
What will it take to roll-out Test and Treat?

Ian Sanne

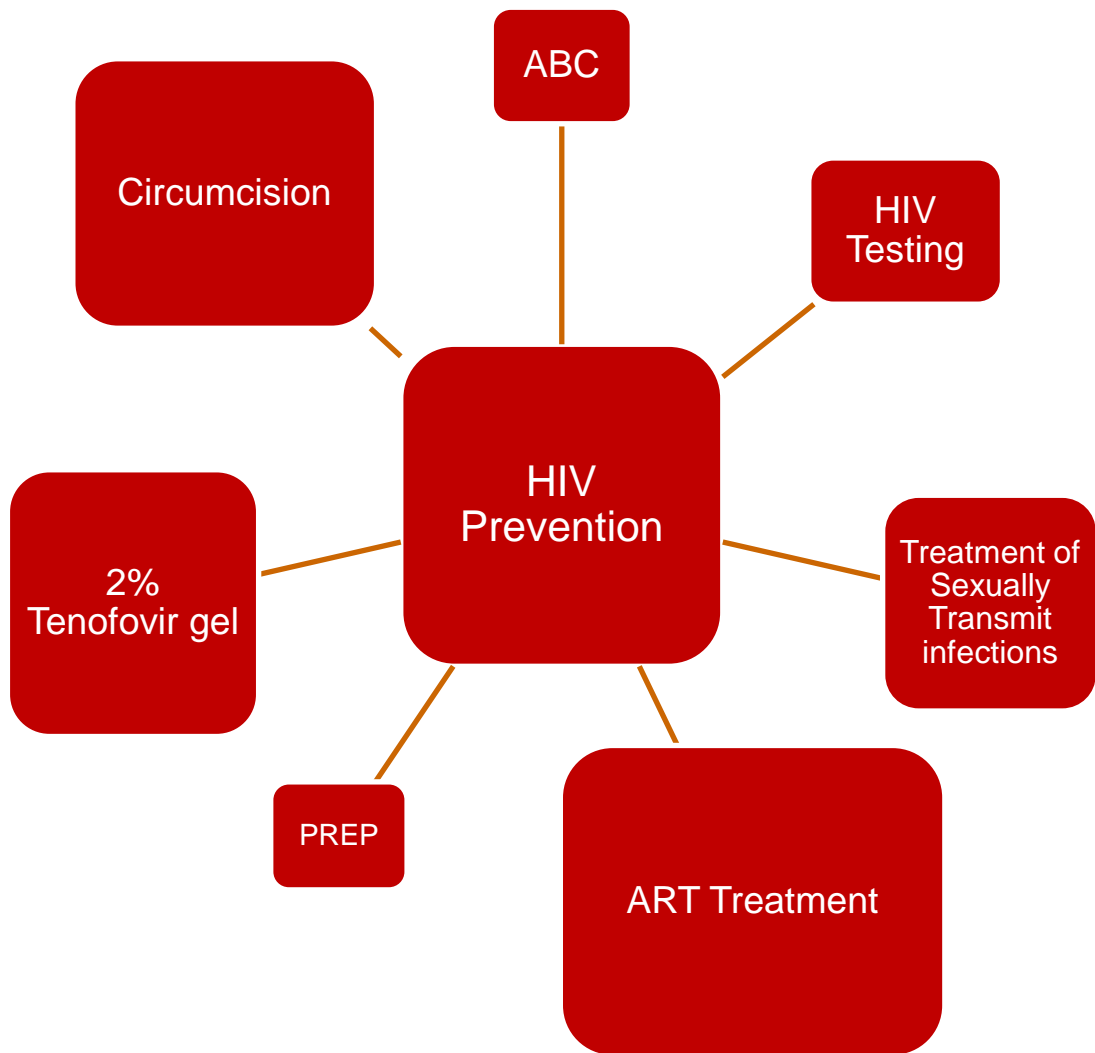
**CTU PI Wits HIV Research Group
International Scientific Officer ACTG**

Outline

- **Combination prevention strategies**
- **Antiretroviral therapy for prevention**
- **Components of treatment expansion**
- **Economics of treatment**
- **Conclusions**

Combination prevention

- **Behavioural interventions – “risk reduction”**
- **HIV testing – “know your status”**
- **Treatment of sexually transmitted infections**
- **Male Medical Circumcision**
- **Treatment**
- **Pre-exposure prophylaxis**
- **Microbicides**
- **Vaccines**



Benefit of early antiretroviral therapy treatment

- **Reduced transmission in discordant couples**
 - HPTN 052 – 96% reduction in HIV transmission
 - Does the observed benefit at an individual level translate to a population benefit?
- **Prevent opportunistic infections and long-term complications**
 - Reduced TB incidence (1, 2, 3)
 - Overall opportunistic infections, hospitalization, absenteeism and societal productivity
 - Non-infectious complications: neurologic, viral associated cancers, cardiovascular and metabolic

Lawn S Lancet 2005; Pape B NEJM 2009
Fox M AIDS 2010, Hosseinipour IAS 2011;

Antiviral treatment as prevention

- **Extensive biological plausibility**
 - The concentration of HIV-1 in blood and genital tract correlates with sexual transmission
 - Antiretroviral agents that concentrate in the genital tract reduce HIV-1 viral load
- **Most observational reports indicate ART reduces transmission of HIV-1 in couples**

Prevention of Transmission of HIV with ART

M Cohen, Y Chen, M McCauley, T Gamble, R Bollinger,
Y Bryson, D Burns, D Celentano, S Chariyalertsak,
F Conradie, L Cottle, G De Bruyn, V Elharrar, S Eshleman,
M Essex, E Filho, S Godbole, B Grinsztejn, J Hakim,
I Hoffman, M Hosseinipour, N Kumarasamy, J Kumwenda,
J Makhema, A Martinez, K Mayer, S Mehendale, L Mills,
K Nielsen, J Pilotto, E Piwowar-Manning, I Sanne, B Santos,
T Taha, L Wang, S Safren, T Fleming,
and the HPTN 052 Protocol Team

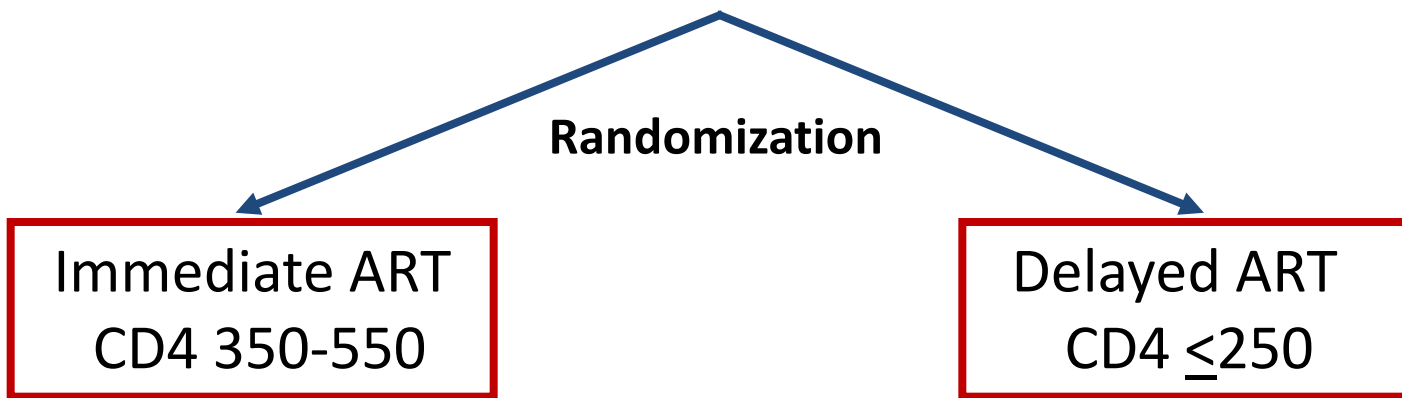


National Institute of Allergy
and Infectious Diseases



HPTN 052 Study Design

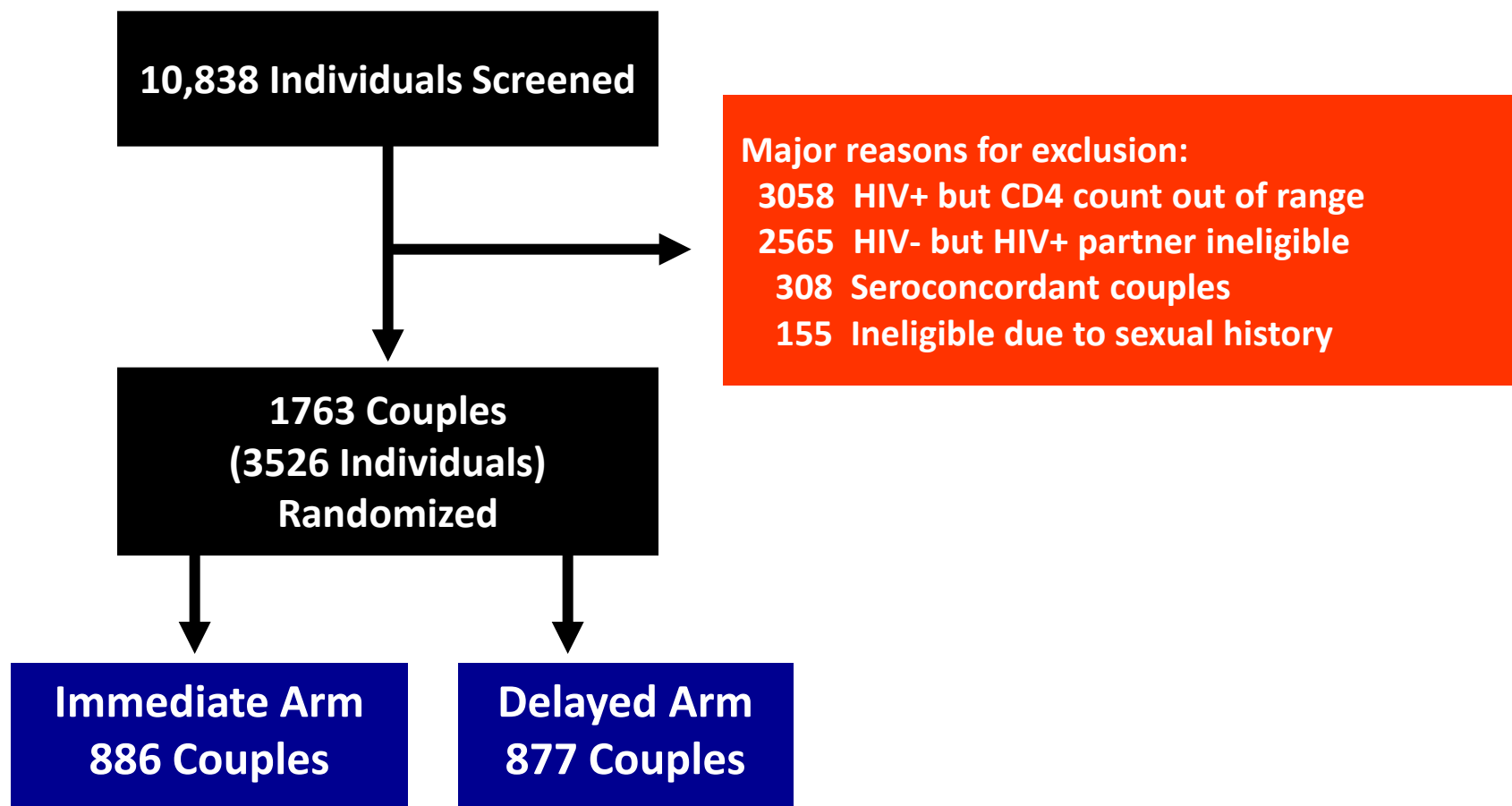
Stable, healthy, serodiscordant couples, sexually active
CD4 count: 350 to 550 cells/mm³



Primary Transmission Endpoint
Virologically-linked transmission events

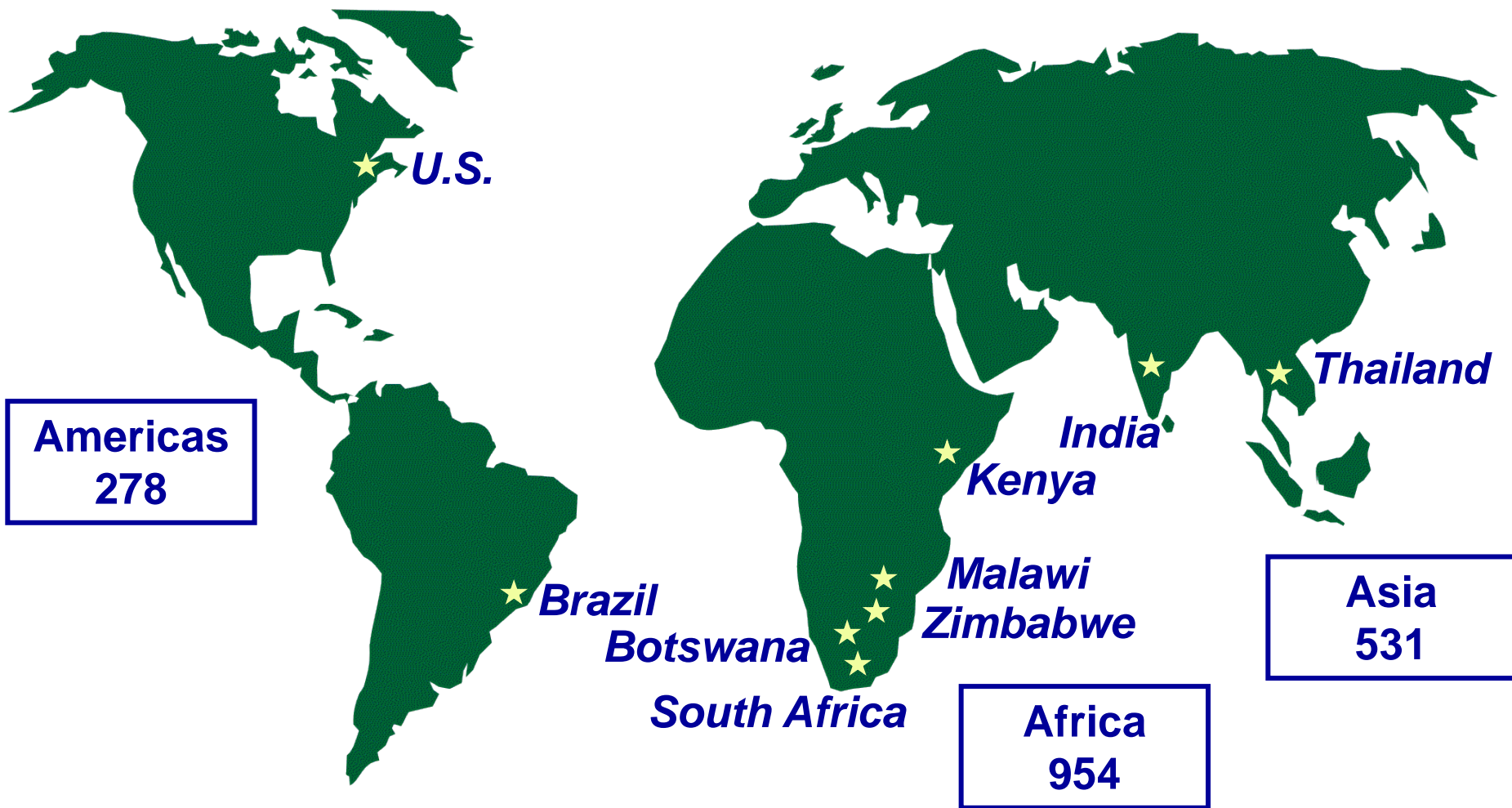
Primary Clinical Endpoint
WHO stage 4 clinical events, pulmonary tuberculosis, severe bacterial infection and/or death

HPTN 052 Enrollment



HPTN 052 Enrollment

(Total Enrollment: 1763 couples)



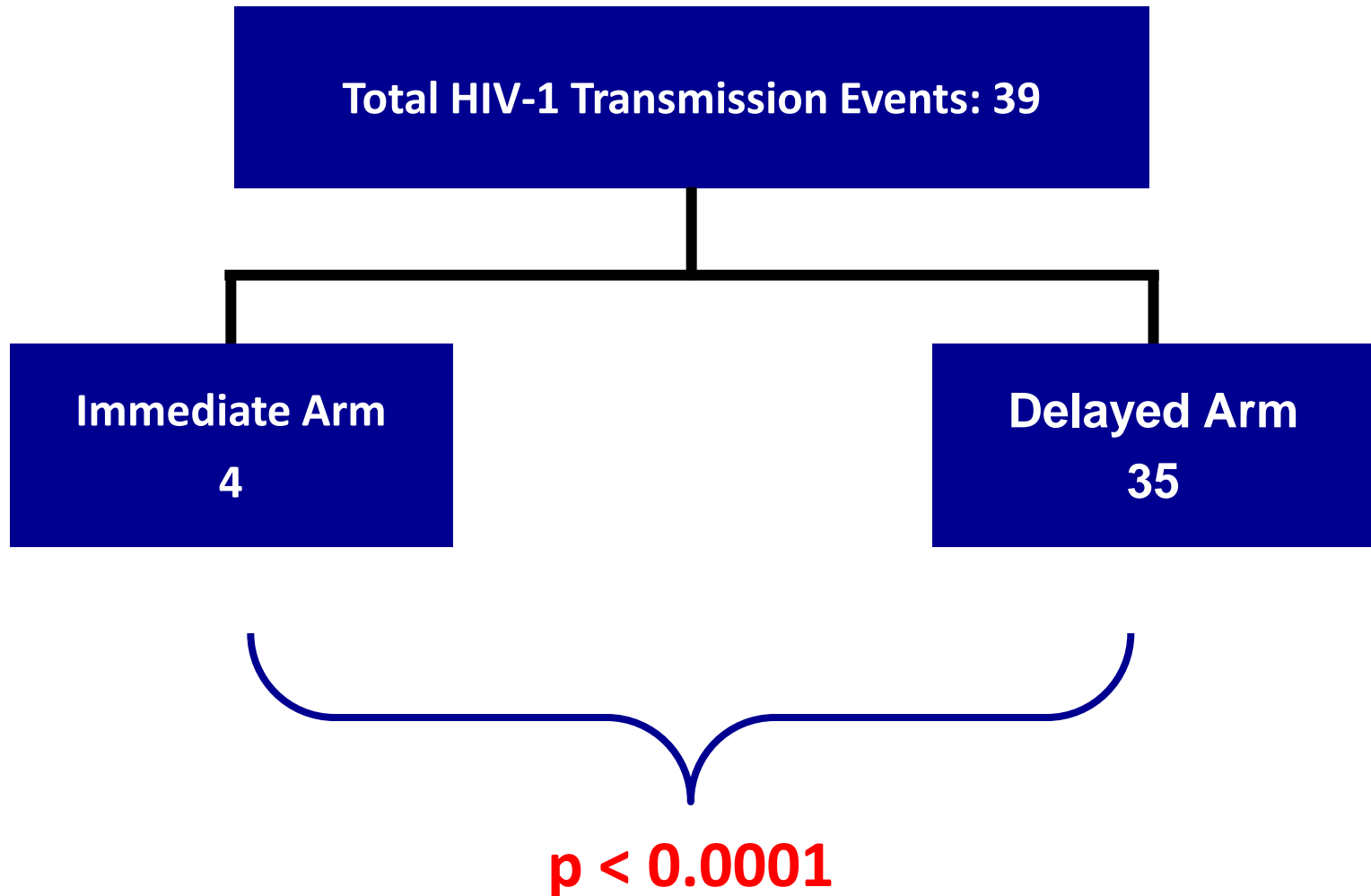
HPTN 052: Baseline Characteristics

	Index		Partner	
	Immediate N = 886	Delayed N = 877	Immediate N = 893	Delayed N = 882
Female	49%	50%	49%	47%
Age (median)	33	32	32	32
Married	94%	95%	93%	94%
Any unprotected sex	6%	8%	8%	8%
CD4 (median [IQR])	442 [373-522]	428 [357-522]	---	---
HIV RNA log₁₀ (median [IQR])	4.4 [3.8-4.9]	4.4 [3.9-4.9]	---	---

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HPTN 052: HIV-1 Transmission



HPTN 052: HIV-1 Transmission

Total HIV-1 Transmission Events: 39

Linked Transmissions:
28

Unlinked or TBD
Transmissions: 11

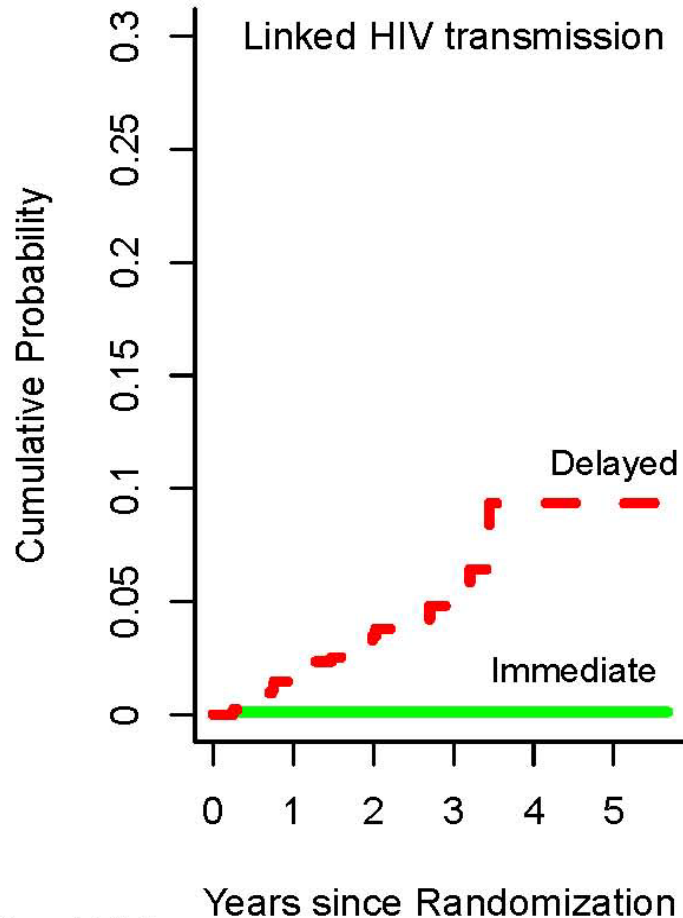
Immediate
Arm: 1

Delayed Arm:
27

$p < 0.001$

- 18/28 (64%) transmissions from infected participants with CD4 >350 cells/mm³
- 23/28 (82%) transmissions in sub-Saharan Africa
- 18/28 (64%) transmissions from female to male partners

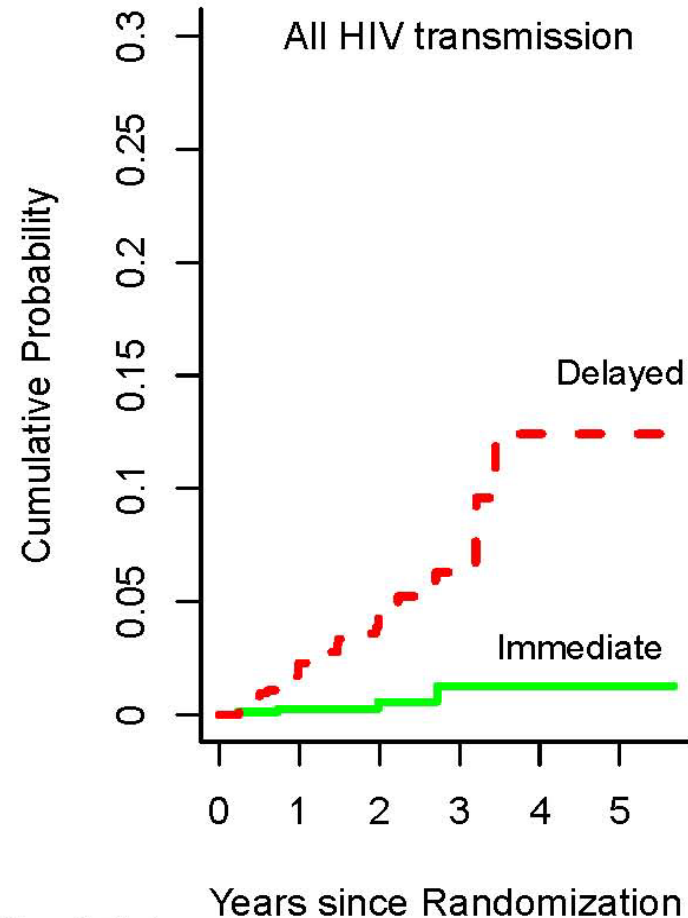
HPTN052: HIV-1 Transmissions



No. at Risk

Immediate 893 658 298 79 31 24

Delayed 882 655 297 80 26 22

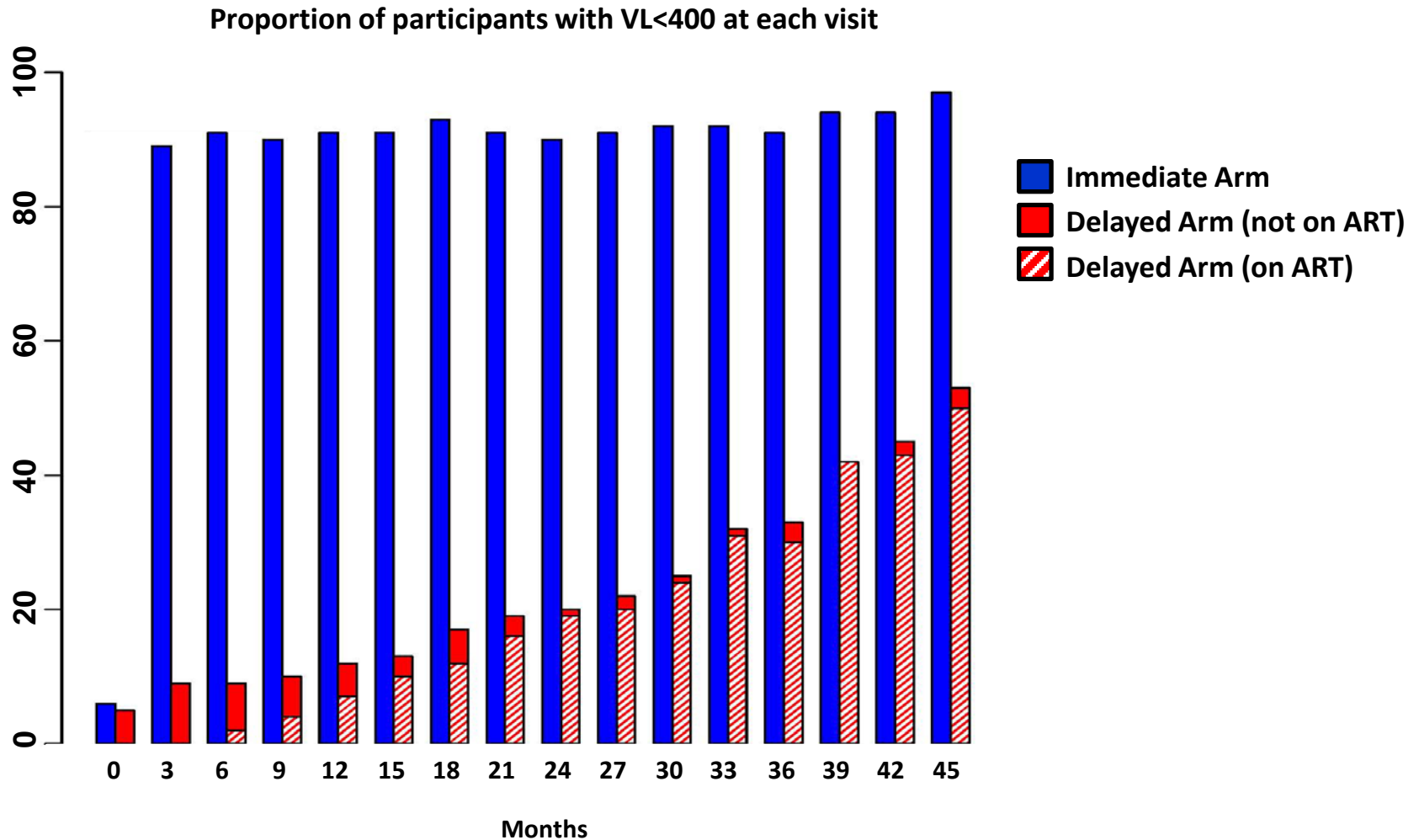


No. at Risk

Immediate 893 658 298 79 31 24

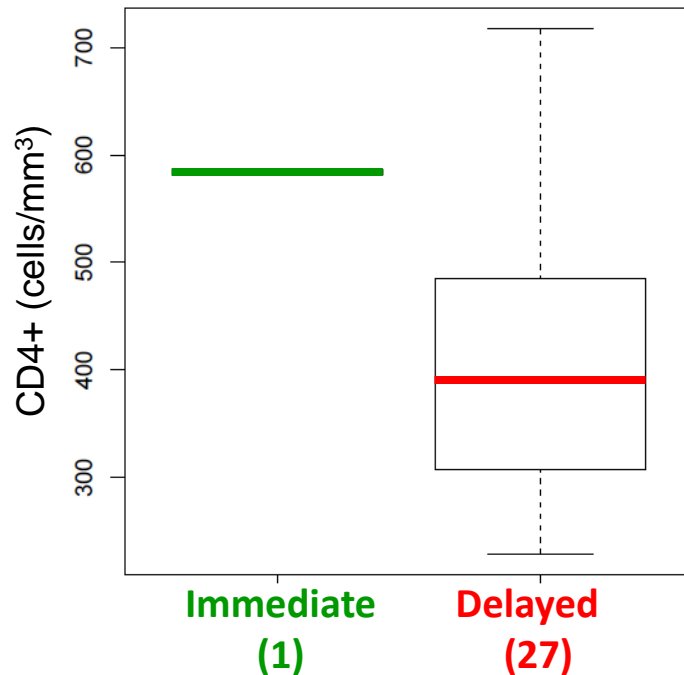
Delayed 882 655 297 80 26 22

HPTN 052: Effect of ART

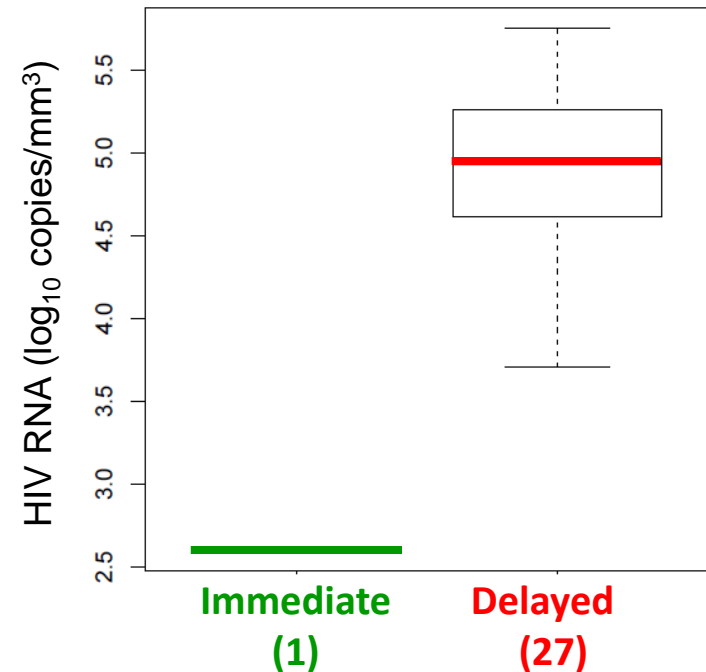


HIV Transmission: CD4 Count and HIV-1 RNA

28 Linked Transmissions



Median proximal CD4 (range): 400 (229-858)
Immediate arm: 584 (584-584)
Delayed arm: 391 (229-858)



Median proximal log₁₀ VL (range): 4.9 (2.6-5.8)
Immediate arm: 2.6 (2.6-2.6)
Delayed arm: 4.9 (2.6-5.8)

HPTN 052 Prevention Conclusion

Early ART that suppresses viral replication led to 96% reduction of sexual transmission of HIV-1 in serodiscordant couples

Total cost and potential cost savings of the national antiretroviral treatment (ART) programme in South Africa 2010 to 2017

**Gesine Meyer-Rath^{1,2,3},
Yogan Pillay⁴, Mark Blecher⁵, Alana Brennan^{1,2,3}, Lawrence Long^{2,3}, Leigh Johnson⁶,
Harry Moultrie^{3,7}, Ian Sanne^{2,3}, Matthew Fox^{1,2,3,8}, Sydney Rosen^{1,2,3}**

¹ Center for Global Health and Development, Boston University, US

² Health Economics and Epidemiology Research Office (HE²RO), Wits Health Consortium, South Africa

³ Faculty of Health Sciences, University of the Witwatersrand, South Africa

⁴ National Department of Health, South Africa

⁵ National Treasury, South Africa

⁶ Centre for Infectious Disease Epidemiology and Research, University of Cape Town, South Africa

⁷ Enhancing Children's HIV Outcomes (ECHO), Wits Health Consortium, South Africa

⁸ Department of Epidemiology, Boston University School of Public Health, US



Scenarios

Old South African Guidelines

Eligibility	Adults: CD4 <200 cells/mm ³ or WHO stage 4 Children: CD4 15% to 20% or WHO stage 3 or 4
Regimens	Adults: d4T + 3TC + EFV/NVP; AZT + ddl + LPV/r Children <3 yrs: d4T + 3TC + LPV/r ; AZT + ddl + NVP

New South African Guidelines

Eligibility	Adults: CD4 <350 cells/mm ³ for TB/HIV co-infected or pregnant pts, <200 cells/mm ³ or WHO stage 4 for all others Children: Early Paediatric Treatment
Regimens	Adults: TDF + 3TC + EFV/NVP for all new initiates; TDF + 3TC + LPV/r if failing d4T- or AZT-containing regimens/ AZT + 3TC + LPV/r if failing TDF-containing regimens Children <3 yrs: ABC + 3TC + LPV/r; AZT + ddl + NVP

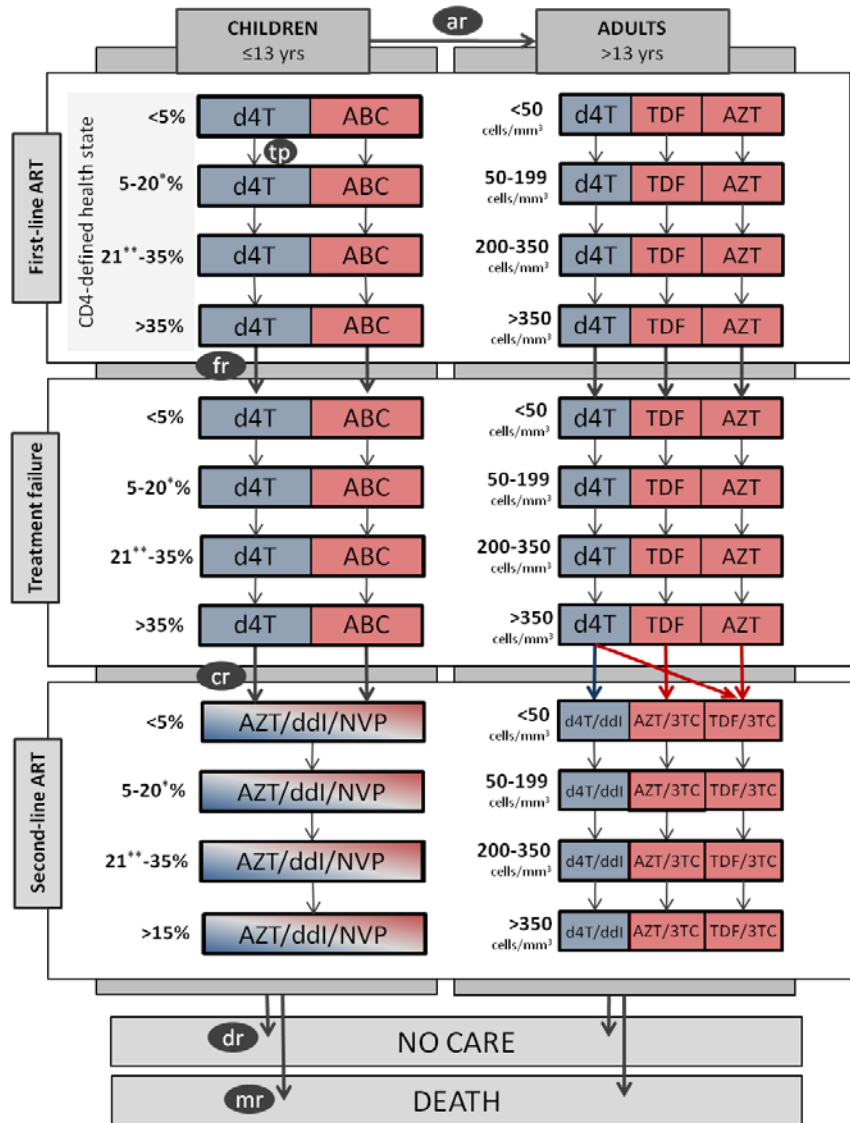
Full WHO Guidelines

Eligibility	Adults: CD4 <350 cells/mm ³ or WHO stage 4 for all Children: Early Paediatric Treatment
Regimens	As in “New South African Guidelines”

Additional conditions

- **New drug purchasing system (RL/FDC):**
 - ARV drugs at prices set in reference list (modelled on CHAI/ GPRM/ SCMS prices)
 - Fixed-dose combination where possible
- **Task shifting (TS):**
 - ARV initiation and management by nurses under physician supervision
 - ARV dispensing by pharmacy assistants under pharmacist supervision

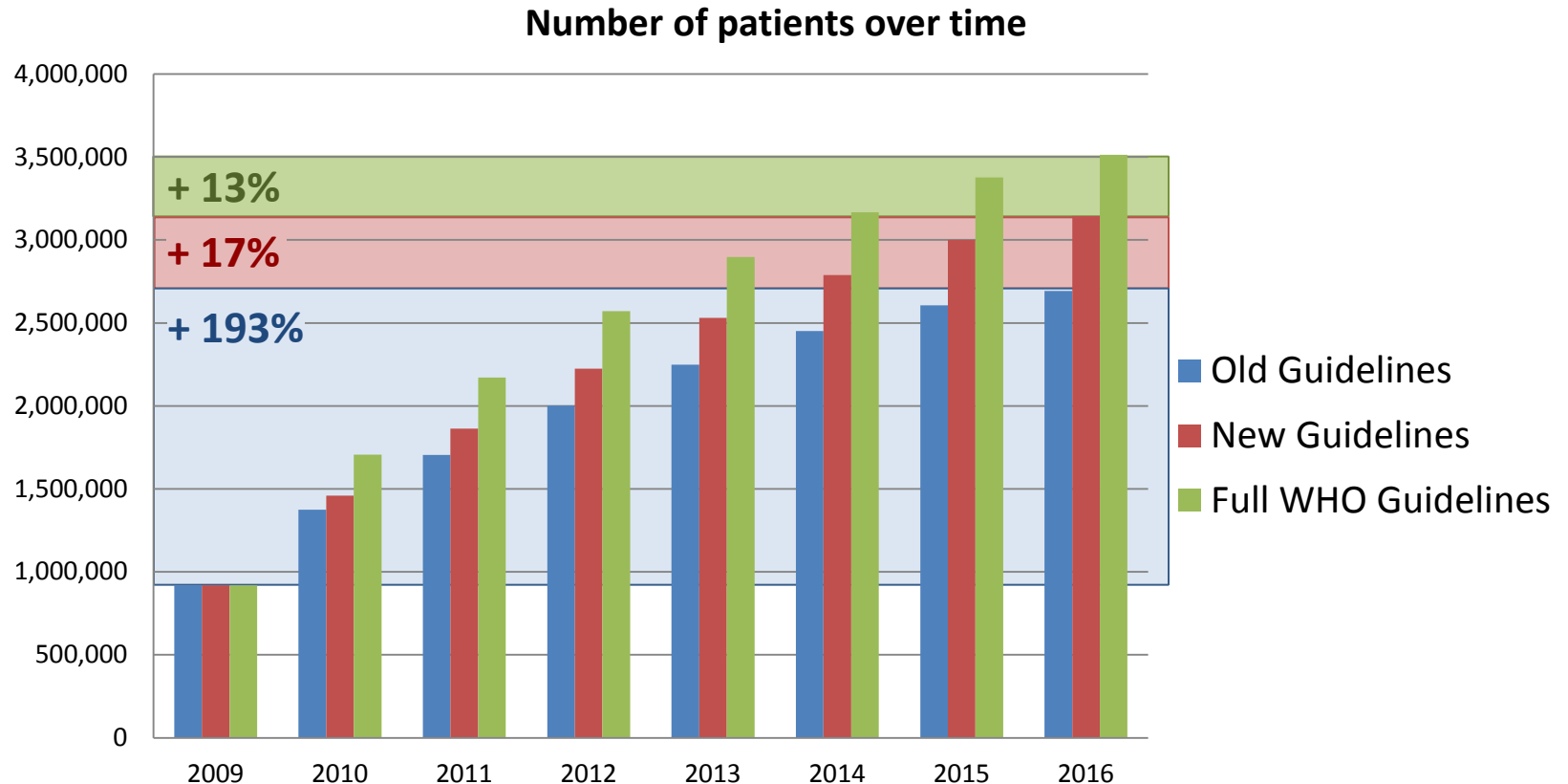
Health-state transition model National ART Cost Model (NACM)



- 6-monthly transitions between types of care and CD4-defined health states
- Number of patients initiating ART from ASSA2003 model
- Initiation rate (coverage of newly eligible pts)
 - 80% in pts with $<200\text{ CD4 cells/mm}^3$
 - 27% in pts with $200-350\text{ CD4 cells/mm}^3$
- Transition probabilities and rates of mortality, loss to follow-up, and first-line treatment failure based on 2 large Johannesburg cohorts:
 - Themba Lethu Clinic Cohort (n= 9,502)
 - Harriet Shezi Children's Clinic (n= 3,748)
- Transition probabilities and rates depend on CD4 cell count/ percentage and, for adult first-line treatment, also on time on treatment
- Model is evaluated for 2010/11 to 2016/17, with a run-in between 2003/4 and 2009/10

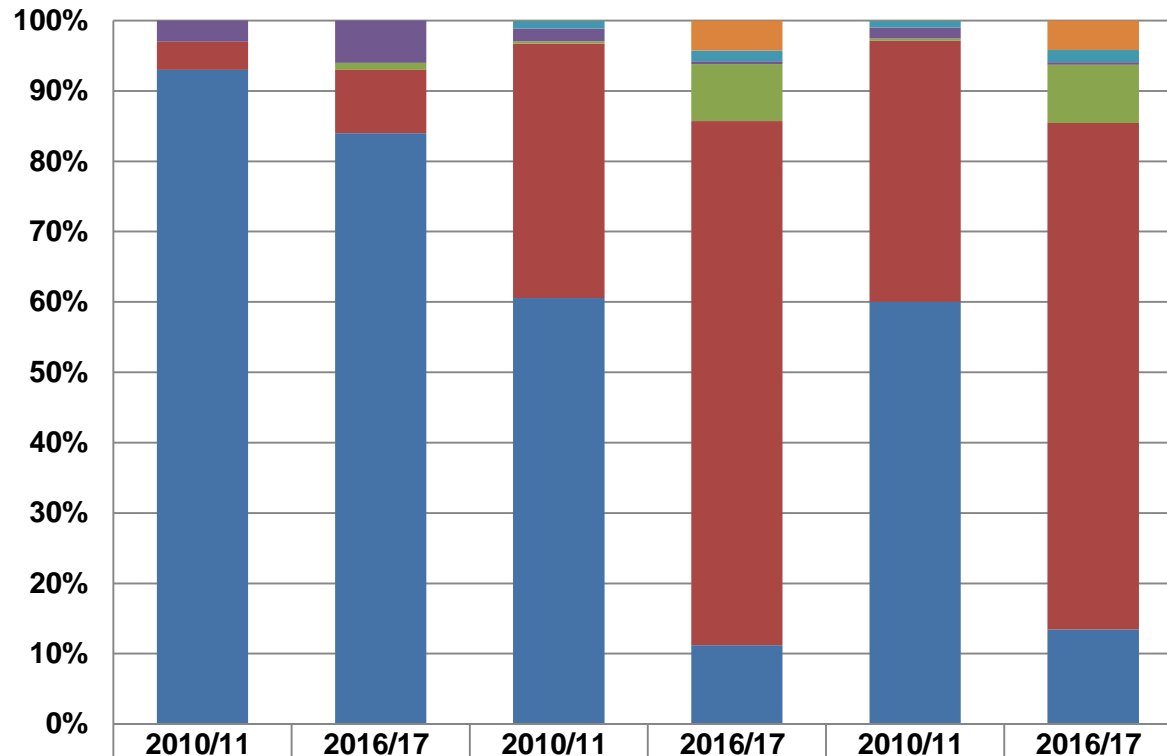
Results:

Total number of patients



→ Growth in number of patients on ART over time as a result of prevalence is higher than growth in patients as a result of increase in eligibility

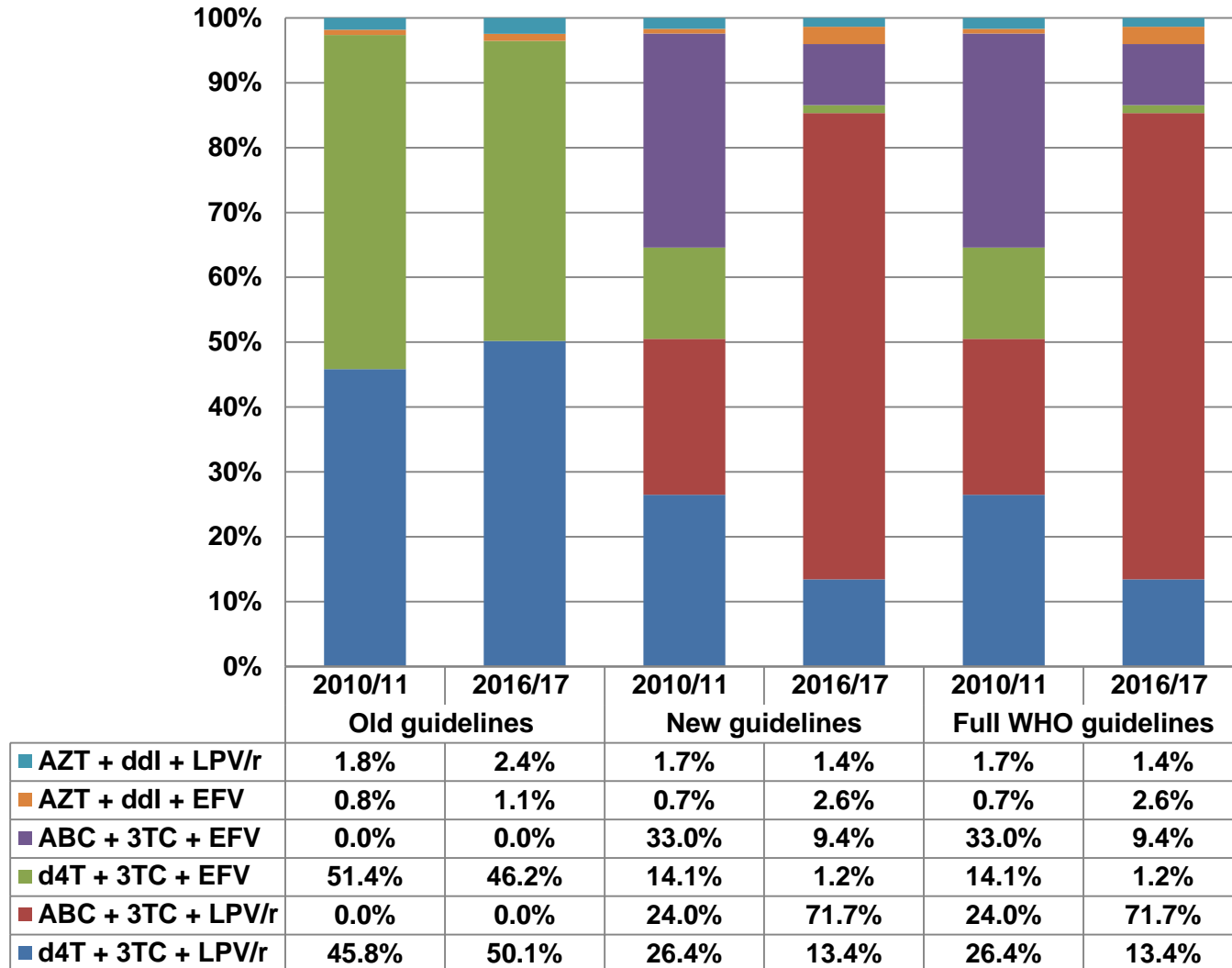
Regimen distribution (Adults)



	2010/11	2016/17	2010/11	2016/17	2010/11	2016/17
	Old Guidelines		New Guidelines		Full WHO Guidelines	
■ AZT+3TC+LPV/r	0%	0%	0.1%	4%	0.1%	4%
■ TDF+3TC+LPV/r	0%	0%	1%	2%	1%	2%
■ AZT+ddl+LPV/r	3%	6%	2%	0.4%	2%	0.4%
■ AZT+3TC+EFV/ NVP	0%	1%	0.3%	8%	0.3%	8%
■ TDF+3TC+EFV/ NVP	4%	9%	36%	75%	37%	72%
■ d4T+3TC+EFV/ NVP	93%	84%	61%	11%	60%	13%

Results:

Regimen distribution (Children)



Results:

Total cost [million 2009 ZAR]

Scenario	Full cost (Staffing and drug cost as current)			Reduced cost (With task-shifting and reference list for drug prices)			
	2010/11	2016/17	Total	2010/11	2016/17	Total	Change on Full cost
Old Guidelines	7,729	19,053	94,647	4,900	12,090	59,961	-33%
New Guidelines	8,317	22,869	110,152	5,190	14,865	70,489	-35%
Change on Old GL (Full cost)	8%	20%	17%	-29%	-22%	-25%	-
Full WHO Guidelines	9,731	25,209	124,925	6,044	16,323	79,565	-33%
Change on Old GL (Full cost)	27%	33%	32%	-11%	-14%	-16%	-

→ The total cost of the programme increases by 17% and 32%, resp., for the New Guidelines and WHO Guidelines scenarios, as a result of both higher numbers of patients and higher drug cost for TDF-containing regimens.

What does it take to test and treat

- **HIV testing as the gate keeper to treatment and prevention**
- **Clinical sites**
 - Infrastructure, health care workers, laboratory monitoring, pharmaceutical supply chain management
 - Primary health care, down-referral, task-shifting
 - Safe, effective treatment regimens, no overlapping toxicity
- **Treatment adherence**
 - Loss to initiation, loss to follow-up
- **Resistance surveillance and treatment efficacy**
- **Procurement, cost and health care funding**

South African National Strategic Plan

- **HIV testing – targeting annual testing**
 - 12 – 15 Million HIV test per annum (cost = R1.5 B/ann.)
- **ART guideline include more populations**
 - CD4+ 350
 - Any opportunistic infection (WHO II)
- **Prevention interventions for HIV negatives**
 - Behaviour intervention
 - Male Medical Circumcision (6,0M ; R3 Billion)
 - Microbicides, PREP etc.
 - Vaccine

Conclusion

Population level viral load will determine future HIV transmission rates

Treatment benefits the individual and their partner(s)

Acknowledgements

- National and Provincial Departments of Health (GP, MP, NC)



- PEPFAR



WORKING IN PARTNERSHIP

- USAID



- NIH

