

Optimizing the HIV Treatment and Care Continuum

Meg Doherty, MD, MPH, PhD
Coordinator Treatment and Care
WHO HIV Department, HQ





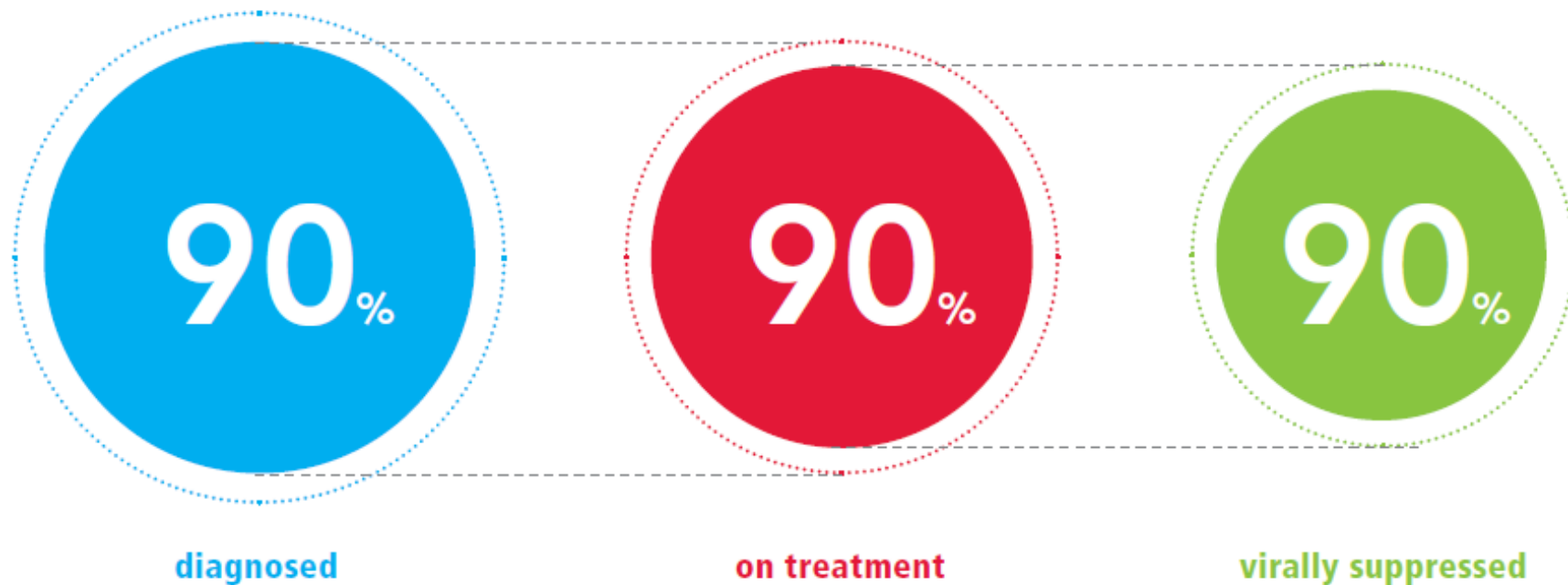
How can we improve the treatment and care continua/um?

- Continua of Treatment, Care and Prevention
- Populations specific examples and interventions
- WHO approach to optimizing the treatment and care continuum
- How this translates into country level implementation and programming



Targets require innovations across the continuum of care

THE TREATMENT TARGET

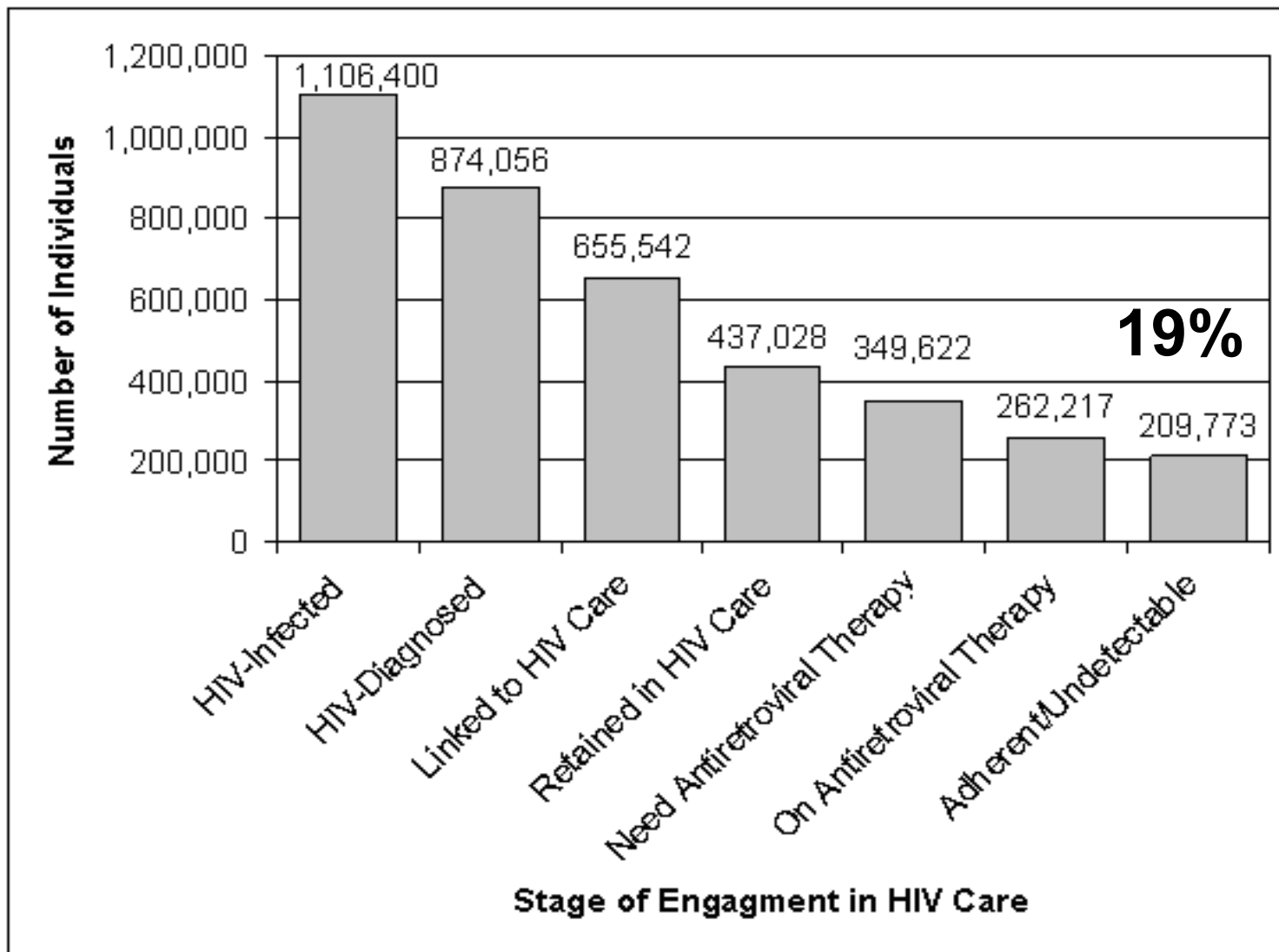


Drugs, diagnostics & service delivery optimization:

- New FDCs (Paeds), simplified second and third line
- Diagnostics for HIV rapid, CD4, and viral load testing
- Community ARV delivery



The Gardner Cascade for HIV in the United States



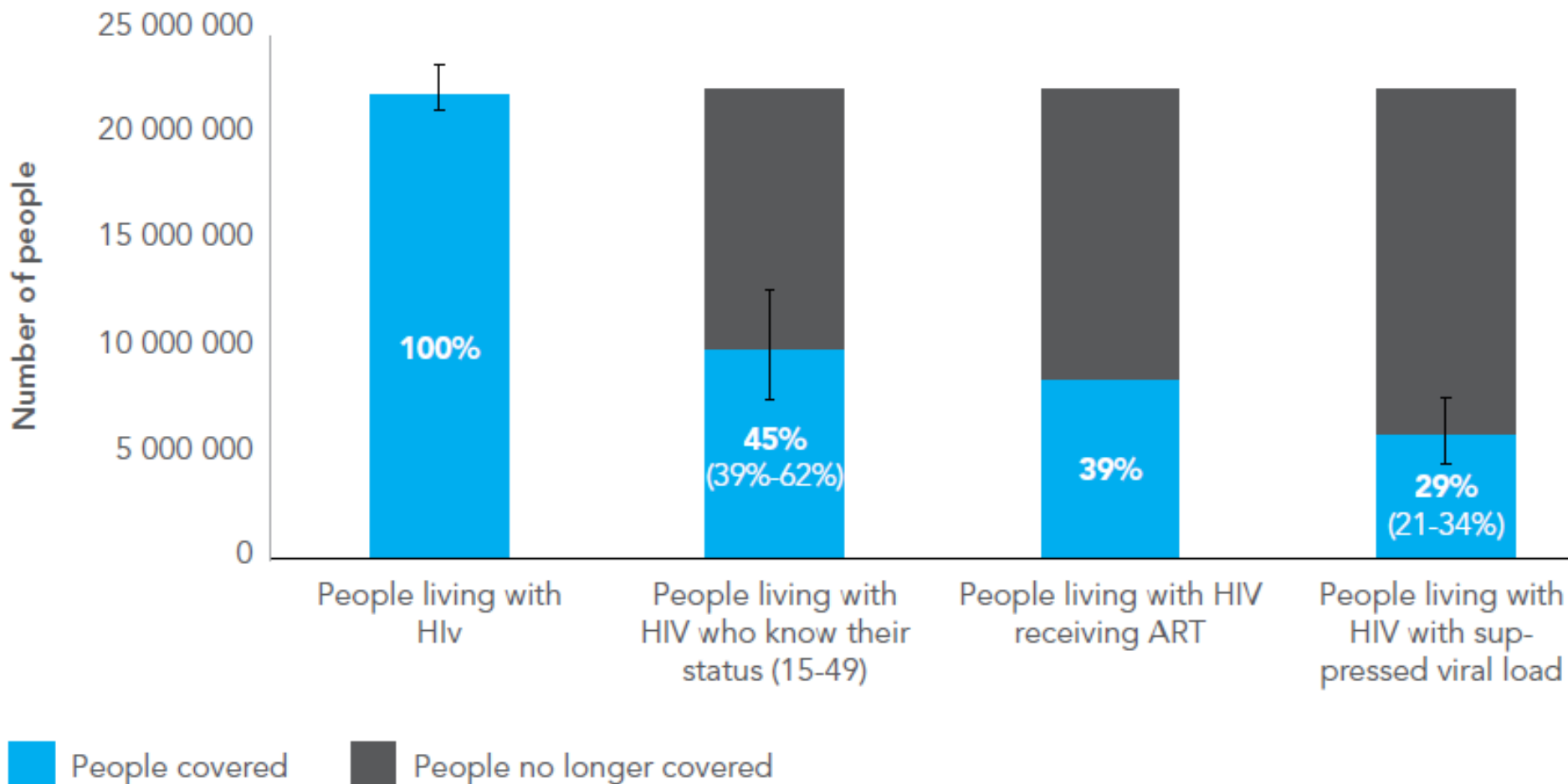
Gardner, et al. 2011. The Spectrum of Engagement in Care and its Relevance to Test and Treat Strategies for Prevention of HIV Infection. Clin Infect Dis. (2011) 52 (6):793-800.doi: 10.1093/cid/ciq243

Source: Gardner et al. Clin Infect Dis. 2011; 52 (6): 793-800



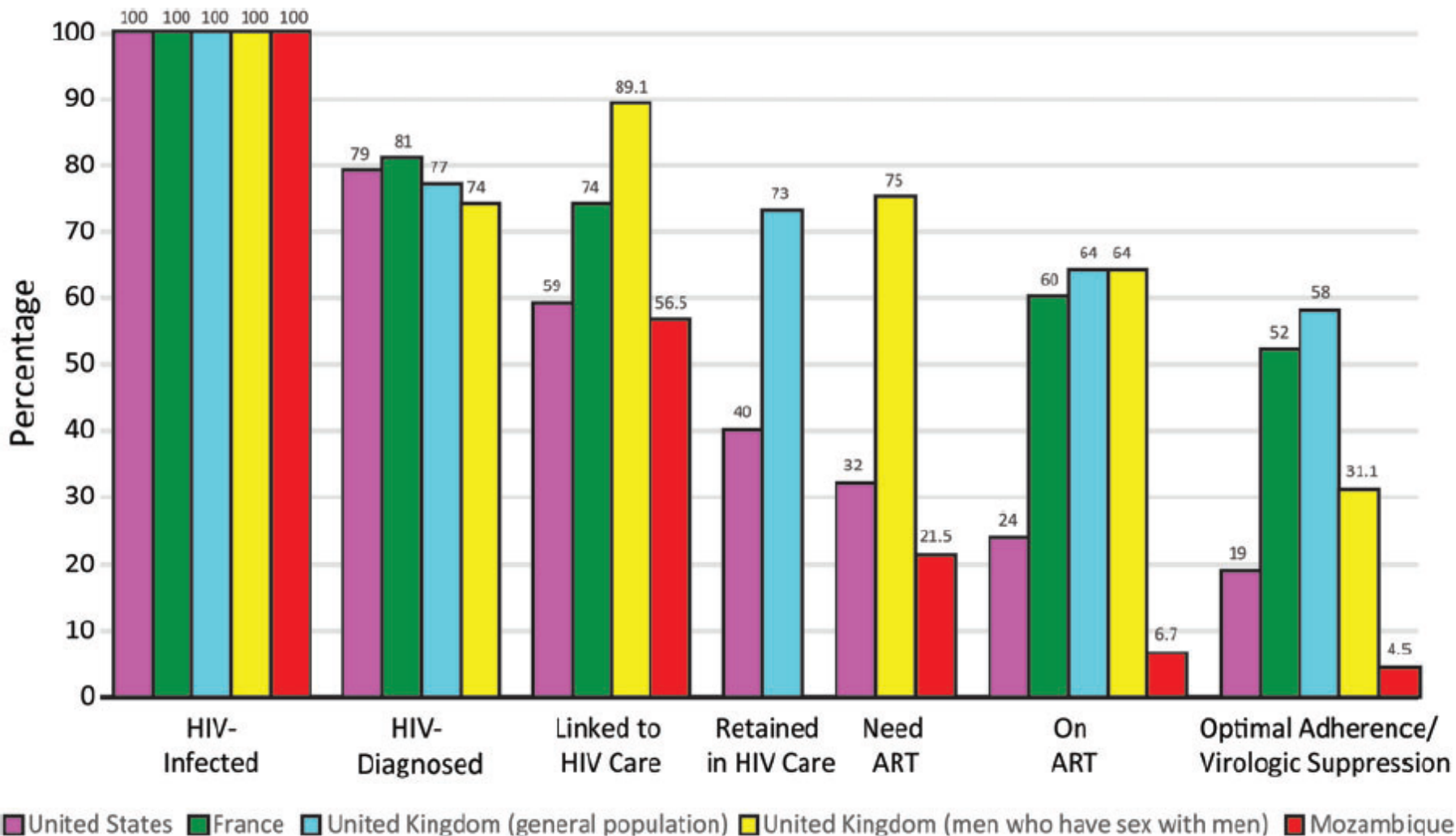
ART scale-up depends on improving every step of the cascade – SS Africa

ABBREVIATED HIV TREATMENT CASCADE FOR ADULTS IN SUB-SAHARAN AFRICA AGED 15 YEARS OR MORE, 2013





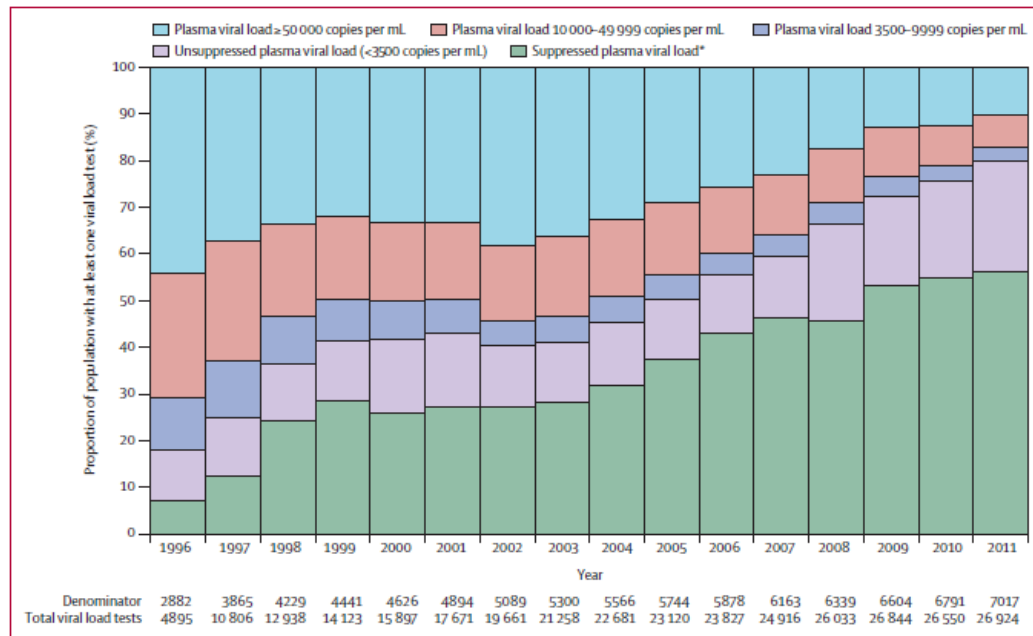
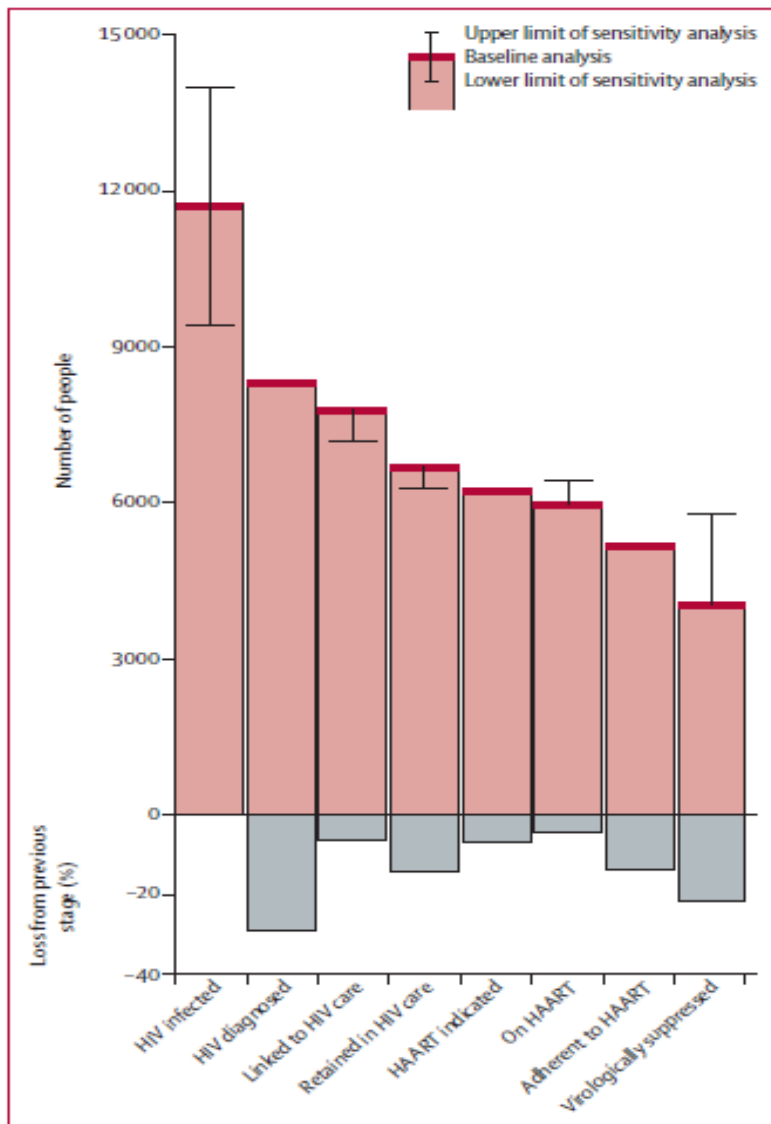
The spectrum of engagement in HIV care in 4 countries



Source: Brown et al , 2013; Gardner et al, 2011; Delpechet al, 2013; Micek et al; 2009; Supervie et al, 2013



The cascade of HIV care in British Columbia, Canada (1996–2011)



Source: Nosyk et al, Lancet ID, Jan 2014



Challenges with the continuum of care



Unaware of HIV Status



Late Diagnosis of HIV Infection



Failure of HIV-Positive Patients to Link to Care



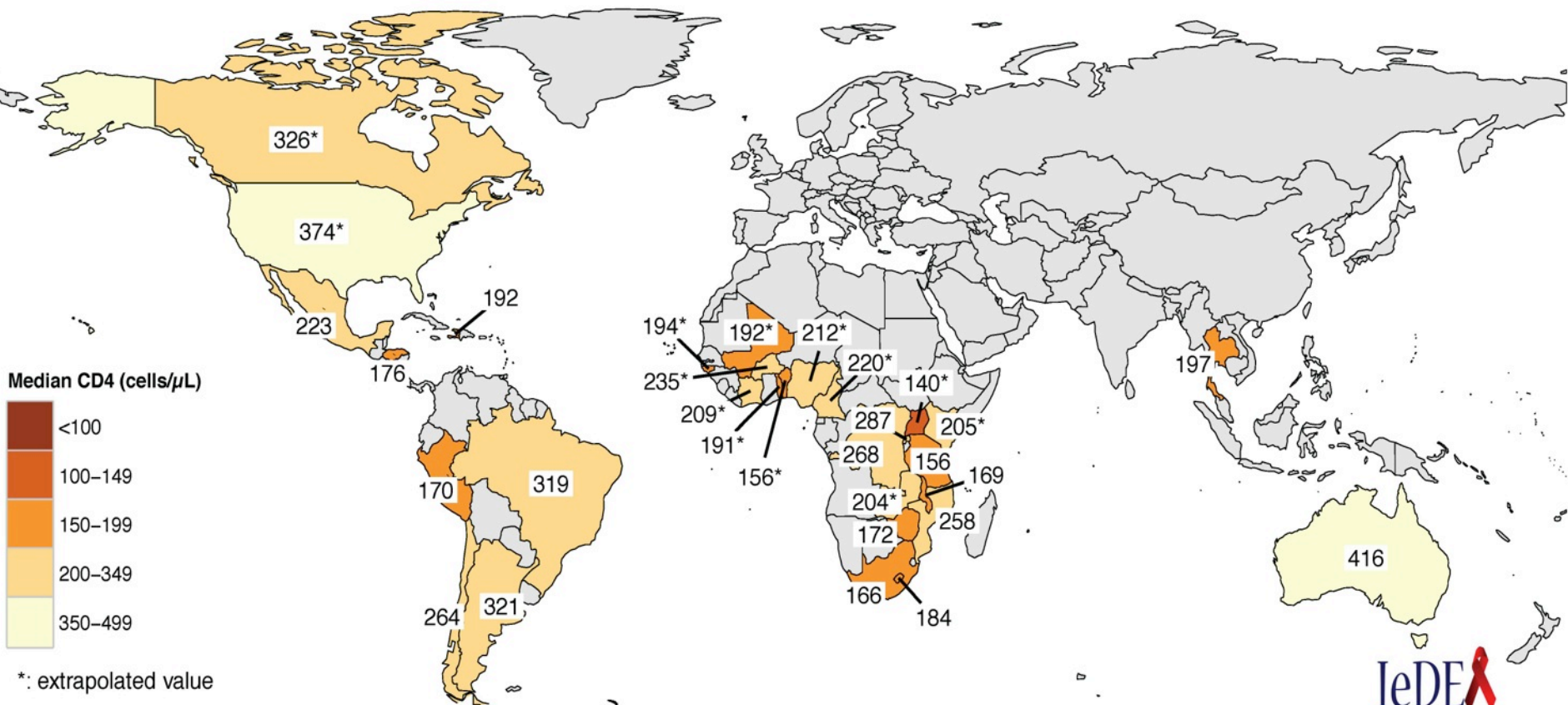
Late Initiation of ART



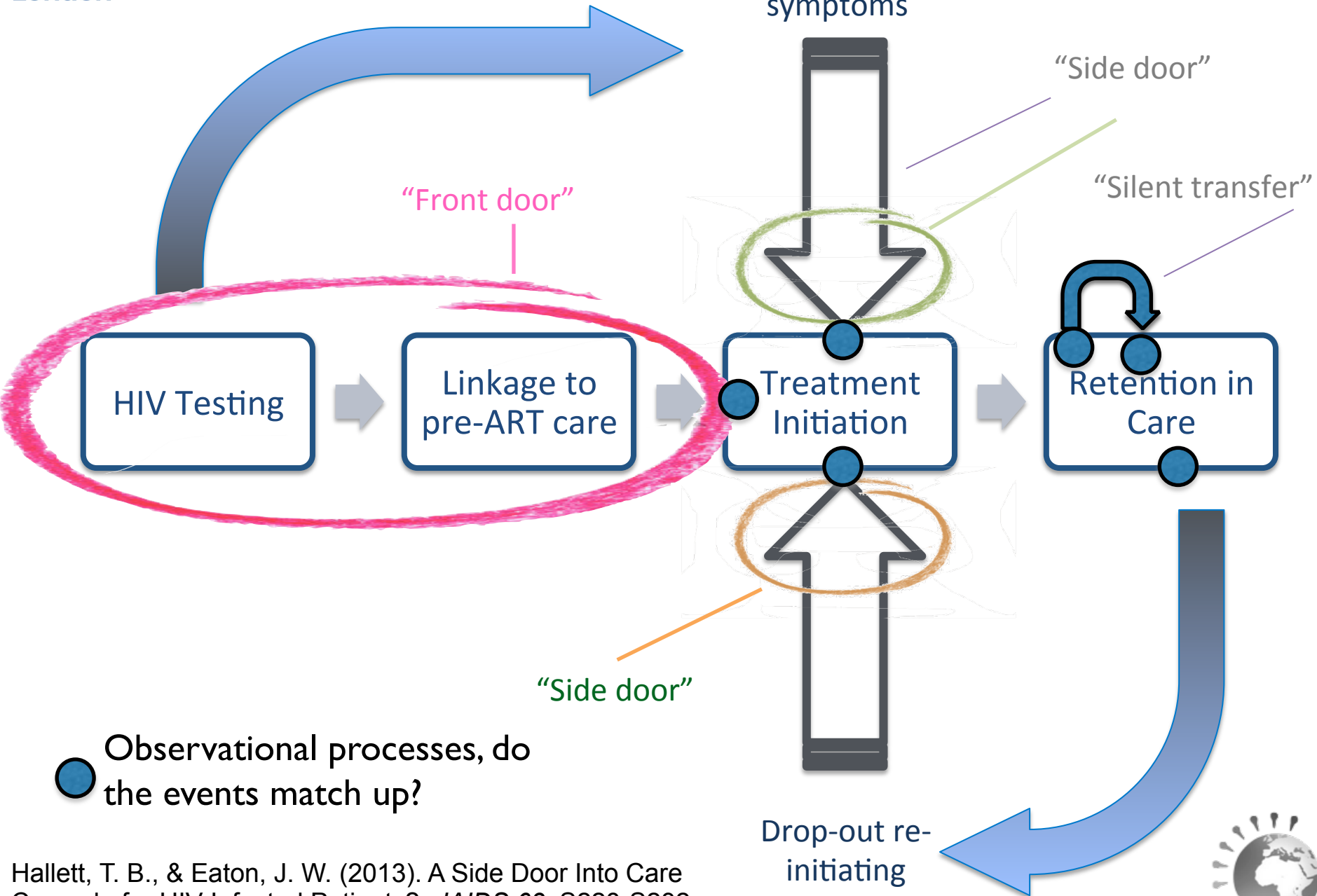
Inability to Achieve and Maintain Viral Suppression

Treatment initiation still late in the large majority of countries

Median CD4 count at start in 2013 (data for some countries extrapolated)



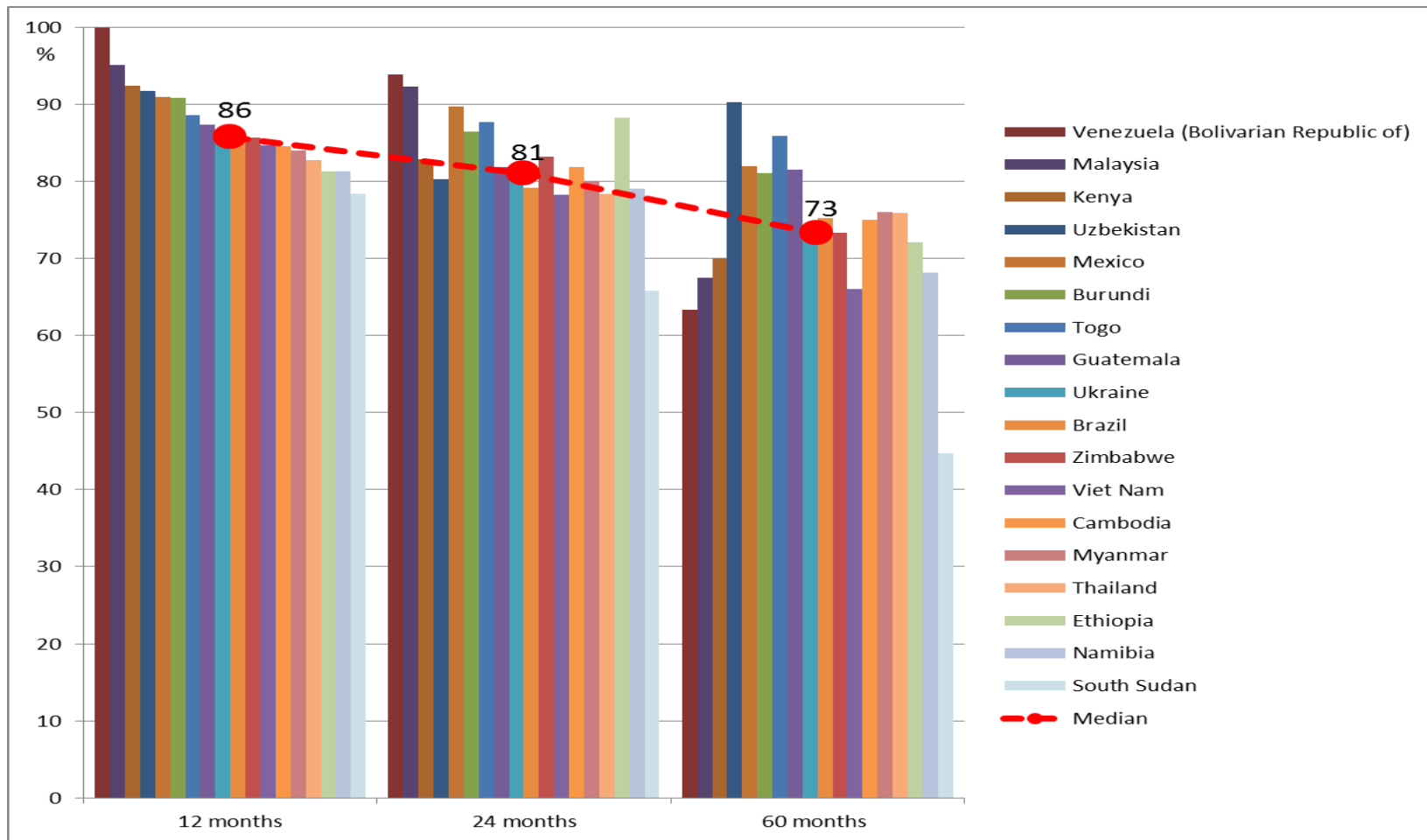
Presentation with
symptoms





Too many people are being lost to follow-up

ART retention rates (%) at 12, 24 and 60 months reported by selected low- and middle-income countries, 2013.



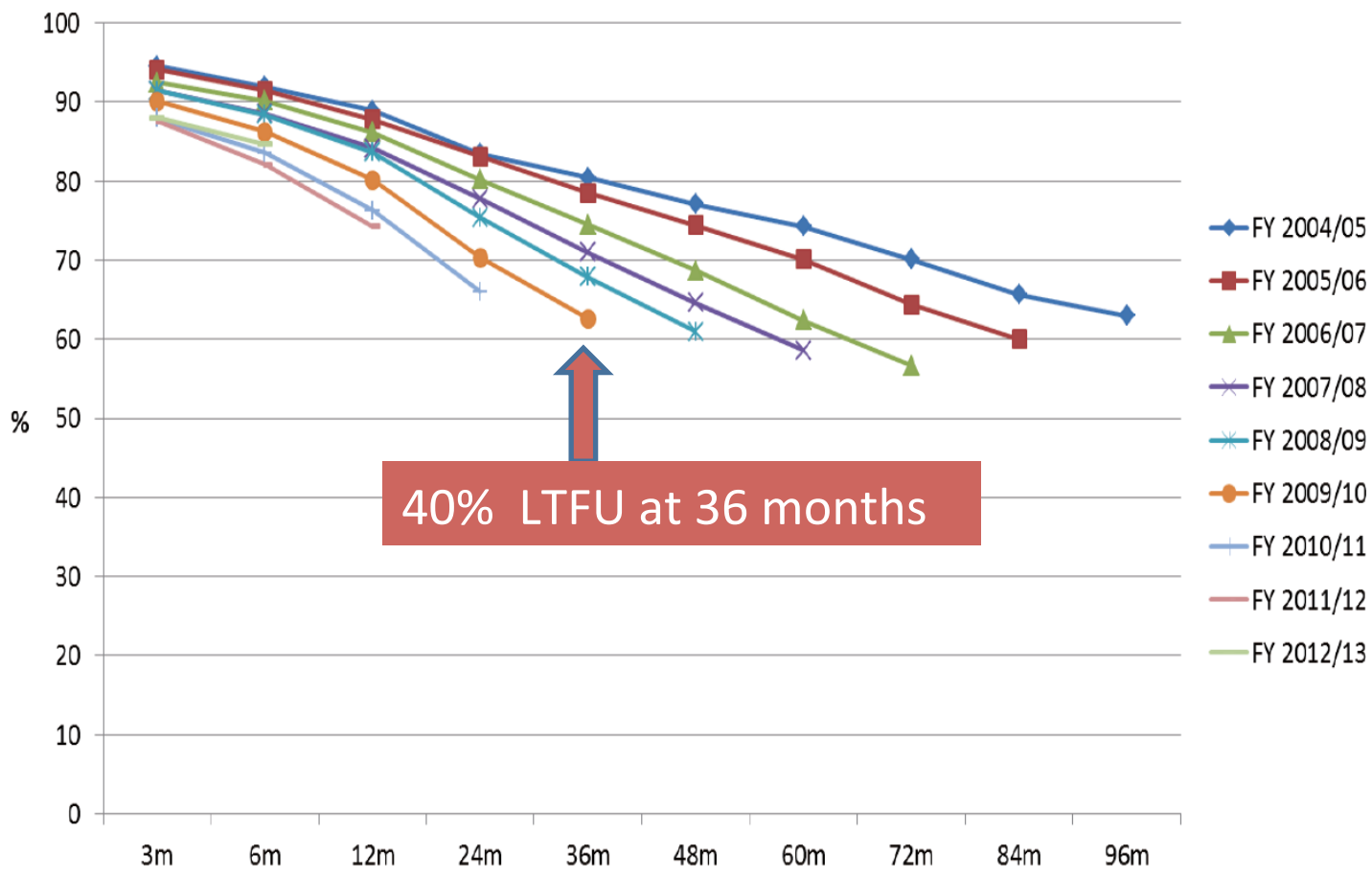
Source: Global AIDS Response Progress Reporting (WHO/UNAIDS/UNICEF).



Too many people are being lost to follow-up: newer cohorts with worse retention

Percentage adults remaining on ART by duration

(Data from 352 phase 6 sites)



40% LTFU at 36 months

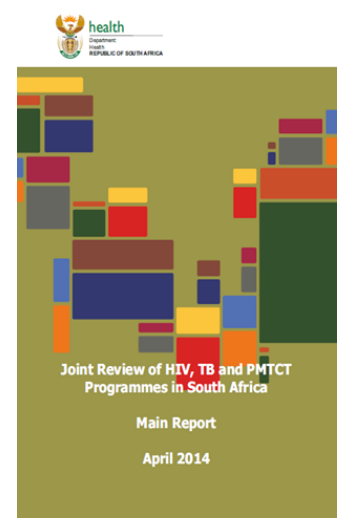
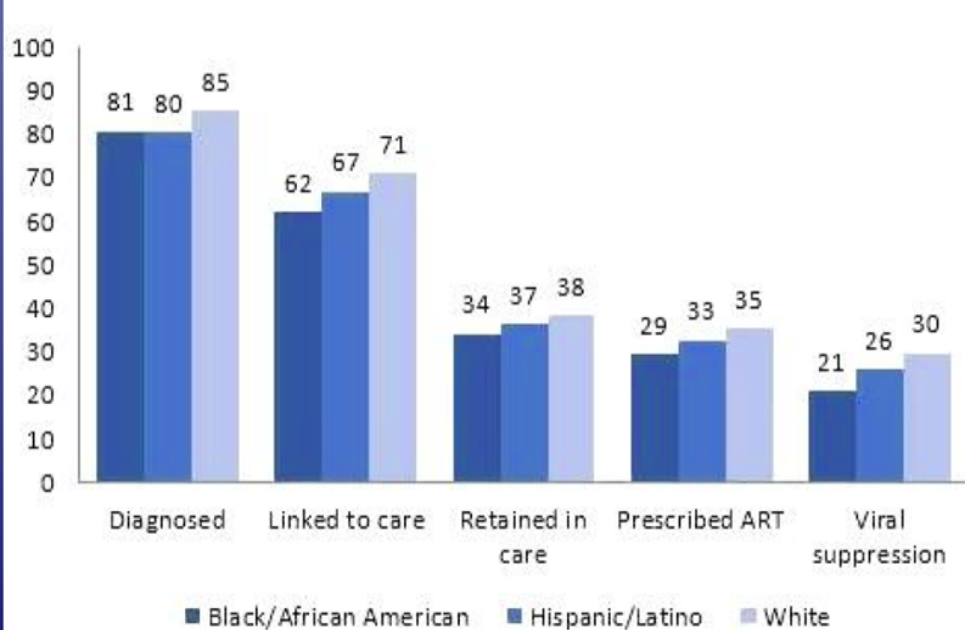
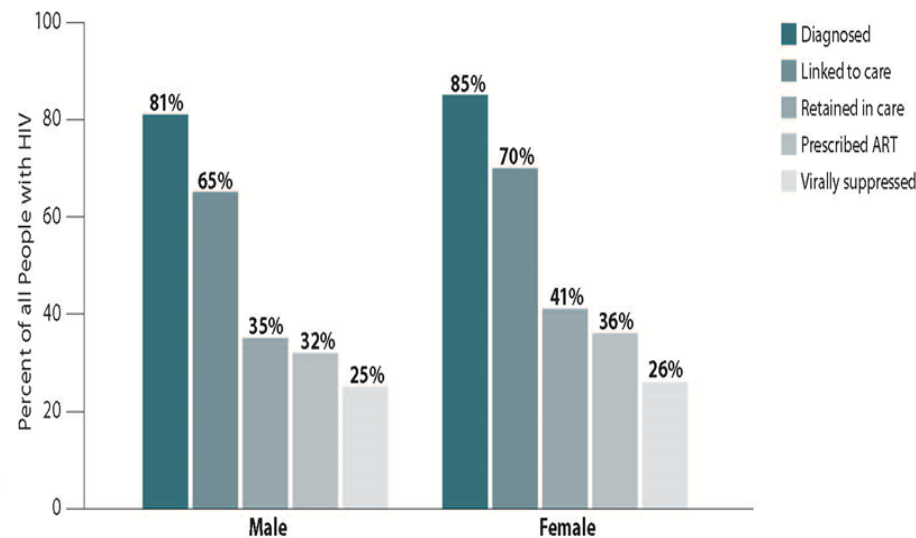


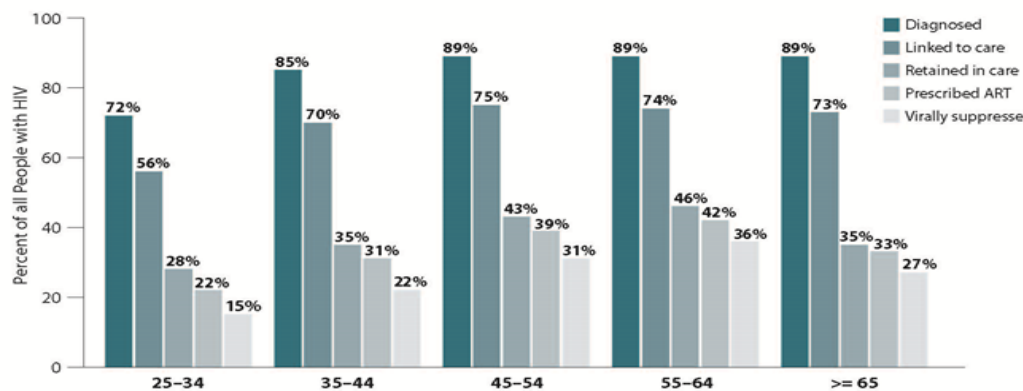
Figure 2. Percentage of persons with HIV engaged in selected stages of the continuum of care, by race/ethnicity -- United States



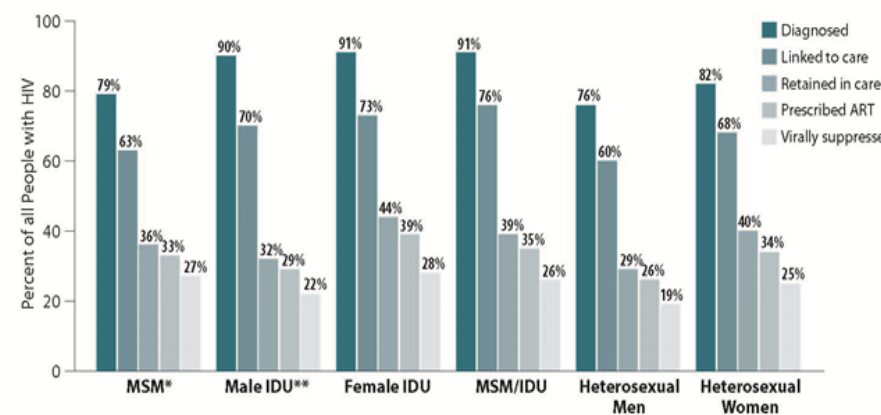
BY GENDER: Although men are less likely to be retained in care, men and women are equally likely to be virally suppressed.



BY AGE: Younger Americans are least likely to be retained in care or have their virus in check; HIV care and viral suppression improve with age, except among those aged 65 and older.



BY RISK GROUP: Across all risk groups, fewer than half are in ongoing care and roughly a quarter have their virus in check.



Note: Although national data were not available to provide estimates of viral suppression for those under the age of 25, the data show that 13-24 year-olds are substantially less likely to have been diagnosed with HIV than other age groups (only 41 percent versus more than 70% for all other age groups).

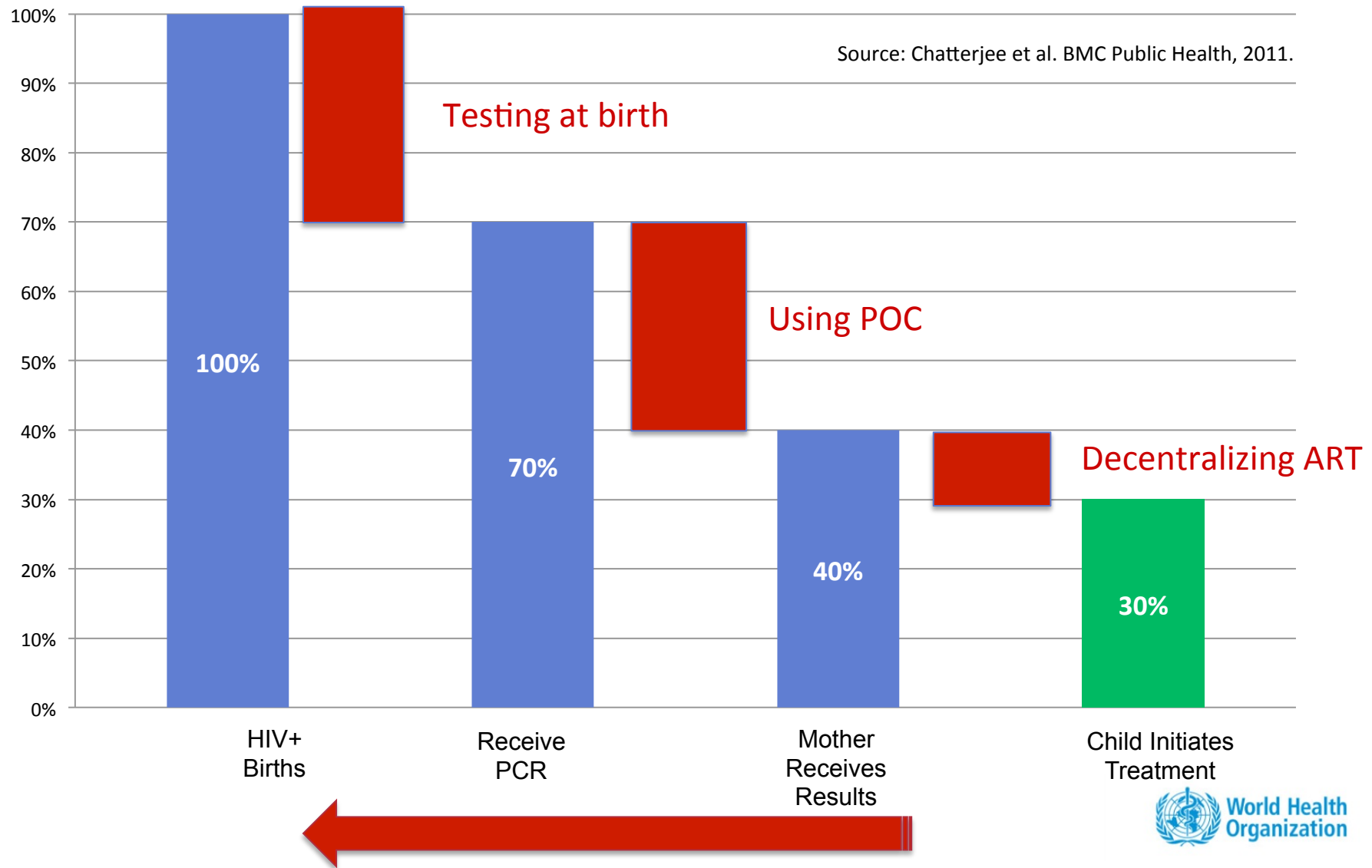
* The term men who have sex with men (MSM) is used in CDC surveillance systems because it indicates the behaviors that transmit HIV infection, rather than how individuals self-identify in terms of their sexuality

** IDU = Injection drug user





Paediatric retention across the cascade





Double Dividend–integration testing and treatment into Child Survival work (ACT & PHTI)



4

REDUCE
CHILD MORTALITY

- Pneumonia and Diarrhea initiatives
- Routine child health services – *EPI*
- Nutrition Initiatives
- Neonatal initiatives



5

IMPROVE
MATERNAL HEALTH

- National Post-natal care programs
- eMTCT – *The Global Plan*
- *Option B+*



6

COMBAT HIV/AIDS,
MALARIA AND OTHER
DISEASES

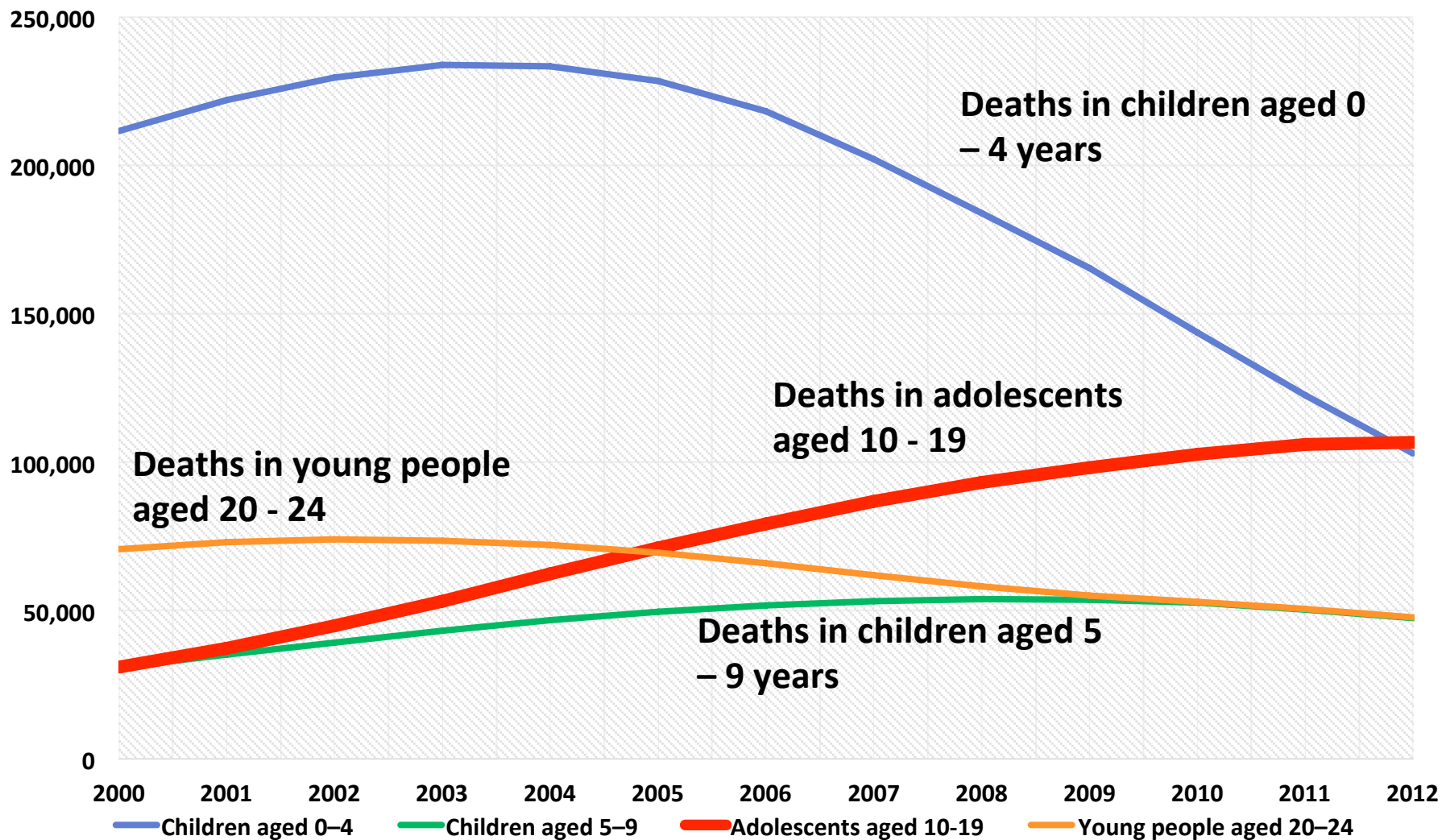
- IATT Paediatric ART working group, simpler regimens – *“Optimal Formulary”*
- WHO recommendations 2014 Supplement;
- Improved SCM of ARTs



Action to **improve survival** of HIV exposed infected and uninfected children in the era of eMTCT and renewed child survival campaigns



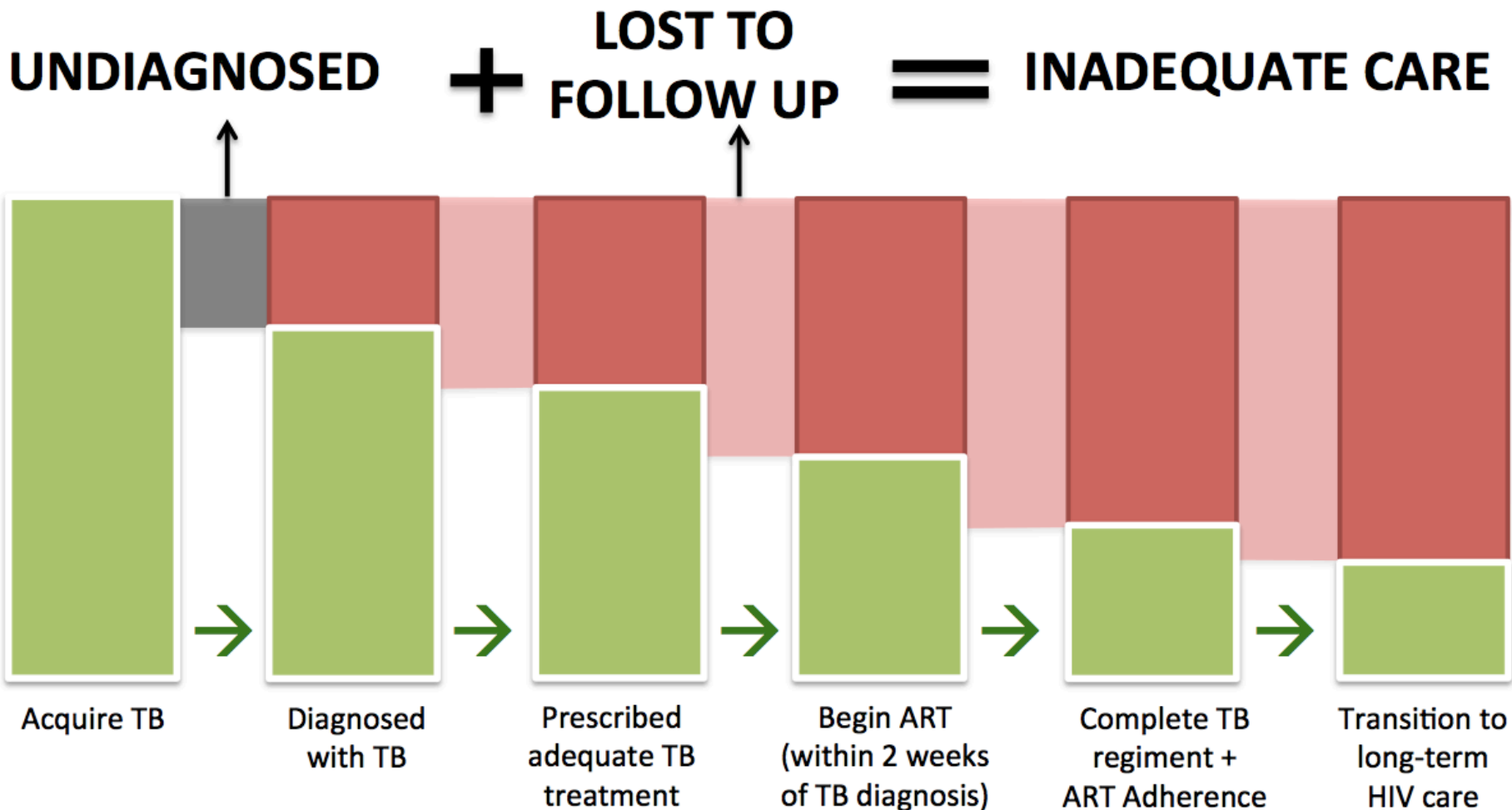
Unacceptable inequality: AIDS deaths rising among adolescents



Source: UNAIDS 2012 HIV and AIDS estimates



TB-HIV Continuum of Care





Xpert MTB/RIF in HIV settings – a vital opportunity



World Health
Organization

TUBERCULOSIS DIAGNOSTICS

Xpert MTB/RIF Test

ABOUT THE XPERT MTB/RIF TEST

The rapid TB test – known as Xpert MTB/RIF- is a fully-automated diagnostic molecular test. It has the potential to revolutionize and transform TB care and control. The test:

- simultaneously detects TB and rifampicin drug resistance
- provides accurate results in less than two hours so that patients can be offered proper treatment on the same day
- has minimal bio-safety requirements and training needs, and can be housed in non-conventional laboratories.



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UPDATED WHO RECOMMENDATIONS

AS OF OCTOBER 2012

Strong recommendation:

- Xpert MTB/RIF should be used as the initial diagnostic test in adults and children presumed to have MDR-TB or HIV-associated TB



Integrate service delivery according to the setting

TB service

One-stop service

HIV service

HIV testing

HIV prevention

CPT

ART

HIV testing

ART

CPT

Condoms

HIV and TB Services provided together

ART

TB diagnosis and treatment

TB screening

IPT

TB diagnosis

TB treatment

TB contact tracing

TB screening

TB diagnosis

TB treatment

Referral to HIV

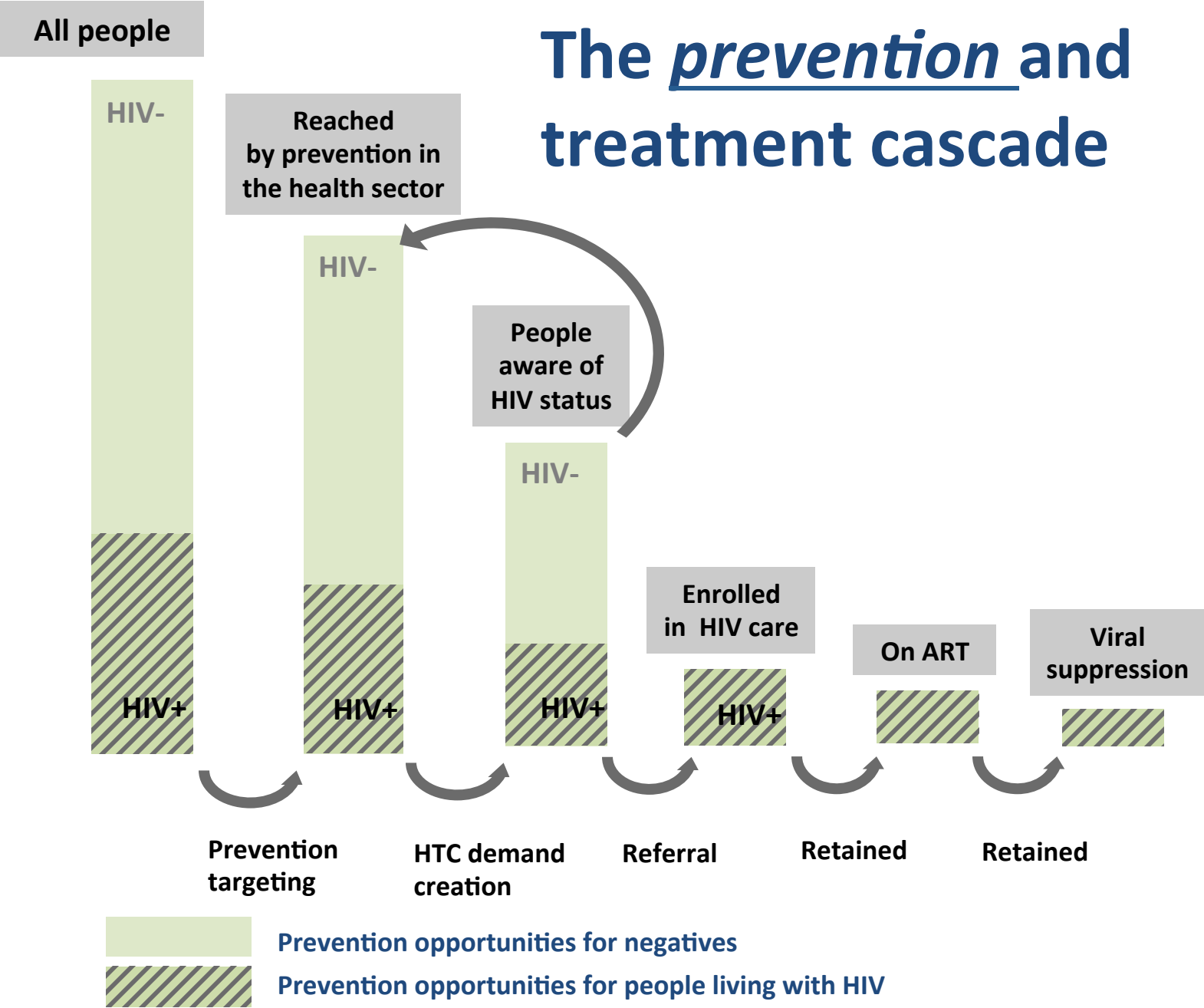
Partially integrated

Co-located Adjacent

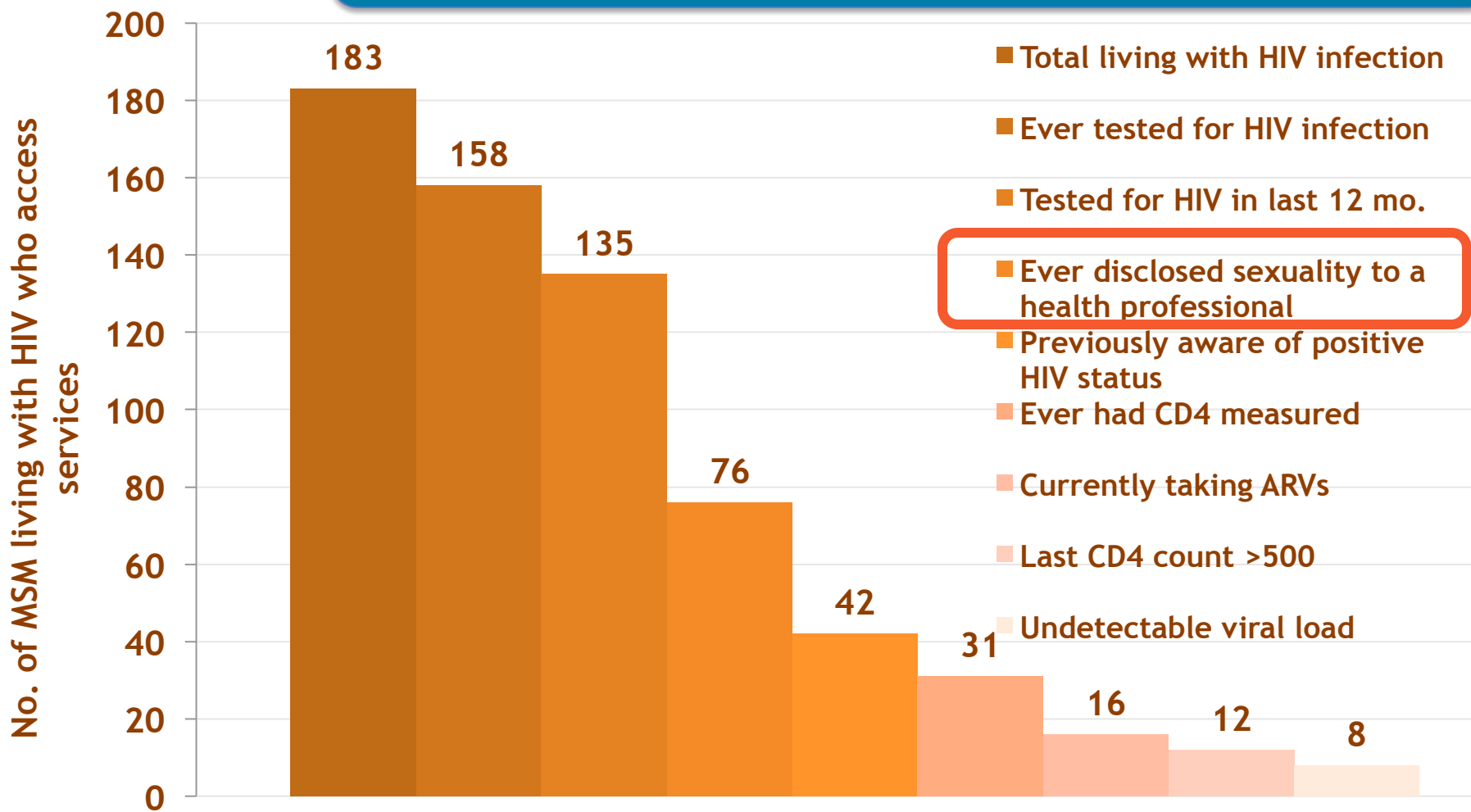
Partially integrated

Referral to TB

The prevention and treatment cascade



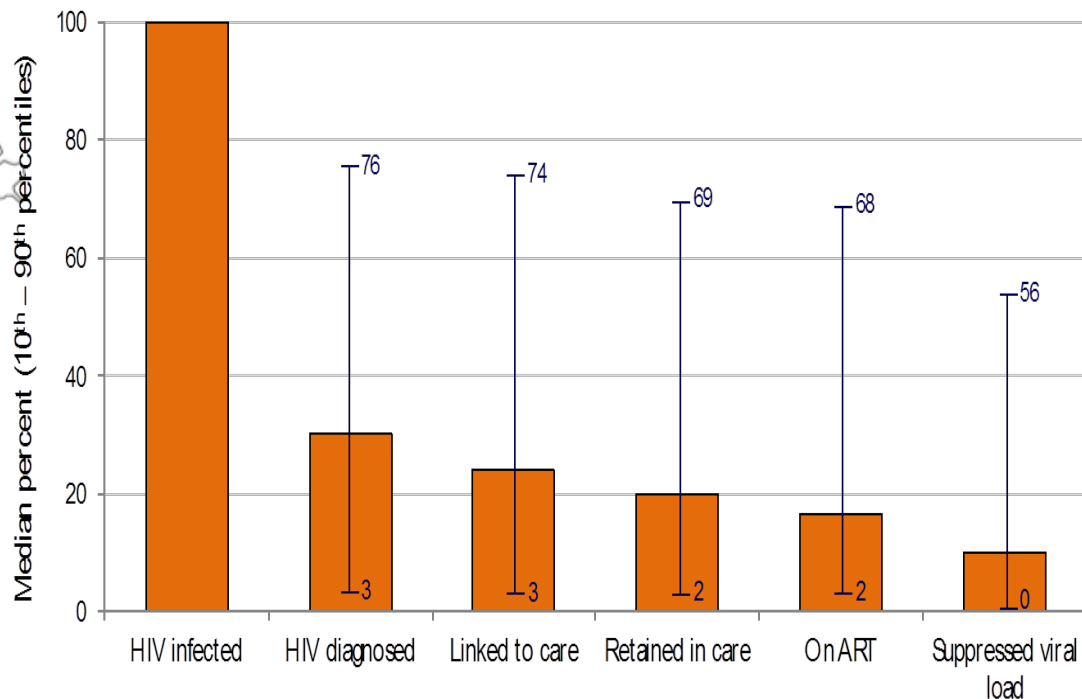
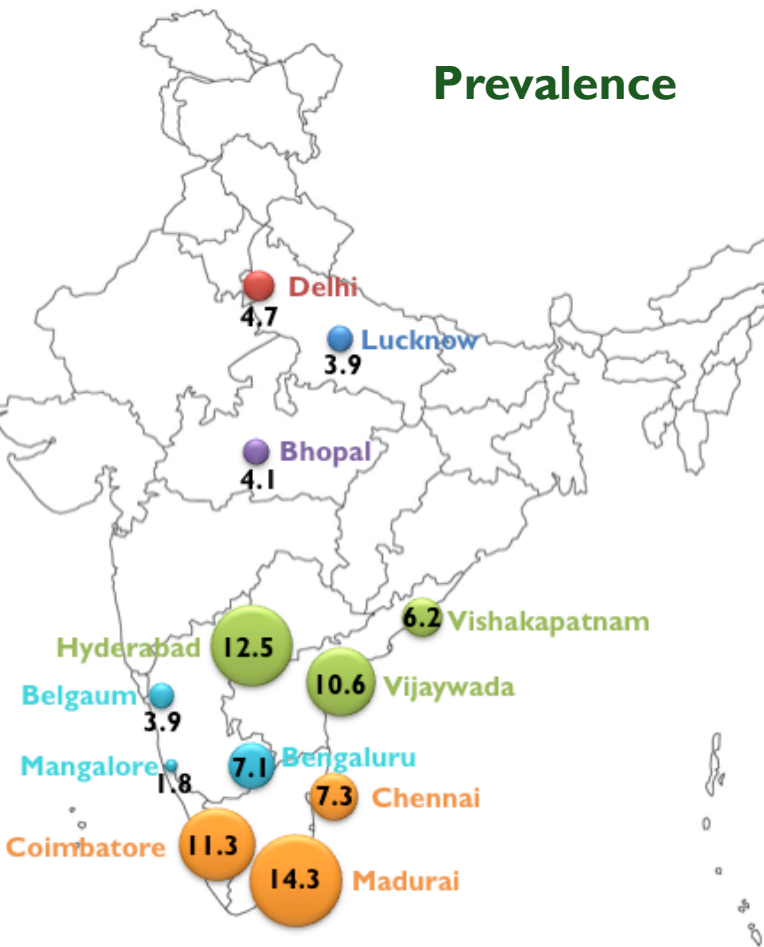
Moscow MSM: HIV Diagnosis and Treatment



HIV prevalence RDS adj: 12.4% (95%CI: 9.3 – 16.1)

HIV Care Cascade Among 1,146 HIV Positive MSM From 12 sites In India

Prevalence



Engagement in care was better in sites with established epidemics where there have been more government-led targeted interventions.

Awareness of status was better among individuals who had received other services (e.g., TB treatment and STI treatment)

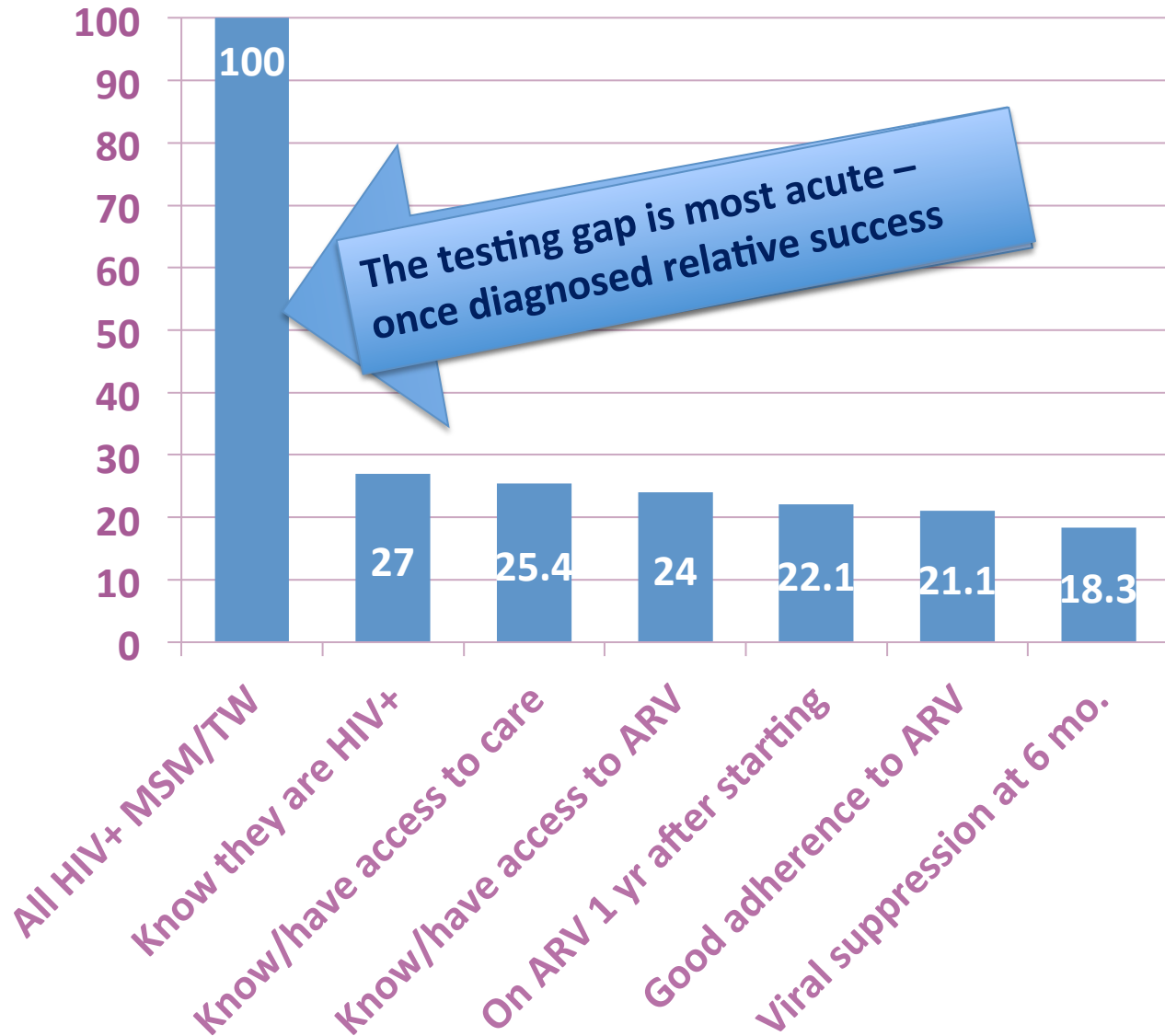
Solomon SS et al IAS 2014 MOPEI500

Mehta SH et al CROI 2014



KEY POPULATIONS

Treatment Cascade in Peru



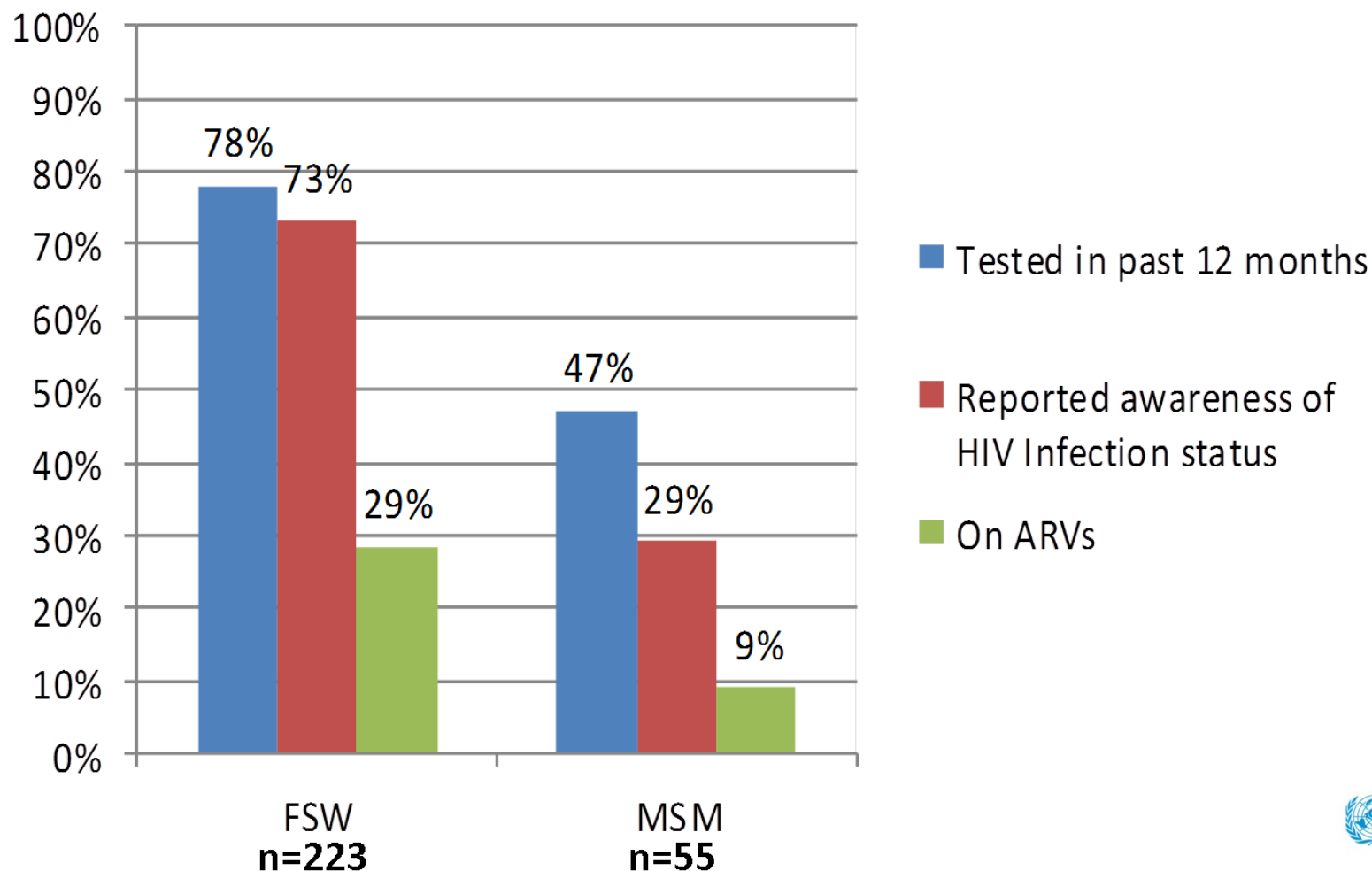
Continuum of Care Cascade for HIV+ MSM/TW in Peru (Est. N = 38,000)

■ % of HIV+ MSM/TW

Carlos F. Cáceres, Cayetano Heredia University, Lima



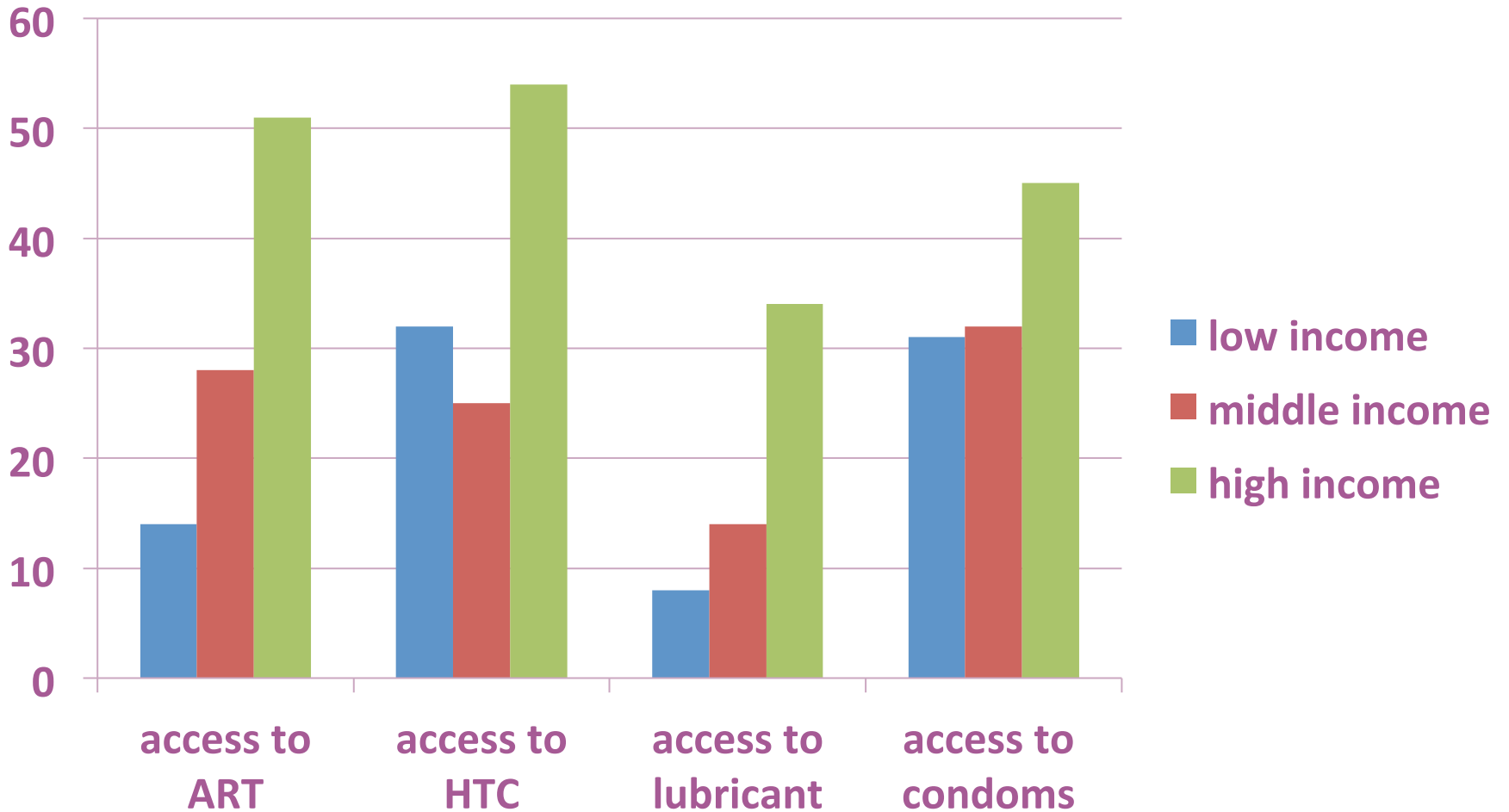
HIV Testing, Knowledge of Infection Status and ARV Use Among Enrolled FSW and MSM Living with HIV in Swaziland





Access to prevention and ART

MSM *(Global Men's Health and Rights Study 2012)*





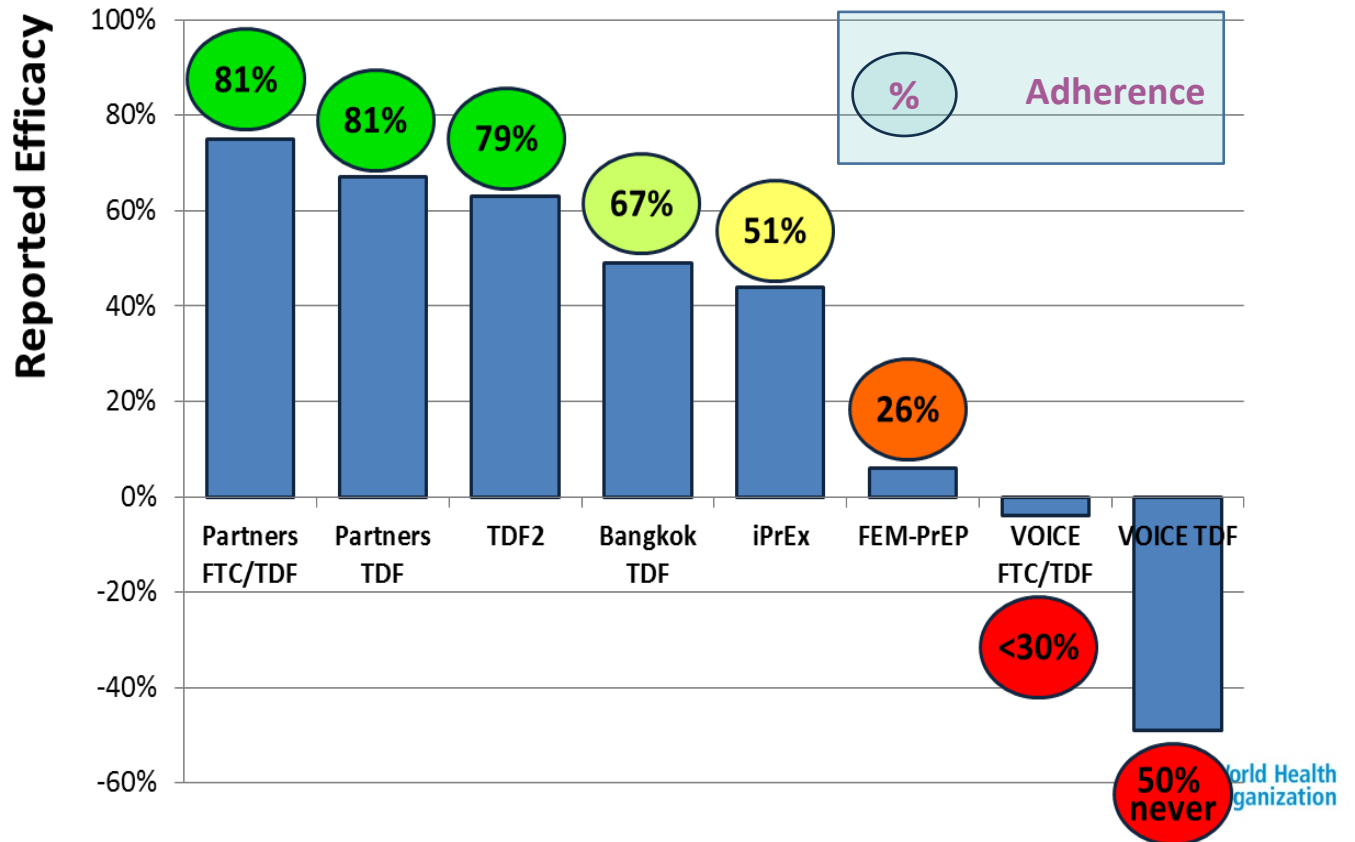
KEY POPULATIONS

New WHO recommendations on PrEP

WHO Consolidated Guidelines on HIV Prevention, Diagnosis, Treatment and Care for Key Populations 2014

- PrEP is effective and safe if taken as prescribed
- Effectiveness trials (Phase II b and III) conducted in MSM, higher risk women & PWID
- OLE in MSM PrEP sites show promising outcomes

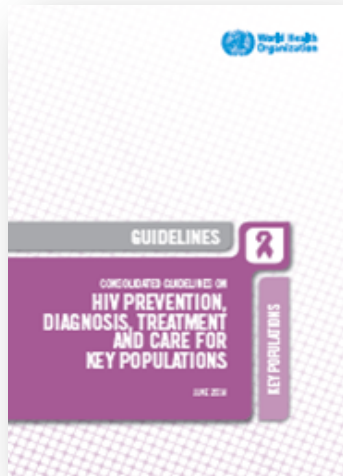
Dose-response relationship between adherence and PrEP efficacy



Type date



New PrEP recommendation in WHO Key Population Guidelines 2014



Among men who have sex with men, PrEP is recommended as an *additional HIV prevention choice* within a comprehensive HIV prevention package

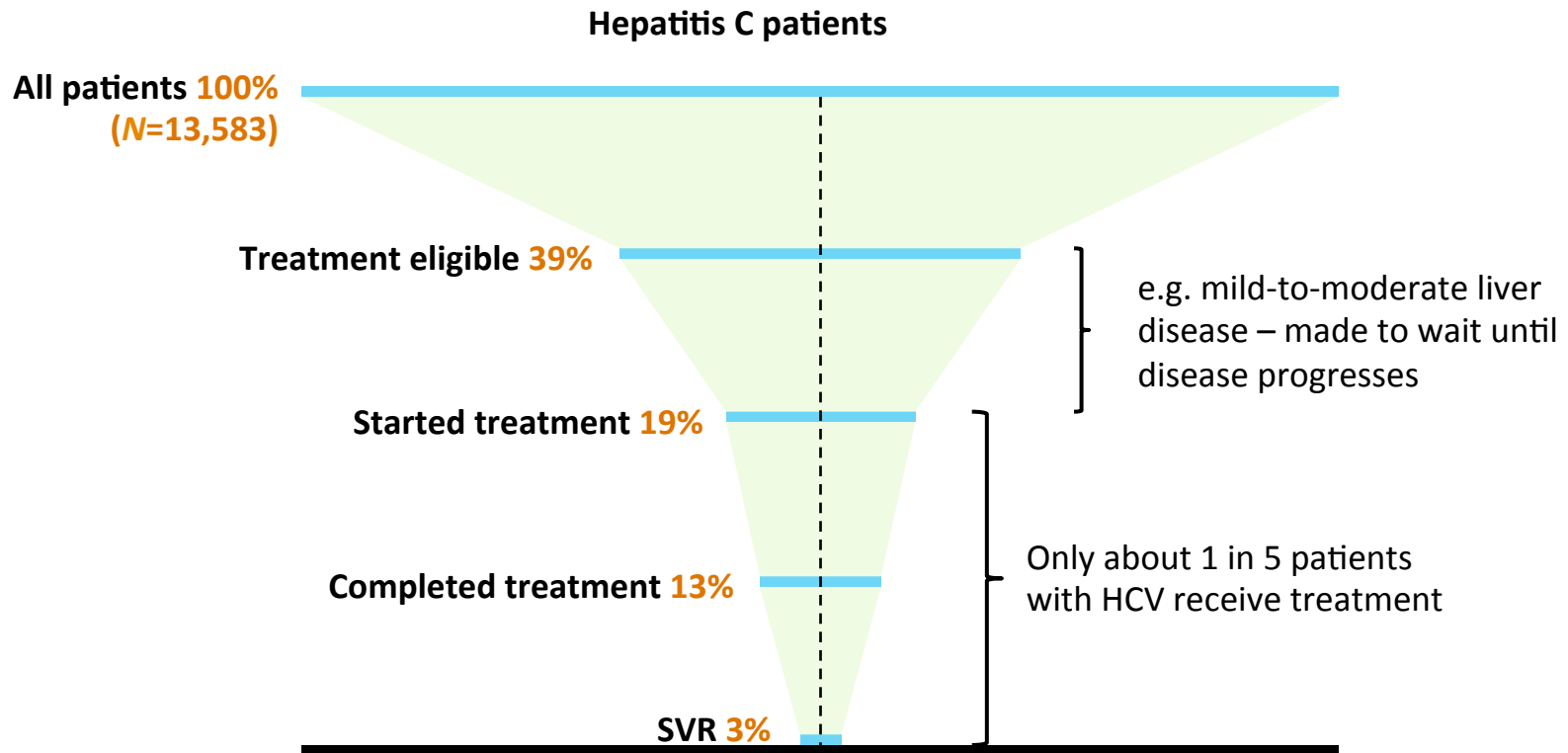
No recommendation was made at this stage concerning the use of PrEP among people who inject drugs

WHO 2012 PrEP conditional recommendation for other KP and people in SDC remains – *for consideration in demonstration projects*



Hepatitis C Treatment Cascade

Review of 25 studies (including 13,583 HCV patients)
HCV treatment experience a clinical care setting

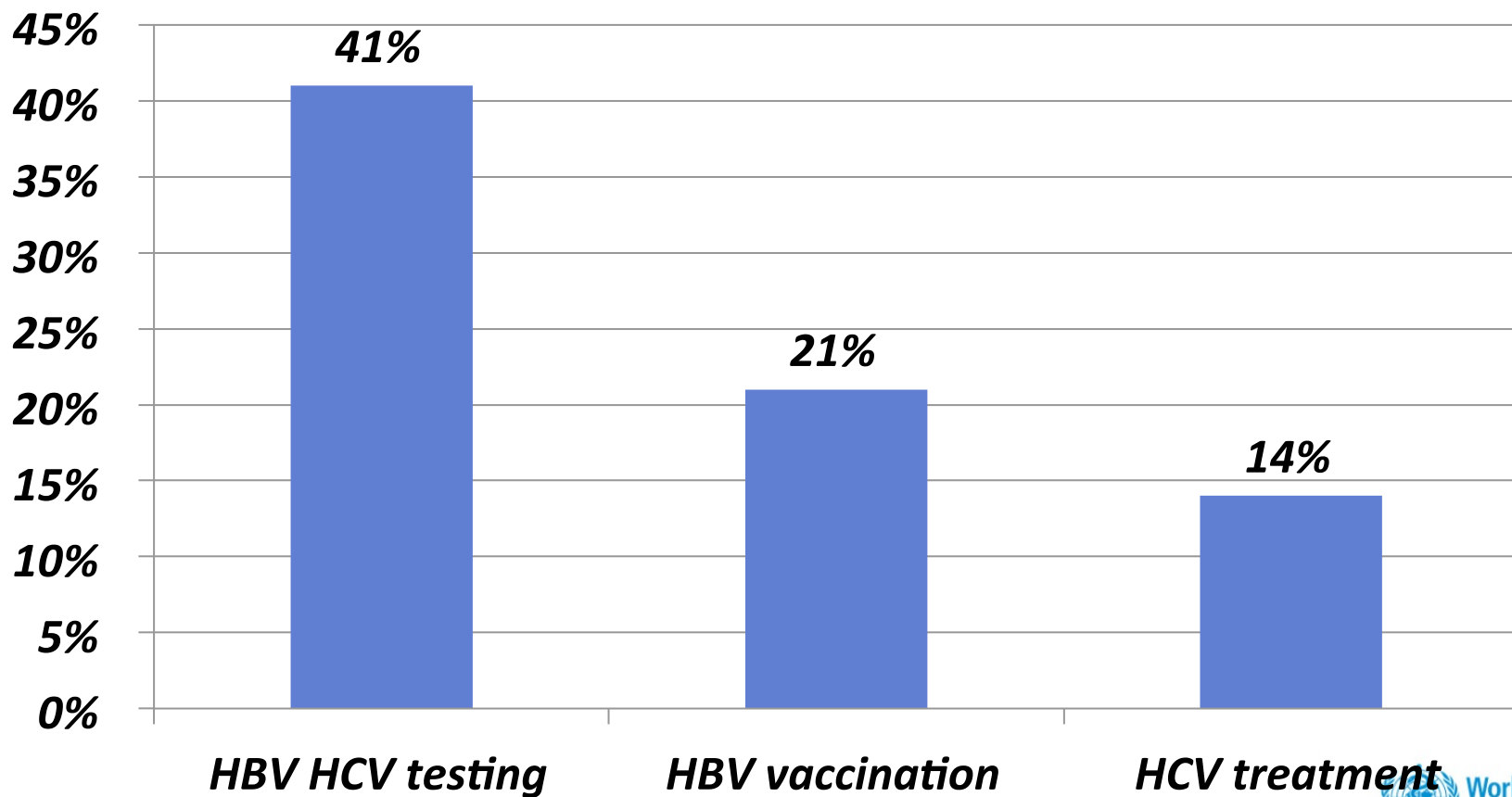


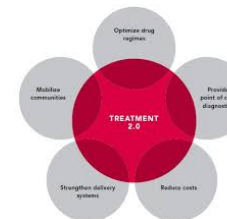


HIV-Hep Service Integration

- **HIV is a service platform for supporting an emerging hepatitis agenda**

Share among 58 WHO HIV focus countries offering hepatitis services in ART clinics, June 2014



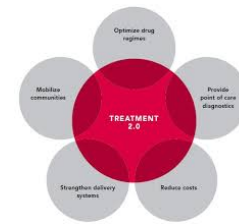


WHO Innovations in HIV Testing

Advantages of HIVST

- Convenience
- Privacy
- Autonomy
- Reduced stigma & normalization
- Less resource intensive for the health care system





WHO Innovations in Drugs

Drug optimization agenda (CADO, PADO, PAWG, Peds Formulary, PHTI):

- Low-dose EFV / low-dose AZT
- Use of new drugs (e.g., dolutegravir, TAF)
- Heat stable FDC for DRV/r; single pill second line
- Paediatric formulations (pellets, injectables, long-acting)

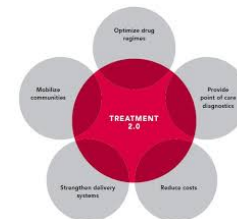




WHO leadership in Drug Optimization



ART Optimization Strategy	Tolerability	Resistance	Convenience	PW, TB, children	Cost Reduction	What action are needed?	Expected Timeline
Low dose EFV	✓	?	✓	?	✓	<ul style="list-style-type: none"> • pK studies (PW & TB) 	1-2 yrs
Low dose DRV/r (as FDC)	✓	?	✓	?	✓	<ul style="list-style-type: none"> • pK studies (DRV:RTV ratio) • RCT (standard vs low dose) 	2-5 yrs
Use of DTG	✓	✓	✓	?	✓	<ul style="list-style-type: none"> • Studies in PW, TB & children • Comparative trials (TDF / TAF in 1st line) • RCT (DRV/r + DTG in 2nd line) 	2-5 yrs
Use of TAF	✓	?	✓	?	✓	<ul style="list-style-type: none"> • Trials DTG • Studies in PW, TB & children 	2-5 yrs
Long-acting formulations	✓	?	✓	✓	✓	<ul style="list-style-type: none"> • Phase II/III studies 	> 5 yrs



WHO Innovations in Service delivery

Bringing ARV services closer to the patient:

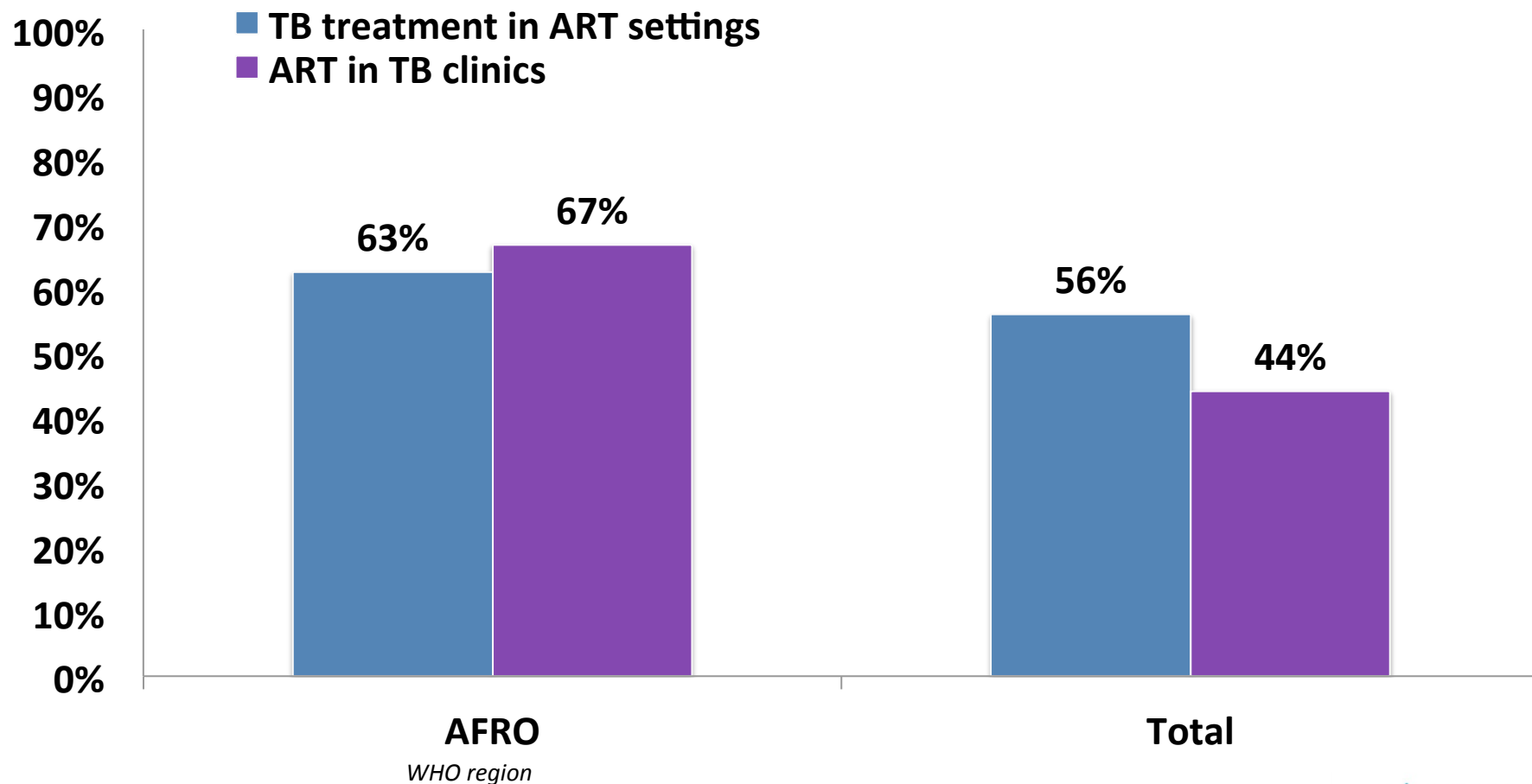
- Task Shifting / sharing
- Integration & Decentralisation
- Community based ARV delivery approaches
- Use of POC CD4 for rapid linkage / engagement





Uptake of 2013 WHO operational and Service Delivery Recommendations as of June 2014

ART and TB Service integration policies, percent (%) of 59 WHO focus countries, by region





WHO consultation on Community ART Delivery (ICASA 2013)



Already happening: DRC, Mozambique, South Africa, Uganda, Zimbabwe

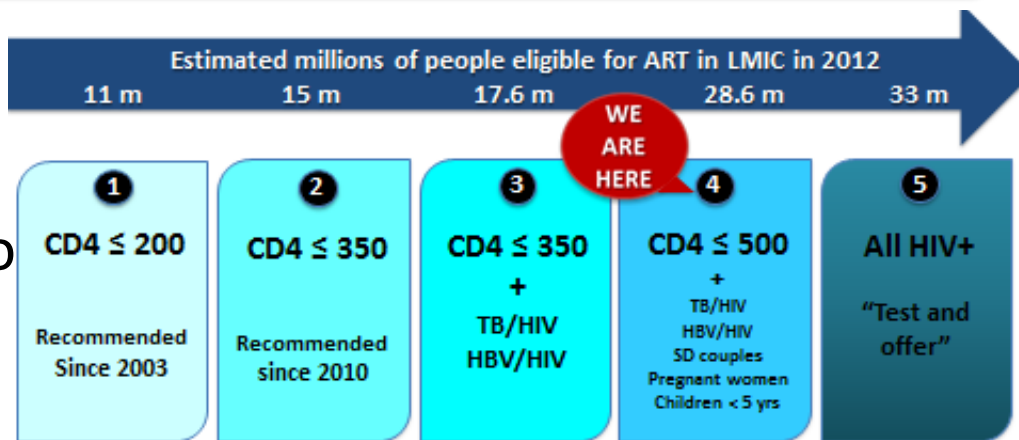
- Models need to be flexible and adapted to context
- Referral mechanisms are critical
- Supportive policy needed, including for support of community health workers
- Simplified, integrated M&E critical

Model of care	Country, implementer and year	Criteria for delivering ART	ART refill interval	Frequency of clinic visit	Patient–provider ratio, human resources used and organization	Remarks
Community adherence groups (14,15)	Mozambique Ministry of Health 2011–present Lesotho, Malawi, South Africa and Zimbabwe	Stable on ART Piloting Inclusion of pre-ART people living with HIV	Monthly (Lesotho and Mozambique), every 2 months (Malawi), every 3 months (Zimbabwe)	Every 6 months (Lesotho, Malawi and Mozambique), annually (Zimbabwe)	Self-forming groups of 6–10 people living with HIV rotate to collect ART for the group. Groups formed with support from clinic staff and local networks of people living with HIV	
Community adherence groups – pilot for the above (15)	Mozambique Médecins Sans Frontières 2008–present	>6 months on ART, absence of adverse drug events, no opportunistic infection, CD4 >200 cells/mm ³	Monthly	Every 6 months	Self-forming groups of six people living with HIV rotate to attend the clinic and collect ART for the group	98% retention in care after 3 years; children in community adherence groups reporting 94% retention (11) Uptake around 50%

Additional interventions to improve the treatment and care cascade

Next guidelines

- Evidence of WHAT
- Greater focus on the HOW to deliver ARVs and context



Optimized Care Package of interventions to improve continua:

Early

Late

Stable

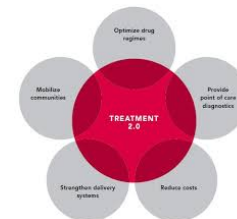
Failing

• Adherence & retention support

• Interventions to reduce mortality and morbidity

• Community ART delivery

• Second and third line support



WHO Innovations in Diagnostics

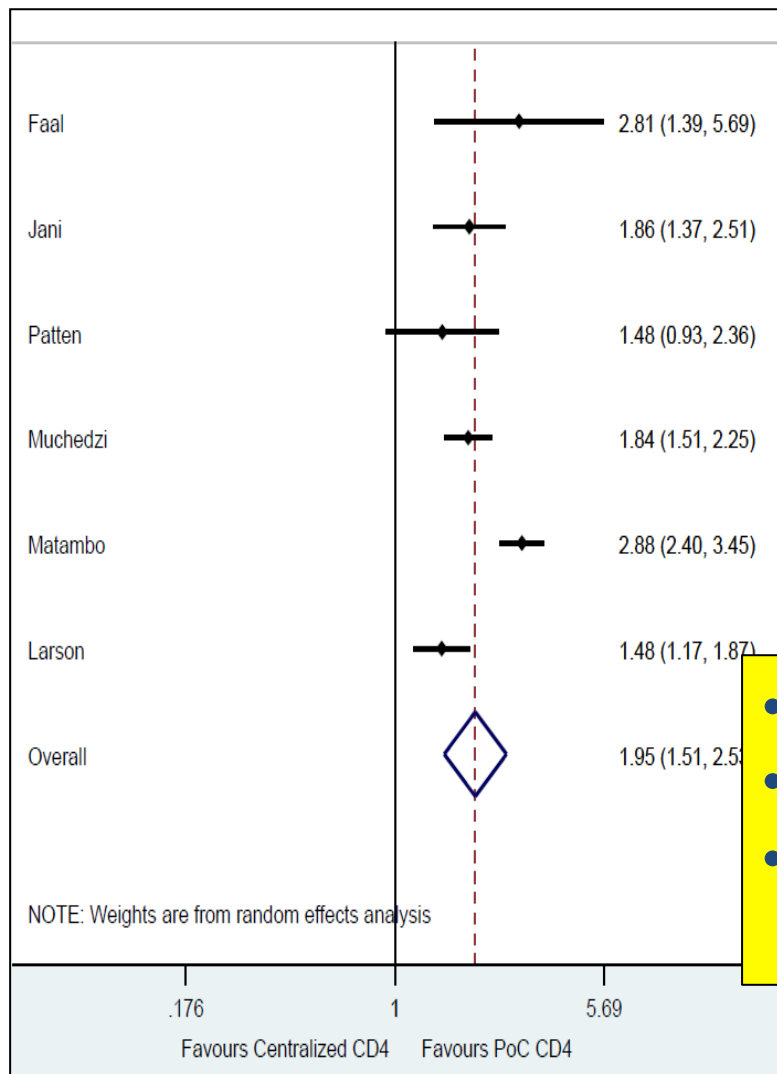
Diagnostics optimization agenda:


- Viral Load implementation guidance with CDC & PEPFAR
- Quality of Care for POCT
- Technical lead to the Diagnostics Access Initiative (DAI)





Impact of Point of care CD4 on linkage/retention in HIV care





Wynberg E et al. *Journal of the International AIDS Society* 2014, 17:1809
<http://www.jaociety.org/index.php/jia/article/view/1809> | <http://dx.doi.org/10.7448/IAS.17.1.1809>

Review article

Impact of point-of-care CD4 testing on linkage to HIV care: a systematic review

Elke Wynberg¹, Graham Cooke^{*1}, Amir Shroufi², Steven D Reid³ and Nathan Ford^{*4,5,6}

^{*}Corresponding author: Nathan Ford, HIV/AIDS Department, World Health Organization, 20 Avenue Appia, 1211 Geneva, Switzerland. Tel: +41 22 791 19 19. (fordn@who.int)

[†]These authors contributed equally to the work.

Abstract
Introduction: Point-of-care testing for CD4 cell count is considered a promising way of reducing the time to eligibility assessment for antiretroviral therapy (ART) and of increasing retention in care prior to treatment initiation. In this review, we assess the available evidence on the patient and programme impact of point-of-care CD4 testing.
Methods: We searched nine databases and two conference sites (up until 26 October 2013) for studies reporting patient and programme outcomes following the introduction of point-of-care CD4 testing. Where appropriate, results were pooled using random-effects methods.
Results: Fifteen studies, mainly from sub-Saharan Africa, were included for review, providing evidence for adults, adolescents, children and pregnant women. Compared to conventional laboratory-based testing, point-of-care CD4 testing increased the likelihood of having CD4 measured [odds ratio (OR) 4.1, 95% CI 3.5–4.9, n=2] and receiving a CD4 result [OR 2.8, 95% CI 1.5–5.6, n=6]. Time to being tested was significantly reduced, by a median of nine days; time from CD4 testing to receiving the result was reduced by as much as 17 days. Evidence for increased treatment initiation was mixed.
Discussion: The results of this review suggest that point-of-care CD4 testing can increase retention in care prior to starting treatment and can also reduce time to eligibility assessment, which may result in more eligible patients being initiated on ART.

Keywords: antiretroviral therapy; HIV/AIDS; point-of-care CD4; retention; treatment initiation.

To access the supplementary material to this article please see Supplementary Files under Article Tools online.

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Introduction
 There is a recognized need for improving the care pathway from HIV diagnosis to timely antiretroviral therapy (ART) initiation, with several recent studies highlighting substantial losses in the continuum of care from HIV testing to ART initiation [1–3]. Reasons reported for such attrition vary and include long waiting times at testing centres, absence of a facility that is often far removed from remote testing centres. In addition, flow cytometry requires technical expertise, complex instrumentation and software, and a reliable data management system to ensure the results are returned promptly to the health worker and patient. A number of PoC CD4 machines are currently available on the market, with more expected in the coming years [4]. Early results show

- Odds of linking to care increased
- Time to testing reduced by 9 days
- Time from testing to receiving the result was reduced by 17 days



Strategic Use of ARVs - SUFA3 (the WHAT and the HOW)

2011

SUFA 1

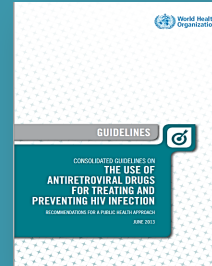
- Clinical science map
- Roadmap to consolidated ARV guidelines

2012

SUFA 2

- HIV programming: from clinical recommendations into policy and practice

2013



- Major capacity building
- Policy dialogue in countries

2014

SUFA 3

- Roadmap to the next generations of WHO ARV guidance
- **Clinical and Implementation Science research agenda**



Distribution of Intervention Approaches at Each Step of the Cascade

Geng, Feb 2014

	Testing	Linkage	Staging	Pre-ART retention	ART initiation	Retention on ART	Adherence	Viral suppression
Delivery Architecture	47%	64%	73%	56%	58%	64%	38%	63%
Counseling	10%	13%	4%	6%	10%	9%	29%	10%
Demand Creation	18%	13%	12%	31%	17%	13%	19%	15%
Management	28%	23%	29%	25%	37%	26%	21%	29%
Social	28%	13%	15%	13%	18%	17%	31%	15%
Technology	9%	16%	21%	19%	10%	14%	13%	13%
Total studies	125	64	52	16	109	115	68	52

White= More Studies

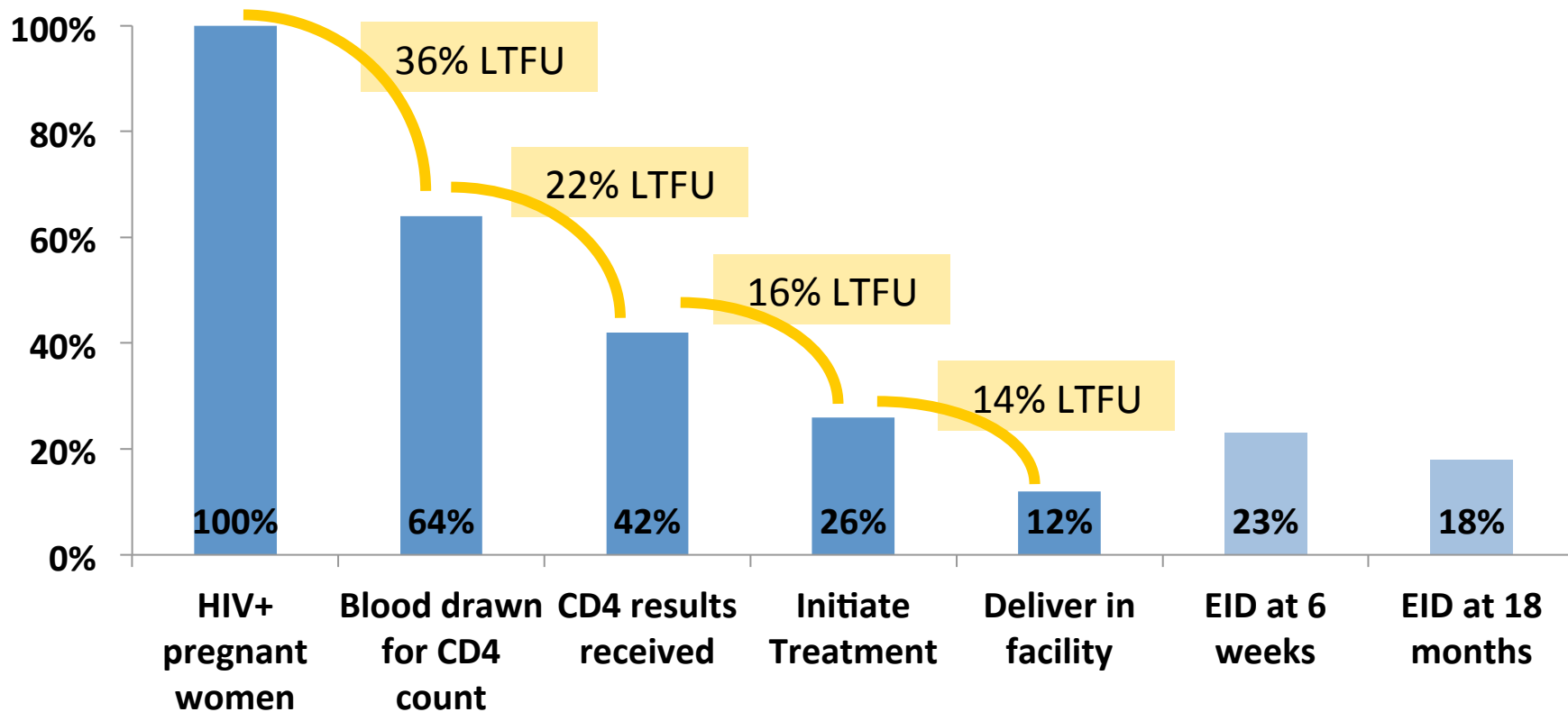


Red= Fewer Studies

- Service delivery approaches are most studied within each step.
- Differences by approach seemed largest for linkage interventions and smallest for adherence interventions.



Retention and the Leaky PMTCT & Paeds Cascade



Among infants testing HIV positive via EID, an estimated 38% will initiate treatment, and an estimated 28% will be retained and alive on treatment after 12 months

Cascade based on Data from Lesotho, Malawi, South Africa, Uganda, Zambia, & Zimbabwe

Sources: Chatterjee et al, BMC Public Health 2011; 11:553;

UNICEF, 2012. Available at: http://www.unicef.org/aids/files/DISCUSSION_PAPER.A_BUSINESS_CASE_FOR_OPTIONS_B.pdf



Cascade Targets Addressed by Interventions for *Children*

	Testing	Linkage	Staging	ART initiation	Pre-ART retention	Retention on ART	Adherence	Viral suppression
Service Delivery	2	1	0	1	0	3	2	2
Counseling	0	0	0	0	0	0	2	1
Demand Creation	0	0	0	0	0	0	0	0
Management	0	0	0	2	0	0	0	0
Social support	0	0	0	0	0	0	0	0
Technology	1	0	0	1	0	0	0	0

White= More Studies



Red= Fewer Studies

- Service delivery approaches were the most common with retention on ART as the most examined outcome
- Overall there is a paucity of approaches and steps in the cascade



Implementation Science Research Priorities/Gaps

Adults

- ART Retention & reengagement
- Pre-ART Retention
- Linkage to care
- Adherence and VL suppression

PMTCT

- How to find those not in ANC
- How to retain mothers starting in B+/B programs
- Retesting late in pregnancy and BF
- Demand creation
- Special management for “high risk” mothers (infants) identified HIV+ at delivery

Children / Youth

- Strategies to target children/ adolescents to test, link to care, create demand, promote adherence
- Tracing LTFU
- Reduction of social/structural barriers for youth testing/care
- Optimal models to deliver care and transition adolescents



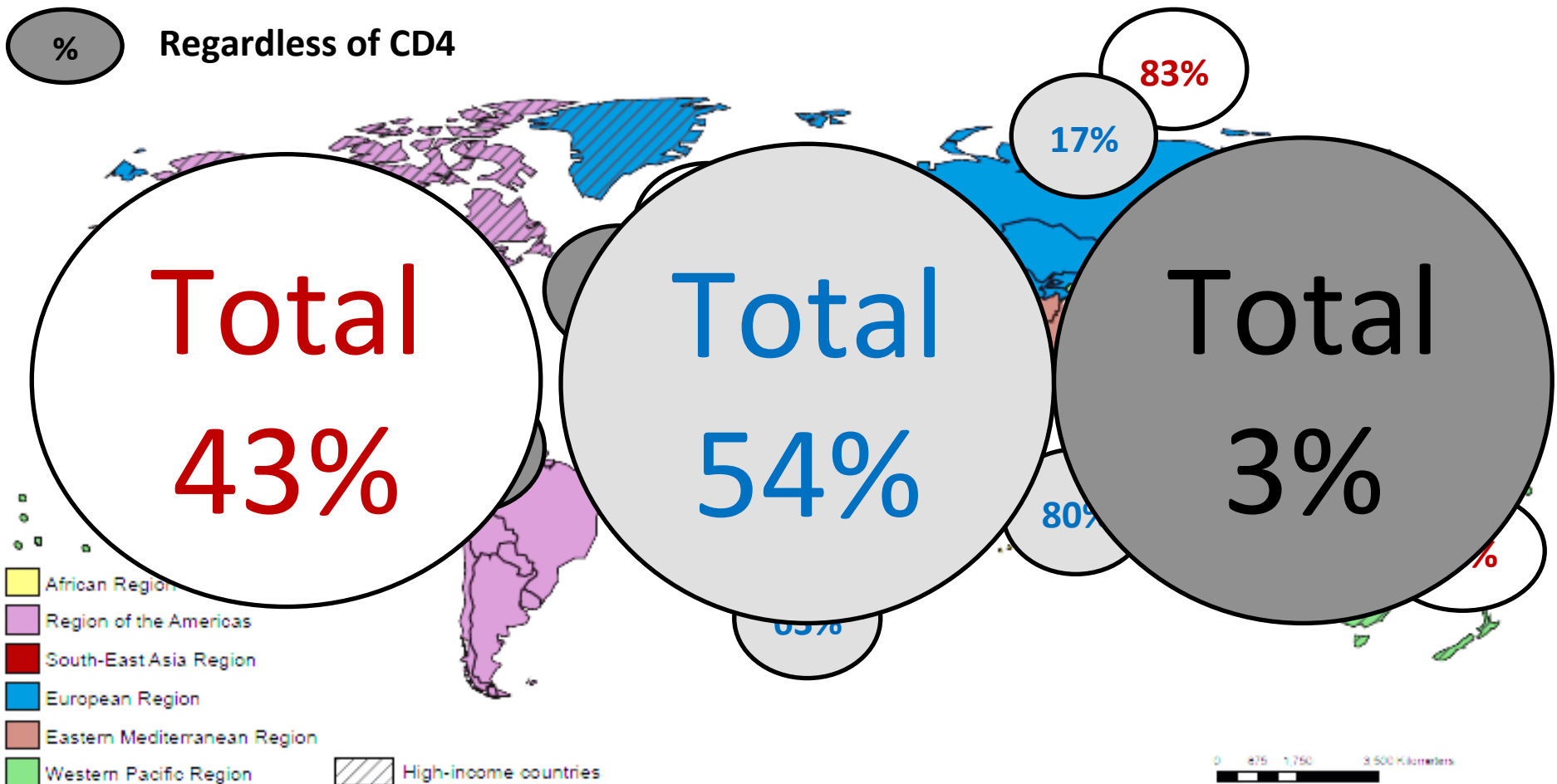
Threshold for ART initiation

Uptake based on 58 WHO focus countries, by region

% CD4 <350

% CD4 <500

% Regardless of CD4



Uptake of 2013 recommendations as of July 2014



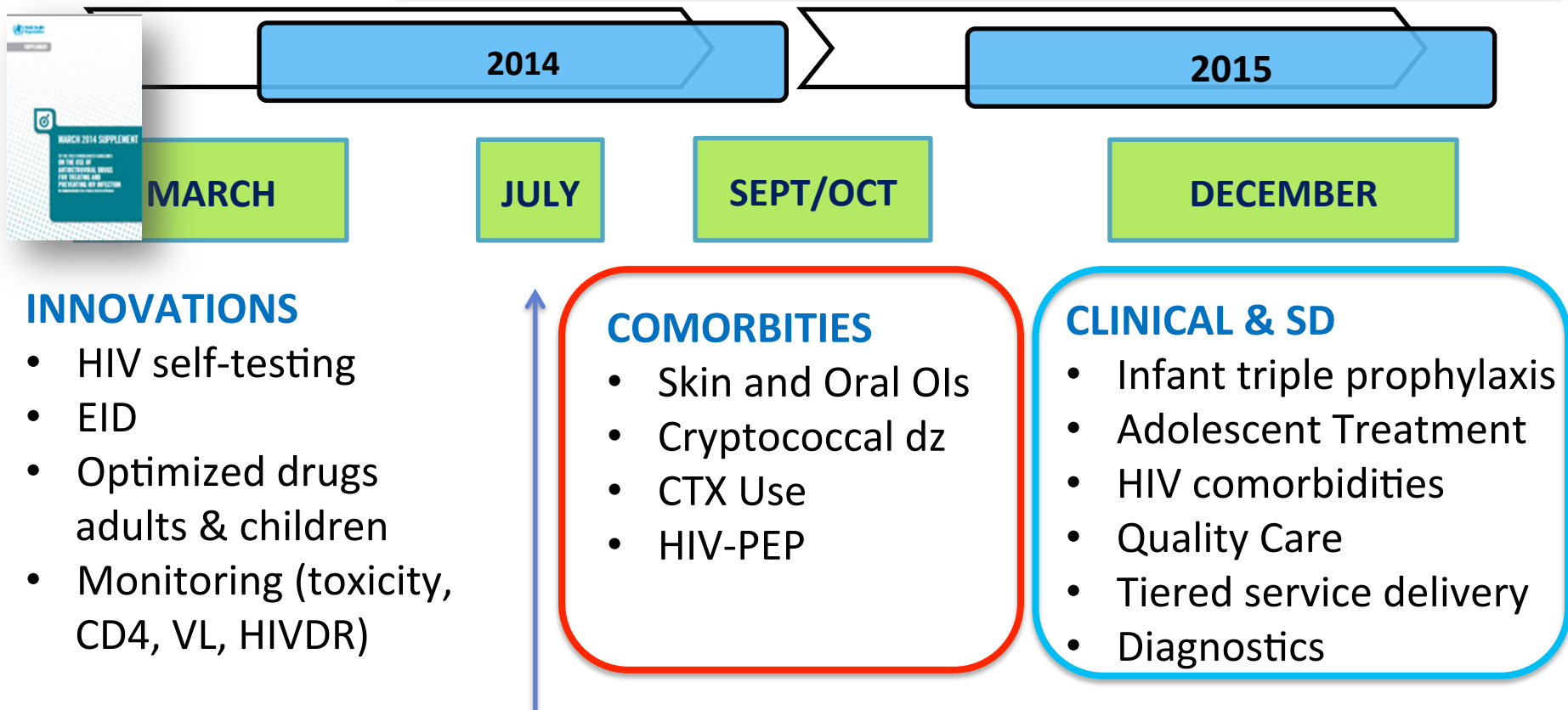
Will the funding be there?

Current Global Fund CN applications & TRP feedback to countries:

- Expanding eligibility—
 - countries are phasing in eligibility to 500 (Moz, Tanz at 350)
 - going to 500 only if extra resources available (e.g. Zim)
 - Choosing non-FDC ARVs or non-recommended first line (Ukraine, Zimbabwe)
- Treatment/prevention balance (e.g. Zambia)
 - are investments well balanced?
 - has the prevention been fully maximized prior to expanding ARVs in high incidence areas
- Routine VL
 - Lower priority in many country CN as counties prioritizing ARVs



Updates to WHO ARV Guidelines: current and future plans



INNOVATIONS

- HIV self-testing
- EID
- Optimized drugs adults & children
- Monitoring (toxicity, CD4, VL, HIVDR)

COMORBIDITIES

- Skin and Oral OIs
- Cryptococcal dz
- CTX Use
- HIV-PEP

CLINICAL & SD

- Infant triple prophylaxis
- Adolescent Treatment
- HIV comorbidities
- Quality Care
- Tiered service delivery
- Diagnostics

1. Technical and operational considerations for implementing viral Load testing
2. Guidance for Improving the Quality of HIV-related Point-of-Care Testing

Assessment of challenges and implementation of new recommendations



Take home messages

- **The treatment, care and prevention continuum is a data use approach to analyze gaps to by populations and location**
- **Optimization / solutions may need to be locally driven and focus on the intermediary hand-offs between each step (quality improvement of care and services)**
- **WHO committed to continue to lead on:**
 - Drugs, Diagnostics & Service Delivery optimization/innovation
 - Guidelines that address the ‘HOW’
 - Promotion Implementation & improvement science research agenda to fill knowledge gaps



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EXTRA SLIDES



MSM



- Efficacy
- Ongoing high incidence in almost all setting
- Current prevention interventions insufficient
- Values and preferences supporting PrEP as an additional prevention choice consistent
- Increasing experience from pilot and OLE studies

PWID



Despite efficacy from 1 RCT

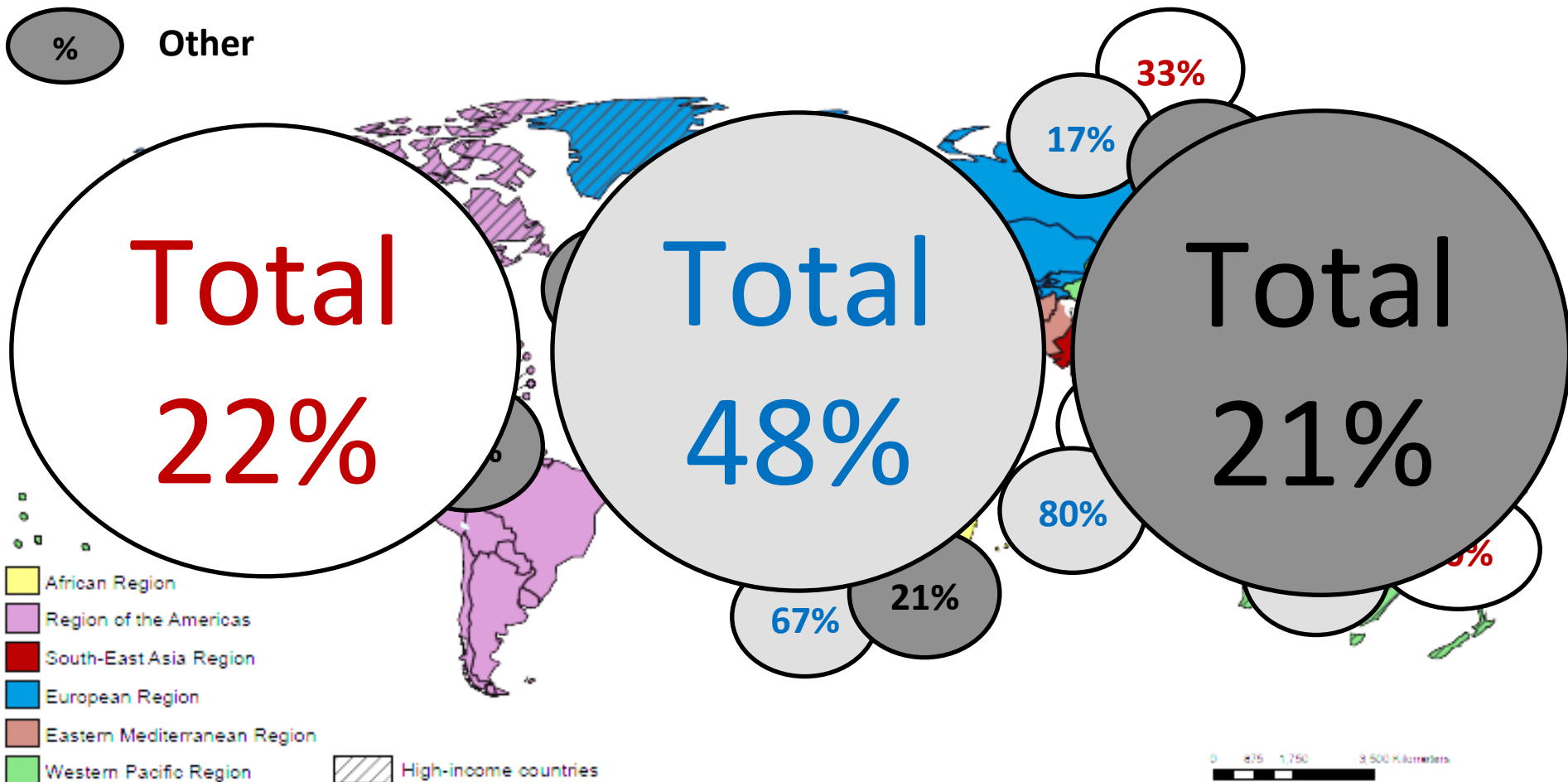
- Only 1 trial site
- Alternative effective HIV prevention interventions available (incl. OST & NSP) with current poor global coverage and reach
- Limited values and preferences – much unfavourable
-



Paediatric ART Age Initiation

Uptake based on 58 WHO focus countries, by region

- % Age < 2 yrs
- % Age < 5 yrs
- % Other



- African Region
- Region of the Americas
- South-East Asia Region
- European Region
- Eastern Mediterranean Region
- Western Pacific Region
- High-income countries



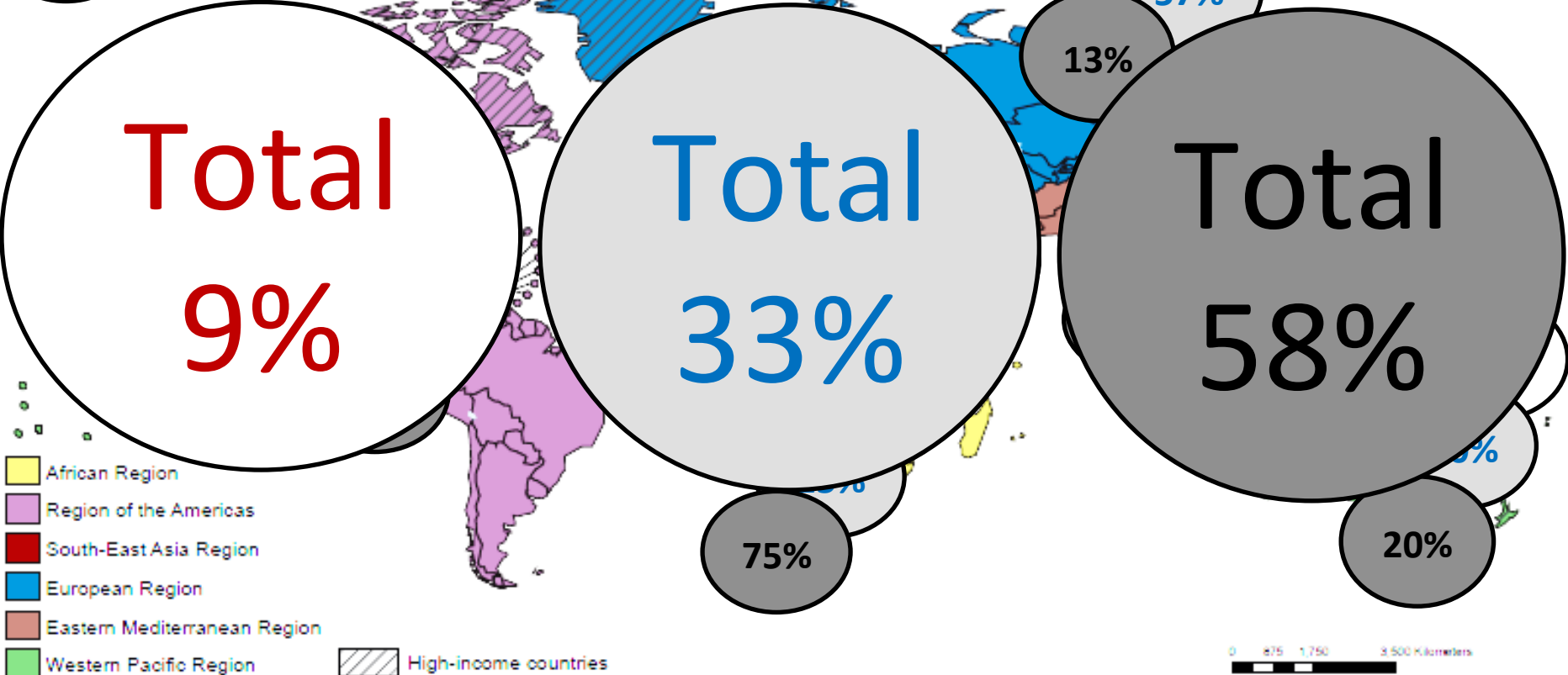
Uptake of 2013 recommendations as of July 2014



Option B / B +

Uptake based on 58 WHO focus countries, by region

- Option A
- Option B
- Option B+





Patterns of ARV use

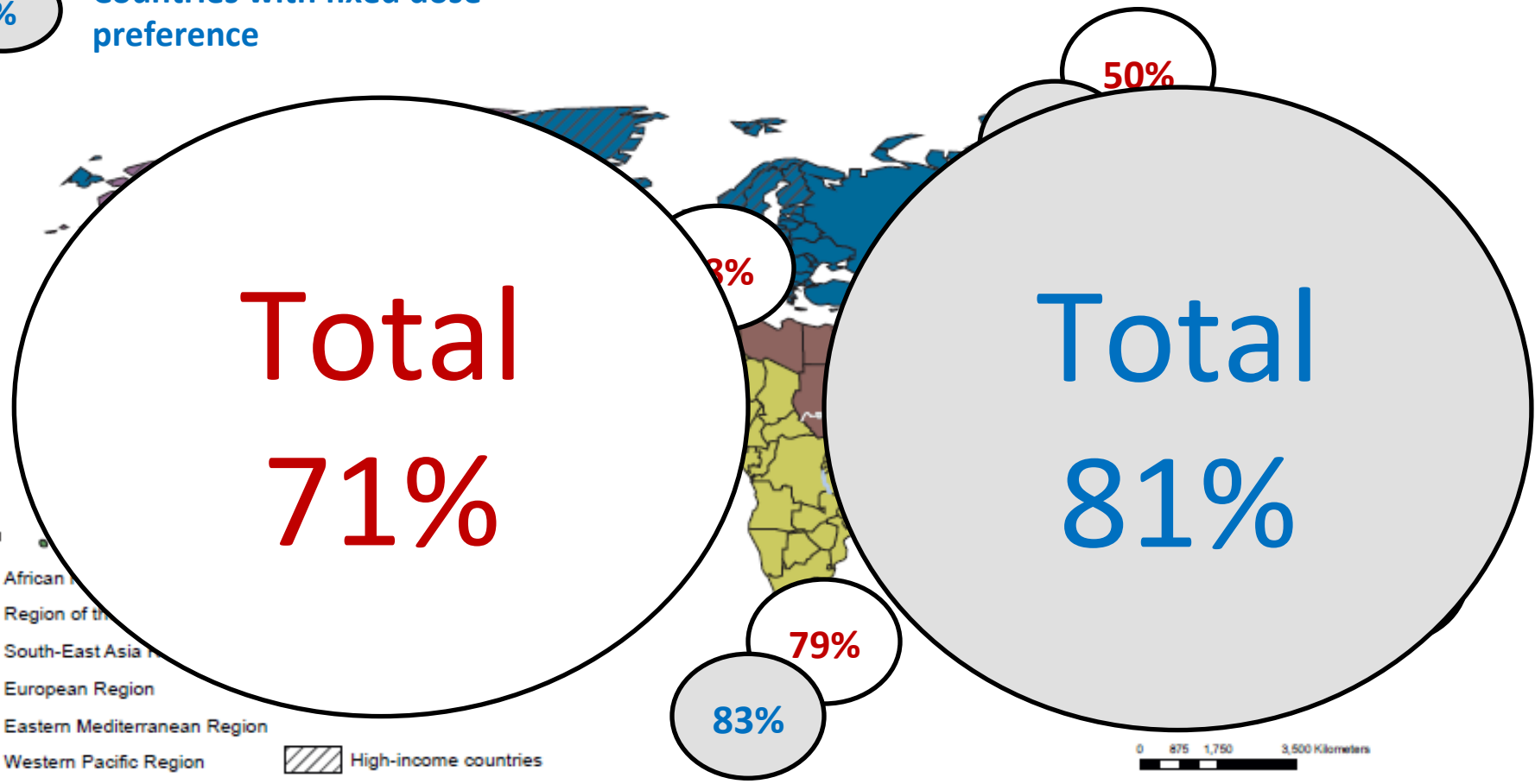
Uptake based on 58 WHO focus countries, by region

%

Preferred 1st line TDF/
3TC(FTC)/EFV

%

Countries with fixed dose
preference



- African Region
- Region of the Americas
- South-East Asia Region
- European Region
- Eastern Mediterranean Region
- Western Pacific Region
- High-income countries

0 875 1,750 3,500 Kilometers