PMTCT GUIDELINES
RATIONALE AND GOING FORWARD

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SA Background

- Population: 48m
- Annual number of deliveries: 1,2m
- 97% of women attend the first ANC
- 71% of women attend 5th ANC visit
- 97% of pregnant women accessing syphilis testing
- 95% have access annual skilled attendance at birth
- 95% deliver at health facilities

Source: Health of our Children, HSRC 2008
Epidemiological data

- HIV prevalence in the general population: 12%
- HIV prevalence among pregnant women: 29.1%
- Uptake of PMTCT >85%
Figure 2: Estimation of timing of mother-to-child HIV-1 transmission in a non-breastfeeding population. Estimates are based on a hypothetical cohort of 100 children born to HIV-infected women without any interventions. Upper line numbers indicate number of children at risk for infection. Adapted from reference 6.
What did we know and when did we know it?
Perinatal HIV Clinical Trial Results

1994 U.S. AZT Trial ACTG 076
- 67% reduction in transmission

1994

1998

Thai Bangkok short AP/IP AZT trial
- 50% reduction in transmission

1998

Cote d'Ivoire short AP/IP AZT trials
- 37% reduction in transmission (breastfeeding)

1999

PETRA AZT/3TC trial (6 wk results)
- 50% reduction with longest arm.
- 38% reduction with the IP/PP arm

1999

1999 Uganda 2-dose IP/PP NVP trial (HIVNET 012)
- 47% reduction in transmission (breastfeeding)

1999

2000

Thailand Long vs short AZT regimens
- 4% TR in LL (non BF)

2000

2002

Cote d'Ivoire DITRAME +
- 6.2% TR with AZT & IP/PP NVP

2002

2003

DITRAME + 1201.1
- 4.7% TR with AZT/3TC & IP/PP NVP

2003

2004

Thailand PHPT
- <2% AZT + NVP

2004
## History of SA PMTCT program

<table>
<thead>
<tr>
<th>Year</th>
<th>Event</th>
<th>Year</th>
<th>Event</th>
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<tbody>
<tr>
<td>1999</td>
<td>HIVNET 012 (13-14%)</td>
<td>2001</td>
<td>Pilot sites (PETRA and SAINT)</td>
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<tr>
<td>2004</td>
<td>Thai regimen – AZT +sd NVP</td>
<td>2003</td>
<td>PMTCT regimen of sd-NVP (20%)</td>
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<td>WHO guidelines in 2006</td>
<td>2008</td>
<td>Guidelines to include AZT from 28wks and HAART for &lt;200</td>
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<td>Rapid advice 2009 / implemented 2010</td>
<td>2010</td>
<td>HAART for &lt;350, Dual for &gt;350 from 14wks AZT for infant x4wks (&lt;5%)</td>
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<td>2006</td>
<td>2009/2010</td>
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<td>----------------------------------------------------------------------</td>
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<tr>
<td>ART eligible – CD 4 &lt;200 or ≤200 or &lt;350 with WHO stages 3 or 4</td>
<td>ART eligible – CD 4 ≤350 or WHO stage 3 or 4</td>
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<tr>
<td>If not, for AZT from 28wks +sd-NVP during labour</td>
<td>Maternal 3 drug regimen seen as equivalent to AZT (+sd-NVP) Start earlier at 14wks</td>
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<tr>
<td>Infant = AZT syrup for 1wk or 4 wks if maternal therapy &lt;28wks</td>
<td>Infant – 4 wks of AZT for all – regardless of maternal therapy</td>
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<tr>
<td>No recommendation for mom or infant ARV’s if mom breastfeeding</td>
<td>Maternal and infant ARV’s if mom breastfeeding</td>
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</tbody>
</table>
WHO eligibility criteria for pregnant women

- CD 4 \( \leq 350 \) regardless of clinical stage
- CD 4 > 350 – if sympt (WHO 3 or 4)
- Start asap irrespective of GA

Preferred regimen –
- AZT +3TC +NVP or
- AZT +3TC +EFV (not 1\textsuperscript{st} trimester)
- Alternative – TDF +3TC (FTC) +NVP (EFV)
Those not qualifying

Option A:
- AZT 300mg bd from 14wks
- AZT 300hr’ly in labour +sd NVP
- Tail cover (?maintained from 2006)

Option B:
triple therapy in pregn +BF

Infant – AZT or NVP daily for 4 - 6wks or until 1wk after cessation of BF
Rationale behind changes

- **Optimal timing and eligibility** for ART initiation in non-pregnant adults
- **Timing of transmission** (with or without b/feeding) and benefits of **early initiation** of ARV during pregnancy
- **Safety** of 3drug regimen for use during pregnancy
- More countries ready to expand more effective PMTCT services
Why 350

- Sufficient data from non-pregn adults of benefits of earlier initiation
- Accounts for 40% of pregn HIV infected women
- Accounts for >75% of MTCT risk and >80% of pp transmission
- Account for 85% of maternal deaths within 2yrs of delivery
Efficacy of ARV in reducing MTCT

- HAART for PMTCT - <2% in developed / developing countries
  - 2.4% in Thai study (20% of women with CD 4 <200)
  - AZT from 28wks +sd-NVP (mom not eligible) – 2% in PHPT-2

- Kesho Bora – women CD 4 200 – 500, btwn 28 - 36wks
  - HAART =1.8% vs dual =2.2% (NS)
What to start

Start one of the following regimens in ART-naïve individuals (for maternal HAART or for PMTCT)

- **Preferred**
  - AZT + 3TC + EFV
  - AZT + 3TC + NVP

- **Alternative**
  - TDF + 3TC or FTC + EFV
  - TDF + 3TC or FTC + NVP

- EFV – no convincing evidence of teratogenicity
- No superiority of AZT over TDF / no concerns of TDF from RCT’s
Drug safety during pregnancy

• NVP associated with hepato-toxicity when initiated at >250

• EFV or alternatively LPV/r
  • Use of PI to avoid this in women >250
  • Side effects –**dislipidaemia** / N/V/loose stools /Hyperglycemia

• No concern of drug resistance after discontinuation

• LPV/r levels reduced during 3\({\text{rd}}\) trimester but no need to adjust dosage
The review of NVP safety in pregnant women with CD4 count 250–350 cells/mm³ did not confirm an increased risk of serious adverse events and the panel concluded that the benefits of using NVP in this situation outweigh the risks of not initiating ART.

The panel was unable to conclude from the evidence reviewed whether there are benefits associated with the use of EFV vis a vis NVP in pregnant women after the first trimester and with higher or unknown CD4 cell counts, although more than half of the panel members preferred EFV in these situations.”
EFV during pregnancy

- Rash and hepatitis can occur
- 5 retrospective cases and 1 prospective case of NTD in humans exposed to EFV in 1st/3
- Meta analysis of 11 prospective and 5 retrospective cases with 1st/3 exposure – 1132 exposed to EFV vs 7163 non exposed – RR=0.87 (0.61-1.24) (Ford, 2010)
- 2.9% overall birth defects
OCTANE (A5208)

- Octane 1 – women with prev exposure to sd-NVP
  - TDF/FTC/NVP (n=120) – VF or death=26%
  - TDF/FTC/LPVR (n=120) VF or death =8% (p=0.0004)
- Octane 2 – women with no prev exposure
  - TDF/FTC/NVP (n=249) – VF or death=17%
  - TDF/FTC/LPVR (n=251) VF or death =20% (NS even with ITT)
Tail therapy

- NVP has long half life and low genetic barrier
- NNRTI resistance if sd exposure to sd-NVP up to 60%
- Resistance can be detected up to 12m ff exposure in plasma and cellular provirus
- 1wk combivir reduced NVP resistance from 60 – 10% but risk not eliminated (TOPS study, McIntyre)
- NNRTI based HAART in women with prev exposure to sd-NVP impaired optimal viral suppression (Octane study)
Truvada

A5207 7 vs 21 days

- AZT /3TC
- Kaletra
- Truvada (TDF + FTC/emtricitabine)

- All equivalent, less resistant mutations if taken for 21 days
- Has long half life, already used in PrEP
- Trials of stat dose vs combivir x7d almost completed
There are two choices for HIV-positive women who breastfeed and are not taking ART:

- If a woman received zidovudine during pregnancy, daily nevirapine is recommended for her child from birth until the end of the breastfeeding period.
- Or
- If a woman received a three-drug regimen during pregnancy, a continued regimen of three-drug prophylaxis is recommended for the mother until the end of the breastfeeding period.
### Table 1: Standardised national ART and ARV regimens for women who are HIV positive and pregnant and their infants

<table>
<thead>
<tr>
<th>Woman</th>
<th>Maternal regimens</th>
<th>Comment</th>
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<tbody>
<tr>
<td>Eligible for lifelong ART (i.e. CD4 ≤ 350 or WHO clinical stage 3 or 4)</td>
<td>TDF + 3TC/FTC + NVP</td>
<td>Start lifelong ART within 2 weeks</td>
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<tr>
<td>Currently on lifelong ART</td>
<td>Continue ART</td>
<td>Substitute EFV with NVP if in first 12 weeks of pregnancy</td>
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<tr>
<td>Contraindication to TDF (renal disease)</td>
<td>AZT + 3TC + NVP</td>
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<tr>
<td>Not eligible for ART i.e. CD4 &gt; 350 and WHO stage 1 or 2</td>
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<tr>
<td>Unbooked and presents in labour</td>
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<td>Assess maternal ART eligibility before discharge</td>
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<tr>
<td>sdNVP + AZT 3hrly in labour</td>
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<td></td>
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<tr>
<td>TDF + FTC single dose (stat) after delivery</td>
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<td>azT from 14 weeks</td>
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Success??

- Evaluation of current PMTCT program done last year, (6\textsuperscript{th} IAS, 2011)
- Good coverage of 6 wks immunization
- DBS from 565 facilities – 30% HIV exposed (vs 31% from national data)
- 34% were on HAART and 20% exclusive BF; 62% no BF
- Exclusive BF and HAART both beneficial
TR

- Nationally – 3.5%
- Provinces
  - NC – 1.7% (15.6%)
  - FS – 6% (31.1%)
  - KZN – 2.8% (43.9%)

(c/section not helpful)
Challenges

- Increase dual therapy uptake in ANC (still 5% unbooked)
- Early initiation of HAART in 40% of pt CD 4<350
  - Contributes to 90% of maternal deaths
- Increased testing for infants
SA and MDG’s

1. To eradicate extreme poverty and hunger
2. To achieve universal primary education
3. To promote gender equality and empower women
4. To reduce child mortality
5. To improve maternal health
6. To combat HIV/AIDS, malaria and other diseases
7. To ensure environmental sustainability
8. To develop a global partnership for development

between 1998 and 2007, the maternal mortality rate leapt from 150 to 625 deaths for each 100,000 live births. That means South Africa, sub-Saharan African’s economic powerhouse, has no hope of meeting the U.N. MDG that require 38 deaths per 100,000 births by 2015.
South Africa
“Stop Making Excuses”
Accountability for Maternal Health Care in South Africa
“Quotes”

- “While many sub-Saharan African countries are not on track to meet their MDG targets, South Africa is one of only six countries in sub-Saharan Africa that made no progress in reducing maternal deaths by 2008, and one of five (together with Botswana, Lesotho, Swaziland, and Zimbabwe) that experienced the largest percentage increases”
Ke a leboga