# The cost-effectiveness of interventions to prevent mother-to-child HIV transmission when mothers do not require treatment for their own health: Case study of Malawi

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# Policy Context

- About 390,000 infants become infected with HIV annually; 90% of whom are in Africa.
- In 2010, the WHO released new PMTCT Guidelines for pregnant women not requiring ART for their own health (CD4 > 350 cells/μL):

  Option A: The mother receives ZDV during pregnancy, perinatal sdNVP and combivir tail; and the child daily nevirapine from birth until one week after end of breastfeeding

  *OR*

  Option B: The mother receives a three-drug regimen during pregnancy, and continued triple therapy to one week after end of breastfeeding

- In 2011, the Ministry of Health Malawi announced it would follow Option B+, providing ARVs for pregnant women for life.

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# Policy Context

## Decision Problem

- Using Malawi as a case study,

  *'How can a resource poor country, struggling to scale-up ART to its population in need, best use its available resources to prevent MTCT amongst mothers not in need of treatment for their own health?'*

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# Details of the Decision Model
## - A probabilistic decision-model, structured as a decision-tree

| | |
|---|---|
| Population: | Known HIV-1 infected pregnant women in Malawi who do not require treatment for their own health, presenting either<br>a) At delivery; or<br>b) Antenatally |
| Interventions: | a) Peri-/postnatally<br>• Standard of care (sd NVP, sc ARVs)<br>• Maternal triple antiretrovirals, with SOC<br>• Infant nevirapine, with SOC<br>b) Antenatally<br>• Maternal triple antiretrovirals (M-ARVs);<br>• Maternal ZVD; or<br>• Nothing |
| Source of clinical evidence: | a) BAN trial (Malawi)<br>b) Kesho Bora trial (Burkina Faso, Kenya, SA)<br>c) Mma Bana trial (Botswana)<br>- Maternal ARVs: AZT/3TC + LPV/r |

# Details of the Decision Model

| | |
|---|---|
| Outcomes: | HIV transmissions averted; QALYs-gained |
| Resource use and unit costs: | - Interventions costed taking a 'health sector perspective'.<br>- Drugs and healthcare visits costed according to Malawian national standards.<br>- Downstream treatment costs incorporated |
| Results: | Presented in terms of Incremental Cost Effectiveness Ratios (ICERS) $\frac{\Delta \text{ Costs}}{\Delta \text{ QALYs}}$ |
| Sensitivity and Scenario analyses: | Results subject to sampling uncertainty, and their robustness tested according to alternative model assumptions:<br>- Changes in drug regimens and prices (TDF/3TC/EFV)<br>- Earlier versus later antenatal initiation<br>- Other model parameters (e.g. discounting) |

| Results – Base Case | ICER per transmission-averted | ICER per QALY-gained |
|---|---|---|
| (1) Initiation at Delivery | | |
| Standard of care (SOC) | - | |
| Infant Nevirapine (I-NVP) | **$264.30** | **$15.57** |
| Maternal Antiretrovirals (M-ARVs) | Dominated | |
| (2) Antenatal Initiation | | |
| Antenatal maternal ZDV; followed by SOC | - | |
| Standard of care from delivery (SOC) | Dominated | |
| Infant Nevirapine (I-NVP) | Dominated | |
| Antenatal maternal ZDV; followed by I-NVP (WHO Option A) | **$667.44** | **$39.39** |
| Antenatal maternal ZDV; followed by M-ARVs | Dominated | |
| Maternal Antiretrovirals from delivery (M-ARVs) | Dominated | |
| Antenatal maternal ARVs; followed by I-NVP | **$172,861** | **$10,325** |
| Antenatal maternal ARVs; followed by M-ARVs (WHO Option B) | Dominated | |
| Antenatal maternal ARVs; followed by SOC | Dominated | |

Increasing in cost

Increasing in cost

# Results – Scenario Analyses (ICERs per QALY-gained)

| | ZDV/3TC + LPV/r | | TDF/3TC/EFV | |
|---|---|---|---|---|
| | Later antenatal initiation* (median of 6.4 weeks pre-delivery) BASE CASE | Earlier antenatal initiation** (median of 11 weeks of ART pre-delivery) | Later antenatal initiation* (median of 6.4 weeks pre-delivery) | Earlier antenatal initiation** (median of 11 weeks of ART pre-delivery) |
| (2) Antenatal Initiation | | | | |
| Antenatal maternal ZDV; followed by SOC | - | | - | |
| Antenatal maternal ZDV; followed by I-NVP (WHO Option A) | **$39.39** | **$38.09** | **$38.50** | **$37.22** |
| Antenatal maternal ARVs; followed by I-NVP | **$10,325** | **$7,236** | **$1,200** | **$603** |

* Effectiveness of interventions with later antenatal initiation from Kesho Bora trial

** Effectiveness of interventions with earlier antenatal initiation from Mma Bana trial

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# Determining Cost-Effectiveness

- Need to know whether ICERs represent a 'good buy'
  - Requires some knowledge over the 'opportunity costs' of resources
- The WHO advise that any intervention offering a unit of health gain (DALY-averted) at <3x GDP p.c. be recommended as *"relatively cost-effective"*, and one <1x GDP p.c. as *"very cost-effective"*
- Based upon Malawian GDP p.c. of $290 in 2009, this would result in an upper threshold of $870.
- It is not clear whether these thresholds do represent opportunity costs – *caution is required when interpreting results*.

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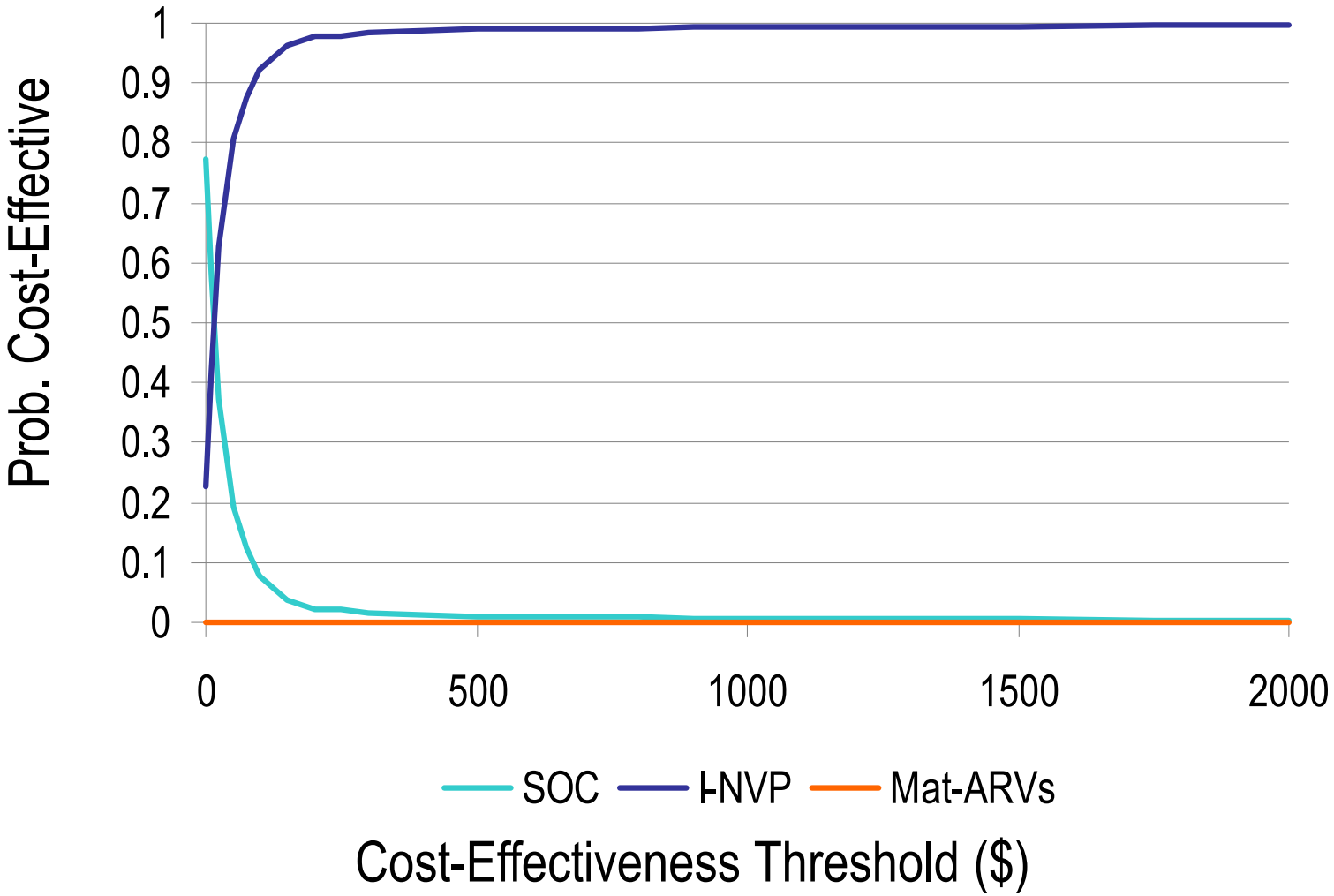
# Cost-Effectiveness Acceptability Curves (QALYs) - Initiation at delivery

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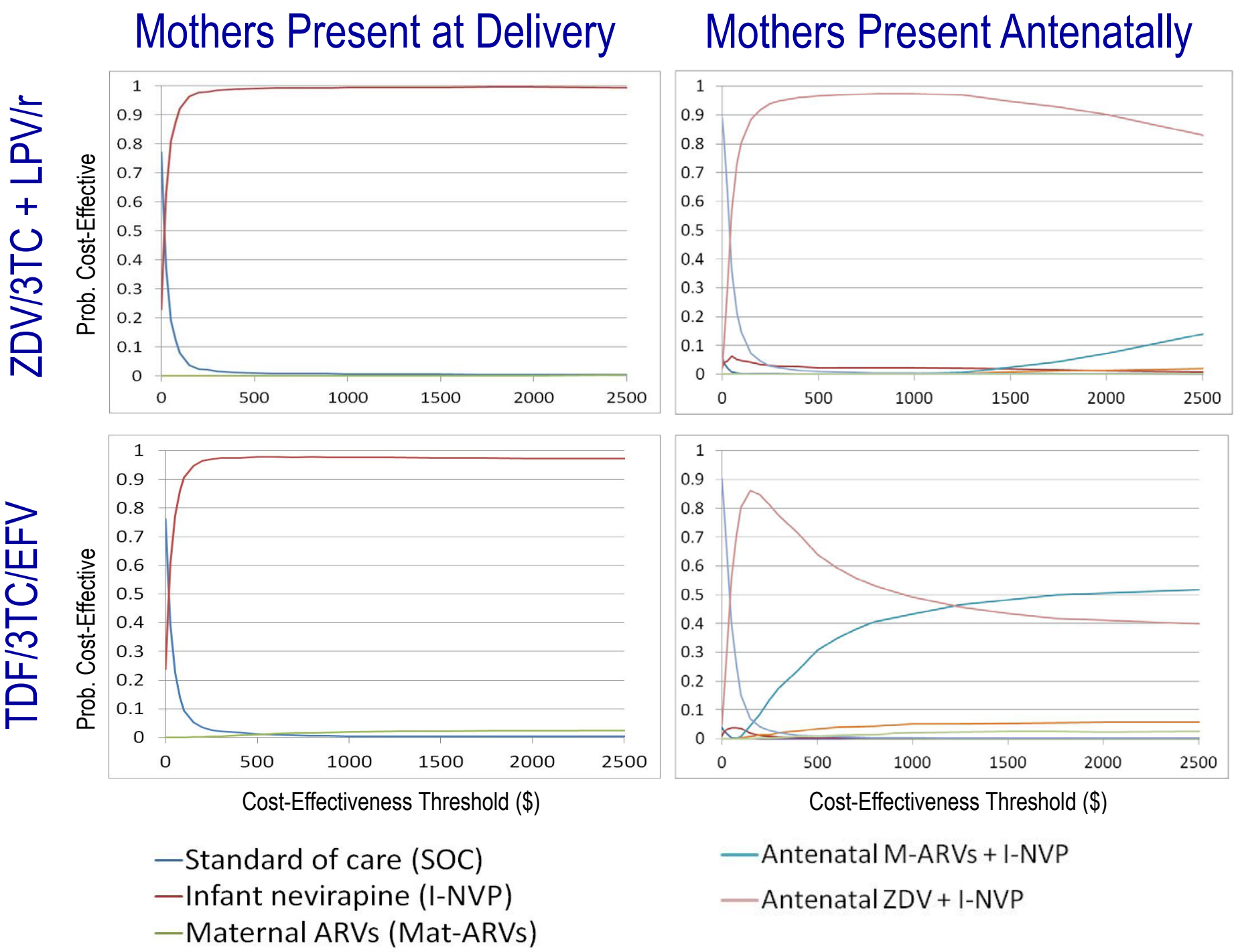
Mothers Present at Delivery
Mothers Present Antenatally
ZDV/3TC + LPV/r
TDF/3TC/EFV
Prob. Cost-Effective
Prob. Cost-Effective
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1
0
500
1000
1500
2000
2500
Cost-Effectiveness Threshold ($)
Cost-Effectiveness Threshold ($)
Standard of care (SOC)
Infant nevirapine (I-NVP)
Maternal ARVs (Mat-ARVs)
Antenatal M-ARVs + I-NVP
Antenatal ZDV + I-NVP

# Aggregate Analysis – Use of $1million Spend

| | | ZDV/3TC + LPV/r | TDF/3TC/EFV |
|---|---|---|---|
| | Antenatal ZDV; Infant NVP | Antenatal triple ARVs; Postpartum triple ARVs | Antenatal triple ARVs; Postpartum triple ARVs |
| Mean Incremental Cost Per Case (compared to SOC) | **$3.63** | **$607.85** | **$83.31** |
| Coverage Per Additional US $1m | **275,658** | **1,645** | **12,003** |
| Transmissions averted (compared to SOC) | **16,793** | **84** | **603** |
| QALYs gained (compared to SOC) | **284,812** | **1,424** | **10,299** |

Antenatal initiation at median of 6.4 weeks pre-delivery

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# Study Findings

- When mothers present at delivery, infant nevirapine during breastfeeding is likely to be a cost-effective strategy
- When mother present antenatally, receipt of ZDV during pregnancy followed by infant nevirapine throughout breastfeeding is likely to be cost-effective
- On the basis of future clinical evidence triple ARVs during pregnancy followed by postnatal infant nevirapine may be cost-effective if supported with sufficient resources and/or with lower ARV prices.

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# Limitations

- The model is based upon a *number of assumptions,* including
  - Predicated on PMTCT generating health gains for infants, not horizontal transmission
  - Used only trial data that was deemed reasonably comparable
  - Relies upon the external validity of trial findings
- There may also be other factors that policy-makers have reason to value

- *What about Option B+?*
  - Lack of data for evaluation
  - Total fertility in Malawi of 6 and mean birth spacing is 37mnths
  - Highly unlikely to be cost-effective for PMTCT because of cost of ARVs between births (when no vertical transmissions are averted)

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# Thank You

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# Are there other means to generate health gains?

Value of implementation analysis

- Based upon a cost-effectiveness threshold of $500:
  - The value of determining eligibility to AZT followed by infant nevirapine is US$688 (MOH EHP listed prices)/US$169 (CHAI listed prices), compared to an estimated cost of CD4 test of $4.50-9.00
  - An investment of up to $190 (MOH EHP prices)/US$191 (CHAI prices) would be worthwhile if it resulted in a mother initiating PMTCT at ANC instead of at delivery.

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