Preference on characteristics of rapid diagnostic tests to identify pregnant women at risk of transmitting HBV to their infants in Africa

2 August 2022

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Incremental approach

Maternal antiviral prophylaxis if high maternal HBV DNA viral load or HBeAg positive

HBsAg testing, linkage to care and follow up of infants. When available, HBIG for infants born to HBsAg+ and HBeAg+ mothers

At least 3 doses of hepatitis B vaccine, including a timely birth dose within 24 hours

WHO guidelines, 2020
MTCT risk despite birth dose & hepatitis B immunoglobulin

Boucheron P et al., Lancet Infect Dis 2021
MTCT risk despite birth dose & hepatitis B immunoglobulin

HBV DNA ≥ 200 000 IU/mL

Risk of mother-to-child transmission (%) vs. Maternal HBV DNA levels during pregnancy (log10 IU/ml)

Boucheron P et al., Lancet Infect Dis 2021
Performance of HBeAg to diagnose HBV DNA ≥ 200,000 IU/mL

Pooled sensitivity 88%
(95% CI: 84-92%)

Pooled specificity 93%
(95% CI: 90-94%)

Boucheron P et al., Lancet Infect Dis 2021
How about rapid diagnostic test (RDT) to detect HBeAg?

Guingané et al. (Burkina Faso)
Sen 64%
Spe 95%

Ségéral et al. (Cambodia)
Sen 76%
Spe 97%

Boucheron P et al., Lancet Infect Dis 2021
• Unlikely to have a perfect rapid diagnostic test
  – Sensitivity: 100%
  – Specificity: 100%
  – Time-to-result: 20 minutes
  – Price: 1 US$

• What is the acceptable level of trade-off between these parameters?

• To assess preference of healthcare workers in Africa on four characteristics of RDTs using a survey & discrete choice experiment (DCE)
<table>
<thead>
<tr>
<th>Parameters</th>
<th>Levels</th>
</tr>
</thead>
<tbody>
<tr>
<td>Price for a patient</td>
<td>US$ 1</td>
</tr>
<tr>
<td></td>
<td>US$ 5</td>
</tr>
<tr>
<td></td>
<td>US$ 15</td>
</tr>
<tr>
<td></td>
<td>US$ 20</td>
</tr>
<tr>
<td>Diagnostic sensitivity</td>
<td>85%</td>
</tr>
<tr>
<td></td>
<td>90%</td>
</tr>
<tr>
<td></td>
<td>95%</td>
</tr>
<tr>
<td></td>
<td>100%</td>
</tr>
<tr>
<td>Diagnostic specificity</td>
<td>90%</td>
</tr>
<tr>
<td></td>
<td>95%</td>
</tr>
<tr>
<td></td>
<td>100%</td>
</tr>
<tr>
<td>Time-to-result</td>
<td>20 minutes</td>
</tr>
<tr>
<td></td>
<td>60 minutes</td>
</tr>
</tbody>
</table>
Scenario

- A healthcare worker in charge of antenatal care in a primary care clinic in a rural area of low-income country.
- In each year, you identify about 1000 women infected with HBV at your antenatal screening services.
- Of these HBV-infected women, about 20% (200 women) have high viral loads and require antiviral drugs to stop the transmission of HBV to their babies.
- The rest (800 women) have low viral loads and do not require antiviral drugs.
- However, most of women do not benefit from antiviral drugs because they cannot afford to bear the cost of PCR (US$ 40) and make a one-day trip to a district hospital for PCR.
- You are now asked about your preference between two fictional rapid tests as a tool to detect HBV-infected pregnant women with high viral loads.
## Example

<table>
<thead>
<tr>
<th>Rapid Test A</th>
<th>Rapid Test B</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Price</strong></td>
<td><strong>Price</strong></td>
</tr>
<tr>
<td>1 US$</td>
<td>15 US$</td>
</tr>
<tr>
<td><strong>Time to result</strong></td>
<td><strong>Time to result</strong></td>
</tr>
<tr>
<td>60 minutes</td>
<td>20 minutes</td>
</tr>
<tr>
<td><strong>Percentage of under-treated (out of 200 needing antivirals)</strong></td>
<td><strong>Percentage of under-treated (out of 200 needing antivirals)</strong></td>
</tr>
<tr>
<td>20% of women who need antiviral drugs don’t get them.</td>
<td>5% of women who need antiviral drugs don’t get them.</td>
</tr>
<tr>
<td><strong>Percentage of over-treated (out of 800 not needing antivirals)</strong></td>
<td><strong>Percentage of over-treated (out of 800 not needing antivirals)</strong></td>
</tr>
<tr>
<td>10% of women get antiviral drugs they don’t need.</td>
<td>10% of women get antiviral drugs they don’t need.</td>
</tr>
</tbody>
</table>
# Characteristics of 555 participants

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Profession</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Doctor</td>
<td>349</td>
<td>62.9</td>
</tr>
<tr>
<td>Nurse</td>
<td>23</td>
<td>4.1</td>
</tr>
<tr>
<td>Midwife</td>
<td>31</td>
<td>5.6</td>
</tr>
<tr>
<td>Lab staff</td>
<td>52</td>
<td>9.4</td>
</tr>
<tr>
<td>Public health practitioner</td>
<td>57</td>
<td>10.3</td>
</tr>
<tr>
<td><strong>Region (Africa)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Central</td>
<td>29</td>
<td>5.2</td>
</tr>
<tr>
<td>East</td>
<td>52</td>
<td>9.4</td>
</tr>
<tr>
<td>North</td>
<td>37</td>
<td>6.7</td>
</tr>
<tr>
<td>South</td>
<td>53</td>
<td>9.5</td>
</tr>
<tr>
<td>West</td>
<td>384</td>
<td>69.2</td>
</tr>
<tr>
<td><strong>Hepatitis B involvement</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>187</td>
<td>33.7</td>
</tr>
<tr>
<td>Yes</td>
<td>368</td>
<td>66.3</td>
</tr>
</tbody>
</table>
Alternative-specific multinominal probit model

- Utility vs. Sensitivity (%)
  \[ y = 0.1158x - 9.8388 \]
  \[ R^2 = 0.998 \]

- Utility vs. Specificity (%)
  \[ y = 0.0579x - 5.1525 \]
  \[ R^2 = 0.8855 \]

- Utility vs. Cost (USD)
  \[ y = -0.0681x + 0.1371 \]
  \[ R^2 = 0.9825 \]

* Isa YS et al., Master’s thesis 2022 *
Interaction

Who cares what?

• Doctors: sensitivity
• Public health: money
• Midwives: time-to-result
Predicted acceptance over PCR

Specificity 95%, Time-to-result 20 min

Predicted acceptance

Sensitivity

0% 10% 20% 30% 40% 50% 60% 70% 80% 90% 100%

70 72 74 76 78 80 82 84 86 88 90 92 94 96 98 100

US$ 1
US$ 5
US$ 15
US$ 20
Predicted acceptance over PCR

Specificity 95%, Time-to-result 20 min

Predicted acceptance vs. Sensitivity

Optimal

Minimal

US$ 1

US$ 5

US$ 15

US$ 20
Optimally/minimally acceptable level of sensitivity

• For a rapid diagnostic test of:
  – Specificity 95%
  – Time-to-result 20 minutes

<table>
<thead>
<tr>
<th>Cost</th>
<th>Sensitivity (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Minimal</td>
</tr>
<tr>
<td>1 USD</td>
<td>82.5</td>
</tr>
<tr>
<td>5 USD</td>
<td>85.0</td>
</tr>
<tr>
<td>15 USD</td>
<td>90.5</td>
</tr>
<tr>
<td>20 USD</td>
<td>93.5</td>
</tr>
</tbody>
</table>

Isa YS et al., Master’s thesis 2022
Summary

• Healthcare workers in Africa particularly care about sensitivity and cost
• However, there is a diversity between the type of healthcare workers
• For a test providing the result in 20 minutes with a specificity of 95%, the sensitivity should be $\geq 82.5\%$ if this costs 1 USD and $\geq 85.0\%$ for 5 USD test
• HBeAg RDT is unlikely to meet these criteria
• Other markers
  – Hepatitis B core-related antigen (HBcrAg)
  – Quantification of hepatitis B surface antigen (qHBsAg)
Thank you!

- Institut Pasteur
  - Yasir Isa
  - Judith Mueller
  - Jeanne Perpétue Vincent
  - Salim Chalal
- Université Paris Cité
  - Jonathan Sicsic
- CGHE
  - John Ward
  - Henry Njuguna
- Society for AIDS Africa
  - Chakroun Mohammed
- Helwan University, Cairo
  - Mohamed El Kassas
- HEPSANET
  - Asgeir Johannessen
  - Alexander Stockdale
  - Edith Okeke
  - Moussa Seydi
  - Gilles Wandeler
  - Mark Sonderup
  - Wendy Spearman
  - Michael Vinikoor
  - Edford Sinkala
  - Hailemichael Desalegn
  - Fatou Fall
  - Pantong Davwar
  - Mary Duguru
  - Tongai Maponga
  - Jantjie Taljaard
  - Philippa C. Matthews
  - Monique Andersson
  - Gibril Ndog
  - Roger Sombie
  - Maud Lemoine