Challenges in Oral PrEP Rollout in South Africa

James McIntyre
October 2015
“The problems of victory are more agreeable than those of defeat, but they are no less difficult”

Winston Churchill
Evidence, Policy, Implementation & Delivery

The Evidence Road

The Policy Map

The Implementation Vehicle

The Delivery Drivers
Evidence, Policy, Implementation & Delivery

The Evidence Road
Building the evidence road for PMTCT

1994 US
PACTG 076: AZT

1999 Thailand
Bangkok CDC: Short AZT

1999 Cote d’Ivoire
Wiktor CDC: Short AZT

1999 Uganda
HIVNET 012: sd NVP

2000 Thailand
PHPT: AZT

2002 Cote d’Ivoire
DITRAME+: Short AZT + sd NVP

2003 E. Africa
SIMBA: Infant ARV

2004 Thailand
PHPT-2: Short AZT + SD NVP

2008 Ethiopia, India, Uganda
SWEN: Infant NVP

2008 Malawi
PEPI-Malawi: Infant NVP

2009 Tanzania
MITRA-plus: Maternal ARV

2010 Botswana
Mma Bana: Maternal ARV

2010 Malawi
BAN: Infant NVP vs. Mat. ART

2011 Africa
HPTN 046: Infant NVP

AP/IP/PP
Building the evidence road for PrEP

2010
- iPrEx

2011
- Partners PrEP

2012
- TDF2
- Fem-PrEP

2013
- VOICE
- CDC BTS

2015
- Ipergay
- PROUD
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The **Policy** Map
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

<table>
<thead>
<tr>
<th>Year</th>
<th>PMTCT</th>
<th>ART</th>
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<tbody>
<tr>
<td>2001</td>
<td>4 weeks AZT; AZT+ 3TC, or SD NVP</td>
<td>No recommendation</td>
</tr>
<tr>
<td>2004</td>
<td>AZT from 28 wks + SD NVP</td>
<td>CD4 &lt;200</td>
</tr>
<tr>
<td>2006</td>
<td>AZT from 28wks + sdNVP +AZT/3TC 7days</td>
<td>CD4 &lt;200</td>
</tr>
<tr>
<td>2010</td>
<td>Option A (AZT +infant NVP)</td>
<td>CD4 ≤350</td>
</tr>
<tr>
<td></td>
<td>Option B (triple ARVs)</td>
<td></td>
</tr>
<tr>
<td>2013</td>
<td>Option B or B+ Moving to ART for all for life</td>
<td>CD4 ≤500</td>
</tr>
<tr>
<td>2015</td>
<td></td>
<td>All, as soon as possible</td>
</tr>
</tbody>
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*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
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.

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.
The **Implementation** Vehicle
ACTG 076: Moving rapidly from evidence to policy and implementation in the US

Feb 18
DSMB stops study

Feb 21
First press report

March
Public Health Service Task Force Set up

Apr 29
Interim guidance for use of AZT in pregnant women

Jun 6
Public hearing to debate guidelines

Aug 4
PHS Task Force issues expanded recommendations for use of AZT for PMTCT

August 8
FDA approves new labeling for AZT to include PMTCT

Dec 5
Medicaid coverage for AZT PMTCT required in all states

Adapted from Mofenson, CROI 2013
Western Cape DOH starts PMTCT at 2 midwife obstetric units in Khayelitsha

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

PHRU starts Soweto PMTCT programme with FSTI and EGPAF support

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

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

Government unsuccessfully challenges Constitutional Court order. PMTCT programme commences.

National framework for eliminating MTCT developed by National Department of Health

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

Revised PMTCT policy: Lifelong ART for women with CD4 < 350, and “Option A” AZT and NVP prophylaxis

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

Government publishes new operational plan for HIV including nevirapine for PMTCT

Adapted from Barron et al. Bull WHO 2013
Lessons from PMTCT and ART
“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
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 alternative 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
PrEP: implementation challenges
Evidence, Policy, Implementation & Delivery

The Users
“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
Can we predict PrEP uptake?
Understand barriers to successful PrEP

**Individual**
- Fear
- Lack of awareness
- Misinformation
- Health concerns
- Non adherence

**Health System**
- Trained staff
- HIV testing services
- Drug supply
- Laboratory services

**Community**
- Stigma
- Criminalization

**HIV TESTING**
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
Applying the ‘PrEP Continuum of Care” approach

Population at risk

Likely to seek PrEP

Access to Healthcare

Likely to receive PrEP

Adherence and Efficacy

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
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, homophobia, 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
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
“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
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.
Thank you