



Understanding new HIV prevention interventions



Professor Francois Venter
Ezintsha, University of the Witwatersrand
2020

Sex is now safe

- PrEP/PEP: Almost total protection
- As treatment: Undetectable = untransmissible
- Partners study sub-study of men¹:
 - Who-have-sex-with-men (MSM)
 - Almost 77 000 unprotected anal sex acts – no transmission
- Intermittent PrEP for gay men
 - “On-demand” – 2 tabs 2–24 hours before sex, 1 tab at 24, then 48 hours
 - 1500 (mainly MSM) – no transmissions
- SA sex worker operational PrEP programme – no transmissions on PrEP



Test and treat seems to be bearing fruit (2018/9)...

- SA: 44% reduction – in only 5 years (2012–2017)!
- Similar in Swaziland, Zimbabwe, Botswana
- And rich countries (PrEP)

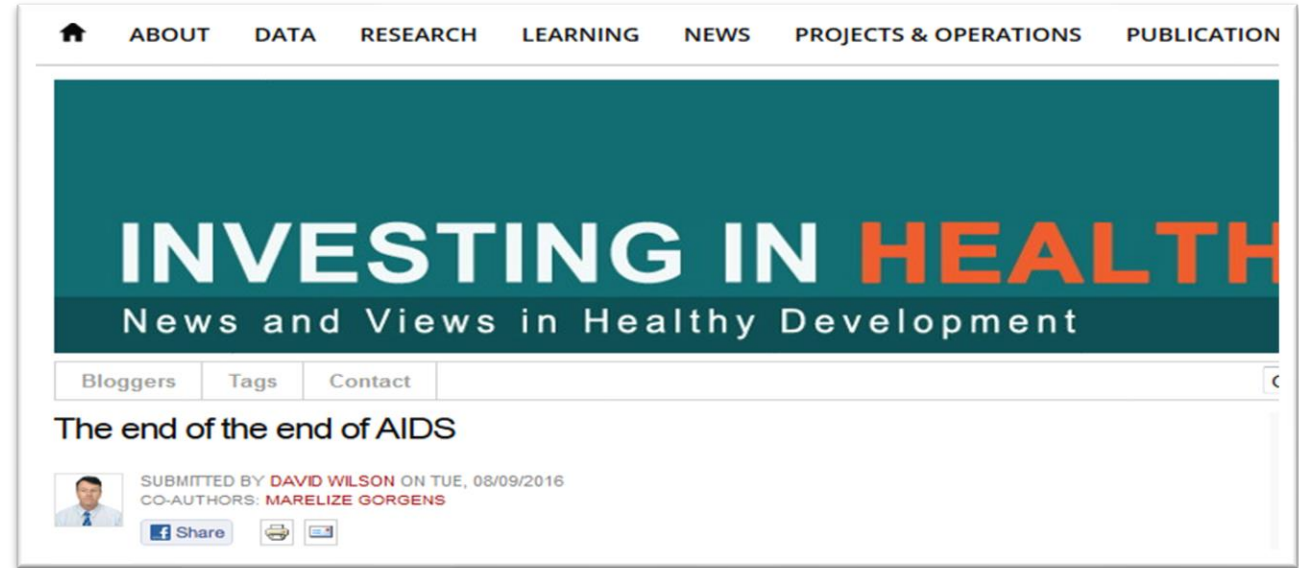


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ACHIEVING THE 90-90-90 TARGET

Sweden the first country to achieve UNAIDS/WHO 90-90-90 target

Michael Carter
Published: 14 September 2016



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The end of the end of AIDS

SUBMITTED BY DAVID WILSON ON TUE, 08/09/2016
CO-AUTHORS: MARELIZE GORGENS

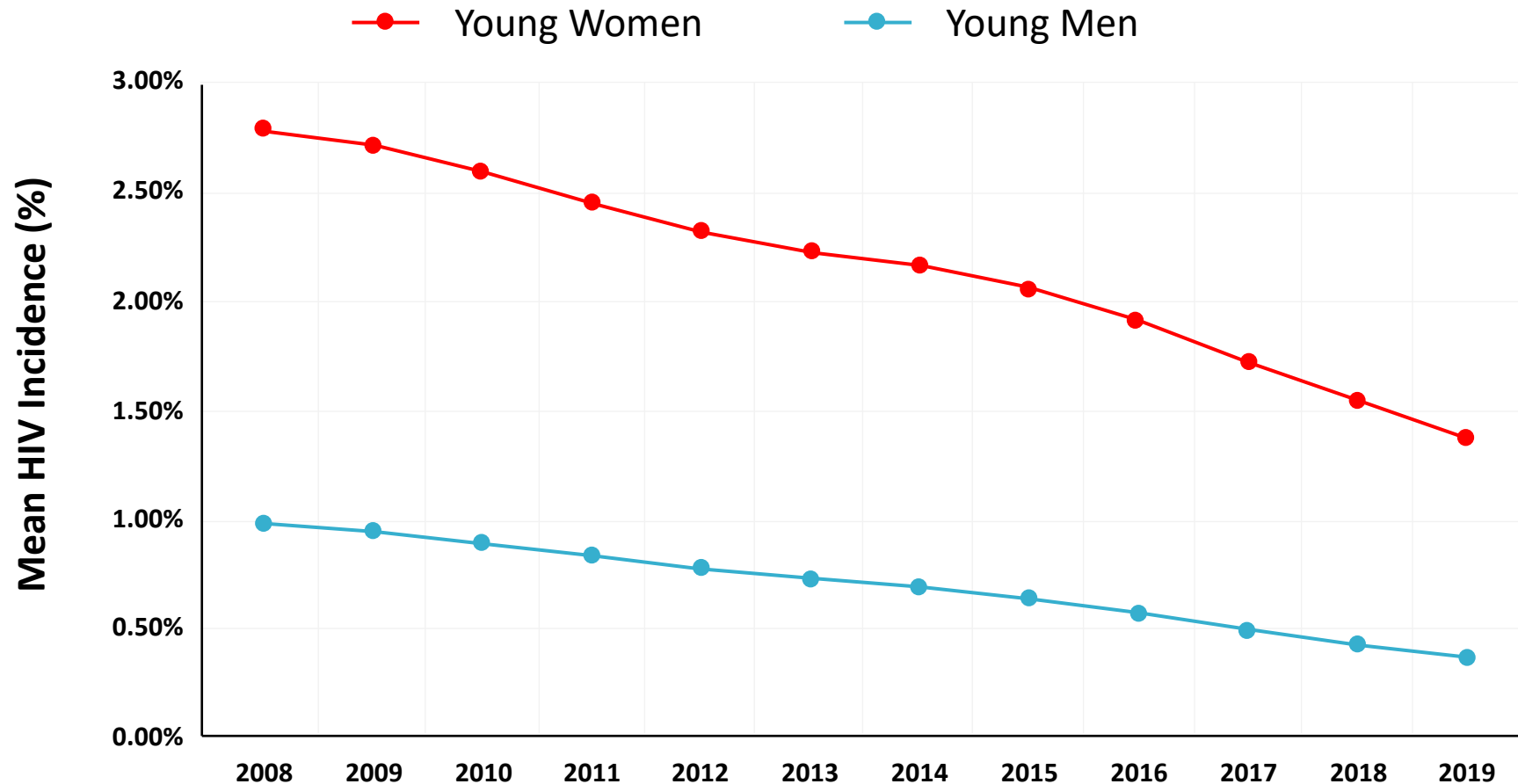
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ART exposure, South Africa, 2017

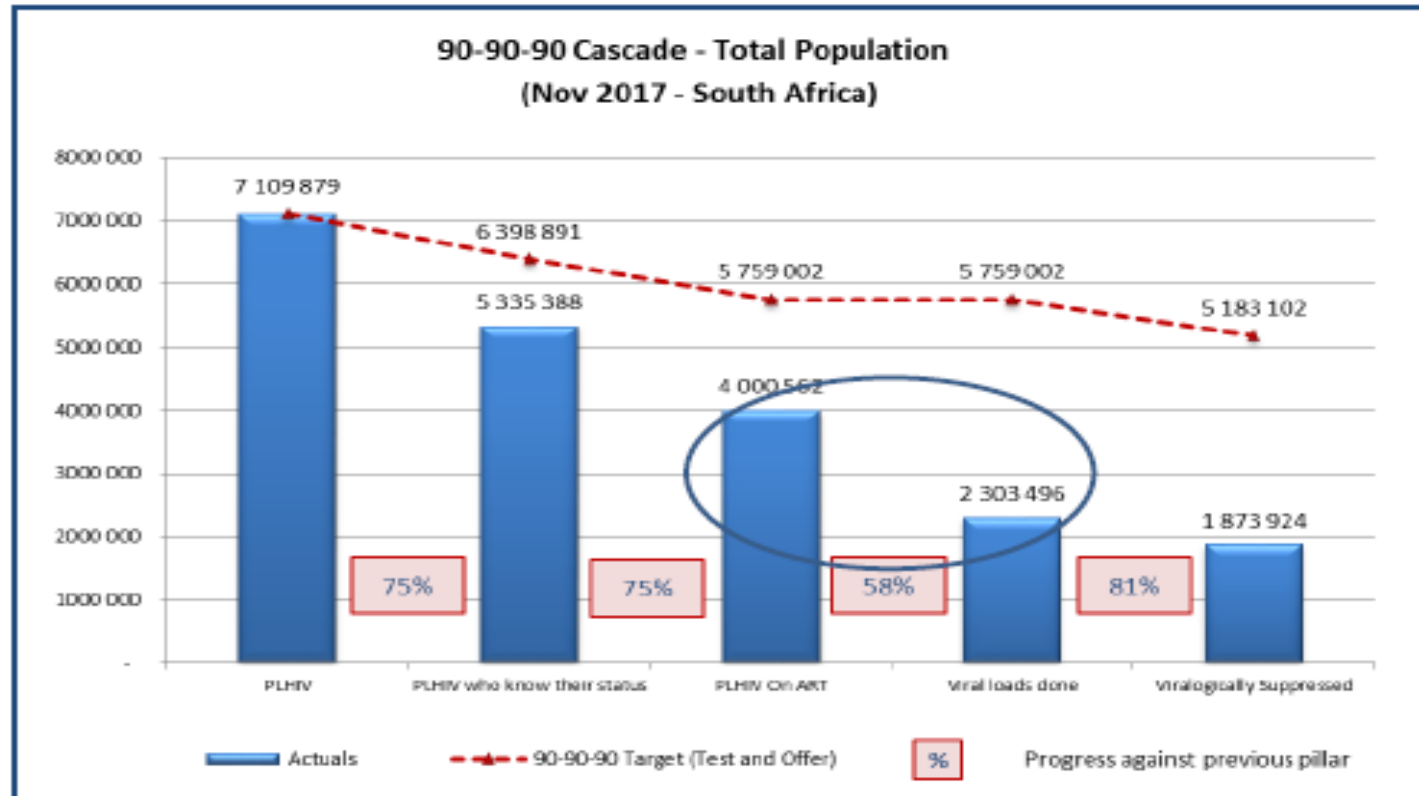
Variable	Estimated number of people on ART (n)	Proportion of people living with HIV on ART (%) 95% CI
National	4,401,872	62.3 (59.2-65.2)
Female	2,998,170	65.5 (62.4-68.4)
Male	1,403,702	56.3 (51.0-61.5)



HIV incidence compared between young men and young women (aged 15–24)



South African progress to 90-90-90 (public sector)



1st 90 (90%) 75%

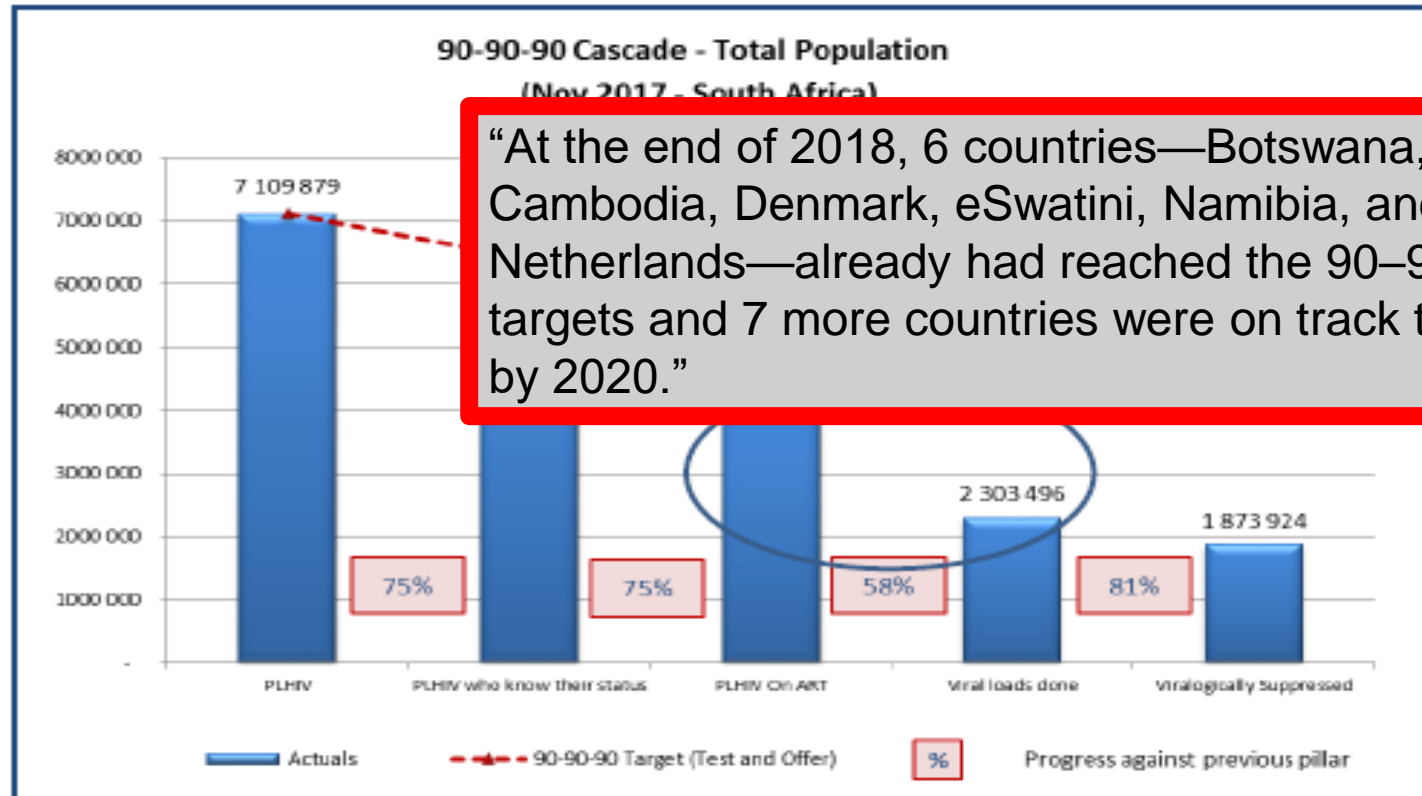
2nd 90 (81%) 56%

3rd 90 (73%)* 26%

* Suppressed and recorded in HIS

Including private sector:
60% PLHIV on ART

South African progress to 90-90-90 (public sector)



“At the end of 2018, 6 countries—Botswana, Cambodia, Denmark, eSwatini, Namibia, and the Netherlands—already had reached the 90–90–90 targets and 7 more countries were on track to do so by 2020.”

(90%) **75%**
 (81%) **56%**
 3rd 90 (73%)* **26%**

* Suppressed and recorded in HIS

Including private sector:
 60% PLHIV on ART

Five African Countries Approach Control of Their HIV Epidemics as U.S. Government Launches Bold Strategy to Accelerate Progress

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September 19, 2017

PEPFAR

U.S. President's Emergency Plan for AIDS Relief

Strategy for Accelerating HIV/AIDS Epidemic Control (2017-2020)



The New York Times



Opinion

In Africa, a Glimpse of Hope for Beating H.I.V.



SEPTEMBER 19, 2017

What do we know?

- Epidemic is raging in 16–32 year olds; after that transmission dynamic less important
- Men and young people missing
- Antiretrovirals, when taken, stop the epidemic in its tracks – treatment and PrEP/PEP

Just imagine....

- We focus on 18–32 year-olds with laser-like focus
- Test, link to care (? incentives), make taking treatment seamless
- PrEP wherever possible, expand PEP as an entry point

So plenty to do in HIV prevention!

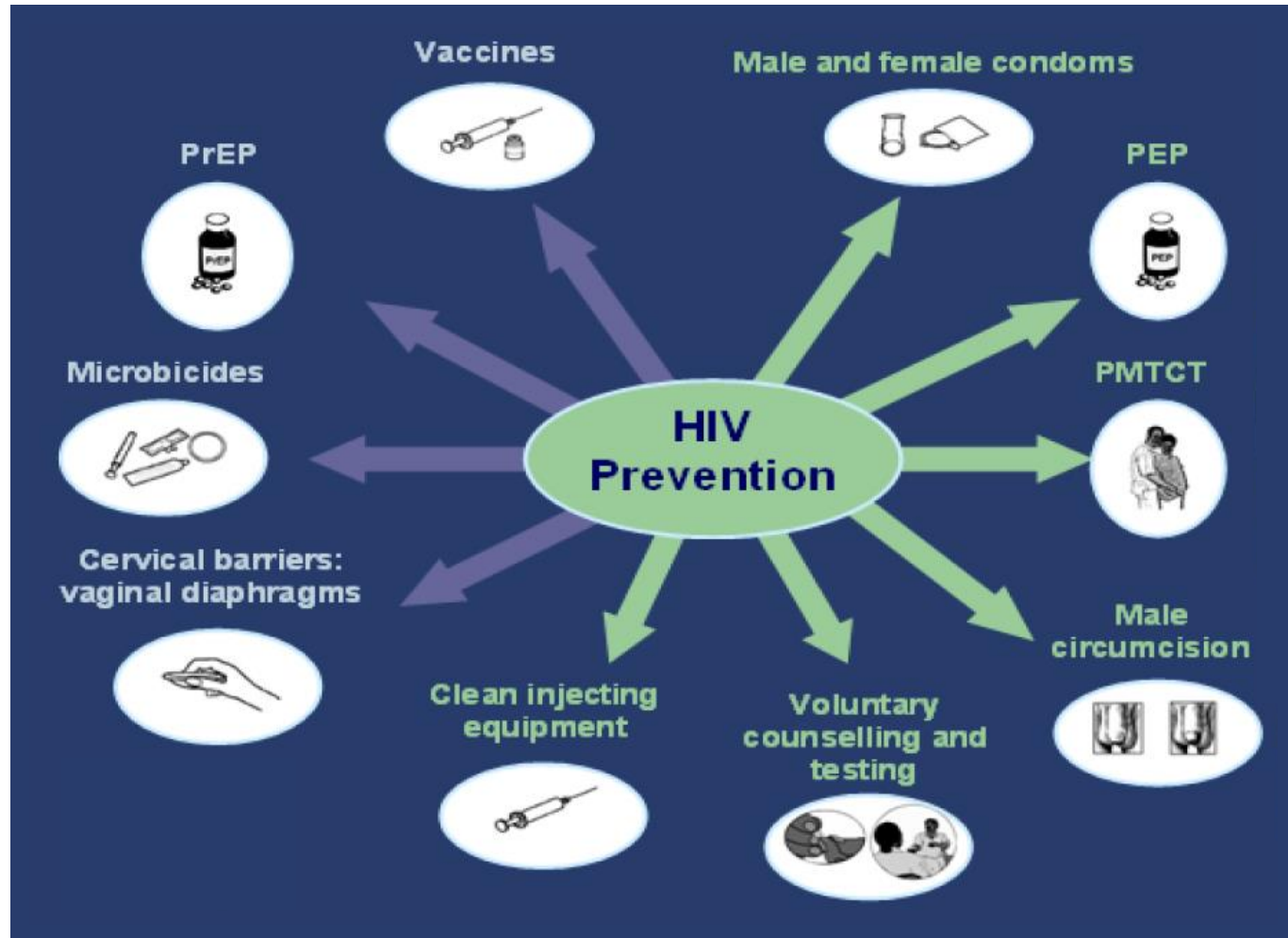
- What is available?

What works for prevention?

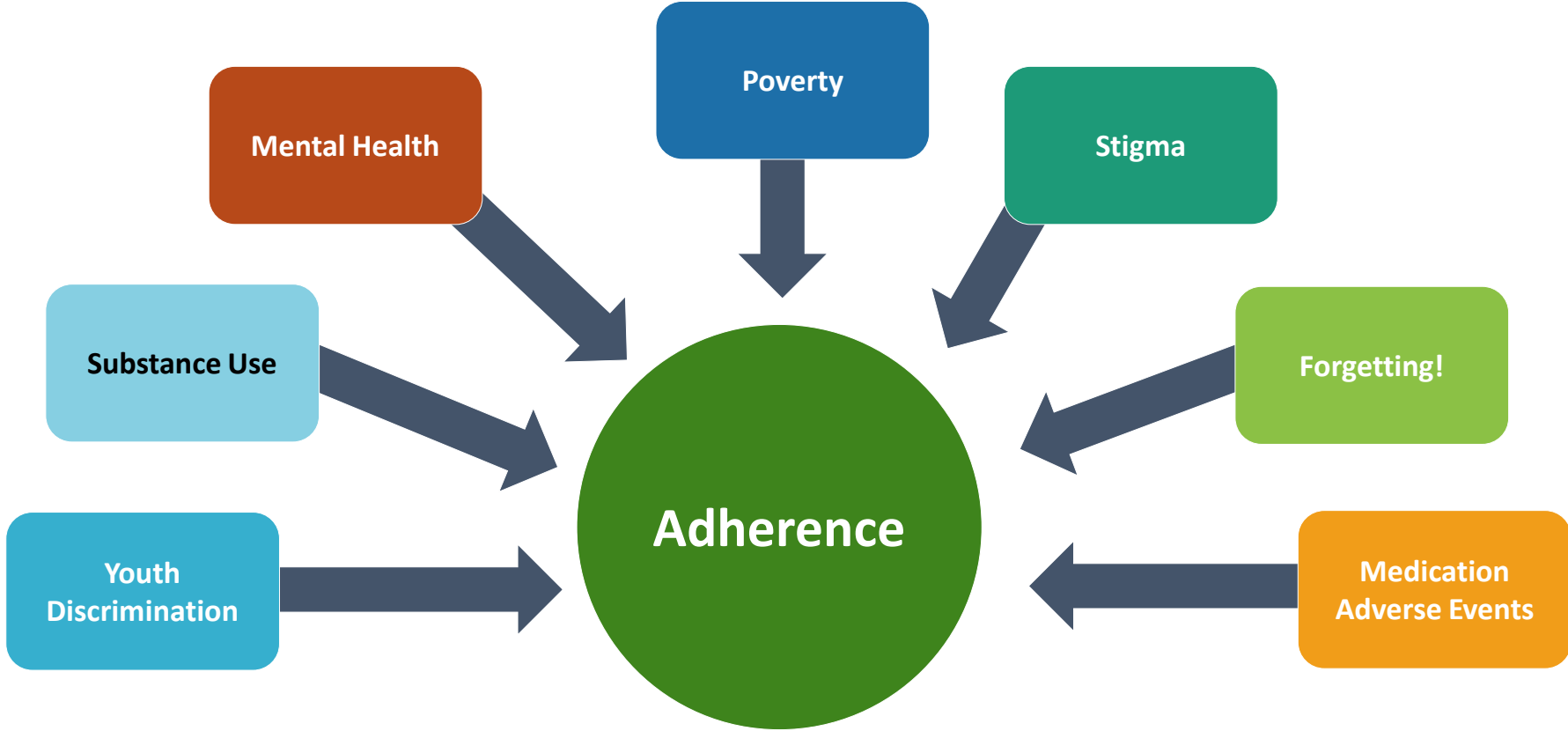
- Treatment
- Mother-to-child prevention
- Circumcision
- Needle exchange
- Post-exposure prophylaxis (PEP)
- Pre-exposure prophylaxis (PrEP)
- Programmes focusing on risk groups
- Condoms



Biomedical HIV prevention research



Assessing barriers to care and treatment



The evolving HIV treatment paradigm



HIV-1 discovered

1983



AZT monotherapy

1987

AZT/3TC



Triple-Drug Therapy

1995

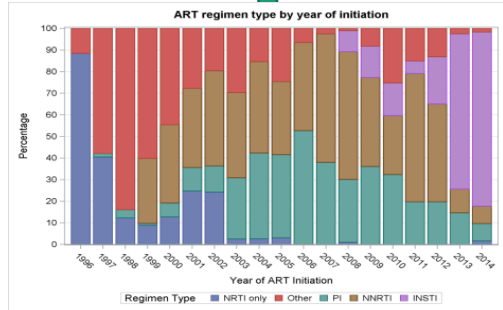
1996



Single-Tablet Regimens

2006

The Integrase Era



2012–2013

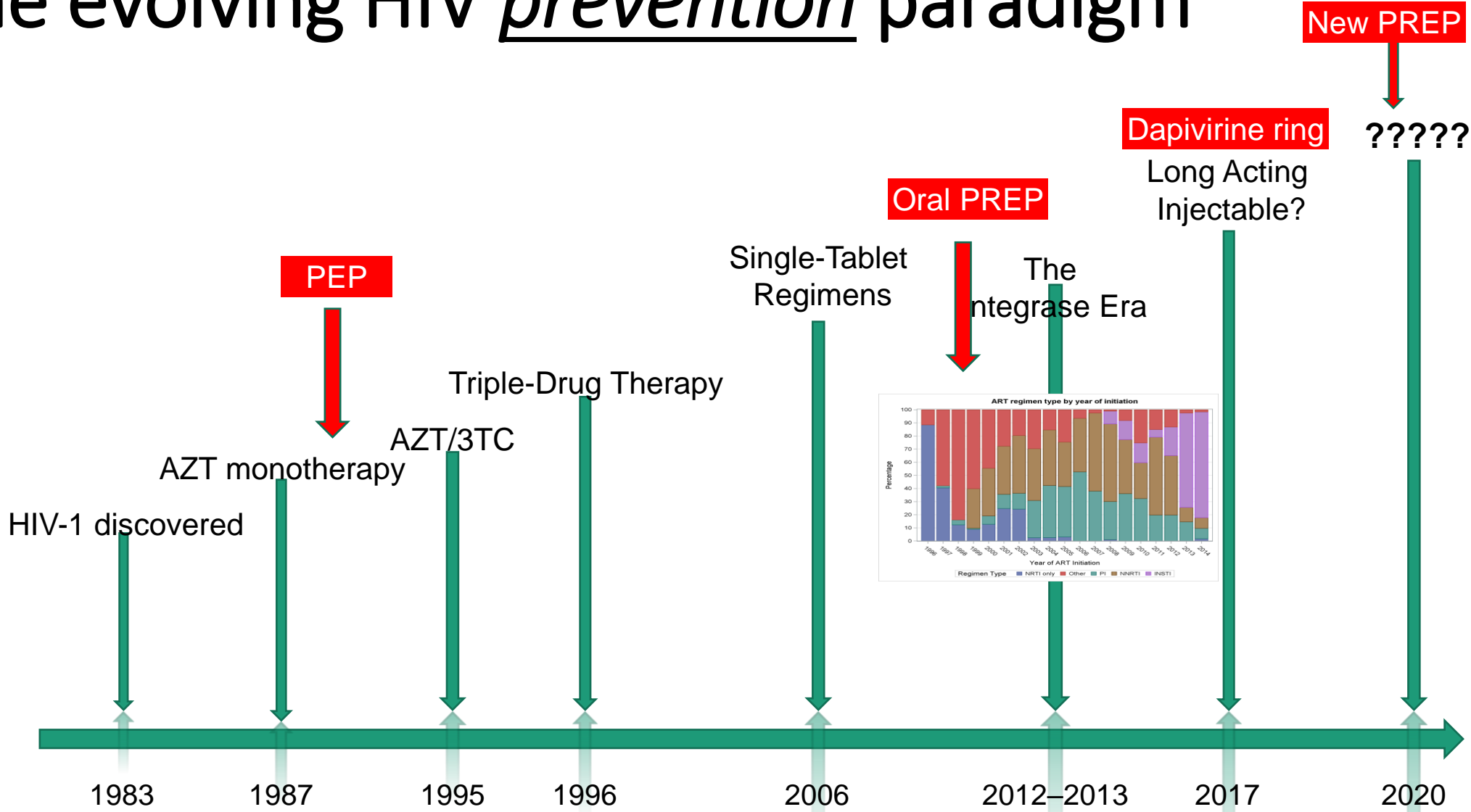
2017

?????

Long Acting Injectable?

2020

The evolving HIV *prevention* paradigm



Current offerings

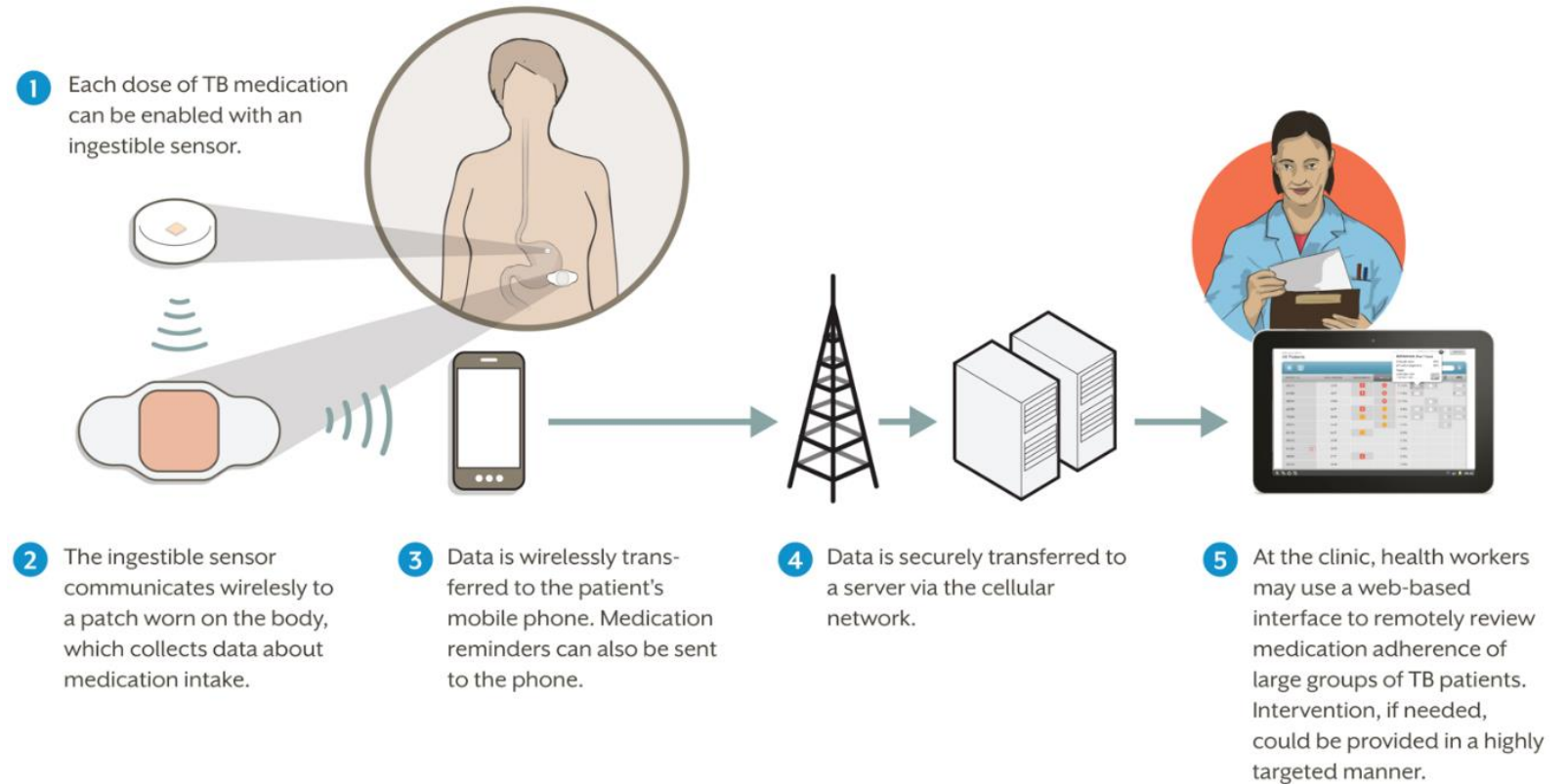
- Oral PEP: largely integrase-based with TDF/TAF+3TC
(modified if resistance in source patient suspected, or renal issues)
- Oral PrEP: TDF/FTC (or 3TC) since 2010
 - On-demand PrEP evidence base growing

Monitoring strategies to improve retention in care

Distance monitoring

- Text messaging services to connect patients with providers^{1,2}
- Wireless drug monitors (smart pill boxes)³
- Digital pills⁴
- Home-based HIV-1 RNA via mailed dried blood spot⁵

Example of Wirelessly Observed Therapy⁶



Overview of current and future prevention strategies

FDA Approved, In Use*

Daily oral FTC/TDF PrEP

Daily oral FTC/TAF PrEP

*<10% of those who could benefit from PrEP
in US are receiving it¹

Late Phase Development

Topical/local approaches
(vaginal ring)

Long-acting injectable formulations

Emerging, Available

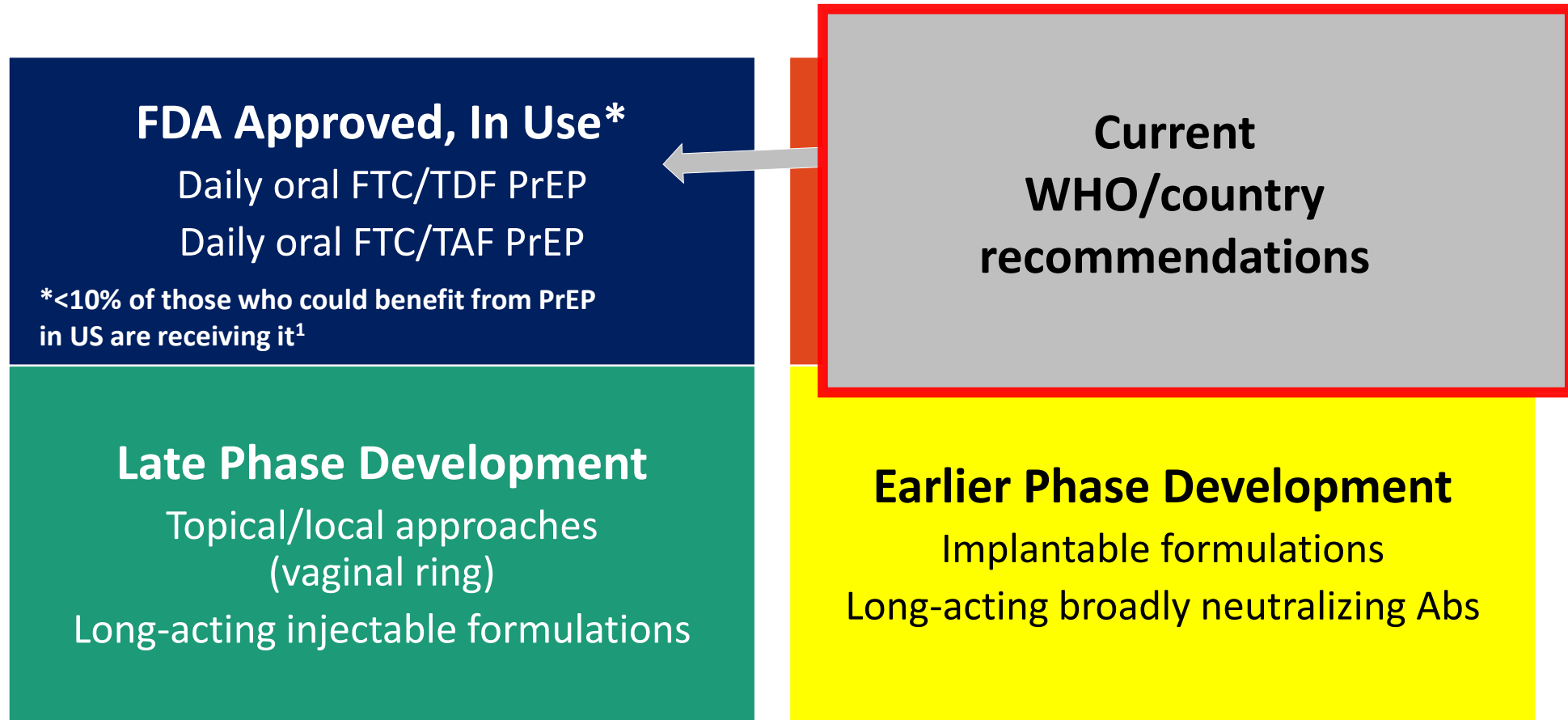
On-demand oral FTC/TDF PrEP

Earlier Phase Development

Implantable formulations

Long-acting broadly neutralizing Abs

Overview of current and future prevention strategies



Oral PrEP with FTC/TDF and FTC/TAF: Indications and recommended dosing

- Oral, once-daily FTC/TDF and FTC/TAF currently FDA approved for at-risk adults and adolescents to reduce the risk of sexually acquired HIV transmission^{1,2}
 - FTC/TAF not indicated to prevent HIV transmission from receptive vaginal sex²

CDC* ³
<ul style="list-style-type: none">▪ FTC/TDF recommended for daily use only▪ Not recommended as coitally timed or other noncontinuous use

IAS-USA* ⁴
<ul style="list-style-type: none">▪ FTC/TDF recommended for daily use▪ Optional recommendation for on-demand FTC/TDF use only for MSM with infrequent sex

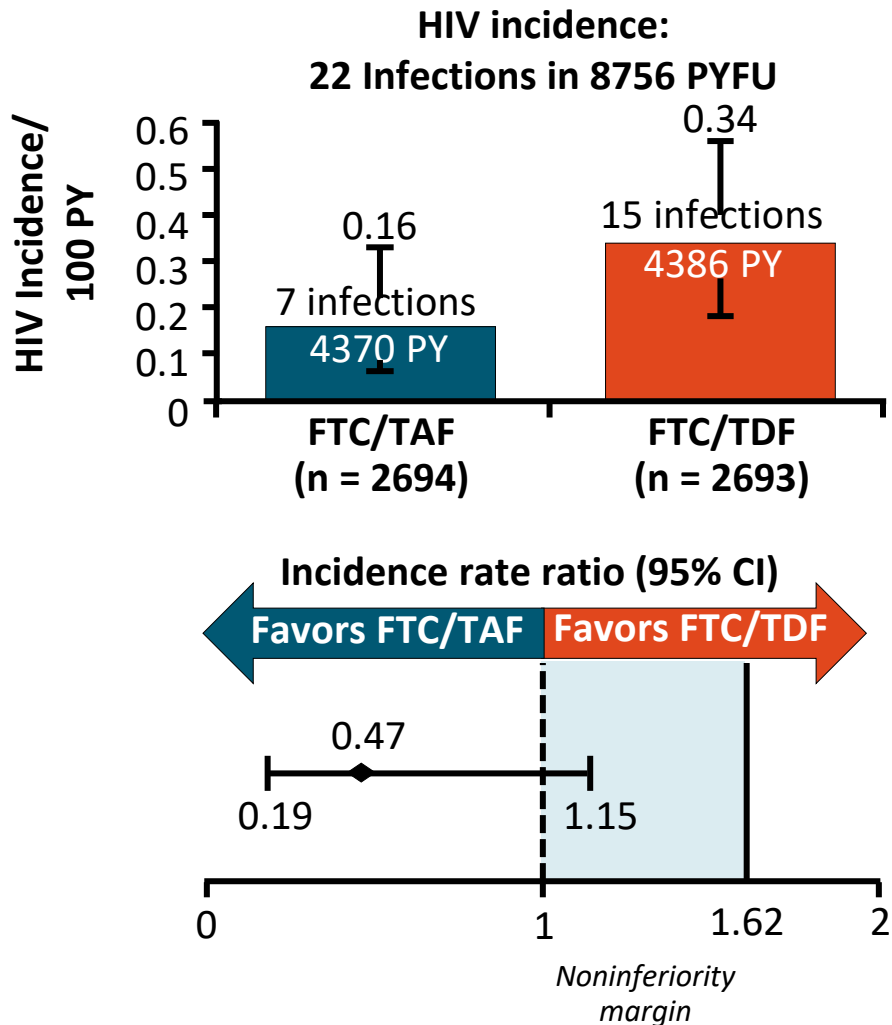
WHO* ⁵
<ul style="list-style-type: none">▪ FTC/TDF recommended for daily use▪ Optional recommendation for on-demand FTC/TDF use only for MSM with infrequent and predictable sex

EACS* ⁶
<ul style="list-style-type: none">▪ FTC/TDF recommended for daily use▪ Daily FTC/TAF shown to be noninferior to daily FTC/TDF in MSM and TGW only▪ Optional recommendation for on-demand FTC/TDF use only for MSM

*Guidelines issued before FDA approval of FTC/TAF as PrEP

▪ **On-demand FTC/TDF use is by 2-1-1 dosing: double dose 2-24 hrs before sex, 1 dose 24 hrs after first dose, 1 dose 48 hrs after first dose^[5-7]**

DISCOVER: FTC/TAF non-inferior to FTC/TDF for efficacy



- Primary analysis conducted when 100% completed Week 48, 50% completed Week 96
- Noninferiority of FTC/TAF maintained in sensitivity analysis excluding suspected BL infections
 - IRR: 0.55 (95% CI: 0.20–1.48)

Outcome, n	FTC/TAF	FTC/TDF
Possible causes of HIV infection	(n = 2694)	(n = 2693)
▪ Suspected BL infection	1	4
▪ Low TFV-DP in DBS	5	10
▪ Medium/high TFV-DP in DBS	1	1
Resistance genotype performed	(n = 6)	(n = 13)
▪ FTC	0	4*
▪ TFV	0	0

*All with suspected BL infection

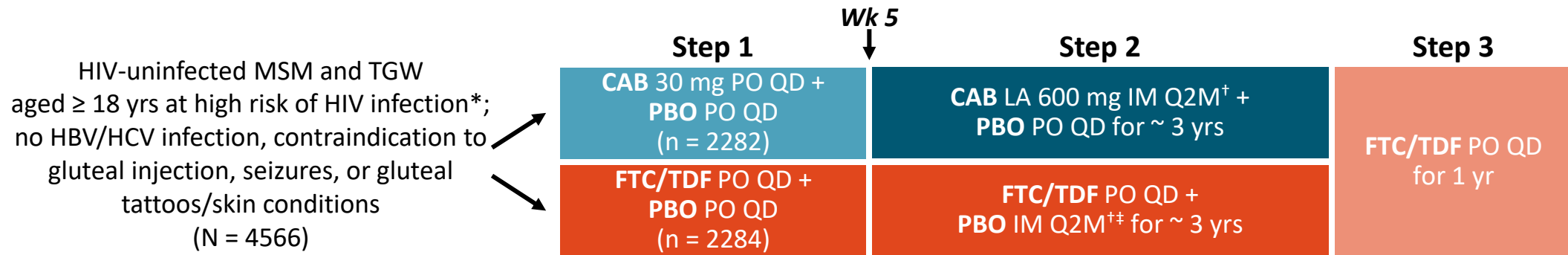
DISCOVER: FTC/TAF non-inferior to FTC/TDF for efficacy



*All with suspected BL infection.

HPTN 083: Study design

- International, randomized, double-blind phase IIb/III study
 - At interim analysis on May 14, 2020, with 25% of endpoints accrued, DSMB recommended termination of blinded study due to crossing of prespecified O'Brien-Fleming stopping bound
 - Planned N = 5000, with $\geq 50\%$ aged < 30 yrs; $\geq 10\%$ TGW; $\geq 50\%$ black participants in US



*Any non-condom receptive anal intercourse, >5 partners, stimulant drug use, incident rectal or urethral STI or incident syphilis in past 6 mos; or SexPro Score ≤ 16 (US only).

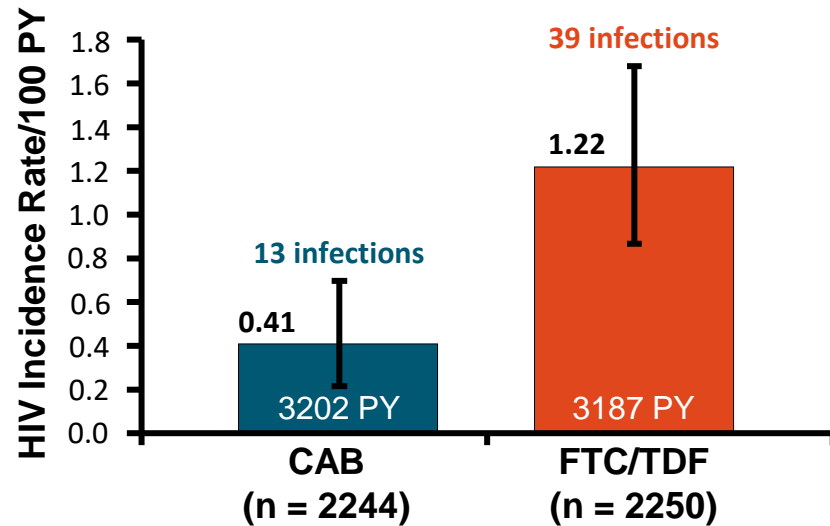
[†]First 2 doses given in Wks 5 and 9 then every 2 mos thereafter.

[‡]PBO for CAB injection was a 20% intralipid solution.

- Primary endpoints: incident HIV infections, grade ≥ 2 clinical and laboratory events

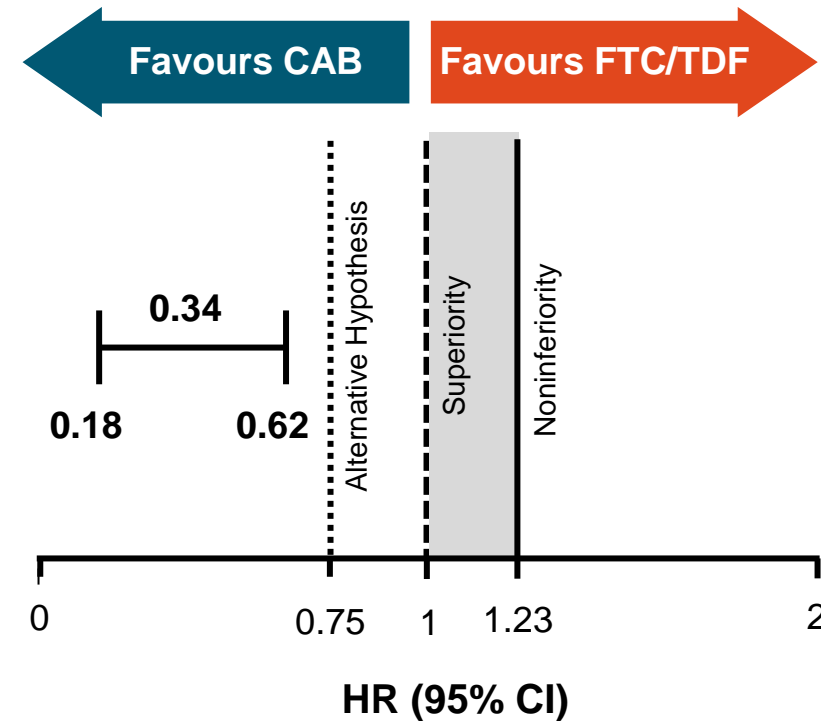
HPTN 083: HIV incidence

- Pooled incidence: 0.81 per 100 PY (95% CI: 0.61-1.07)
 - 52 HIV infections in 6389 PYFU



Median follow-up per participant: 1.4 yrs (IQR: 0.8-1.9).

- LA CAB met alternative hypothesis (HR: 0.75) and demonstrated statistically significant superiority vs FTC/TDF



084 just halted!

- Similar results – safe, highly effective vs TDF/FTC

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Wits University hails breakthrough for HIV prevention as historic

10 November 2020, 1:45 PM | Thabile Mbhele | @SABCNews



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UPDATED 10 NOVEMBER 2020

HIV prevention injection hailed as a 'major breakthrough' for women

Early results from a pivotal trial of an HIV prevention injection announced by the University of the Witwatersrand researchers have been hailed as being a “game-

The future?

- New injectables and implantables in phase 1, 2, 3 – preliminary safety data are promising
- Ring being licensed – ? role
- Cost will be a major issue
- LAI implementation also an issue – where will the injections be given?

Thank you!

