

The new challenges around Test and Treat

(and a little on new regimens)

Durban October 2016



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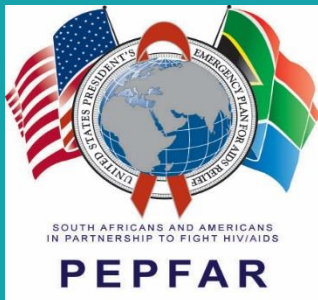
WITS RHI

Disclosures...

- Part of optimisation collaborations – grants to improve testing, new drug regimens, linkage to care
- Pharma (including drug donations for studies) and managed care



O P T I M I Z E



Talk structure:

- The history of Test & Treat (Test and Start)
- What happened at and around IAS?
- Why does it not seem to work....
- Some options and some new drug regimens for SA



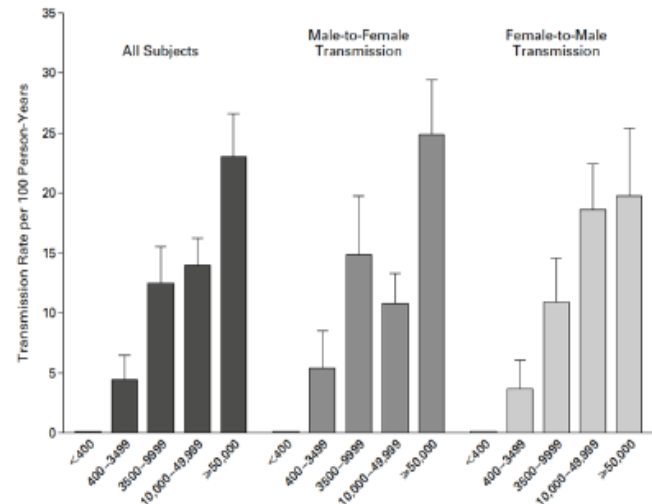
Talk structure:

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HIV-1 levels & HIV-1 infectiousness

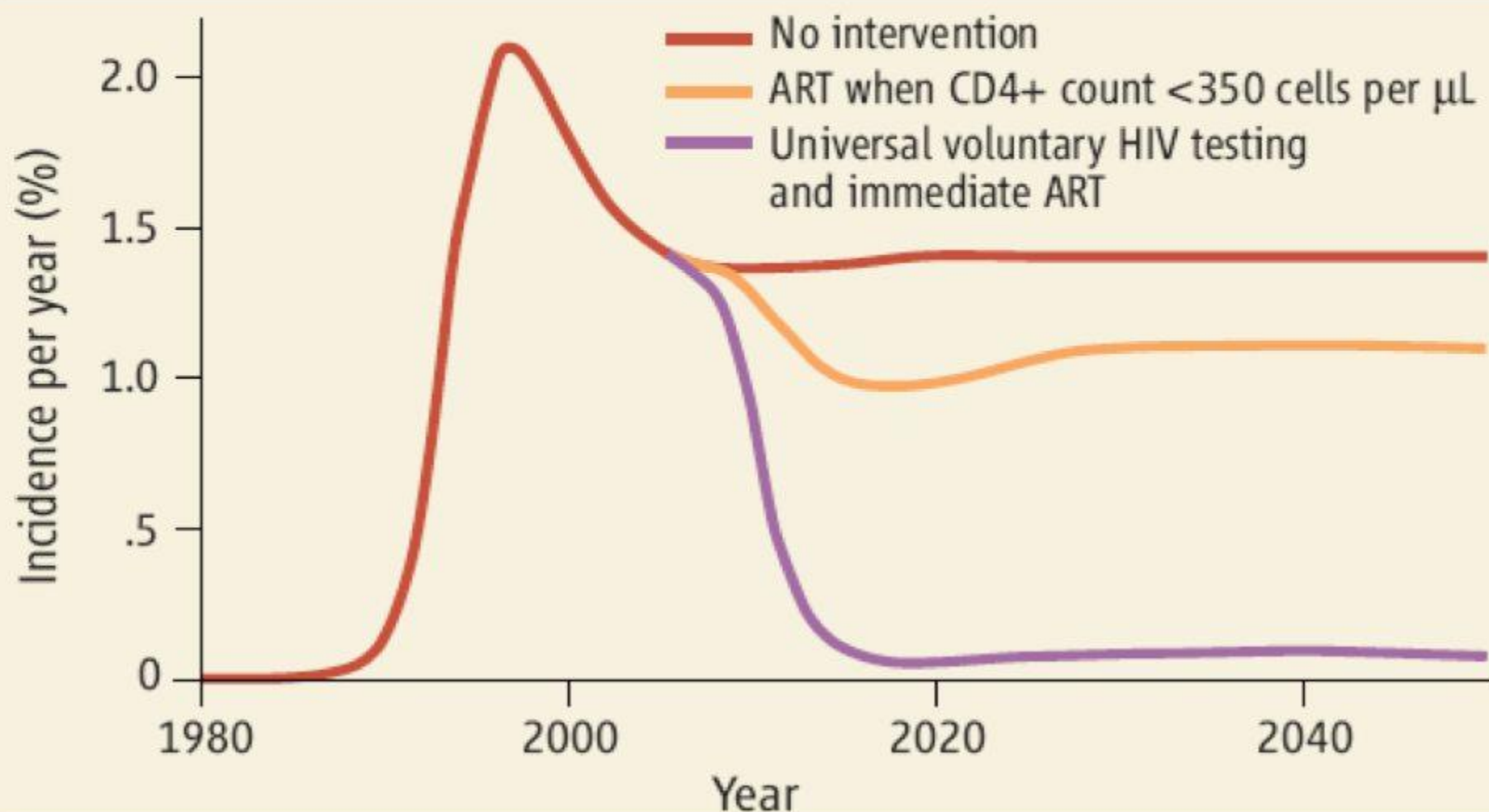
- High plasma HIV-1 RNA concentrations are associated with increased HIV-1 transmission risk
- Plasma and genital HIV-1 levels are correlated (coefficient ~0.5-0.6)
 - But, genital HIV-1 more variable than plasma and tight correlation not found in all individuals

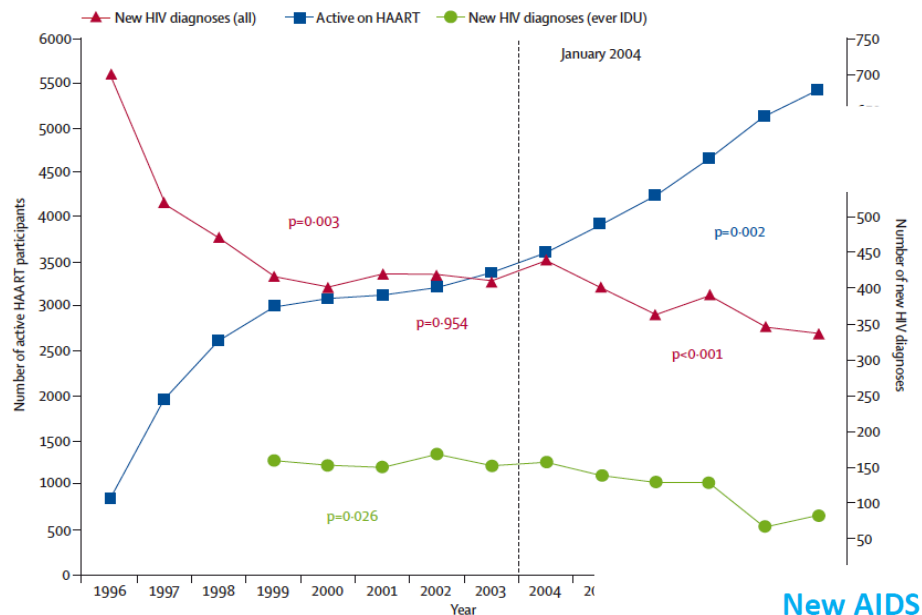


Quinn et al NEJM 2000

Universal voluntary HIV testing with immediate antiretroviral therapy as a strategy for elimination of HIV transmission: a mathematical model

R Granich, C Gilks, C Dye, K De Cock, B Williams. The Lancet Nov 26th 2008

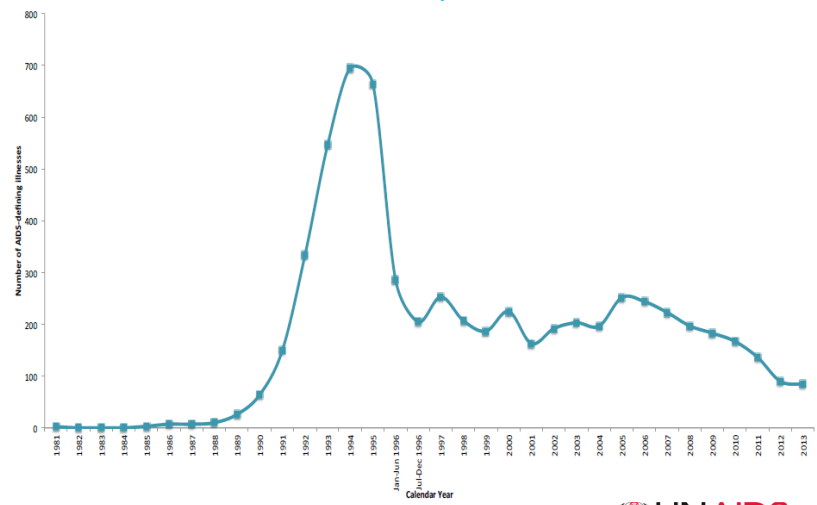




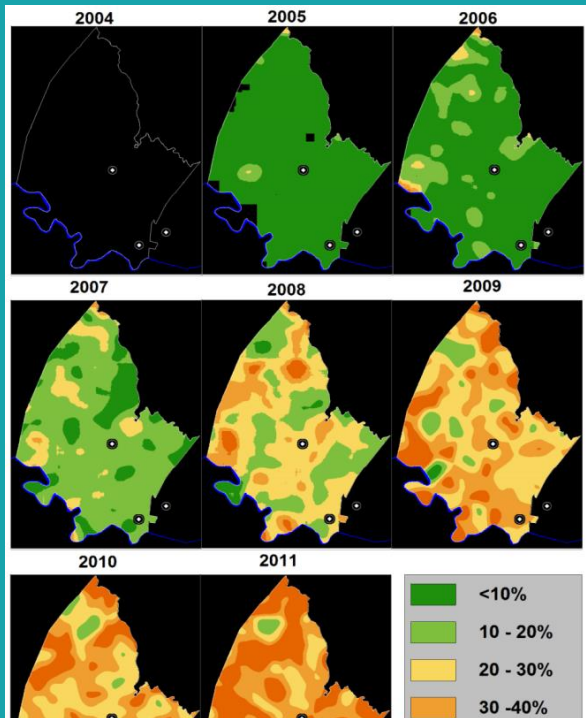
Number at risk														
Active on HAART	837	1960	2597	2994	3079	3120	3211	3356	3585	3911	4141	4271	4414	4441
New HIV diagnoses (all)	702	519	471	416	400	420	418	408	441	411	381	351	321	311
New HIV diagnoses (ever IDU)	NA	NA	NA	159	152	149	168	149	156	141	131	121	111	101
HIV tests done in BC (per 1000)	138	140	137	135	135	135	145	142	154	161	161	161	161	161

Figure 1: Number of active HAART participants and number of new HIV diagnoses per year in British Columbia. p values are for trend and were obtained from the generalised additive model. Injecting drug user (IDU) refers to in HAART=highly active antiretroviral therapy. BC=British Columbia. NA=not available.

New AIDS Cases Diagnosed by Year British Columbia, Canada



ART coverage significantly decreased individual risk, KwaZulu Natal, South Africa (2004-11)



- Africa Centre longitudinal surveillance cohort with community and individual data
- Between 2004 and 2011, 1395 HIV seroconversions and over 53,042 person-years of observation (crude HIV incidence rate of 2.63 (95% C.I. 2.50 to 2.77) per 100 person-years

Every % point increase in ART coverage among all HIV+ adults in a community, was associated with a 1.7% decline in the hazard of HIV acquisition ($p < 0.001$)

REPORTS

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

Frank Tanser,^{1*} Till Bämigehausen,² Erolil Grapsa,³ Jaffer Zaidi,³ Marie-Louise Newell^{1,3}

The landmark HIV Prevention Trials Network (HPTN) 052 trial in HIV-discordant couples demonstrated unequivocally that treatment with antiretroviral therapy (ART) substantially lowers the probability of HIV transmission to the HIV-uninfected partner. However, it has been vigorously debated whether substantial population-level reductions in the rate of new HIV infections could be achieved in "real-world" sub-Saharan African settings where stable, cohabiting couples are often not the norm and where considerable operational challenges exist to the successful and sustainable delivery of treatment and care to large numbers of patients. We used data from one of Africa's largest population-based prospective cohort studies (in rural KwaZulu-Natal, South Africa) to follow up a total of 16,667 individuals who were HIV-uninfected at baseline, observing individual HIV seroconversions over the period 2004 to 2011. Holding other key HIV risk factors constant, individual HIV acquisition risk declined significantly with increasing ART coverage in the surrounding local community. For example, an HIV-uninfected individual living in a community with high ART coverage (30 to 40% of all HIV-infected individuals on ART) was 38% less likely to acquire HIV than someone living in a community where ART coverage was low (<10% of all HIV-infected individuals on ART).

One of the most successful public health interventions ever undertaken has been the provision of combination antiretroviral therapy (ART) to more than 6.2 million people in sub-Saharan Africa (1). The ART scale-up

the trial can be extrapolated to communities where stable, cohabiting couples are not the norm (2). The existing global evidence of the population effect of HIV treatment as prevention has been based on "ecological" associations (correlations

HIV Treatment mid-2012 treatment than 20,000 patients characterized by high adults aged 15 y levels of poverty 67% of adults area were using 17 community-based counselors using ART. The treatment crossed to CD4+ and tuberculosis new threshold v adults in Aquarius observation, no po treatment initiati Within the F Centre demograp resident individu lance at any give 2006, all women 15 to 54 years were eligible fo for the HIV s

Maps s
(≥15

~4 YEAR LAG BETWEEN SCALE UP OF ART AND DECLINE IN MTB INCIDENCE

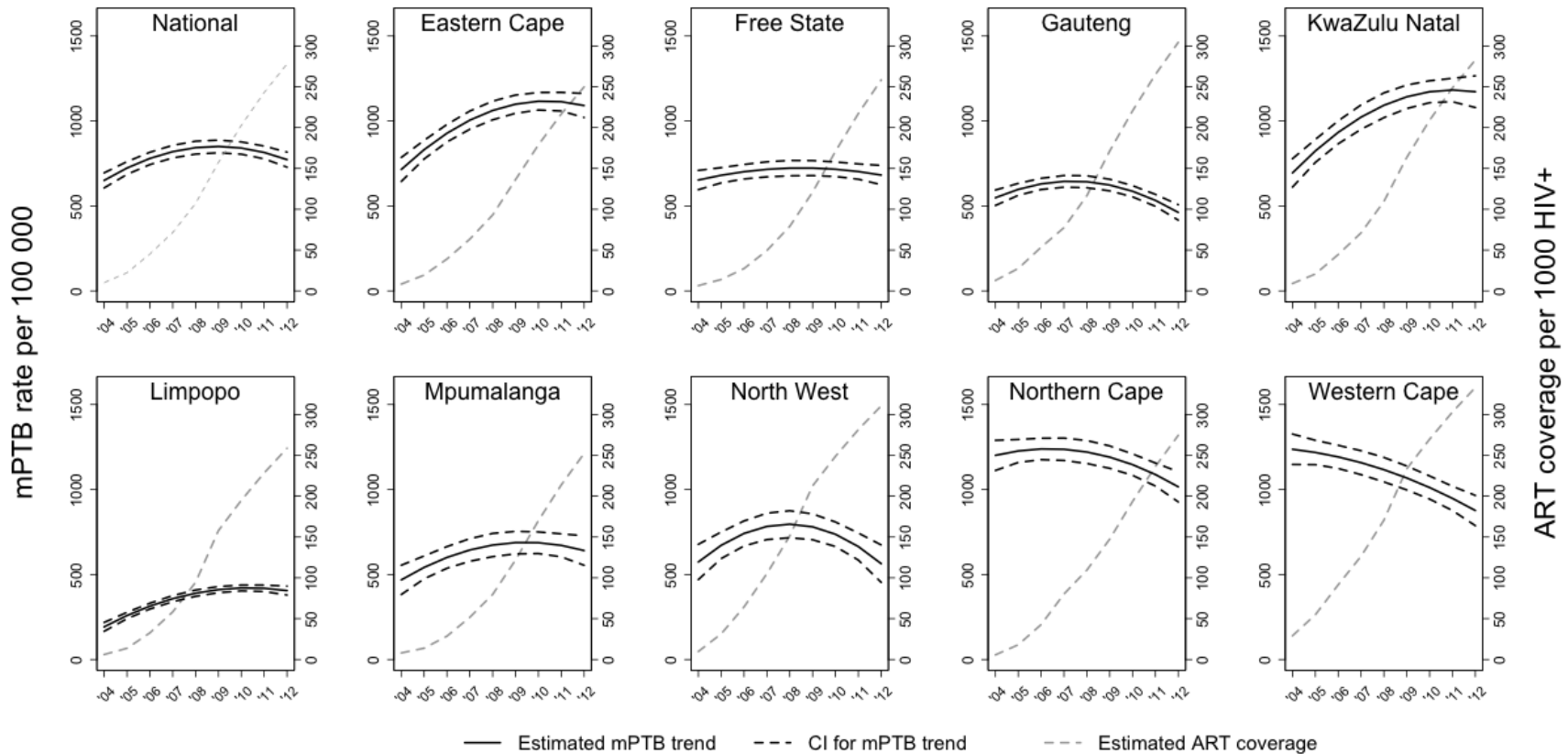
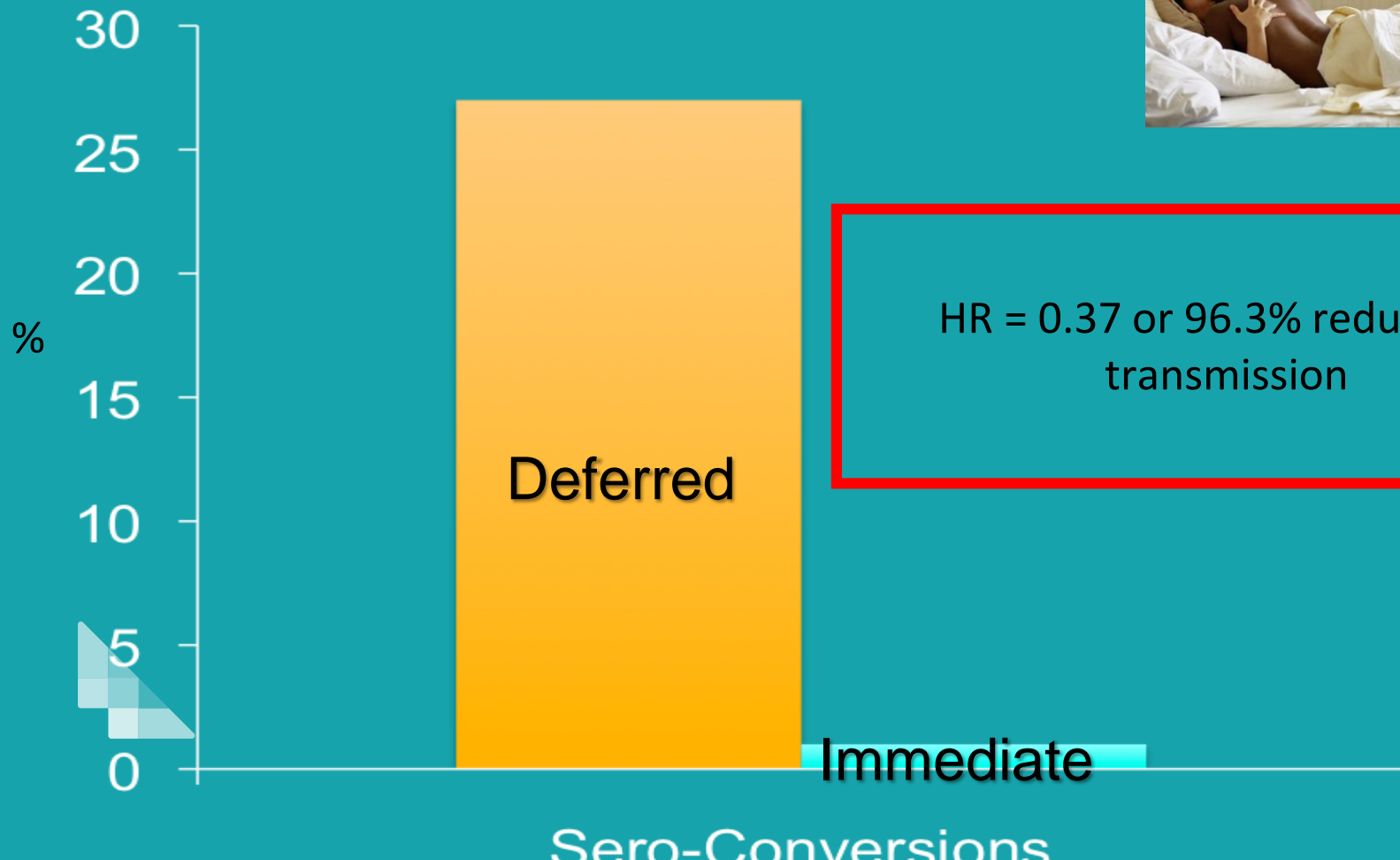


Figure 1: Incidence of microbiologically-confirmed pulmonary tuberculosis (per 100,000 population) and antiretroviral treatment coverage rates in HIV-infected individuals nationally in South Africa nationally and provincially from 2004 to 2012

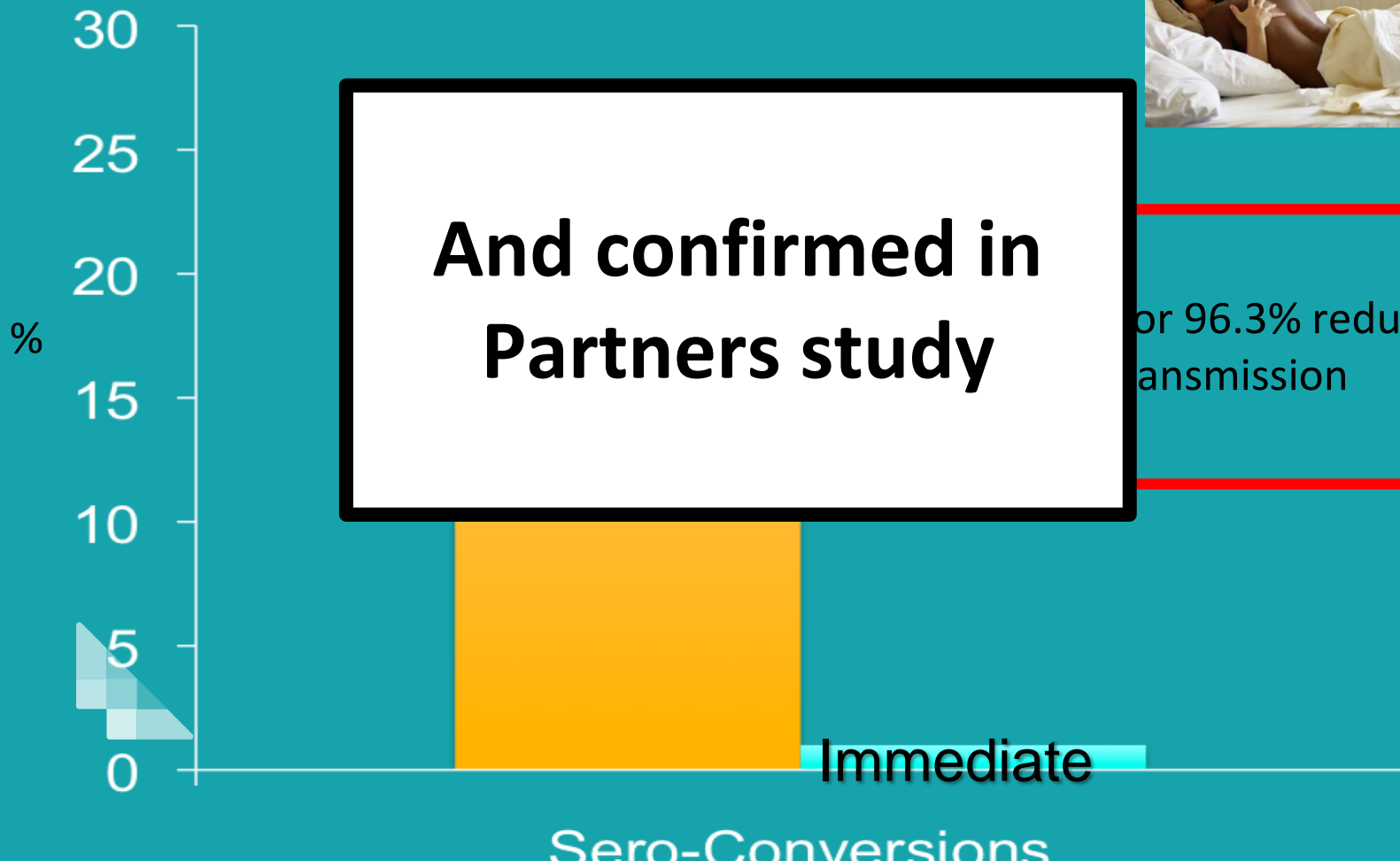
The solid black line represents the estimated trend in PTB incidence per 100,000 population over the study period and the dotted black line the corresponding 95% confidence interval. The overlaid dotted grey line is the ART coverage per 1000 HIV positive individuals based on data from the ASSA 2008 model.

Nanoo A, Izu A, Ismail, NA, Ihekweazu C, Abubakar I, Mamejta D, Madhi SAM. 2015. Nationwide and regional decline in incidence of microbiologically-confirmed pulmonary tuberculosis in South Africa: a time series analysis from 2004 to 2012. *The Lancet Infectious Diseases*, In press

Is sex safe? HPTN 052



Is sex safe? HPTN 052



Thorn in T&T side: Individual benefit

- Conflicting observational studies
- 052 not convincing re individual data

Comparative effectiveness of immediate antiretroviral therapy versus CD4-based initiation in HIV-positive individuals in high-income countries: observational cohort study

Sara Lodi, Andrew Phillips, Roger Logan, Ashley Olson, Dominique Costagliola, Sophie Abgrall, Ard van Sighem, Peter Reiss, José M Miró, Elena Ferrer, Amy Justice, Neel Gandhi, Heiner C Bucher, Hansjakob Furrer, Santiago Moreno, Susana Monge, Giota Touloumi, Nikos Pantazis, Jonathan Sterne, Jessica G Young, Laurence Meyer, Rémonie Seng, Francois Dabis, Marie-Anne Vandehende, Santiago Pérez-Hoyos, Inma Jarrin,

Interpretation The benefits of immediate initiation of ART, such as prolonged survival and AIDS-free survival and increased virological suppression, were small in this high-income setting with relatively low CD4 count at HIV diagnosis. The estimated beneficial effect on AIDS is less than in recently reported randomised trials. Increasing rates of HIV testing might be as important as a policy of early initiation of ART.

Funding National Institutes of Health

START and Temprano fixed this

Table 1: Severe morbidity in TEMPRANO study at 30 months

	% events	n	Rate / 100 PY	adj HR	p
WHO ART	11.4%	111	4.9		
Early ART	6.6%	64	2.8	0.56	0.0002
No IPT	10.7%	104	4.7		
IPT	7.2%	71	3.0	0.65	0.005

Table 1. Primary endpoint and its components in open DSMB report (15 May 2015)

	Early ART (arm A)		Deferred ART (arm B)		Hazard Ratio
	N	rate/100 PY	N	rate/100 PY	Arm A/B (95% CI)
AIDS, serious non-AIDS, or death (primary)	41	0.60	86	1.25	0.47 (0.32 to 0.68)
AIDS or AIDS death	14	0.20	46	0.66	0.30 (0.17 to 0.55)
Serious non-AIDS or non-AIDS death	28	0.41	41	0.59	0.67 0.42 to 1.09) NS**

* PY = patient years, ** NS = non significant

Thanks: Simon Collins



Treatment for life

Expect a normal life expectancy:

May et al. AIDS 2014

- UK CHIC: 21 388 people started ART 2000-2010

If 35 year old man started ART:

	life expectancy		
CD4	Baseline	1 year ART	5 years ART
<200	71		& VL>50 54
200-349	78	78	
>350	77	81	& VL<50 80
General population	78		

Conclusion: If diagnosed, in care and on effective ART: life expectancy is normal

Great information to give to people newly diagnosed and encourage good adherence



Thanks: Julie Fox, Guys

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Several things happened....

- The individual benefits were confirmed (but VERY small in health people at high CD4 counts)
- 90-90-90 success stories (Botswana, Havlir, Sweden)
- But failure to link to care in some RCTs - Swaziland, KZN
- And no impact on new incidence (KZN)



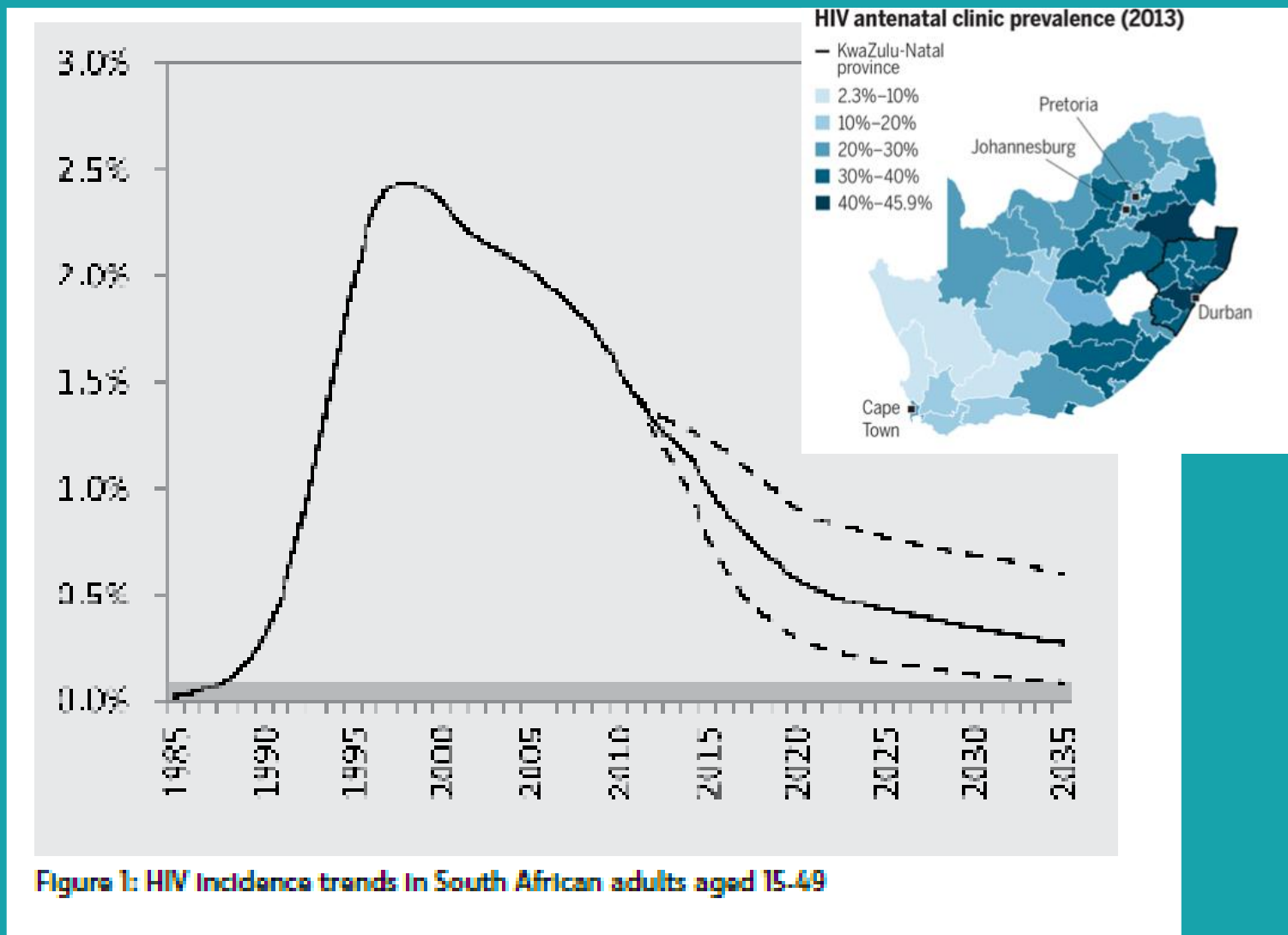
Incidence still remains stubbornly high...

New HIV infections among people aged 15 years and over, by region, 2010–2015



Source: UNAIDS 2016 estimates.

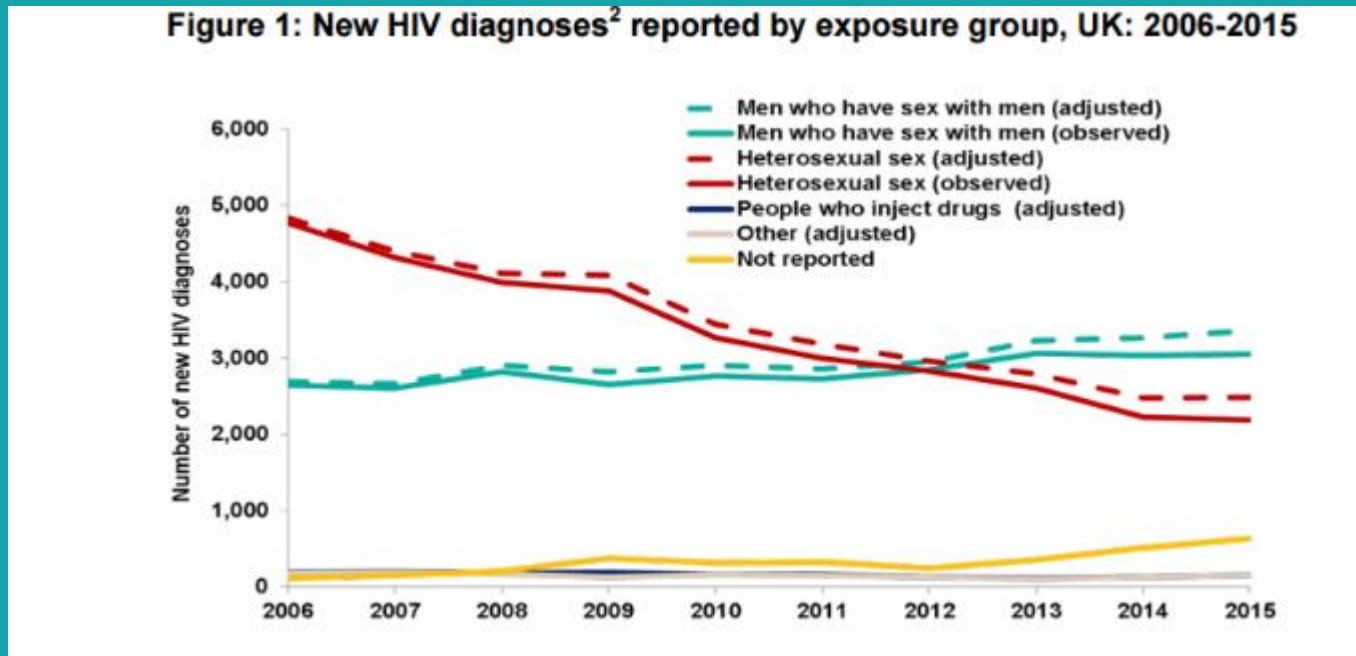
And does not correlate well with ART...



Source: Leigh Johnson, Spotlight, 2016

Troubling....

- Julio Montagner in Vancouver: MSM vs intravenous drug users



Source: Public Health England, 2016

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Linkage to care?

- Massive challenge in Swaziland, KZN – if they take too long, is the damage done?

HIV TREATMENT

Even in settings with good testing & ART coverage, treatment cascades still show important leakages...

WV/AIDS Department

Cascade of HIV care – Sub-Saharan Africa

Stage	Count	Percentage
Living with HIV	24.7 million	-
Diagnosed	11.11 million	45%
Linked to care	-	-
In care	-	-
On ART	9.63 million	39%
Adherent to ART	-	-
Virally suppressed	7.14 million	29%

Reference: UNAIDS Gap Report 2014

Cascade of HIV Care – Brazil, 2013

Stage	Count	Percentage
Living with HIV	724,000	-
Diagnosed	589,000	80%
Linked to care	537,000	73%
In care	448,000	61%
On ART	365,000	48%
Adherent to ART	-	-
Virally suppressed	293,000	40%

Reference: Brazilian Ministry of Health. Cascade of continuous care in Brazil, 2013. HIV epidemiology report, October 2014, Brazil.

Cascade of HIV care – United States

Stage	Count	Percentage
Living with HIV	1,201,100	-
Diagnosed	1,022,800	86%
Linked to care	-	-
In care	478,000	40%
On ART	441,961	37%
Adherent to ART	-	-
Virally suppressed	304,495	30%

Reference: Heather Bradley, PhD, L. H. Irene Hall, PhD, L. Richard J. Wolcott, et al. HIV Diagnosis, Care, and Treatment Among Persons Living with HIV – United States, 2011. Morbidity and Mortality Weekly Report 2013; 62(15):3115-3127 available at <http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6215a1.htm>

Cascade of HIV care – Russia

Stage	Count	Percentage
Living with HIV	1,363,330	-
Diagnosed	515,403	49%
Linked to care	481,783	38%
In care	156,858	11%
On ART	127,054	9%

Reference: Petrova, A., Pappa, A., Jensen, T., et al. The cascade of HIV care in Russia. BMC Public Health 2010, 10:1151.

Cascade of HIV care – British Columbia (CA)

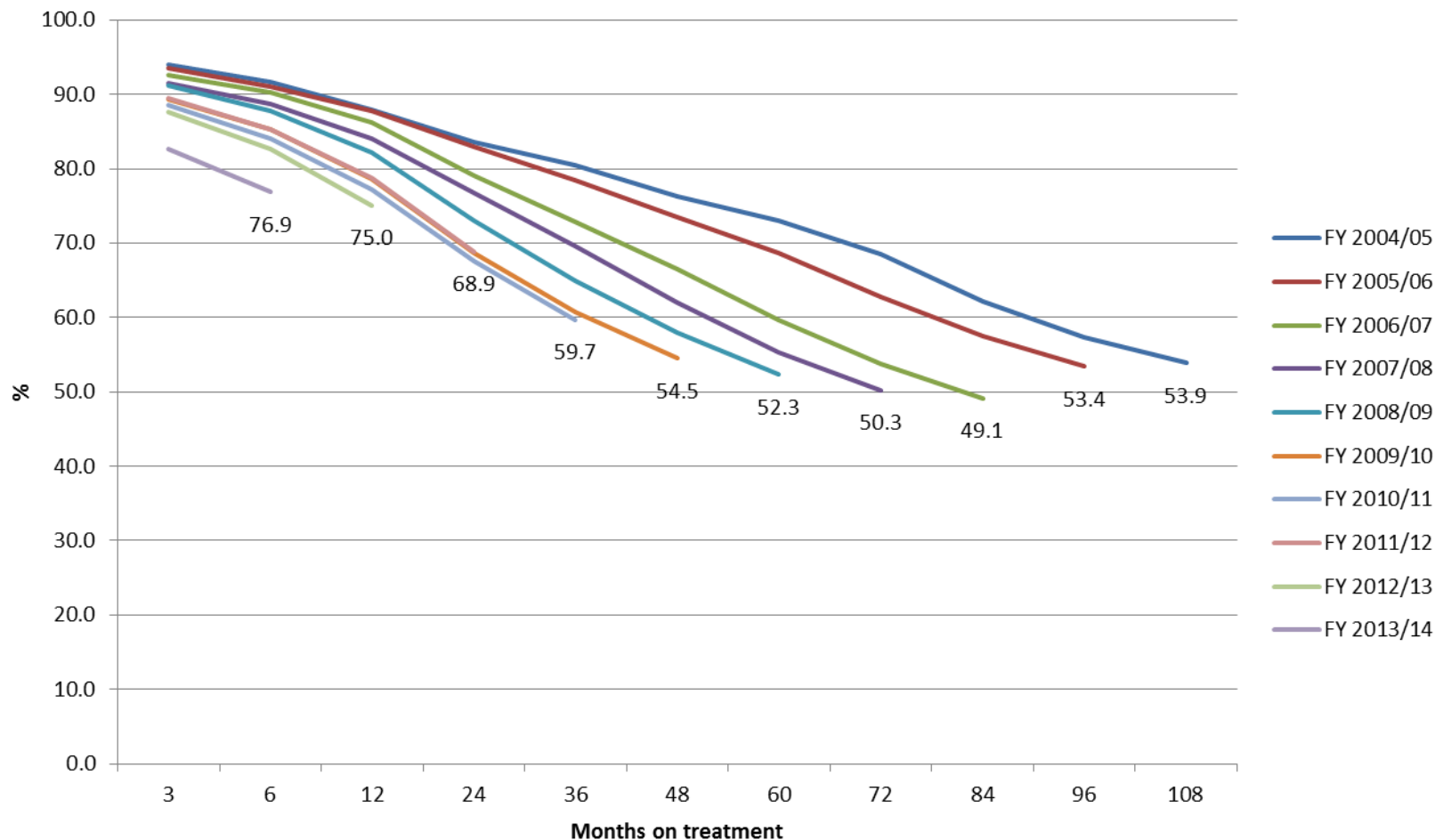
Stage	Count	Percentage
Living with HIV	72,000	-
Diagnosed	51,120	71%
Linked to care	48,240	67%
In care	41,040	57%
On ART	36,720	51%
Adherent to ART	31,680	45%
Virally suppressed	24,912	35%

Reference: Nook, B., Manser, J.S., Colley, G., Lima, V.D., Chan, K., Heath, K., Yip, B., Samji, H., Gilbert, M., Barrios, R., Goulet, R., Hogg, R.S. STDP HIV/AIDS Study Group. The cascade of HIV care in British Columbia, Canada, 1996-2011: a population-based retrospective cohort study. The Lancet Infectious Diseases 2014;14:40-49.

Hill et al. CROI 2015 [abstr 1118]

Retention in care

National: Percentage of adults remaining on ART, by duration and year started ART



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

Thanks: Andrew Boule



health

Department:
Health
REPUBLIC OF SOUTH AFRICA

Insufficient VL suppression?

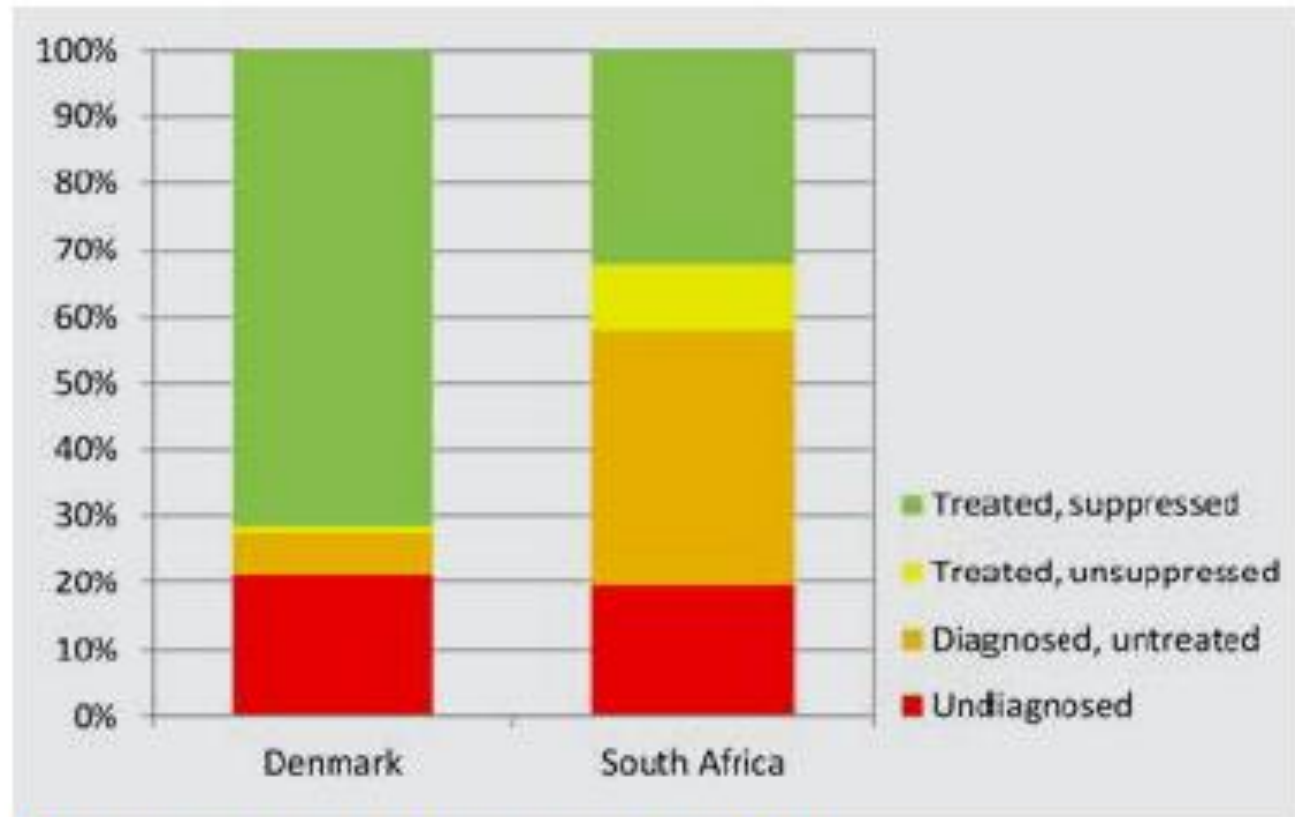


Figure 2: Treatment cascades in Denmark and South Africa in 2013

Source: Spotlight 2016

Do we have a resistance problem?



VL expansion poor!

TABLE 1. Selected treatment and monitoring indicators for viral load (VL) monitoring scale-up during pre- and post-scale-up periods, by country – sub-Saharan Africa, 2013–2015

Country	VL monitoring periods			Cumulative no. of ART patients		No. of ART patients with ≥1 VL test		ART patients with ≥1 VL ART patients with ≥1 VL		VL tests with viral suppression (%)*		Turnaround time†		Established target number of VL tests	
	Yr of scale-up	Pre-scale-up	Post-scale-up	Pre-scale-up	Post-scale-up	Pre-scale-up	Post-scale-up	Pre-scale-up	Post-scale-up	Pre-scale-up	Post-scale-up	Pre-scale-up	Post-scale-up	2015	2016
Côte d'Ivoire	2015	2014	2015	129,993	138,365	4,922	3,687	4	3	66	53	10	10	50,000	112,000
Kenya	2014	2013	2014–2015	631,503	798,188	53,012	280,645	8	38	64	83	18	31	1,200,000‡	1,393,557
Malawi¶	2014	2013	2014–2015	472,865	536,438	28,315**	61,227**	6	11	86	84	18	29	132,275	212,598
Namibia	2014	2013	2014–2015	126,779	131,721	76,716**	138,604**	54	95	74	86	5	4	192,616	206,520
South Africa	2014	2013	2014–2015	2,609,275	2,951,159	1,878,927	2,119,890	72	75	75	78	3	3	3,600,000	3,900,000
Tanzania	2015	2014	2015	600,886	758,344	14,334	22,772	2	3	80	72	10	4	87,589	363,314
Uganda	2014	2013	2014–2015	507,663	757,703	25,000	79,207	5	10	90	94	18	6	250,000	800,000

Abbreviation: ART = antiretroviral therapy.

* The percentage of viral load tests with viral suppression might include multiple tests per patient. In Kenya, the viral load suppression rate for pediatrics is 63% and represents 13% of the cumulative number of ART patients.

† Average time from specimen collection to return of test results to referring facility (days).

‡ Might represent more than one viral load test per person.

¶ In the post-scale-up period, viral load testing is conducted every 2 years in Malawi compared to annual testing in other countries.

** The number of viral load tests could not be disaggregated at the individual level for adult patients in Côte d'Ivoire and Malawi. The number of tests for these two countries is therefore overestimated for these two countries. In Namibia, pediatric patients account for approximately 10% of the total number of tests. In Malawi, approximately 10% of the total number of tests with one or more viral load test were assumed to be duplicates and were subtracted from the total number of tests.



GROUPING: Quarter: **Q1 2015**

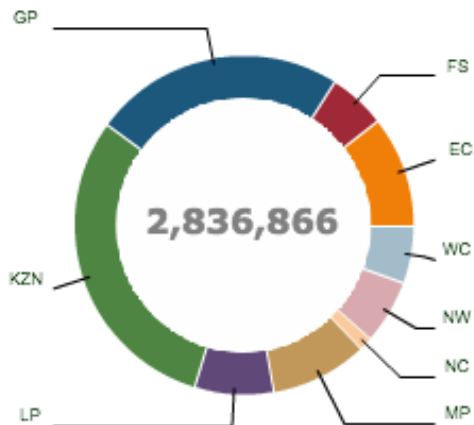


Summary indicators for CCMT M&E in SA - Adults

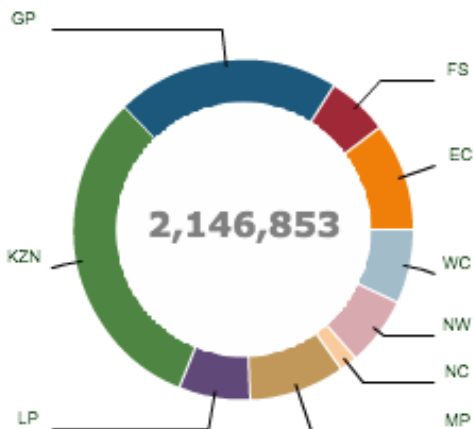
Period: from Q1 2012 to Q1 2015

Select Age Category: **Adults** Children <15 years

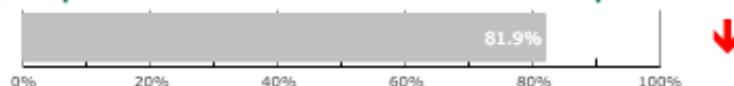
People on treatment (DHIS)



People with a VL test done in the last 12 months



% People in care and on ART with a VL <= 1000 copies/ml



% People in care and on ART, who have a VL done at least annually



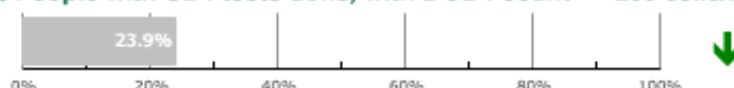
% People with CD4 tests done, with a CD4 count <= 500 cells/mm3



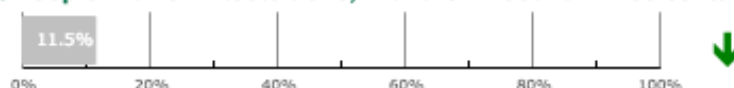
% People with CD4 tests done, with a CD4 count <= 350 cells/mm3



% People with CD4 tests done, with a CD4 count <= 200 cells/mm3



% People with CD4 tests done, with a CD4 count <= 100 cells/mm3



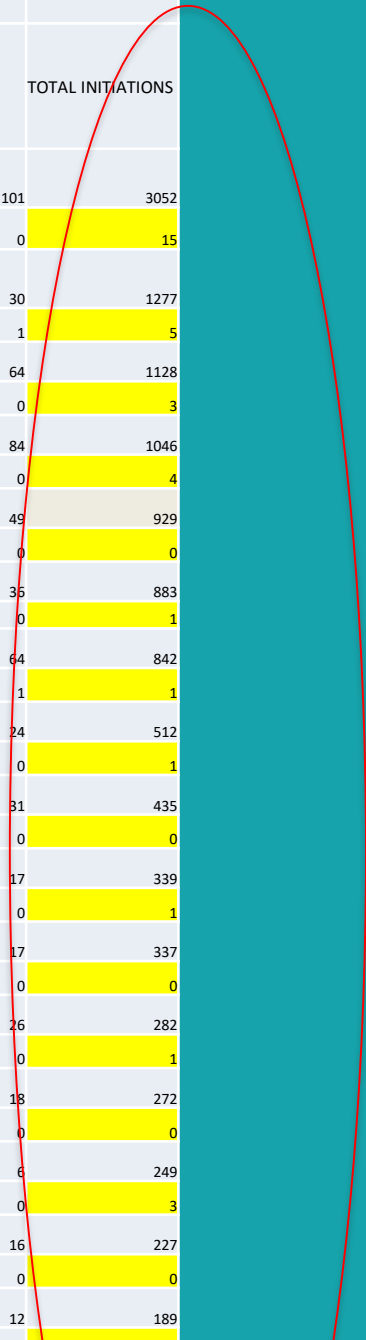
Clinics in central Johannesburg

Thanks to Sam Lalla-Edwards and team, M&E Dept, RHI

First and Second line regimens at ART initiation for Jan to Dec 2015														
Facility name		JAN	FEB	MAR	APR	MAY	JUN	JUL	AUG	SEP	OCT	NOV	DEC	TOTAL INITIATIONS
HCHC	1st Line	166	217	232	175	796	227	235	254	221	268	160	101	3052
	2nd Line	2	0	2	2	0	3	2	1	0	2	1	0	15
Yeoville	1st Line	69	97	144	160	135	104	140	109	106	104	79	30	1277
	2nd Line	0	2	0	1	0	0	0	0	1	0	0	1	5
80 Albert	1st Line	78	91	91	86	110	100	135	91	90	91	101	64	1128
	2nd Line	0	1	0	0	0	1	0	0	1	0	0	0	3
Jeppe Clinic	1st Line	76	95	76	75	113	75	96	83	73	84	116	84	1046
	2nd Line	0	1	2	0	0	0	0	0	0	1	0	0	4
Joubert Park	1st Line	81	81	82	71	92	71	81	79	83	86	73	49	929
	2nd Line	0	0	0	0	0	0	0	0	0	0	0	0	0
Rosettenville	1st Line	57	105	81	77	105	88	68	62	61	84	59	36	883
	2nd Line	0	0	0	0	0	0	0	0	1	0	0	0	1
Malvern	1st Line	78	66	67	77	73	79	75	69	61	70	63	64	842
	2nd Line	0	0	0	0	0	0	0	0	0	0	0	1	1
Jeppe Street	1st Line	36	34	50	28	55	56	47	32	44	51	55	24	512
	2nd Line	1	0	0	0	0	0	0	0	0	0	0	0	1
Bellavista	1st Line	32	40	59	44	40	26	36	36	26	28	37	31	435
	2nd Line	0	0	0	0	0	0	0	0	0	0	0	0	0
Crown Gardens	1st Line	17	31	39	25	27	32	32	30	29	33	27	17	339
	2nd Line	0	0	0	0	0	0	0	0	0	0	1	0	1
Mayfair	1st Line	10	29	38	37	34	18	39	28	37	24	26	17	337
	2nd Line	0	0	0	0	0	0	0	0	0	0	0	0	0
Bezvalley	1st Line	10	11	20	18	22	33	25	30	23	45	19	26	282
	2nd Line	0	0	1	0	0	0	0	0	0	0	0	0	1
Glenanda	1st Line	10	23	28	29	24	30	18	28	21	21	30	18	272
	2nd Line	0	0	0	0	0	0	0	0	0	0	0	0	0
SRH	1st Line	30	45	37	38	20	15	17	6	5	13	17	6	249
	2nd Line	0	1	1	1	0	0	0	0	0	0	0	0	3
South Hills	1st Line	15	32	20	10	19	17	23	23	12	20	20	16	227
	2nd Line	0	0	0	0	0	0	0	0	0	0	0	0	0
Kibler Park	1st Line	12	14	22	15	19	12	11	10	25	15	22	12	189
	2nd Line	0	0	0	0	0	0	0	0	0	0	0	0	0
CMJAH	1st Line	34	27	26	25	16	30	26	27	35	42	28	16	332
	2nd Line	0	0	0	0	0	3	0	0	0	3	0	0	6

First and Second line regimens at ART initiation for Jan to Dec 2015

FEB	V 1 3	APR	MAY	JUN	JUL	AUG	SEP	OCT	NOV	DEC	TOTAL INITIATIONS
2172	2	175	796	227	235	254	221	268	160	101	3052
02	1	2	0	3	2	1	0	2	1	0	15
974	4	160	135	104	140	109	106	104	79	30	1277
20	9	1	0	0	0	0	1	0	0	1	5
911	10	86	110	100	135	91	90	91	101	64	1128
10	7	0	0	1	0	0	1	0	0	0	3
956	12	75	113	75	96	83	73	84	116	84	1046
8	8	0	0	0	0	0	0	1	0	0	4
812	10	71	92	71	81	79	83	86	73	49	929
00	8	0	0	0	0	0	0	0	0	0	0
1051	00	77	105	88	68	62	61	84	59	35	883
00	6	0	0	0	0	0	1	0	0	0	1
667	00	77	73	79	75	69	61	70	63	64	842
00	5	0	0	0	0	0	0	0	0	1	1
340	00	28	55	56	47	32	44	51	55	24	512
00	5	0	0	0	0	0	0	0	0	0	1
409	00	44	40	26	36	36	26	28	37	31	435
00	3	0	0	0	0	0	0	0	0	0	0
319	00	25	27	32	32	30	29	33	27	17	339
00	3	0	0	0	0	0	0	0	1	0	1
298	00	37	34	18	39	28	37	24	26	17	337
00	2	0	0	0	0	0	0	0	0	0	0
110	01	18	22	33	25	30	23	45	19	26	282
01	2	0	0	0	0	0	0	0	0	0	1
238	00	29	24	30	18	20	21	21	30	18	272
00	3	0	0	0	0	0	0	0	0	0	0
457	11	38	20	15	17	6	5	13	17	6	249
11	2	1	0	0	0	0	0	0	0	0	3
320	00	10	19	17	23	23	12	20	20	16	227
00	2	0	0	0	0	0	0	0	0	0	0
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00		0	0	0	0	0	0	0	0	0	0



Global epidemiology of drug resistance after failure of WHO recommended first-line regimens for adult HIV-1 infection: a multicentre retrospective cohort study

*The TenoRes Study Group**

Summary

Background Antiretroviral therapy (ART) is crucial for controlling HIV-1 infection through wide-scale treatment as



- “Researchers at University College London said the study could mean that, after a year of treatment, up to 15% of people in sub-Saharan Africa and 10% in South Africa were resistant to the drug.”

Latest news News by topic HIV update News feeds Conference news

RESISTANCE

Tenofovir resistance may develop in more than half of patients failing treatment in sub-Saharan Africa

Keith Alcorn

Published: 01 February 2016

Home > The Times > Article >

No rise in SA's ARV resistance

Katharine Child | 03 February, 2016 00:54



But the director of the Centre for the Aids Programme of Research in SA, Salim Karim, said resistance to antiretrovirals was not high. File photo
Image by AFP/Debraj Singh/REUTERS/Butterstock.com

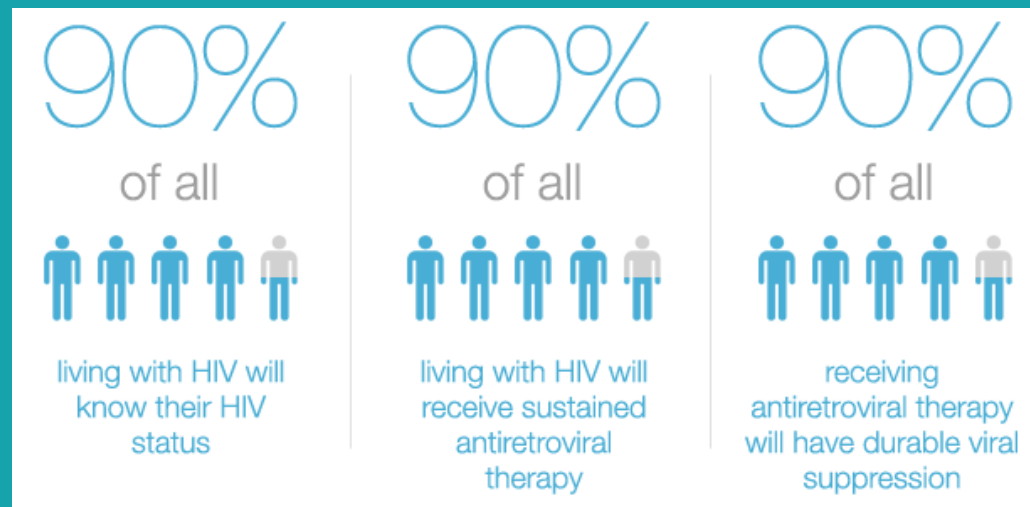
Some ideas

- Is the data just wrong?



Some ideas why: missing men?

- We are probably very close to the 3rd 90
- Second 90: probably there for women; not men – and that's a huge problem

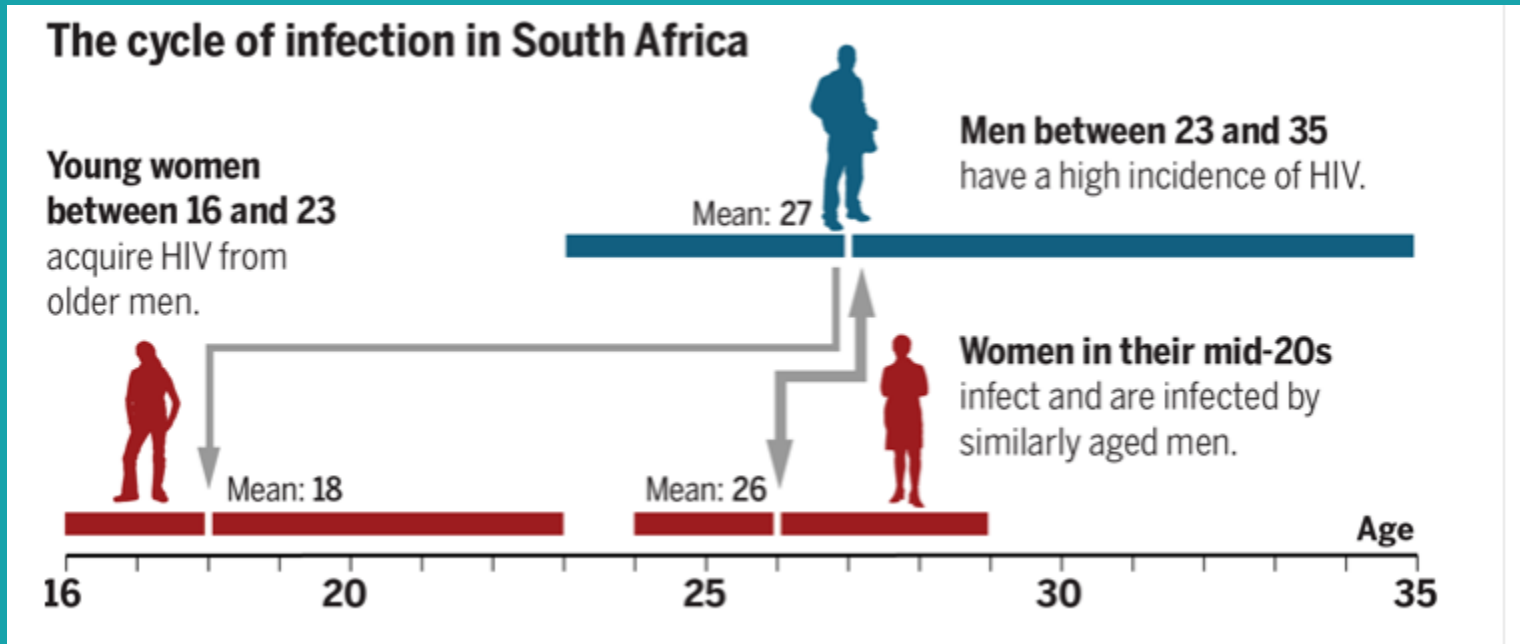


Some ideas why: missing populations?

- Sex workers and gay men? But smallish population



Or is it something else?



Prevention still suffers from intuitive thinking

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HIV/Aids

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21 JULY 2016

'Sugar daddies' and 'blessers' increase HIV/Aids risk

Lebogang Motsumi, 27, still remembers the moment when she learnt she had contracted HIV from a man a decade her senior.

0

Lebogang Motsumi, 27, still remembers the moment when she learnt she had contracted [HIV](#) from a man a decade her senior.

Money and gifts

"It was August 15, 2009, at 1:00pm," she said, recalling the instant when her life changed



Talk structure:

- The history of Test & Treat (Test and start)
- What happened at and around IAS?
- Why does it not seem to work....
- Some options and some new drug regimens for SA



OPTIMIZE

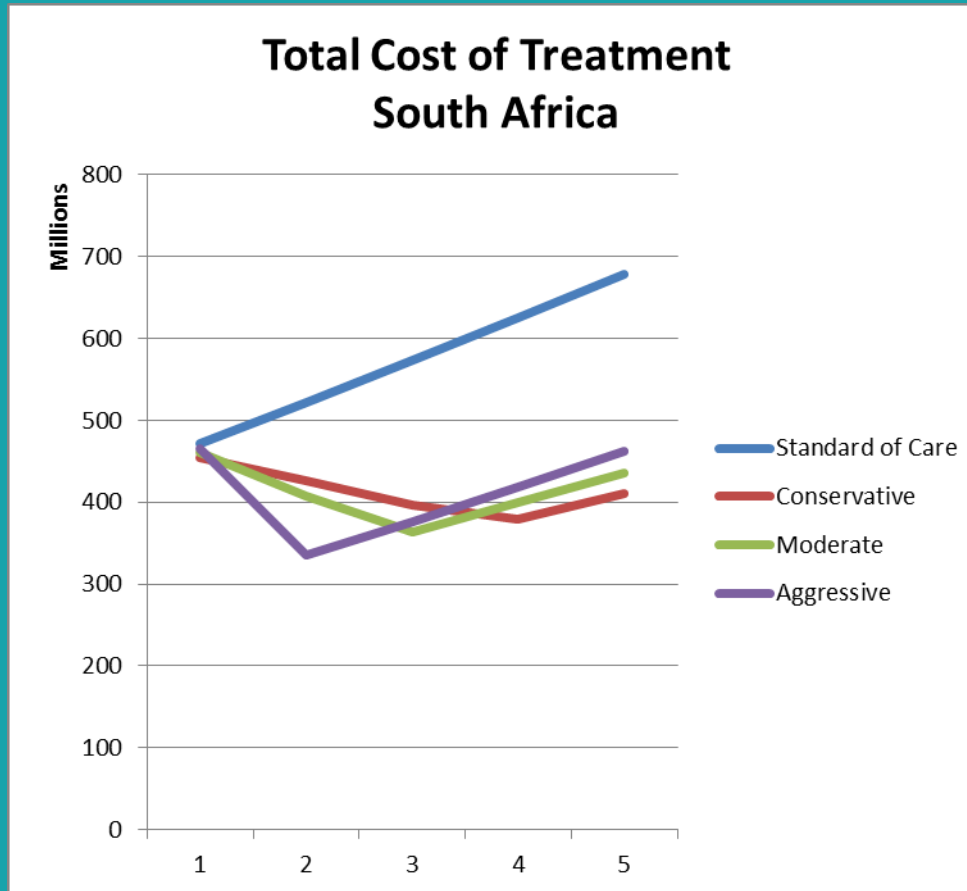


So, lifetime treatment means...

- Less and less tolerance for “nuisance” side effects
- Far less focus on the initiation period, sickness
- Interest in contribution of ARVs & HIV to other non-communicable disease risk factors
- Focus on costs – especially of drugs
- Focus on longer-acting injectables, implantables
- Interest in “cure”
- Unacceptable to have “lesser” drugs in lower-income countries – complex!
- Harmonisation between paedics and adults



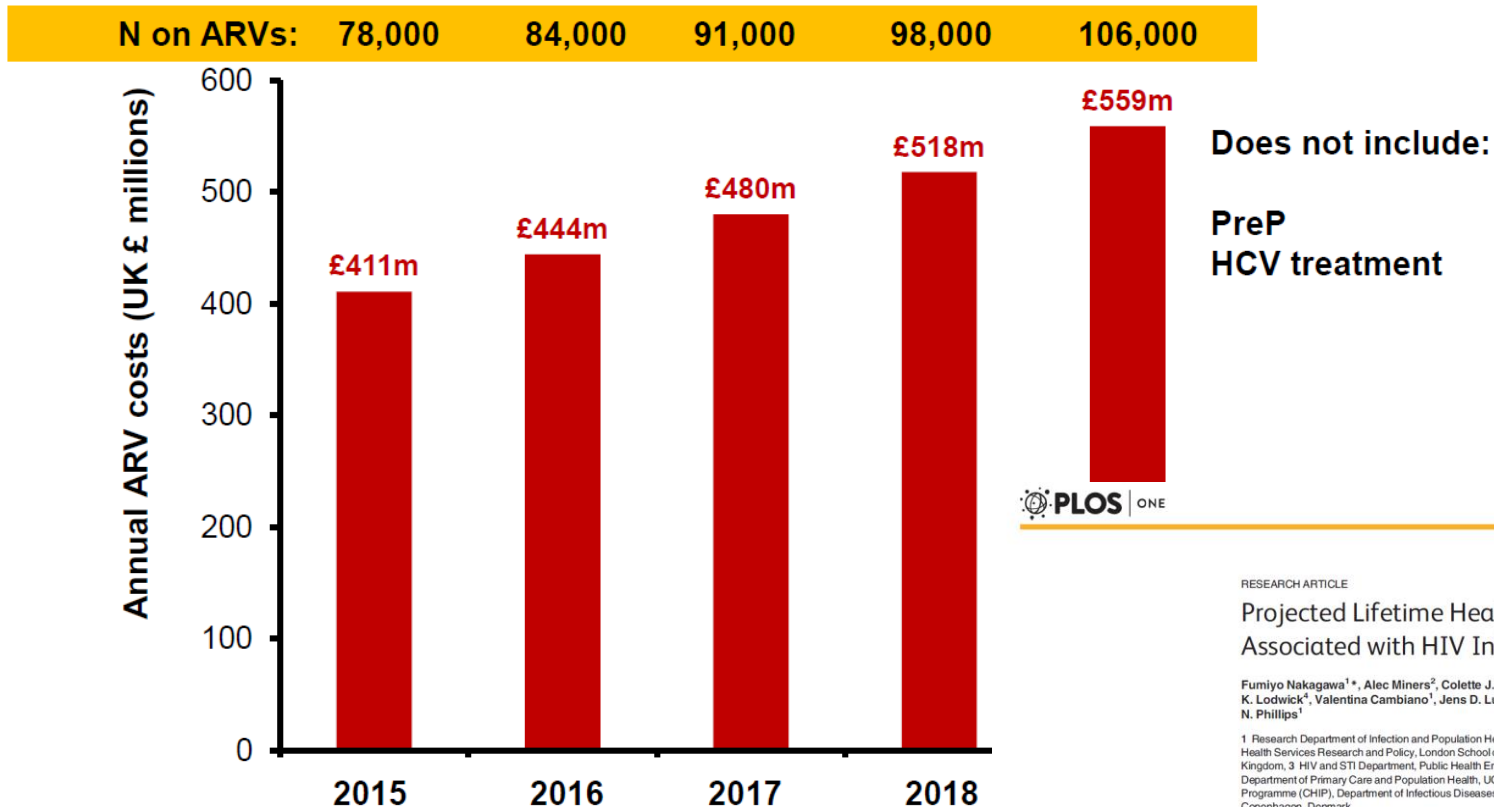
SA cost....



In press, SAMJ

Rich countries too

Projected UK ARV costs, if branded drugs used (8% growth/year)



PLOS ONE

RESEARCH ARTICLE

Projected Lifetime Healthcare Costs Associated with HIV Infection

Fumiyo Nakagawa^{1*}, Alec Miners², Colette J. Smith¹, Ruth Simmons², Rebecca K. Lodwick⁴, Valentina Cambiano¹, Jens D. Lundgren⁵, Valerie Delpech², Andrew N. Phillips¹

¹ Research Department of Infection and Population Health, UCL, London, United Kingdom, ² Department of Health Services Research and Policy, London School of Hygiene & Tropical Medicine, London, United Kingdom, ³ HIV and STI Department, Public Health England, London, United Kingdom, ⁴ Research Department of Primary Care and Population Health, UCL, London, United Kingdom, ⁵ Copenhagen HIV Programme (CHIP), Department of Infectious Diseases (8632), Rigshospitalet, University of Copenhagen, Copenhagen, Denmark

* f.nakagawa@ucl.ac.uk

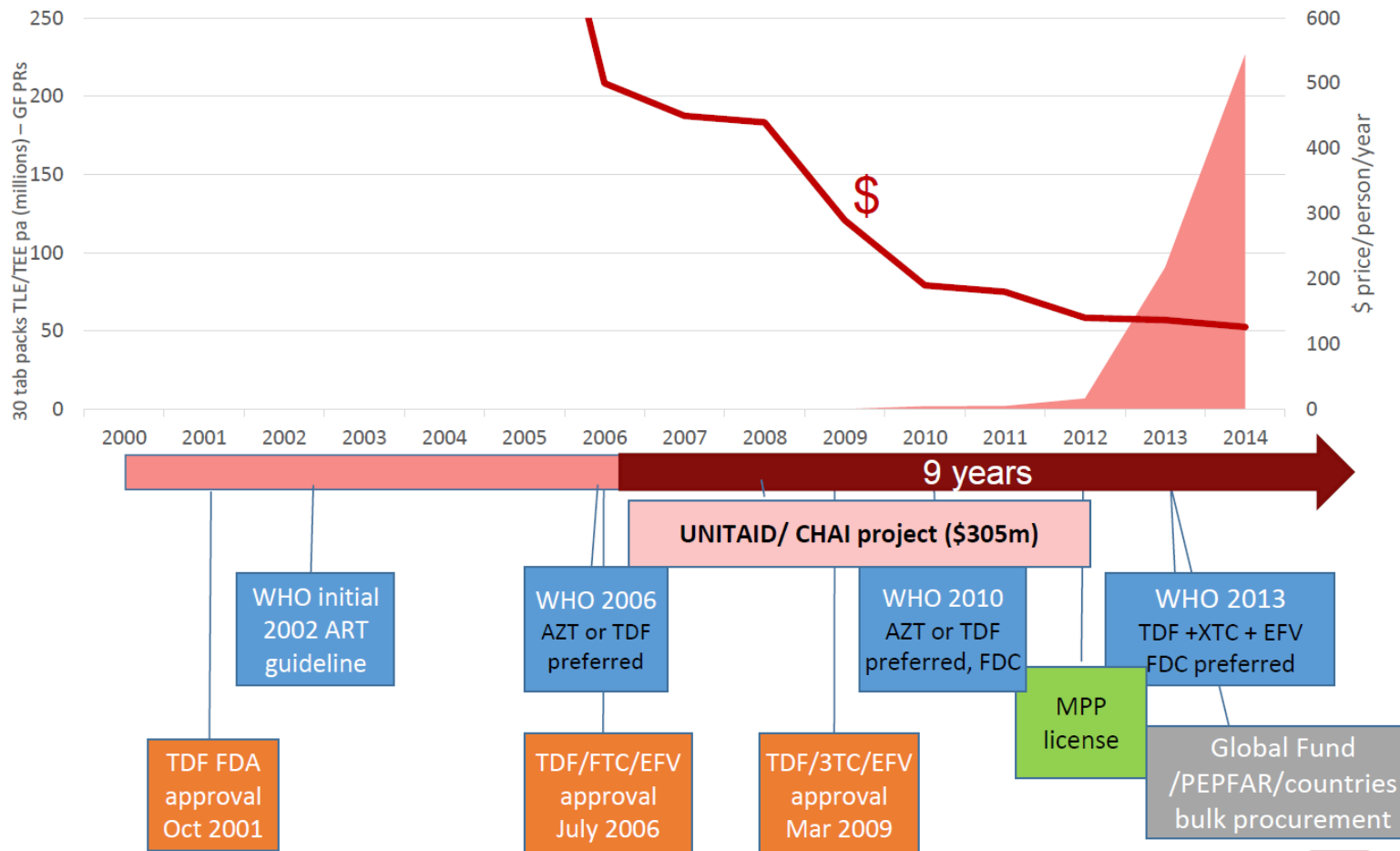


Abstract

Thanks: Andrew Hill

We need things to go faster

Approvals, licenses and uptake: TDF-first-line ART case study



Thanks Joe Eron

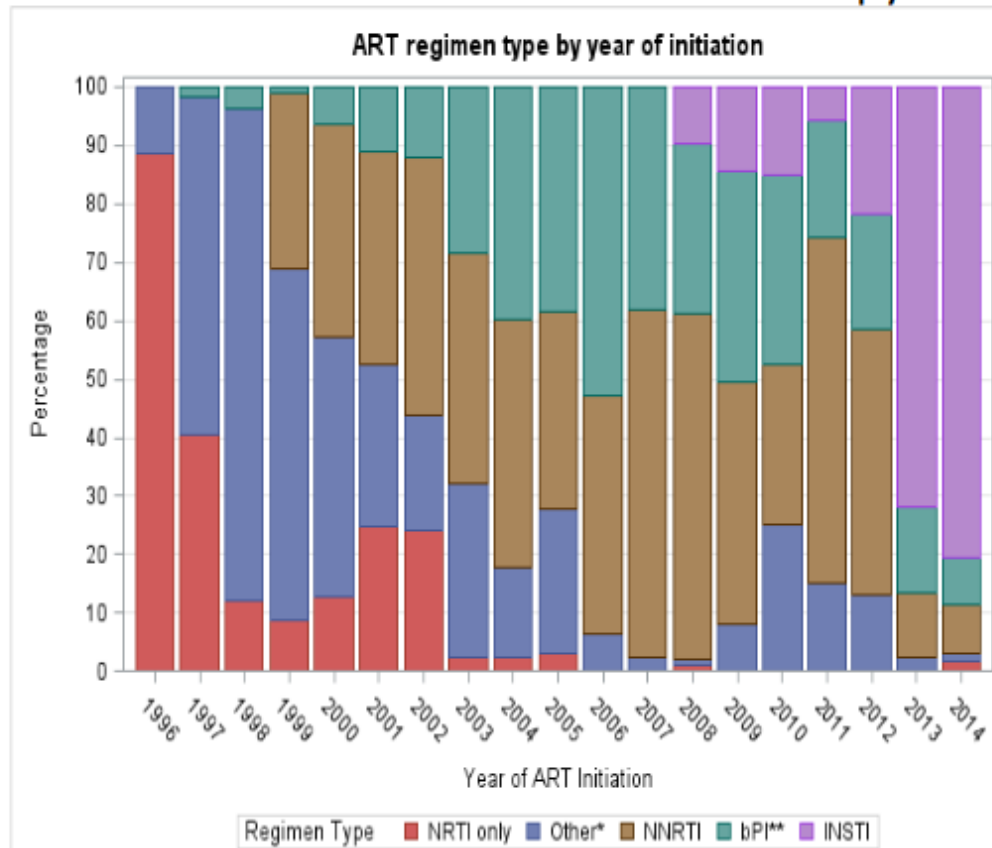
“The integrase inhibitor era”

UCHCC: UNC
CFAR HIV
Clinical Cohort

Shift To Integrase Inhibitor-based Therapy



Initial Antiretroviral Therapy



1,773 patients
initiating ART
between 1996
and 2014 in the
UCHCC,
follow-up
through 2015

bPI = LPV/r, DRV/r or ATV/r therapy

Other = includes unboosted PI and other bPI combinations

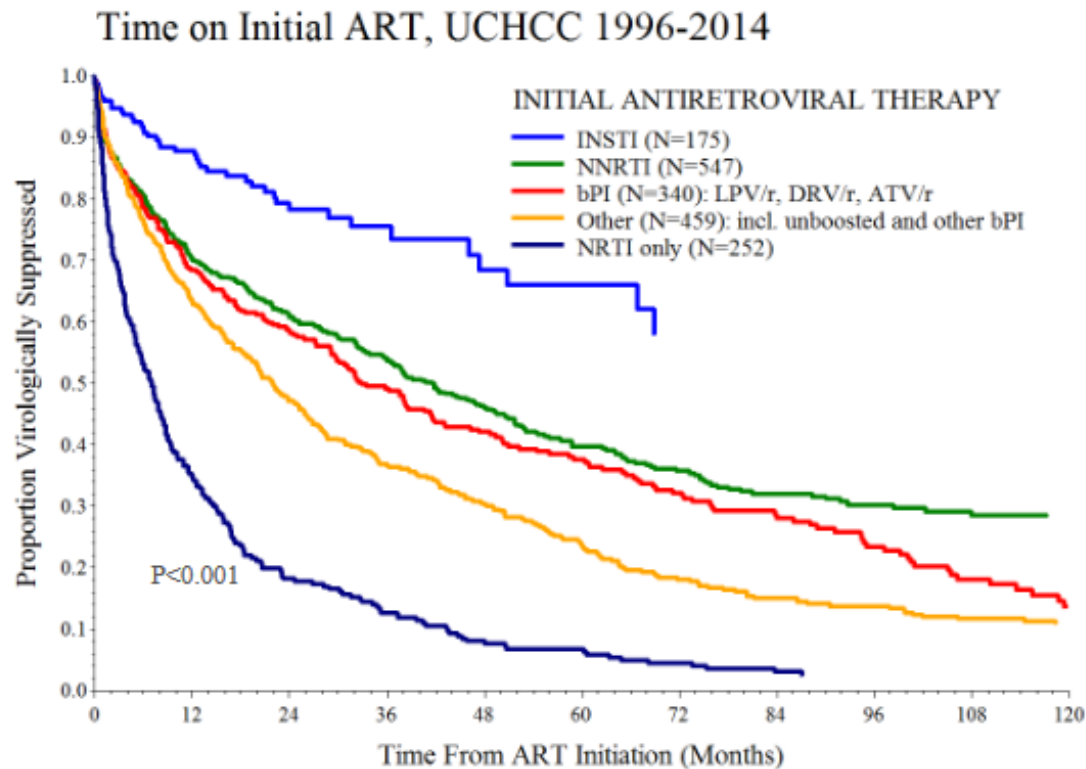
Courtesy of Thibaut Davy and Sonia Napravnik

And they do well in the real (US) world!

UCHCC: UNC CFAR HIV Clinical Cohort



Persistence of Initial ART



In CNICS cohort integrase inhibitor use was strongly associated with HIV RNA suppression

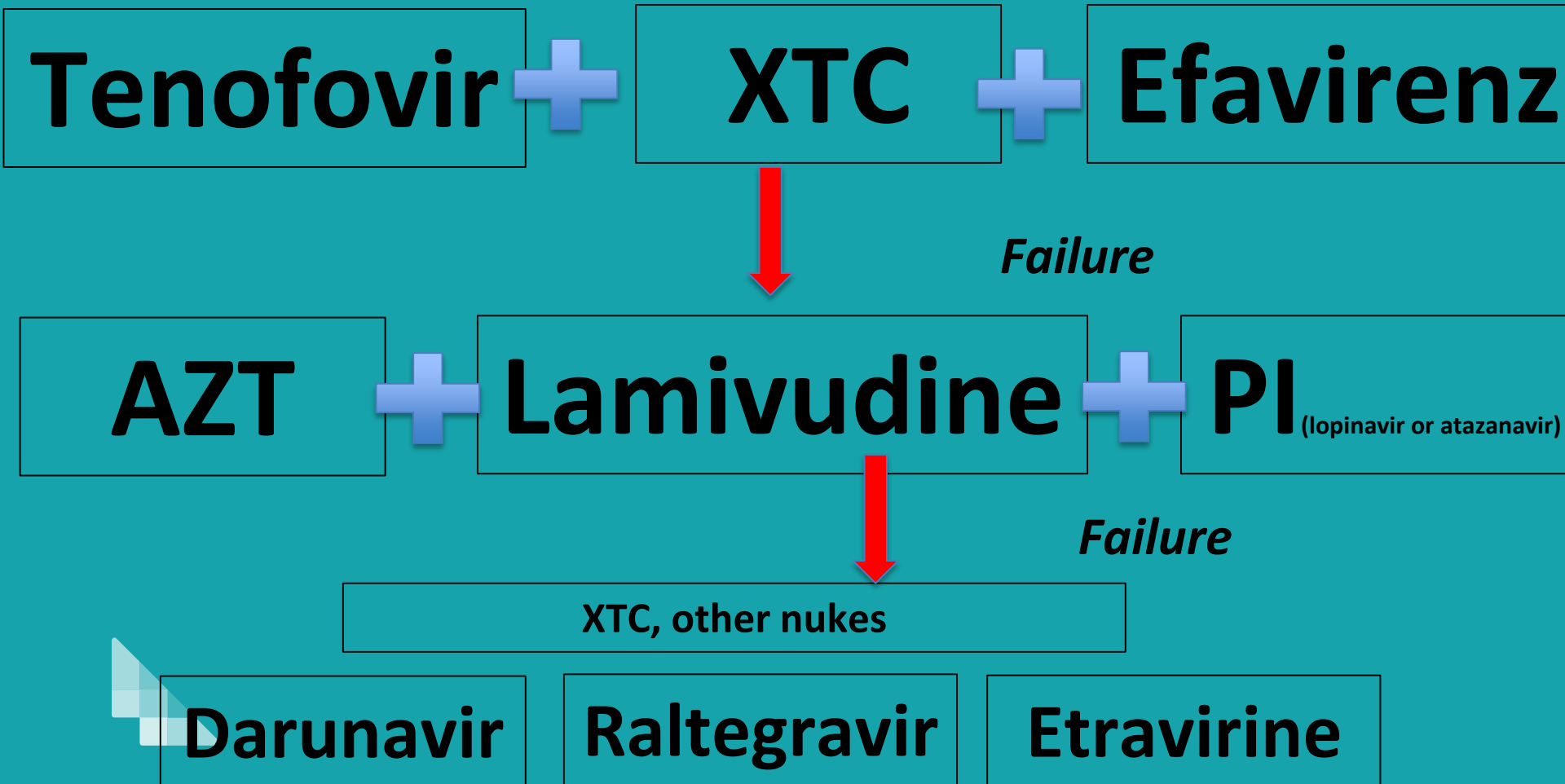
Thanks Joe

But.... Not in WHO guidelines

- Or SAHCS
- And not used anywhere (Botswana moving to dolutegravir)



WHO regimens pre-2015



1st line....



Cost driver



**Side effect (and
size) driver,
resistance weak
link**



1st line....



Cost driver



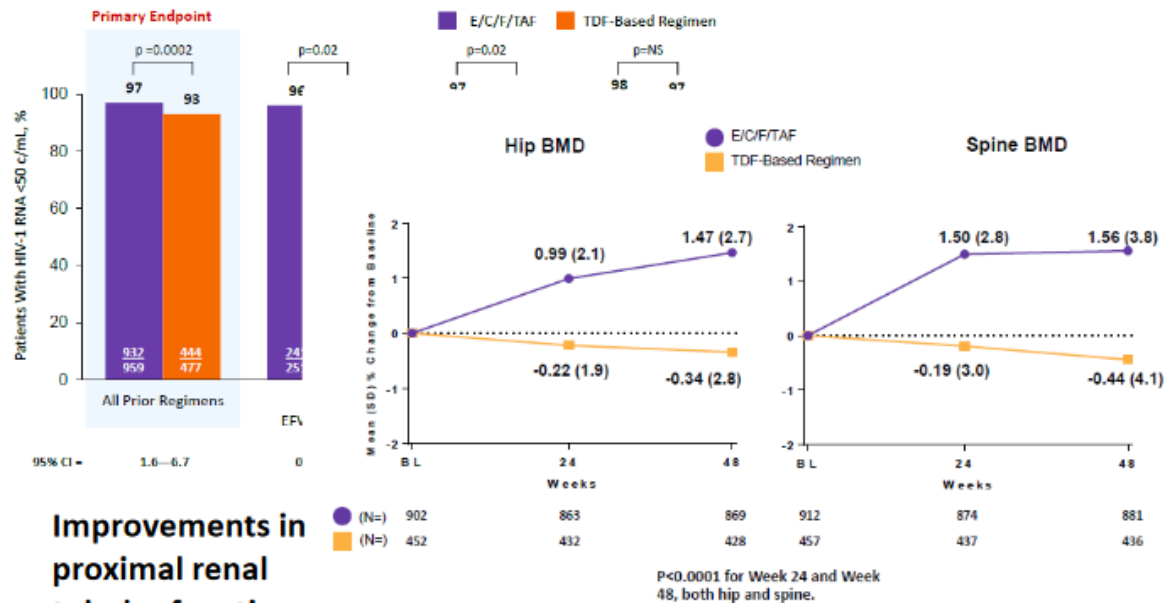
**400mg? Other
NNRTI?**



TAF vs tenofovir

ART to Decrease Long-term Toxicity

Switch from Tenofovir DF to Tenofovir alafenamide-containing therapy in patients with suppressed plasma HIV RNA levels.



1st line....



Safer, cheaper



**Safer, ?2nd line
need, cheaper**

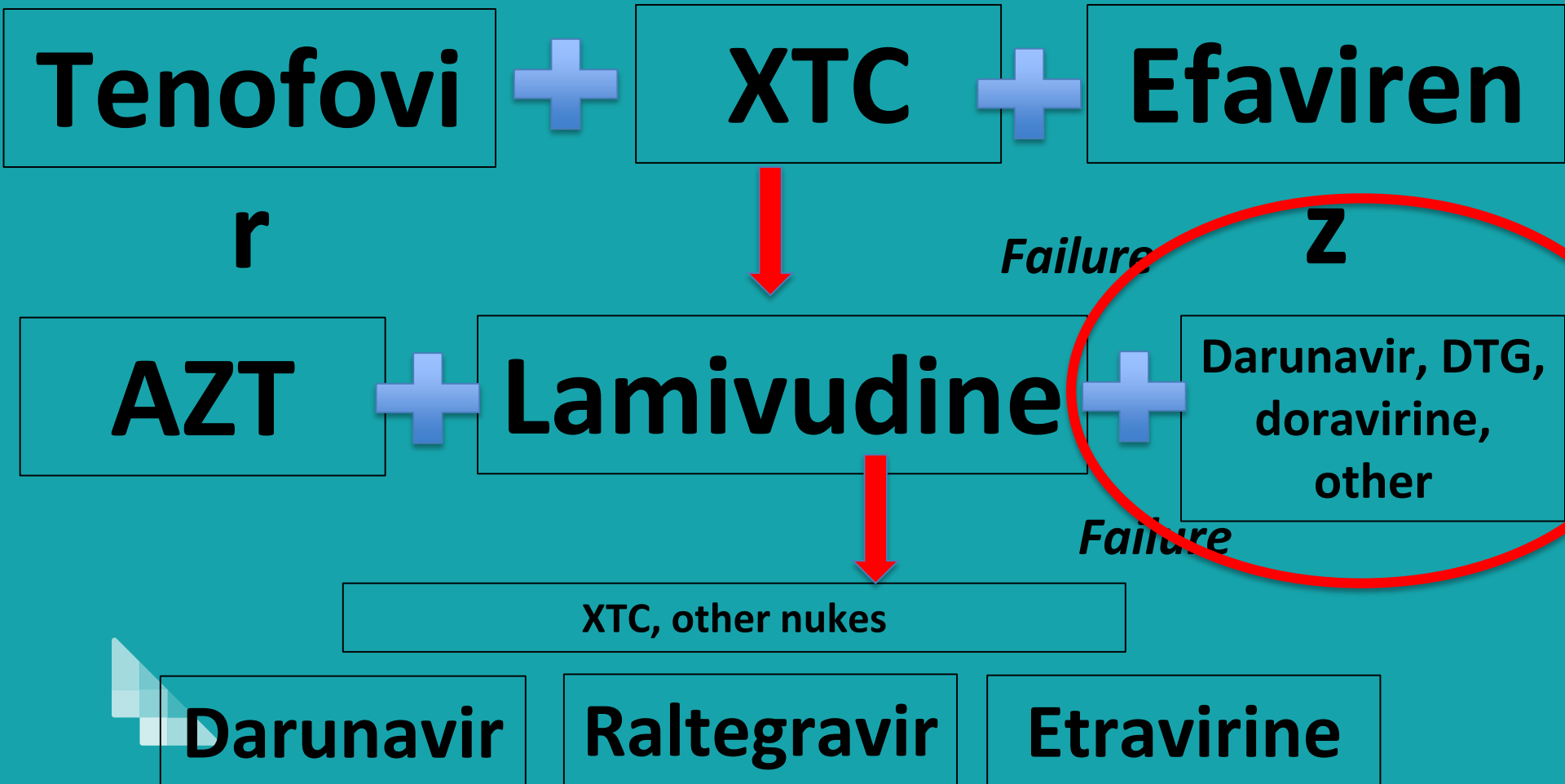


Why aren't these drugs available?

- Many not registered
- Limited TB/pregnancy data (almost all new drugs)
- Cost: abacavir, all integrase inhibitors – hope for dolutegravir; co-formulations: Not available



WHO regimens pre-2015





Should we start treatment on the
day of diagnosis?


Francois Venter

Thanks Sydney Rosen and
her team

 OPEN ACCESS  PEER-REVIEWED

RESEARCH ARTICLE

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

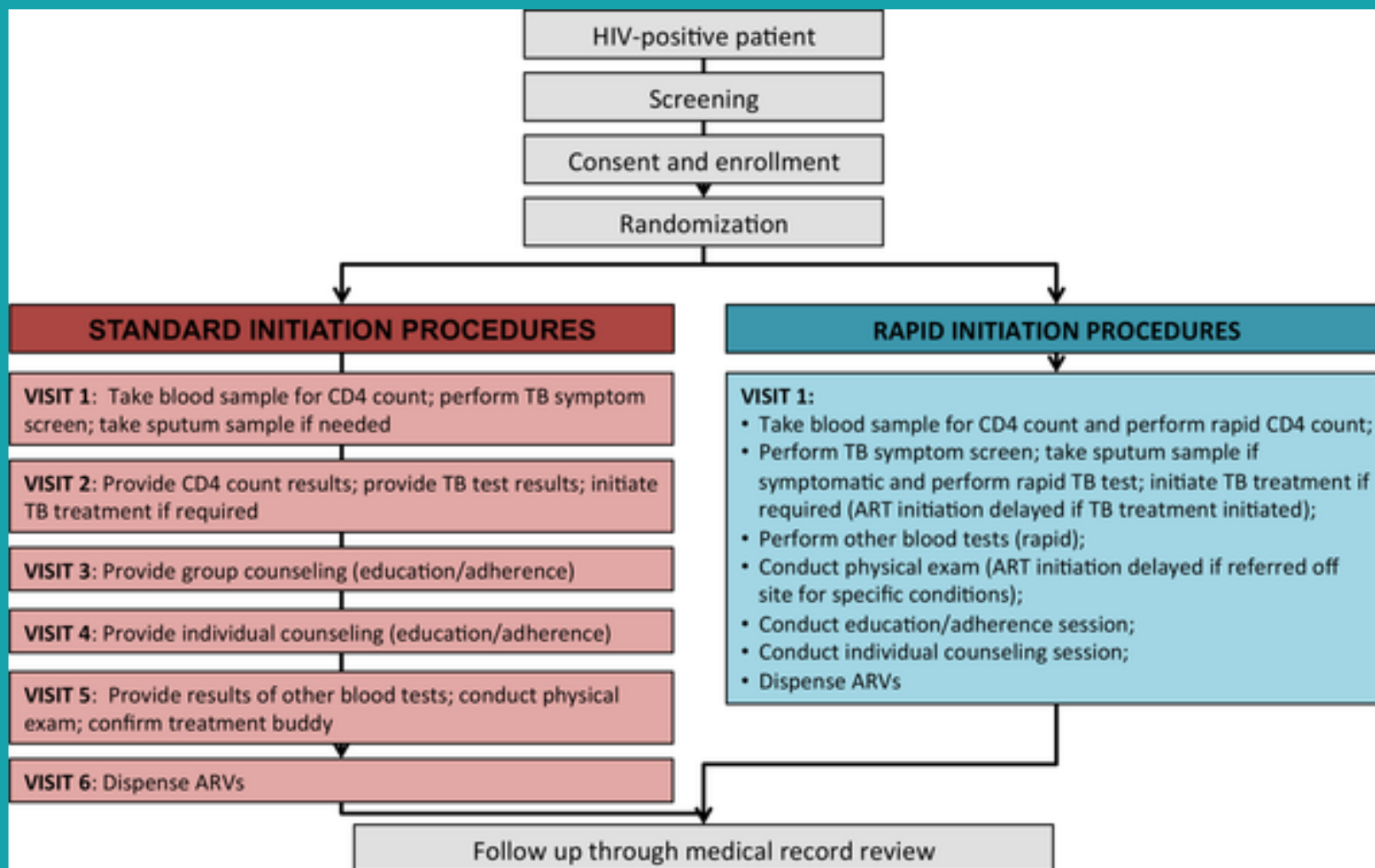
Sydney Rosen , Mhairi Maskew, Matthew P. Fox, Cynthia Nyoni, Constance Mongwenyana, Given Malete, Ian Sanne, Dorah Bokaba, Celeste Sauls, Julia Rohr, Lawrence Long

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

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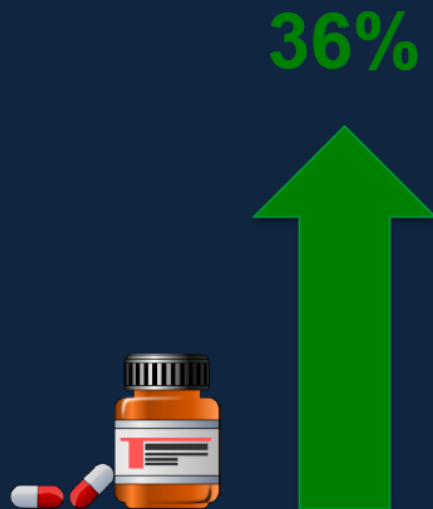
Fig 1. Standard initiation of treatment and rapid initiation procedures and visit schedule.



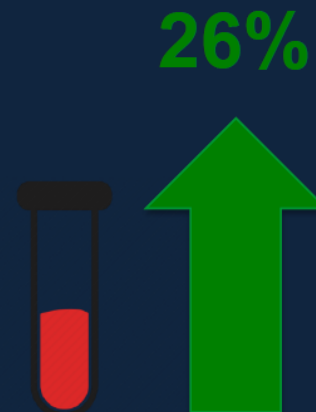
Rosen S, Maskew M, Fox MP, Nyoni C, Mongwenyana C, et al. (2016) Initiating Antiretroviral Therapy for HIV at a Patient's First Clinic Visit: The RapIT Randomized Controlled Trial. *PLoS Med* 13(5): e1002015. doi:10.1371/journal.pmed.1002015
<http://journals.plos.org/plosmedicine/article?id=info:doi/10.1371/journal.pmed.1002015>

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

Effect Modification by Site and by Age and Sex

Initiated \leq 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 \geq 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 \geq 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

Advocate:

- Good surveillance (and interpretation!)
- Single patient identifiers
- Better HIV testing and linkage
- Expanded VL monitoring
- Evidence-based interventions
- And prepare for the new regimens to be implemented fast



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