Data needs and use for PEPFAR PMTCT impact modeling

Tracy Creek, MD
Centers for Disease Control and Prevention
Global AIDS Program
PMTCT Team

Goals of (little) model

- Estimate (grossly) the population-level MTCT rate using:
  - New WHO guidelines
  - PEPFAR coverage targets (test 80% of women, give drugs to 85% of positives)
- Estimate costs to PEPFAR of implementing new guidelines

Data needed

- # Pregnant HIV-infected women
- MTCT rates over 1 year of BF for
  - Eligible women on ART
  - Option A and B
- Percent of women eligible for ART
- Drug costs

Assumptions

- Number of HIV+ pregnant women in 15 PEPFAR focus countries taken from the 2009 UN Universal Access Report
- PEPFAR's published target: among HIV+ pregnant women, 80% tested, 85% of those receive appropriate ARV (68% coverage)
  - All eligible women get HAART
  - All other women get option A or B
  - All women breastfeed for 12 months
- This is a simplified best case scenario (for policy discussion purposes only), but I tried to use some realism for the rest of the assumptions
- "Eligible women" CD4<350 or stage 3-4
  - CHAI meta-analysis says 40% CD4<350
  - Louise Kuhn recent paper says 68% CD4<350 or stage 3-4
  - 68% hasn't been documented anywhere else (probably because nobody is doing good staging, which is not going to improve fast), so I used halfway between the two, 54%

Transmission rate data used

- Data compiled
  - Mma Bana
  - Kesho Bora
  - Kibs
  - Mitra Plus
  - BAN
  - MTCT-Plus initiative
  - Botswana program data

Which transmission rates are realistic?

- Mma Bana shows the least MTCT - mothers started ARVs at 26-29 weeks
- Most studies had shorter ARV times and more MTCT
- 14 week start will be rare despite WHO guidelines – ANC median start 22 weeks, often later
- Real world will have wide range of start times, few at earlier end, more at later end
- The wide range of MTCT rates seen in the trials will probably be seen in reality too
- For this exercise, not worthwhile modeling 14 week start

The unstudied second six months of BF

- Data exists for first six months
- Extrapolate to the second six months – HOW?
  - Mothers on ART could have lower transmission rate since viral load will be dropping
  - Infant NVP will probably have similar efficacy the whole time since maternal viral load is ~static or increasing some
  - May or may not have decreasing baseline MTCT risk (independent of drugs) over time (depends on which data you use, ZEBS, BAN show different things)
  - Maybe an increase in MTCT around the weaning period? Theoretically possible, more engorgement, higher milk viral load, discussed in various papers. Maybe no increase if on drugs.
  - Net of all these – we just don't know. I decided to assume the same transmission rate through the whole year and take a median of all the studies.

Regimen	Mom CD4	Study/ country	MTCT 2- 6 wks	MTCT first ~6 months of BF	Estimated MTCT months ~6-12 of BF	Extrapolated total MTCT
Women/infants receiving PMTCT prophylaxis similar to PMTCT option A or B. Median MTCT risk=6%						
AZT/3TC/LPV from 28 weeks through BF	200-500	Kesho Bora/ Kenya, Burkina Faso, RSA	3.3%	1.9% in median 21 weeks BF* *Recalculated*	0.36% per month= 2.7% in 7 months	7.9%
AZT/3TC/NVP (or NLF) 34 weeks through 6m BF	>200	Mitra Plus/Tanzania	4.1%	1.2% at 6m, 97% BF, 17% still BF at 26 wk	0.2% per month= 1.2% in 6 months	6.5%
AZT started ~28 weeks +/- SD-NVP	>200 or unknown CD4	Botswana program data 2008-9	2.9%	N/a	N/a	6%
daily infant NVP during BF	>250	BAN/Malawi	N/a	1.7% in 7 months	0.2% per month= 1.0% in 5 months	
AZT/3TC/NVP (or NLF) from 36 weeks through BF	>250	KiBS/Kenya	3.8%	1.1% by 6m, told to wean at 6m	0.18% per month= 1% in 6 months	5.9%
ABC/AZT/3TC through pregnancy and BF	>200	Mma Bana/Botswana	1.4%	0.7% in 6 months	0.12% per month= 0.7% in 6 months	2.8%
LPV/r/AZT/3TC through pregnancy and BF	>200	Mma Bana/Botswana	0.4%	0 in 6 mos	0	0.4%

Regimen	Mom CD4	Study/ country	MTCT 2- 6 wks	MTCT first ~6 months of BF	Estimated MTCT months ~6-12 of BF	Extrapolated total MTCT
Women receiving HAART for their own health (median MTCT risk=9%)						
Cohort A: AZT/3TC/NVP through pregnancy (avg 7wk) and BF	<200	Kesho Bora/Kenya, Burkina Faso, RSA	3.7%	5.8% in median 20 weeks** *Recalculated*	1.2% per month= 8.4% in 7 months	17.9%
AZT/3TC/NVP from median 30 weeks through BF	<200	MTCT-Plus Initiative, Cote d'Ivoire	2.2%	1.9%-3.9%*** in avg 4.6 months	0.4-0.8% per month= 3.0- 5.9% in 7.4 months	7.1-12%**
AZT/3TC/NVP from 34 wks through BF	<250	KiBS/Kenya	4.3%	0.9% in 6 months	0.15% per month= 0.9% in 6 months	6.1%
AZT/3TC/NVP through pregnancy and BF	<200	Mma Bana/Botswana	0.6%	0 in 6 mos	0	0.6%

*The poster reported 1.6%, but **only 76% BF**, so I recalculated (413 infants, 76% bf so actually 314 infants, 6 transmissions=1.9%)
Paper reported 3.9%. Recalculated because of 111 women, only **61% breastfed (68 women, page 6 of paper). 4 infections out of 68 women=5.8%.
***Higher assumes all infections of unknown timing were postnatal; lower is if none were postnatal.

Another way of looking at it
(as explained by Lynne Mofenson)

- BAN control group (CD4>250) showed decreasing MTCT over time without drugs
  - 2-6 weeks 0.5% MTCT per week
  - 6-12 weeks 0.27% MTCT per week
  - 12-29 weeks 0.12% per week
- *ZEBS showed about 1% per month throughout the first year, so did Zvitambo (sicker women though).*
- Use the last, lowest rate, extrapolate to last six months =0.48% per month x 6=2.9%
- Then assume 90% efficacy in preventing transmission, because that's what the BAN infant NVP arm showed when compared to the BAN control group
- So reduce 2.9% by 90%= **0.3% total for the whole 6-12 month period**

Model outputs

- For presentation to OGAC, I used Lynne's way of looking at the second six months
- If you do this, and plug in 0.3% for the whole second 6 months for all the trials, the median MTCT rate for both prophylaxis and treatment is exactly 5%.

Estimated MTCT in PEPFAR countries using new WHO 2009 guidelines

80% counseling and testing x 85% ARV coverage = 68% overall ARV coverage

Drug regimen	Estimated MTCT rate	% HIV+ women receiving regimen	Number HIV+ women receiving regimen	Number of infant infections	Infant infections averted
None	35%	32%	308,544	107,990	0
HAART	5%	31% (46% of the 68% receiving drugs)	298,902	14,945	89,671
WHO Option A or B regimen	5%	37% (54% of the 68% receiving drugs)	356,754	17,838	107,026
		TOTAL	964,200	140,773 **(15% MTCT)**	196,697

Cost range in US$ depending on which regimen is used: $75,936,053 - $287,176,075

Alternative scenarios

Change to previous page	New population MTCT rate
Use my original estimate of 9% for HAART and 6% for Option A and B	16%
Use 85% ARV coverage instead of PEPFAR target of 68%	10%

Final thoughts

- Mma Bana shows us the promise of what could happen, at least for Option B, but we don't know what WILL happen
- Option A will be most widely used, least studied
- Over an entire year in the real world, expect more variable compliance than during short period a clinical trial – can't dismiss high outlier results
- Exactly what transmission rate we use does not change population MTCT rate dramatically
- Coverage level does change MTCT rate dramatically – this is what drives transmission in reality and in models - we need to focus on getting our numerators and denominators right!