

# WHO recommendations

Diagnostic testing in infants

# Recommendations 2- testing in infants

| Intervention   | Reco   | QoE      | Comment  |
|--|--------|----------|--|
| At or around 6 weeks of age is most efficient time at which to perform a viral test for an HIV exposed infant                        | Strong | Low      | Programmatic expedience governed this recommendation- most infants are seen at this time and sensitivity and specificity for detection of infection acquired at or around delivery is >95% |
| Presumptive diagnosis of severe HIV may be made on clinical grounds with a history of HIV exposure and positive HIV antibody testing | Strong | Very low | Pragmatic and based on fact that early diagnosis not yet universally available   |

| <b>DNA</b>  |  |  |
|---|--|--|
| <b>Assay</b>  | <b>Advantages</b>  | <b>Disadvantages</b>   |
| <b>Amplicor DNA PCR</b>   | <ul style="list-style-type: none"> <li>✓ Widely used and validated</li> <li>✓ Not affected by exposure to antiretroviral medicines</li> <li>✓ Standardized reagents and kits</li> </ul>  | <ul style="list-style-type: none"> <li>+ Not useful in predicting the need for antiretroviral therapy</li> <li>+ Not licensed or approved for diagnostic purposes</li> </ul>   |
| <b>RNA</b> (also useful in assessing the likelihood of disease progression)   |  |  |
| <b>Assay</b>  | <b>Advantages</b>  | <b>Disadvantages</b>   |
| <b>AMPLICOR Monitor HIV-1 v1.5:</b> uses PCR to detect HIV, which is then made visible with a probe bound to an enzyme                                    | <ul style="list-style-type: none"> <li>✓ Uses an automated system that combines all amplification and reading steps in one instrument</li> <li>✓ Used for most types of HIV</li> <li>✓ High throughput</li> <li>✓ 0.2–0.5 ml of plasma, DBS</li> <li>✓ Can be used for other diseases</li> </ul>                                 | <ul style="list-style-type: none"> <li>+ Requires Cobas Ampliprep</li> <li>+ Potential for amplification errors</li> <li>+ Concern about possible low level RNA if using RNA DBS</li> <li>+ No standardized reagents and kits for diagnosis</li> <li>+ Not licensed or approved for diagnostic purposes</li> </ul> |
| <b>Branched DNA (bDNA) test:</b><br>RNA is released from plasma and then amplified prior to detection using enzymes that produce measurable colour change | <ul style="list-style-type: none"> <li>✓ Less risk of contamination than PCR</li> <li>✓ High throughput without the need of full automation, although full automation is possible</li> <li>✓ Can be used for other diseases</li> <li>✓ Uses plasma or DBS plasma</li> </ul>  | <ul style="list-style-type: none"> <li>+ Requires 1.0 ml of plasma</li> <li>+ May not be as reliable with non-B subtypes</li> <li>+ Concern about possible low level RNA if using RNA DBS</li> <li>+ Not licensed or approved for diagnostic purposes</li> </ul>   |
| <b>Nucleic acid sequence-based amplification NASBA</b><br><b>Nuclisens HIV-1 assay:</b>   | <ul style="list-style-type: none"> <li>✓ 0.1–0.2 ml of plasma, DBS or serum</li> <li>✓ High throughput and short turnaround time</li> <li>✓ Rapid results</li> <li>✓ Fully automated</li> <li>✓ Used for most types of HIV</li> <li>✓ Can be used with all specimen types</li> <li>✓ Can be used for other biomarkers</li> </ul> | <ul style="list-style-type: none"> <li>+ Concern about possible low level RNA if using RNA DBS</li> </ul>  |

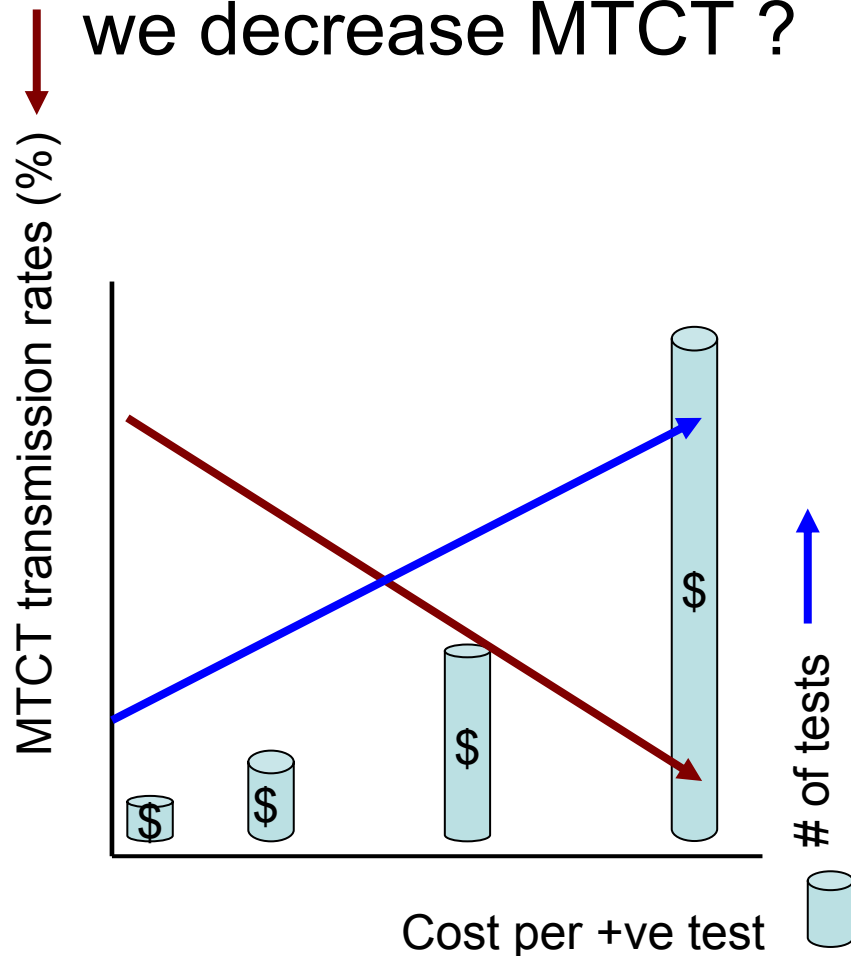
# Costing –test only

- Rapid tests 0.5 -1.20 USD
- HIV DNA PCR 12-18 USD
- HIV RNA 24-36 USD

Not costed: Lab staff, transport, communications, logistics, EQA, supervision.

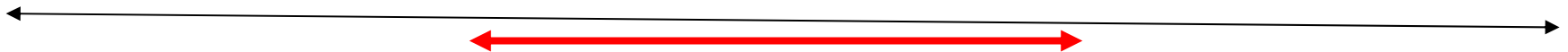
# PMTCT EID testing

- How will this change as we decrease MTCT ?



| HIV prev in population tested | Cost per positive test (USD) |
|-------------------------------|------------------------------|
| 1%                            | 2000                         |
| 5%                            | 400                          |
| 20%                           | 100                          |

# Feasibility

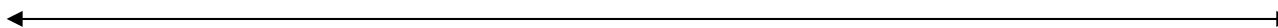
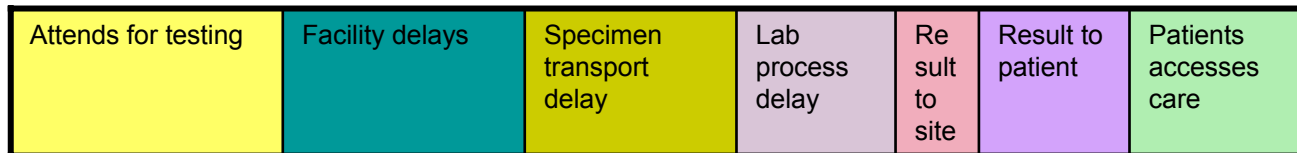


T = 2 months or >

? T = < 1 mo to avert death



T = 6 weeks



(Median Kenya 70 days  
(IQR 39 to 99))

# Clinical algorithms

## ***HIV infection considered :***

- IMCI- recognise those needing testing  
Horwood et al.'s study – clinical assess 690 hospital outpatients, aged 2–59 months, HIV seroprevalence setting of 28.7%. sensitivity of 70%, specificity of 80% (PPV) of 59%, 38% of infants were infected,

## ***SEVERE HIV recognised***

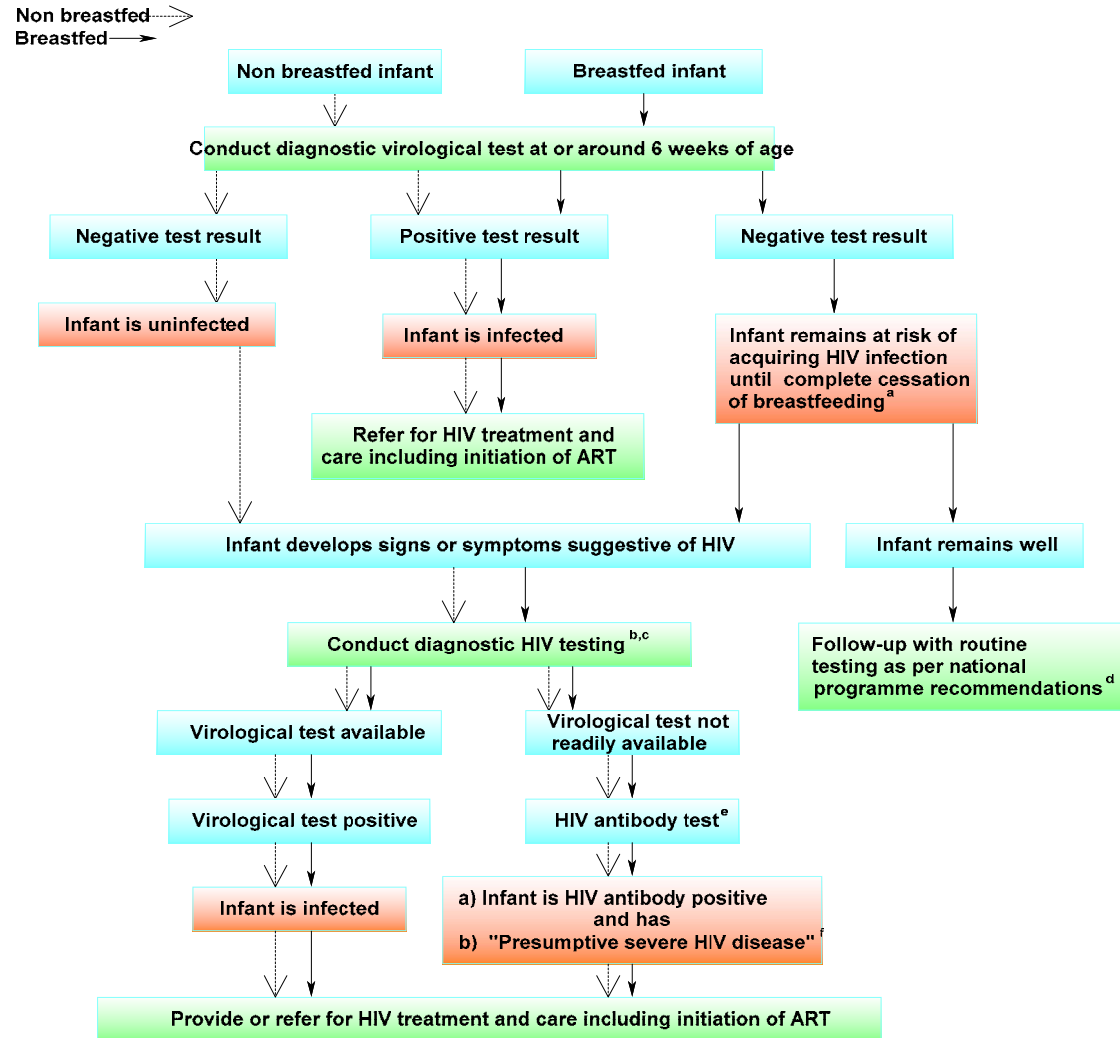
- WHO presumptive severe disease  
(HIV Ab + severe signs, wt loss, OC, severe sepsis, specific OIs)  
Being validated
- Illif Zimbabwe Data part of Zvitambo Study  
Suggests clinical algorithm based on low weight can detect most infants who need ART
- ANECCA  
Study ongoing to validate HIV antibody and clinical symptom complex

# Lab based

- CD4 + signs + symptoms + antibody testing (ANECCA study, & others ongoing)
- RT: - rule out infection in >30% (17 of 54) of infants as early as 3 to 6 months of age and in 66% (31 of 47) of 6- to 9-month-old infants.
- RT screening for infants would save \$4.05/infant based on current Uganda MoH guidelines (PCR  $\leq$ 18 months) and \$2.51/infant based on current WHO recommendations (PCR  $\leq$ 12 months), but would have missed 2 early infections.  
(Homsy Abstract 668 CROI 2008).

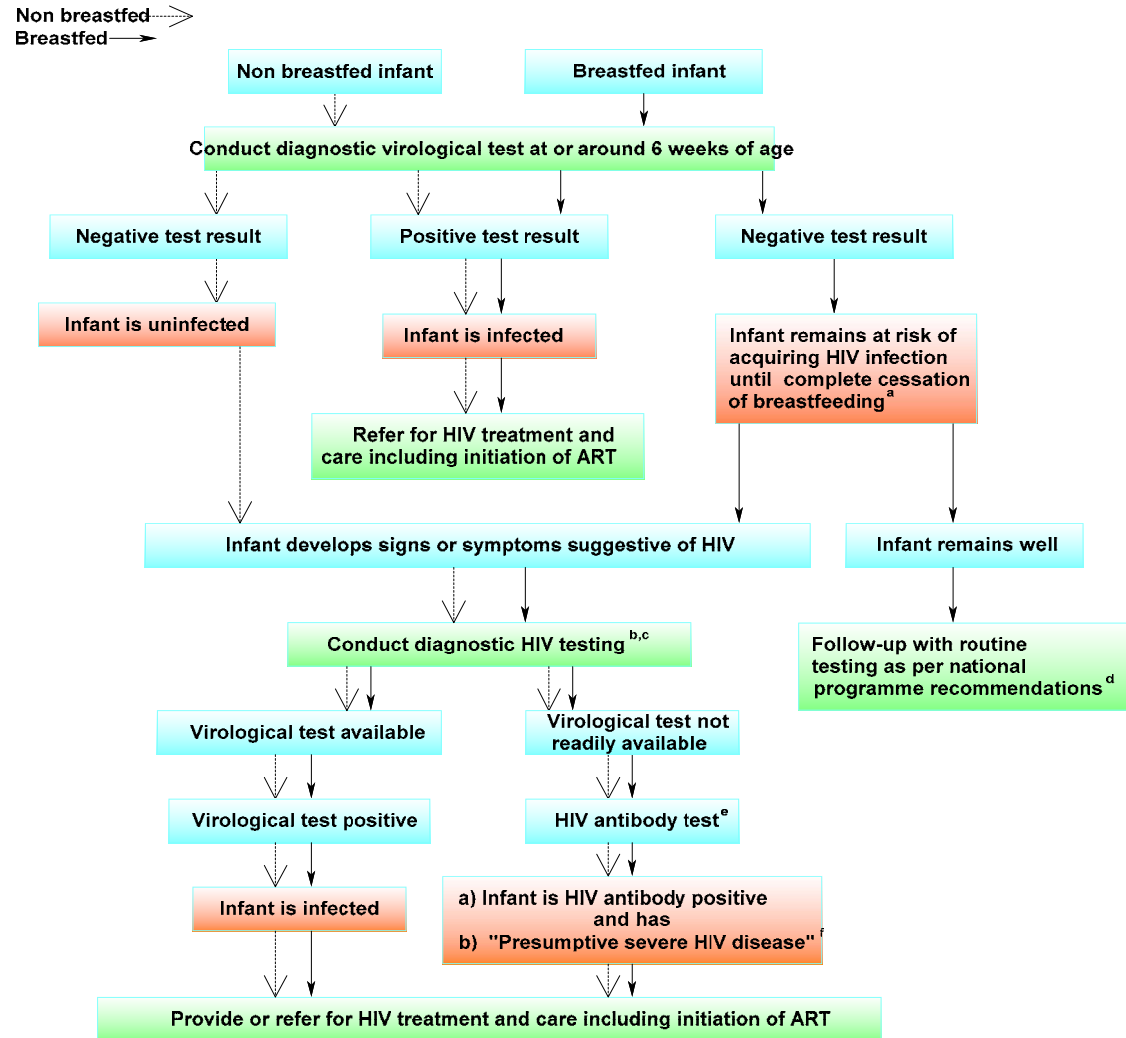
One other CROI abstract suggesting high rates false negatives with HIV Ab

## 6 Week Visit of Exposed or Suspected Exposed Infant



- a The risk of HIV transmission remains if breastfeeding continues beyond 18 months of age  
 b Infants over 9 months of age can be tested initially with HIV antibody test, as those who are HIV Ab negative are not usually HIV infected, although still at risk of acquiring infection if still breastfeeding.  
 c In children older than 18 months antibody testing is definitive  
 d Usually HIV antibody testing from 9-18 months of age  
 e Where virological testing is not readily available, and HIV antibody testing should be performed, it may be necessary to make a presumptive clinical diagnosis of severe HIV disease in HIV seropositive children. Confirmation of diagnosis should be sought as soon as possible.  
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