Objectives of this Presentation

• To describe the global response to PMTCT
• To implement the essential programmatic components of PMTCT
  – The four pillars of PMTCT
  – The elements of the PMTCT cascade
  – PMTCT /SRH integration
• To implement evidence based solutions to address the challenge of retention in PMTCT programmes
Global PMTCT Coverage

77% coverage of ART in PMTCT

29% Nigeria
95% South Africa
Global Targets: UNAIDS

- Reach and sustain 95% of pregnant women living with HIV with lifelong HIV treatment by 2018

START FREE STAY FREE AIDS FREE

A SUPER-FAST-TRACK FRAMEWORK FOR ENDING AIDS AMONG CHILDREN, ADOLESCENTS AND YOUNG WOMEN BY 2020

START FREE

STAY FREE

AIDS FREE

START FREE

- Eliminate new HIV infections among children (aged 0-14) by reducing the number of children newly infected annually to less than 40,000 by 2018 and 20,000 by 2020.
- Reach and sustain 95% of pregnant women living with HIV with lifelong HIV treatment by 2018.
• **International standard** to allow validation to be carried out using a credible, **systematic approach**

• Monitoring of EMTCT achievement globally

• **Recognition of countries that have successfully eliminated** (and sustained elimination) of MTCT of HIV and/or syphilis
The four pillars of PMTCT?

1. Primary prevention
2. Family Planning
3. Testing and ARV Intervention for mum and baby
4. Keeping mum, dad and any positive baby alive ad well
Pillar 1: Primary prevention of HIV

- 8 elements of prevention in antenatal and postnatal care (WHO 2017)
  - HIV testing
  - HTS for all sexual and drug injecting partners
  - Partner referral for ART if HIV positive
  - Male partner referral for VMMC
  - STI screening and management
  - Condom promotion
  - Risk reduction counselling
  - Offer, start or continue PreP
Pillar 1: Primary prevention in pregnancy in context of PreP

- WHO 2017 released guidance on role of PreP in pregnancy and breastfeeding
- Support the safety of PreP during pregnancy and breastfeeding
Who to prioritise for PreP

Assessment of ongoing risk (risk scores may be used)
- Unknown partner status in high prevalence settings
- HIV positive partner not on ART or with unknown viral load
- Current STI including syphilis
- High risk exposures (female sex work; injecting drug use)
Pillar 2: Family Planning

• All HIV positive women should have access to family planning and should be given a choice of methods
• FP services should be integrated into ART clinics and provided as a one stop service
• For stable HIV clients receiving a differentiated model of ART refill, provision for FP must be made – ideally through use of a long lasting method or community delivery of FP
• Women should also be encouraged to “plan their families” – aiming to conceive when they are well and their viral load is suppressed
Pillar 2: Family Planning

- Longs acting methods are preferred
  - IUDs and IUS devices can be safely used by HIV positive women
  - Progestogen injections can be safely used – refer to local guidelines for frequency of use
- Oral combined contraceptives should not be used in combination with NNRTIs
- There is some evidence that the effectiveness of implants may be reduced when used in combination with EFV based regimens. However where supply of other forms of contraception may be limited this may remain an acceptable option. (see next slide partners for prevention study – real world use) Women should be counselled about the possible interaction with EFV and condom use advised as per all other methods of contraception
- Use of condoms should be advised with all contraception methods
Results were no different when limited to women using NVP.

Note: Arrows represent adjusted hazard ratios.
Pillar 3:
Identification of HIV positive women
Delivery of maternal ART
Management of the exposed infant
The PMTCT cascade

Attending ANC

Testing

HAART antenatal

HAART Delivery

HAART Postnatal

Exposed baby follow up

Community awareness to increase ANC attendance early
Use of pregnancy tests at community level
HIV Testing and Re-testing

• All pregnant women with unknown or negative status should be tested at their first antenatal visit
• Re-testing of HIV negative women is then recommended in the third trimester, at delivery (depending on timing of previous test) and regularly (6 mthly) during breast feeding
• Re-testing identifies sero-convertors and is an opportunity to re-identify those lost to follow up
• Where to re-test postnatally to catch these women? Re-testing may be integrated into EPI
• In low prevalence settings the frequency of re-testing should be adapted
## Example of PMTCT Re-testing guidance Zimbabwe

### Re-testing HIV negative pregnant and lactating women

<table>
<thead>
<tr>
<th>TIME OF PRESENTATION</th>
<th>WHEN TO TEST</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st or 2nd trimester: HIV-negative status known</td>
<td>Re-test in third trimester</td>
</tr>
<tr>
<td>1st or 2nd trimester: HIV-negative status unknown</td>
<td>Offer HIV test; re-test in third trimester</td>
</tr>
<tr>
<td>3rd trimester: HIV-negative status known</td>
<td>Re-test 6 weeks post delivery</td>
</tr>
<tr>
<td>3rd trimester: HIV-negative status unknown</td>
<td>Offer HIV test; re-test at 6 weeks post delivery</td>
</tr>
<tr>
<td>Labour and delivery: HIV-negative status known from third trimester</td>
<td>Re-test at 6 weeks post delivery</td>
</tr>
<tr>
<td>Labour and delivery: HIV-negative status known from 1st or 2nd trimester</td>
<td>Re-test immediately, then 6 monthly</td>
</tr>
<tr>
<td>Labour and delivery: HIV status unknown</td>
<td>Offer HIV test, then 6 monthly</td>
</tr>
<tr>
<td>Breastfeeding woman: HIV-negative status known</td>
<td>Re-test every 6 months until cessation of breastfeeding</td>
</tr>
<tr>
<td>Breastfeeding woman: HIV-negative status unknown</td>
<td>Offer HIV test immediately; re-test every 6 months until cessation of breastfeeding</td>
</tr>
</tbody>
</table>
Re-testiing in EPI experience from Malawi: IAS 2017

- A cross-sectional, non-experimental implementation pilot was conducted in 15 randomly selected health centres in two districts between June and November 2016.
- Mothers with an unknown HIV status, a previous HIV-negative result greater than 3 months prior to their visit, or a known HEI that had missed a scheduled HIV test were eligible for enrolment.
- Following routine immunisation services, eligible and consenting mothers were offered on-site referral for HIV testing and counselling for themselves and/or their infants.

Piloting the integration of routine maternal HIV screening in Malawi's immunisation programme: Stillson et al IAS 2017
3675 mothers were screened during immunisation visits at 15 health centres.

Of these women, 1977 were eligible and 1400 enrolled in the pilot.

Most mothers reported having a previous HIV test (94%), with a median time from last test of 6 months and median time since delivery of 3.3 months.

Of those enrolled, 96% received HIV testing and counselling, yielding 0.30% positive, 99% negative, and 0.37% indeterminate results.

54 eligible HEIs were identified and referred for testing, yielding 5.5% positive, 76% negative, and 18.5% unknown results.

Piloting the integration of routine maternal HIV screening in Malawi's immunisation programme: Stillson et al IAS 2017
Pillar 3: Antiretroviral Interventions for PMTCT: The Mother

- All HIV positive women should be started on lifelong TDF 3TC EFV when diagnosed antenatally, at delivery or postnatally.
- For further details on the clinical management of PMTCT refer to the guideline section on the PMTCT resource page.
Pillar 3: The Challenge of Maternal Retention on ART

Experience from MSF Malawi and Zimbabwe

(ICASA Dec 2015)
• 25 articles included - majority being from sub-Saharan Africa.
• For HIV+ pregnant and breastfeeding women, pooled retention estimates were 81% [95%CI: 73-87; I²=88%] at 6 months and 70% [95%CI: 62-77; I²=98%;] at 12 months on ART.
• Pooled proportion of HIV-exposed infants tested for HIV by PCR at 6-8 week post-partum was 66% [95%CI: 57%-75%; I²=86%].
• Frequent reported reasons for poor retention were initiation of ART on the same day as HIV diagnosis, facility resource constraints (e.g. long waiting hours, staff and drug shortages) and high-volume health facilities.
Malawi Thyolo: Characteristics of women at enrolment in PMTCT (N = 1,874)

- 98.5% WHO Stage 1 or 2
- 51% CD4 ≤350 cells/µl
- 76% CD4 ≤500 cells/µl

83% pregnant

98.5% WHO Stage 1 or 2

51% CD4 ≤350 cells/µl
76% CD4 ≤500 cells/µl
Malawi Thyolo: Time on ART prior to delivery

- Majority on ART for > 4 weeks – WHO definition for high risk infant < 4 weeks (but many countries saying < 8 weeks)
- PMTCT programmes should address reasons for late attendance to ANC
Malawi Thyolo: Retention in PMTCT

- Only 10.5% had a 6-month viral load test
- Of these, 94.4% virologically suppressed (VL <1,000 copies/ml)
Malawi National PMTCT Programme
30mth outcomes

- In facility-level data, **79.9% (52,525/65,749)** and **75.0% (40,509/54,029)** of all patients were still in care **6 and 12 months** after ART initiation. After **24 months**, **70.6% (17,257/24,245)** were retained, 26.8% were LTF, 1.5% had died and 0.6% stopped ART.

- In six large facilities with individual-level data, slightly more patients defaulted or discontinued treatment: **24 and 30 months after ART initiation retention was 67.2% and 62.6%**.

- Most patients were lost early and many did not return after the first visit (Figure 1), but after 18 months, further LTF was low.
Zimbabwe Gutu: Characteristics of women included in the analysis

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in years, median (IQR)</td>
<td>28 (22 to 33)</td>
</tr>
<tr>
<td>Pregnant at initiation, n (%)</td>
<td>435 (73.5%)</td>
</tr>
<tr>
<td>WHO Stage 1 or 2, n (%)</td>
<td>574 (98.0%)</td>
</tr>
<tr>
<td>CD4 &gt; 500 cells/µl, n (%)</td>
<td>142 (43.7%)</td>
</tr>
</tbody>
</table>
Zimbabwe Gutu: Retention in PMTCT

- 10.4% of clients did not return after initiation
- After 12 months attrition was very low
Zimbabwe Gutu: Factors associated with loss to follow up

- Risks for lost to follow up included:
  - Being initiated during pregnancy versus postnatally
  - Being initiated in a larger (district hospital) facility – unable to track silent transfer post delivery
  - Being a young adults
  - Having more advanced disease at presentation
Zimbabwe Gutu: Silent Transfers on ART

- Of the 56.5% traced, 31.5% of the women were still on ART at other facilities.
Zimbabwe Gutu: Reasons for defaulting

- Disclosure still remains the most common reason for defaulting in PMTCT.
Zimbabwe Gutu: Coverage of viral load testing & viral suppression

3 months on ART

- Eligible: 374
- Tested: 234 (63%)
- Suppressed: 215 (92%)

12 months on ART

- Eligible: 226
- Tested: 109 (48%)
- Suppressed: 92 (84%)
Pillar 3: Strategies to support maternal retention in PMTCT

- Integration of PMTCT and SRH Services: antenatally, at delivery and postnatally (mother infant pair clinics/ family approach)
- Quality counselling and adherence support
- Peer to peer support – “Mother Mentors”
- Male involvement – invitation letters
- Community engagement and awareness
Service Integration of PMTCT with ANC, delivery and PNC interventions

- One stop service (same day, same room, same health care worker);
  - ART delivered in ANC
  - Mother infant pair clinics (including EPI ideally)
- Cluster randomised controlled trial in Kenya (Turan et al. JAIDS 2015) comparing integrated with non-integrated services demonstrated
  - higher (69% versus 36%) rates of enrolment on ART
  - and faster (0 versus 8 days) rates of enrolment on ART
  - along with more frequent testing of the infant
Quality Counselling:
MSF PMTCT counselling tools

HIV / AIDS

P
Preventing
M
Mother
T
To
C
Child
T
Transmission

Tools available on SAMU website PMTCT resources
Implementation tools section
Patient Tracing

Identification of missed appointments

Communication to tracer

Tracer calls or visits patient

Tracer communicates back to HC
Peer to peer (mother to mother) support in PMTCT

RCT (M2M vs SOC) in South Africa showed significant impact on:

- RIC at 12 months: 91% vs 64%
- Disclosure rates: 82% vs 69%
- Return of the infant for early infant diagnosis: 60% vs 31%
- Schmitz et al IAS 2015
Male Involvement: Invitation letters

- Invitation card for partner of women who presents alone at 1\textsuperscript{st} ANC
- RCT invitation card vs SoC: 28\% vs 19\% presented with partner at ANC
Community Awareness

- Messages on importance of:
  - attending early for ANC
  - starting ART early
  - testing as a couple

Examples of IEC materials available on SAMU website
PMTCT resources – Implementation tools section

ALL HIV positive women that are pregnant or breastfeeding now qualify for ARVs at any CD4 count!
Viral Load Monitoring in PMTCT

• WHO does not currently make any different recommendation regarding the timing or frequency of VL testing in PMTCT
• Several national guidelines have made adaptations e.g.
  – For clients already on ART to perform a VL at first antenatal visit if previous VL more than 3-6 months ago
  – For newly initiated clients to perform the first VL at 3 months
  – For women initiating ART to perform the first VL earlier (mth 3 on ART)
  – To increase frequency of VL testing during pregnancy and breast feeding to 6 monthly
A cross-sectional study of HIV-infected pregnant women on ART at the first ANC under PMTCT Option B+ at Bwaila Hospital in Lilongwe, Malawi from June 2015 to December 2016.

A total of 434 women were tested for ART treatment failure
- 343 (82%) were in HIV-WHO stage 1
- 353 (82%) attended first ANC during the 2nd trimester.
- The overall prevalence of ART treatment failure was 7.1% (95% confidence interval (CI): 5.1 - 10.0).
- For women who knew their partners HIV status, women with HIV-infected partners had an indication of reduced odds of having developed treatment failure (OR = 0.45, 95% CI: 0.10 - 2.03) compared to those with HIV-uninfected partners.

Prevalence of antiretroviral therapy (ART) treatment failure among HIV-infected pregnant women at first antenatal care:
PMTCT Option B+ in Malawi (Chagomerana M et al IAS 2017)
Pillar 3: Management of the exposed infant
Pillar 3: Antiretroviral prophylaxis for the exposed infant

• The choice of antiretroviral prophylaxis for the exposed infant will depend on whether the infant is classified as high or low risk

• WHO defines a high risk HIV exposed baby to be born to mother
  – born to women with established HIV infection who have received less than four weeks of ART at the time of delivery, OR
  – born to women with established HIV infection with VL >1000 copies/mL in the four weeks before delivery, if VL available, OR
  – born to women with incident HIV infection during pregnancy or breastfeeding, OR
  – identified for the first time during the postpartum period, with or without a negative HIV test prenatally

• Some national guidelines have adapted these definitions
Pillar 3: Antiretroviral prophylaxis for the exposed infant

- **Low risk babies should receive**
  - If breastfeeding 6 weeks of infant prophylaxis with daily NVP
  - If having replacement feeding they should receive 4-6 weeks of daily NVP (or twice daily AZT)

- **High risk babies should receive**
  - Dual prophylaxis with daily AZT and NVP for 6 weeks whether they are breast or formula fed
  - Breast fed high risk infants should continue NVP or AZT alone for a further 6 weeks
Pillar 3: OI prophylaxis for the exposed infant

- All exposed infants should commence cotrimoxazole prophylaxis at 6 weeks.
- Cotrimoxazole prophylaxis is stopped once negative HIV status is confirmed 12 weeks after cessation of breastfeeding.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Strength of tablet or oral liquid (mg or mg/5ml)</th>
<th>3-5.9 kg</th>
<th>6-9.9 kg</th>
<th>10-13.9 kg</th>
<th>14-19.9 kg</th>
<th>20-24.9 kg</th>
<th>25-34.9 kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>CTX Suspension 200/40 per 5ml</td>
<td>2.5ml</td>
<td>5ml</td>
<td>5ml</td>
<td>10ml</td>
<td>10ml</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Tablets (dispersible) 100/20 mg</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>4</td>
<td>4</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Tablets (scored) 400/80 mg</td>
<td>-</td>
<td>half</td>
<td>half</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Tablets (scored) 800/160 mg</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>half</td>
<td>half</td>
<td>1</td>
<td></td>
</tr>
</tbody>
</table>
Pillar 3: HIV testing of exposed infants

- The EID algorithm can be found in the WHO and PMTCT guidelines in the guideline section of the PMTCT resource page.
- All exposed infants should be tested between 4-6 weeks using nucleic acid testing (NAT).
- In some countries birth EID may be introduced – in some contexts only for high risk infants; in some contexts for all infants.
- If tested negative at birth exposed infants should be re-tested at 6 weeks.
- Exposed infants are then re-tested with antibody test at 9 months, 3 mths after cessation of breast feeding and at any time the child presents with symptoms suggestive of HIV.
Pillar 3: HIV testing of exposed infants

- To improve the turn around time of EID results several point of care technologies are now available.
- These include
  - Xpert EID
  - Alere Q
- MSF has carried out a number of validation studies of these point of care technologies in Malawi, Zimbabwe and Kenya
- In Zimbabwe a study has been carried out to look at the use of Xpert for polyvalent testing for TB, VL and EID (and in the future HPV)
Pillar 3:
MSF experience of birth HIV testing in Khayelitsha South Africa

• Birth PCR testing was implemented using centralised testing on **high risk infants** in April 2014.

• From July 2015, PCRs were done on **all HIV-exposed infants**, using POC testing in addition to Roche PCR. A nurse was working seven days a week and an on-call doctor was available for neonatal ART initiation.
MSF Experience Birth EID: Khayletisha South Africa - Results

• Laboratory verification of the POC test was 100% specific and sensitive.
• 483 infants were tested using POC PCR in the clinic yielding one positive test (positivity rate 0.2%).
• All mothers received the POC PCR results.
• Median time to initiation for the positive infant on POC was 12 hours compared to a median of three days (range: 2-16 days) for 5 infants positive by Roche PCR.
Birth EID : Discussion Points

• Positivity rate was very low and all negative baby’s need subsequent testing at 6 weeks
• Cost of this additional testing versus the yield and impact on initiation of ART need to be assessed in other settings including rural sites where POC may not be at every facility
• Impact on retention and time to initiation on ART for any HIV positive infant needs further assessment in a range of contexts
PMTCT: Research Gaps

• VL monitoring in PMTCT
  – Impact and cost effectiveness of additional VL monitoring
• Re-testing in postpartum period
  – Feasibility of maternal repeat HIV testing in EPI
• Use of birth EID in programmatic settings
  – Feasibility
  – Yield
  – Impact on time to initiation
  – Cost effectiveness
• Feasibility of classification of exposed infants (high/low risk) and correct use of infant dual / single prophylaxis
PMTCT – Take home messages

• Globally there has been a successful scale up but still wide country variation exists
• All pillars of PMTCT need to be addressed for successful programming
• Each step of the PMTCT cascade need to be monitored to determine a successful programme
• Retention in PMTCT is a challenge – evidence based strategies to improve retention should be implemented
• The new WHO guidance on defining exposed infants as high and low risk with differing prophylaxis interventions requires further assessment in programme settings
• At birth testing if implemented should be documented in programme settings to assess the impact related to the additional costs