel(s) of test & treat

- Access to HIV Testing
- Linkage to care
- Retention in care & return to care
- Adherence adherence adherence





Achilles heel(s) of 'test & treat'

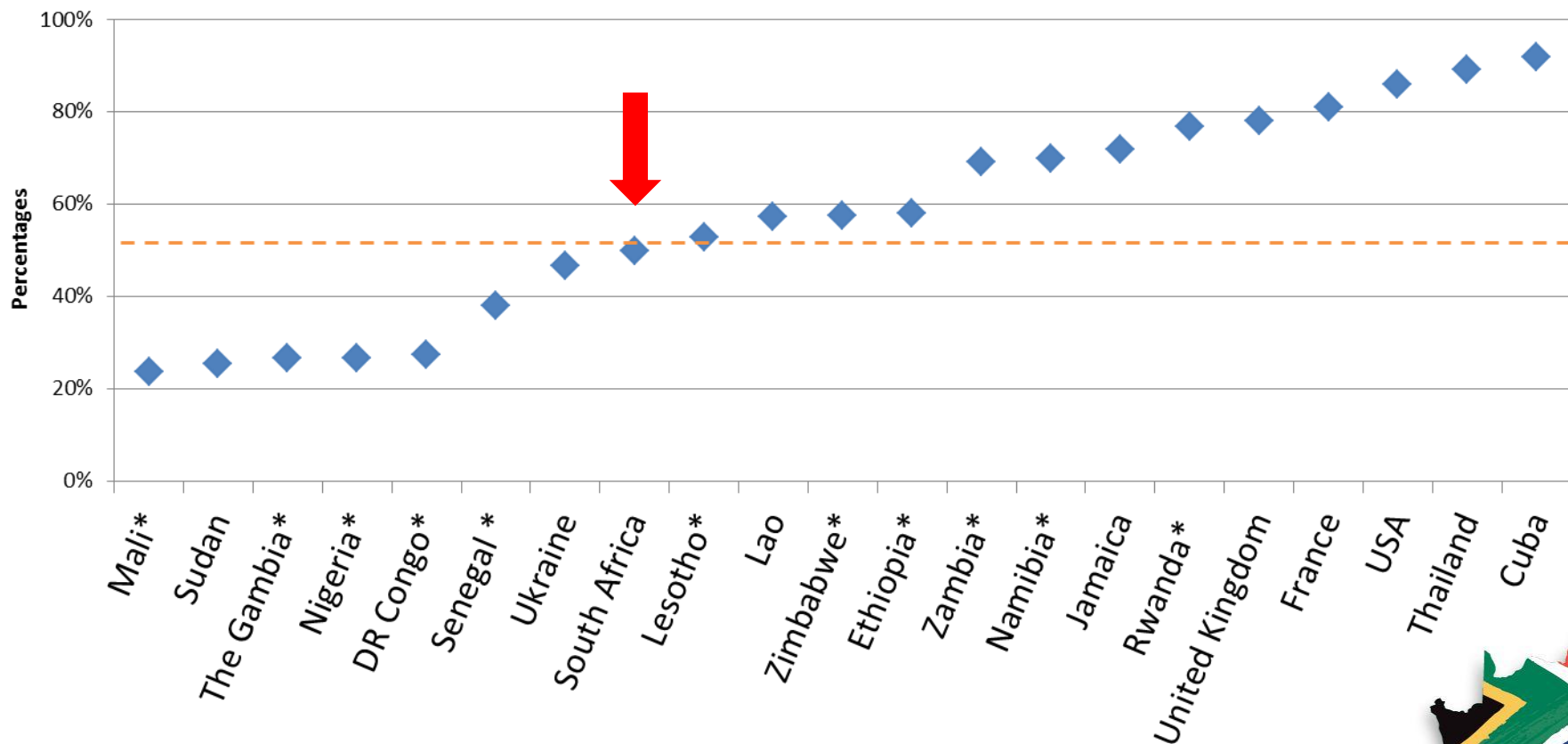
- Client factors
 - Socio-economic & demographic factors (disease-related stigma, transport, age, psychosocial support etc.)
 - Knowledge , perceptions and beliefs regarding risk, disease, prevention & treatment
 - Affective factors (depression, anxiety, shame, etc.)
 - Behavioural factors (e.g. missed appointments)
 - Comorbidity, treatment burden, drug side effects & interactions
- Health system factors
 - Human resource capacity – skills, tools, attitudes, external stigma
 - Accessibility - waiting times, distance, lack of integration, centralized
 - Tracking, recording and reporting
 - Supply chain management – stock outs – reliance on global manufacturing and API
 - Sustainability – escalating costs





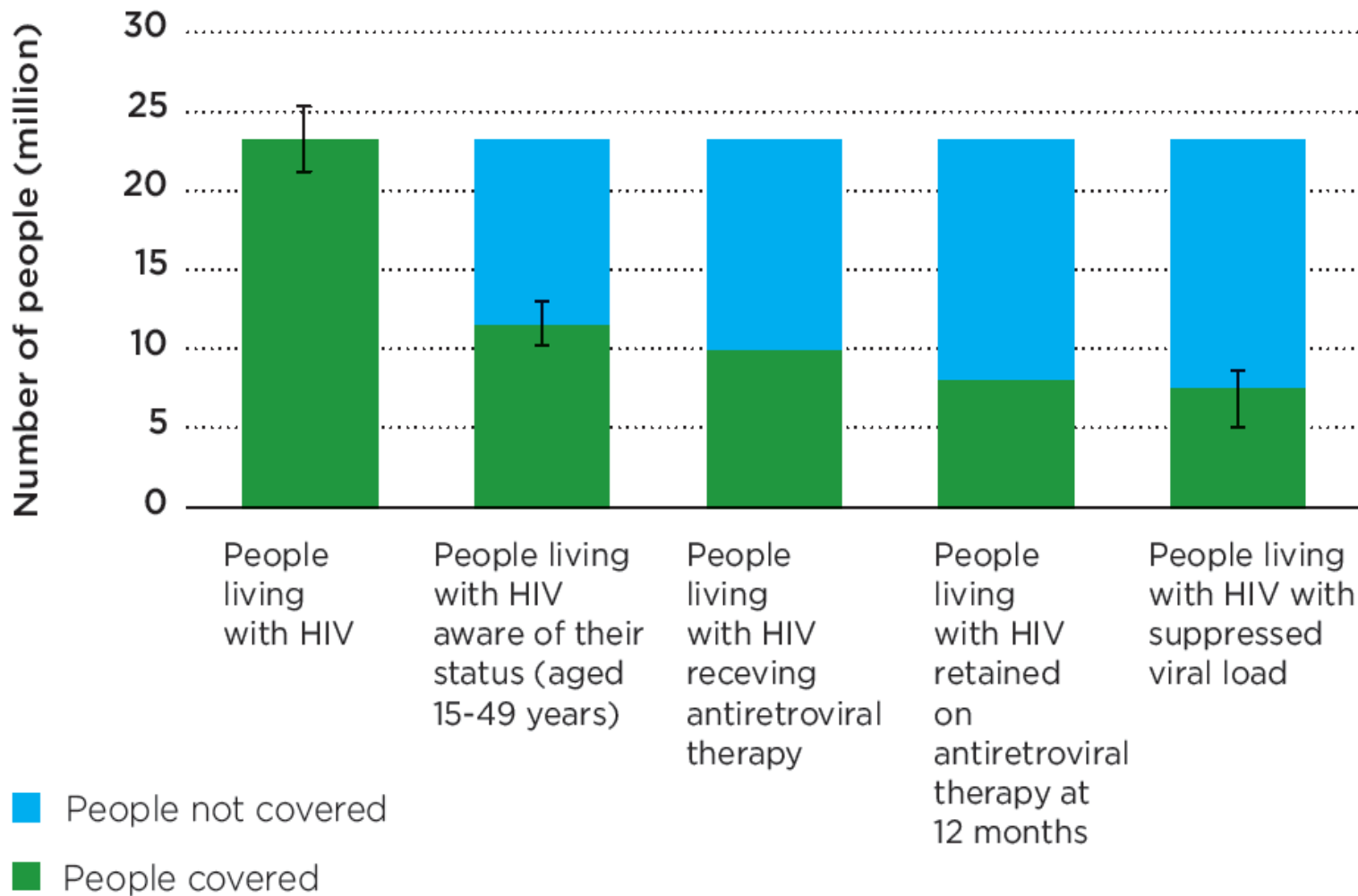
Diversity in progress towards the first 90 – access to HCT

Awareness estimates of HIV status among PLHIV
in selected countries





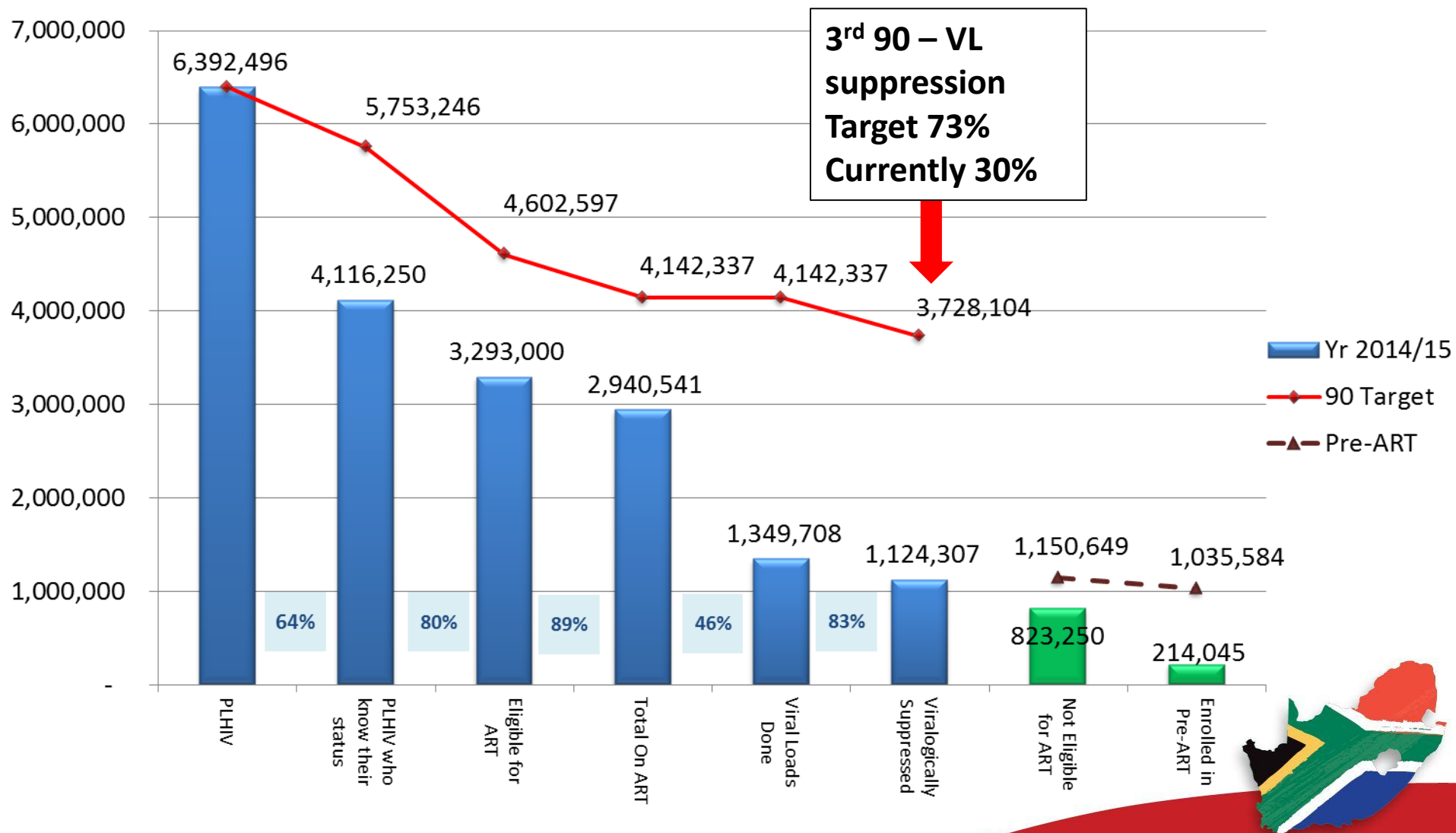
HIV treatment cascade for people aged 15+ sub-Saharan Africa, 2014





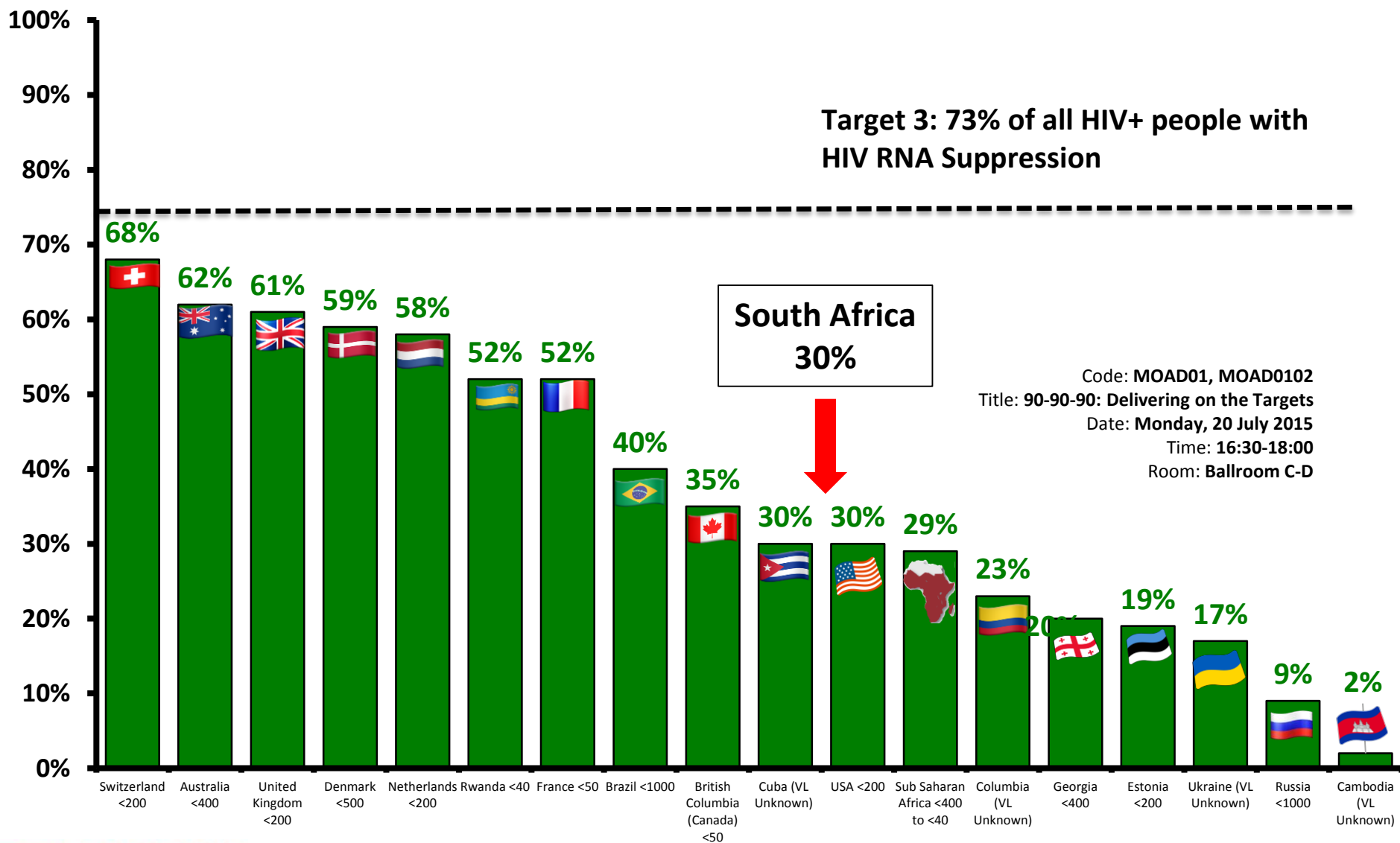
SA Treatment Cascade

Adult (15 years and older) HIV Care and Treatment Cascade



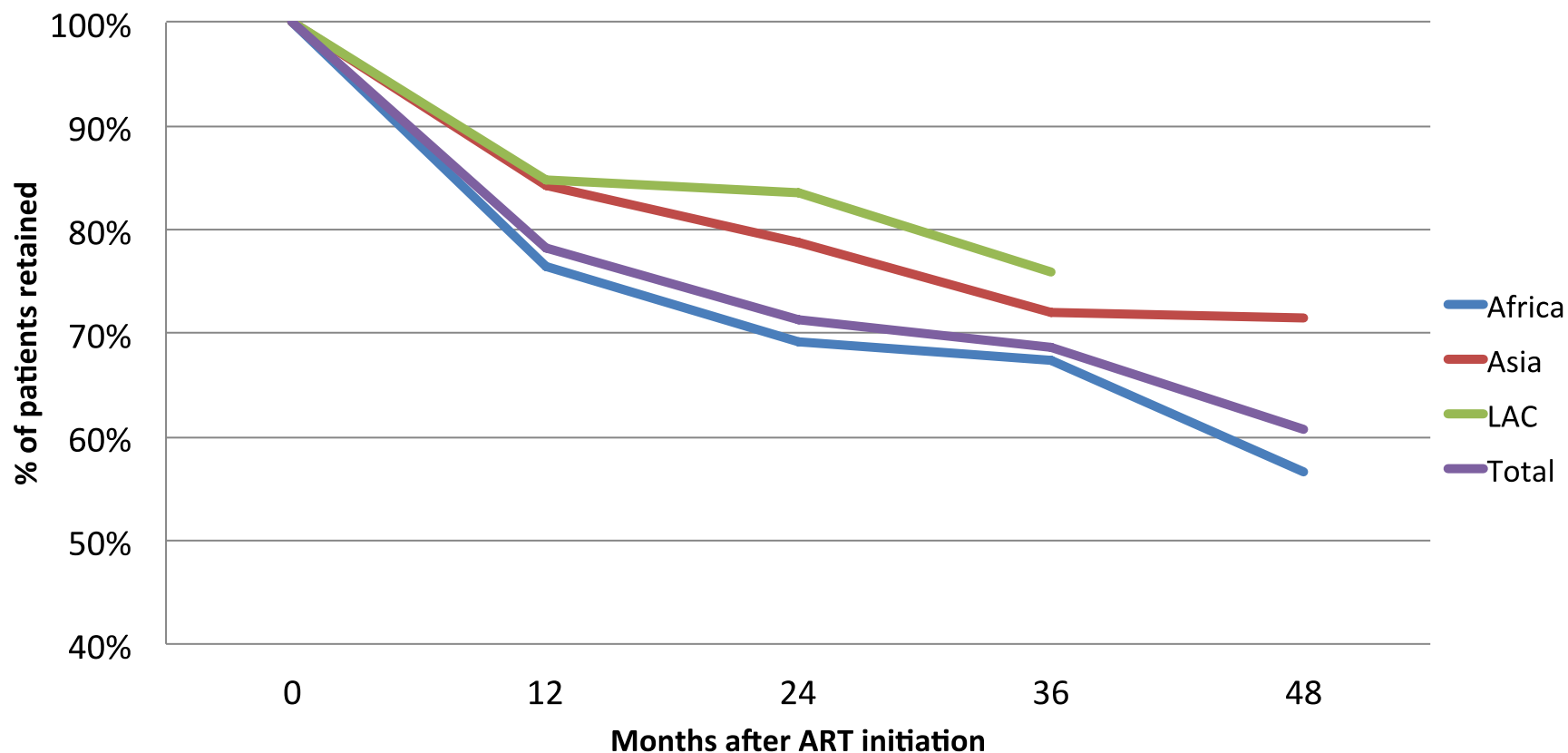


3rd 90 - % of PLHIV on ART with viral load suppression





Starting people on ART is easy Keeping them on treatment is the challenge Retention in care



* Note: Y axis starts at 40%

Figures

Figure 1. Average retention at specified time points, by region*

Fox MP, Rosen S, Retention of Adult Patients on Antiretroviral Therapy in Low- and Middle-Income Countries: Systematic Review and Meta-analysis 2008-2013, J Acquir Immune Defic Syndr. 2015 May





GLOBAL GUIDELINES WHEN TO START ART





Global Guidelines on ART

- **WHO guidelines 2013** – Recommend start ART at CD4<500 – currently under review in light of new evidence
- **USA & UK** recently recommend starting ART at initial HIV diagnosis regardless of CD4 count
- **Lancet – Vancouver Consensus Statement**
 - IAS HIV Pathogenesis meeting – July 2015
 - Signed by 500 researchers, clinicians & civil society experts
 - Recommends *'all PLHIV should have access to ART at diagnosis'* in context of combination HIV prevention





SA Consolidated National Guidelines

National consolidated guidelines for the prevention of mother-to-child transmission of HIV (PMTCT) and the management of HIV in children, adolescents and adults

24 December 2014



health

Department:
Health
REPUBLIC OF SOUTH AFRICA





SA National Guidelines – 1st Jan 2015

Start ART CD4 <500

6.6.4 When to start: ART eligibility in late adolescents ≥ 15 years and adults living with HIV

Box 19: ART eligibility criteria

Eligible to start ART

CD4 count ≤ 500 cells/ μ l irrespective of clinical stage
(Prioritise those with CD4 <350 cells/ μ l)

OR

Severe or advanced HIV disease (WHO clinical stage 3 or 4), regardless of CD4 count

OR

Irrespective of CD4 count or clinical stage:

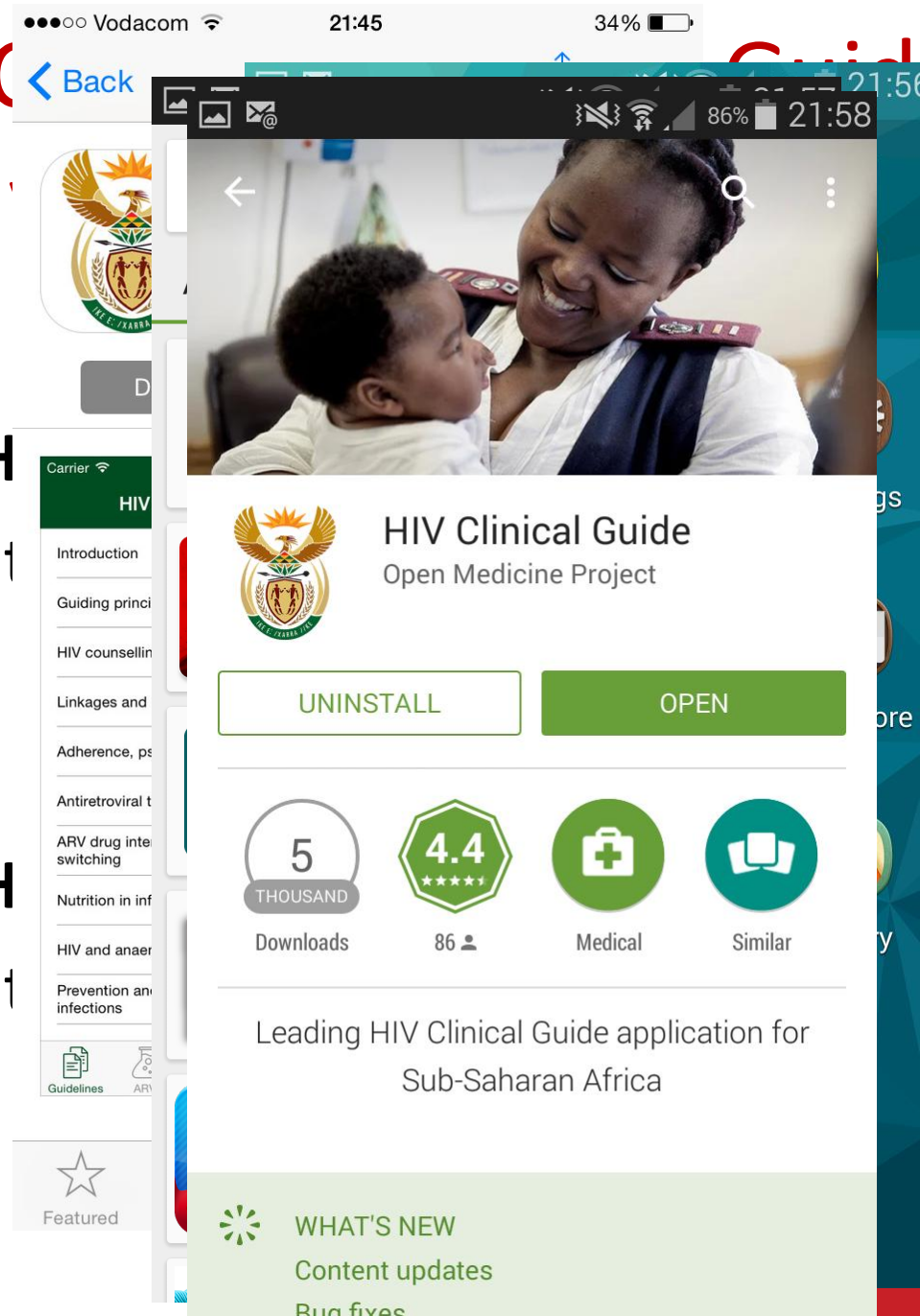
- Active TB disease (including drug-resistant and EPTB)
- Pregnant and breastfeeding women who are HIV-positive
- Known hepatitis B viral (HBV) co-infection
- Prioritise those with CD4 ≤ 350 cells/ μ l or advanced HIV disease





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Guidelines on

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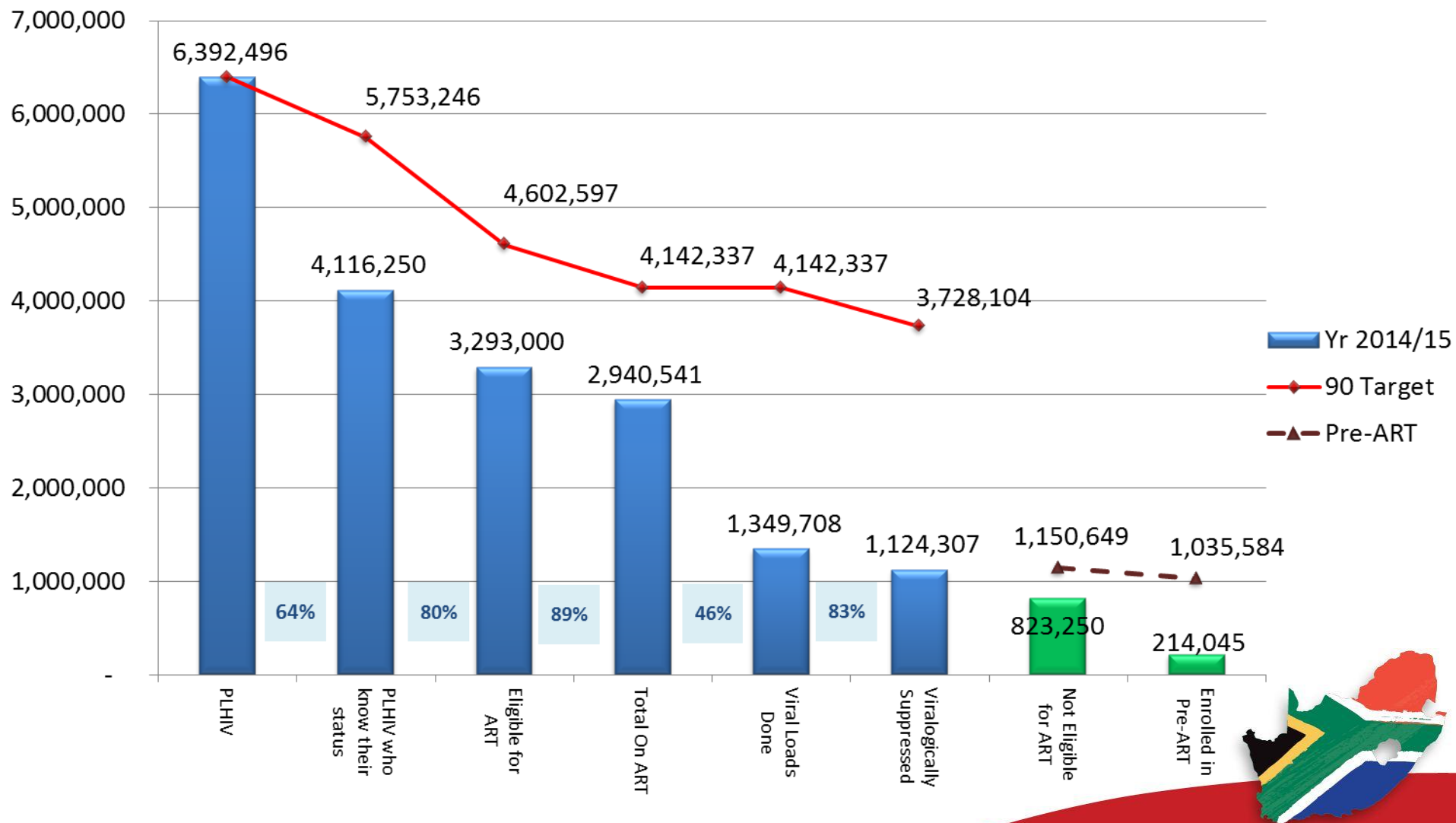
HIV Clinical Guidelines App - screenshots





SA Treatment Cascade

Adult (15 years and older) HIV Care and Treatment Cascade





Take home messages – CD4 <500 for now..

- Don't forget those we are already leaving behind
- HIV counselling & testing is critical first step to increase access to ART
- Need to ensure that those tested are linked to care, started on treatment, kept on treatment and treated successfully
 - Adherence will make or break the ART response
 - Capturing 'unique patient identifier' (national ID number, passport, drivers license) is only way to track clients
- Client experience – friendly, competent, fast, decentralised
- All in the context of combination HIV prevention and non-discrimination





Acknowledgements

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- Alasdair Reid, Erasmus Morah & Martina Brostrom
UNAIDS

