Outline

• Aims of P/EMTCT
• Burden of Disease
• Timing and Determinants of Transmission
• Evolution of Prevention Science
• Evolution of Policy
• Current WCP Guidelines
  – Prophylaxis
  – Feeding
  – Testing
• The future.....
AIMS OF PMTCT
Aims of PMTCT/EMTCT

- Care of HIV-infected women and their babies during pregnancy, breastfeeding and early childhood to
  - Prevent vertical transmission
    (Eliminate Paediatric HIV)
  AND
  - Optimise maternal and infant health and survival
Effective PMTCT underpinned by...

- Preventing new HIV infections in the fertile.
- HIV + women avoiding unintended pregnancies

And its success depends on....

- Early pregnancy test and early antenatal care
- Routine early HIV testing and counseling
- ART initiation before 20 weeks gestation
- Viral suppression
- Avoidance of interventions that harm child health
In the developing world ….  

6. Determinants of poor health outcome in vertical HIV exposure
BURDEN OF DISEASE
Global HIV infections: 2007

- 33 million in world
- 2011 - 34.2 million
- 8 million on HAART
- 22 million in SSA
- 2011 - 23.5 million
- 2011
- 5.7 million in SA
- 1.7 million on HAART

12 countries account for 75% of world’s HIV-positive pregnant women
South Africa has less than 1% of world’s population but 17% of HIV infections

From ppt by Prof G Theron
Now > 6 million PLHIV in RSA !!! > 3 million on ART

Figure 5: The HIV epidemic curve among antenatal women, South Africa, 1990 to 2013. (Source: NDoH, 2014).

### WHO/UNAIDS MODEL

<table>
<thead>
<tr>
<th>Indicator</th>
<th>UNAIDS 2008</th>
<th>UNAIDS 2009</th>
<th>UNAIDS 2010</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total HIV population (Adults &amp; children)</td>
<td>5 570 000</td>
<td>5 630 000</td>
<td>5 575 096</td>
</tr>
<tr>
<td>HIV+ Adults(15+)</td>
<td>5 240 000</td>
<td>5 300 000</td>
<td>5 056 294</td>
</tr>
<tr>
<td>Adult (15-49) prevalence (%)</td>
<td>17.9</td>
<td>17.8</td>
<td>17.9</td>
</tr>
<tr>
<td>Adult HIV+female population(15+)</td>
<td>3 230 000</td>
<td>3 270 000</td>
<td>2 945 686</td>
</tr>
<tr>
<td>HIV population (children &lt;15)</td>
<td>325 000</td>
<td>334 000</td>
<td>518 802</td>
</tr>
<tr>
<td>Total annual AIDS deaths</td>
<td>330 000</td>
<td>314 000</td>
<td>282 578</td>
</tr>
<tr>
<td>AIDS orphans</td>
<td>1 850 000</td>
<td>1 950 900</td>
<td>2 138 909</td>
</tr>
<tr>
<td>Adult AIDS deaths (15+)</td>
<td>297 000</td>
<td>284 000</td>
<td>252 348</td>
</tr>
<tr>
<td>Adult New HIV infections (15+)</td>
<td>352 000</td>
<td>344 000</td>
<td>332 512</td>
</tr>
<tr>
<td>New infections (children&lt;15)</td>
<td>49 800</td>
<td>42 700</td>
<td>48 088</td>
</tr>
<tr>
<td>Need for ART among adults (15+)</td>
<td>1 475 000</td>
<td>1 584 000</td>
<td>1 407 026</td>
</tr>
<tr>
<td>Need for ART(children)</td>
<td>156 800</td>
<td>158 600</td>
<td>304 535</td>
</tr>
<tr>
<td>Infected mothers needing PMTCT</td>
<td>218 700</td>
<td>213 800</td>
<td>260 280</td>
</tr>
</tbody>
</table>

The National Antenatal Sentinel HIV and Syphilis Prevalence Survey, South Africa 2010

2016 RXH HIV Symposium
Figure 2.2  iMMR from 2005 to 2013

More ART-based PMTCT

Saving Mothers 2011-2103
Fig. 2.2. Distribution of underlying causes maternal deaths 2008-2010


Fig. 4. Trend in causes of maternal deaths, 1997-2009 (source: own calculations from data from Stats SA).
Emergence of a peak in early infant mortality Bourne et al.  
*AIDS* 2009, 23:101–106

**Fig. 2.** Graphical representation of likely HIV/AIDS-related deaths, at ages 1–11 months, in South Africa during 1997–2002.
MDG 4: Child Mortality ↑

Figure 4.1: Under-Five Mortality Rate in South Africa since 1998, and the 2015 MDG

- 2015 MDG Target: 20
- 2007: 104
- 2001: 97
- 1998 (SADHS): 59

Under-five mortality rate per thousand live births

Source: 1998 South Africa Demographic and Health Survey, 2001 Census & 2007 Community Survey, South Africa

Poor progress!
TIMING AND DETERMINANTS OF MTCT
Timing of HIV Transmission
(Pre ART, non Breast-Feeding cohort)

Transmission risk is small prior to 28 weeks gestation, rises towards term and peaks during labour and delivery.

- Maternal IP Rx reduces IP but not IU risk
- Infant PEP reduces IP proportion and PP risk


**Figure 2.** Estimated distribution of the dates of transmission.

- **Infant & Maternal sdNVP**
- **Dual Rx/HAART**

IU infection: Birth PCR pos
Early ART = early disease control
Maternal ARVs and infant PEP target intense IP transmission risk but not IU transmission.
8-12 hours of labour has the same risk of transmission as 18 months of breastfeeding !!!

Transmission risk intensity low during breastfeeding even with No ARVs but, over time, cumulative risk high

4% Transmission of HIV for every 6 months of breast-feeding
Determinants of *in utero* risk

- **High maternal viral load** (advanced disease, inadequate ART, viral rebound or new infection)
- Maternal immune status (80% of VT in CD4<350)
- **Co-morbidity** (TB, Syphilis, ?CMV, HSV?)
Determinants of *intra partum* risk

- **High maternal viral load** (advanced disease, inadequate ART, viral rebound or new infection)
- Maternal immune status (80% of VT in CD4<350)
- Avoidance of labour (NVD > Emergency C/S > Elective C/S) + Invasive obstetric procedures.
- Duration of ROM > 4hrs; chorioamnionitis;
- SPTL & PPROM.
- **Co-morbidity** (TB, Syphilis, ?CMV, HSV?)
Determinants of *post partum* risk

- **High maternal viral load** (advanced disease, inadequate ART, viral rebound or new infection)
- Maternal immune status (80% of VT in CD4<350)
- ? Immature gut
- Compared to EBF, early mixed feeding increases transmission (*solids + BF* = 11x; *BF + FF* 2-3x); breast feeding risk cumulative over time
EVOLUTION OF PREVENTION SCIENCE
Milestones In PMTCT Research

• Early 1980s: MTCT documented
• 1985: BF MTCT reported (CDC = avoid BF)
• 1994 (NEJM): PACTG 076 (AZT \(\downarrow\) VT 67%)
• 1999 (Lancet): HIVNET 012 (sdNVP) and “Thai AZT Study” – \(\downarrow\)MTCT 50% - simple
• 2003: Thai AZT + sdNVP (Targeted ART if CD4 < 200) – MTCT reduced dramatically to only 1-2%
• HAART/FF virtually eliminates MTCT
HIV transmission and/or deaths between 1 to 6 months according to pre-delivery length of ART (n= 2,161 infants)

Adequate Duration of Pre-delivery ARVs is a Key Determinant of Vertical Transmission

<table>
<thead>
<tr>
<th></th>
<th>1-30 days</th>
<th>31-90</th>
<th>&gt;90</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV+</td>
<td>3.6</td>
<td>1</td>
<td>0.3</td>
</tr>
<tr>
<td>HIV+ &amp; Death</td>
<td>5.7</td>
<td>2.9</td>
<td>2</td>
</tr>
</tbody>
</table>

\[ p = <0.001 \]
\[ p = 0.011 \]

DREAM COHORT

Marazzi MC et al. 5th IAS, Cape Town 2009
Treatment vs Prophylaxis

• HAART for PMTCT common in developed world

• PROMISE HS (CROI 2015) – compares Options A, B and B+:

<table>
<thead>
<tr>
<th>OUTCOME (N in analyses)</th>
<th>Arm A ZDV/NVP</th>
<th>Arm B ZDV/3TC/LPV-r</th>
<th>Arm C TRV/LPV-r</th>
<th>P Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>All women, N= 3523; (3240 1077BF; 283 1077FF)</td>
<td>N=1543 (V3, N=413)</td>
<td>N=1541 (V3, N=410)</td>
<td>N=439 (V3, N=406)</td>
<td>A vs B A vs C B vs C</td>
</tr>
<tr>
<td>Infant HIV Infection Rates by Age 14 Days (N=3096)</td>
<td>1.8% (25/1386)</td>
<td>0.5% (7/1385)</td>
<td>0.6% (2/325)</td>
<td>Combined Triple ARV arms vs Arm A: -1.28% (-2.11%, -0.44%)**</td>
</tr>
</tbody>
</table>
HPTN 052

- Discordant couples
- Immediate vs deferred treatment of infected partner (CD4 350 – 550)
- 96% reduction in transmission

PROMISE Study, CROI 2015:
- Maternal cART significantly better PMTCT than prophylactic maternal AZT & sdNVP (Option A)

Hot off the press!!!!

- Zero transmissions in 58,000 condomless sexual exposures in sero-different couples where infected partner was on suppressive ART. Rodger et al. JAMA 2016

Treatment as Prevention

- Game-changer !!!!
Cautionary note......unintended consequences.

<table>
<thead>
<tr>
<th>OUTCOME (N in analyses)</th>
<th>Arm A (ZDV/NVP)</th>
<th>Arm B (ZDV/3TC/LPV+)</th>
<th>Arm C (TRV/LPV-r)</th>
<th>P Value* A vs B</th>
<th>A vs C</th>
<th>B vs C</th>
</tr>
</thead>
<tbody>
<tr>
<td>All women, N= 3523; (3240 1077BF; 283 1077FF)</td>
<td>6.7% (22/329)</td>
<td>4.3% (14/332)</td>
<td>9.2% (29/314)</td>
<td>-</td>
<td>0.25</td>
<td>0.02</td>
</tr>
<tr>
<td>(Version 3 (V3), N= 1229)</td>
<td></td>
<td></td>
<td></td>
<td>0.3% (1/315)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Severe 'Adverse Pregnancy Outcome' (N=965)</td>
<td></td>
<td></td>
<td></td>
<td>0.6% (2/319)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>VLBW &lt;1500 g (N=935)</td>
<td></td>
<td></td>
<td></td>
<td>2.0% (6/301)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>VPTD &lt;34 weeks (N=1022)</td>
<td></td>
<td></td>
<td></td>
<td>-</td>
<td>0.06</td>
<td>0.17</td>
</tr>
<tr>
<td>Infant Deaths by Age 14 Days (All infants, N=2851)</td>
<td>2.0% (28/1432)</td>
<td>1.2% (17/1412)</td>
<td>4.0% (15/373)</td>
<td>0.13</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Infant Deaths by Age 14 Days (V3 infants, N=1036)</td>
<td>3.2% (11/349)</td>
<td>0.6% (2/346)</td>
<td>4.4% (15/341)</td>
<td>-</td>
<td>0.43</td>
<td>0.001</td>
</tr>
</tbody>
</table>

#1077BF and 1077FF refer to the breast-feeding (1077BF) and formula-feeding (1077FF) genotypes.

May require improvements in neonatal care – MSSN!!
Another Unintended Consequence: Infant Mortality In Trials From Not BF e.g. HPTN 046

• Daily infant NVP for 6wk vs 6 months

• Overall VT @ 6/12: **NVP = 1,2%;** Placebo = 2,4%; p=0,048 (Loses significance after 6 months)

• Maternal CD4 > 350: @ 9/12: **NVP = 0,9%** and Placebo = 3,3% (p=0,014)

★ 2/3 deaths in 2\textsuperscript{nd} 6 months \textbf{after} BF cessation

Maldonado: CROI 2011
Developing World Feeding Policy Evolution

• HIV burden is greatest in the developing world and in communities with high background IMR
• HIV infected infants have greatest mortality
• HIVEU infants > mortality than non-HIVE
• Avoiding breastfeeding prevents postnatal vertical transmission but incurs significant mortality and morbidity.
Breastfeeding: Cornerstone of Child Survival

Relative risk of infectious disease mortality from never breastfeeding

- < 2 mths: 5.8 [95% CI: 3.4–9.8]
- 4–5 mths: 2.6 (95% CI: 1.6–3.9)
- 6–8 mths: 1.8 (95% CI: 1.2–2.8)
- 9–11 mths: 1.4 (95% CI: 0.8–2.6)


Pooled data from 6 countries.
Research on making breastfeeding safer

• 1999 (pre-ARVs): Exclusive breastfeeding reduces risk of postnatal VT (Coutsoudis & Coovadia)

• 2004: Ross & Piwoz model (Pre ARVs): If background IMR > 40 mortality from not breastfeeding > mortality from breastfeeding)

• Post 2004:
  – BF and infant NVP: SWEN, PEPI, BAN, HPTN 046
  – BF and maternal ART: Kesho Bora, Mma Bana, HPTN 046, etc. VT<1%
  – PROMISE HS, BF and FF
Timing the Introduction of Replacement Feeding According to Background Infant Mortality Rate
BAN: Probability HIV positive by week 28 visit in infants uninfected at birth (maternal CD4>250)

Control vs Maternal HAART: p = 0.0032
Control vs Infant NVP: p <0.0001
Maternal HAART vs Infant NVP: p = 0.1203
The Game-Changer: ARVs reduce the Risk Of BF Transmission to less than 1%

Answer: Reduce VT risk of breastfeeding!
BF Transmission Is Reduced To < 1% By EBF And ARVs So There’s No Safe Time To Introduce Replacement Feeding In Developing World

Additional Risk of Death

Not Breastfed

Breastfed

Lines don’t intersect so No optimum age to introduce formula

Age
PROMISE 1077BF: Postnatal MTCT (Primary Analysis)

At 6 months of age, estimate 0.3% (95% CI, 0.1-0.6)

At 9 months of age, estimate 0.5% (95% CI, 0.2-0.8)

At 12 months of age, estimate 0.6% (95% CI, 0.4-1.1)
Infant 12-month survival rate was extremely high (98.9%) and did not differ significantly by study arm.
EVOLUTION OF POLICY AND ITS EFFECT
Timing of HIV Transmission (Pre ART, non Breast-Feeding cohort)

- Transmission risk is small prior to 28 weeks gestation, rises towards term and peaks during labour and delivery.
- Maternal IP Rx + infant PEP reduce IP but not IU risk.
- Infant PEP reduces IP proportion and PP risk.
- Boosted infant PEP targets brief period of intense IP risk.

**Infant & Maternal sdNVP**

**Dual Rx/HAAART**

**IU infection: Birth PCR pos**

**Early ART = early disease control**
Regimens
Short-short targeted IP risk
Short-long when IP risk high but couldn’t reduce IU MTCT
Long-long approach covers IU, IP and PP
Treatment as prophylaxis
Test and treat, no delay

PREVENTION POLICY EVOLUTION
### Table 1. Three options for PMTCT programmes

<table>
<thead>
<tr>
<th></th>
<th>Woman receives:</th>
<th>Prophylaxis (for CD4 count &gt; 350 cells/mm²)</th>
<th>Infant receives:</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Option A</strong></td>
<td>Triple ARVs starting as soon as diagnosed, continued for life</td>
<td>Antepartum: AZT starting as early as 14 weeks gestation</td>
<td>Daily NVP from birth through 1 week beyond complete cessation of breastfeeding; or, if not breastfeeding or if mother is on treatment, through age 4–6 weeks</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Intrapartum: at onset of labour, sdNVP and first dose of AZT/3TC</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Postpartum: daily AZT/3TC through 7 days postpartum</td>
<td></td>
</tr>
<tr>
<td><strong>Option B</strong></td>
<td>Same initial ARVs for both:</td>
<td>Triple ARVs starting as early as 14 weeks gestation and continued intrapartum and through childbirth if not breastfeeding or until 1 week after cessation of all breastfeeding</td>
<td>Daily NVP or AZT from birth through age 4–6 weeks regardless of infant feeding method</td>
</tr>
<tr>
<td></td>
<td>Triple ARVs starting as soon as diagnosed, continued for life</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Option B+</strong></td>
<td>Same for treatment and prophylaxis:</td>
<td>Regardless of CD4 count, triple ARVs starting as soon as diagnosed, continued for life</td>
<td>Daily NVP or AZT from birth through age 4–6 weeks regardless of infant feeding method</td>
</tr>
</tbody>
</table>

Note: *Triple ARVs* refers to the use of one of the recommended 3-drug fully suppressive treatment options.

* Recommended in WHO 2010 PMTCT guidelines

* True only for EFV-based first-line ART; NVP-based ART not recommended for prophylaxis (CD4 > 350)

* Formal recommendations for Option B+ have not been made, but presumably ART would start at diagnosis.
Option B+

- **All** pregnant women eligible for ART at diagnosis, **continued for life**
- FDC (EFZ, FTC and TDF): one tablet once a day – promotes adherence, affordable
- Simplifies Program
- Strongly supports breastfeeding
- Preconception ART for next pregnancy
- Reduces horizontal transmission in the community – Public Health Benefit
- Individual Health Benefits
PMTCT Is Effective

Figure 3: The HIV prevalence epidemic curve among antenatal women, South Africa, 1990 to 2012 (Source: NDoH, 2013)
### Perinatal Infant HIV-Exposure and MTCT: Weighted Results by Province and National % (95% CI)

<table>
<thead>
<tr>
<th>Province</th>
<th>2010</th>
<th>2011</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Infant HIV-Exposed</td>
<td>MTCT % (95% CI)</td>
</tr>
<tr>
<td>Eastern Cape</td>
<td>30.0 (26.3-33.7)</td>
<td>4.7 (2.4-7.0)*</td>
</tr>
<tr>
<td>Free State</td>
<td>31.1 (28.9-33.3)</td>
<td>5.9 (3.8-8.0)</td>
</tr>
<tr>
<td>Gauteng</td>
<td>30.2 (27.7-32.8)</td>
<td>2.5 (1.5-3.6)</td>
</tr>
<tr>
<td>KwaZulu Natal</td>
<td>43.9 (39.7-48.0)</td>
<td>2.9 (1.7-4.0)</td>
</tr>
<tr>
<td>Limpopo</td>
<td>22.6 (20.4-24.8)</td>
<td>3.6 (1.4-5.8)</td>
</tr>
<tr>
<td>Mpumalanga</td>
<td>36.2 (33.6-38.9)</td>
<td>5.7 (4.1-7.3)</td>
</tr>
<tr>
<td>Northern Cape</td>
<td>15.6 (13.0-18.3)</td>
<td>1.4 (0.1-3.4)*</td>
</tr>
<tr>
<td>Northwest</td>
<td>30.9 (28.6-33.1)</td>
<td>4.4 (2.9-5.9)</td>
</tr>
<tr>
<td>Western Cape</td>
<td>20.8 (16.8-24.9)</td>
<td>3.9 (1.9-5.8)</td>
</tr>
<tr>
<td><strong>National</strong></td>
<td><strong>31.4% (30.1-32.6%)</strong></td>
<td><strong>3.5 (2.9-4.1)</strong></td>
</tr>
</tbody>
</table>

*Note unstable estimates due to smaller sample size realisation precision is low*
Transmission Rate: W Cape

Year | Percentage
---|---
2003 | 17.6
2004 | 10.3
2005 | 6.1
2006 | 5.4
2007 | 5
2008 | 4.5
2009 | 3.6
2010 | 3.2
2011 | 1.9

From ppt Prof G Theron
Thanks to Pearl van Niekerk, PMTCT coordinator
Further gains to EMTCT and child survival ARE possible...
More ART-based PMTCT

Saving Mothers 2011-2103
Overall MTCT is down especially due to a reduction in IP and BF transmission. Suboptimal ANC/PMTCT explains relatively high proportion due to IU transmission.

**FIGURE 1:** Risks of HIV transmission with (in red) and without (in purple) antiretroviral drugs occurring during the intrauterine, intrapartum and during months 1–9 via breastfeeding. The risks of transmission amongst mothers who are non-adherent, failing therapy or drug resistant are likely to lie between these two estimates.

Kuhn, Kroon. S Afr J HIV Med. 2015
Maternal
Infant Prophylaxis
Infant Feeding
Infant Testing

CURRENT WCP GUIDELINES
The Western Cape Consolidated Guidelines for HIV Treatment:
Prevention of Mother-to-Child Transmission of HIV (PMTCT),
Children, Adolescents and Adults.
2015 (Amended Version)

2016 RXH HIV Symposium

NATIONAL CONSOLIDATED GUIDELINES APP FROM OPEN MEDICINE PROJECT
Maternal testing, treatment and VL monitoring

- Test at booking, 20 weeks, 32 weeks, delivery, every 3 months during breastfeeding
- If positive: initiate ART (1st line is FDC: Tenofovir 300mg, Emtricitibine 200mg, Efavirenz 600mg)
- VL Monitoring after 3 months ART and if > 1000, adherence counselling and repeat VL in 4 weeks.
- Complex viral load monitoring algorithm - depends on result, gestation and response to intensified adherence counselling
Increased Risk Scenarios

• Undiagnosed until labour: stat NVP, Truvada and 3 hourly AZT
• VL > 1000 despite intensified adherence support (might consider El. C/S)
• VL unknown even if adequate ART duration (usually caregiver oversight)
• Viral rebound
• SPTL, PPPROM, Chorioamnionitis
• Other co-morbidities
CURRENT WCP GUIDELINES
Low Risk

• Counsel on importance of ARV adherence to prevent transmission
• Demonstrate administration and back demonstration
• Daily NVP for 6 weeks, return if problems

Table 3: Post-exposure prophylaxis (PEP) in HIV-exposed infants#

<table>
<thead>
<tr>
<th>Subgroup of HIV-exposed infants</th>
<th>ARVs for PEP</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Low risk of HIV transmission at birth:</td>
<td>Nevirapine daily for 6 weeks (regardless of feeding choice)</td>
</tr>
<tr>
<td>• Mother on ART with documented VL &lt;1000 copies/ml &lt;12 weeks before delivery</td>
<td></td>
</tr>
</tbody>
</table>

Do HIV PCR* at birth or at first presentation to facility. If positive, do confirmatory PCR and transition to ART. If negative, repeat PCR at 10 weeks and 6 weeks after final breastfeed.
Table 5: Oral dosing of Nevirapine for PEP in HIV-exposed infants

<table>
<thead>
<tr>
<th>Birth Weight</th>
<th>Age at exposure</th>
<th>Daily Dosage</th>
<th>Daily Volume</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;2.0kg</td>
<td>Birth to 2 weeks</td>
<td>2mg/kg</td>
<td>0.2 ml/kg</td>
</tr>
<tr>
<td></td>
<td>2 to 6 weeks</td>
<td>4mg/kg</td>
<td>0.4 ml/kg</td>
</tr>
<tr>
<td>2.0 – 2.5kg</td>
<td>Birth to 6 weeks</td>
<td>10mg</td>
<td>1ml</td>
</tr>
<tr>
<td>&gt;2.5kg</td>
<td>Birth to 6 weeks</td>
<td>15mg</td>
<td>1.5ml</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Age at exposure</th>
<th>Daily Dosage</th>
<th>Daily Volume</th>
</tr>
</thead>
<tbody>
<tr>
<td>*6 weeks to 6 months</td>
<td>20mg</td>
<td>2ml</td>
</tr>
<tr>
<td>6 months to 9 months</td>
<td>30mg</td>
<td>3ml</td>
</tr>
<tr>
<td>9 months to 12 months</td>
<td>40mg</td>
<td>4ml</td>
</tr>
</tbody>
</table>

*Consider dose of 4mg/kg if still an in-patient and weighs <2kg at 6-12 weeks. Also consider weight-based dosing if severely underweight for age at discharge.
Increased Risk

- **In utero transmission**
  - No ART or started > 28 weeks gestation
  - High VL or Viral rebound
  - Co morbidity (TB, Syphilis)
  - Symptomatic baby

- Urgent result of birth PCR and, if positive, urgent ART
- cARP as likely ↑ IP risk too

- **Intra partum transmission**
  - VL > 1000 during labour
  - Chorioamnionitis
  - PPPROM
  - SPTL

- Needs combination PEP (AZT & NVP) for 6 weeks as PEP for IP exposure and if BF, extended NVP for BF exposure until VL<1000
- Birth PCR as likely ↑ IU risk too
### METRO WEST Jan-June 2013

<table>
<thead>
<tr>
<th></th>
<th>2010</th>
<th>2011</th>
<th>2012</th>
<th>2013 Jan-June</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Caesarean Section Rate</strong></td>
<td>24.2%</td>
<td>25.3%</td>
<td>27.8%</td>
<td>28%</td>
</tr>
<tr>
<td><strong>Births Before Arrival</strong></td>
<td>3.6%</td>
<td>3.5%</td>
<td>3.2%</td>
<td>2.9%</td>
</tr>
<tr>
<td><strong>No Antenatal care “UNBOOKED”</strong></td>
<td>5.8%</td>
<td>5.9%</td>
<td>5.1%</td>
<td>5.5%</td>
</tr>
</tbody>
</table>

- Thanks to Metro West PPIP Team
- Dr C Nelson, Dr L Dietrich, Dr D Nage and Dr L Jacobs
HPTN 040: cARP Halves Intrapartum Transmission When No Prelabour ART

Proportion with HIV transmission

Nielsen Saines NEJM 2012;366: 2368-79

2016 RXH HIV Symposium
2015 WCP Consolidated Guidelines (amended and corrected)

Non-Low-Risk

2. High risk of HIV transmission at birth:
   - Mother on ART with most recent VL ≥1000 copies/ml
   - Mother on ART with VL unknown <12 weeks before delivery**
   - Mother not on ART or initiated ART <12 weeks before delivery
   - Mother newly diagnosed HIV-positive during labour or <72 hours postpartum
   - Increased risk of HIV transmission during labour and delivery (irrespective of maternal VL):
     o Clinical chorioamnionitis
     o Spontaneous preterm labour (<37 weeks gestation)
     o Prolonged rupture of membranes > 18 hours
   - Unknown maternal HIV status or abandoned/orphaned infant (exposure confirmed with rapid HIV antibody test)

If breastfeeding:

- Nevirapine daily for at least 12 weeks
- Zidovudine twice daily for 6 weeks
(Only stop NVP once maternal VL <1000 copies/ml.)

If formula feeding:

- Nevirapine daily for 6 weeks
- Zidovudine twice daily for 6 weeks

Do HIV PCR* at birth or at first presentation to facility. If positive, do confirmatory PCR and transition to ART. If negative, repeat PCR at 10 weeks, around 18 weeks (6 weeks after stopping NVP) and 6 weeks after final breastfeed.
Table 4: Oral dosing of Zidovudine for PEP in HIV-exposed infants

<table>
<thead>
<tr>
<th>Zidovudine (AZT) syrup (10mg/ml)</th>
<th>Birth weight / gestational age</th>
<th>Age at exposure</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>If gestational age &lt;35 weeks</td>
<td>Birth to 6 weeks</td>
<td>2 mg/kg/dose 12 hourly (0.2 ml/kg/dose 12 hourly)</td>
<td></td>
</tr>
<tr>
<td>&lt;3 kg and &gt;35 weeks</td>
<td>Birth to 6 weeks</td>
<td>4 mg/kg/dose 12 hourly (0.4 ml/kg/dose 12 hourly)</td>
<td></td>
</tr>
<tr>
<td>&gt;3 kg and &gt;35 weeks</td>
<td>Birth to 6 weeks</td>
<td>12 mg 12 hourly (1.2 ml 12 hourly)</td>
<td></td>
</tr>
<tr>
<td>&gt;3 kg</td>
<td>&gt;6 weeks</td>
<td>Dose according to weight-based dosing chart (2013)</td>
<td></td>
</tr>
</tbody>
</table>

CTX prophylaxis: From 6 weeks until 10 week PCR neg if FF or until post weaning PCR neg if BF.
If PCR pos extended prophylaxis from 4-6 weeks of age
Testing

CURRENT WCP GUIDELINES
### Table 2: HIV testing in HIV-exposed infants

<table>
<thead>
<tr>
<th>Time of HIV test</th>
<th>Who should be tested</th>
<th>Which test should be used</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>At birth</strong></td>
<td>All HIV-exposed infants Abandoned newborns/orphans (HIV-exposure confirmed with Rapid Determine * test</td>
<td>HIV PCR test If positive, confirm with a 2\textsuperscript{nd} HIV PCR test</td>
</tr>
<tr>
<td><strong>At 10 weeks</strong></td>
<td>All HIV-exposed infants not on ART (irrespective of feeding choice)</td>
<td>HIV PCR test If positive, confirm with a 2\textsuperscript{nd} HIV PCR test</td>
</tr>
<tr>
<td><strong>Around 18 weeks</strong></td>
<td>Breastfeeding HIV-exposed infants who received NVP for 12 weeks then stopped *If NVP is extended beyond 12 weeks, do this test 6 weeks after final NVP</td>
<td>HIV PCR test If positive, confirm with a 2\textsuperscript{nd} HIV PCR test</td>
</tr>
<tr>
<td><strong>6 weeks after final breastfeed</strong></td>
<td>All HIV-exposed infants who were breastfed</td>
<td>Age appropriate test</td>
</tr>
</tbody>
</table>

Birth PCR test detects *in utero* transmissions. It cannot detect *intra partum* transmissions. Ten week PCR test detects both IU and IP transmissions but may miss some IP transmissions especially if extended NVP.
Overall MTCT is down especially due to a reduction in IP and BF transmission. Suboptimal or late ANC booking and PMTCT explains relatively high proportion due to IU transmission.

**FIGURE 1:** Risks of HIV transmission with (in red) and without (in purple) antiretroviral drugs occurring during the intrauterine, intrapartum and during months 1–9 via breastfeeding. The risks of transmission amongst mothers who are non-adherent, failing therapy or drug resistant are likely to lie between these two estimates.

Kuhn, Kroon. S Afr J HIV Med. 2015
Emergence of a peak in early infant mortality Bourne et al.  
*AIDS 2009, 23:101–106*  

Fig. 2. Graphical representation of likely HIV/AIDS-related deaths, at ages 1–11 months, in South Africa during 1997–2002.

Six week PCR too late for many of IU transmissions

EID @ 6 Weeks is too late for IU infected babies
HPTN 040: PCR@6 Weeks Misses A Third Of IP Transmission

Nielsen Saines NEJM 2012;366: 2368-79
Feeding

CURRENT WCP GUIDELINES
Low risk intensity:
8-12 hours of labour has the same risk of transmission as 18 months of breastfeeding !!!

Health gains from breastfeeding, need >6 wks NVP or suppressive maternal cART
Overall MTCT is down especially due to a reduction in IP and BF transmission. The proportion due to IU transmission is increased because of late access to ANC/PMTCT.

**FIGURE 1:** Risks of HIV transmission with (in red) and without (in purple) antiretroviral drugs occurring during the intrauterine, intrapartum and during months 1–9 via breastfeeding. The risks of transmission amongst mothers who are non-adherent, failing therapy or drug resistant are likely to lie between these two estimates.

Kuhn, Kroon. S Afr J HIV Med. 2015
PROMISE 1077BF: Postnatal MTCT
(Primary Analysis)

At 6 months of age, estimate 0.3%
(95% CI, 0.1-0.6)

At 9 months of age, estimate 0.5%
(95% CI, 0.2-0.8)

At 12 months of age, estimate 0.6%
(95% CI, 0.4-1.1)
Feeding

• EBF with maternal ART cover is default
• Actively assess if feeding choice is best. If not, explore reasons and advise.
• FF only if AFASS compliant, medical indication or failing 2\textsuperscript{nd} line ART (and AFASS compliant?)
• Extended infant DNP if inadequate maternal suppression?
• May be role for heat-treatment of EBM esp with prems – preserves option of EBF.
• Human Milk Banking
MOST IMPORTANT

• Viral control by optimising maternal ART
• Exclusive breastfeeding for the first 6 months of life and thereafter complementary feeding to 12 months of age is the ideal but not always possible in real life
  – Some mixed feeding in first 6 months is not a reason to stop breastfeeding altogether
  – If unable to EBF for first 6 months, it is not a reason to avoid breastfeeding altogether
Increased Risk Scenarios

• New HIV infection during breastfeeding
• No maternal ART
• Failing 2\textsuperscript{nd} line ART
• Early mixed feeding with solids and breast milk
• Formula feeding in low resource settings
<table>
<thead>
<tr>
<th>RECOMMENDATIONS</th>
<th>Strength of the recommendation</th>
<th>Quality of the evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. The duration of breastfeeding by mothers living with HIV: For how long should a mother living with HIV breastfeed if she is receiving ART and there is no evidence of clinical, immune or viral failure?</td>
<td>Strong</td>
<td>12 months: low</td>
</tr>
<tr>
<td>Mother's living with HIV should breastfeed for at least 12 months and may continue breastfeeding for up to 24 months or longer (similar to the general population) while being fully supported for ART adherence (see the WHO consolidated guidelines on ARV drugs for interventions to optimize adherence).</td>
<td></td>
<td>24 months: very low</td>
</tr>
<tr>
<td>The Guideline Development Group agreed that recommendation 1 should be framed by the following statement.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>In settings where health services provide and support lifelong ART, including adherence counselling, and promote and support breastfeeding among women living with HIV, the duration of breastfeeding should not be restricted.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>“Mothers known to be HIV-infected (and whose infants are HIV uninfected or of unknown HIV status) should exclusively breastfeed their infants for the first six months of life, introducing appropriate complementary foods thereafter and continue breastfeeding.”</td>
<td></td>
<td></td>
</tr>
<tr>
<td>“Breastfeeding should then only stop once a nutritionally adequate and safe diet without breast milk can be provided.”</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Table 2. 2016 guiding practice statements

<table>
<thead>
<tr>
<th>GUIDING PRACTICE STATEMENTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. When mothers living with HIV do not exclusively breastfeed</td>
</tr>
<tr>
<td>If a mother living with HIV does not exclusively breastfeed, is mixed feeding with ART better than no breastfeeding at all?</td>
</tr>
<tr>
<td>Mothers living with HIV and health-care workers can be reassured that ART reduces the risk of postnatal HIV transmission in the context of mixed feeding. Although exclusive breastfeeding is recommended, practising mixed feeding is not a reason to stop breastfeeding in the presence of ARV drugs.</td>
</tr>
<tr>
<td>2. When mothers living with HIV do not plan to breastfeed for 12 months</td>
</tr>
<tr>
<td>If a mother living with HIV plans to return to work or school, is a shorter duration of planned breastfeeding with ART better than no breastfeeding at all?</td>
</tr>
<tr>
<td>Mothers living with HIV and health-care workers can be reassured that shorter durations of breastfeeding of less than 12 months are better than never initiating breastfeeding at all.</td>
</tr>
</tbody>
</table>
THE FUTURE….. (IS NOW!)
THE FUTURE

• Guideline stability
• Systems strengthening
  • Improve coverage, uptake and access to ART
  • Task shifting (self testing/lay testers/ART clubs)
  • Preconception ART
  • Early ANC
  • Adherence and retention
  • Local innovations
• VEID and linkage to care
  • PCR POCT
  • Neonatal ART
• ART at diagnosis for all
• Unrestricted breastfeeding
### METRO WEST Jan-June 2013

<table>
<thead>
<tr>
<th></th>
<th>2010</th>
<th>2011</th>
<th>2012</th>
<th>2013 Jan-June</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Caesarean Section Rate</strong></td>
<td>24.2%</td>
<td>25.3%</td>
<td>27.8%</td>
<td>28%</td>
</tr>
<tr>
<td><strong>Births Before Arrival</strong></td>
<td>3.6%</td>
<td>3.5%</td>
<td>3.2%</td>
<td>2.9%</td>
</tr>
<tr>
<td><strong>No Antenatal care “UNBOOKED”</strong></td>
<td>5.8%</td>
<td>5.9%</td>
<td>5.1%</td>
<td>5.5%</td>
</tr>
</tbody>
</table>

- Thanks to Metro West PPIP Team
- Dr C Nelson, Dr L Dietrich, Dr D Nage and Dr L Jacobs
Behaviour change has not worked........

Test and treat and Treatment as prophylaxis may reduce incidence

- 15-24 years is key indicator group
- 47.5% of survey population
- MDG Target is 5.3% (75% less than baseline of 23.1%)!
Alere q HIV-1/2 Detect

Real Time PCR system targeting unspliced HIV RNA

Throughput 1 sample per instrument and cartridge taking approx 55 mins

Sample input 25 µl whole blood

Report qualitative result of HIV-1 and HIV-2 separately on printed sheets

Cartridge based point-of-care nucleic acid test for HIV-1/2
## Field performance: POC vs SOC.

<table>
<thead>
<tr>
<th></th>
<th>Alere q (first test)</th>
<th>Roche CAP/CTM HIV-1 PCR</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pos</td>
<td>Neg</td>
</tr>
<tr>
<td>Positive</td>
<td>11</td>
<td>1</td>
</tr>
<tr>
<td>Negative</td>
<td>1</td>
<td>242</td>
</tr>
<tr>
<td>Error</td>
<td>2</td>
<td>29</td>
</tr>
<tr>
<td>Total</td>
<td>14</td>
<td>272</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Alere q (first test)</th>
<th>Roche CAP/CTM HIV-1 PCR</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pos</td>
<td>Neg</td>
</tr>
<tr>
<td>Positive</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>Negative</td>
<td>0</td>
<td>162</td>
</tr>
<tr>
<td>Error</td>
<td>0</td>
<td>19</td>
</tr>
<tr>
<td>Total</td>
<td>4</td>
<td>181</td>
</tr>
</tbody>
</table>

- False positive recorded as “Equivocal” on SOC repeat test. (final status unknown)
- False negative on POC after 10 days infant combination prophylaxis (VL 1146 copies/ml)

NPV 89% [95% CI, 84-92%]  
NPV 90% [95% CI, 84-94%]

*7 patients tested at Mowbray were >21 days (PPV affected-75%)
Test and treat

• From 1 September 2016, it will be national policy that all HIV infected people will be eligible for ART
• This will be implemented from 1 April 2017 in WCP
PMTCT Can Be So Simple.....

• Identify HIV Positive reproductive age women (intensive testing and retesting)
• Initiate ART (FDC) and continue throughout pregnancy, breastfeeding and lifelong
• Ensure adherence and confirm with VL monitoring
• Test and retest their babies and treat positives immediately
• Breastfeed for as long as possible (ensuring adherence and VL suppression)
THANK YOU