Birth Testing for HIV Diagnosis in Children: Considerations & Controversies

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Infant Birth Testing

- Global update
- Primer on diagnosing HIV infection in infants
- Early Infant Diagnosis (EID) implementation
- Birth testing: considerations & controversies
GLOBAL UPDATE
### Global HIV epidemic in women and children, 2015

<table>
<thead>
<tr>
<th>Metric</th>
<th>Global</th>
<th>sub-Saharan Africa</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estimated number of women 15+ years living with HIV</td>
<td>17.8 million</td>
<td>14.2 million</td>
<td>80%</td>
</tr>
<tr>
<td>Estimated number of pregnant women living with HIV</td>
<td>1.4 million</td>
<td>1.3 million</td>
<td>90%</td>
</tr>
<tr>
<td>Estimated number of children &lt;15 years living with HIV</td>
<td>1.8 million</td>
<td>1.6 million</td>
<td>87%</td>
</tr>
<tr>
<td>Estimated number of children &lt;15 years newly infected with HIV</td>
<td>150,000</td>
<td>120,000</td>
<td>84%</td>
</tr>
<tr>
<td>Estimated number of children &lt;15 years dying of AIDS related causes</td>
<td>110,000</td>
<td>91,000</td>
<td>86%</td>
</tr>
</tbody>
</table>

*Children & AIDS Statistical update; Source UNAIDS 2016 HIV and AIDS estimates; www.childrenandaids.org*
Nationally recommended PMTCT approach, low and middle income countries, 1st quarter 2016

“Treat All” for pregnant and breastfeeding women adopted in 95% of 144 LMIC in 2016
Dramatic increases in ART coverage in pregnancy with Option B+

**Malawi**

national programme evaluation, 2011-2015

**Swaziland** stepped-wedge evaluation, 2013-2015

<table>
<thead>
<tr>
<th></th>
<th>Total n=2315</th>
<th>Option A N=1272</th>
<th>Option B+ N=1043</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ever starting ART</td>
<td>35% (440)</td>
<td>94% (979)</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>CD4 &lt;350 starting ART</td>
<td>66% (263)</td>
<td>94% (351)</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Start ART 1st ANC visit</td>
<td>2% (18)</td>
<td>86% (896)</td>
<td>&lt;0.001</td>
<td></td>
</tr>
</tbody>
</table>

Gupta SK et al. CROI 2016 Boston Abs 789; adapted courtesy of L. Mofenson; Abrams EA et al. CROI 2016 Abs 34
Global increase in number of pregnant women with HIV receiving ARVs for PMTCT, 2005-2015

- HIV+ pregnant women receiving ARVs for PMTCT
- HIV+ pregnant women needing ARVs for PMTCT

Compiled data including Children & AIDS Statistical update: [www.childrenandaids.org](http://www.childrenandaids.org); UNAIDS, Prevention Gap Report 2016
Percentage of pregnant women living with HIV receiving most effective ARVs for PMTCT, 21 sub-Saharan Global Plan countries, 2015

- South Africa: >95%
- Uganda: >95%
- Namibia: >95%
- Mozambique: >95%
- Swaziland: 95%
- Botswana: 92%
- Burundi: 89%
- Zambia: 87%
- United Republic of Tanzania: 86%
- Zimbabwe: 84%
- Cameroon: 82%
- Malawi: 80%
- Côte d'Ivoire: 79%
- Kenya: 74%
- Lesotho: 70%
- Democratic Republic of the Congo: 67%
- Ghana: 63%
- Chad: 46%
- Angola: 40%
- Nigeria: 30%
## Malawi Option B+ National Evaluation: MTCT 4-12 week old infants

<table>
<thead>
<tr>
<th></th>
<th>Total N</th>
<th>HIV-Infected</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall results</td>
<td>1785</td>
<td>4.1% (95%, CI 3.2-5.2%) (N=73)</td>
</tr>
<tr>
<td>By Maternal ART Status (p&lt;0.001):</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Not on ART</td>
<td>118</td>
<td>20.3% (95% CI 15.2-26.7%) (N=24)</td>
</tr>
<tr>
<td>• On ART</td>
<td>1,669</td>
<td>2.9% (95% CI 2.2-4.0%) (N=49)</td>
</tr>
</tbody>
</table>

### Time ART Initiation* (Chi square for trend p<0.01)

<table>
<thead>
<tr>
<th></th>
<th>Total N</th>
<th>HIV-Infected</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before pregnancy</td>
<td>836</td>
<td>1.4% (N=12)</td>
</tr>
<tr>
<td>1st or 2nd trimester</td>
<td>665</td>
<td>4.1% (N=27)</td>
</tr>
<tr>
<td>3rd trimester</td>
<td>138</td>
<td>4.3% (N=6)</td>
</tr>
<tr>
<td>Postpartum</td>
<td>30</td>
<td>13.3% (N=4)</td>
</tr>
<tr>
<td>Not on ART</td>
<td>118</td>
<td>20.3% (N=24)</td>
</tr>
</tbody>
</table>
Estimated vertical transmission rates, sub-Saharan Africa, 2000-2015

Final mother-to-child transmission rate
Perinatal mother-to-child transmission rate (within 6 weeks of birth)
Percentages of adults and children <15 years living with HIV receiving ART in all low- and middle-income countries, 2000-2015
Percentage of children <15 years living with HIV receiving ART, by UNICEF Regions, 2005-2015

The numbers: summary and key points

• An estimated 150,000 new pediatric infections in 2015 attributed to MTCT
• Accelerated access to effective PMTCT among HIV+ pregnant women
  – High national uptake of Option B+;
    high uptake of ART with Option B+
  – 60% decline in new pediatric infections, 2009 → 2015
• Estimated rates of early MTCT decreasing
  – Doubling of MTCT rate through postnatal period
  – Wide variation by region/country
• Number of HIV-infected children receiving ART still shockingly low
Nothing is simple

DIAGNOSING HIV INFECTION IN INFANTS AND CHILDREN
Why is infant HIV diagnosis so complicated?

• Maternal antibody is transmitted trans-placentally and can be detected for as long as ~18 months. Therefore a positive antibody identifies infant HIV exposure rather than infection status
  – Virologic testing (using a nucleic acid amplification test [NAAT]) is required to diagnose HIV infection in infants
    • Current commercial platform requires high level laboratory with trained technicians
• EID testing historically included a single test scheduled at optimal time to capture most infections (in utero and intrapartum) and most infants (first immunization visits)
  – Cost and capacity limitations
Early Infant Diagnostic Testing

• Now understood that infant diagnosis is an ongoing process requiring multiple tests over time
  – Maturation of PMTCT services
  – New emphasis on retention in long term care

• Given the long duration of exposure, from conception through cessation of breast feeding, **multiple diagnostic tests** over time are necessary to:
  – Diagnose infection as early in life as possible in infants
    • To initiate treatment and prevent disease progression and death
  – Finalize infection status at the end of the exposure period
    • Identify children with HIV acquired during breast feeding
    • Declare uninfected children ‘HIV-free’
### Timing of transmission and timing of diagnosis of HIV infection

#### Transmission Timeline

<table>
<thead>
<tr>
<th>Antenatal</th>
<th>Postpartum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early</td>
<td>Early</td>
</tr>
<tr>
<td>Late</td>
<td>Late</td>
</tr>
</tbody>
</table>

- **Pregnancy**: 10-25%<br>  |<28wks | >28wks |
- **Labor & Delivery**: 35%-40%<br>  |0-1 mo | 1-6 mos | 6-24 mos |
- **Breastfeeding**: 35%-40%<br>  |<28wks | >28wks |

#### Testing Timeline

- **Birth testing**
- **4-12 weeks testing**
- **9 months testing**
- **12 weeks post-breastfeeding**
Rationale for *addition of HIV diagnostic testing at birth*

- Diagnose HIV infection earlier in life
  - Diagnose infants with *in utero* infection
    - With better PMTCT coverage total number of HIV infections decreases but proportion attributed to *in utero* vs intrapartum transmission increases
    - Infants with *in utero* infection at higher risk for rapid disease progression and death
  - Initiate ART earlier
    - Prevent mortality and disease progression
    - Essential to CURE agenda, reduce latent reservoir with very early ART
Highest probability of death among untreated infants with peri-partum

Becquet R et al, PlosOne 2012
Peak in early mortality at 2-3 months of age in untreated HIV infection

Bourne DE, AIDS 2007
Early ART initiation prevents mortality in infants, CHER trial

![Graph showing the probability of death over months with two lines representing deferred and early treatment.](Violari, et al, NEJM, 2008)
To treat *early* infant diagnosis must be done *early*
Estimated vertical transmission rates, sub-Saharan Africa, 2000-2015

- Final mother-to-child transmission rate
- Perinatal mother-to-child transmission rate (within 6 weeks of birth)

--- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
Rate | 32% | 32% | 32% | 31% | 31% | 30% | 29% | 27% | 26% | 23% | 20% | 18% | 16% | 13% | 11% | 9% | 4% |
To treat all diagnosis must be done late as well, when transmission risk has ended
Implementation and experiences

EARLY INFANT DIAGNOSIS (EID)
Globally, in 2015, 51% received a virologic test by 2 months of age.
Percentage of infants born to HIV+ pregnant women receiving a virological test for HIV <2 months of age, by UNICEF Regions, 2009-2015
Percentage of HIV-exposed infants <2 months of age receiving a virological test for HIV, 21 Global Priority countries, 2015
EID – more than a heel prick

HIV positive pregnant woman on ART

Infant enrolled in PMTCT follow-up

EID sample obtained at 4-6 weeks of age

Sample transported to laboratory

Sample tested for HIV at laboratory

EID results returned to the clinic

EID results returned to the family

Retained in care; repeat testing at end of transmission risk

Immediate ART initiation
Retention outcomes for women initiating ART under Option B+, Malawi, 2011-2013

• Aggregated facility-level data, 546 facilities, retention in care:
  – 76.8% (20,475/26,655) after 12 months
  – 70.8% (18,306/25,849) after 24 months
  – 69.7% (17,787/25,535) after 36 months

• Patient-level data, 20 large facilities with EMR, retention in care, n=14,630 beginning Option B+:
  – 68.5% (95%CI 67.7-69.2) at 12 months
  – 61.1% (95%CI 60.3-61.9) at 24 months
  – 56.3% (95%CI 55.4-57.2) at 36 months

Haas et al, Lancet HIV, 2016
Lower retention with B+ compared with ART for eligible adults, Malawi

Women initiating ART during pregnancy:
• ~5 times more likely to have no follow-up visit
• 1.6 times more likely to be lost to follow-up during year 1 compared with non-pregnant adults

Haas et al, Lancet HIV, 2016
Entry into care and diagnostic testing in HIV-exposed infants, Malawi, June 2014-June 2015

Charts constructed using data from the Malawi Ministry of Health Q2 (April-June 2015) report
ICAP Mozambique EID Uptake
Jul 2015-Mar 2016

% HEI tested by 2 months

- Jul-Sep 2015: 38%
- Oct-Dec 2015: 33%
- Jan-Mar 2016: 29%

Source: ICAP URS 2016
# Findings from rapid assessment 40 health facilities in Cameroon

<table>
<thead>
<tr>
<th>Facilities conducting DBS collection for EID</th>
<th>PMTCT Facilities</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>%</td>
</tr>
<tr>
<td>40</td>
<td>75% of all PMTCT facilities</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Transport system for DBS samples used</th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>32</td>
<td></td>
<td>80%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Turnaround time for DNA PCR result</th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>2-4 weeks</td>
<td>3</td>
<td>8%</td>
</tr>
<tr>
<td>4-6 weeks</td>
<td>8</td>
<td>20%</td>
</tr>
<tr>
<td>&gt;6 weeks*</td>
<td>29</td>
<td>72%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>SMS printers for EID results</th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>15</td>
<td></td>
<td>38%</td>
</tr>
</tbody>
</table>

*Respondents reported turnaround times of >6 months as well as indicating that in many cases, test results were never received

Source: ICAP Rapid Assessment 2015
Turnaround time for EID results among 254 facilities with on-site specimen collection, ICAP 2015

Source: ICAP PFaCTS, August 2015
Even in well functioning programs, time to ART initiation is often delayed.
HIV disease progression prior to early ART initiation, South Africa, 2007-2010

• 403 children in Cape Town and Soweto initiating ART <3 months of age (~CHER)
  – Median age ART initiation 8.4 weeks [IQR 7.2-9.7]
• 62% of infants with advanced disease
  – CD4%<25% or CD4 count <1500 cells/mm³
  – Only 20% with normal CD4, WHO 1 or 2
• Each month increase in age at ART initiation increased odds of advanced disease at ART start (R: 1.69, CI:1.05-2.71)

Innes S et al JIAS 2014
Innovations to improve the EID cascade

- SMS printers for returning results to clinics
- Telephone hotlines to obtain results
- Appointment and tracking systems for HIV-exposed infants
- Expansion of HIV and EID testing to entry points other than PMTCT (immunization and outpatient clinics, inpatient wards)
- Introduction of Point-of-Care (POC) technology
- Addition of birth testing

Essajee S et al., JIAS 2015
HIV Infant Tracking System improves EID quality and retention, Kenya

Innovative on-line system, algorithm-based computer alerts for staff and text messaging alerts to mothers
EID implementation: summary and key points

• Slow but steady scale-up of EID in LMIC over the last decade
  – Majority of exposed infants still not being tested early
  – Wide variation by country/region primarily using dried blood spots with centralized laboratory testing
  – Provided a precedent for introduction of routine viral load testing in low resource settings

• Multiple *gaps* along the EID cascade
  – *Retention in care*, testing access, delayed return of results
  – Resulting in *late* or *no* ART for those infants determined to be HIV infected
HIV BIRTH TESTING

Game changer or one more gap to mind?
Guidance for infant diagnostic testing

<table>
<thead>
<tr>
<th>Source</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>US DHHS (Recommendations for Use of Antiretroviral Drugs in Pregnant</td>
<td>Virologic tests are required to diagnose HIV infection in infants aged &lt;18</td>
</tr>
<tr>
<td>HIV-1-Infected Women, 2015)</td>
<td>months and should be performed: 14 to 21 days of life and at ages 1 to 2 months</td>
</tr>
<tr>
<td></td>
<td>and 4 to 6 months</td>
</tr>
<tr>
<td>New York State DOH, 2010</td>
<td>HIV nucleic acid testing (NAT) to detect HIV RNA or DNA should be performed:</td>
</tr>
<tr>
<td></td>
<td>within 48 hours of birth, at 2 weeks, 4 to 6 weeks, first 2 weeks after</td>
</tr>
<tr>
<td></td>
<td>cessation of PEP, and the second at least 6 weeks after cessation of PEP). For</td>
</tr>
<tr>
<td></td>
<td>babies born with high risk of transmission, an additional PCR test midway</td>
</tr>
<tr>
<td></td>
<td>through PEP is recommended to allow earlier identification of infected infants.</td>
</tr>
<tr>
<td>WHO Consolidated guidelines on the use of ARVs for treating and</td>
<td>Addition of nucleic acid testing (NAT) at birth to existing early infant</td>
</tr>
<tr>
<td>preventing HIV infection, 2016</td>
<td>diagnosis (EID) testing approaches can be considered to identify HIV infection</td>
</tr>
<tr>
<td></td>
<td>in HIV-exposed infants (conditional recommendation, low-quality evidence).</td>
</tr>
<tr>
<td></td>
<td>Virologic test at 4-6 weeks or the earliest time thereafter</td>
</tr>
<tr>
<td>South Africa DOH (National consolidated guidelines for PMTCT,</td>
<td>Birth PCR to all exposed infants 10w PCR to all infants who tested negative at</td>
</tr>
<tr>
<td>updated June 2015)</td>
<td>birth 18w PCR to all infants on extended 12w NVP PCR 6w post cessation of BF</td>
</tr>
<tr>
<td></td>
<td>Rapid HIV test at 18m</td>
</tr>
</tbody>
</table>

All guidelines recommend immediate ART for HIV-infected infants to prevent disease progression and mortality.
Birth testing – potential pathway to earlier ART and improved outcomes

From a public health approach, the addition of birth testing to the EID schedule could result in more infants starting ART and starting ART earlier

Lilian, PIDJ 2013
Birth testing – a critical pathway to remission

Newborn diagnostic testing is essential to the cure agenda

• Critical importance of diagnosing infants as close to birth as possible to:
  • Initiate ‘immediate ART’
  • Limit reservoir size
  • Promote normal immune and brain development

Early ART is important in the Journey towards HIV Remission

Growing into deficits
  Executive function
  Risk behaviors
  Assimilate into work force

Potentially best outcome
If institute very early ART
  Restricted reservoirs
  Normal immune and brain development

Timing matters
Lowest reservoirs in treated Fiebig I
Partially reversible CD4 depletion and immune activation

Adapted from Ananworanich J, HIV Center grand rounds, 2016
Limited experience with birth testing in low and middle income countries

• National guidelines in South Africa changed in June 2015 to include routine birth PCR for all HIV-exposed infants + repeat testing at 10 weeks for those with negative test at birth
  • Layered onto a highly successful EID testing program. Implementation has required:
    • Meticulous planning, innovation and supervision
    • Financial investments
    • New tools, standard operating procedures,
    • Informed, capable health care workers
    • Continued monitoring & support

• Several other countries are implementing (Thailand) or planning/piloting (Kenya) introduction of birth testing for infant diagnosis
South Africa Infant HIV Diagnosis Program

<table>
<thead>
<tr>
<th>Sub-District</th>
<th>Facility</th>
<th>Ward</th>
<th>Folder No</th>
<th>Patient Name</th>
<th>Patient DOB</th>
<th>Patient Address</th>
<th>Patient Tel</th>
<th>Patient Age</th>
<th>Test Date</th>
<th>Result</th>
<th>Test Date</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>City of Tshwane</td>
<td>Tshwane General</td>
<td>1</td>
<td>12345</td>
<td>John Doe</td>
<td>01/01/2016</td>
<td>123 Main St</td>
<td>123-456-7890</td>
<td>10 years</td>
<td>01/01/2016</td>
<td>Positive</td>
<td>01/01/2016</td>
<td>Negative</td>
</tr>
<tr>
<td>City of Tshwane</td>
<td>Tshwane General</td>
<td>2</td>
<td>54321</td>
<td>Jane Smith</td>
<td>02/02/2016</td>
<td>234 Park Ave</td>
<td>987-654-3210</td>
<td>15 years</td>
<td>02/02/2016</td>
<td>Negative</td>
<td>02/02/2016</td>
<td>Positive</td>
</tr>
</tbody>
</table>

Weekly results:

- gp Tshwane 2 Health sub-District:
  - 31 Delivery: 6 cases
  - 34 Live birth to HIV positive woman: 4 cases
  - 56 Targeted birth PCR test: 70 cases
  - 57 Targeted birth PCR test positive: 1 case

- gp Refentse Clinic (Odi):
  - 31 Delivery in facility total: 57 cases
  - 34 Live birth to HIV positive woman: 10 cases
  - 56 Targeted birth PCR test: 7 cases
  - 57 Targeted birth PCR test positive: 0 cases

- gp Tembe CHC:
  - 31 Delivery in facility total: 54 cases
  - 34 Live birth to HIV positive woman: 14 cases
  - 56 Targeted birth PCR test: 20 cases
  - 57 Targeted birth PCR test positive: 0 cases

Feucht U, SA Clinicians Society Conference, Apr 2016
Birth testing program at Rahima Moosa, Johannesburg, South Africa

• Screen ~1000 women/month, 30/day
  – Brief interview to ascertain HIV status
  – HIV test women with negative or unknown status

• ~200 HIV-exposed deliveries/month, 8-10/day
  – 4 full-time counselors: counsel mothers on postnatal ward
  – 1 full-time nurse: supervise counselors, draw blood
  – 2 data-capturers: registers and electronic database to document testing activities and results, patient tracking
  – Weekly clinic where moms obtain results (integrated with routine ARV/EID clinic)
# High uptake of birth HIV PCR testing, Kwazulu Natal, RSA

**EID coverage** (6000 HIV-exposed infants born/month)

<table>
<thead>
<tr>
<th>Time</th>
<th>Coverage Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 weeks</td>
<td>92% for 2014-2015</td>
</tr>
<tr>
<td>Birth</td>
<td>81% in the first year 2015-2016</td>
</tr>
<tr>
<td></td>
<td>94% in final quarter of the first year</td>
</tr>
<tr>
<td>10 weeks</td>
<td>79% in the first year of birth testing</td>
</tr>
</tbody>
</table>

**Percent positivity**

<table>
<thead>
<tr>
<th>Time</th>
<th>Positivity Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 weeks</td>
<td>1.3% for 2014-2015</td>
</tr>
<tr>
<td>Birth</td>
<td>0.7% in the first year</td>
</tr>
<tr>
<td>10 weeks</td>
<td>undetermined (unable to de-duplicate)</td>
</tr>
</tbody>
</table>
Modest proportion of all HIV-infected infants identified through birth testing

Proportion of all positive HIV PCR tests from different clinical settings and decreasing HIV positivity rate in the Western Cape province, South Africa, 2009 – 2015

Option B+
Begins in the Western Cape mid-2013

Maritz CROI 2016; slide courtesy of L. Mofenson
One-year Survival
HIV-infected: Testing Once

Testing once: 6 weeks is clinically and economically superior to birth or 10 weeks

Francke et al, JID 2016
One-year Survival (HIV-infected): Testing Twice

Testing twice: markedly improves outcomes and is cost-effective in South Africa compared to 6 weeks alone

Francke et al, JID 2016
Clinical impact and cost-effectiveness of EID in South Africa

• Testing once: 6 weeks is clinically and economically superior to birth or 10 weeks
• Testing twice: markedly improves outcomes and is cost-effective in South Africa, compared to 6 weeks alone
• If scale-up costs are comparable, programs with incomplete 6-week EID coverage should scale up 6-week programs before adding birth testing
• Avoiding loss to follow-up after birth testing is critical
  – If >37% of infants with negative birth test fail to return at 6 weeks, clinical benefits of adding birth testing are lost
Antiretroviral treatment for newborns: nothing simple about it

- Only a limited number of ARVs can be used in the first weeks of life (ZDV, NVP, 3TC, D4T); liquid formulations; frequent dose adjustments as the child ages and grows
- High rates of prematurity, low birth weight, co-morbid conditions
- Limited global experience with newborn ART; Under what conditions is it feasible and safe to routinely initiate ART in newborns? By whom? And where?

Table 4 (C). Drug dosing of liquid formulations for twice-daily dosing in infants less than 4 weeks of age*
NOTE: LPV/r not recommended for use in infants less than 2 weeks of age

<table>
<thead>
<tr>
<th>Drug</th>
<th>Strength of liquid (mg/mL)</th>
<th>2-3 kg</th>
<th>3-4 kg</th>
<th>4-5 kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>AZT</td>
<td>10 mg/mL</td>
<td>1 mL</td>
<td>1.5 mL</td>
<td>2 mL</td>
</tr>
<tr>
<td>NVP</td>
<td>10 mg/mL</td>
<td>1.5 mL</td>
<td>2 mL</td>
<td>3 mL</td>
</tr>
<tr>
<td>3TC</td>
<td>10 mg/mL</td>
<td>0.5 mL</td>
<td>0.8 mL</td>
<td>1 mL</td>
</tr>
<tr>
<td>LPV/r*</td>
<td>80/20 mg/mL</td>
<td>0.6 mL</td>
<td>0.8 mL</td>
<td>1 mL</td>
</tr>
</tbody>
</table>

*WHO dosing annex, in review, 2016*
How can technologies enhance infant diagnosis programs?

• Role of Point-of-Care (POC) and other diagnostic innovations
  – Several evaluations demonstrating high sensitivity, specificity of POC technologies (Alere Q, Xpert HIV-1 Cepheid) for EID

• NAAT platforms - impact of ARV exposures; sensitivity, specificity, positive/negative predictive value

• SMS printers, SMS reminders, dashboards – approaches to communication, monitoring, evaluation

Time from phlebotomy to return of result using Point of Care (POC PCR) Xpert® HIV-1 Qual – Cepheid vs Standard of Care lab PCR, Rahima Moosa
  – Result release POC PCR: 2.6 hours (95% CI: 2.3-3.1)
  – Result release LAB PCR: 43 hours (95% CI: 31-54)

Techanau K, 8th Pediatric HIV Workshop 2016
Routine birth testing?
More questions than answers

- What are the optimal models for implementing birth testing programs?
  - Where to test? When to test? Who to test? Who should do the testing?
  - How to ensure results are returned to the family?
    - With linkage to treatment and ART initiation for those testing positive
    - Retention in care and repeat testing for those testing negative

- What criteria should national programs use to determine if, when and how to recommend birth testing?

- Will the addition of birth testing to national programs improve infant diagnosis?
  - Possible risk of destabilizing fragile EID programs - $\$, supplies, priority, retention and repeat testing

- Will the addition of birth testing improve long-term outcomes of children with HIV infection?
In Summary

• Diagnostic testing at birth offers a unique opportunity to catalyze infant diagnostic services
  – To improve existing EID to services to reach all HIV-exposed children with testing and results
  – To effectively engage and treat all infants and children diagnosed with HIV infection
• Much work is yet to be done to achieve these objectives
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