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Point-of-Care Testing

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London School of Hygiene & Tropical Medicine
Point-of-care Testing

• Why do we need POC tests for Sexually transmitted infections?
• Benefit vs risks of POC testing
• What is on the horizon - advances in diagnostic technologies
• The way forward
Access to STI diagnostics is limited in areas with high disease burden

WHO: Estimated incidence of 4 curable STIs is >400 million new cases/year
## Performance of WHO Vaginal Discharge algorithm with Risk Assessment for detection of CT/NG

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>Prev</th>
<th>Sens/Spec (%)</th>
<th>PPV (%)</th>
<th>Gold Standard</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tanz</td>
<td>628 preg</td>
<td>8%</td>
<td>46/82</td>
<td>18</td>
<td>CT-EIA, GC-Cult</td>
</tr>
<tr>
<td></td>
<td>395</td>
<td>11%</td>
<td>62/64</td>
<td>18</td>
<td></td>
</tr>
<tr>
<td>Brazil</td>
<td>334</td>
<td>15%</td>
<td>68/49</td>
<td>19</td>
<td>CT- IF, GC-Cult</td>
</tr>
<tr>
<td>Benin</td>
<td>192</td>
<td>8%</td>
<td>87/42</td>
<td>11</td>
<td>CT-EIA, GC-Cult</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>93/34 (S)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Malawi</td>
<td>550</td>
<td>20%</td>
<td>43/73</td>
<td>28</td>
<td>CT- EIA, GC-Cult</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>62/61 (S)</td>
<td>27</td>
<td></td>
</tr>
<tr>
<td>USA</td>
<td>102</td>
<td>12%</td>
<td>42/74</td>
<td>34</td>
<td>CT-EIA; GC-Cult</td>
</tr>
<tr>
<td>Peru</td>
<td>324</td>
<td>15%</td>
<td>98/13</td>
<td>16</td>
<td>CT- LCR, GC- Cult</td>
</tr>
<tr>
<td>Kenya</td>
<td>621</td>
<td>16%</td>
<td>59/61</td>
<td>22</td>
<td>CT- PCR, GC- Cult</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>78/42 (S)</td>
<td>20</td>
<td></td>
</tr>
</tbody>
</table>

(S) - with speculum exam.
POC Testing for Sexually Transmitted Infections

- To improve specificity of syndromic management, especially for vaginal discharge
- To improve access to testing, especially for at risk populations
- To empower individuals to take responsibility for their health
ASSURED Tests to Improve Global Health

A = Affordable
S = Sensitive
U = User-friendly
R = Rapid and robust
E = Equipment-free
D = Deliverable

✓ Cheap
✓ Accurate
✓ Fast/Simple

“Pick 2 of 3, you can’t have them all.”
Diagnostics: Access vs Performance vs Cost

Urban
Semi urban
Rural

Urban
Semi urban
Rural

Urban
Semi urban
Rural

Accurate ✓✓✓
Cheap ×
Fast/simple ×

Accurate ✓✓
Cheap ✓
Fast/simple ✓

Accurate ✓
Cheap ✓✓
Fast/simple ✓✓
What is the Ideal Diagnostic?

**DIRECT METHODS**
- (Microscopy) Culture
- Genome detection
- Antigen detection

**INDIRECT METHODS**
- Serology IgM
- Serology IgG

**Time to Result:**
- Days
- Hours
- Hours/Minutes

Adapted with permission from J. Cardosa
FDA Approves over-the-counter Sales of Oral HIV Tests, July 2012

Aspirin? Check. Shampoo? Check. Free HIV Test — Check?

Oct 22, 2013: European Parliament votes favourably for home use of IVDs
## Performance of Oral HIV Test

<table>
<thead>
<tr>
<th>Performance Measure</th>
<th>Minimum Recommended Performance</th>
<th>Professional Use OraQuick Test Performance (2-sided 95% CI*)</th>
<th>Minimum Recommended Performance</th>
<th>Over-the-Counter OraQuick Test Performance (2-sided 95% CI*)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>98% (lower bound of the 2-sided 95% CI)</td>
<td>99.3% (98.4 - 99.7%)</td>
<td>95% (lower bound of the 2-sided 95% CI)</td>
<td>92.98% (86.64 – 96.92%)</td>
</tr>
<tr>
<td>Specificity</td>
<td>98% (lower bound of the 2-sided 95% CI)</td>
<td>99.8% (99.6 – 99.9%)</td>
<td>95% (lower bound of the 2-sided 95% CI)</td>
<td>99.98% (99.90 – 100%)</td>
</tr>
</tbody>
</table>

*95%CI = 95% Confidence Interval
Risk Benefit analysis

• The FDA performed a risk analysis to understand the public and individual health implications of approving a test with these performance characteristics.
  – estimated the net transmissions averted
  – The impact of switching from professional testing to self-testing
  – The impact of who will use the test
  – Do the benefits outweigh the risks?

• A risk assessment model showed that in the first year of use, there would be:
  – A net increase of ~4,500 new HIV infections identified among those not aware of their HIV status
  – ~2,700,000 who would test negative.
  – ~4,000 transmissions would be averted, outweigh the individual risk of increased numbers of false negative results (approximately 1,100).

• Individual risk remained which prompted FDA to address this risk through messages in the test kit labeling:
  – A positive result with this test does not mean that you are definitely infected with HIV, but rather that additional testing should be done in a medical setting.
  – A negative result with this test does not mean that you are definitely not infected with HIV, particularly when exposure may have been within the previous three months.
  – Testing is recommended if you test negative and continue to engage in behavior that puts you at risk for HIV infection.
  – A negative result does not imply it is safe to engage in risk behavior for HIV infection.
Rapid Tests for Syphilis

Procedure:
1. Use dropper provided, dispense 1 drop of serum/whole blood to sample well S
2. Add 2 drops of diluent buffer to sample well S
3. Read results after 15 minutes

- Negative
- Positive
- Invalid
<table>
<thead>
<tr>
<th>Test</th>
<th>Specimen</th>
<th>Sensitivity* (%)</th>
<th>Specificity* (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abbott Determine</td>
<td>serum</td>
<td>89-100</td>
<td>96-98</td>
</tr>
<tr>
<td></td>
<td>whole blood</td>
<td>60-89</td>
<td>98-99</td>
</tr>
<tr>
<td>Standard Bioline</td>
<td>serum</td>
<td>91-100</td>
<td>96-99</td>
</tr>
<tr>
<td></td>
<td>whole blood</td>
<td>86-100</td>
<td>98-99</td>
</tr>
<tr>
<td>Qualpro Syphicheck I</td>
<td>serum</td>
<td>67-98</td>
<td>98-99</td>
</tr>
<tr>
<td></td>
<td>whole blood</td>
<td>64-84</td>
<td>98-100</td>
</tr>
<tr>
<td>Omega VisiTect</td>
<td>serum</td>
<td>84-98</td>
<td>98-99</td>
</tr>
<tr>
<td></td>
<td>whole blood</td>
<td>73-96</td>
<td>99-100</td>
</tr>
</tbody>
</table>

Mabey et al. STI 2006; 82 Suppl V: v13-16
Dual Path Technology: HCV/HIV/Syphilis Assays

HCV, HIV and Syphilis Test
Performance of DPP Combo Test

<table>
<thead>
<tr>
<th>DPP</th>
<th>RPR</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-Trep</td>
<td></td>
<td></td>
</tr>
<tr>
<td>+</td>
<td>739</td>
<td>11</td>
</tr>
<tr>
<td>-</td>
<td>95</td>
<td>756</td>
</tr>
<tr>
<td>Total</td>
<td>834</td>
<td>767</td>
</tr>
</tbody>
</table>

Concordance of DPP NON-Trep with:
RPR+ = 98.4%; RPR- = 98.6%

<table>
<thead>
<tr>
<th>DPP Trep</th>
<th>TPPA</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>+</td>
<td>972</td>
<td>27</td>
</tr>
<tr>
<td>-</td>
<td>35</td>
<td>567</td>
</tr>
<tr>
<td>Total</td>
<td>1007</td>
<td>594</td>
</tr>
</tbody>
</table>

Concordance of DPP Trep with:
TPPA+ = 96.5%; TPPA- = 95.5%

HCV POC Tests

• The U.S. FDA approved HCV POC tests for finger stick and venipuncture specimens
• OraQuick tests using oral samples or blood have shown to be comparable to laboratory-based enzyme immunoassays with better specificity and sensitivity compared to four other POC tests
• U.S. premarket studies in the field and laboratory demonstrated high sensitivities and specificities for the OraQuick fingerstick assay, although two other POC tests were less sensitive and produced false negatives in patients who were co-infected with HIV
# Meta-analysis of Performance of POC HCV Tests

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Sensitivity (95% CI)</th>
<th>Specificity (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Within-Study Oraquick Oral Fluid</td>
<td>98.1% (92.4, 99.5)</td>
<td>98.5% (93.3, 99.7)</td>
</tr>
<tr>
<td>Within-Study Oraquick Whole Blood and Fingerstick</td>
<td>99.8% (98.6, 100)</td>
<td>99.9% (99.4, 100)</td>
</tr>
<tr>
<td>Other Whole Blood and Fingerstick Blood Tests</td>
<td>86.2% (83.3, 88.6)</td>
<td>89.9% (34.1, 99.4)</td>
</tr>
<tr>
<td>Serum and Plasma Tests</td>
<td>98.8% (88.2, 99.9)</td>
<td>99.8% (99, 100)</td>
</tr>
</tbody>
</table>

Why don’t we have good rapid tests for chlamydia and gonorrhoea?
## Performance of Clearview Chlamydia Test

STD clinic and re-education centres in China

N = 1,497 women; 13%

<table>
<thead>
<tr>
<th></th>
<th>cervical swab</th>
<th>vaginal swab</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>sensitivity</strong></td>
<td>50%</td>
<td>33%</td>
</tr>
<tr>
<td><strong>specificity</strong></td>
<td>98%</td>
<td>99%</td>
</tr>
<tr>
<td><strong>PPV</strong></td>
<td>78%</td>
<td>86%</td>
</tr>
</tbody>
</table>

*Performance vs. PCR (Yin et al. STI 2006; 82 Suppl V: v33-7)
Sample In, Answer Out: A Multi-disease, Random Access Real-time PCR Platform with Remote Quality Control

MTB/RIF
MRSA
CT/Ng
HIV Viral Load

5 20 80 Samples per shift 500-1000
Rapid VS Point-of-Care Tests

Courtesy of Dr. Ray Waters

K. Senior Lancet ID 9:467 2009
HIV Viral Load Product Pipeline

- 2013: SAMBA VL (DDU/Cambridge)
- 2014: Liat™ Analyser (IQuum), EOSCAPE HIV™ Rapid RNA Assay System (Wave 80 Biosciences)
- 2015: Cepheid, LYNX Viral Load Platform (NWGHF)
- 2016: Cavidi AMP, Viral Load Assay with BART (Lumora), RT CPA HIV-1 (Ustar, Gene-RADAR, Nanobiosym)

Point-of-Care CD4 Technologies in the Pipeline*

*Estimated; timeline and sequence may change.
POC Dx Initiative Goals

• Develop an open point of care instrument platform capable of delivering optimum performance

• Establish interoperability standards to encourage menu expansion by competing companies/sources

• Reduce barriers to entry into global health markets by eliminating the need for expensive instrument development

• Achieve a harmonized regulatory environment
POC Diagnostics Initiative

Bacteria vs virus vs fungus?

Platform 1
- TB
- HIV
- STIs
- Fever

Platform 2
- TB
- HIV
- STIs
- Fever

Platform 3
- TB
- HIV
- STIs
- Fever
Barcoding Pathogens and Resistance Hot Spots

- simultaneous genomic and proteomic profiling of multiple pathogens at point-of-care.
- over 100 uniquely barcoded nanobeads (barcoded with embedded quantum dots) providing unique spectral emissions for each nanobead


Nanocrystals absorb light then re-emit the light in a different color – the size of the nanocrystal (at the Angstrom scale) determines the color.

Six different quantum dot solutions are shown excited with a long wave UV lamp.
Moving Forward

- There is a promising pipeline of technologies that can improve access to at risk populations; need:
  - oral rapid tests to screen for HIV/syphilis, other viral STIs
  - test menus for STI syndromes

- Regulatory authorities and control programmes need to balance benefit vs risks of POC tests for HIV/STIs
  - need to model the benefit of access vs risks

- Strategic placement of new technologies in health systems to maximize impact
  - consider changing patient pathways
Thank you