Challenges in Oral PrEP Rollout in South Africa

James McIntyre

October 2015

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"The problems of victory are more agreeable than those of defeat, but they are no less difficult"

Winston Churchill

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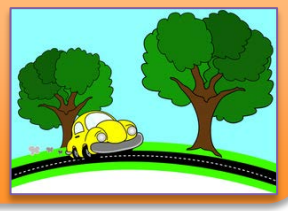
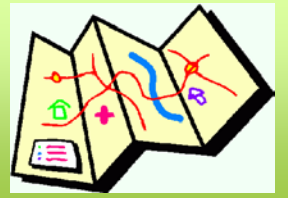
Evidence, Policy, Implementation & Delivery

The **Evidence** Road



The **Policy** Map



The **Implementation** Vehicle

The **Delivery** Drivers

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The **Evidence** Road

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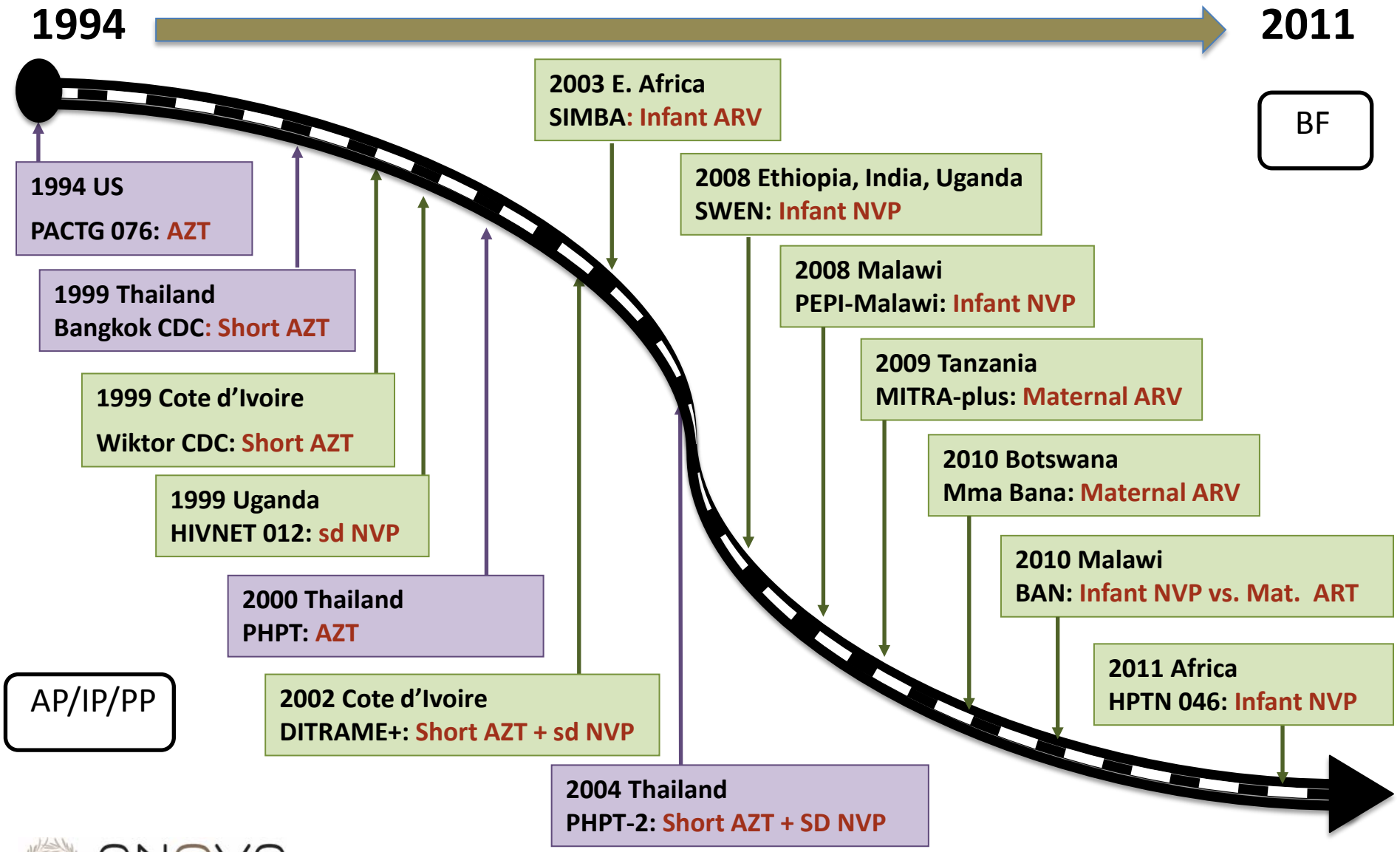
Building the evidence road for PMTCT



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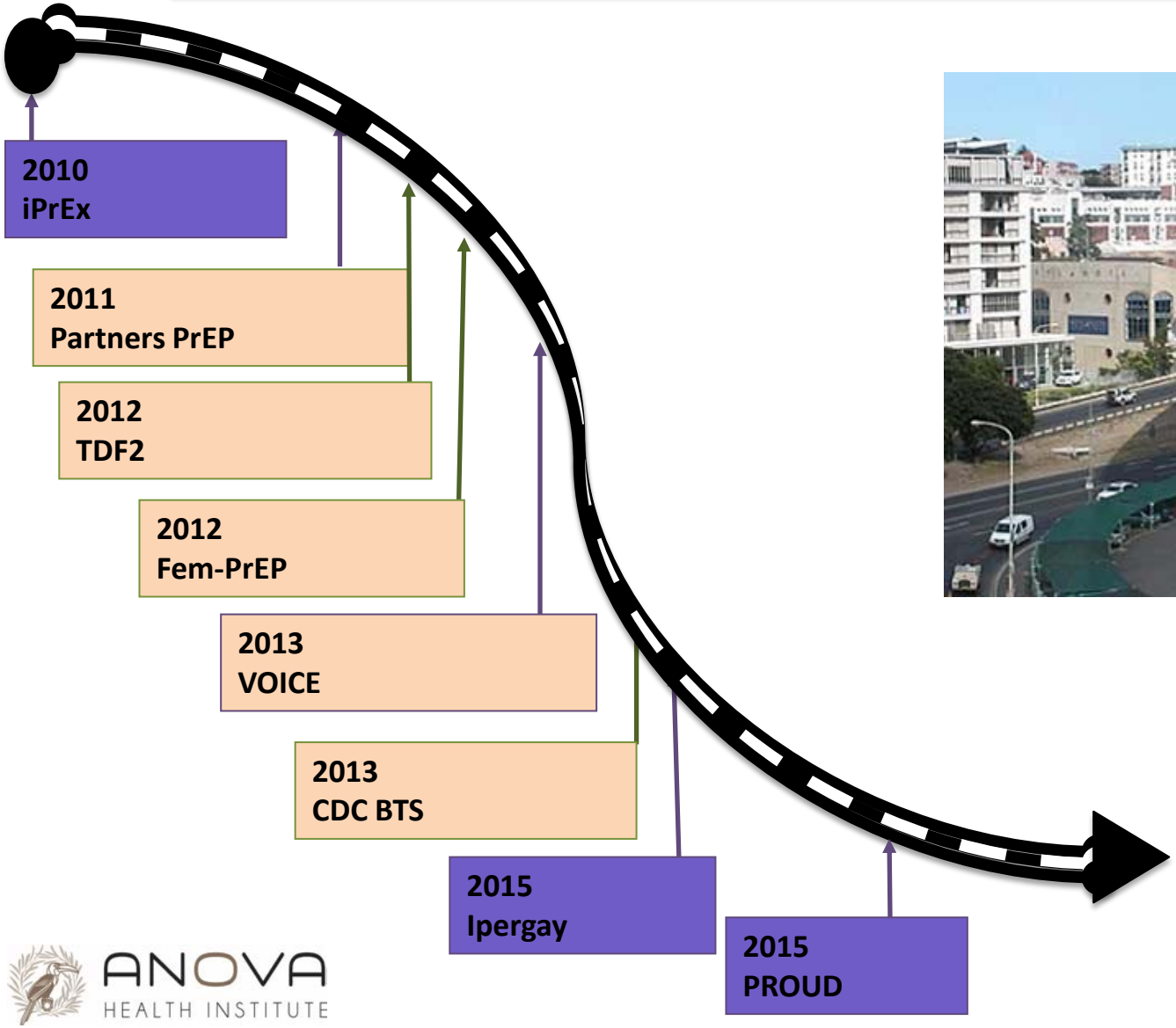
Building the evidence road for PrEP

2010 → **2015**



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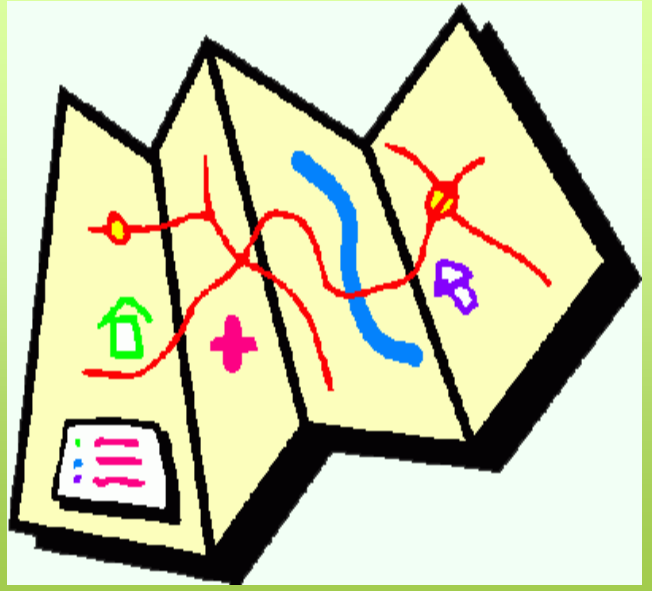
The **Policy** Map



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Scientific Evidence ≠ Policy ≠ Implementation

From evidence to policy: lessons from PMTCT & ART

Strong Scientific Evidence ≠ Policy

- PMTCT policies for resource-limited settings have been driven since 2000 by WHO normative guidance,
- WHO guidelines are intended to be adapted at country level and lead to local guidelines
- More recently, PEPFAR guidance and Global Fund requirements have been very influential, although complementary to WHO guidelines

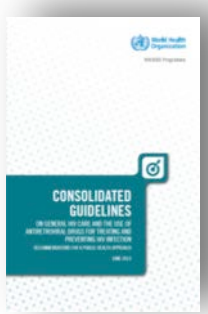
Evolution of WHO PMTCT ARV Recommendations

2001

2004

2006

2010



2013

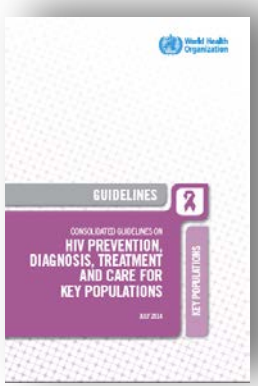
2015

PMTCT	4 weeks AZT; AZT+ 3TC, or SD NVP	AZT from 28 wks + SD NVP	AZT from 28wks + sdNVP +AZT/3TC 7days	**Option A** (AZT +infant NVP) **Option B** (triple ARVs)	**Option B or B+** Moving to ART for all for life	
ART	No recommendation	CD4 <200	CD4 <200	CD4 ≤350	CD4 ≤500	All, as soon as possible

Move towards: more effective ARV drugs, extending coverage throughout MTCT risk period, ART for the mother's health, ***increased consideration of operational and program implementation issues***

Adapted from Shaffer, WHO 2013

Evolution of WHO PrEP Recommendations



2014

Among men who have sex with men:

Pre-exposure prophylaxis (PrEP) is recommended as an additional HIV prevention choice within a comprehensive HIV prevention package.

2015

For HIV-negative individuals at substantial risk of HIV infection:

Oral PrEP (containing TDF) should be offered as an additional prevention choice for people at substantial risk of HIV infection as part of combination prevention approaches

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The **Implementation** Vehicle

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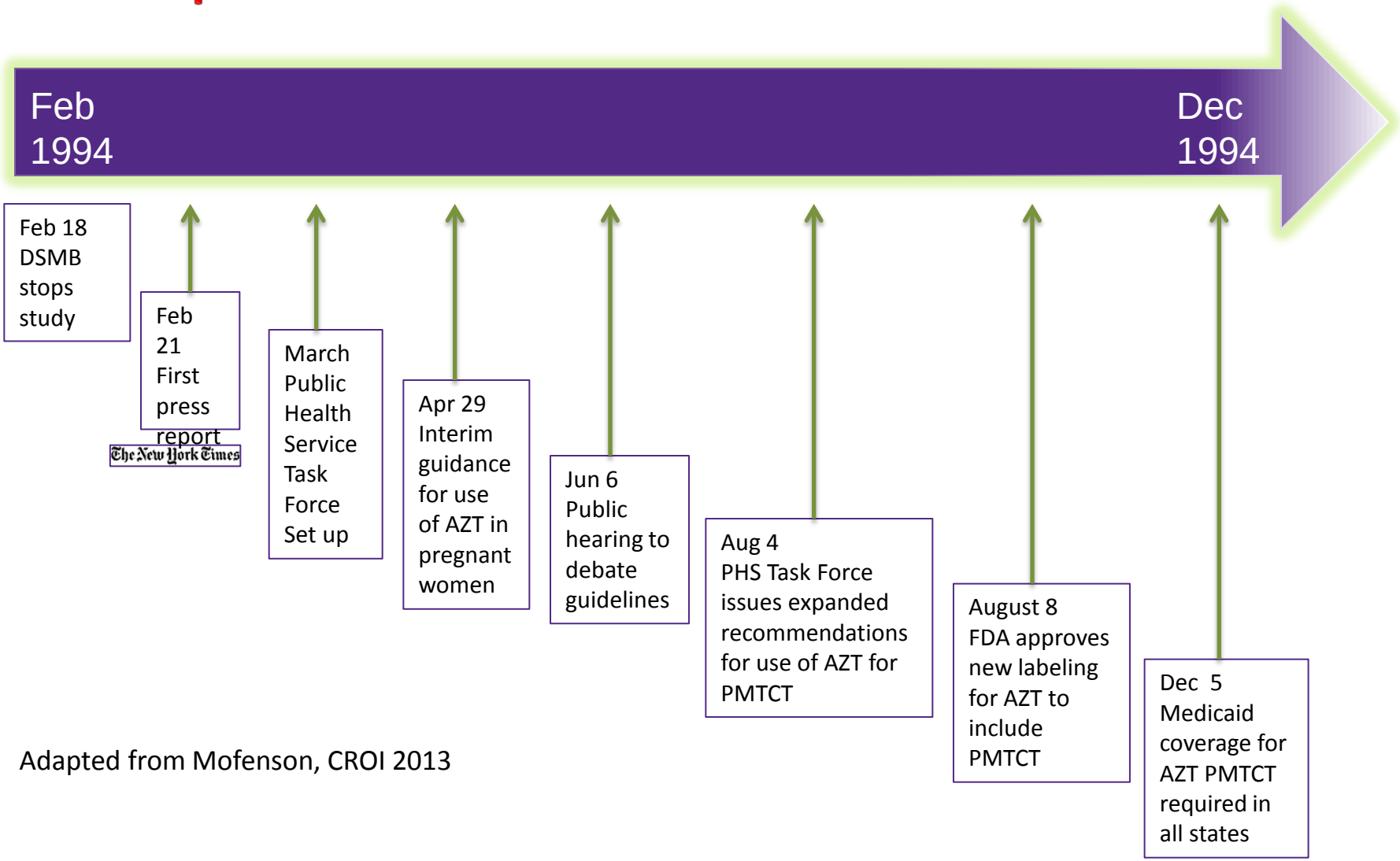
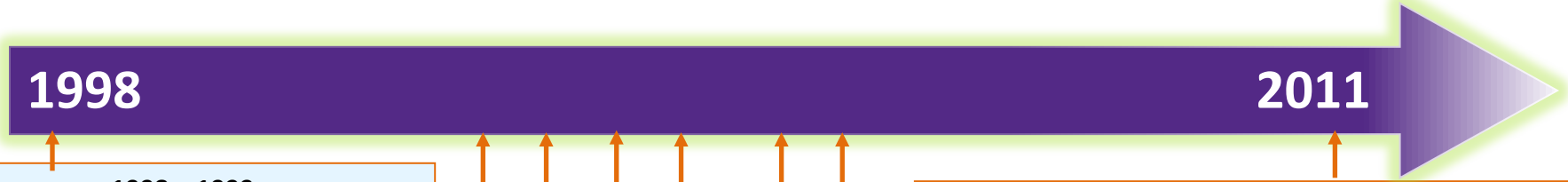
ACTG 076: Moving rapidly from evidence to policy and implementation in the US



Adapted from Mofenson, CROI 2013

Moving slowly to implement PMTCT in South Africa



1998 – 1999
Western Cape DOH starts PMTCT at 2 midwife obstetric units in Khayelitsha

2000
Durban AIDS conference : Studies from Africa Confirm ARV effectiveness for PMTCT

2000
PHRU starts Soweto PMTCT programme with FSTI and EGPAFsupport

2001
South African Ministry of Health endorses establishment of 2 research sites in each province as PMTCT pilots

2001
Constitutional Court orders government to develop a fully capable and effective national PMTCT programme

2002
Government unsuccessfully challenges Constitutional Court order. PMTCT programme commences.

2003
Government publishes new operational plan for HIV including nevirapine for PMTCT

2004
Introduction of CCMT plan including ART for pregnant women with CD4 < 200

2010
Revised PMTCT policy: Lifelong Art for women with CD4 <350, and "Option A" AZT and NVP prophylaxis

2011
Ministry of Health endorses exclusive breastfeeding for all HIV+ mothers and phasing out of formula supply

2011
National framework for eliminating MTCT developed By National Department of Health

Adapted from Barron et al. Bull WHO 2013

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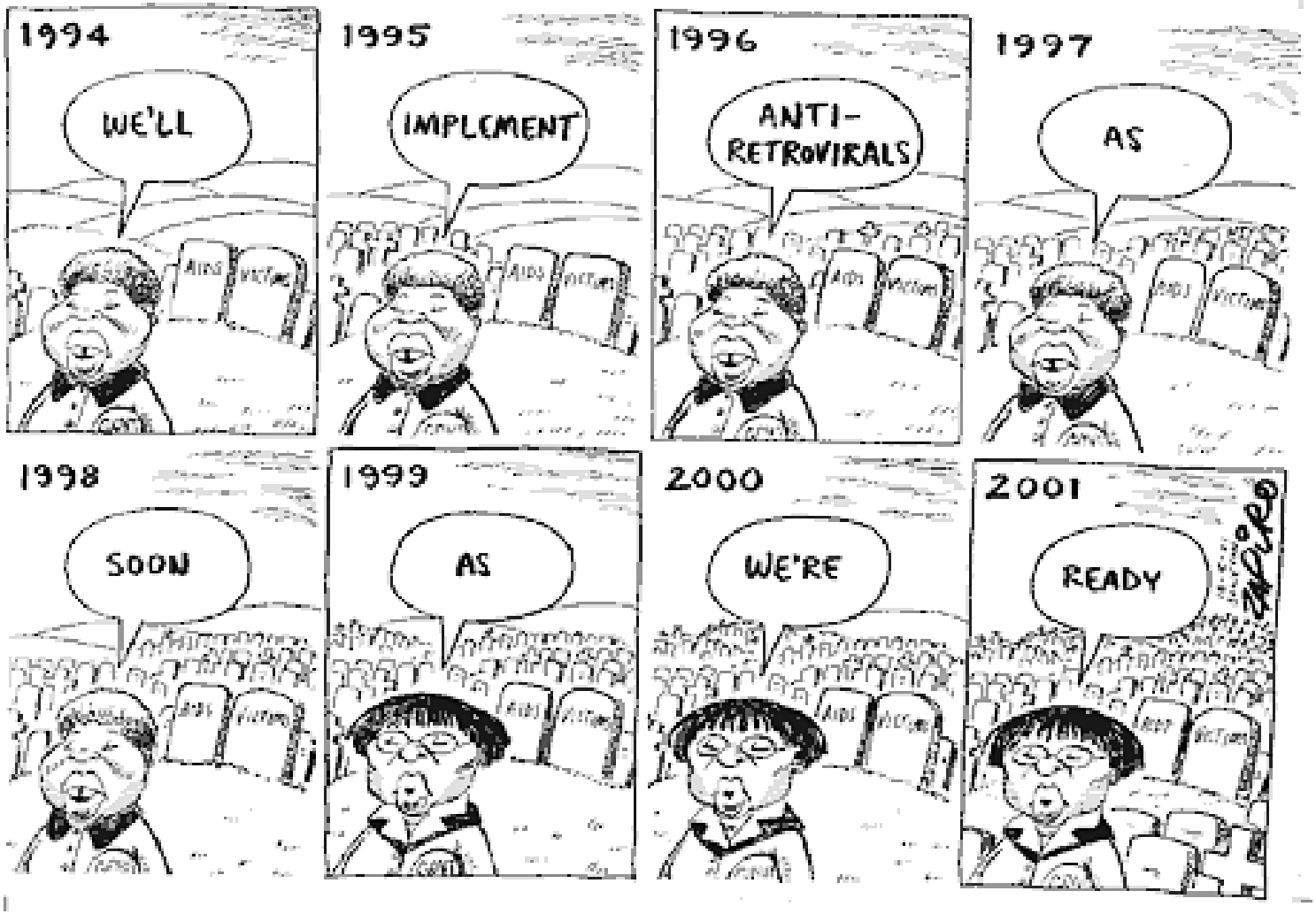
Lessons from PMTCT and ART



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“I have been asked many times if we can afford to do this. I always have one answer. Can we afford not to?”

Minister Aaron Motsoaledi,
on ARV expansion
AIDS 2014 Conference

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From policy to implementation

Policy ≠ Implementation

- Policy provides a route map to move implementation forward along the path set by evidence

- PMTCT global policies have historically been based on clinical trial data, advising on antiretroviral regimens and infant feeding data, but with very little emphasis on health systems issues, or advising on "how" rather than "what" to do

- Successful implementation needs the right service vehicle and effective drivers

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The **Delivery** Drivers

Delivery challenges

PrEP and ARV treatment

- PrEP implementation will need to be in parallel with expanded access to treatment in line with WHO guidance

- In South Africa: estimated that:
  - 6.4-million people infected with HIV
  - 4.2-million know their status, and
  - 3.1-million were on treatment by March 2015

- SA government 90-90-90 goals by 2020

Delivery challenges

Regulatory Approval

- Gilead application to MCC for prevention indication for Truvada® under review
- No application made for TDF alone
- Registration likely to be required for state sector guideline
- “Off licence” use currently permitted by prescription by physician in private sector, but wider rollout will require trained nurse dispensing or alternative distribution structures

Delivery challenges

Drug Supply and cost

- Antiretroviral stockouts being reported in treatment programme (which is based on fixed dose combination)
- Generic TDF/FTC available: retail cost varies from R270 – R480
- Government tender price approximately R65/month
- SA government provision in medium-term expenditure framework for steadily expanding HIV treatment,
  - HIV/AIDS conditional grant rising from R13.7bn in 2016-16 to R15.4bn in 2016-17, and R17.4bn in 2017-18

Delivery challenges

Health services

- Health services already over burdened by treatment needs
- Not optimal for prevention strategies or long term interventions
- HIV testing schedules and clinical monitoring requirements (such as creatinine and STIs) make alterative distribution challenging
- No local models evaluated yet, but community based distribution approaches are being extended for ARV treatment programmes
- Possible consideration of NGO-delivered programmes for rapid expansion (as with medical male circumcision)

Delivery challenges

"PrEP should be seen as an additional prevention choice based on a comprehensive package of services, including HIV testing, counselling and support, and access to condoms and safe injection equipment." (WHO)

- Comprehensive package of prevention services requires staff, counselling times, supply of and access to commodities

Lessons from PMTCT

- PMTCT was successful within a vertical programme for an easy-to-access population
- Nurses were initially reluctant to fully participate – seen as “other people’s work”
- Health worker acceptance of ARV treatment and PMTCT may not translate into acceptance of ARV prevention
- Drug supply is important, but testing is essential

PMTCT in South Africa: community demand

HIV testing access is central to PrEP and "Test and Treat"

- Access to initial and follow up HIV testing must be expanded for PrEP access
- Reaching marginalised groups is essential
- HIV testing outside of health facilities needs to be scaled up
- Self testing may be a key component

PrEP: why are we waiting?

The Lancet HIV

October 2015

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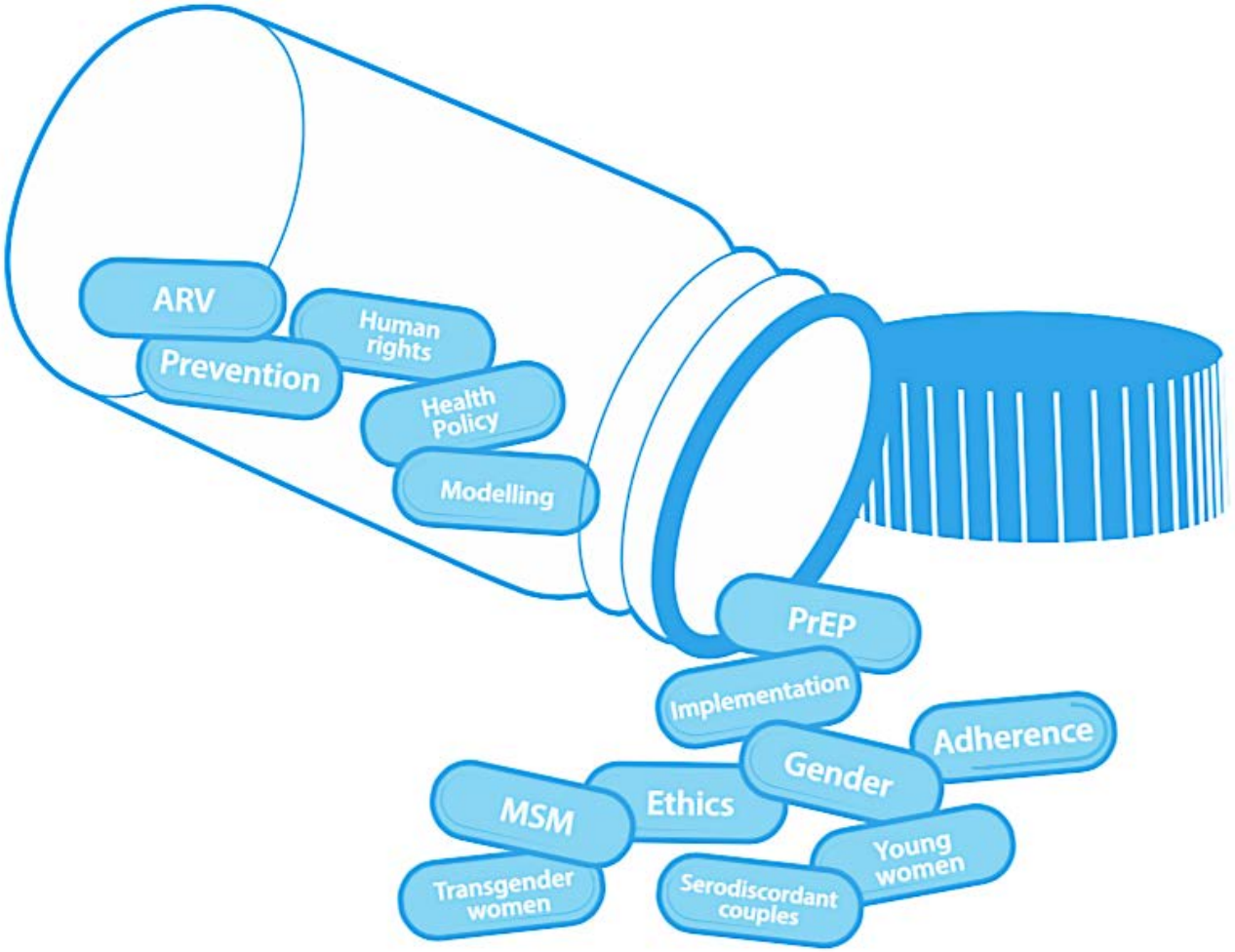
PrEP: implementation challenges



JIAS & NEMUS 2014

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The **Users**

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“The Baeten Rules of ARV prevention”

- When taken, they work.
- You don’t always have to be perfect to be good enough.
- The barriers are real … and sometimes they are us.
- PrEP is wanted. It is also not forever, not for everyone, and not one size fits all.
- There are risks in doing, but the greater risk is not doing enough.

Baeten, HIVR4P, 2014

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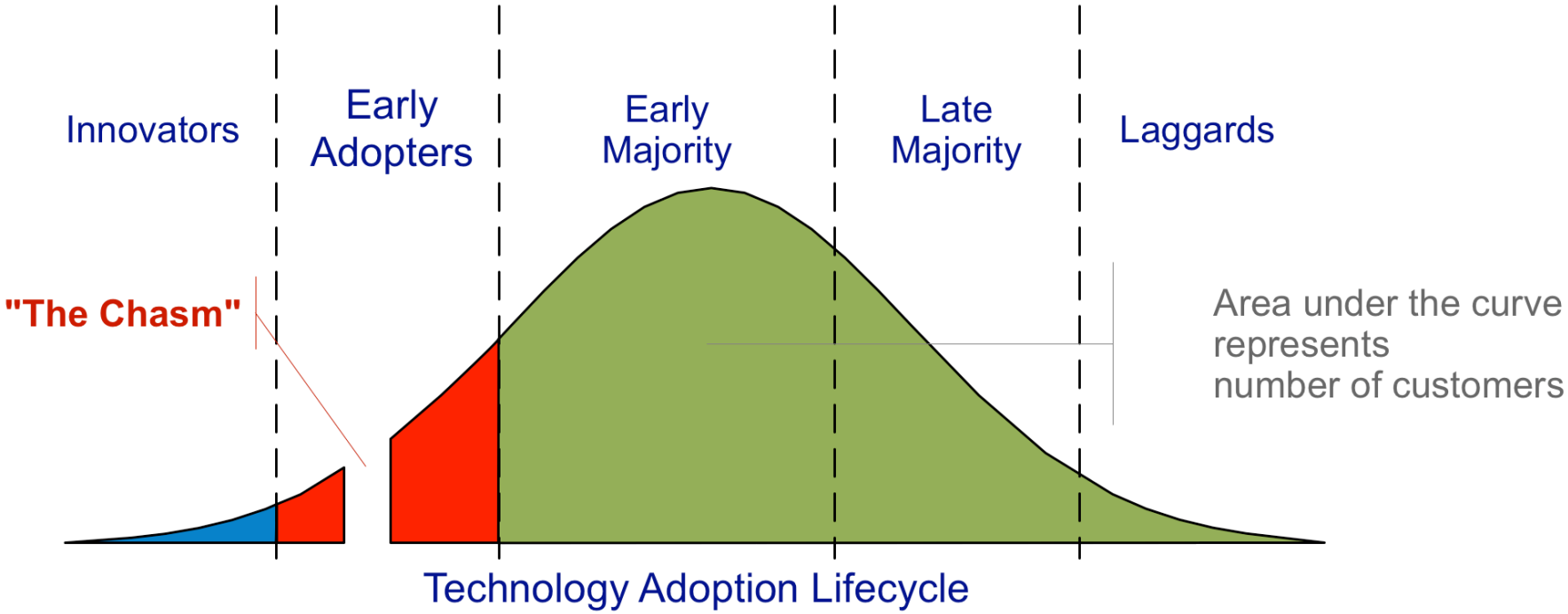
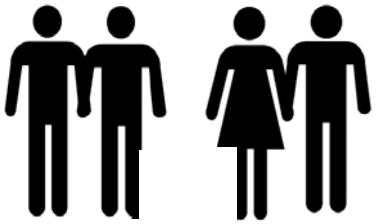
Can we predict PrEP uptake?





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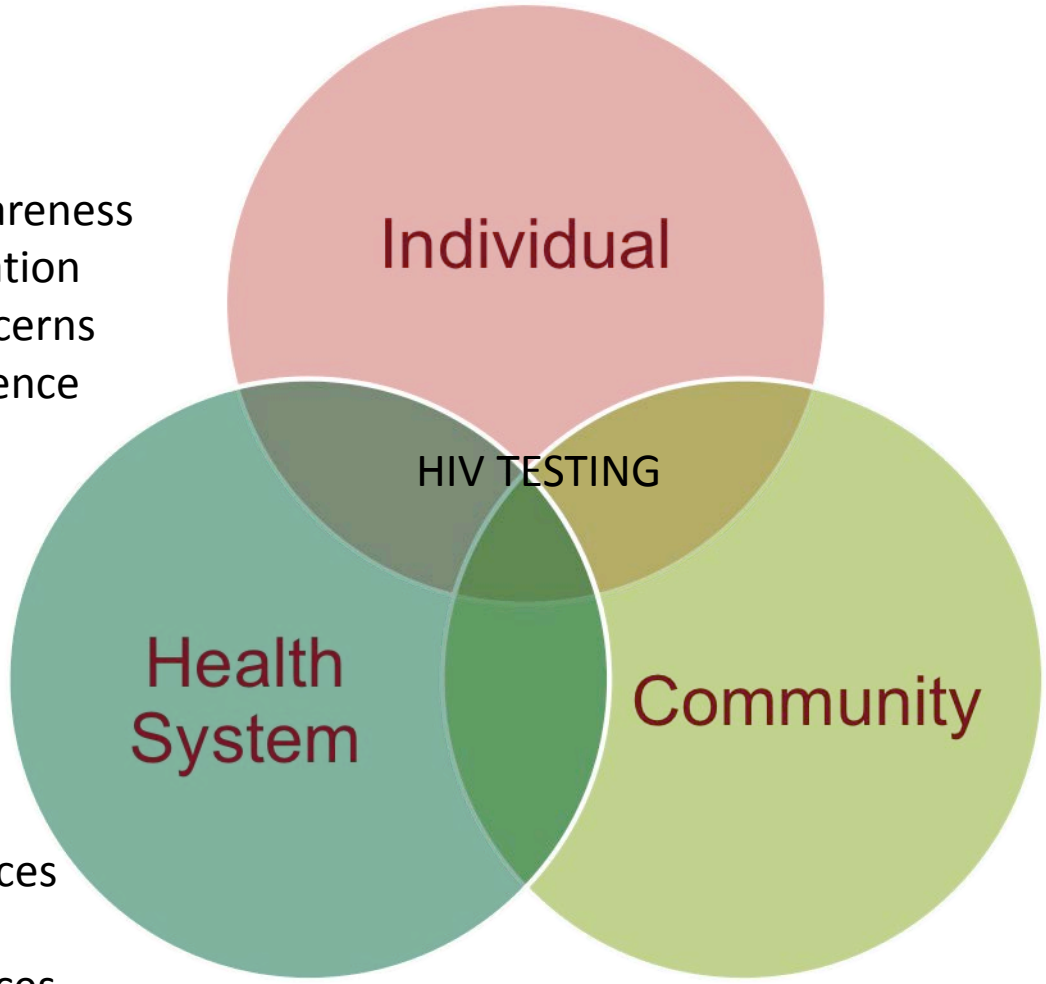
Understand barriers to successful PrEP

Fear
Lack of awareness
Misinformation
Health concerns
Non adherence



Trained staff
HIV testing services
Drug supply
Laboratory services

Stigma
Criminalization

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Who should get PrEP in South Africa?

"We would start with the most vulnerable groups in South Africa – female sex workers, men who have sex with men, discordant couples and young women between the ages of 15 and 24"

Dr Yogan Pillay,
as quoted in the Mail And Guardian,
30 September 2015

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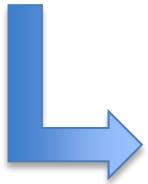
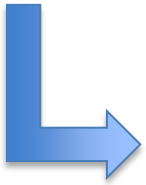
Applying the 'PrEP Continuum of Care" approach

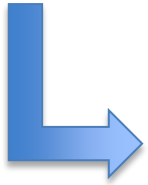
Population at risk



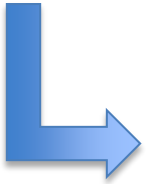
Likely to seek PrEP



Access to Healthcare



Likely to receive PrEP



Adherence and Efficacy

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Kelley et al, CID, 2015

Understanding the need: two approaches…

"IN GOD WE TRUST;
ALL OTHERS MUST
BRING DATA."
- W. EDWARDS DEMING

If we have data,
let's look at data.
If all we have are
opinions, let's go
with mine.

Jim Barksdale
NETSCAPE

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PrEP for Female Sex Workers in South Africa

- Population size uncertainties:
  - Estimated population: 160 000 – 180 000
  - HIV Prevalence: 60%

- Population at risk: 65 000
  - Willing to take and likely to receive: 30,000 ??

- Demonstration project underway in Pretoria & Johannesburg (Wits RHI)

- Other networks and services exist: could expand access

- Need to accelerate demonstration projects, awareness and access

PrEP for MSM in South Africa

- Population size uncertainties:
  - Estimated population: 750 000 – 1 200 000
  - HIV Prevalence: 33%

- Population at risk: 500 000 – 800 000
  - Willing to take and likely to receive: 200 000 – 400 000 ??

- Demonstration project starting October 2015 in Cape Town & Johannesburg

- Private sector provision also required: education needed

- Need to accelerate demonstration projects, awareness and access

Policy Challenges

“HIV-negative individuals at substantial risk of HIV infection”

- Who decides?
- How can provision of PrEP for marginalised and vulnerable populations be operationalized
- Will self identification be required to access PrEP
- Stigma, homoprejudice, service access, sex work criminalisation likely to limit implementation
- Can/should PrEP be integrated into health services?

PrEP for Young Women in South Africa

- Population size:
  - Estimated population: 4 800 000
  - HIV Prevalence: 17%

- Population at risk: 4 000 000
  - Willing to take and likely to receive: 1 000 000 – 2 000 000

- No evidence yet for appropriate delivery models, messaging, demand creation

- No evidence for uptake or adherence rates

- Do not yet know how Aspire and Ring Study results may influence thinking

PrEP for Young Women in South Africa

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PrEP for Young Women in South Africa

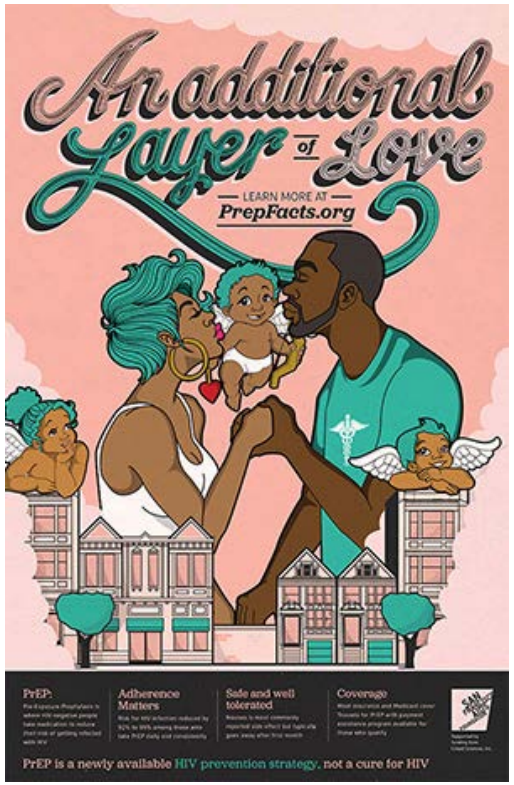
Uncertainties on :

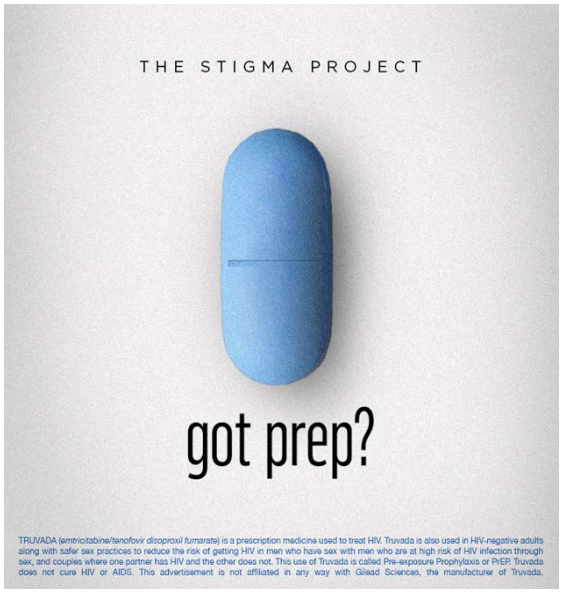
- Target age: in school or out of school
  - Modelling suggests 15 – 19 age group would have most impact
  - Young women hard to reach after leaving school

- Delivery sites:
  - Schools, health facilities, community based venues?
  - Contraception services
  - Pregnant women (Mean age at first birth 22.5 years)

- Attitudes:
  - peers, parents, providers
  - social marketing, adherence support

Messaging to build demand





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Answering PrEP critics

"Denying PrEP to patients because they might have unsafe sex makes about as much sense as our colleagues who treat high cholesterol denying statins to theirs because they might eat more ice cream."

Susan Buchbinder,
San Francisco City Health Department

The New York Times

OCT. 5, 2015

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Lessons from PMTCT

- Implementing antiretroviral prevention saves lives
  - Mother to child transmission in South Africa dropped from >25% in 1994 to around 2% in 2015

- Even imperfect strategies can be effective whilst evolving to better approaches

- According to UNAIDS estimates, expanding ART to all people living with HIV and expanding prevention choices can help avert
  21 million AIDS-related deaths and
  28 million new infections by 2030.

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Thank you

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