How are we doing with Universal Test and Treat?

Francois Venter

October 2018

University of the Witwatersrand
WITS RHI

Thanks DoH, WHO, PEPFAR, CHAI, UCT, Joep Lange Institute, Celicia Serenata, Steve Smith, David Allen

UNIVERSITY OF THE WITWATERSRAND
JOHANNESBURG

Optimising ART Consortia

The **USAID**-funded OPTIMIZE consortium includes five leading private and public sector partners, and led by Wits RHI. OPTIMIZE leverages efforts by a wide range of donors and key stakeholders (e.g., Unitaid and its implementing partners, WHO and Global Fund).

OPTIMIZE operates under the assumption that aligning the collective power of scientists, regulators, drug companies, donors, programmers and advocates to achieve its singular goal -- accelerating access to simpler, safer and more affordable HIV treatment -- can rapidly advance ART optimization efforts.

Unitaid finds new and better ways to prevent, test and treat HIV, tuberculosis and malaria quickly and more affordably. It takes game-changing ideas and turns those into practical solutions that can help accelerate the end of the three diseases. Established in 2006 by Brazil, Chile, France, Norway and the United Kingdom, Unitaid plays an important part in the global effort to defeat HIV, tuberculosis and malaria. For more information, please visit: www.unitaid.org

USAID FROM THE AMERICAN PEOPLE

SOUTH AFRICANS AND AMERICANS IN PARTNERSHIP TO FIGHT HIV/AIDS PEPFAR

Unitaid Innovation in Global Health

saMRC advancing life

Why is South Africa important?

- Almost a fifth of global HIV-positive population
- 5 of 7.9 million people on ART
- Sustainable programme – mostly funded off SA tax base
- Almost halving of incidence in last 5 years in some demographics – HSRC, July 20128

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Why is test and treat so important?

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More ART coverage= less death…

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Number of AIDS-related deaths, by sex, sub-Saharan Africa, 1990–2017

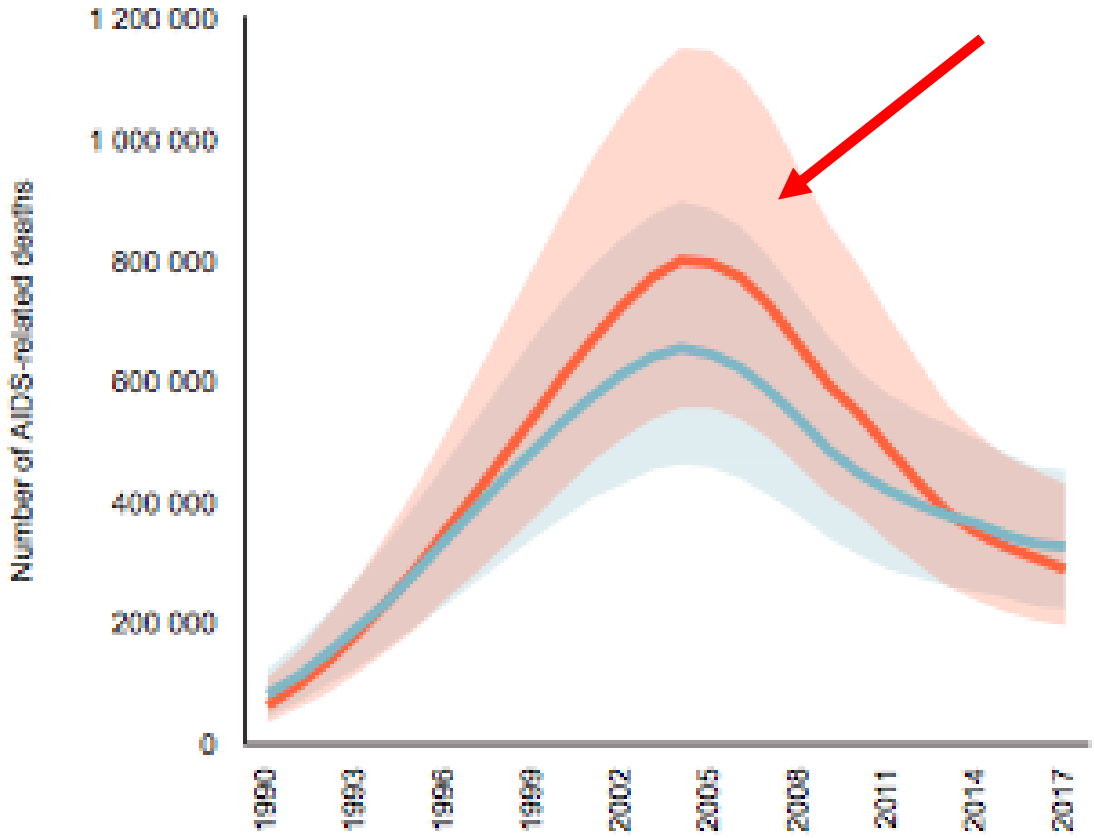

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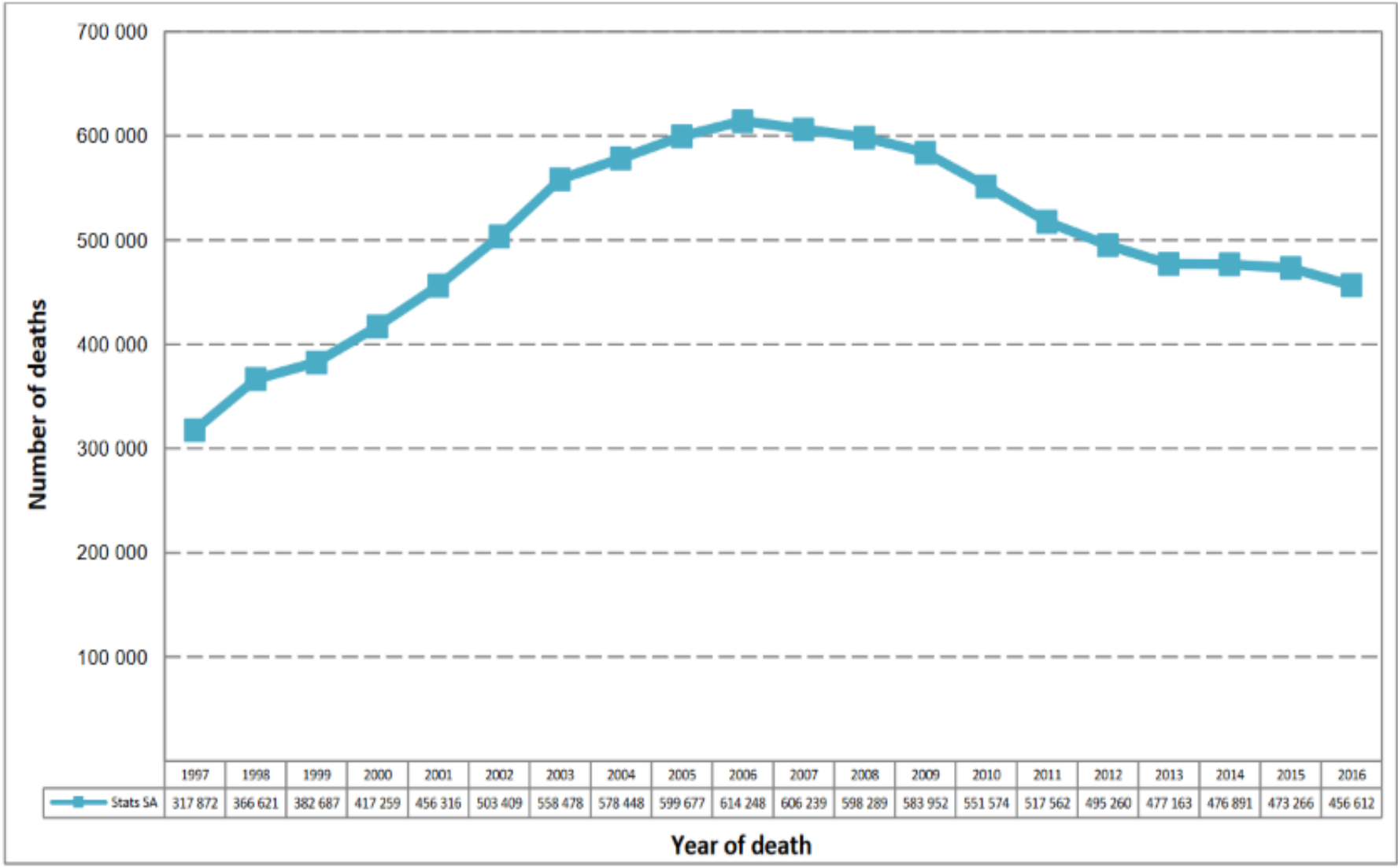
Figure 3.1: Number of registered deaths by year of death, 1997–2016*

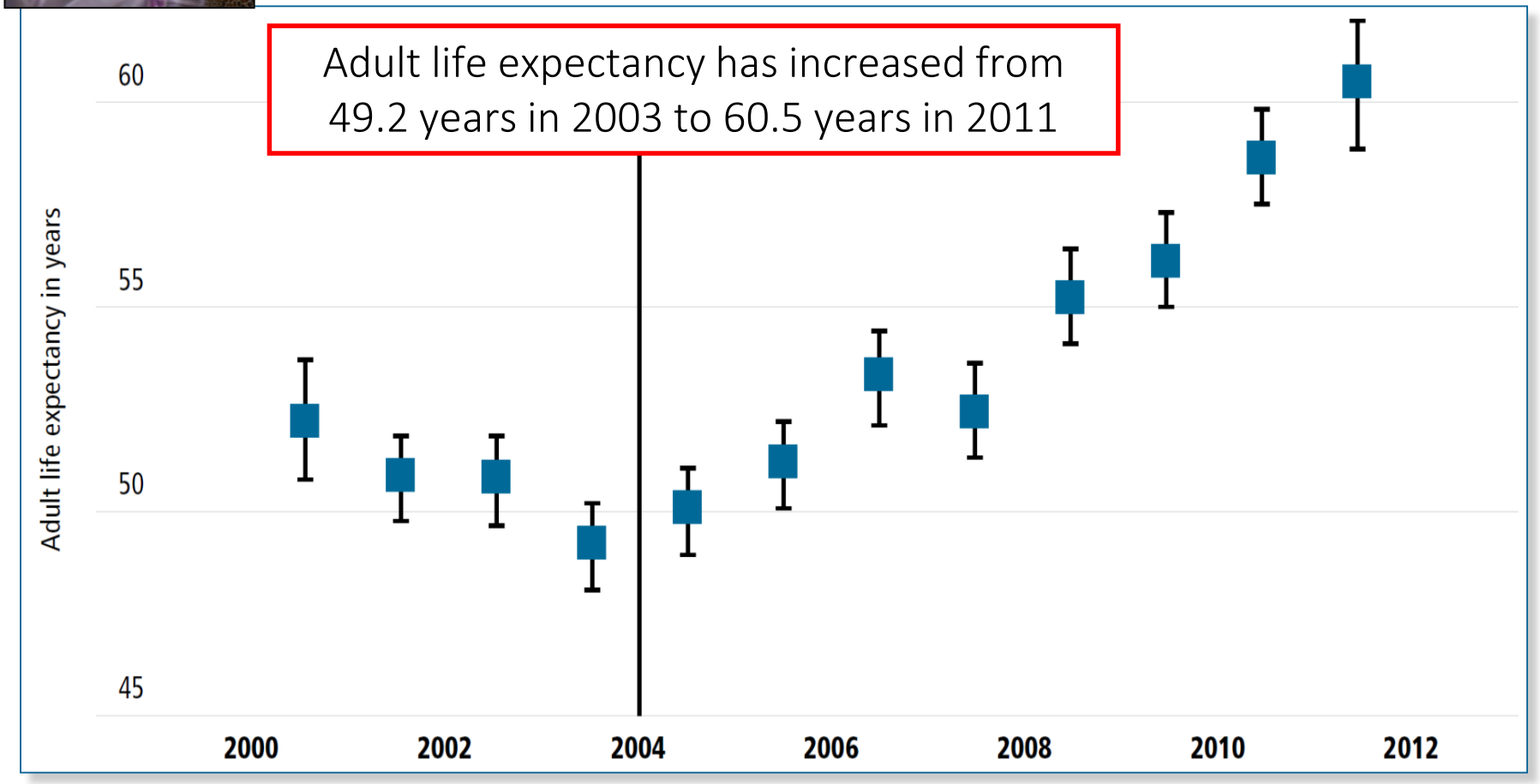


	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016
Stats SA	317 872	366 621	382 687	417 259	456 316	503 409	558 478	578 448	599 677	614 248	606 239	598 289	583 952	551 574	517 562	495 260	477 163	476 891	473 266	456 612

*Data for 1997–2015 have been updated with late registrations/delayed death notification forms processed in 2016/2017.

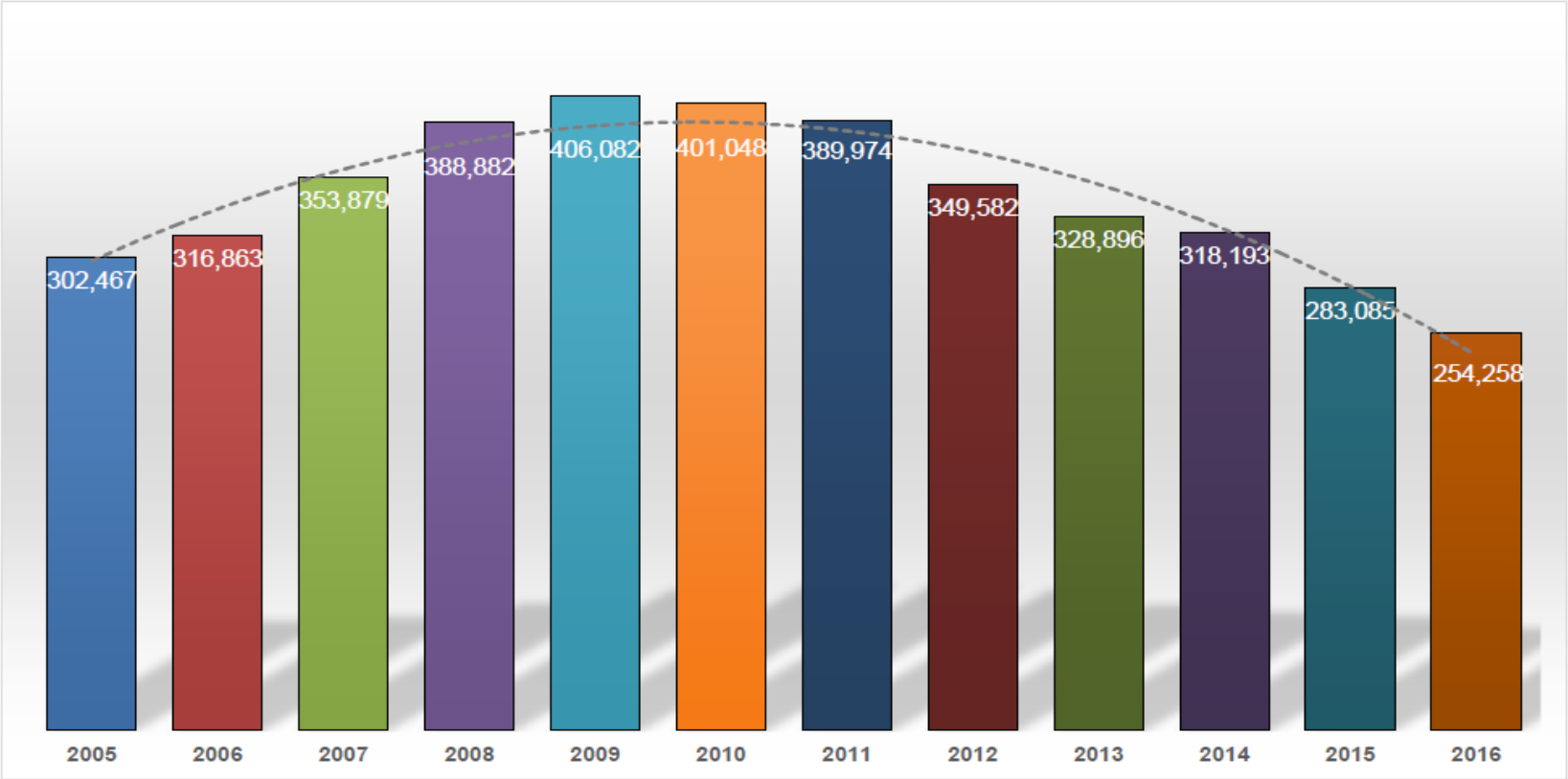
Increases in Adult Life Expectancy in Rural South Africa: Valuing the Scale-Up of HIV Treatment

Jacob Bor,[1,2]* Abraham J. Herbst,[1] Marie-Louise Newell,[1,3] Till Bärnighausen[1,2]



Source: Bor *et al*. Increases in adult life expectancy in rural South Africa: valuing the scale-up of HIV treatment. Science, 2013, 339:961–965.

Trends of TB registration from 2005 to 2016



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And CD4 count is rising

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PEOPLE INITIATING TREATMENT EARLIER, BUT MANY STILL START WITH ADVANCED DISEASE

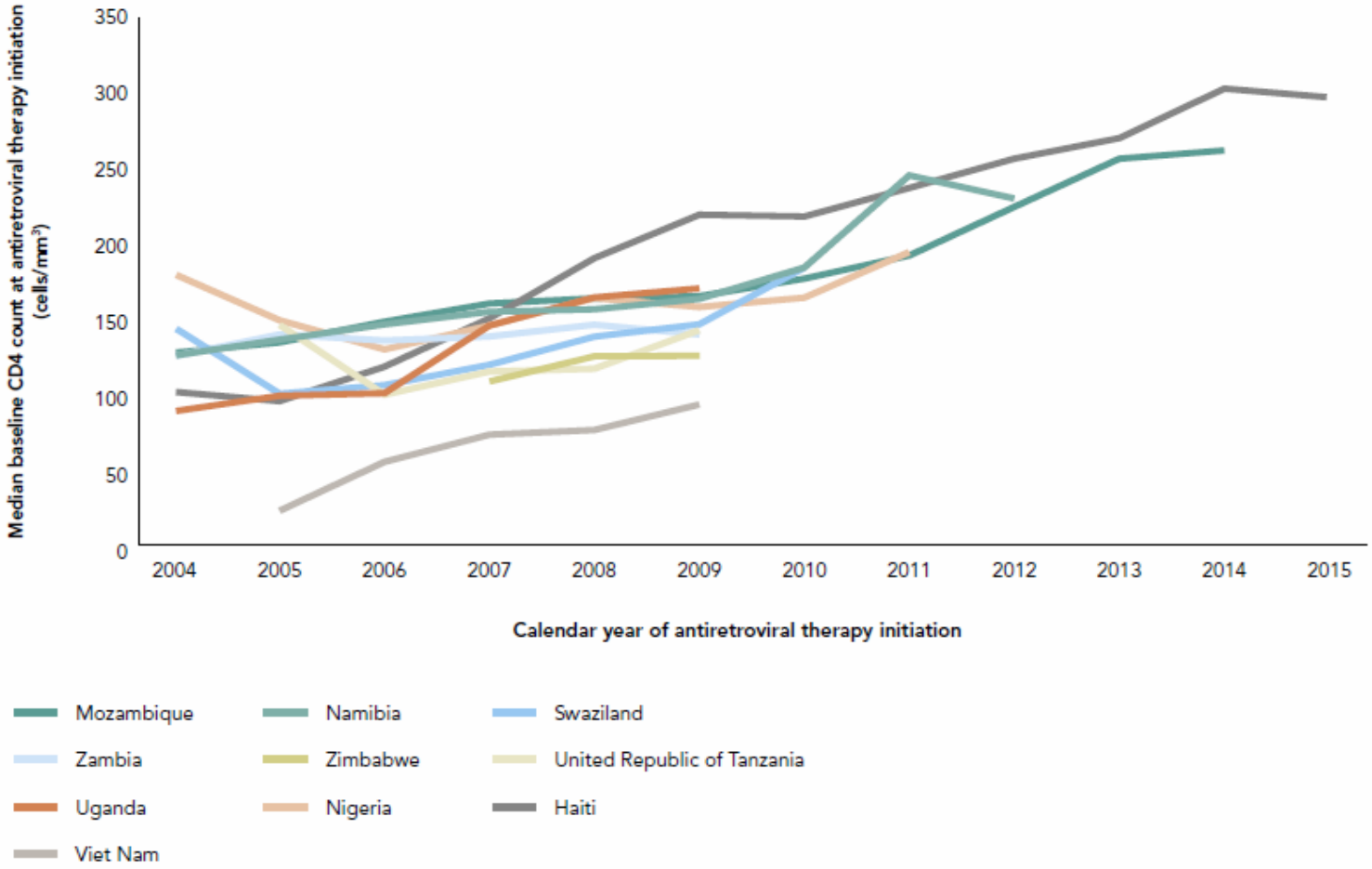
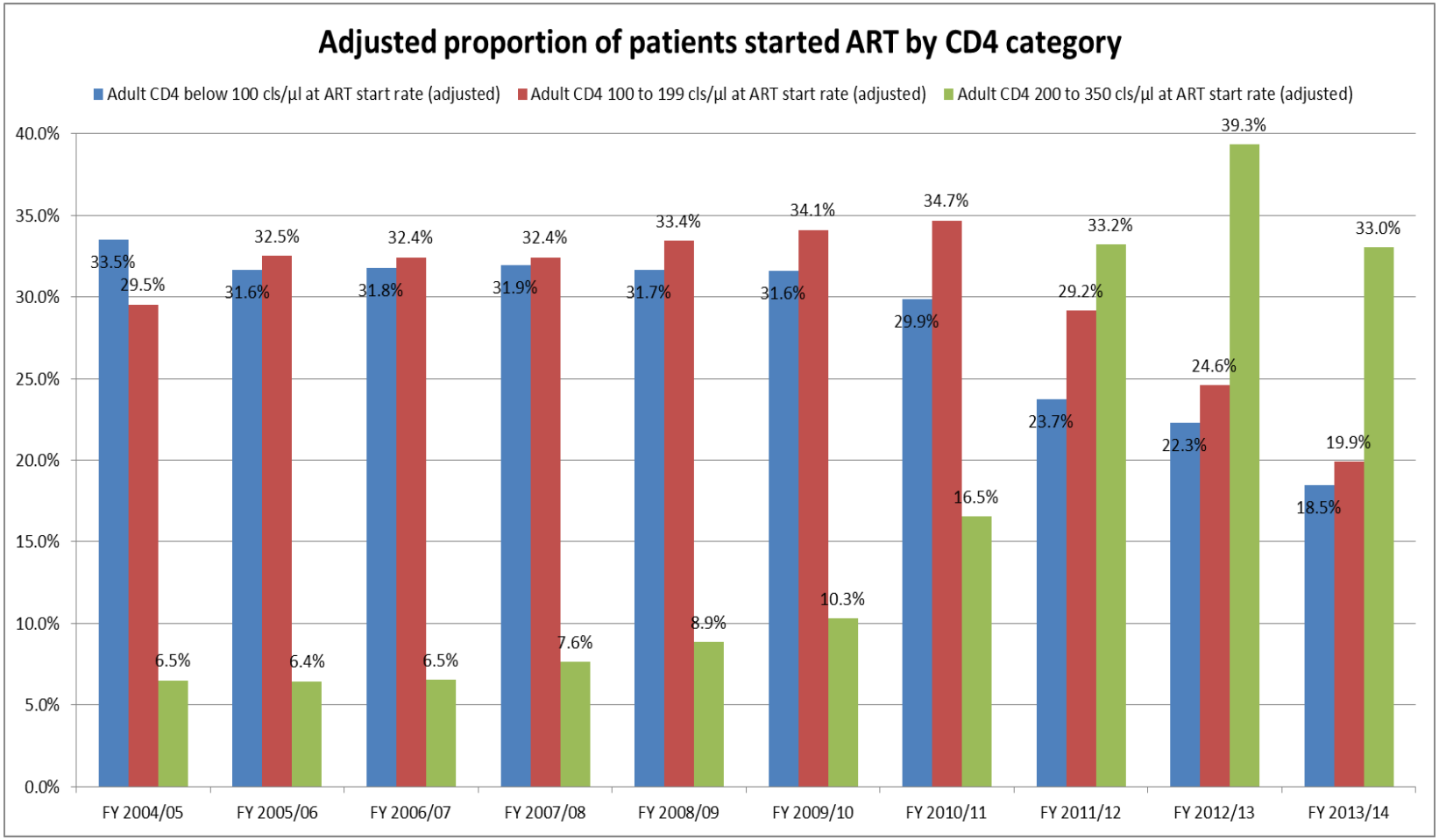


FIGURE 3.9. TRENDS IN MEDIAN CD4 T-CELL COUNT AT ANTIRETROVIRAL THERAPY INITIATION, 10 COUNTRIES, 2004–2015

Source: Auld AF, Shiraishi RW, Oboho I et al. Trends in Prevalence of Advanced HIV Disease at Antiretroviral Therapy Enrollment—10 Countries, 2004–2015. MMWR Morb Mortal Wkly Rep 2017;66:558–563. doi: http://dx.doi.org/10.15585/mmwr.mm6621a3.

Changing disease severity over time



Thanks: Andrew Boulle

Source: Consolidated National report covering monthly and quarterly ART data to end March 2014

health
Department:
Health
REPUBLIC OF SOUTH AFRICA

	Period 1		Period 2		Period 3		*P**
Group–*n* (%)							
Men	6,643	(27.6)	2,640	(30.9)			
Women < 40 years old	13,851	(57.5)	4,867	(57.0)			
Women ≥40 years old	3,588	(14.9)	1,028	(12.1)	1,071	(12.8)	
CD4 count (cells/μL) - median [IQR]							
In men	180 [71–341]		183 [74–335]		229 [100–386]		<0.001
In women <40 years old	307 [164–481]		288 [158–458]		349 [213–520]		<0.001
In women ≥40 years old	258 [135–432]		242 [119–419]		333 [161–522]		<0.001
Age (years)-median [IQR]							
In men	36.5 [30.4-44.5]		34.8 [28.7-43.0]		34.5 [28.3-42.0]		<0.001
In women <40 years old	27.5 [23.4-32.6]		26.5 [22.5-31.2]		26.7 [22.4-31.6]		<0.001
In women ≥40 years old	46.8 [43.2-51.9]		46.9 [42.9-53.0]		48.0 [43.7-53.4]		<0.001

IQR: Inter-Quartile Interval

Period 1: January 1, 2007–March 31, 2010; Period 2: April 1, 2010–July 31, 2011; Period 3: August 1, 2011–September 15, 2012

Change of treatment guidelines and evolution of ART initiation in rural South Africa: data of a large HIV care and treatment programme

Mélanie PLAZY, François DABIS, Kevindra NAIDU, Joanna ORNE-GLIEMANN, Till BARNIGHAUSEN and Rosemary DRAY-SPIRA

BMC Infectious Diseases 2015 **15**:452

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Change of treatment guidelines and evolution of ART initiation in rural South Africa: data of a large HIV care and treatment programme

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BMC Infectious Diseases 2015 **15**:452

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But late presentation remains a problem

- % presenting < 200, 100 not significantly changed
- Cryptococcal meningitis levels

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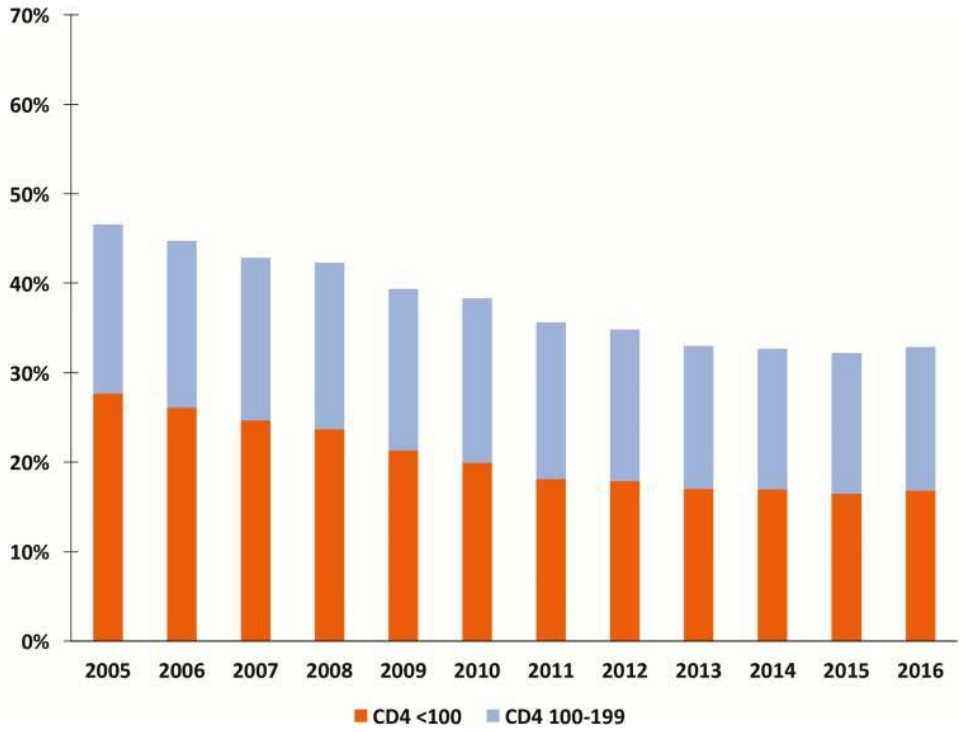
Clin Infect Dis. 2018 Apr 1; 66(Suppl 2): S111–S117.
Published online 2018 Mar 4. doi: [10.1093/cid/ciy045]

PMCID: PMC5850436
PMID: 29514238

Persistent High Burden of Advanced HIV Disease Among Patients Seeking Care in South Africa's National HIV Program: Data From a Nationwide Laboratory Cohort

Sergio Carmona,[1,2] Jacob Bor,[3,4,5] Cornelius Nattey,[3] Brendan Maughan-Brown,[6] Mhairi Maskew,[3] Matthew P Fox,[3,4,5] Deborah K Glencross,[1,2] Nathan Ford,[7] and William B MacLeod[3,4]



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PLOS ONE | A Peer-Reviewed, Open Access Journal

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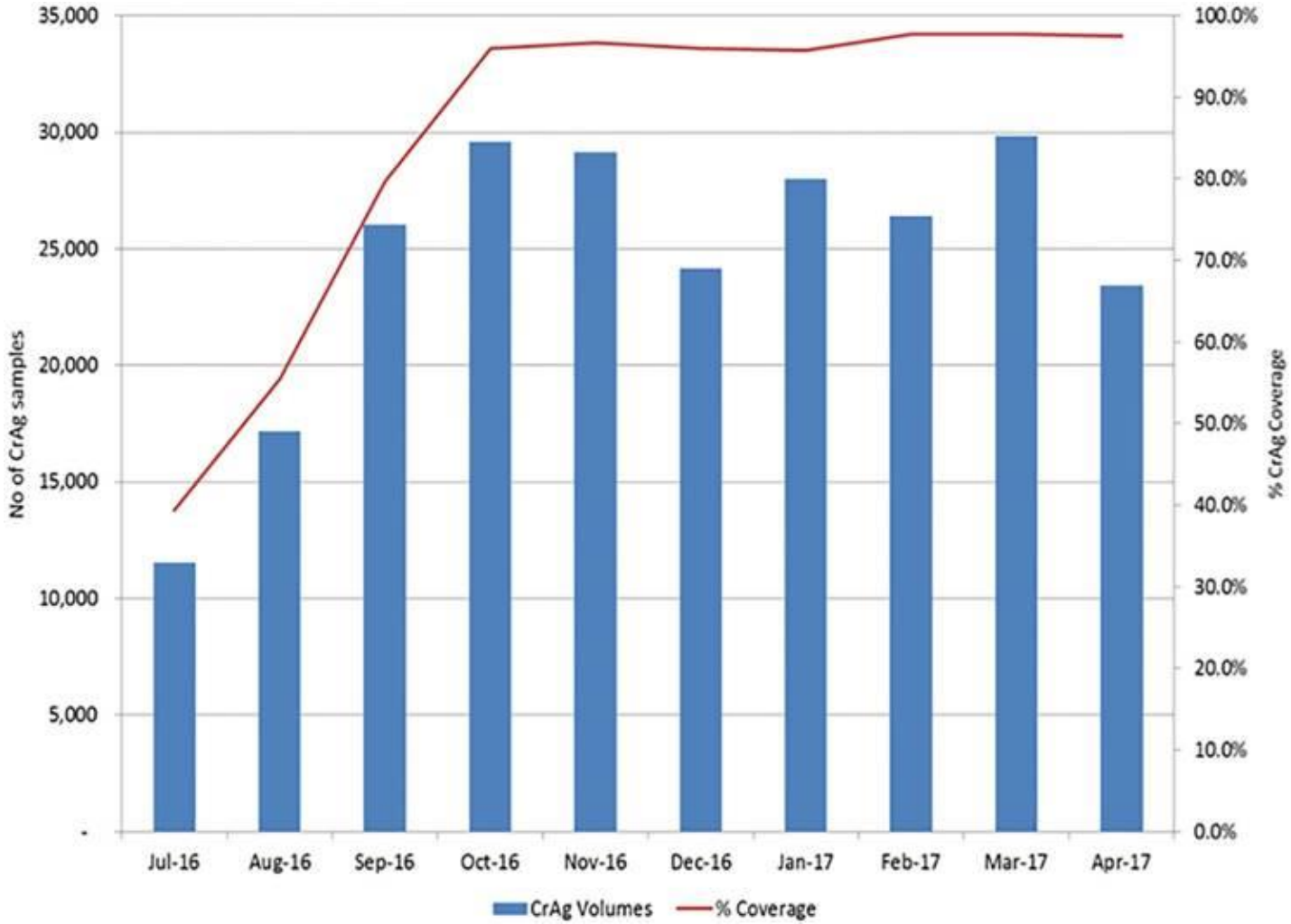
PLoS One. 2018; 13(6): e0198993.
Published online 2018 Jun 12. doi: [10.1371/journal.pone.0198993]

PMCID: PMC5997320
PMID: 29894509

Cryptococcal antigen positivity combined with the percentage of HIV-seropositive samples with CD4 counts <100 cells/μl identifies districts in South Africa with advanced burden of disease

Lindi-Marie Coetzee, Conceptualization, Data curation, Formal analysis, Methodology, Validation, Writing – original draft, Writing – review & editing,[1,2,*] Naseem Cassim, Conceptualization, Data curation, Formal analysis, Methodology Software, Writing – original draft, Writing – review & editing,[1,2] Charlotte Sriruttan, Resources, Writing – review &



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Less new infection

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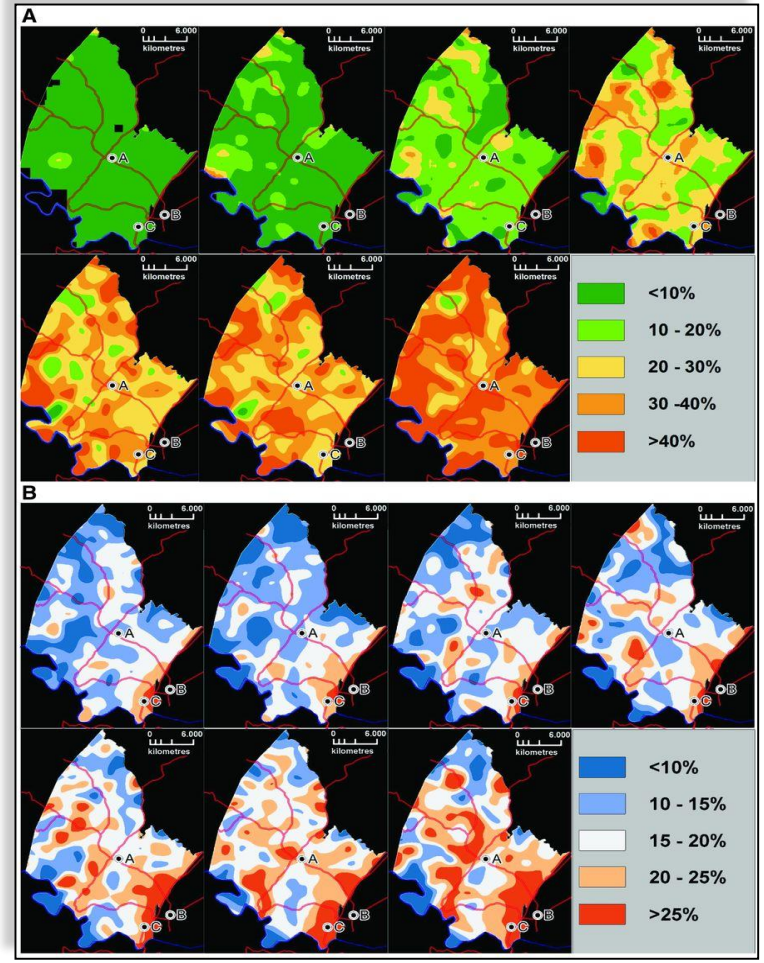
High Coverage of ART Associated with Decline in Risk of HIV Acquisition in Rural KwaZulu-Natal, South Africa

Frank Tanser,[1*] Till Bärnighausen,[1,2] Erofili Grapsa,[1] Jaffer Zaidi,[1] Marie-Louise Newell[1,3]



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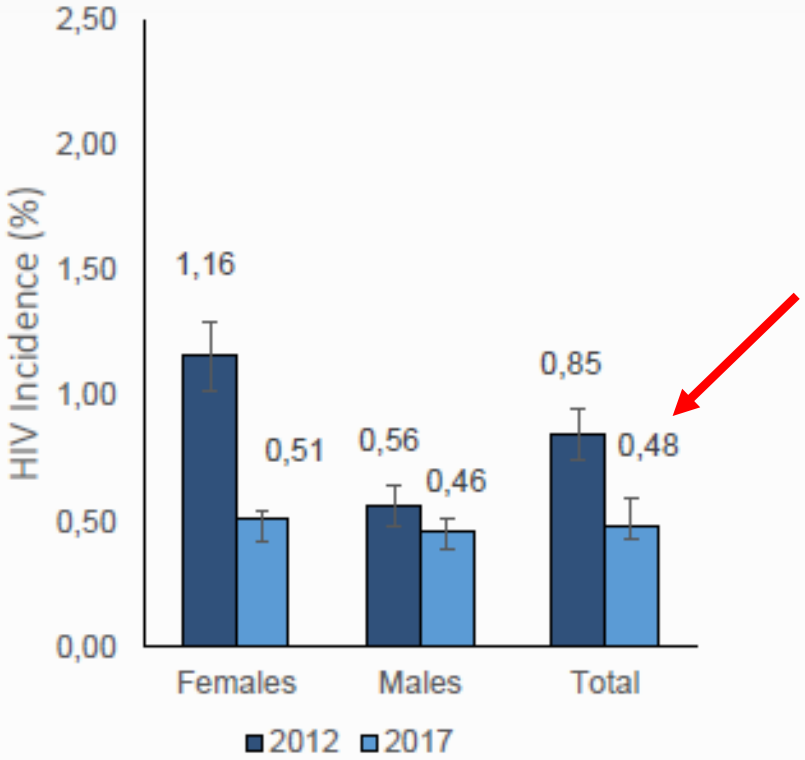
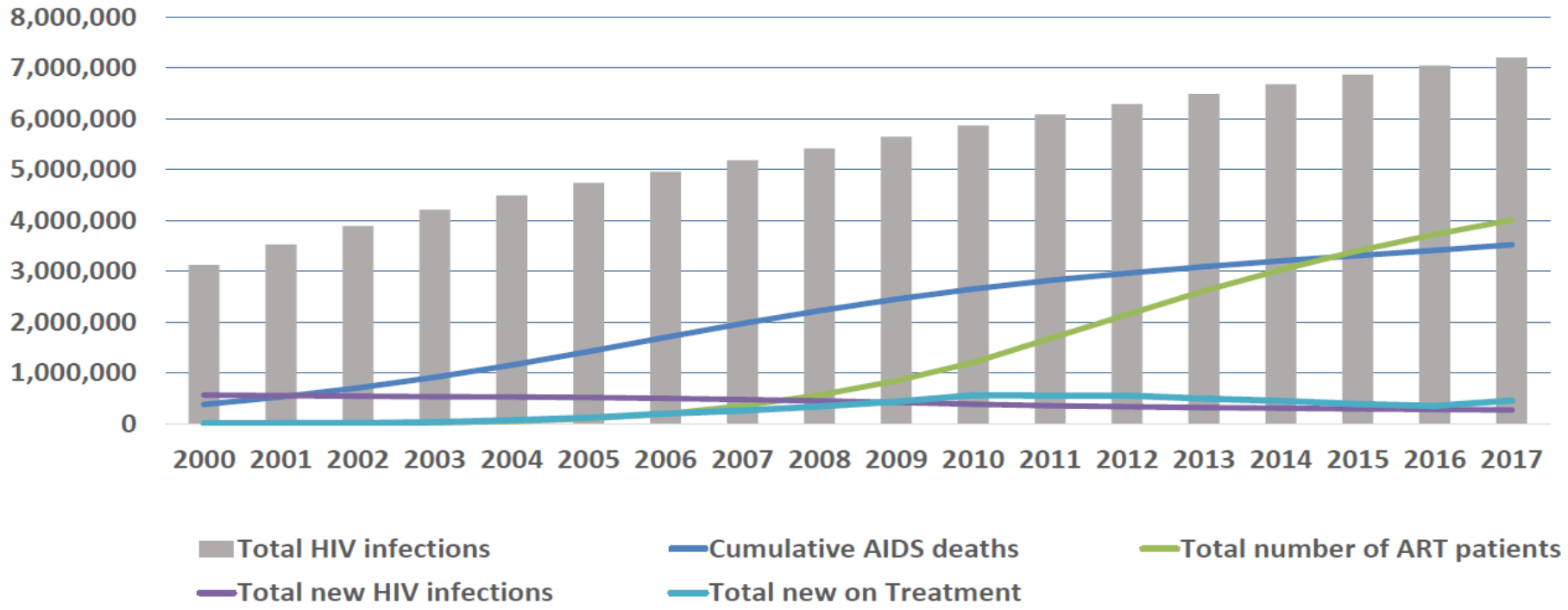
Changes to HIV Incidence among those aged two years and older by Sex, South Africa, 2012-2017

- NB. The 2012 results were re-calculated using the 2017 test parameters
- The overall HIV incidence has significantly dropped by 44%.
- The largest decline (56%) in incidence was among females.
- Among males the incidence declined by 18%



South Africa: Decreasing Incidence, Increasing Treatment



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Similar drops in…

- Botswana
- Zimbabwe
- Swaziland
- (Melbourne, San Francisco)

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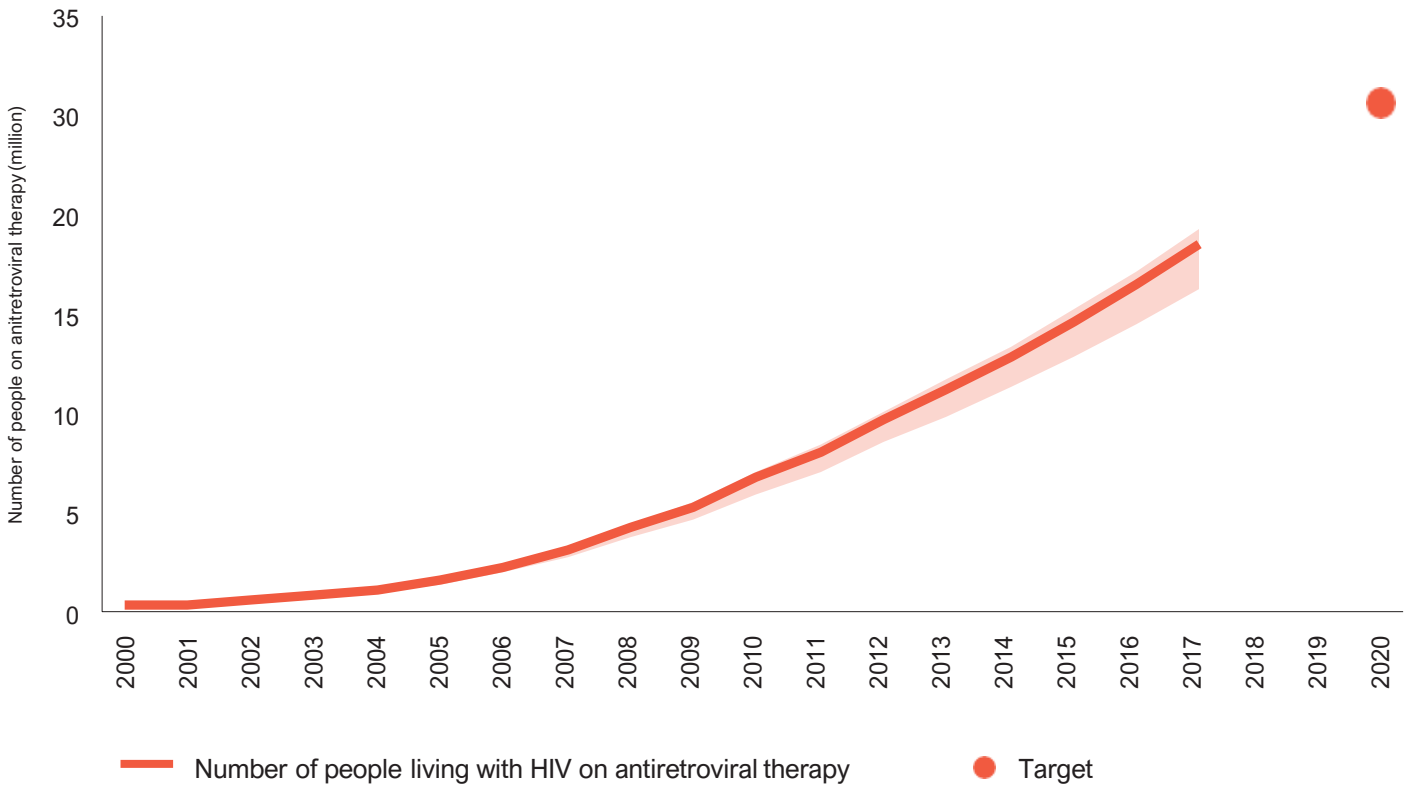
…making the treatment target in adults one of the first ones to be on trajectory to be attained by 2020

Number of people living with HIV accessing antiretroviral therapy, global, 2000–2017 and 2020 target



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Source: UNAIDS 2018 estimates. Global AIDS Monitoring, 2018.

Test and treat is now the standard of care in most countries, increasing eligibility for ART

Estimated millions of people eligible for ART in LMIC in 2012

11 m | 15 m | 17.6 m | 28.6 m | 33 m

1

CD4 ≤ 200

Recommended **Since 2003**

2

CD4 ≤ 350

Recommended **since 2010**

3

CD4 ≤ 350 + TB/HIV HBV/HIV

4

CD4 ≤ 500 + TB/HIV HBV/HIV

5

All HIV+

"Test and treat"

WE ARE HERE

Initiate ART regardless of CD4 count for:

- Serodiscordant couples
- Pregnant women
- Children < 5 years

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The Evolving HIV Treatment Paradigm

- 3TC=lamivudine; ZDV=zidovudine

HIV-1 discovered

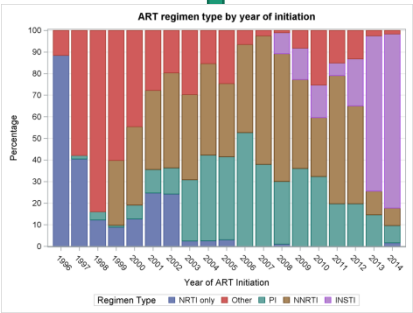
ZDV monotherapy

ZDV/3TC

Triple-Drug Therapy

Single-Tablet Regimens

The Integrase Era



Long Acting Injectable?

?????

1983 | 1987 | 1995 | 1996 | 2006 | 2012–2013 | 2017 | 2020

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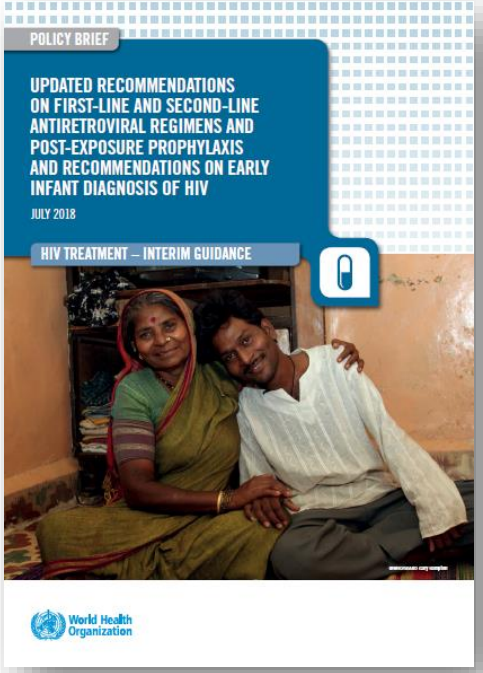
WHO: new recommendations for first-line ART regimens



BOX 1. RECOMMENDATIONS: FIRST-LINE ARV DRUG REGIMENS

1. A DTG based regimen may be recommended as a preferred first-line regimen for people living with HIV initiating ART *(conditional recommendation)*
   - Adults and adolescents *(moderate-certainty evidence)*
   - Women and adolescent girls of childbearing potential[a] *(very-low-certainty evidence)*
   - Infants and children with approved DTG dosing[b] *(low-certainty evidence)*

NEW

WHO 2018

“Dolutegravir in first line therapy has by far the highest impact in getting to the last 90 for South Africa”

Professor Gesine Meyer-Rath -
Boston University/HE^{2}RO

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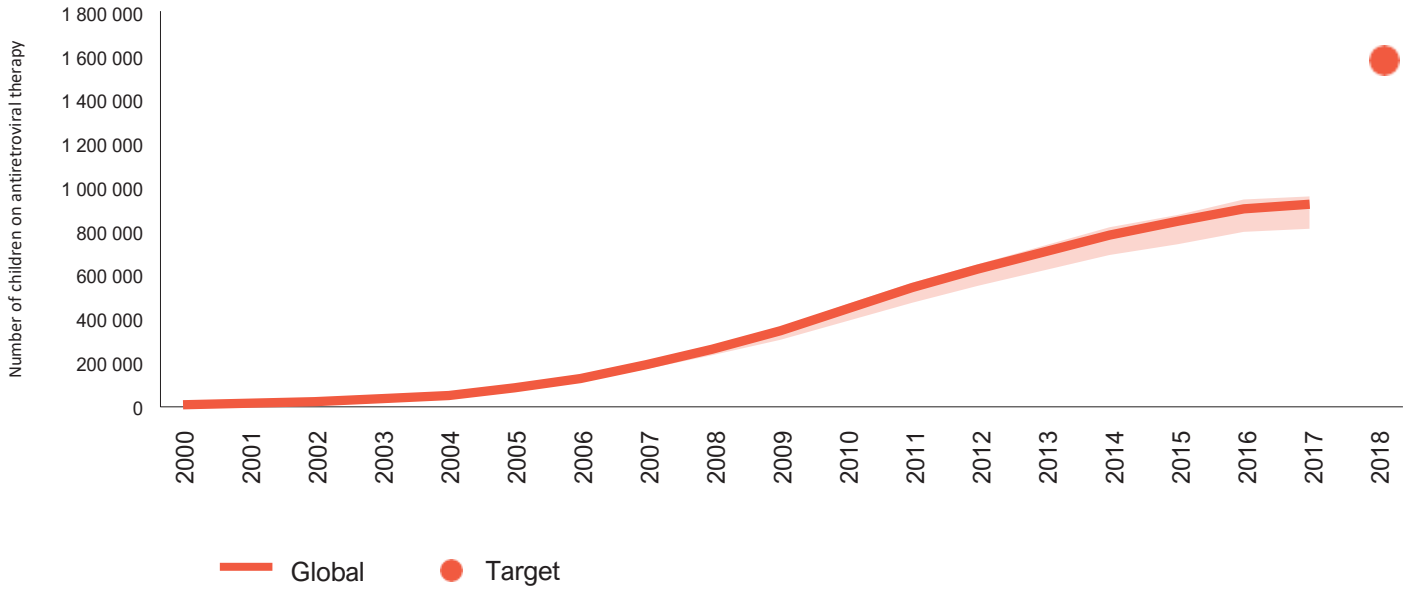
ART exposure, South Africa, 2017

Variable	Estimated number of people on ART (n)	Proportion of people living with HIV on ART (%) 95% CI
National	4,401,872	62.3 (59.2-65.2)
Female	2,998,170	65.5 (62.4-68.4)
Male	1,403,702	56.3 (51.0-61.5)

However, children lag far behind in ART treatment coverage…

Number of children (aged 0–14 years) accessing antiretroviral therapy, global 2000–2017 and 2018 target



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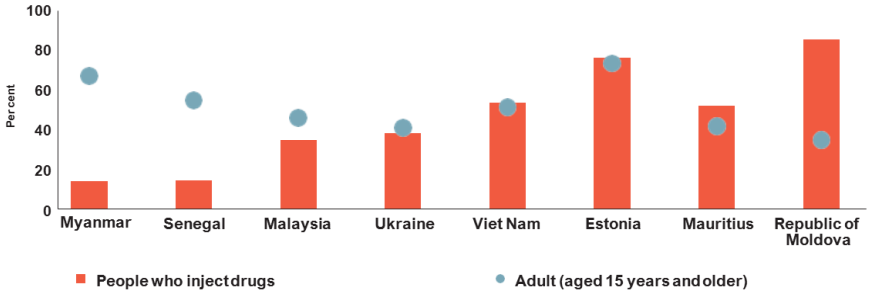
Source: UNAIDS 2018 estimates; Global AIDS Monitoring, 2018.

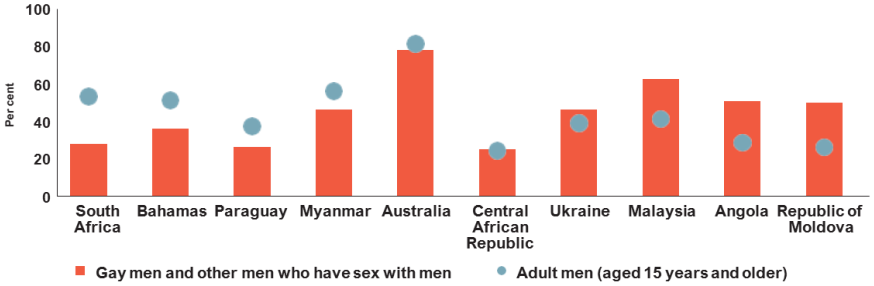
…as do key populations

Antiretroviral therapy coverage, by population, select countries, 2014–2017

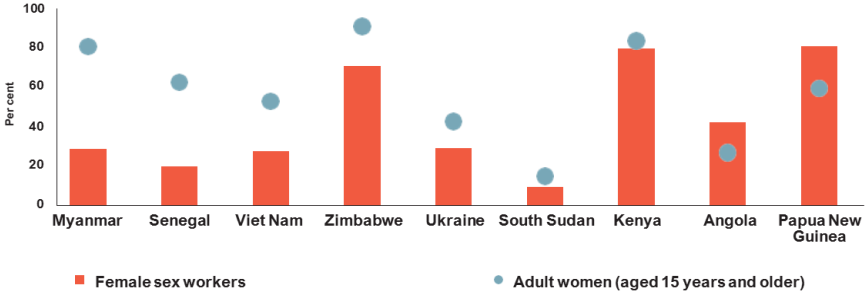
People who inject drugs and all adults
(aged 15 years and older), 2014–2017



Gay men and other men who have sex with men and adult men
(aged 15 years and older), 2016–2017



Female sex workers and adult women
(aged 15 years and older), 2016–2017



Source: Global AIDS Monitoring, 2018.

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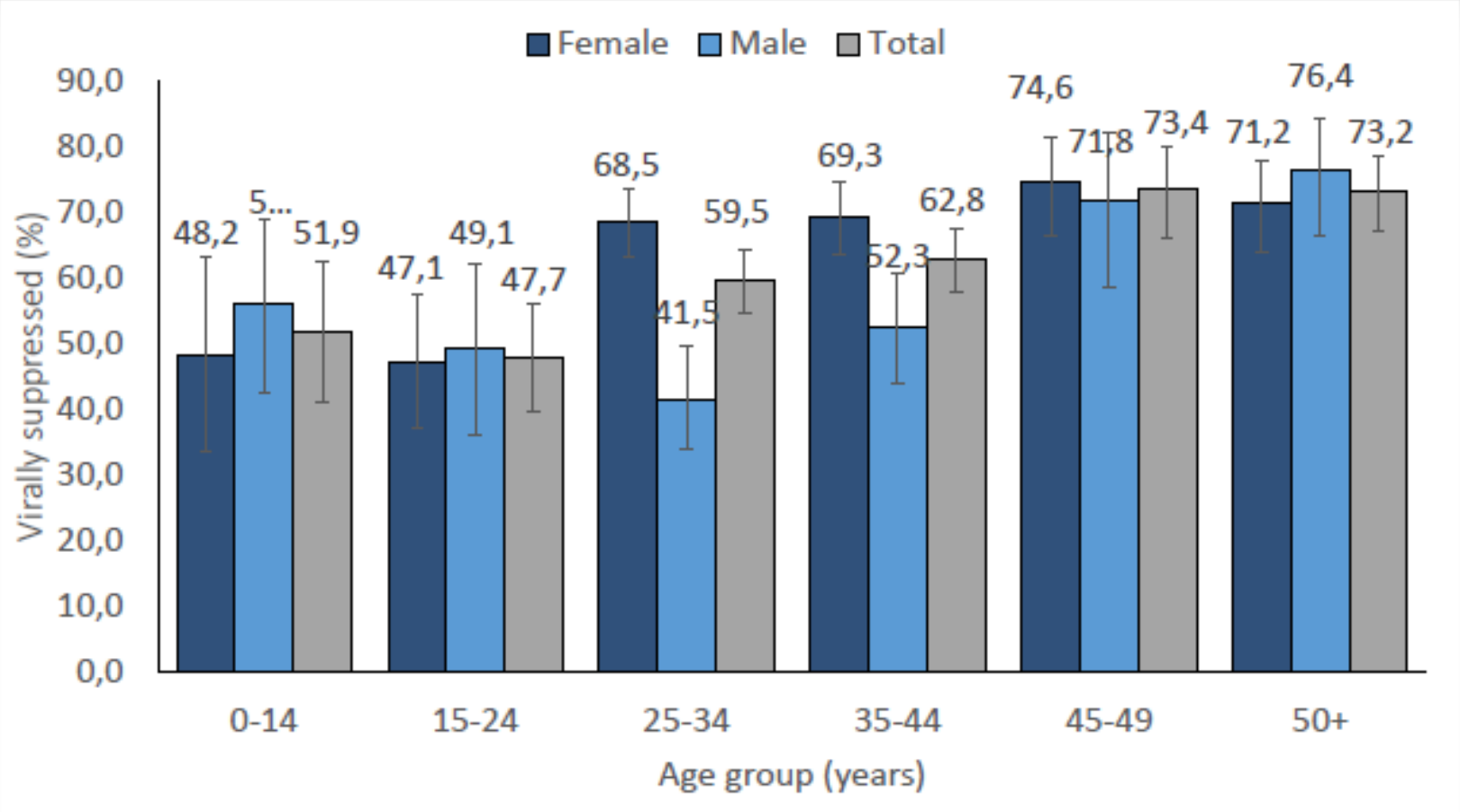
ART exposure by age group, South Africa, 2017

Age group (years)	Estimated number of people on ART (n)	Proportion of people living with HIV on ART (%) 95% CI
Total	4,401,872	62.3 (59.2-65.2)
0-14	131,052	50.0 (36.6-63.3)
15-24	273,981	39.9 (32.1-48.3)
25-49	3,243,819	63.1 (59.2-66.8)
50 and older	753,020	76.7 (71.3,81.4)
15-49	3,517,800	60.4 (57.0-63.6)

Viral suppression among all PLHIV irrespective of treatment by age and sex, South Africa, 2017

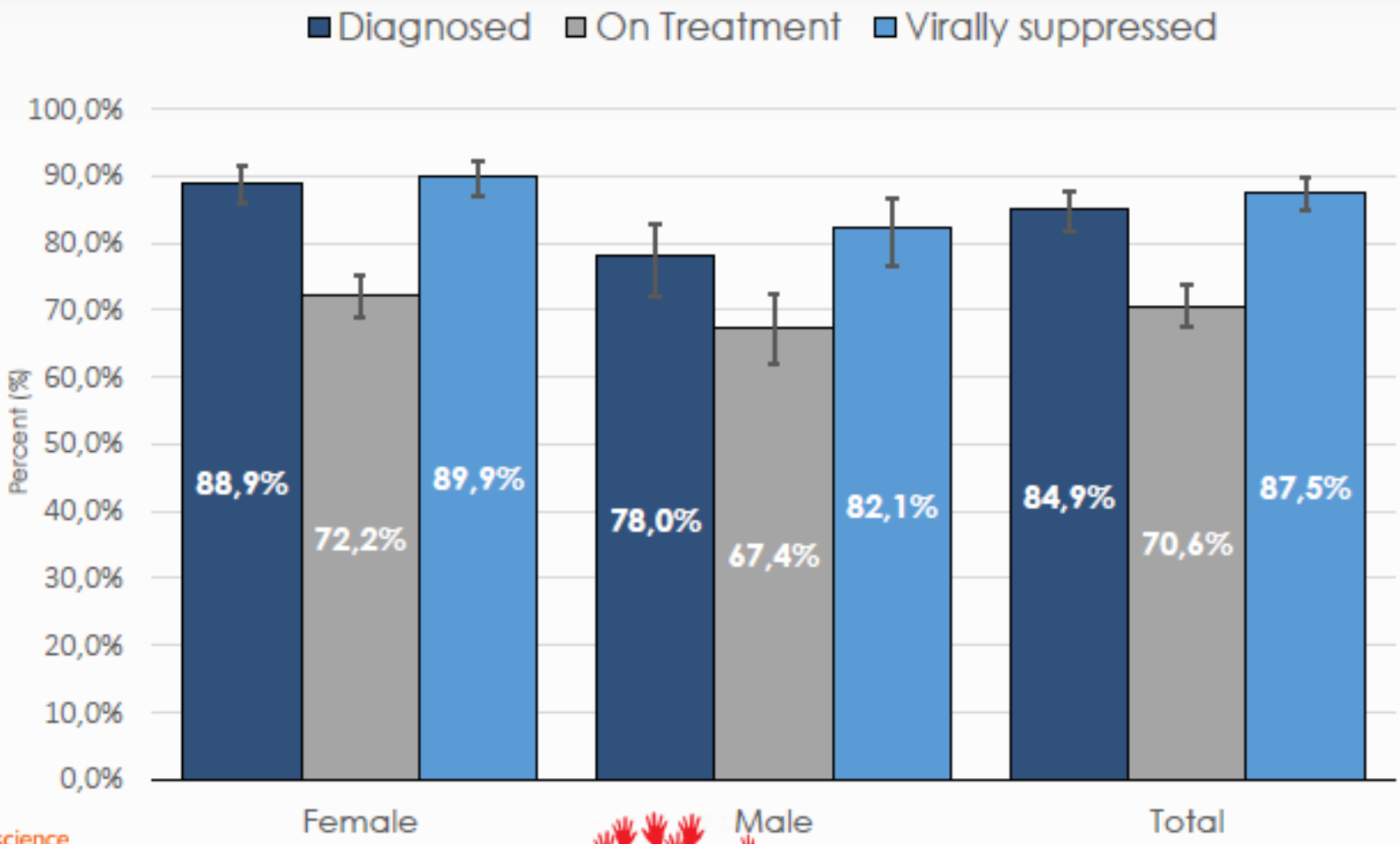


science & technology
Department Science and Technology
REPUBLIC OF SOUTH AFRICA

SABSSM V

50/90

90-90-90 - 15 to 64 years of age



HSRC Human Sciences Research Council

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Department Science and Technology
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SABSSM V

50/90

Same-day initiation?

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OPEN ACCESS PEER-REVIEWED

RESEARCH ARTICLE

Initiating Antiretroviral Therapy for HIV at a Patient's First Clinic Visit: The RapIT Randomized Controlled Trial

Sydney Rosen, Mhairi Maskew, Matthew P. Fox, Cynthia Nyoni, Constance Mongwenyana, Given Malete, Ian Sanne, Dorah Bokaba, Celeste Sauls, Julia Rohr, Lawrence Long

Published: May 10, 2016 • http://dx.doi.org/10.1371/journal.pmed.1002015

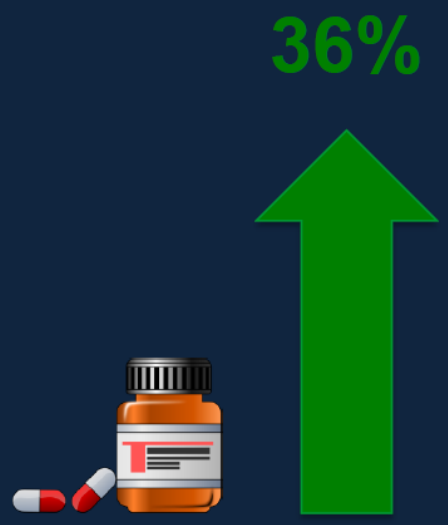
Effect Modification by Site and by Age and Sex

Initiated ≤ 90 days and retained and suppressed by 10 months	Standard arm	Rapid arm	Crude relative risk [95% CI]*
Full sample	96/190 (51%)	119/187 (64%)	1.26 (1.05-1.50)
Site			
Primary health clinic	46 (43%)	67 (64%)	1.50 (1.15-1.95)
Hospital-based HIV clinic	50 (61%)	52 (63%)	1.04 (0.82-1.32)
Age and sex			
Male < 35	12/32 (38%)	32/45 (71%)	1.90 (1.17-3.08)
Male ≥ 35	31/53 (58%)	28/45 (62%)	1.06 (0.77-1.47)
Female < 35	28/60 (47%)	32/53 (60%)	1.29 (0.91-1.83)
Female ≥ 35	25/45 (56%)	27/44 (61%)	1.10 (0.78-1.57)

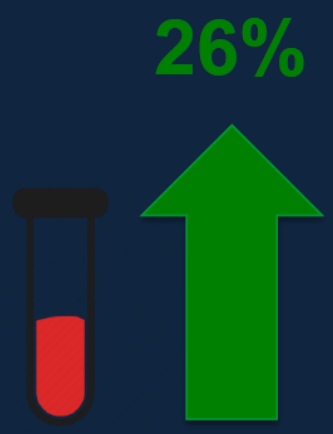
*Effect observed in study; p-values for interaction terms for absolute risk differences were not significant

Conclusions

It is possible to initiate nearly all eligible patients on ART (75% on the same day) and improve overall health outcomes



ART Initiation



Viral Suppression

South Africa ART Surge Targets

		Baseline	FY 17/18	FY18/19		FY19/20		FY19/20	
		Sep-17	Mar-18	Sep-18	Mar-19	Sep-19	Mar-20	Sep-20	Dec-20
All Districts	Baseline (No Surge)	3,960,000	4,100,000	4,240,000	4,380,000	4,520,000	4,660,000	4,800,000	4,870,000
All Districts	Baseline + Acceleration + Surge	3,960,000	4,280,000	4,600,000	5,000,000	5,400,000	5,800,000	6,000,000	6,100,000
All Districts	Baseline + Surge + Private sector	4,356,000	4,708,000	5,060,000	5,500,000	5,940,000	6,380,000	6,600,000	6,710,000
27 Districts	Baseline + Surge (27 Districts)	3,168,000	3,424,000	3,680,000	4,000,000	4,320,000	4,640,000	4,800,000	4,880,000

ART SURGE TARGETS

Increase of 2.1M on ART

6.1M: 90-90-90

6.7M: 95-95-95

health
Department:
Health
REPUBLIC OF SOUTH AFRICA

Phila

2030 NDP

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In summary:

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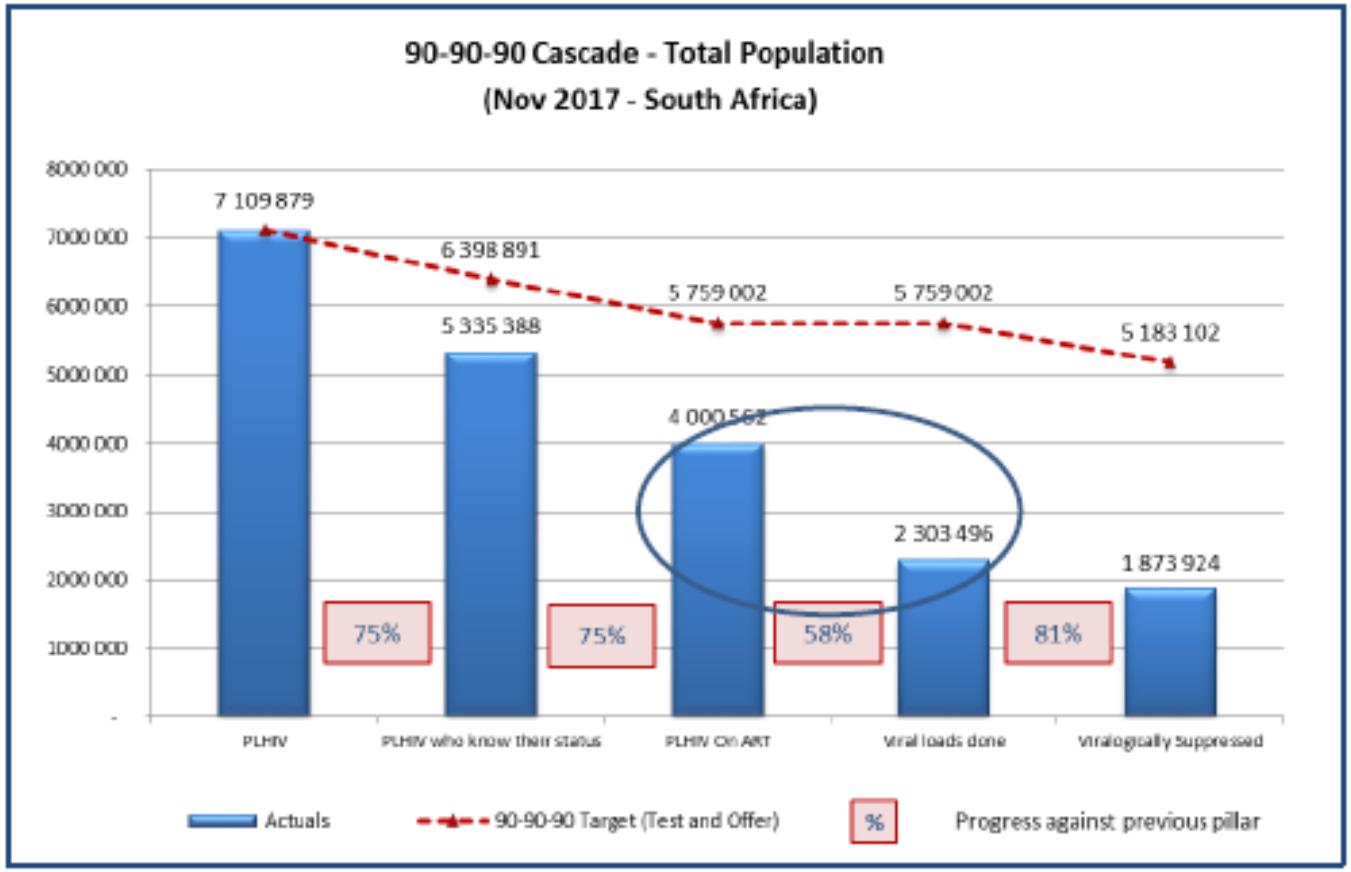
South Africa Progress to 90-90-90 (public sector)



1st 90 (90%) **75%**

2nd 90 (81%) **56%**

3rd 90 (73%)* **26%**

*Suppressed and recorded in HIS

Including private sector:
60% PLHIV on ART

health
Department:

BUT! A strong caution…

- Most patient who interrupt therapy do NOT do so for side effects
- Life challenges:
  - Stockouts, healthcare inaccessibility
  - Depression/anxiety
  - Relationship breakdown
  - Changing/losing jobs
  - Alcohol use
  - Inability to pay
- Poverty and healthcare access remain a major challenge

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Conclusions

- South Africa is a mature programme – reaping large prevention and morbidity/mortality benefits
- Close to 90-90-90 but key people left behind
- CD4 at initiation rising – but getting complex to interpret
- DTG introduction is important but complex
- System failures huge risk – poor linkage, drug stockouts, poor attention to clinical monitoring, M&E dependent on lab
- Attention to drug supply security and adherence vital for epidemic control
- Social context needs loud voices

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Thank you


USAID
FROM THE AMERICAN PEOPLE


SOUTH AFRICANS AND AMERICANS
IN PARTNERSHIP TO FIGHT HIV/AIDS
PEPFAR


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