Overview of Multi-disease Integrated Testing

May 2019
Across sub-Saharan Africa, infant case finding lags behind testing rates in adults.

Progress in the 1st 90 for infants is not being realized at a similar rate as for adults.

Figure 11. Nearly half of HIV-exposed infants are not tested
Percentage of children born to women living with HIV who were tested for HIV within eight weeks of birth, 23 focus countries, 2017

52% of HEI tested by 8 weeks of age compared to...

75% [55-92%] of PLHIV know their HIV status.
Monitoring PLHIV on ART is critical to achieving viral suppression targets

Though more people are being diagnosed and placed on treatment, the gap in the 3\textsuperscript{rd} 90 is growing

\textbf{EASTERN AND SOUTHERN AFRICA}

- **Testing gap**: Percentage of people with HIV who do not know their status and are not on treatment
- **Treatment gap**: Percentage of people living with HIV who know their status but are not on treatment
- **Viral suppression gap**: Percentage of people living with HIV who are on treatment but not virally suppressed
- **Virally suppressed**: Percentage of people living with HIV who are on treatment and virally suppressed

\textit{"The ‘viral suppression gap’ is growing more prominent."} - UNAIDS 2018

Source: UNAIDS special analysis, 2018.
Point-of-care (POC) testing offers an opportunity to address coverage and quality gaps in molecular testing

Services to manage PLHIV have been tremendously decentralized

Centralized laboratory systems maximize throughput but often do so at the expense of rapid result availability

- May lead to missed opportunities for more critical clinical decisions, such as HIV diagnosis for infants or management of clients with unsuppressed VL

POC testing for EID and CD4 has been shown to increase rates and timeliness of clinical action\(^1\) (linkage to care, ART initiation)

- But management of decentralized testing fleets can be capital, resource intensive and complex without accompanying supportive systems

Initial implementation strategy to offer POC testing is Multi-disease integrated testing on existing GeneXpert devices. Integration represents an opportunity to increase access and minimize costs for POC testing

\(^1\) Vojnov L et al 2016, Mwenda R et al 2018, Jani IV et al 2018
POC testing is currently being considered for certain priority populations who could most benefit from rapid DNA-PCR test results.

- **HIV exposed infants (HEI)**
  - to ensure timely diagnosis and improve rates of early treatment initiation

- **Pregnant and breast feeding HIV+ women**
  - to promote re-suppression and avert vertical transmission (20-25% risk of MTCT from women with unsuppressed VL)

- **Children/adolescents**
  - to ensure early detection of virological failure, can have higher rates of unsuppressed VL

- **Persons with advanced HIV disease**
  - ensure more rapid viral suppression and lower the risk of disease progression

- **Patients on ART failing 1\textsuperscript{st} VL**
  - to ensure early ARV switch, can have increased morbidity & mortality with prolonged elevated VL
There are currently 3 POC products approved by regulatory authorities to offer EID and/or HIV VL

<table>
<thead>
<tr>
<th></th>
<th>Cepheid GeneXpert</th>
<th>DRW Samba II</th>
<th>Abbott m-PIMA (formerly AlereQ)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Assay</strong></td>
<td>HIV-1 Qual (EID)</td>
<td>HIV-1 VL</td>
<td>HIV-1/2 Detect (EID)</td>
</tr>
<tr>
<td><strong>Regulatory</strong></td>
<td>WHO PQ, CE-IVD</td>
<td>WHO PQ, CE-IVD</td>
<td>WHO PQ, CE-IVD</td>
</tr>
<tr>
<td><strong>Sample</strong></td>
<td>1 DBS, 100ul WB</td>
<td>1ml plasma</td>
<td>25ul WB</td>
</tr>
<tr>
<td><strong>Time to result</strong></td>
<td>1h55m (DBS) 95 mins (WB)</td>
<td>95 mins</td>
<td>52 mins</td>
</tr>
<tr>
<td></td>
<td></td>
<td>95 mins</td>
<td>70 mins</td>
</tr>
</tbody>
</table>
A large existing fleet of GeneXpert devices established through National TB Programs has multiplexing capability to run different disease assays.

Over 2,800 GeneXpert systems have already been procured for TB testing in PEPFAR-focus countries.

Current utilization of existing devices is generally less than 50%.

<table>
<thead>
<tr>
<th>Assay</th>
<th>HIV-1 Qual (EID)</th>
<th>HIV-1 VL</th>
<th>HCV VL</th>
<th>HPV VL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regulatory</td>
<td>WHO PQ, CE-IVD</td>
<td>WHO PQ, CE-IVD</td>
<td>WHO PQ, CE-IVD</td>
<td>WHO PQ, CE-IVD</td>
</tr>
<tr>
<td>Sample</td>
<td>1 DBS, 100ul WB</td>
<td>1ml plasma</td>
<td>1ml plasma</td>
<td>Cervical swab</td>
</tr>
<tr>
<td>Time to result</td>
<td>1h55m (DBS) 90 min (WB)</td>
<td>90 mins</td>
<td>90 mins</td>
<td>60 mins</td>
</tr>
</tbody>
</table>

Source: Cepheid 2017

HBV VL released in Dec 2018
A range of centralized platforms can also offer integrated testing

*National programs have invested heavily in nucleic acid amplification testing (NAT) platforms (which detect DNA and RNA) that are capable of testing a range of diseases and may have spare capacity*

<table>
<thead>
<tr>
<th>Test Menu</th>
<th>Roche CAP/CTM 96</th>
<th>Roche 4800/6800/8800</th>
<th>Abbott m2000sp</th>
<th>Hologic Panther</th>
</tr>
</thead>
<tbody>
<tr>
<td>Max daily throughput (incl. controls)</td>
<td>168 (8hrs); 312 (24hrs)</td>
<td>384/960 (8hrs); 1,344/3,072 (24hrs)</td>
<td>96 (8hrs); 288 (24hrs)</td>
<td>320 (8hrs); 1,220 (24hrs)</td>
</tr>
<tr>
<td>HCV VL</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>HBV VL</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>HIV EID</td>
<td>✓</td>
<td>✗²</td>
<td>✓</td>
<td>✗³</td>
</tr>
<tr>
<td>HIV VL</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>MTB</td>
<td>✗</td>
<td>✓</td>
<td>✓</td>
<td>✗</td>
</tr>
<tr>
<td>HPV</td>
<td>✗</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>

²Cobas 4800 offers regulatory-approved EID; ³Currently under validation in the US
Multi-disease integrated testing can leverage existing instrument fleet

Multi-disease integrated testing brings benefits to all programs sharing infrastructure:
- Cost-sharing for fixed costs to maximize utilization and reduce all-in cost per test
- Increasing access to devices and sites that would be otherwise unaffordable
- Improved quality by increasing and coordinating monitoring and training
- Increased negotiating power for test prices and S&M
- Leverage on data management, sample transport and supply chain systems
Integration of care services can be realized in most of the system areas and is expected to generate efficiencies and better services provided to the patients.
There are many areas where multiplexing can yield improved efficiency, not only through higher utilization of the device, but also through leveraging and combining laboratory support systems, such as training, mentorship, and connectivity.
Integration Implementation Framework

**Key Activities**

1. Advocacy with key opinion leaders for policies enabling TB/HIV/HCV/HPV Integration
   - Site mapping with existing and expected devices
   - Capacity assessment: existing and projected (HR, infrastructure, equipment, S&M, ST, etc.)
   - Current and future resource assessment
2. Consultative meetings
3. Agreement on well-defined responsibilities
4. Commitment to contribute to the program and take action

**Outcome**

- Strong commitment & collaboration between programs
- Leverage existing resources & share operational costs to ensure sustainability
- Achieve milestones according to set targets
- Operationalize with well defined roles and cost implications
- Integrated services available across the country
- Anticipate and address challenges, share best practices

**MoH (NTP, NACP, HIV, HCV, Cancer program, and Labs) Leadership and Partner Coordination**

1. Testing models based on assessment
2. Identification and mapping of target facilities - onsite, referrals
3. Set volume targets, and define test/sample type prioritization, as appropriate
4. Timeline for phased implementation

1. Program plan (Who, When, What, Where, How)
2. Site & product selection
3. Process flows and SOPs
4. Data management & information flow
5. Funding gap analysis

1. Pilot sites visit & coordination
2. Conduct trainings and awareness campaign
3. Lab workflow and patient flow optimization
4. Pilot findings dissemination (gaps, actions and best practices)
5. Scale-up plan

1. Routine monitoring and supportive supervision visits
2. Tracking and Reporting against KPIs
3. Identification of low performance service areas
4. Service improvement plan of actions
Thank you!